

2006-2007 Research Abstracts

CASE SURGERY

A compilation of investigations made by Case Surgery Physicians, research scientists and distinguished colleagues.



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Surgery



Dear Colleague:

I am pleased to share with you our 2006-2007 research abstracts. The Department of Surgery provides a unique multi-specialty academic environment where ideas are exchanged and cooperative research programs are planned.

The 2006-2007 academic year has been a fruitful and productive one for the department and its members. The work produced has been presented at national and international forums and published in prestigious journals.

The Department of Surgery will continue to expand its research and educational endeavors in the coming year.

We welcome your interest in our Department's research and clinical studies. If you would like additional information, please call 216.844.3209 or visit our web site at www.casesurgery.com

Sincerely,

Jeffrey L. Ponsky, MD
Oliver H. Payne Professor and Chair

Special thanks to the Case School of Medicine Biologic Research Unit for their continued support.

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Section 1

**Cardiovascular and
Cardiothoracic
Surgery**

“MITRAL REPAIR” FOR ISCHEMIC MITRAL REGURGITATION

Arie Blitz, MD

Numerous studies over the past several decades have demonstrated that successful mitral repair is preferable to replacement when it is feasible. Correction of IMR is usually performed in conjunction with coronary bypass surgery. Ischemic mitral regurgitation (IMR) is one of the more challenging types of valvular insufficiency to repair, and the results may not be as durable as for other types of repair. Reduced durability may occur after a complex repair, use of too large an annuloplasty ring, or repair for acute IMR. Reduced durability may also be due to changes in ventricular geometry caused by the natural history of ischemic coronary artery disease that cannot be managed by ring annuloplasty alone.

In the acute scenario when the patient is ill and unstable, mitral valve replacement may be the best alternative. The value of prophylactic techniques to control ventricular remodeling following an acute myocardial infarction are unknown. In the chronic scenario, IMR is usually due to papillary muscle displacement, ventricular wall motion abnormalities, annular dilatation or some combination thereof. Techniques that can deal successfully with preservation of ventricular performance, progressive ventricular dilatation and diastolic dysfunction, when added to annuloplasty, in certain circumstances, may improve long term results. When compensated heart failure progresses to decompensated failure, and ventricular performance is on the back side of the Starling curve too far, a ventricular assist device or heart transplantation may be considered.

A variety of rings are available that are tailored to correct the altered geometry of IMR

A variety of techniques and devices have been proposed for control of ventricular remodeling. In this presentation we will review the repair techniques for IMR, as well as the clinical results of IMR repair.

OUTCOMES AFTER COMPLEX AORTIC VALVE/ASCENDING AORTIC SURGERY REQUIRING CIRCULATORY INTERRUPTION WITH ANTEGRADE CEREBRAL PERFUSION

A.S. Aharon; A. Blitz; P. Dumicz; Y. Elgudin; M. McGee; K. Johnson; A. H. Markowitz

BACKGROUND: We retrospectively examined factors contributing to mortality and neurologic outcomes in patients with complex aortic valve (AV) pathology requiring concomitant ascending aortic/hemiarch (AA/HA) replacement for aneurysmal dilatation and/or severe atherosclerotic disease.

METHODS: From Nov 1997 to June 2006, 102 patients undergoing AV surgery using a stentless full-root prosthesis (full root {86} or modified subcoronary {14} implantation) or valve-sparing procedure (2) had concomitant AA/HA replacement with hypothermic circulatory arrest, right axillary cannulation (RAC), and continuous antegrade cerebral perfusion (CACP). Seventy-four (73%) had aneurysmal dilatation and 28 (27%) had "untouchable" atherosclerotic disease. Median age was 69 years (range 23-91), and there were 67 (66%) males and 35 (34%) females. Twenty-two (22%) were reoperations and concomitant procedures included CABG (27), mitral valve surgery (7), Maze (7) and tricuspid valve repair (4).

RESULTS: There were 3 (2.9%) early deaths, 3 strokes (2.9%) and no transient ischemic attacks. Univariate analyses identified only prior cerebrovascular accident (CVA) as a risk factor for postoperative stroke ($p < 0.005$). Multivariate analysis did not reveal AA atherosclerotic disease, aneurysmal dilatation, advanced age, prior stroke, reoperative surgery, and diminished EF as risk factors for early death or CVA.

CONCLUSIONS: Complex AV/AA surgery can be performed with low operative mortality and stroke risk using RAC, CACP, and avoidance of any aortic manipulation. This technique compares favorably to complete circulatory arrest and allows for aggressive resection of dilated and/or highly calcified aortas in properly selected patients.

RADIAL ARTERIES VS SAPHENOUS VEIN BYPASS GRAFTS FOR CABG

Arie Blitz, MD and Richard F. Brodman, MD*

The benefits of unilateral and bilateral internal thoracic artery (ITA) for revascularization are well known. For more than 25 years, use of a variety of alternative arterial bypass grafts has increased because saphenous vein bypass grafts degenerate over time. The radial artery (RA) was abandoned in the 1970s because of unacceptably poor early patency of about 50%. Mechanical intimal trauma used intra-operatively doomed the RA to failure in the '70s. The advent of calcium channel blockers, better harvesting techniques, and excellent early patency of RA grafts led to a resurgence in the use of the RA in the 1990's. Nonetheless, its use still ignites some controversy.

The RA is easy to harvest, is more uniform in size than the ITA, generally has a larger internal diameter than the ITA, is easier to work with than the ITA, and is of ample length for any coronary target. However, the RA is more disposed to vasospasm than the ITA. Proper harvest technique and surgical management of the RA, though not difficult, is critical to success. The results of coronary revascularization using the RA in the present era are excellent. In a recent prospective randomized study, Desai and colleagues compared the patency of RA grafts to saphenous vein grafts. The patency rate of RA grafts at 1 year was 91.8% and saphenous vein grafts 86.4% ($p=0.009$). A finding in this study, as well as others, is that RAs are best used to graft coronary vessels that have high grade stenosis.

We will present our technique for RA harvest, a 12 year single surgeon experience using the RAs as second and third bypass grafts of choice after the LITA, and a review of the recent literature on RA and saphenous vein graft patency. We will include a brief video of ulnar artery harvest technique.

CONCLUSION: The RA plays an indispensable role in the current era of total arterial revascularization. As long as meticulous attention is paid to details of its harvesting, preparation, and target selection, it will continue to be an integral part of coronary bypass surgery.

CASE STUDIES IN THE DIFFICULT AORTA

Alan Markowitz, M.D. and Alon S Aharon, M.D.

CASE REPORT - 1

Patient profile

AB is an 83-year-old woman who had previously undergone LIMA-LAD bypass in 1982. The patient has had a long history of severe peripheral vascular disease including; (1) angioplasty of both iliac arteries, (2) angioplasty of the right renal artery, (3) bilateral carotid endarterectomies, and most recently, (4) an axillary-to-axillary artery crossover graft with graft extension to the left carotid artery from the left subclavian artery. The patient was noted to have severe aortic stenosis (aortic valve area of 0.5cm²) with severe concentric left ventricular hypertrophy and an ejection fraction of 50%. Coronary angiography demonstrated a 90% LAD/D1 lesion with left-to-right collaterals filling an occluded dominant right coronary artery. Computerized axial tomographic (CAT) scan of the chest showed diffuse calcification in the ascending aorta, transverse arch and descending aorta with occlusion of the left carotid artery, and left subclavian artery at their origins. In addition, diffuse arteriosclerotic obstruction of the innominate artery extending into the right subclavian and right carotid arteries were noted. Arteriography demonstrated occlusion of the axillary graft and a non-patent LIMA. Delayed filling of the left subclavian and carotid arteries through the graft was also observed. The patient had no palpable pulse in either groin, and both lower extremity indices were diminished.

Surgery

Both axillary arteries were grafted end-to-side with the two opposite branches of a 4-branched aortic arch Dacron graft (arterial perfusion channel plus one of the arch branches). A second branch was cannulated for arterial return, and the third reserved as a source for anticipated CABG. Percutaneous venous cannulation through the right femoral vein completed the circuit. Cardiopulmonary bypass was initiated slowly, ultimately achieving 3.25 l/min flow in this 1.5 sq m patient, which was adequate for systemic cooling. While approaching 18C, SVG - D1/LAD and SVG - PDA were performed. Both retrograde and antegrade cardioplegia were given simultaneously and the heart was vented during peripheral circulatory arrest. Continuous antegrade cerebral perfusion was initiated at 700cc/min to maintain a cerebral perfusion pressure of 70-80. The ascending aorta and root were resected and replaced with the branched graft and a Freestyle valve was placed in modified subcoronary position after aortic endarterectomy (performed secondary to extensive aortic calcification). The proximal saphenous vein anastomosis was anastomosed to the unused branch of the graft, and the axillary artery grafts were left intact at the conclusion of the procedure.

Post-operative course

AB tolerated the procedure well; she was extubated the following morning neurologically intact with normal renal function and was discharged to a skilled nursing facility on post operative day seven, fully ambulatory.

CASE REPORT - 2

Patient profile

MM is an 83-year-old female with a history of giant cell arteritis, who underwent aortic valve repair for aortic insufficiency in 1995. The patient was subsequently noted to have progressive aortic insufficiency with dilatation of the ascending aorta to 4.5 cm and required aortic valve replacement (AVR) with a pericardial bioprosthesis two years following aortic valve repair. The aortic aneurysm was not addressed at the second intervention. Three months prior to the patient's most recent admission, chest x-ray revealed a widened mediastinum. Computerized axial tomographic (CAT) scan of the chest demonstrated a 10 cm aneurysm of the ascending aorta. The patient refused surgical intervention at that time. Thirty-six hours prior to the operative intervention (described below), MM was admitted emergently to an outside hospital with acute chest pain radiating to the back, and syncope from hypotension. Repeat CAT scan demonstrated hemorrhage in the mediastinum. Following fluid resuscitation, the patient was immediately transferred to our institution for surgical intervention. On admission, the patient's vital signs were stable and her hematocrit was 22%.

From our prior Heartport experience, remote coronary sinus cannula and a pulmonary artery vent were placed via the right internal jugular vein; cardiopulmonary bypass was initiated using direct right axillary artery cannulation and a long percutaneous venous cannula placed via the right femoral vein. When the patient's temperature reached 18 C, she was exanguinated into the oxygenator, the sternum and aneurysm were opened simultaneously and the head continually perfused at 800 cc/min yielding antegrade cerebral pressures of 70-80 mmHg. The innominate artery was clamped and the left carotid artery internally occluded with a balloon catheter. Distal hemi-arch anastomosis was performed using a beveled Dacron graft. Following completion of the distal anastomosis, the graft was reclamped, cardiopulmonary bypass resumed and the patient rewarmed. The entire ascending aorta which was extremely friable (secondary to the arteritis) and was resected with preservation of the coronary ostia. A 3 cm tear-through old suture line was found to be the source of hemorrhage. The 10-year-old aortic pericardial bioprosthesis demonstrated yellowed leaflets with no calcification or evidence of degeneration. The aortic sewing skirt was cleared of layered endocardial growth and sutured to the Dacron graft. The coronary buttons were then reimplanted and the graft-graft anastomosis completed (the antegrade cerebral perfusion time was 22 minutes, crossclamp time 123 minutes, and cardiopulmonary bypass time 212 minutes). The patient was returned to the intensive care unit with minimal inotropic support.

Post-operative course

The patient twice failed extubation over the next week and was subsequently weaned from the ventilator with tracheostomy on post-operative day 10. MM was transferred to a skilled nursing facility on post-operative day 17 following tracheostomy removal. The patient is living independently one year later.

ROUND PEG IN A SQUARE HOLE: STENTLESS REPLACEMENT OF THE QUADRICUSPID AORTIC ROOT

Alon S. Aharon, MD, Alan H. Markowitz, MD, Michelle J. Capdeville, MD, Robert C. Gilkeson, MD

We report two patients with severe aortic insufficiency (AI) who underwent root replacements with stentless porcine prostheses in the presence of either pre-operatively or intraoperatively diagnosed quadricuspid aortic valves (QV) and significant concomitant pathology. Literature review suggests the full-root bioprosthesis, either homograft or heterograft, can be reliably performed despite anatomical complexity or the addition of other procedures. Suggestions to simplify implantation are offered.

INTRODUCTION: The QV is a rare congenital anomaly occurring in 0.008% of cases at autopsy and 0.013% of 60,446 echocardiograms performed at the Mayo Clinic. [1] 45% of patients with known QV's required surgery, most for AI in the 5th and 6th decades [2]. QV's are associated with other congenital malformations in 18% of cases, with coronary ostial displacement most frequent [2]. Previously, prostheses have been predominantly employed but pulmonary autografts [3] have been recently implanted. We describe the first documented stentless valve insertions.

CASE REPORTS

Patient #1

M.G. is a 45 year-old female with a history of progressive, exertional dyspnea, orthopnea, chest pain and AI. Transesophageal echocardiography (TEE) (Fig. 1) revealed a QV with 4+AI, LV enlargement, severe LVH and ejection fraction (EF) 65%. Gated CT scan (Fig. 2) and three-dimensional reconstruction (Fig. 3) defined a type b QV (3 equal cusps and 1 smaller), an enlarged left main coronary ostium and mid-ascending 4.5 cm aortic diameter. Intraoperative findings confirmed the pre-operative diagnosis of type b QV (Fig. 4) with the supernumerary cusp located between the right and non-coronary leaflets. The coronary ostia were 140° apart and normally positioned relative to the aortic valve posts. The aortic valve leaflets were thickened and retracted, producing the central regurgitant jet seen on TEE; leaflet histology showed fibrous thickening without significant calcification.

Through a mid-line sternotomy with direct cannulation of the right axillary artery, cardiopulmonary bypass (CPB) was initiated, the aorta cross-clamped, and retrograde cardioplegia delivered. During systemic cooling to 18°C the ascending aorta was incised transversely 2-3 cm distal to the right coronary ostium or the sinotubular ridge. The aortic leaflets were resected and the coronary buttons isolated (fig. 5). When 18°C was reached, cardiopulmonary bypass was discontinued and clamps were applied to the innominate and left carotid arteries. Ascending aorta/hemi-arch replacement with a 32mm Gel-weave graft was performed with continuous antegrade cerebral perfusion, monitored through a pressure channel in the axillary cannula, and systemic circulatory arrest. The Freestyle sizer displays 120° spokes, and was used to determine the site of the Freestyle posts to accommodate the native coronary ostia (fig.6). The prosthesis was rotated 120° to give the native left coronary the broadest reimplantation target. The interrupted inflow suture line was tied around a circumferential autologous pericardial strip, coronary buttons reimplanted, and distal suture line completed. Postoperative course was uneventful.

Patient #2

B.D. is a 74 year-old female with progressive shortness of breath, orthopnea, syncope, class IV heart failure, severe aortic and mitral insufficiency, moderate pulmonary hypertension, progressive ventricular dysfunction and paroxysmal atrial fibrillation. TEE disclosed a QV with severe aortic and mitral insufficiency, dilated LV, PFO, and EF of 25%. The patient underwent aortic root replacement with a 25mm Freestyle valve as described Patient 1, mitral valve repair via 27mm Duran ring, PFO closure, and Maze. The patient was discharged home in sinus rhythm after an uneventful hospital course.

COMMENTS: QV is a rare congenital malformation often presenting as AI later in life [2]. Associated anomalies like displacement of the left and right coronary orifices and single coronary ostium [4], may result in severe operative complications if unrecognized during aortic valve surgery. The most common variation (seen in our 2 patients) is one smaller extramurary cusp [5] located between the right coronary and non coronary leaflets in the atrioventricular nodal conduction tissue region [6]. Embryologically, abnormal cusp formation may result from abnormal fusion of the aorticopulmonary septum or abnormal proliferation in the common aortopulmonary trunk [5].

Stentless full-root bioprosthesis availability has made root replacement virtually interchangeable with aortic valve replacement using the same prosthesis, and has given the cardiac surgeon the opportunity to implement either procedure with expectations of the same results [7]. The Freestyle will not fit into a quadricuspid aortic root as a modified subcoronary implant, and should be used as a full-root only. The native coronary ostia will dictate the porcine commissural posts alignment (Fig.6), which is delineated via marking pen (fig. 5). The interrupted inflow suture line is tied around a circumferential autologous pericardial strip, rarely requiring additional topical hemostatic agents. A longitudinal line drawn from the L-N post distally prior to complete ascending aortic transection can be later used to prevent inadvertent misalignment upon reconstruction of the Freestyle-aortic suture line.

The majority of QV's requiring replacement underwent mechanical or stented bioprosthetic valve implantation [2]. The freestyle valve offers excellent hemodynamics and durability [7] compared to other bioprosthetic valves [8] and cryopreserved aortic allografts. Freedom from moderate or greater AI has been reported higher than 97 percent at 10 years when the freestyle bioprosthesis implantation using the full root technique [8]. Full root implantation also provides a larger effective orifice area in patients with a small aortic root [8]. The full root technique provides appropriate orientation and tailoring of the stentless bioprosthesis to accommodate both the abnormally shaped quadricuspid aortic root and the malaligned coronary ostia often seen in the QV. We advocate the use of the freestyle stentless bioprosthesis as a full root in patients with QV's.

FIGURES

Fig. 1

Transesophageal echocardiographic basal short axis view of a quadricuspid aortic valve in diastole. Note large left main coronary (LCA) artery at level of left coronary cusp.

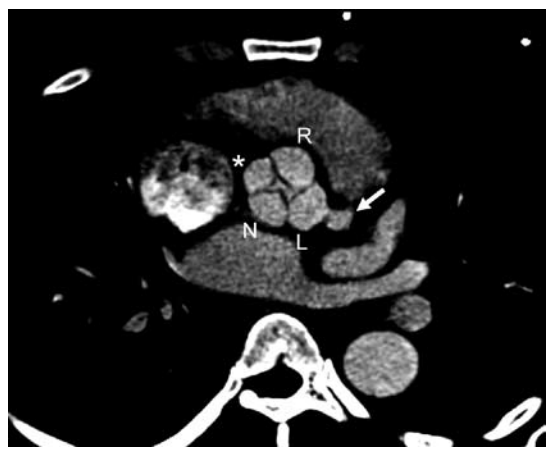


Fig. 2

Axial oblique MIP image of the aorta demonstrates quadricuspid aortic L=left cusp R=right cusp N=non coronary cusp . *=supernumerary cusp. Note dilated left main coronary artery (arrow) There is lack of coaptation of the valve leaflets in diastole.

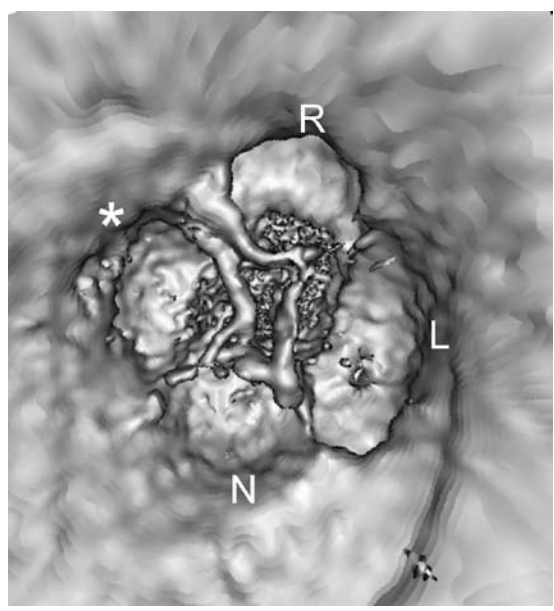


Fig. 3

Virtual CT endoscopic view of the aorta demonstrates quadricuspid aortic L=left cusp R=right cusp N=non coronary cusp . *=supernumerary cusp.

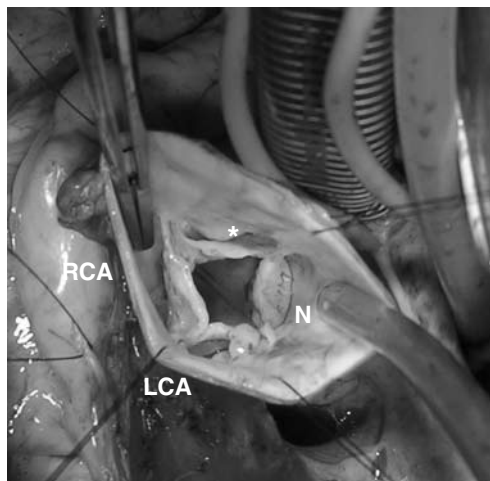


Fig. 4
Intraoperative photograph of the quadricusp aortic valve.
(L=left cusp R=right cusp N=non coronary cusp. *=supernumerary cusp)

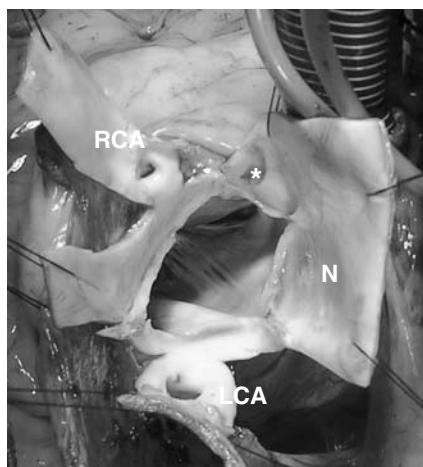


Fig. 5
Intraoperative photograph illustrating the quadricusp aortic annulus with isolated right and left coronary buttons. The native commissural posts are delineated with a marking pen thus simplifying alignment of the porcine commissural posts. (RCA=right coronary artery, LCA=left coronary artery, N=non coronary cusp. *=supernumerary cusp)

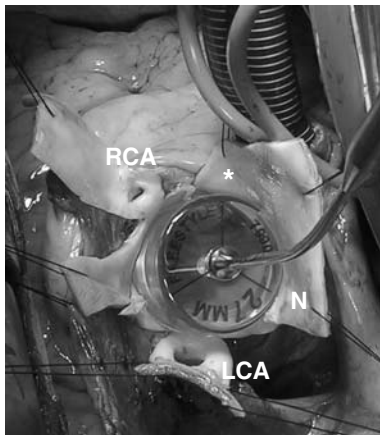


Fig. 6

The native coronary ostia will dictate the alignment of the porcine commissural posts.

(RCA=right coronary artery, LCA=left coronary artery, N=noncoronary cusp. *=supernumerary cusp)

THE UTILITY OF THE FULL ROOT BIOPROSTHESIS IN COMPLEX REOPERATIVE AORTIC VALVE SURGERY

Alon Aharon¹, Arie Blitz¹, Ihab Halaweish¹, Michelle Capdeville¹, Robert Gilkeson¹, James Fang¹, Alan Markowitz¹

OBJECTIVES: Aortic root replacement following previous operation of the aortic valve (AV) combined with additional complex cardiac procedures represents a high-risk patient group. We review our 9-year experience of reoperative AV surgery using the Freestyle Valve (FV) placed in the full root (FR) position.

METHODS: From March 1998 to February 2007, 1,212 patients underwent AVR; 21 had reoperative AVR using the FV as a FR. 25 concomitant procedures performed included: aortic hemiarch/arch replacement 9(43%), Maze 4(19%), coronary artery bypass 6(29%), mitral valve 5(24%), and tricuspid valve surgery 1(5%). 11 (52%) were in NYHA class III/IV; 3(14%) were emergent and 19/21 (90%) had one valve size or greater implanted. Surgical techniques included remote (axillary artery and percutaneous femoral vein) cannulation with cardiopulmonary bypass initiation before sternotomy and continuous antegrade cerebral perfusion when aortic hemiarch/arch replacement was required. Internal mammary artery (IMA) grafts were left to freely perfuse the myocardium allowing IMA flow to augment myocardial protection. Coronary effluent was continuously returned to the pump via small ostial cannulae.

RESULTS: There were 2 early deaths (10%) and 1 (5%) CVA. The stroke occurred in a patient with an intra-cranial bleed 1 year before surgery. Univariate analysis did not identify any significant STS risk factors for early death. Advanced NYHA class trended toward poor outcome.

CONCLUSIONS: The FV allows for FR implantation in complex aortic reoperative surgery with acceptable early results. Remote cannulation, initiation of presternotomy CPB and utilization of the IMA as a cardioplegic conduit are useful techniques in these patients.

Section 2

Colorectal Surgery

A RESIDENT'S EXPERIENCE WITH HAND-ASSISTED VS STRAIGHT LAPAROSCOPY FOR LEFT COLECTOMY: IS THERE REALLY A DIFFERENCE?

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BACKGROUND: Several studies comparing the effectiveness of hand-assisted colectomy (HAC) and straight laparoscopic colectomy (SLC) have been published. It has been suggested that HAC may help residents progress along the learning curve but there is currently no evidence to support this claim. These previous studies include procedures performed by staff surgeons or residents at various skill levels and report operative times and conversion rates as their primary endpoints. Furthermore, the actual role of the resident or staff surgeon as either the first assistant or primary surgeon is routinely not addressed. We report the experience of a single resident, training with both HAC and SLC techniques during residency and fellowship. We feel that the percentage of cases completed by the resident as the operating surgeon is the most important primary endpoint in determining the most effective approach for teaching laparoscopic colectomy.

METHODS: All patients who underwent left-sided HAC or SLC by a single resident, starting as the primary surgeon, were included. If the assisting attending assumed the role of the operating surgeon during the case it was recorded as an incomplete case for the resident. Operative times and conversions were included as secondary endpoints. All values below are reported as mean (range).

RESULTS: A single resident started 147 laparoscopic colectomies as the primary surgeon during residency and colorectal fellowship including 81 left sided procedures. There were 44 patients in the HAC group and 37 SLC patients. There were no differences in patient demographics, diagnoses, ASA class, number of previous surgeries, and type of surgery. Cases done by straight laparoscopy were more likely to be completed by the resident than those done by HAC (SLC 88%, HAC 72%; $p=.06$). There were also differences in operative time favoring SLC (HAC 142 min (100-170) vs. SLC 133 min (95-195); $p = 0.04$).

Complications were similar in the two groups (HAC 19% vs. SLC 21%) as were conversions (HAC 5.6% vs. SLC 4.5%). There was also no difference in length of hospital stay (HAC 4.9 days (2-10) vs. SLC 4.4 days (2-13); $p = 0.17$).

2

SAFETY OF ALVIMOPAN, A HIGHLY SELECTIVE, POTENT, PERIPHERALLY ACTING MU-OPIOID RECEPTOR (PAM-OR) ANTAGONIST, IN MORE THAN 1,900 PATIENTS UNDERGOING BOWEL RESECTION

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INTRODUCTION: In postoperative ileus (POI) trials, alvimopan accelerated GI recovery and reduced length of hospital stay after bowel resection (BR). However, these benefits must be associated with acceptable risk to permit widespread use of alvimopan in this population.

Methods: Adult patients who received alvimopan 12mg or placebo, underwent laparotomy for BR, and were scheduled for postoperative IV-PCA were included in this pooled safety analysis of two phase II and five phase III POI trials. Treatment-emergent adverse events (TEAEs: any AE occurring between first study dose and within 7 days after the last dose) and serious AEs (SAEs: AEs resulting in death, persistent/substantial disability, prolonged hospitalization, or readmission; life threatening; requiring intervention to prevent permanent impairment/damage within 30 days of the last study medication) from the POI worldwide safety database were used to develop a clinically relevant safety profile of alvimopan in BR patients.

Results: 986 placebo patients and 999 alvimopan 12mg patients were included in this analysis. The most common TEAEs included GI disorders (placebo, 65%; alvimopan 12mg, 60%), surgical complications such as POI, wound complications, anastomotic leak, etc. (placebo, 23%; alvimopan 12mg, 17%), respiratory disorders (placebo, 22%; alvimopan 12mg, 19%), laboratory test abnormalities (placebo, 22%; alvimopan 12mg, 18%), vascular disorders (placebo, 22%; alvimopan 12mg, 21%), cardiac disorders (placebo, 17%; alvimopan 12mg, 15%), renal/urinary disorders (placebo, 13%; alvimopan 12mg, 13%), and hepatobiliary disorders (placebo, 0.2%; alvimopan 12mg, 0.2%). The most common SAEs were POI (placebo, 5.2%; alvimopan 12mg, 1.2%), postoperative infection (placebo, 1.6%; alvimopan 12mg, 1.5%), and small bowel obstruction (placebo, 1.9%; alvimopan 12mg, 1.6%). Incidence rate for all-cause mortality was 0.7% for each treatment group.

Conclusions: In this large pooled safety database from the worldwide POI trials, alvimopan 12mg demonstrated a favorable risk profile supporting the clinical benefit in BR patients.

CLINICAL OUTCOMES AND RESOURCE UTILIZATION ASSOCIATED WITH LAPAROSCOPIC AND OPEN COLECTOMY USING A LARGE NATIONAL DATABASE

Conor P. Delaney, MCh, PhD, Eunice Chang, PhD, Michael Suer, Michael Broder, MD, MSHS

BACKGROUND: Although laparoscopic colectomy (LC) has emerged as the preferred approach for colectomy, the broader implications of LC have not been addressed. This study compared clinical and utilization outcomes between patients having LC or open colectomy (OC) using a large national database.

METHODS: Patients who underwent elective segmental colectomy from 07/01/2004-06/30/2006 were identified using appropriate ICD-9 codes from a dataset from Premier Inc., from more than 400 hospitals (SAY REAL NUMBER – SAVES WORDS). Using standard instrument charge descriptions, patients could be assigned to LC or OC cohorts. Rates of transfusion, complication, readmission, reoperation, length of stay (LOS), and total hospitalization costs were evaluated. Multivariate analyses adjusted for differences in patient, surgeon, and hospital characteristics.

RESULTS: Of a total 32,733 patients (mean age 64 ± 14 years), 11,044 (34%) had LC and 21,689 (66%) had OC. LC patients had lower rates of transfusions (OR, 0.68; $P < 0.0001$), complications (OR, 0.89; $P < 0.0001$), readmissions (OR, 0.89; $P = 0.0051$), but higher reoperation rates (OR, 1.8; $P = 0.0020$) compared with the OC cohort. The LC cohort had shorter mean LOS and slightly higher mean hospitalization costs than the OC cohort (7.0 vs 8.1 days; $P < 0.0001$ and \$8,076 vs \$7,678; $P = 0.0002$). LC discharge disposition was: 84.4% to home, 9.4% with home nursing, and 4.4% to a nursing facility, compared with 74.3%, 14.1%, and 8.0%, respectively, in the OC group. These differences were highly significant (OR, 0.70 for home with nursing vs. home, OR, 0.67 for nursing facility vs. home, $P < 0.0001$ for both comparisons).

CONCLUSION: Using a national database to assess resource utilization, these data confirm the clinical benefit (fewer complications and transfusions, and shorter LOS) of LC. Although costs are marginally increased, this is outweighed by the reduction in hospital utilization, readmission rates, and nursing utilization after discharge.

ACCELERATED GI RECOVERY AND REDUCED LENGTH OF STAY FOLLOWING MODIFIED PRE-OP DOSE TIMING WITH ALVIMOPAN: RESULTS OF A LARGE RANDOMIZED PLACEBO-CONTROLLED STUDY IN PARTIAL BOWEL RESECTION (BR)

Kirk Ludwig, Warren Enker, Conor Delaney, Bruce Wolff, Wei Du, Lee Techner

OBJECTIVE: To study the efficacy of alvimopan 12-mg administered 30-90 minutes prior to and bid until hospital discharge (or 7 days) after laparotomy for small/large BR surgery with primary anastomosis.

METHODS: This was the first randomized, double-blind, placebo-controlled phase IIIb study of alvimopan including only patients undergoing BR. Adult patients scheduled for postoperative IV opioid-based patient-controlled analgesia were enrolled June-04–November-05. Treatment effects on time-to-events in the modified intent-to-treat (MITT) population were analyzed using Cox proportional hazards model. Magnitude of treatment effect was expressed using difference in Kaplan-Meier means for time-to-event endpoints. The primary endpoint was GI₂, a 2-component composite measure=maximum of time to lower (bowel movement) and upper GI (solid food) recovery. Other endpoints included uncensored length of hospital stay (LOS; defined by distribution of discharge order written [DOW] by postoperative day [POD]). Incidence of POI-related postoperative morbidity (POM; defined as NGT insertion or complications of POI [POI resulting in prolonged stay/readmission]) was evaluated using Fisher's exact test. Patients were monitored for adverse events (AEs).

RESULTS: A total of 654 patients were randomized. The MITT population included 629 patients with a mean age of 60 years, 51% of whom were women. The most common primary reasons for BR were colon cancer (36%) and diverticulitis (16%).

Endpoint	Placebo N=313	Alvimopan N=317	
GI₂ (Hazard ratio)	—	1.53	$P<0.001$
Mean, hrs	111.8	92.0	$\Delta=19.8$
LOS, DOW by POD	6.2	5.2	$P<0.001$
Incidence of POI-related POM (%)	14.4	6.9	$P=0.003$

The 3 most commonly reported AEs were nausea (alvimopan, 57.8%; placebo, 66.2%; $P=0.030$), vomiting (alvimopan, 14.0%; placebo, 24.6%; $P<0.001$), and abdominal distension (alvimopan, 17.6%; placebo, 20.3%; $P=0.425$).

CONCLUSIONS: Alvimopan 12-mg administered 30-90 minutes before surgery and bid following surgery accelerated upper and lower GI recovery, reduced hospital LOS and reduced POI-related POM. This new study provides further data on the efficacy, dose, and optimal dose timing of alvimopan.

OUTCOME OF DISCHARGE WITHIN 24-72 HOURS OF LAPAROSCOPIC COLORECTAL SURGERY

Conor P Delaney MD, Brad Champagne MD, Harry L Reynolds MD

Although laparoscopic colorectal surgery (LC) may permit early recovery and discharge from hospital, short lengths of stay are not routinely achieved. This is partly because accelerated recovery programs with early discharge are associated with high readmission and complication rates, especially after open colorectal surgery. This study examines safety and outcomes after LC in cases discharged within 72 hours of surgery.

118 consecutive patients (mean age 60 years) underwent elective LC by a single surgeon over a 12 month period, and were followed in a prospective IRB-approved database. Patients were managed with an accelerated recovery program using an intravenous PCA overnight, and diet and oral analgesia on postoperative day 1. Standardized discharge criteria were used.

Operations included: segmental colectomy (n=64), proctosigmoidectomy/APR (n=27), total colectomy/ileal pouch (n=10), rectopexy/reversal of Hartmans (n=8), adhesiolysis/stoma (10). Mean BMI was 28.5 (range 20-45). Mean operative time was 142 minutes with no mortality, and median stay of 3 days. 20% had a complication within 30 days, but only 2.5% had a serious complication. LC permitted 82 (70%) of patients to be discharged within 72 hours of surgery (10 day 1; 46 day 2; 26 day 3). Patients were grouped and analyzed by day of discharge. Discharge on day 1-2 was associated with significantly lower complication rates than seen for all patients. Although patients discharged on day 1-2 had the lowest readmission rate, this was not statistically significant.

	Mean stay (days)	Complications (%)	Readmissions (%)
All (n=118)	3.7	20	8.5
Day 1-2 (56)	1.8	7*	5.4
Day 3 (26)	3.0	15	7.7

* p<0.05 vs all patients

Readmission and complication rates are low in patients discharged on day 1, 2 or 3 after laparoscopic colorectal surgery. Patients who fulfill standardized discharge criteria and have adequate support at home, can safely be discharged early after laparoscopic colorectal surgery.

EFFICACY OF ANAL FISTULA PLUG IN CLOSURE OF CROHN'S ANORECTAL FISTULAS

O'Connor L, Champagne BJ, Ferguson MA, Orangio GR, Schertzer ME, Armstrong DN.

PURPOSE: The efficacy of Surgisis anal fistula plug in closure of Crohn's anorectal fistula was studied.

METHODS: Patients with Crohn's anorectal fistulas were prospectively studied. Diagnosis was made by histologic, radiographic, or endoscopic criteria. Variables recorded were: number of fistula tracts (primary openings), presence of setons, and current antitumor necrosis factor therapy. Under general anesthesia and in prone jackknife position, patients underwent irrigation of the fistula tract by using hydrogen peroxide. Each primary opening was occluded by using a Surgisis anal fistula plug. Superficial tracts amenable to fistulotomy were excluded.

RESULTS: Twenty consecutive patients were prospectively enrolled, comprising a total of 36 fistula tracts. At final follow-up, all fistula tracts had been successfully closed in 16 of 20 patients, for an overall success rate of 80 percent. Thirty of 36 individual fistula tracts (83 percent) were closed at final follow-up. Patients with single fistulas (with 1 primary opening) were most likely to have successful closure using the anal fistula plug. Successful closure was not correlated with the presence of setons or antitumor necrosis factor therapy.

CONCLUSIONS: Closure of Crohn's anorectal fistula tracts using Surgisis anal fistula plug is safe and successful in 80 percent of patients and 83 percent of fistula tracts. Closure rates were higher with single tracts than complex fistulas with multiple primary openings.

2

EFFICACY OF ANAL FISTULA PLUG IN CLOSURE OF CRYPTOGLANDULAR FISTULAS: LONG-TERM FOLLOW-UP

Champagne BJ, O'Connor LM, Ferguson M,, Orangio GR, Schertzer ME, Armstrong DN.

PURPOSE: The long-term efficacy of Surgisis anal fistula plug in closure of cryptoglandular anorectal fistulas was studied.

METHODS: Patients with high cryptoglandular anorectal fistulas were prospectively studied. Additional variables recorded were: number of fistula tracts, and presence of setons. Under general anesthesia and in prone jackknife position, patients underwent irrigation of the fistula tract by using hydrogen peroxide. Each primary opening was occluded by using a Surgisis anal fistula plug, which was securely sutured in place at the primary opening and tacked to the periphery of the secondary opening.

RESULTS: Forty-six patients were prospectively enrolled during a two-year period. Follow-up was six months to two years (median, 12 months). At final follow-up, all fistula tracts had been successfully closed in 38 patients, for an overall success rate of 83 percent. Seven patients had multiple tracts, for a total of 55 fistula tracts in the series. Of the 55 individual tracts, 47 (85 percent) were closed at final follow-up. Patients with one primary opening were most likely to have successful closure by using the anal fistula plug, although this was not significant. Successful closure was not correlated with the presence of setons.

CONCLUSIONS: Long-term closure of cryptoglandular anorectal fistula tracts using Surgisis anal fistula plug is safe and successful in 83 percent of patients and 85 percent of tracts.

GENERAL SURGERY RESIDENT'S DEMONSTRATE DECREASED OPERATIVE TIME'S AND CONVERSION RATES FOR STRAIGHT LAPAROSCOPIC SIGMOID COLECTOMY IN A MENTORSHIP BASED TRAINING PROGRAM

Champagne B, Lee E, Valerian B, Singh P

INTRODUCTION: The ideal approach to teach general surgery residents laparoscopic colectomy is not well established. This study demonstrates the impact of a unique advanced laparoscopic mentorship rotation on resident's ability to perform LSR for diverticular disease.

METHODS: All attempted laparoscopic sigmoid resection's for diverticular disease by senior or chief resident's assisted by a single colorectal surgeon from 1999-2005 were included. Residents at our institution participate in a three month mentorship with an advanced laparoscopic surgeon before or after their colorectal clerkship. The operating resident's exposure to this mentorship dictated which group each patient was assigned to.

RESULTS: There were 88 patients who underwent LSR by previously mentored resident's (MR) and 63 patients by those resident's who had not completed the laparoscopic rotation (R). There was no difference in patient demographics or indication for surgery. There was a statistically significant difference in operative time favoring MR (MR 115 min (65-175) vs R 161 min (105-205); $p < .01$). Complications were similar in the two groups (MR 17% vs, R 15%) as well as length of hospital stay (MR 4.2 days (2-9) vs R 4.4 days (3-10); $p = 0.73$). There were fewer conversions in the mentored group (MR 4.5% vs. R 13%; $p < 0.01$).

CONCLUSIONS: A ten week advanced laparoscopic mentorship rotation appears to significantly enhance general surgery residents ability to perform straight laparoscopic colectomy as demonstrated by both decreased operative times and a lower conversion rate.

IMPACT OF AN EXPERIENCED LAPAROSCOPIC COLORECTAL SURGEON TO AN EXISTING TRADITIONAL COLORECTAL PRACTICE IN AN ACADEMIC MEDICAL CENTER

Vincent J. Obias MS MD, Farhad Zeinali MD, Harry L. Reynolds MD, Brad Champagne MD, Conor P. Delaney MD PhD

INTRODUCTION: Laparoscopic colectomy (LAC) is steadily gaining acceptance. The potential benefits of LAC have been reported by high volume institutions with established laparoscopic programs, however introduction of LAC has often been associated with prolonged operative times, increased costs and no reduction in hospital stay over that seen with open surgery. There are no published data looking at the impact of introducing an experienced laparoscopic colorectal surgeon using fast-track post-operative care pathways on an established and experienced colorectal practice.

METHOD: A consecutive group of 73 patients undergoing LAC performed during the first 11 months of a new practice were compared to a case matched group of patients undergoing open colectomy (OC). Patients were identified from a prospective database and matched for age, gender, DRG and operation. Open complication data were obtained from electronic medical record review. Patients were compared for outcome and direct costs. Hospital information was collated using integrated hospital cost management system and decision software (Transition Systems Inc. Boston, MA; TSI). Statistics were performed with Paired t test and Fishers exact test.

RESULTS: Median age was 66.5 for the LAC group and 63.0 for the OC group ($p=0.1935$). Surgical procedures were: right colectomy $n=63$, left/sigmoid colectomy $n=26$, subtotal colectomy $n=18$, total proctocolectomy $n=8$, anterior resection $n=27$ and abdominoperineal resection $n=4$. Laparoscopic operative times were a mean of 152 minutes. Overall morbidity for LC was 19.2% and for OC was 16.4% ($p=0.829$). There was no mortality. Median length of stay was: LC=3.0 days; OC= 7.0 ($p=0.0001$). Median direct cost per LAC was \$4396 versus \$6500 for OC ($p=0.0013$). Bundled anesthesia and surgical costs were \$2438 for LAC and \$2612 for OC, while bundled post-operative care expenses (ICU, nursing, pharmacy, laboratory, radiology, and rehab) were \$1315 for LAC and \$3010 for OC.

CONCLUSION: The results demonstrate the benefit of an experienced laparoscopic colorectal surgeon to an already established colorectal practice. LAC significantly reduced direct costs and resource utilization, with similar morbidity to OC. Hospital stay was also significantly reduced. Although surgical costs were similar, post-operative care costs were reduced yielding a significant overall net financial benefit to the institution.

2

INCIDENCE OF COLONIC ISCHEMIA AFTER REPAIR OF RUPTURED ABDOMINAL AORTIC ANEURYSM WITH ENDOGRAFT

Champagne BJ, Lee EC, Valerian B, Mulhotra N, Mehta M.

BACKGROUND: Colonic ischemia after open repair of ruptured abdominal aortic aneurysm (rAAA) has been reported to be as high as 42% and is associated with high mortality rates when transmural necrosis is involved. With the evolution of endovascular aortic repair (EVAR) devices, some centers now primarily use this technique for rAAA. The objective of this study was to determine the incidence of colonic ischemia after EVAR of rAAA.

STUDY DESIGN: All patients who underwent EVAR of rAAA from January 2002 to January 2006 were included in this review. All flexible sigmoidoscopies were performed within 48 hours, ischemia was graded consistently, and treatment was initiated per protocol based on grade of ischemia. Patients with grades I and II ischemia were followed up with medical management and in some cases, repeat colonoscopy. All patients with grade III ischemia underwent bowel resection.

RESULTS: Forty-four patients underwent EVAR of rAAA during the study period. Operative mortality was 11%. Sigmoidoscopy was performed in 36 of 39 patients who survived longer than 24 hours. Bowel ischemia was documented in 8 of the 36 patients (23%). Of these, five had grade I or grade II ischemia at both initial and repeat endoscopy, so these patients did not progress to resection. Three patients underwent exploratory laparotomy with bowel resection because of grade III ischemia; one of these procedures was performed for worsening ischemia discovered at repeat colonoscopy.

CONCLUSIONS: This study demonstrated that the overall incidence of colonic ischemia (23%) after EVAR of rAAA is less than that reported for the open repair. We would continue to recommend mandatory flexible sigmoidoscopy for these patients

INTRAOPERATIVE RADIATION THERAPY INTRODUCTION AND UTILIZATION IN A COLORECTAL UNIT

C Williams, H Reynolds, C Delaney, B Champagne, V Obias, Y Joh, J Merlino,

T Kinsela

PURPOSE: The introduction of an intraoperative electron beam radiation therapy unit (IORT) offers the colorectal surgeon more extensive treatment options for locally advanced primary and recurrent neoplasms.

METHODS: We retrospectively review the subset of colorectal patients treated with IORT following introduction of the Mobetron unit in 1999, examining both indications and outcomes. This unit permits radiation of a cone of tissue up to 10cm in diameter using an electron accelerator with excellent tissue penetration.

RESULTS: A review of all patients treated with IORT since 1999 revealed 40 patients who underwent colectomy or proctectomy. All patients had evidence of local extension to contiguous structures and based on preoperative staging were deemed likely to have incomplete resection by the operating surgeon. 14 underwent abdominal perineal resection, 10 low anterior resection, 5 low anterior resections with low Hartmann's, 5 segmental colectomy, 2 pelvic exenteration, 1 colostomy, 1 colectomy and duodenectomy, and 2 underwent local excision of recurrences. 26 out of the 40 underwent adjacent organ, abdominal wall or pelvic sidewall excision. IORT was selected as an alternative to sacrectomy or exenteration for a close margin in 10 patients. IORT dose ranged from 9 to 12Gy.

	n	Stage***				Number with Positive margins (%)	Median Follow up after Surgery in months (range)	Number with local Recurrence	Number Surviving to Date (%)
		4	3	2	1				
Primary Rectal	15	5	5	4	1	3 (20)	21 (1-84)	0	8 (53)
Recurrent Rectal	11	2	5	4	0	4 (36)	42 (6-90)	0	9 (81)
Recurrent Colon	7	4	2	1	0	1 (17)	49 (22-83)	1*	4 (57)
Primary Colon	2	1	1	0	0	0	28 (16-39)	0	2 (100)
Appendiceal	2	0	0	2	0	0	20 (11-37)	0	2 (100)
Other**	3	1	2	0	0	2 (67)	24 (6-47)	0	4 (100)
Totals	40	14	13	11	2	10 (25)	29 months	1	28 (70)

* IORT to gross Tumor, **Other includes colon and duodenal primaries, 1 ovarian cancers with rectal involvement, & 1 endometrial cancer recurrence with rectal involvement.

***Pathologic stage post Pre-operative chemo and radiation

CONCLUSION: The introduction of IORT has allowed us to selectively approach locally advanced primary and recurrent neoplasms which traditionally would have been deemed unresectable. The one local recurrence occurred in a patient who received IORT to gross tumor. Sacrectomy and other extended resections may be avoided in selected patients with low local recurrence rates and good median survival for such a high risk group of patients.

LAPAROSCOPIC TOTAL COLECTOMY AND ILEORECTAL ANASTOMOSIS

Yong-Geul Joh, Vincent Obias, Conor P. Delaney

INTRODUCTION: This video is a laparoscopic total colectomy and ileorectal anastomosis for thirty seven-year-old female with chronic, severe constipation.

METHODS: After exposure of the ileocecal pedicle, blunt dissection was used to develop the plane between the vessels and the retroperitoneum. The ileocolic pedicle was transected with the Ligasure device. After medial dissection, lateral dissection was performed to the cecum. Careful dissection of the terminal ileal mesentery was done. The omentum was carefully dissected off the transverse colon. After the splenic flexure was mobilized, the left colic, mid colic, and right colic vessels were ligated by the Ligasure device. After lateral dissection of the sigmoid colon, the sigmoid arteries were transected by the Ligasure device. The rectosigmoid junction was divided by using the Endo GIA 60-mm through the RLQ port. And then the mesocolon was transected by the Ligasure device. The colon was exteriorized through the 4-cm Pfannenstiel incision. After confirming orientation of the proximal bowel, an end to end anastomosis was fashioned with the CEEA.

RESULTS: The operative time was 160 minutes. The estimated blood loss was 20ml. The patient was discharged on the second postoperative day without uneventable recovery.

CONCLUSION: Laparoscopic total colectomy and ireorectal anastomosis was performed safely and rapidly with Ligasure device.

STANDARDIZATION OF A PORCINE MODEL TO TEACH LAPAROSCOPIC PROCTOSIGMOIDECTOMY?

Yong-Geul Joh, Farhad Zeinali, Vincent Obias, Conor P. Delaney

INTRODUCTION: Laparoscopic colorectal surgery is associated with a significant learning curve. The porcine model is generally regarded as too easy, while cadaver tissues are unlike live surgery. We demonstrate a porcine laparoscopic colectomy model, replicating the anatomical steps for human laparoscopic sigmoid colectomy in a live operative model.

METHODS: Under an approved training protocol, a four port laparoscopic proctosigmoidectomy was performed by a resident with an attending assisting. The inferior mesenteric vessels is dissected close to the aorta with a medial to lateral approach. After division of the vessels, the descending colon mesentery is dissected off the retroperitoneum. The lateral attachments of the descending colon and rectum are mobilized, and the rectum and mesorectum transected. The specimen is exteriorized through a left lower quadrant incision, an anvil inserted, and a laparoscopic anastomosis fashioned.

RESULTS: This procedure permits teaching of a medial-lateral approach in a live operative model.

CONCLUSIONS: The technical skills necessary to perform laparoscopic colon surgery in patients can be practiced, using a careful, anatomical, multiple step approach to porcine laparoscopic colectomy.

LAPAROSCOPIC VS. OPEN RESECTION WITH RECTOPEXY FOR RECTAL PROLAPSE

Champagne B, M.D., Orangio G, M.D., Ambroze W, M.D., Schertzer M, M.D., Armstrong D, M.D., Choat D, M.D., Atlanta, Ga

PURPOSE: Laparoscopically-assisted resection with rectopexy is an effective treatment for rectal prolapse. Prior studies comparing laparoscopic procedures with open resection and posterior rectopexy (ORR) are scarce and have been limited in sample size and included a variety of technical approaches in the open repair group. The purpose of this study was to evaluate the effectiveness of laparoscopic resection with posterior rectopexy (LRR) for rectal prolapse compared to ORR.

METHODS: Between June 2001 and June 2005 the study included 31 patients who underwent LRR and 55 patients who underwent ORR for rectal prolapse. Patients who underwent Ripstein or Altmeier repairs and those who had rectopexy without resection were excluded from the study. A retrospective chart review was performed on both groups.

RESULTS: There was no significant difference between the groups in age, sex, ASA class, number of previous abdominal operations, prior repairs for prolapse, and recurrence after surgery. The mean difference in length of stay was statistically significant ($p < 0.001$) and was 4.3 days in the laparoscopic group and 6.4 days in the open group. Complications requiring re-operation including ventral hernia, small bowel obstruction, and recurrent prolapse were more common in the open group (21%), compared to the laparoscopic group (6%; $p = 0.043$).

CONCLUSIONS: Laparoscopic resection with rectopexy for rectal prolapse can be performed with morbidity and recurrence rates comparable to open procedures. In addition we found a statistically significant advantage in terms of shorter length of hospital stay and decreased need for reoperation in the laparoscopic group.

LAPAROSCOPY AND COLORECTAL METASTASIS

Champagne BC, Delaney CP

Laparoscopic colon resection for cancer has been proven to be safe, and oncologically equivalent to conventional surgery, while reducing hospital stay, shortening recovery times, and reducing postoperative complications. Of patients newly diagnosed with colorectal cancer, approximately 20% are found to have synchronous metastases while 30% develop metastases within 3 years according to the most recent population-based studies. Patients with metastatic disease are now living twice as long as they were one decade ago. With the increasing life expectancy for colorectal cancer we are beginning to see a considerable number of patients with metastatic disease surviving long periods of time with acceptable and improved quality of life. Although there is increasing application of laparoscopy for primary treatment of colorectal cancer, the appropriate role for laparoscopy in patients with metastatic disease has yet to be defined.

Laparoscopic staging in surgical oncology has been employed to define radiologically occult intraparenchymal and extra hepatic disease and to spare the patient the risk and discomfort of a non-therapeutic laparotomy. Investigators also demonstrated that laparoscopic identification of patients with unresectable disease shortened hospital stay and reduced total hospital charges.

The role of laparoscopy for resection in patients with known synchronous lesions is dependent on numerous variables. The presence of extra-hepatic disease or other absolute or relative contraindications to resection of liver metastases is the most important factor in determining treatment strategy. The severity of the patients symptoms necessitating an urgent intervention and the location of the tumor also dictate the appropriate approach. Recent evidence also suggests that the survival benefit from surgical resection of hepatic metastases may be determined by the biological behavior of the neoplasm rather than by early detection or size and number of lesions. Early studies have demonstrated that laparoscopic resection of the primary tumor in patients requiring a staged resection allows for a quick recovery and low morbidity which may allow earlier postoperative treatment with chemotherapy in tumors with favorable biologic properties.

The role of laparoscopic fecal diversion as a palliative intervention in patients with diffuse metastatic colorectal cancer has also been well documented. In either open or laparoscopic surgery for palliation the surgeon should choose an operation with the lowest morbidity. Lastly, it appears that we are now entering an era that challenges the traditional beliefs regarding the incurability of patients with extra hepatic metastasis. If this trend persists, the role of laparoscopy and laparoscopic US will continue to be of great demand as a staging modality to prevent unnecessary laparotomy.

LAPAROSCOPY AND RECTAL CANCER

Champagne BC and Delaney CP

Laparoscopic colectomy has been proven oncologically equivalent to conventional surgery and is now generally agreed to offer patients a reduced length of stay, shorter recovery times and improved cosmesis. In contrast, acceptance of laparoscopic proctectomy for rectal cancer has been very delayed and the enthusiasm of early studies has met considerable skepticism. For rectal cancer, it has been demonstrated that there is considerable variation between surgeons in disease-free survival and local pelvic recurrence after open proctectomy for rectal cancer. These differences are likely to be magnified when the technical challenge of laparoscopy is added to proctectomy. Minimally invasive approaches to rectal cancer need to demonstrate equivalent oncologic outcomes and maintenance or improvement in quality of life. This review will outline the current evidence for laparoscopy as a treatment option for patients with rectal cancer, emphasize the need for standardized approaches amongst multi-disciplinary teams, and highlight the technical details of different laparoscopic operations for rectal cancer.

FEASIBILITY OF TRANSRECTAL NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC SURGERY (NOTES) IN THE PORCINE MODEL

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BACKGROUND: NOTES: Access via a transrectal approach may be a beneficial alternative to transgastric approaches by providing superior visualization and eliminating need for endoscopic retroflexion. Transrectal NOTES may also introduce a second point for tissue retraction and triangulation when used in conjunction with transgastric NOTES. The optimal means of performing transrectal NOTES has not been described.

METHODS: Transrectal NOTES was performed in 6 pigs using various techniques to evaluate means of peritoneal access and closure. Using a rigid operating anoscope, 2 animals had a 1.5 cm transmural proctotomy made by conventional hand-held electrocautery which enabled peritoneal passage of a flexible endoscope. Transrectal NOTES access was achieved in 2 other animals by endoscopic balloon dilation over a transmural access wire. Finally, in 2 animals, an endoscopic needle-knife papillotome made a transmural incision enabling passage of the endoscope without dilation. Once feasibility of access was demonstrated, closure of the rectal defect was attempted. 2 animals had direct sutured closure under anoscopic visualization with a continuous absorbable suture. A third animal underwent closure with the NDO Plicator, an endoscopic tissue plicating device.

RESULTS: In all animals, transrectal access was achieved quickly and easily without injury to adjacent organs. In the first 2 animals, a laparoscope was used to provide guidance until the learning curve was completed. In 2 subsequent animals, guidance was obtained with a transgastric NOTES endoscope and combined transgastric and transrectal NOTES cholecystectomy was performed. In the last 2 animals, the transrectal endoscope was passed directly into the peritoneal cavity without additional video guidance. Direct suture closure of the proctotomy was easily performed under anoscopic visualization and demonstrated negative leak tests in vivo. Endolumenal closure with the NDO Plicator was easily performed; however one small leak was present on ex vivo tissue examination.

CONCLUSIONS: Transrectal NOTES, either as a standalone procedure or combined with transgastric NOTES, is feasible and provides safe access to the peritoneal cavity. Closure of the proximal rectal NOTES access point can be done by hand with suture. Despite one small leak, Plicator closure of rectal defects is intuitive and promising. Additional survival studies are required to determine the long-term effects of transrectal NOTES.

INFLUENCE OF LAPAROSCOPIC COLORECTAL SURGERY AND FAST-TRACK CARE PATHWAYS ON RESOURCE UTILIZATION IN AN EXISTING TRADITIONAL ACADEMIC COLORECTAL PRACTICE

Vincent J. Obias MS MD, Farhad Zeinali MD, Harry L. Reynolds MD, Brad Champagne MD, Conor P. Delaney MD PhD

INTRODUCTION: Laparoscopic colectomy (LAC) and fast-track care pathways (FT) are not always associated with major reductions in length of stay (LOS). Results are variable and limited to those of single groups or institutions. Introduction of LAC may be associated with long operative times, high costs, and no reduction in LOS for LAC or open colectomy (OC). Although clinical and financial implications are enormous, no data are available assessing the potential of adding a laparoscopic colorectal surgeon experienced in FT to an established colorectal practice.

METHOD: We compared 110 OC or LAC patients of an experienced laparoscopic colorectal surgeon during the first 11 months of a new practice (NEW) to case matched patients undergoing surgery by an established, experienced colorectal surgeon (EST). Patients were identified from a prospective database and matched for age, gender, DRG and operation. Direct costs were assessed using integrated hospital cost management system decision software (Transition Systems Inc., Boston, MA). Statistics were with Paired t test and Fishers exact test.

RESULTS: Procedures included segmental (n=111) or subtotal colectomy (n=26), proctocolectomy n=9, proctosigmoidectomy n=41, APR n=13, Hartmann's /end ileostomy reversal n=14 and rectopexy n=6. There were 85 NEW LAC vs 5 EST LAC (p<0.0001). Median age was 65 for NEW and 62 for EST patients (p=0.48). Mean operative times were 158 min NEW vs 226 min EST, and morbidity was 24% NEW and 27% EST (p=0.6). Bundled anesthesia/surgical costs were \$2281 for NEW and \$2762 for EST (p<0.0001). Bundled post-operative care expenses (ICU, nursing, pharmacy, laboratory, radiology, and rehab) were \$1327 for NEW and \$3490 for EST (p<0.0001).

	N	Laparoscopic	Median LOS	Direct cost (\$)
NEW	110	85*	4.0*	4368*
EST	110	5	7.0	6856

* p <0.0001 for NEW vs EST

CONCLUSION: These results demonstrate the benefit of an experienced laparoscopic colorectal surgeon familiar with FT, even to an institution with an established and experienced traditional colorectal practice. Direct costs, LOS and other resource utilization were significantly reduced, without adverse changes in morbidity. As these changes occurred within one year of the NEW practice, these benefits should easily be transferable to other institutions.

LAPAROSCOPIC PROCTOCOLECTOMY WITH END ILEOSTOMY FOR CROHN'S COLITIS WITH COLO-VAGINAL FISTULA

Vincent Obias MD, Yong-Geul Joh MD, Conor Delaney MD PhD.

INTRODUCTION: Laparoscopy is increasingly used for colorectal surgery, however conversion rates are high with inflammatory disease, internal fistulas, and pelvic surgery. This video demonstrates a totally laparoscopic proctocolectomy and end ileostomy with transanal specimen removal in a patient with Crohn's disease and a rectovaginal fistula.

METHODS: A 75 year old female with a 3 year history of colitis had 10 bloody bowel movements a day, incontinence requiring a pad, weight loss and anemia. As she had failed medical management, she was scheduled for surgery.

RESULTS: The right and transverse colon were mobilized, preserving the greater omentum. The ileocolic and inferior mesenteric pedicles were divided with a stapler, and the middle colic vessels with clips. The splenic flexure and left colon were mobilized. The colovaginal fistula was taken down and the rectum mobilized laparoscopically to the mid-anal canal. An intersphincteric dissection was performed, and the specimen removed transanally. The vaginal fistula was closed laparoscopically, and the ileostomy matured. Estimated blood loss was 150ml and hospital stay 5 days.

CONCLUSION: Complex cases can be completed in a complete laparoscopic fashion permitting a rapid recovery with less pain, and a lower risk of hernia formation and adhesions.

IMPACT OF AN EXPERIENCED LAPAROSCOPIC COLORECTAL SURGEON TO AN EXISTING TRADITIONAL COLORECTAL PRACTICE IN AN ACADEMIC MEDICAL CENTER

Vincent J Obias MD, Farhad Zeinali MD, Harry L Reynolds MD, Brad Champagne MD, Conor P Delaney MD, University Hospitals of Cleveland, Case Medical Center

INTRODUCTION: Laparoscopic colectomy (LAC) is steadily gaining acceptance. The potential benefits of LAC have been reported by high volume institutions with established laparoscopic programs, however, introduction of LAC has often been associated with prolonged operative times, increased costs and no reduction in hospital stay over that seen with open surgery. There are no published data looking at the impact of introducing an experienced laparoscopic colorectal surgeon using fast-track post-operative care pathways on an established and experienced colorectal practice.

METHOD: A consecutive group of 73 patients who underwent LAC performed during the first 11 months of a new practice were compared to a case-matched group of patients who underwent open colectomy (OC). Patients were identified from a prospective database and matched for age, gender, DRG and operation. Open complication data were obtained from electronic medical record review. Patients were compared for outcome and direct costs. Hospital information was collated using integrated hospital cost management system and decision software (Transition Systems Inc. Boston, MA; TSI). Statistics were performed with Paired t test and Fishers exact test.

RESULTS: Median age was 66.5 for the LAC group and 63.0 for the OC group ($p=0.1935$). Surgical procedures were: right colectomy ($n=63$), left/sigmoid colectomy ($n=26$), subtotal colectomy ($n=18$), total proctocolectomy ($n=8$), anterior resection ($n=27$), and abdominoperineal resection ($n=4$). Laparoscopic operative times were a median of 142 minutes. Overall morbidity for LAC was 19.2% and for OC was 16.4% ($p=0.829$). There was no mortality. Median length of stay was: LAC=3.0 days; OC= 7.0 ($p=0.0001$). Median direct cost per LAC was \$4396 versus \$6500 for OC ($p=0.0013$). Bundled anesthesia and surgical costs were \$2438 for LAC and \$2612 for OC, while bundled post-operative care expenses (ICU, nursing, pharmacy, laboratory, radiology, and rehabilitation) were \$1315 for LAC and \$3010 for OC.

CONCLUSION: The results demonstrate the benefit of an experienced laparoscopic colorectal surgeon to an already established colorectal practice. LAC significantly reduced direct costs and resource utilization, with similar morbidity to OC. Hospital stay was also significantly reduced. Although surgical costs were similar, post-operative care costs were reduced yielding a significant overall net financial benefit to the institution.

DEVELOPMENT OF STANDARDIZED ALGORITHMS FOR MANAGEMENT OF ANASTOMOTIC LEAKS AND ABDOMINAL AND PELVIC ABSCESES AFTER COLORECTAL SURGERY

R Phitayakorn, CP Delaney, HL Reynolds, BJ Champagne, AG Heriot, P Neary, AJ Senagore, and the International Anastomotic Leak Study Group

Although anastomotic leak (AL) is a major complication of intestinal surgery, management practices are variable and generally based on non-evidence based traditions learned during training. This may be especially problematic for surgeons in low volume institutions who do not often see anastomotic complications. This paper develops standardized algorithms for managing AL.

Published literature from 1973 to 2005 was reviewed for the terms AL and abdominal abscess. A five-round modified-Delphi technique via email was utilized to establish consensus for AL management among an international group of 45 experienced international colorectal surgeons and radiologists from America, Australasia, and Europe.

Clinical scenarios were grouped into intraperitoneal anastomoses, extraperitoneal (low pelvic) anastomoses, and anastomoses with a proximal diverting stoma. Management of intraperitoneal AL is dependent on the patient's clinical presentation. Patients with high-grade sepsis or generalized peritonitis should undergo an operation with fecal-diversion, and management of the anastomosis based on the size of the defect. Patients with extraperitoneal AL (usually posterior, low pelvic) require antibiotics with interventional drainage, depending on the anatomic location and abscess size. Diverted patients with AL are selectively treated with observation or intervention depending on the site and size of the AL.

These algorithms establish widely acceptable guidelines for the management of AL and intraabdominal abscess after colorectal surgery. They provide an opportunity for comparison of results, and for prospective research to define the optimal intervention for these potentially devastating complications.

BASILINE VIRTUAL REALITY ENDOSCOPIC PERFORMANCE AMONG NOVICES

R Phitayakorn MD and CP Delaney MCh, PhD, FRCSI

BACKGROUND: The use of endoscopic simulation in the training and assessment of medical and surgical residents is a rapidly expanding field of study. To date, there have been no published benchmark studies on baseline endoscopic performance in true novices.

METHODS: Non-medical, novice participants were enrolled in a prospective evaluation of colonoscopy ability on the virtual reality endoscopic simulator GI Mentor II™. Participants were asked to complete an anonymous demographic sheet that included: occupation, prior endoscopy exposure, age, gender, height, and prior video game experience including estimated amount of hours per week and types of games played.

Participants were then given a brief, standardized orientation on the purpose of colonoscopy and the basic use of a colonoscope. Each participant was then given five minutes to negotiate the colonoscope from the anus to the cecum on GI Mentor II™ colonoscopy module 1, level 1. Endoscopic metrics including: % mucosal surface examined, % of time with a clear view, number of times lost view of the lumen, number of times with excessive pressure, % of time patient spent in pain, number of times with loop formation, and amount of loop time were all prospectively collected for each participant and correlated with their respective demographic data.

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RESULTS: Forty-two participants (30 male, 12 female) from a wide variety of non-medical occupations were enrolled in this study with a mean age of 30 ± 10 years. Fifteen participants (36%) reached the cecum within the designated time limit. These participants had significantly higher percentages of mucosal surface examined ($p < 0.001$) and time with a clear view ($p < 0.006$) compared to participants who did not reach the cecum. Participants with prior video game experience ($n=20$) did not reach the cecum more frequently ($p > 0.10$) or with higher metric scores ($p > 0.10$) than participants without video game experience. Participant age, gender, height were not significantly associated with ability to reach the cecum.

CONCLUSION: For novices, the metrics of percentage of mucosal surface examined and time with a clear view may be the most reliable in establishing baseline endoscopic performance when using the GI Mentor II™. This result sets a benchmark by which future studies can demonstrate learning with instruction on this virtual reality simulator. Prior video game experience, as well as a learner's age, gender, or height is not significantly associated with endoscopic facility in true medical novices. The reason why some participants have a much higher baseline ability to perform a simulated colonoscopy requires further evaluation.

EXPERT BENCHMARK FOR THE GI MENTOR II

R Phitayakorn MD, JM Marks MD, HR Reynolds MD, and CP Delaney MCh, PhD, FRCSI

BACKGROUND: There is increasing interest in the use of virtual-reality simulators in general surgery residency training. Many simulators lack a benchmark against which trainees can measure competence and skill.

METHODS: Surgeons who had performed over 1000 colonoscopies were evaluated on Module 1, Case 5 of the GI Mentor I or II™ virtual reality endoscopy simulator (Simbionix, Cleveland). Participants were given five minutes to familiarize themselves with the simulator, and then performed the study case with standardized instructions. Metrics were recorded by the previously calibrated simulator.

RESULTS: Twenty-three surgeons (21 male, 2 female) participated. Mean height was 69.6 ± 2.6 inches, mean age 51 ± 9 years, median surgical glove size 7.5, and surgeons had 18.4 ± 10.2 years of practice, and did 8 ± 6 colonoscopies weekly. Ten participants had advanced training in endoscopy, laparoscopy, or colorectal surgery, eight had used the simulator before, of whom six had used it once. Mean time to complete the study case was 13.6 ± 5.3 minutes and time to reach the cecum was 6.5 ± 4.3 minutes. Participants examined $92.3 \pm 3.6\%$ of the simulated colonic mucosa with a clear view of the lumen $89.5 \pm 4.2\%$ of the time. Total time the colon was looped was 22 ± 35 seconds (range=0-133). The overall efficiency of screening was $70.33 \pm 23.45\%$ (range=20 to 94%). Participants tended to mistake normal simulated colonic structures as pathology.

CONCLUSION: Performance on a virtual reality endoscopic simulator has a wide amount of variability even among a group of experienced endoscopists. Expert benchmark tests should be performed on simulators that will be used for resident assessment prior to any attempts at certification of competence.

2

INTRAOPERATIVE RADIATION THERAPY INTRODUCTION AND UTILIZATION IN A COLORECTAL UNIT

C Williams, H Reynolds, C Delaney, B Champagne, V Obias, Y Joh, J Merlino, T Kinsella

PURPOSE: The introduction of an intraoperative electron beam radiation therapy unit (IORT) offers the colorectal surgeon more extensive treatment options for locally advanced primary and recurrent neoplasms.

METHODS: We retrospectively review the subset of colorectal patients treated with IORT following introduction of the Mobetron unit in 1999, examining both indications and outcomes. This unit permits radiation of a cone of tissue up to 10cm in diameter using an electron accelerator with excellent tissue penetration.

RESULTS: A review of all patients treated with IORT since 1999 revealed 40 patients who underwent colectomy or proctectomy. All patients had evidence of local extension to contiguous structures and based on preoperative staging were deemed likely to have incomplete resection by the operating surgeon. 14 underwent abdominal perineal resection, 10 low anterior resection, 5 low anterior resections with low Hartmann's, 5 segmental colectomy, 2 pelvic exenteration, 1 colostomy, 1 colectomy and duodenectomy, and 2 underwent local excision of recurrences. 26 out of the 40 underwent adjacent organ, abdominal wall or pelvic sidewall excision. IORT was selected as an alternative to sacrectomy or exenteration for a close margin in 10 patients. IORT dose ranged from 9 to 12Gy.

	n	Stage***				Number with Positive margins (%)	Median Follow up after Surgery in months (range)	Number with local Recurrence	Number Surviving to Date (%)
		4	3	2	1				
Primary Rectal	15	5	5	4	1	3 (20)	21 (1-84)	0	8 (53)
Recurrent Rectal	11	2	5	4	0	4 (36)	42 (6-90)	0	9 (81)
Recurrent Colon	7	4	2	1	0	1 (17)	49 (22-83)	1*	4 (57)
Primary Colon	2	1	1	0	0	0	28 (16-39)	0	2 (100)
Appendiceal	2	0	0	2	0	0	20 (11-37)	0	2 (100)
Other**	3	1	2	0	0	2 (67)	24 (6-47)	0	4 (100)
Totals	40	14	13	11	2	10 (25)	29 months	1	28 (70)

* IORT to gross Tumor, ** Other includes colon and duodenal primaries, 1 ovarian cancers with rectal involvement, & 1 endometrial cancer recurrence with rectal involvement.

*** Pathologic stage post Pre-operative chemo and radiation

CONCLUSION: The introduction of IORT has allowed us to selectively approach locally advanced primary and recurrent neoplasms which traditionally would have been deemed unresectable. The one local recurrence occurred in a patient who received IORT to gross tumor. Sacrectomy and other extended resections may be avoided in selected patients with low local recurrence rates and good median survival for such a high risk group of patients.

GI RECOVERY RESPONDER ANALYSIS: RESULTS OF PHASE III TRIALS OF ALVIMOPAN (ALV) 12 MG VERSUS PLACEBO (PLA) IN PTS UNDERGOING BR

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INTRODUCTION: A responder analysis was performed to examine alv, a peripherally acting mu-opioid receptor (PAM-OR) antagonist, in the management of postoperative ileus (POI). The proportion of patients who achieved GI recovery and hospital discharge after BR was analyzed in multicenter, randomized, double-blind NA trials.

Methods: Adult pts undergoing laparotomy for BR scheduled for postoperative IV patient-controlled opioid analgesia received oral alv 12 mg or pla preoperatively and twice-daily postoperatively until hospital discharge or for 7 postoperative days (PODs). This pooled post hoc analysis examined the proportion of responders (pts who achieved the event without developing complications of POI) on POD5 and 7 for efficacy endpoints of GI-2 recovery (composite of time to first bowel movement [BM] and toleration of solid food) and time to hospital discharge order (DCO) written. Treatment effects on time to events were analyzed using the Cox proportional hazards model. P values were calculated using Fishers exact tests.

Results: Alvimopan significantly accelerated GI-2 recovery and DCO written (hazard ratio=1.5 and 1.4, respectively; $P<0.001$). More pts in the alv group achieved GI recovery and DCO written. For ex, 80% of pts in the alv group achieved GI-2 recovery by POD5 compared with 66% of pts in the pla group.

CONCLUSION: In this responder analysis, a significantly greater proportion of pts who received alv 12 mg achieved GI-2 recovery and DCO written by POD7 compared with pts who received pla. This pooled analysis suggests that by accelerating GI recovery, alv also reduces the proportion of pts with a prolonged hospital stay.

	Pla n = 695	Alv 12 mg n = 714	
GI-2, PODs 5, 7	66.3%, 74.7%	80.1%, 84.5%	$P<0.001$
DCO, PODs 5, 7	61.0%, 80.0%	77.0%, 90.2%	$P<0.001$

ADOPTION OF LAPAROSCOPIC COLECTOMY IN THE UNITED STATES: 2002-2006 TRENDS IN LAPAROSCOPIC VS OPEN COLECTOMIES

Anthony J. Senagore, MD, Conor P Delaney, MD, Janet K. Young, M.D., Dennis Dunn, PhD.

Spectrum Health and Michigan State University, Grand Rapids, MI 1, Case Western Reserve University, Cleveland, OH2, Solucient, a Thomson business, Evanston, Illinois3.

Laparoscopic colectomy adoption rates have lagged, primarily due to issues related to management of colorectal cancer. We conducted a study to determine whether there has been an increase in laparoscopic colectomies for both benign and malignant disease since the publication of several studies demonstrating efficacy data for laparoscopic colorectal cases.

The study population was defined by merging data from several databases. We used January 1, 2002 through June 30, 2006 data from the MarketScan Hospital Drug database, a proprietary database managed by Thomson and the International Classification of Diseases-9th Revision, Clinical Modification (ICD-9-CM) procedure codes to identify inpatient hospitalizations related to colectomy. Severity was classified by 3M's All Patient Refined DRGs (APR-DRG) version 15 severity class.

During the study period annual inpatient colectomies for cancer decreased from 86,600 to 77,800, while laparoscopic volume increased from 6.3% of colon to 20.1%. Despite the lower volume of cancer resections, there has been a nearly 11% increase in the most severe cases (severity level 4). Conversely, non-cancer colectomies increased from 141,000 to 155,000 in the same period. A laparoscopic approach increased from 12.1% to 20.1% during the study period.

The data presented in this study demonstrate that clinical evidence is essential in stimulating adoption of new surgical techniques, particularly when related to oncologic surgery where long term outcome is more important than short term benefits. Coordinated education will be essential to encourage implementation from the current group of early adopter surgeons.

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ALVIMOPAN IS ASSOCIATED WITH REDUCED HOSPITAL LENGTH OF STAY, LOWERED READMISSION RATES, AND DECREASED COSTS AFTER BOWEL RESECTION: POOLED DATA FROM 4 CLINICAL TRIALS

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PURPOSE: The objective of this evaluation was to assess the economic impact of postoperative ileus (POI) in patients undergoing laparotomy for large or small bowel resection (BR) and treated with a peripherally active mu-opioid receptor (PAM-OR) antagonist, alvimopan. This analysis was performed on the 12-mg alvimopan and placebo groups in 4 institutional review board-approved, multicenter, double-blind, placebo-controlled, phase III US and Canadian efficacy trials. All patients provided informed written consent. The alvimopan 12 mg dose was the only dose of alvimopan common to all 4 trials.

METHODS: A post hoc assessment of 4 randomized phase III efficacy trials of alvimopan for the management of POI was performed to determine the following: 1) hospital length of stay (LOS) (based on day of surgery to the day that discharge order was written) and 2) rate of hospital readmissions attributable to POI within 7 days of initial hospital discharge (based on serious adverse event reports). Cost data were not collected in the clinical trials, so hospital and readmission cost data were obtained from Premier's Perspective (TM) Comparative Database (01/01/05 to 12/31/05), a nationwide hospital database with about 5 million discharges annually. Day-specific hospital costs were estimated using DRG codes 148 and 149, and readmissions were estimated using information from patients who had a primary admission ICD-9 diagnosis code of 560.1 (paralytic ileus) or 997.4 (digestive system complications not otherwise identified) [Premier data 01/01/05 to 03/31/05]. Readmissions within 7 days of discharge were included because, in general, hospitals are unable to obtain additional reimbursement for up to 30 days after discharge for readmissions that are directly related to the initial hospitalization. The cost of alvimopan has not yet been established, thus was not included in the analysis. All other costs are reported in 2005 US dollars.

RESULTS: From the 4 clinical trials, 1,401 patients underwent BR (n, 710 [alvimopan 12 mg]; n, 691 [placebo]). The mean hospital LOS for patients receiving alvimopan was significantly lower (6.6 days) compared with the LOS for patients receiving placebo (7.6 days), a reduction of a full day (P equal to 0.001). This full day reduction of LOS may translate to an additional 15 percent increase in the number of BRs per bed per year (alvimopan, 55 surgeries; placebo, 48 surgeries). In addition, the alvimopan group had a lower rate of rehospitalization attributable to POI than the placebo group (1.0 percent vs. 2.0 percent; P equal to 0.127). Hospital mean per-patient cost for the alvimopan group was 12,234 US dollars compared with 13,674 US dollars for the placebo group. Mean per-patient hospital readmission cost for the alvimopan group was 82 US dollars compared with 169 US dollars per patient for the placebo group. The total mean per-patient cost associated with the alvimopan treatment group was 12,316 US dollars compared with 13,843 US dollars for the placebo group.

CONCLUSION: Use of alvimopan 12 mg was associated with a decrease in hospital LOS and readmission rates. These post hoc analyses show that the per-patient economic reduction associated with the alvimopan treatment group compared with the placebo group is 1,527 US dollars. Although the cost of the drug is not currently established, alvimopan could provide a positive economic benefit through reductions in hospital and readmission costs. The LOS reduction associated with alvimopan may also provide the opportunity for hospitals to accommodate 7 additional BRs per year per surgical bed.

STANDARDIZED ALGORITHMS FOR MANAGEMENT OF ANASTOMOTIC LEAKS AND RELATED ABDOMINAL AND PELVIC ABSCESSSES AFTER COLORECTAL SURGERY

R Phitayakorn, CP Delaney, HL Reynolds, BJ Champagne

The risk factors and incidence of anastomotic leak following colorectal surgery are well reported in the literature. However, the management of the multiple clinical scenarios which may be encountered has not been standardized.

The medical literature from 1973-2006 was reviewed using PubMed for papers relating to anastomotic leaks and abdominal abscess, with a specific emphasis on predisposing factors, prevention strategies, and treatment approaches. A six-round modified Delphi research method was utilized to find consensus among a group of expert colorectal surgeons and interventional radiologists regarding standardized management algorithms for anastomotic leaks. Management scenarios were divided into those for intraperitoneal anastomoses, extraperitoneal (low pelvic) anastomoses, and anastomoses with proximal diverting stomas. Management options were then based on the clinical presentation and radiographic findings and organized into three inter-connected algorithms

SAFETY OF ALVIMOPAN, A HIGHLY SELECTIVE, POTENT, PERIPHERALLY ACTING MU-OPIOID RECEPTOR (PAM-OR) ANTAGONIST, IN MORE THAN 1,900 PATIENTS UNDERGOING BOWEL RESECTION

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INTRODUCTION: In postoperative ileus (POI) trials, alvimopan accelerated GI recovery and reduced length of hospital stay after bowel resection (BR). However, these benefits must be associated with acceptable risk to permit widespread use of alvimopan in this population.

METHODS: Adult patients who received alvimopan 12mg or placebo, underwent laparotomy for BR, and were scheduled for postoperative IV-PCA were included in this pooled safety analysis of two phase II and five phase III POI trials. Treatment-emergent adverse events (TEAEs: any AE occurring between first study dose and within 7 days after the last dose) and serious AEs (SAEs: AEs resulting in death, persistent/substantial disability, prolonged hospitalization, or readmission; life threatening; requiring intervention to prevent permanent impairment/damage within 30 days of the last study medication) from the POI worldwide safety database were used to develop a clinically relevant safety profile of alvimopan in BR patients.

RESULTS: 986 placebo patients and 999 alvimopan 12mg patients were included in this analysis. The most common TEAEs included GI disorders (placebo, 65%; alvimopan 12mg, 60%), surgical complications such as POI, wound complications, anastomotic leak, etc. (placebo, 23%; alvimopan 12mg, 17%), respiratory disorders (placebo, 22%; alvimopan 12mg, 19%), laboratory test abnormalities (placebo, 22%; alvimopan 12mg, 18%), vascular disorders (placebo, 22%; alvimopan 12mg, 21%), cardiac disorders (placebo, 17%; alvimopan 12mg, 15%), renal/urinary disorders (placebo, 13%; alvimopan 12mg, 13%), and hepatobiliary disorders (placebo, 0.2%; alvimopan 12mg, 0.2%). The most common SAEs were POI (placebo, 5.2%; alvimopan 12mg, 1.2%), postoperative infection (placebo, 1.6%; alvimopan 12mg, 1.5%), and small bowel obstruction (placebo, 1.9%; alvimopan 12mg, 1.6%). Incidence rate for all-cause mortality was 0.7% for each treatment group.

CONCLUSIONS: In this large pooled safety database from the worldwide POI trials, alvimopan 12mg demonstrated a favorable risk profile supporting the clinical benefit in BR patients.

DISCOVERY PROTEOMICS IN HUMAN COLORECTAL CANCERS

Markowitz S, Chance M, Nibbe R, Reynolds H, Willis

Colorectal cancers (CRC) are the second leading cause of cancer and cancer death in adult Americans. A number of research efforts are ongoing trying to elucidate the cellular and molecular mechanism that causes the onset of CRC, and its progression through increasingly more severe pathological stages (0-IV). We are using a proteomics approach to further our understanding of the mechanistic cause of CRC, and to potentially identify biomarkers that indicate the stage, severity, and prognosis of the disease. A pathologic database at the Case Cancer Center contains matched (normal/tumor) tissue samples collected during surgery from an extensive variety of patients diagnosed with varying stages of CRC. As an initial attempt to use discovery proteomics to examine CRC, we obtained twelve matched tissue samples (normal/stage IV) and performed differential gel electrophoresis (2D-DIGE) to evaluate significant changes in the expression of proteins common to both the normal and diseased tissues. 58 spots are differentially expressed ($\pm 50\%$) between normal and cancer tissue with statistical significance ($p \leq 0.05$). These proteins have been identified by mass spectrometry, and the involved metabolic and cell signaling pathways will be reported. Such pathways may present new targets for adjuvant chemotherapy. Using the protein abundance values on the gels, a supervised learning technique is under development to train a support vector machine (SVM), which in turn could be used to classify an electrophoretic gel pattern as "cancer" or "no-cancer."

ALVIMOPAN (ALV), A PERIPHERALLY ACTING MU-OPIOID RECEPTOR (PAM-OR) ANTAGONIST, SIGNIFICANTLY ACCELERATED GI RECOVERY AFTER SMALL BR

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INTRODUCTION: Time to GI recovery and hospital discharge order (DCO) written were examined after sBR in trials of alv for the management of postoperative ileus.

METHODS: This was a pooled subset analysis of adult pts scheduled for postop IV opioid-based pt-controlled analgesia who underwent sBR. Pts received alv 12 mg or placebo (pla) preop then twice-daily postop until hospital discharge or for 7 PODs. Treatment effects were analyzed using the Cox proportional hazards model (HR) and Kaplan-Meier means (hours). Efficacy endpoints included GI-2 recovery (time to first BM & toleration of solid food), and DCO written. Nausea and vomiting (N/V) were reported as adverse-events.

RESULTS: Efficacy and safety results are presented in the table.

CONCLUSION: Alvimopan 12 mg significantly accelerated GI recovery and hospital discharge compared with pla in this subset analysis of phase III trials. Alv was well tolerated with a lower incidence of nausea and vomiting compared with pla. Moreover, this analysis is consistent with results from the larger population of all BRs in alv phase III trials.

	Placebo (n = 50)	Alv 12 mg (n = 65)	
GI-2, HR	—	2.5	$P < 0.001$
GI-2, mean hrs	115.6	78.0	-37.6 (33%)
DCO, HR	—	2.0	$P < 0.001$
DCO, mean hrs	131.7	98.0	-33.7 (26%)
N/V	57%/25%	44%/20%	—

Section 3

General Surgery

HAND-ASSIST LAPAROSCOPIC DISTAL PANCREATECTOMY

Jeffrey M. Hardacre, MD FACS, Amitabh Chak, MD, and Michael Rosen, MD

INTRODUCTION: Cystic pancreatic neoplasms are being found with increasing frequency. Surgical management has traditionally employed an open operative approach. Laparoscopic procedures are increasingly being used.

METHODS: We describe the technique of hand-assist laparoscopic distal pancreatectomy. The patient is a 25 year-old woman who presented with left-sided abdominal pain. A CT showed a 3.9 cm cystic lesion in the body of the pancreas.

An EUS-guided aspirate of the cyst fluid yielded a CEA of 1450 ug/L.

RESULTS: The operation lasted 200 minutes, and the estimated blood loss was 50 ml. The patient developed a pancreatic fistula that closed with conservative management. The lesion proved to be a mucinous cystic neoplasm.

CONCLUSION: Hand-assist laparoscopic distal pancreatectomy provides excellent exposure and visualization. It allows tactile sensation through a small incision that would be needed for specimen removal. It is an excellent alternative to an open operation in select patients.

QUANTIFYING THE INFLUENCE OF OBESITY ON PROTEIN SYNTHESIS IN VIVO: TOWARDS THE APPLICATION IN BARIATRIC PATIENTS

Peter Hallowell, Danielle Gilge, Stephanie Anderson, Alison Steiber and Stephen Previs.*

BACKGROUND: It is well known that proteins are continuously synthesized and degraded and that the synthesis of some proteins is stimulated during feeding. We have developed and validated the use of $2\text{H}_2\text{O}$ (a stable, non-radioactive isotope method) for measuring rates of protein synthesis in vivo. In addition, using rodent models we have demonstrated that protein synthesis in liver (and plasma albumin) and skeletal muscle are responsive to food intake.

METHODS: A rodent model of diet-induced obesity, i.e. high-fat fed vs. low-fat fed C57BL/6J mice was used. $2\text{H}_2\text{O}$ was injected intraperitoneally. The mice were sacrificed 5 hours later.

RESULTS: We observed comparable rates of protein synthesis in skeletal muscle in the basal (i.e. fasted) state but an impaired response following a liquid meal, in obese vs. lean mice, respectively. Those studies also found a tendency for reduced liver and plasma albumin synthesis in the basal state with virtually no effect on the response of either liver or albumin synthesis during the meal, in obese vs. lean mice, respectively.

CONCLUSION: This method is unique in that it is possible to (i) quantify protein turnover in free-living subjects and (ii) determine the influence of an acute perturbation (e.g. meal-feeding) on protein synthesis in vivo. Studies are now being planned to apply our $2\text{H}_2\text{O}$ method in patients undergoing bariatric surgery. For example, we will quantify rates of albumin synthesis in free-living patients before and after surgery. This will allow us a better understanding of protein metabolism during the profound changes after bariatric surgery.

AN AGGRESSIVE SURGICAL APPROACH IS WARRANTED IN THE MANAGEMENT OF CYSTIC PANCREATIC NEOPLASMS

J.M. Hardacre, M.F. McGee, T.A. Stellato, and J.A. Schulak

BACKGROUND: Cystic pancreatic neoplasms encompass a range of benign to malignant disease. This study assesses the incidence of malignancy in these neoplasms and establishes a strategy for their surgical management.

METHODS: The pathology database at our institution was queried for the spectrum of cystic pancreatic neoplasms from January 1996 through December 2005. Hospital and physician charts were retrospectively reviewed. Neoplasms were grouped into Serous Cystic Neoplasms (SCN), Mucinous Cystic Neoplasms (MCN) Adenoma/Borderline, MCN Invasive, Intraductal Papillary Mucinous Neoplasms (IPMN) Adenoma/Borderline, IPMN Carcinoma-in-Situ (CIS), and IPMN Invasive.

RESULTS: During the study period 60 resections were performed for 16 SCNs, seven MCNs, and 37 IPMNs. The mean age of the patients was 65 years, and 63% were female. Thirty-seven percent (22/60) of the lesions were found incidentally. Forty-five percent (10/22) of incidental lesions were mucinous. Twenty-nine distal pancreatectomies, 23 pancreaticoduodenectomies, five total pancreatectomies, two enucleations, and one central pancreatectomy were performed. There were two peri-operative deaths (3.3%). The overall median length of stay was 8 days. Fifty-eight percent (33/57) of patients suffered at least one complication. Endoscopic ultrasound-guided fine-needle aspiration biopsy failed to diagnose invasive cancer in the three patients with cancer that had this procedure performed. Twenty-five percent (15/60) of all neoplasms contained invasive cancer, 34% (15/44) of mucinous neoplasms contained invasive cancer, and 4.5% (1/22) of incidental neoplasms contained invasive cancer. Sixty percent (9/15) of patients with invasive cancer had lymph node metastases. Sixty-seven percent (10/15) of patients with invasive cancer had invasive cancer within one mm of a final surgical margin. Fifty-three percent (8/15) of patients with invasive cancer developed a recurrence. No patients with SCN or MCN Adenoma/Borderline died during the study period. Patients with MCN or IPMN Invasive neoplasms experienced significantly diminished overall five-year survival compared to patients with IPMN CIS neoplasms and to patients with MCN or IPMN Adenoma/Borderline neoplasms (22% vs 73% vs 94%, $p=0.004$).

CONCLUSION: Given the poor long-term survival of patients with cystic pancreatic neoplasms containing invasive cancer and the current inability to pre-operatively distinguish among the various types of lesions in a reliable manner, our data support an aggressive surgical approach to the management of cystic pancreatic neoplasms.

OPEN RNY GASTRIC BYPASS PROVIDES EXCELLENT SHORT TERM OUTCOMES IN PATIENTS WITH BMI's 65 AND OVER

Peter T. Hallowell, MD, Thomas A. Stellato, MD, John J. Jasper, MD, Margaret Schuster, RN, Kristen Graf, RN, and Ann Robinson BA.

BACKGROUND: Bariatric surgery has become increasingly popular in the treatment of morbid obesity and its co morbid conditions. Controversy remains over the appropriate procedures for patients especially those who are super morbidly obese. We report our experience with open RNY gastric bypass in patients with a BMI \geq 65.

METHODS: Retrospective review of prospectively maintained database. 962 patients from 1998 – Oct. 2006 were reviewed. Revisions were excluded. 923 patients were identified, of those 54 patients with a BMI \geq 65 and 869 patients with a BMI < 65.

RESULTS: Demographic and complication data are listed below.

	Mean Age	Mean BMI	Mean ASA	Mean OR Time	Mean LOS	ICU Stay	Leak	Death
BMI \geq 65	41.1	70.4	2.9	165	3.2	7 %	3.7%	1.9%
BMI < 65	43.3	49.3	2.9	164	3.3	4.0 %	1.4%	0.2%
p value	NS	<0.0001	NS	NS	NS	NS	NS	NS

CONCLUSIONS: Open RNY gastric bypass can be performed safely in super obese patients with low morbidity and mortality. In the setting of an experienced program, length of stay and ICU utilization are minimal. The percentage of death, Leak and ICU stay is higher in patients with a BMI over 65 verses patients with a BMI < 65 these differences were not statistically significant.

RISING PARATHYROID HORMONE (PTH) AFTER GASTRIC BYPASS SURGERY APPEARS TO BE OF A SECONDARY NATURE

Judy Jin MD, Ann V. Robinson BA, Peter T. Hallowell MD, John J. Jasper MD, Thomas A. Stellato MD, Scott M. Wilhelm MD

INTRODUCTION: Endocrine changes, particularly elevated PTH occurring after gastric bypass procedures have been reported but are not well characterized.

METHODS: We retrospectively reviewed patients who underwent Roux-en-Y gastric bypass (short limb (SL) = 75 cm, long limb (LL) = 150 cm) procedures at our institution from January-December 2005. Patient demographics, laboratory values of calcium, vitamin D, phosphorous, alkaline phosphate and PTH were followed at quarterly intervals for one year.

RESULTS: One hundred and forty patients were identified. Mean age for the group was 45 ± 10 years old and 90% of patients were female. The average BMI was 49.2. The mean PTH levels increased from 29.4 post-op to 43.1 ng/ml ($p < 0.001$) over one year. Seven percent of the patients had hyperparathyroidism (PTH > 53 ng/ml) immediately post-op, the ratio then rose to 29% at one year. Only two patients had evidence of true primary hyperparathyroidism with elevated PTH and hypercalcemia. Sixty percent of patients had at least 10 ng/ml increase in PTH level at the end of one year, reflecting a 30% increase from baseline levels. Vitamin D levels < 20 ng/ml were identified in 45 patients (32%) initially post-op and they continued to be low compared to the rest of the population ($p = 0.004$). Vitamin D levels did vary with seasonal sun exposure and were highest in the third quarter (July- September). Sub-analysis of the group showed that patients with LL bypass had lower vitamin D levels (14 vs 22 ng/ml, $p = 0.14$) compared to SL patients.

CONCLUSION: While pre-operative endocrine abnormalities are present in patients undergoing gastric bypass procedures, the derangements intensify after surgery. A 4-fold increase in patients with elevated PTH deserves special attention. When combined with the concurrent prevalence of low vitamin D and normocalcemia in this population, we propose that this is a disorder of secondary hyperparathyroidism requiring medical treatment with vitamin D supplementation.

ELIMINATING RESPIRATORY ICU STAY FOLLOWING GASTRIC BYPASS

PT Hallowell, TA Stellato, MC Petrozzi, M Schuster, K Graf, A Robinson, and JJ Jasper*

BACKGROUND: The Bariatric patient is one of the most complex in General Surgery. The patient's morbid obesity and multiple co-morbidities create a higher likelihood for intensive care services. Some Bariatric centers routinely admit patients post operatively to the intensive care unit (ICU). Sleep apnea (OSA) is an often unrecognized co-morbidity that may lead to increased respiratory events and ICU admissions in bariatric surgery patients.

HYPOTHESIS: Identifying and treating occult OSA may decrease the need for ICU utilization

DESIGN: Retrospective review of prospectively maintained Bariatric database

SETTING: Academic Tertiary Care Medical Center

PATIENTS AND METHODS: From 1998 to 2005 a total of 890 bariatric procedures were performed at our center: 858 primary gastric bypasses, and 32 revisions. All patients undergo extensive preoperative education including mandatory attendance at support group meetings, 3 month cessation of smoking, and an exercise program prior to gastric bypass. Patients undergo comprehensive pulmonary and anesthesia evaluations. Prior to 2004 patients were selectively evaluated for sleep apnea, since 2004 all patients have had a sleep study.

RESULTS: Overall 30 day mortality for these 890 pts. is 0.3%. A post operative ICU stay was required in 43 patients (4.8%). During the period (1998-2003) when OSA evaluation was not mandatory, a respiratory related ICU stay was necessary in 11 of 572 patients. When OSA evaluation was mandated in all patients (2004-2005), there were no respiratory related ICU stays. (0/318) *Statistics using GraphPad InStat computer Fisher's software.

	1998- 2003	2004-2005	Totals
# of bypass patients	572	318	890
BMI (mean) Primary Gastric Bypasses	51.1	49.6	ns
BMI (range) Primary Gastric Bypasses	36-87	36-75	----
ICU stay respiratory related	11	0	*P < 0.01
ICU stay non-respiratory related	21	11	ns

CONCLUSION: Multiple variables such as increased surgical experience, patient education, and smoking cessation unquestionably lead to a decrease in ICU stay. Our study shows that recognizing and treating occult sleep apnea may further improve this quality metric. In our center mandatory OSA screening and aggressive preoperative treatment has actually eliminated the need for respiratory related ICU stay.

EVALUATION FOR BARIATRIC SURGERY EXPOSES UNRECOGNIZED SLEEP APNEA

Hallowell, P.T., Stellato, T.A., Crouse, C. Schuster, M., Graf, K. Robinson, A., Jasper, J.J.

BACKGROUND: Many patients undergoing Bariatric surgery have identified severe co- morbidities, such as diabetes, hypertension and obstructive sleep apnea (OSA). We suspected that sleep apnea was under diagnosed in our population. Starting in December of 2003 we required all patients undergoing Roux en Y gastric bypass to have a pre operative sleep study. This report details our findings comparing an era prior to universal sleep study and after.

METHODS: A retrospective chart review of our database was conducted from July 2003 until December 2005. Era 1 consisted of 101 patients from July to November 2003. Era 2 consisted of 249 patients from December 2003 to December 2005. All patients had either a laparoscopic or open RNY gastric bypass. Age, Gender, Race, BMI, DM, HTN and OSA were documented from the initial evaluation.

RESULTS: Demographic data is summarized in the table below.

	Era 1 (101)	Era 2 (249)	
Mean Age	43.6 (21 – 63)	44.6 (19 – 66)	NS
Mean BMI	49.2 (36.8 – 87.0)	49.6 (37.5 – 74.6)	NS
Gender female	86.1 % (87)	87.6 % (218)	NS
Race	Cauc. 79.2 % (80) AA 18.8% (19) Hisp 2.0% (2)	Cauc. 74.3% (185) AA 24.9% (62) Hisp. 1.0% (2)	NS
HTN	46.5 % (47)	52.6 % (131)	NS
DM	18.8 % (19)	30.5 % (76)	NS

In Era 1 18.8% (19) patients presented with a diagnosis of sleep apnea. 46 of the remaining 82 patients had a sleep study, of those 41 (89.1%) were positive for sleep apnea. In Era 2 19.7% (49) patients presented with sleep apnea as a co morbidity. 200 patients had sleep studies 89.5% (179) were positive.

CONCLUSIONS: In our study population the prevalence of OSA when all patients were evaluated for Bariatric surgery was 91.5% (228). Prior to mandatory evaluation for sleep study only 59% (60) of patients were diagnosed with sleep apnea. Sleep apnea continues to be under diagnosed in the morbidly obese. In Era 1 19% of patients presenting for evaluation for Bariatric surgery had a diagnosis of sleep apnea. In era 2 this remained the same 19.7% despite increasing literature highlighting the association of sleep apnea and morbid obesity. Despite clinical evaluation 32.5% of patients in Era 1 were undiagnosed. An overnight polysomnogram is the most sensitive test for sleep apnea in the morbidly obese patient. The most significant risk factor for OSA is obesity but still rarely evaluated in morbidly obese patients. This is of great importance to both Bariatric Surgeons and Primary Care Physicians.

OUTCOME OF PHEOCHROMOCYTOMA MANAGEMENT IN THE LAPAROSCOPIC ERA

CC Solorzano, JI Lew, S Wilhelm, RE Montano, W Wu, W Huang, RA Prinz

INTRODUCTION: Laparoscopic adrenalectomy (LA) is the currently preferred approach for adrenal pheochromocytomas (pheos). This study reports the changes in diagnosis, management and outcome of pheos treated since the advent of widespread LA.

METHODS: 91 patients with pheochromocytomas were operated at three tertiary referral centers between 1995-2006. Clinical, biochemical and pathologic data were collected retrospectively.

RESULTS: There were 51 females and 40 males. Mean age was 46 yrs (12-81). Tumors were found incidentally in 35% of patients. Of this group of 91 patients, 11 (12%) had familial syndromes. CT or MRI localized the adrenal lesion in all patients. MIBG was obtained in 28 patients with 7 having negative studies and 2 with misleading information. Of these MIBG patients, 18 were concordant with CT, and this modality changed the approach in only one VHL patient. Mean tumor size was 5.6cm (1.5-14.5). There were 87 adrenal pheos and 9 paragangliomas. Laparoscopy was successful in 63/70(90%) patients, with 19/63(30%) having tumors ≥ 6 cm. Conversions to open procedures due to bleeding were performed in patients with 4 right, 2 left pheos and one paraganglioma. Twenty-one patients had a planned open procedure performed due to suspicion of malignancy or large size tumors. LA complications included hematoma (3), wound infection (1), pulmonary (3) and death (1) from hemorrhage after paraganglioma removal. Two of 87 (2.3%) adrenal pheos and 4 of 9 (44%) paragangliomas were malignant. Tumor necrosis correlated positively with tumor size but not with intraoperative adverse events. Average long term follow-up was 27mos (1-122). There were 7 recurrences (3 contralateral adrenals, 4 metastases). Postoperative biochemical tests available in 59 patients were normal in 91%.

CONCLUSION: The diagnosis of pheochromocytoma is made incidentally in 35% of patients. MIBG is not necessary for non-hereditary pheos localized by CT/MRI. LA is possible in most patients with excellent results including lesions ≥ 6 cm without preoperative or intraoperative evidence of invasion. Laparoscopy should be used cautiously for paragangliomas because of a high rate of malignancy.

MEDICARE DATABASE COMPLICATIONS CAN BE AVOIDED IN OLDER OBESE PATIENTS UNDERGOING GASTRIC BYPASS

Peter T. Hallowell, M.D.; Thomas A. Stellato, M.D., Margaret Schuster, RN, BSN, Kristin Graf, RN, BSN, Ann Robinson, B.A., and John J. Jasper, M.D.*

BACKGROUND: The success of bariatric surgery for morbid obesity has spurred surgeons to expand this therapy for the elderly. A recent review of the Medicare database by Flum suggests increased mortality in Medicare beneficiaries especially those that are elderly. Our experience in patients 60 years and older and in Medicare recipients undergoing gastric bypass does not support these findings.

HYPOTHESIS: With carefully evaluated and managed Medicare and elderly patients, there is no increase in perioperative morbidity and mortality

DESIGN: Retrospective review of prospectively maintained Bariatric database.

SETTING: Academic Tertiary Care Medical Center

PATIENTS AND METHODS: We reviewed our database of 928 consecutive patients from 1998 thru May of 2006. Of these, 36 underwent revisional surgery and were excluded. Of the remaining 892 patients, 46 were 60 to 66 years of age; the remainder were 18-59 years of age. These two groups were compared in terms of demographics, morbidity, and mortality. Additionally, the subset of Medicare beneficiaries undergoing gastric bypass were compared with all non Medicare patients.

RESULTS: There is no difference in outcomes between groups, older verses younger and Medicare verses non Medicare, for any post-operative complication or mortality.

CONCLUSION: In our experience bariatric surgery can be performed in carefully selected Medicare recipients and patients age 60 and over with acceptable morbidity and mortality. There is no difference in the occurrence of complications in Medicare patients, patients younger than age 60 or those above the age of 60. We believe these results reflect careful patient selection, intensive preoperative education and expert operative and perioperative management. Our results indicate bariatric surgery should not be denied solely based on age or Medicare status.

A PRIMER ON NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC SURGERY

(NOTES): BUILDING A NEW PARADIGM

Michael F. McGee, MD; Michael J. Rosen, MD; Jeffrey Marks, MD; Raymond P. Onders, MD; Amitabh Chak, MD; Ashley Faulx, MD; Victor K. Chen, MD, MPSH; Jeffrey Ponsky, MD

Access to the abdominal cavity is required for diagnostic and therapeutic endeavors for a variety of medical and surgical diseases. Historically, abdominal access has required a formal laparotomy to provide adequate exposure. Natural Orifice Transluminal Endoscopic Surgery (NOTES) is an emerging experimental alternative to conventional surgery that eliminates abdominal incisions and incision-related complications by combining endoscopic and laparoscopic techniques to diagnose and treat abdominal pathology. During NOTES, commercially available flexible video-endoscopes are used to create a controlled transvisceral incision via natural orifice access to enter the peritoneal cavity. Common incision-related complications such as wound infections, incisional hernias, post-operative pain, aesthetic disdain, and adhesions could be minimized or eliminated by NOTES.

NOTES has evolved from over two centuries of technological innovations and continued growth in the field of surgical endoscopy. Innovative surgical endoscopists have slowly developed means to surpass the constraints of the gastrointestinal lumen by using a flexible endoscope. The future of surgical endoscopy may be the shared entity of NOTES, which further integrates endoscopy, gastroenterology, minimally invasive and general surgery. Although the promise of NOTES is electrifying to surgeons and endoscopists, several key issues need to be characterized prior to the incorporation of NOTES into routine practice. This manuscript reviews the status, contemporary body of literature, limitations, and the potential future implications accompanying the development of NOTES.

COMPLETE ENDOSCOPIC CLOSURE OF GASTROTOMY FOLLOWING NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC SURGERY (NOTES) USING THE NDO PLICATOR

McGee, Michael; Marks, Jeffrey; Onders, Raymond; Chak, Amitabh; Jin, Judy; Williams, Christina; Schomisch, Steve; Ponsky, Jeffrey

BACKGROUND: The NDO Plicator is a device developed for endoscopic treatment of gastroesophageal reflux disease (GERD) by approximating tissues together with a double pledgeted u-stitch. It was theorized that this device may facilitate transgastric NOTES, since closure of the transgastric defect remains a key component for advancement of this new technology.

METHODS: A standardized 12 mm gastrotomy was created endoscopically in 4 pigs with a combination of needle knife cautery and balloon dilation. As the endoscope was removed, a Savory soft-tipped wire was introduced into the stomach and the NDO Plicator was subsequently advanced over the wire. Each defect was identified and the device was positioned. If necessary, the Plicator tissue grasper was used to hold the superior aspect of the gastrotomy and bring the opposed borders of the defect within the jaws of the device. The device was fired three times, leaving three pledgeted suture bundles to close the gastric defect. Following closure, each animal was explored and the integrity of closure was assessed. Animals underwent in vivo contrast fluoroscopy and ex vivo burst pressure testing studies to assess leakage at the closure site.

RESULTS: The first animal was used to test feasibility, refine techniques, and develop a standard procedure. Of the next three animals studied, all showed complete sealing of the gastrotomy site without evidence of contrast extravasation on multi-planar fluoroscopic imaging. Each stomach was excised, submerged under water, and subjected to a pressurized air leak test. No leaks were noted until pressures exceeded 55 mmHg.

CONCLUSION: This study supports the use of the NDO Plicator for closure of standardized gastric defects in a porcine model. In addition to closing NOTES gastrotomies, the NDO Plicator may be a particularly useful tool in obtaining complete closure of gastric perforations, anastomotic leaks, and performing stomal reduction following gastric bypass procedures. The mechanical properties of a closure are not the only factor in determining if a leak will develop. Tissue opposition, ischemia, and tension are important factors that are not easily or reliably measured. The physiologic relevance of gastric bursting pressure is not known; therefore corollary studies with longer term evaluation in animals are necessary prior to proceeding to clinical trials.

INFECTIOUS IMPLICATIONS IN THE PORCINE MODEL OF NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC SURGERY (NOTES) WITH PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) TUBE CLOSURE: A QUANTITATIVE BACTERIOLOGIC STUDY

Michael F. McGee, MD; Jeffrey M. Marks, MD, Raymond P. Onders, MD; Amitabh Chak, MD; Michael J. Rosen, MD; Christina P. Williams, MD; Judy Jin, MD; Steve J. Schomisch, MD; Jeffrey L. Ponsky, MD

BACKGROUND: Obtaining reliable closure of trans-visceral defects is an important barrier currently limiting NOTES. PEG tubes have been proposed as means of managing a NOTES gastrotomy while providing chronic enteral access. NOTES PEG closure has not been studied in survival animals, nor have the microbiological implications of NOTES been characterized.

METHODS: 19 pigs received gastric lavage with saline, chloramphenicol or no lavage and then underwent transgastric NOTES peritoneoscopy. Quantitative cultures were obtained endoscopically at discrete points during each surgery. A sterile foreign body (silicone coated wire) was placed percutaneously under NOTES guidance into the peritoneal cavity and left in place. The gastrotomy was closed with a standard 20-French PEG tube. Animals were followed for 14 days and then underwent sterile laparotomy and sacrifice. Completion cultures for both wire and peritoneal cavity were obtained.

RESULTS: 19 animals successfully underwent NOTES and 18 (94.7%) survived the entire post-operative period without observable sequelae. 1 animal died on post-operative day #2 after the PEG tube dislodged. At 14 days, 5 animals (27.8%) demonstrated intra-abdominal abscesses, 8 (44.4%) had positive peritoneal wash cultures, and 9 (50%) foreign bodies were contaminated on culture. 11 animals (61%) had either abscess, positive peritoneal, or positive wire culture at the end of the study. Infectious complications were not altered by type of gastric lavage or peritoneal bacterial inoculum at introduced at time of surgery. Pre-procedural lavage was not effective in completely evacuating gastric succus, as 8 of 18 animals (44.4%) intra-operative NOTES peritoneal fluid cultures grew greater than 10^3 CFU/ml of bacteria.

CONCLUSION: In the pig, PEG closure of a NOTES gastrotomy is associated with subclinical intra-abdominal abscess formation, and can result in death when the tube is dislodged during the early post-operative period. Pre-procedural gastric lavage does not alter the intra-abdominal bacterial burden introduced at time of surgery or subsequent infectious outcomes in the porcine model. Infectious complications may represent failure of gastrotomy management, intra-operative seeding and deposition of succus during peritoneoscopy, or conditions unique to the pig such as inability to evacuate bezoars, dependent positioning of the PEG, and quadrupedism. These concerning findings necessitate additional studies to determine if porcine models are appropriate and applicable to human subjects in the NOTES setting.

NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC SURGERY (NOTES)

Jeffrey Marks MD., Michael F. McGee MD., Michael J. Rosen MD., Raymond Onders MD., Amitabh Chak MD., Jeffrey Ponsky MD

INTRODUCTION: Natural Orifice Transluminal Endoscopic Surgery (NOTES) involves novel techniques to access the peritoneal cavity without creating abdominal scars. This study evaluates the separate components of NOTES as well as the potential applications of this new modality.

METHODS: In porcine models, NOTES was performed via 3 distinct transgastric access techniques. Gastrostomy sites were inspected at laparotomy for size of defect created and surrounding tissue injury. To test degree of intraabdominal insufflation, pneumoperitoneum was measured via a pressure insufflator through a percutaneous transabdominal catheter, as well as catheters at the tip of the scope and in the biopsy channel. The endoscope was used to explore all quadrants of the abdominal cavity and to perform intraabdominal therapies. A standard Pull PEG tube was withdrawn back through the gastrostomy, leaving the internal mushroom bumper in the gastric lumen. The animals were sacrificed at two hours, or in survival studies, at two weeks.

RESULTS: Needle knife cautery and subsequent balloon dilation provided the most reliable and reproducible access technique. No thermal injuries to surrounding structures occurred. Pressure correlation curves revealed that scope tip and biopsy channel pressures were strongly correlative with true intra-abdominal pressures. Complete abdominal exploration was possible in all cases. Endoscopic guided biopsies, adhesiolysis, diaphragm visualization, small bowel evaluation, and cholecystectomy were successfully performed. All animals showed complete sealing of the gastrostomy site in the survival study. There was also no evidence of extravasation in any of the acute study animals.

CONCLUSION: To better assess this new modality, we have studied the separate components of NOTES. Future applications of this technology may include identification of unrecognized sources of abdominal sepsis, diaphragm stimulation, or organ removal. These initial encouraging results warrant eventual prospective human trials to assess safety and efficacy of this novel technique.

PEG “RESCUE”: A PRACTICAL NOTES TECHNIQUE

Jeffrey M Marks, MD; Jeffrey L Ponsky, MD; Jonathan P Pearl, MD; Michael F McGee, MD

Dislodged PEG tubes occur commonly and may require urgent surgical intervention in a susceptible patient population. Natural orifice transluminal endoscopic surgery (NOTES) may facilitate “PEG Rescue” and avoid the morbidity associated with contemporary surgical techniques. We report a case of a dislodged PEG tube in the early post-operative period with evidence of incomplete gastrocutaneous tract formation and intra-abdominal leakage. Bedside transgastric NOTES exploration facilitated peritoneoscopy, evacuation of intra-abdominal fluid, and re-establishment of the PEG tube through the original gastrotomy tract. Tube feeds were resumed and post-operative contrast fluoroscopy demonstrated no intra-abdominal leakage from the replaced PEG tube. No post-operative complications related to the NOTES procedure were noted at 30 days of follow-up. PEG “Rescue” represents a unique, practical, and empowering application of the burgeoning experience of NOTES.

SYSTEMIC INFLAMMATION AND PHYSIOLOGIC BURDEN OF TRANSGASTRIC NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC SURGERY (NOTES) PERITONEOSCOPY: A CONTROLLED, PROSPECTIVE COMPARISON BETWEEN NOTES AND LAPAROSCOPY

Michael F. McGee, Steve J. Schomisch, Jeffrey M. Marks, Conor P. Delaney, Judy Jin, Christina Williams, Amitabh Chak, Jamie Andrews, Jeffrey Ponsky

BACKGROUND: Although NOTES affords incisionless access to the abdomen and may represent the ultimate minimally invasive approach to surgery, contamination of the peritoneal cavity by enteric bacteria may cause more physiologic stress than initially thought. Measurement of Interleukin-1 (IL-1), Interleukin-6 (IL-6) and Tumor Necrosis Factor-Alpha (TNF-) is a validated method to quantify surgical stress in human and animal models. A prospective, controlled trial was designed to compare the physiologic stress induced by NOTES and laparoscopy.

METHODS: Ten anesthetized 40 kg female swine underwent transgastric NOTES peritoneoscopy (n=6) or diagnostic laparoscopy (DL, n=4). Four control animals underwent anesthesia alone. Plasma levels of IL-1, IL-6 and TNF- were determined pre-operatively, at the completion of surgery, and at 1 hour, 2 days, 7 days and 14 days post-operatively. Animals underwent sacrifice and laparotomy on post-operative day 14. Additional swine (n=2) underwent nonsurvival procedures simulating gastric perforation with diffuse peritonitis to serve as positive controls for cytokine assays.

RESULTS: All survival animals thrived and gained weight post-operatively. Baseline cytokine levels were similar in all groups. Post-operative TNF-, IL-1, and IL-6 profiles demonstrated no significant differences between NOTES, DL, and negative control groups. Cytokine values for positive control animals were significantly higher than the remaining study groups for most time points. TNF- levels were lower in NOTES than DL animals at the completion of surgery (137.8 v. 147.2 pg/mL, p=0.85), and at one hour (111.3 v. 199.7 pg/mL, p=0.28), two days (40.1 v. 57.8 pg/mL, p=0.55), 7 days (34.7 v. 94.3 pg/mL, p=0.07), and 14 days (23.9 v. 69.2 pg/mL, p=0.10) post-operatively. 59% (46 of 78) of IL-1 levels and 68.1% (49 of 72) of IL-6 levels were undetectable at any time for NOTES, DL, and negative control animals.

CONCLUSION: Physiologic stress induced by transgastric NOTES peritoneoscopy is similar to that of DL or anesthesia alone in the chronic swine model. A non-significant, but consistent reduction in TNF-levels was noted in animals undergoing NOTES peritoneoscopy when compared to DL animals. Low levels of IL-1 and IL-6 in NOTES, DL, and negative control animals were undetectable by conventional ELISA methods at most time points.

OBJECTIVE ANALYSIS OF THE ACCURACY AND EFFICACY OF A NOVEL FASCIAL CLOSURE DEVICE

Williams, Christina P; Rosen, Michael J; Jin, Judy; McGee, Michael F; Schomisch, Steve J; BS, Ponsky, Jeffery MD

BACKGROUND: Abdominal fascial closure after midline laparotomy can be time consuming, inaccurate, and is a common time for needle-stick injuries. The SutureTek 360° Fascial Closure Device is designed to provide a secure fascial closure in a timely fashion while reducing the risk of needle-stick injury. To date the accuracy and efficacy of the fascial closure obtained with this device have never been objectively determined.

METHODS: 10 pigs averaging 18Kg were euthanized and underwent a midline laparotomy. Idealized suture locations were pre-marked through the fascia. The animals were then randomly assigned to either a traditional suture closure or the SutureTek device for fascial closure. Surgeons were instructed to place sutures through the idealized markers. Surgeons were then evaluated based on the time to close fascia and distance from the markers. Abdominal bursting pressures were obtained using a manometric balloon.

RESULTS: The SutureTek device resulted in a faster closure time when compared to traditional closure (5.9 ± 0.6 vs 7.7 ± 1.0 minutes: $p=0.012$) with a similar accuracy of placement from the idealized markers ($4.3\text{mm} \pm 2.1$ vs $4.7 \pm$: $p=0.21$). Bursting pressures were similar between the two groups $470\text{mmHg} \pm 71$ for SutureTek versus 453 ± 94 for Traditional closure ($p=0.76$).

CONCLUSIONS: The SutureTek device resulted in a faster fascial closure with similar accuracy and strength when compared to traditional open techniques. The potential reduction in serious needle-stick injuries warrants prospective trials.

RESULTS OF DIAPHRAGM PACING IN AMYOTROPHIC LATERAL SCLEROSIS (ALS): DECREASING THE DECLINE IN RESPIRATORY FAILURE AND INCREASING DIAPHRAGM MOVEMENT

RP Onders, AR Ignagni, B Katirji, R Schilz, MJ Elmo

BACKGROUND: Respiratory insufficiency continues to be the major cause of mortality in patients with ALS. Mechanical ventilation with attendant limitations is the only current therapeutic option for patients developing respiratory compromise. Therapeutic electrical stimulation has been shown to maintain the strength of other peripheral muscles in ALS by maintaining physiologic activity, contractile properties and calcium levels. Motor units can be compensated for by collateral axon sprouting and the rate of sprouting increases with electrical stimulation. We postulate that ongoing therapeutic diaphragm stimulation using the laparoscopic diaphragm pacing system (DPS) is a low-risk outpatient system to stimulate and condition the diaphragm which may delay respiratory failure in patients with ALS and declining respiratory function.

OBJECTIVE: To evaluate in a Phase I trial that the DPS system can be safely implanted and used for conditioning the diaphragm in ALS patients. Secondary objectives are to show that life threatening respiratory muscle dysfunction may be delayed with diaphragm pacing.

METHODS: Patients diagnosed with ALS and forced vital capacity (FVC) above 50% predicted are eligible. Each patient had three lead-in assessments, at four week intervals, prior to implantation with pulmonary function tests, fluoroscopic evaluation of diaphragm movement, speech phonation times, ultrasound analysis of diaphragm thickness, phrenic nerve conduction tests and quality of life tests. Patients underwent laparoscopic mapping of their diaphragm to locate the phrenic nerve motor points and two electrodes were implanted in each hemidiaphragm. Two weeks after surgery, stimulus/output characteristics of each electrode were determined. The patients will then condition the diaphragm with five 30 minute sessions of therapeutic electrical stimulation per day. Patients were similarly assessed post-operatively.

RESULTS: Eight patients have been safely implanted and begun on diaphragm conditioning with the DPS system with no adverse events. There have been no deaths or need for tracheostomy. In all patients, more fluoroscopically observed diaphragm excursion occurs with diaphragm stimulation than under maximal voluntary effort. The first 4 patients (average FVC at implantation was 49%) have an average 12 month follow-up. Their monthly decline in FVC went from 4.1% pre-implant to 1.4% post implant. Patient 3 utilizes DPS continuously to augment respiration and has no diaphragm movement without DPS. Phonation time has improved and muscle thickness (mass) has increased with DPS. Except patient 3, there has been no change in the respiratory sub-score of the ALSFRS_r, although overall score has declined. There has been no decline in the SF-36 emotional domain quality of life scores although the SF-36 physical function has declined.

CONCLUSION: The diaphragm pacing system can be safely implanted and utilized in patients with ALS. There has been a documented decrease in the decline of respiratory failure which leads to an increased survival. The ability to cause more diaphragm movement with DPS is a surprising and beneficial finding. This may be best explained by intact phrenic nerve motor neurons that are no longer controlled by the medullary respiratory center, cerebral cortex, or central or peripheral chemoreceptors; but can be stimulated with DPS. DPS may also have a trophic effect on increasing the survival of these motor neurons. DPS also converts the remaining motor units to usable slow twitch oxidative units. These additional findings of DPS may lead to improved nighttime ventilation, decreased posterior lung lobe atelectasis and subsequent pneumonia

SAFE COMBINED PLACEMENT OF THE LAPAROSCOPIC DIAPHRAGM PACING STIMULATION SYSTEMS(DPS) AND PERCUTANEOUS ENDOSCOPIC GASTROTOMY(PEG) TUBES: RESULTS OF A PHASE ONE STUDY IN AMYOTROPHIC LATERAL SCLEROSIS(ALS)

Elmo RN, Bashar Katirji MD, Robert Schiltz DO, Anthony R Ignangi MS

BACKGROUND: ALS (Lou Gehrig's Disease) is a progressive neurodegenerative disease affecting 6,000 patients annually and respiratory failure is the usual cause of death. The laparoscopic DPS system has been shown to be 96% effective in replacing mechanical ventilation in spinal cord injured patients. The DPS system is being evaluated in ALS patients to decrease the decline in forced vital capacity (FVC) and delay the need for ventilators. ALS patients become malnourished because of progressive bulbar symptoms leading to a need for enteral access. The goal of this study is to assess the surgical outcomes of patients undergoing combined laparoscopic DPS placement and PEG tubes.

METHODS: Patients who met FDA and IRB approved criteria for the DPS system and also required a feeding tube were evaluated. Patients underwent laparoscopic mapping of their diaphragm to locate the phrenic nerve motor points with two electrodes implanted in each hemidiaphragm. The electrodes are a Teflon coated double helix of fourteen stainless steel strands that allow tissue ingrowth. The electrodes leave the abdominal cavity in the epigastric area and are tunneled to a percutaneous exit site on their right chest. Patients then underwent PEG tube placement.

RESULTS: Eleven ALS patients underwent DPS placement with an average FVC of 57% predicted at time of surgery. One patient had a PEG prior to DPS and this was excluded from the field for DPS placement. One patient had a PEG placed after the DPS with no compromise of the abdominal wires. 5 patients underwent combined DPS and PEG placement. There were no operative adverse events with the combined placement and with an average follow-up of 8.5 months no patients developed any wire infections. In post-implant data after conditioning the diaphragm with the DPS, patients show an average rate of decline in FVC of 1% per month from the pre-implantation decline of 3.1% a month, which extrapolates to an additional 20 months of ventilator free survival for these patients.

CONCLUSION: ALS patients are at a surgical risk because of their declining respiratory function with reported morbidity from PEG alone. This study confirms that these patients can undergo combined placement of the DPS system during a clean-contaminated PEG decreasing the possible need for two surgical procedures. The lack of infection also opens the possibility that the DPS system could be implanted with NOTES techniques at the same time as a PEG.

DIAPHRAGM PACER-CARDIAC PACEMAKER INTERACTION: CONCEPTUAL, BENCH EXPERIMENTAL AND HUMAN STUDIES CONFIRMING SAFETY IN VENTILATOR DEPENDENT SPINAL CORD INJURED PATIENTS

R.P. Onders, M.J. Elmo, H. Aiyar, A. R. Ignagni, B.S. Stambler, J.A. Mackall, R. Schilz, B. Katirji and J. T. Mortimer

INTRODUCTION: The diaphragm pacing stimulation (DPS) system is an excellent alternative for ventilator dependant spinal cord injured patients. Patients with high level spinal cord injury are also predisposed to bradycardia and atrioventricular block which at times necessitates placement of a cardiac pacemaker. With spinal cord injured population changing to an older group there is also an increased likelihood of pre-existing cardiac pacemakers. Presently the FDA does not allow two separate pacing devices. The objectives of this study were: 1) determine theoretical values for cardiac capture resulting from the diaphragm pacer stimulus 2) using an in vitro set-up, test the interaction of the diaphragm pacer with a cardiac pacemaker, and 3) confirm safety in a human trial under IRB and FDA protocols.

METHODS: Based on the characteristics (settings) of the cardiac pacemaker and the DPS, conditions where an interaction would occur were identified. The bench approach involved using a saline bath to mimic the "implanted" situation. The interaction between the cardiac pacemaker's ventricular lead and the stimulating lead of the diaphragm pacemaker was tested at distances of 1 mm to > 8cm and sensitivity level of the pacemaker was varied between .62 mV and 2.5 mV. In the human study, we implanted the DPS system and interrogated the pacemaker during DPS use.

RESULTS: If the stimulus from the DPS is detected by cardiac pacemaker, the cardiac pacemaker will respond by introducing paced events (ventricular contractions). These events will depend on the duration of the DPS and "added" to the heart's intrinsic cardiac rhythm. This can lead to an increase cardiac rate of 12 to 36 beats per minute. The saline bath showed that at distances greater than 3 cm no interaction between the two devices was observed. Three patients (out of a total of 38 implanted DPS systems) had cardiac pacemakers and were implanted with the DPS and no device to device interaction was detected.

CONCLUSIONS: Ventilator dependant spinal cord injured patients with cardiac pacemakers can safely undergo implantation of the DPS system to obtain freedom from mechanical positive pressure ventilation. This will allow the DPS system to be utilized by patients with cardiac pacemakers in our other trials involving patients with Congenital Central Hypoventilation Syndrome (Ondine's Curse) and Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's disease).

PATIENT AND CAREGIVERS PERCEPTIONS OF THE DIAPHRAGM PACING STIMULATION (DPS) SYSTEM

Mary Jo Elmo ACNP; Laszlo Nagy; Raymond P. Onders M.D.; Sarah Bell; Anthony R. Ignagni

INTRODUCTION: Spinal cord injury is an overwhelming, devastating experience and the addition of a ventilator adds to the complexity of daily care. Motor point stimulation of the diaphragm is a low-risk, cost-effective outpatient system for ventilatory support. This study analyzes how patients and caregivers perceive the effects of DPS on activities.

DESIGN: Prospective FDA trial of the DPS System for electrical activation of the diaphragm for ventilatory assist in tetraplegics.

PARTICIPANTS/METHODS: After successful implantation and conditioning of the diaphragm to provide at least 4 continuous hours of DPS ventilation, a survey was sent to patients and caregivers to assess DPS effect on their activities. This survey was repeated one year later and the answers analyzed.

RESULTS: The response rate was 92% (22/24). All patients are presently living at home with the primary caregiver being the mother in 14 patients. 64% of patients report fewer secretions with 68% of caregivers reporting less suctioning. 82% of patients report "more normal breathing". 77% of caregivers state caring for the paced patient is less work than the mechanical ventilator. 91% of caregivers say the pacer is easy to use. Other comments included: DPS as life saving during hurricanes and power outages (3); the silence of pacing enabled sleeping well for the first time since their injury (2); attending classes or church easier; traveling for the first time ever since injury (1); transfer from ventilator ward to assisted living or home(2) and air travel now possible(4). 100% of patients describe an increase in mobility. 95% of patients report more freedom and feeling of independence. 100% of patients would recommend it to other tetraplegics.

CONCLUSIONS: DPS stimulation provides natural negative pressure ventilation utilizing the patient's own diaphragm but the most important benefit is allowing patients greater integration into society without the stigma of the ventilator.

UTILITY OF THE DIAPHRAGM PACING STIMULATION (DPS) SYSTEM IN AMYOTROPHIC LATERAL SCLEROSIS (ALS): RESULTS OF PHASE 1 TRIAL

RP Onders, R Schilz, B Katirji, AR Ignagni, MJ Elmo

BACKGROUND: Respiratory insufficiency is the major cause of mortality in patients with ALS. The motor point diaphragm pacing stimulation (DPS) system has become a standardized minimally invasive laparoscopic technique that can provide ventilation in spinal cord injured patients. We postulate that therapeutic DPS will delay respiratory failure in ALS patient.

OBJECTIVE: To review the results of the completed Phase I trial of DPS in ALS patients.

METHODS: ALS patients with forced vital capacity (FVC) above 50% predicted were eligible. Each patient had three extensive lead-in assessments that were continued post implantation of the DPS system. Specific attention was given to respiratory and diaphragm evaluation including pulmonary function tests, fluoroscopic evaluation of diaphragm movement and ultrasound analysis of diaphragm thickness.

RESULTS: Fifteen patients have been safely implanted and begun on diaphragm conditioning with the DPS system with no adverse events. Feeding tubes were safely simultaneously placed. In all patients, more fluoroscopically observed diaphragm excursion occurs with diaphragm stimulation than under maximal voluntary effort. DPS significantly increases muscle thickness when assessed with ultrasound (p-value 0.02). After conditioning the diaphragm with the DPS, preliminary results show an average rate of decline in FVC of 1.3% per month from the pre-implantation decline of 3.1% a month, which extrapolates to an additional 15 to 19 months of ventilator free survival. Additional findings include: DPS can convert fast twitch glycolytic (IIb) to functional slow twitch oxidative muscle (I) fibers; DPS improves posterior lobe lung ventilation; DPS increases lung compliance leading to decreased work of breathing; and patients have started utilizing DPS to improve nighttime ventilation.

CONCLUSIONS: The DPS system can be safely implanted and utilized in ALS patients, with a documented decrease in the decline of respiratory failure leading to increased survival. A multi-center pivotal trial is now enrolling patients and collecting data.

DIAPHRAGM PACING STIMULATION (DPS) SYSTEM: PATIENT VARIABLES AFFECTING INITIAL DIAPHRAGM CONDITION AND SUBSEQUENT FUNCTION WITH ELECTRICAL STIMULATION

Raymond P. Onders M.D.; Mary Jo Elmo ACNP; Anthony R. Ignagni

INTRODUCTION: Minimally invasive motor point stimulation of the diaphragm has demonstrated 100% success rate in providing adequate tidal volumes for ventilation of tetraplegics with intact phrenic nerves. This study analyzes patient variables affecting the initial function of the deconditioned diaphragm and the length of time needed to reach 4 continuous hours of DPS ventilation.

DESIGN: Prospective FDA trial of the DPS System for electrical activation of the diaphragm for ventilatory assist in tetraplegics.

PARTICIPANTS/METHODS: Patients underwent laparoscopic mapping of the diaphragm to locate phrenic nerve motor points for electrode implantation. Two weeks after surgery stimulation of each electrode was set to provide tidal volume for ventilation and patients underwent conditioning of the diaphragm. Pre-operative variables were assessed in relation to when patients met the criteria of 5-7cc/Kg tidal volume for 4 or more continuous hours of ventilation with the DPS system.

RESULTS: A total of 28 patients were implanted, there was a failure to pace in the second patient due to a false positive phrenic nerve study. The amount of time and daily episodes of conditioning the diaphragm affect speed to DPS ventilation. Age and time from injury directly affects conditioning time to achieve 4 continuous hours with DPS from less than 1 week for 18 to 20 year olds on a ventilator for less than one year to 14 weeks for 40 to 50 year olds on ventilators for great than 5 years. Both patients over 65 years took 21 weeks. Two patients requiring surgical correction of scoliosis prior to implantation have required prolonged conditioning to achieve adequate tidal volumes.

CONCLUSIONS: DPS has been demonstrated to work in all innervated diaphragms. Earlier implantation facilitates weaning from the ventilator and should decrease the complications from positive pressure ventilation. Geriatric tetraplegics and patients with significant scoliosis require increased diaphragm conditioning.

LAPAROSCOPIC MOTOR POINT DIAPHRAGM PACING STIMULATION (DPS) SYSTEM: CLINICAL RESULTS FOR TETRAPLEGIA

Raymond Onders MD, Mary Jo Elmo RN, Anthony Ignagni

OBJECTIVE: Ventilator dependent tetraplegics face not only the stigma of being on a ventilator but also the associated significant risks of pneumonia and barotrauma. This study outlines the experience with the Diaphragm Pacing Stimulation (DPS) system for tetraplegics with ramifications for anyone on positive pressure ventilation.

METHOD: In a prospective trial, spinal cord injured (SCI) patients underwent outpatient laparoscopic diaphragm motor point mapping and subsequent electrode implantations. Stimulus/output characteristics of each electrode were determined and diaphragm conditioning was initiated. The patients were weaned from their ventilators at home.

RESULTS: A total of 30 patients have been successfully implanted. DPS provided tidal volumes to free 97% of tetraplegics from ventilators. The results also showed DPS leads to an increase in diaphragm muscle thickness and strength, conversion of fast twitch glycolytic (IIb) to the functional slow twitch oxidative muscle fibers(I), reduction in airway pressure, return to negative chest pressure, 64% decrease in secretions, improved posterior lobe ventilation and increased lung compliance leading to decreased work of breathing.

CONCLUSIONS: The DPS system is a low risk, low cost system that should replace the ventilator for SCI patients. These benefits provided the basis for ongoing research to decrease ventilator times for any patients.

HOME-BASED VENTILATOR WEANING IN TETRAPLEGIA: RESULTS OF THE DIAPHRAGM PACING STIMULATION SYSTEM

Raymond P. Onders M.D.; Mary Jo Elmo ACNP; Anthony R. Ignagni

OBJECTIVE: For high spinal cord injured patients with chronic respiratory insufficiency, electrically induced diaphragm pacing is an alternative to long-term positive pressure ventilation. The goal of this study was to demonstrate the effectiveness of a home-based ventilator weaning program after outpatient laparoscopic implantation of the DPS system.

DESIGN: Prospective FDA trial of the NeuRx RA/4 DPS System for electrical activation of the diaphragm for ventilatory assist in spinal cord injured patients with intact phrenic nerves.

PARTICIPANTS/METHODS: Patients underwent laparoscopic mapping of their diaphragm to locate the phrenic nerve motor points for electrode implantation. Two weeks after surgery, stimulus/output characteristics of each electrode were determined for optimal settings. Caregivers were trained to use the DPS system and a Wright Spirometer. Progressively lengthening conditioning (weaning) sessions would involve turning off the ventilator and turning on the DPS system with documentation of time used, oxygen saturation, tidal volumes and a modified Borg scale of respiratory difficulty. Weekly electronic communication with investigators allowed for input and changes of stimulation parameters by exchange of devices.

RESULTS: Eighteen patients have been implanted with the DPS system. All procedures were performed on an outpatient basis with no intra-operative complications. One patient had a false positive preoperative phrenic nerve conduction study and therefore was never able to pace. The remaining 17 patients (94%) achieved greater than their predicted tidal volume during stimulation with fifteen patients undergoing weaning from the ventilator at home. Ten patients use the device full time, 6 use it 12-24 hours a day resulting in over 25 years of cumulative active implantation time. The home-based weaning protocol allows patients to maintain caregiver support, work, and significantly lower expenses.

CONCLUSIONS: The results show the laparoscopic DPS system to be a low-risk, cost-effective outpatient system for ventilatory support with home-based weaning from the ventilator.

DIAPHRAGM PACING STIMULATION (DPS) SYSTEM IN TETRAPLEGICS WHO WERE INJURED AS A CHILD

Raymond P. Onders M.D.; Mary Jo Elmo ACNP; Anthony R. Ignagni

INTRODUCTION: Tetraplegic children with chronic respiratory insufficiency are a difficult population because of the risks and stigma associated with mechanical ventilators. The DPS system has proven to be an excellent minimally invasive alternative to mechanical ventilation in adult tetraplegics.

METHODS: Review of patients in a prospective FDA trial of DPS System for electrical activation of the diaphragm for ventilatory assist who were injured at age 18 or earlier. The procedure involves laparoscopic mapping of the diaphragm to locate the phrenic nerve motor points for electrode implantation. Two weeks after surgery, stimulus/output characteristics of each electrode are determined for optimal settings to obtain an adequate tidal volume for ventilation. Patients then undergo a home-based weaning protocol from the ventilator.

RESULTS: Of the total of 28 patients implanted with the DPS System, ten patients sustained cervical SCI as children. The age at the time of injury ranged averaged 13 years (ranged 1.5 to 17). Age at the time of implantation ranged from 18 years to 34 years. The length of time from injury to implantation averaged 9.7 years (range 0.8 to 19). All patients tolerated the outpatient implantation procedure. Four patients have achieved full time (24/7) pacing, three patients pace part time and three patients are still actively conditioning their diaphragms. Two patients required surgical correction of their scoliosis prior to implantation. All patients prefer breathing with the DPS and would recommend it to others, 4 patients specifically identified attending college or church without a ventilator eases their integration into society.

CONCLUSIONS: The results show the laparoscopic DPS system to be a low-risk, cost-effective outpatient system for ventilatory support with home-based weaning from the ventilator. The data to date justify the expansion of this study to include patients under the age of 18 and to implant earlier to the time of injury.

THE HURRICANES OF 2005 AND VENTILATORS: THE BENEFITS OF DIAPHRAGM PACING STIMULATION (DPS) SYSTEM

Raymond P. Onders M.D.; Mary Jo Elmo ACNP; Anthony R. Ignagni

OBJECTIVE: During hurricanes the wide spread loss of electricity can cause significant problems for high spinal cord injured patients dependent on ventilators. This study demonstrates the difficulty these patients have during natural disasters associated with power loss and the benefits of the DPS system.

DESIGN: Retrospective analysis of patients who live in hurricane ravaged areas involved or evaluated in an FDA trial of the DPS System for electrical activation of the diaphragm for ventilatory assist.

PARTICIPANTS/METHODS: Patients in effected areas were interviewed concerning their responses to hurricanes Dennis(7/05), Katrina(8/05) and Rita(9/05). Ventilator batteries last from only 1-8 hours before requiring electricity for recharging while the DPS system uses a standard disposable external battery that lasts 500 hours and patients have a stock of batteries.

RESULTS: In summary, all patients experienced loss of electricity during the hurricanes. The problems of being on a ventilator during hurricanes included: risks and fuel shortage with external generators to power ventilators, evacuation centers not equipped for quadriplegics (a special need shelter refused entry of one patient as being too "sick"), hospitals not willing to accept patients just for ventilator power, and traveling with ventilator to areas out of the threat of loss of power is difficult, expensive and time consuming. In three patients with the DPS system the benefits included: loss of electricity alone no longer a concern, evacuation easier(less packing) and transportation simplified; less need for space or additional personnel. One patient with the DPS system who lost her home to Rita states the lack of noise and space from a ventilator simplifies living in a crowded temporary facility.

CONCLUSIONS: Hurricanes are devastating and a significant cause of anxiety in ventilator dependent quadriplegics. The DPS system improves the quality of life during these events by decreasing anxiety, easing evacuation, and simplifying temporary housing.

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DIAPHRAGM PACING STIMULATION (DPS) SYSTEM IN AMYOTROPHIC LATERAL SCLEROSIS (ALS): RESULTS OF PHASE ONE TRIAL AND PLANS FOR MULTI-CENTER PIVOTAL TRIAL

Raymond Onders, MD

Respiratory insufficiency continues to be the major cause of mortality in patients with ALS. Mechanical ventilation with attendant limitations is the only current therapeutic option for patients developing respiratory compromise. Therapeutic electrical stimulation has been shown to maintain the strength of other peripheral muscles in ALS by maintaining physiologic activity, contractile properties and calcium levels. Motor units can be compensated for by collateral axon sprouting and the rate of sprouting increases with electrical stimulation. Therapeutic diaphragm stimulation using the laparoscopic diaphragm pacing system (DPS) is a low-risk outpatient system to stimulate and condition the diaphragm which delays respiratory failure in patients with ALS.

Twelve patients have been safely implanted and begun on diaphragm conditioning with the DPS system with no adverse events. Five of the patients underwent simultaneous feeding tube placement. Patient's lung compliance increases with DPS pacing by decreasing posterior lobe atelectasis and therefore can decrease the work of breathing. Their monthly decline in FVC went from 2.8% pre-implant to 1.0% post implant. For a patient implanted at 60% predicted FVC this would lead to a 20 month increase in time until requiring continuous positive pressure ventilation. In extensive evaluation no adverse effects of DPS pacing was identified. In all patients, more fluoroscopically observed diaphragm excursion occurs with DPS diaphragm stimulation than under maximal voluntary effort. The ability to cause more diaphragm movement with DPS is a surprising and beneficial finding. This may be best explained by intact phrenic nerve motor neurons that are no longer controlled by the medullary respiratory center, cerebral cortex, or central or peripheral chemoreceptors; but can be stimulated with DPS. DPS may also have a trophic effect on increasing the survival of these motor neurons. DPS also converts the remaining motor units to usable slow twitch oxidative units. These additional findings of DPS may lead to improved nighttime ventilation, decreased posterior lung lobe atelectasis and subsequent pneumonia

A multi-center trial is now underway to confirm the preliminary results and identify patient variables that may optimize use of DPS. Patients diagnosed with ALS and forced vital capacity (FVC) above 50% predicted are eligible. Each patient has three lead-in assessments, prior to implantation with pulmonary function tests, fluoroscopic evaluation of diaphragm movement, and quality of life tests. Patients undergo laparoscopic mapping of their diaphragm to locate the phrenic nerve motor points and two electrodes are implanted in each hemidiaphragm. Two weeks after surgery, stimulus/output characteristics of each electrode are determined. The patients will then condition the diaphragm with five 30 minute sessions of therapeutic electrical stimulation per day. Patients are similarly assessed post-operatively at two month intervals for 8 months.

EXPERT BENCHMARK FOR THE GI MENTOR II

R Phitayakorn MD, JM Marks MD, HR Reynolds MD, and CP Delaney MCh, PhD, FRCSI

BACKGROUND: There is increasing interest in the use of virtual-reality simulators in general surgery residency training. Many simulators lack a benchmark against which trainees can measure competence and skill.

METHODS: Surgeons who had performed over 1000 colonoscopies were evaluated on Module 1, Case 5 of the GI Mentor I or II™ virtual reality endoscopy simulator (Simbionix, Cleveland). Participants were given five minutes to familiarize themselves with the simulator, and then performed the study case with standardized instructions. Metrics were recorded by the previously calibrated simulator.

RESULTS: Twenty-three surgeons (21 male, 2 female) participated. Mean height was 69.6 ± 2.6 inches, mean age 51 ± 9 years, median surgical glove size 7.5, and surgeons had 18.4 ± 10.2 years of practice, and did 8 ± 6 colonoscopies weekly. Ten participants had advanced training in endoscopy, laparoscopy, or colorectal surgery; eight had used the simulator before, of whom six had used it once. Mean time to complete the study case was 13.6 ± 5.3 minutes and time to reach the cecum was 6.5 ± 4.3 minutes. Participants examined $92.3 \pm 3.6\%$ of the simulated colonic mucosa with a clear view of the lumen $89.5 \pm 4.2\%$ of the time. Total time the colon was looped was 22 ± 35 seconds (range=0-133). The overall efficiency of screening was $70.33 \pm 23.45\%$ (range=20 to 94%). Participants tended to mistake normal simulated colonic structures as pathology.

CONCLUSION: Performance on a virtual reality endoscopic simulator has a wide amount of variability even among a group of experienced endoscopists. Expert benchmark tests should be performed on simulators that will be used for resident assessment prior to any attempts at certification of competence.

ABSENCE OF INTESTINAL GLUCONEOGENESIS IN RATS AND ZBD DOGS

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We investigated the potential for intestinal gluconeogenesis in 48 hr-fasted rats and in 48 hr-fasted hepatectomized dogs. The arterio-venous balances of concentration and labeling of [6,6-2H₂]glucose were determined across the intestine (in rats and dogs) and across the muscle and kidney (in dogs). The gas chromatography-mass spectrometry data were integrated using a recently developed method for integrating peaks that amplifies the apparent labeling while improving the precision of the measurements. In 48 hr-fasted rats receiving a constant infusion of [6,6-2H₂]glucose, we could not detect any difference in glucose enrichment across the intestine (n = 7 rats, with 4 pairs of samples per rat). To test whether deep hypoglycemia would induce intestinal glucose production, we did a series of experiments in 5 dogs acutely hepatectomized after 48 hr of fasting. When the liver was clamped, we injected a 1.1 mmol bolus of [6,6-2H₂]glucose. Over the next 2 hr, arterial glucose concentration decreased linearly from ~ 5 mM to ~ 0.5 mM. In parallel, arterial glucose enrichment decreased linearly from ~ 1.25% to ~ 0.25%. This resulted from some glucose production in the kidney, demonstrated by a small detectable difference in glucose enrichment between arterial and renal vein plasma. However, this renal glucose production did not prevent very deep hypoglycemia. In addition, there was no detectable difference in glucose enrichment or concentration between arterial and portal vein plasma (n = 5 dogs, with a minimum of 8 pairs of samples per dog). We conclude that there is no detectable intestinal gluconeogenesis in dogs and rats in vivo.

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ABDOMINAL HERNIA REPAIR WITH BRIDGING ACELLULAR DERMAL MATRIX – AN EXPENSIVE HERNIA SAC

Jeffrey Blatnik BA, Judy Jin MD, Michael Rosen MD.

INTRODUCTION: The ability of biologic mesh to remodel into native fascia and prevents hernia recurrence in complicated repairs is appealing. However, little long term data exists evaluating these products in the setting of bridging fascial defects. These collagen based mesh products are costly and long term evaluation of hernia recurrence rates are necessary to justify their expense.

METHODS: We retrospectively reviewed our institutions experience with the use of Alloderm for bridging fascial defects in ventral hernia repair. The indication, defect characteristics, reconstructive techniques, complications, cost, and surgical outcomes were evaluated.

RESULTS: Eleven patients with Alloderm bridging a fascial defect were identified between January 2004 and December 2005. Indications for repair included resection of enterocutaneous fistula, infected mesh and/or ventral hernia repair. A mean of 175 cm² (8-456 cm²) of Alloderm were used, and secured to the fascial edges with 2 to 3 cm underlay, completed with skin coverage in each patient. The mean follow up was 22 months (15-33 mo). One patient died on POD 20. Eight out of ten (80%) patients had recurrences seven underwent further surgery for repair, one patient reported laxity, but refused repair. The total cost of Alloderm for these eleven patients were \$61,1926. The costs for the eight patients with recurrences were \$41,390, a mean cost of \$5,180 per patient.

CONCLUSION: While bridging fascial defects with Alloderm can be an appealing substitute in extremely complicated cases, our data demonstrates an exceedingly high recurrence rate. The long term outcome of bridging fascial defects with biologic prosthesis does not justify the expense of the product.

THE USE OF ACELLULAR DERMAL MATRIX (ALLODERM) FOR COMPLICATED VENTRAL HERNIA REPAIR: DOES TECHNIQUE AFFECT OUTCOMES?

Judy Jin MD, Michael Rosen MD, Jeffrey Blatnik BA, Michael McGee MD, Christina Williams MD, Jeffrey Marks MD, Jeffrey Ponsky MD

INTRODUCTION: The ideal technique for the use of Alloderm in complicated ventral hernia repair has not been defined. The expense of these products mandate careful evaluation to justify their widespread use. We compared two techniques of fascial bridging versus fascial reinforcement repair with regard to their long term recurrence rate using Alloderm.

METHODS: We retrospectively studied patients with abdominal defects repaired with Alloderm at our institution.

RESULTS: Thirty seven patients with abdominal wall repairs using Alloderm were identified between January 2004 and December 2005. Eleven patients underwent bridged fascial repair while 26 patients had reinforced fascial repair. No statistical significance exists between the two groups in terms of average age (57 vs 52 yo), BMI (35 vs 29), ASA score (2.9 vs 2.5) or the number of prior abdominal surgeries (3.4 vs 3.5). The average size of Alloderm utilized was 175 cm² for bridged and 89 cm² for reinforced repair ($p=0.005$). In patients with reinforced closure, primary repair was achieved with lateral component separation in 22/26 patients. The mean follow up was 21.4 months (15-36 mo). For the bridged group, one patient died on POD 20. Of the remaining ten patients, eight patients (80%) developed recurrences. Seven patients required reoperation while one patient refused repair. In the reinforced group, four patients were lost to follow up and 2 patients died. Four of the remaining 20 patients (20%) developed recurrences that required repair; that is significantly different from the bridged group ($p=0.009$).

CONCLUSION: This study demonstrates that the method in which Alloderm is utilized in abdominal wall reconstruction has a significant impact on recurrence rates. Based on our findings, Alloderm should be used only as a reinforcement after primary fascial reapproximation.

LAPAROSCOPIC COMPONENT SEPARATION IN THE SINGLE STAGE TREATMENT OF INFECTED ABDOMINAL WALL PROSTHETIC REMOVAL

M. J. Rosen, MD, J. Jin MD, M. F. McGee MD, C. Williams MD, J. Marks MD, J.L. Ponsky MD

BACKGROUND: The ideal surgical treatment for complicated ventral hernias remains elusive. Traditional component separation provides local advancement of native tissue for tension free closure without prosthetic materials. This technique requires an extensive subcutaneous dissection with division of perforating vessels predisposing to skin flap necrosis and complicated wound infections. Laparoscopic separation of components provides a minimally invasive alternative to open techniques while eliminating the potential space and subsequent complications of large skin flaps. We report our initial experience with a minimally invasive component separation with early postoperative outcomes.

METHODS: We retrospectively reviewed the medical records of all patients who underwent a minimally invasive component separation for abdominal wall reconstruction during the resection of an infected prosthetic. Pertinent details included baseline demographics, reason for contamination, operative technique and details, postoperative morbidity, mortality and recurrence rates.

RESULTS: Between August 2006 and January 2007, 7 patients were identified who underwent a laparoscopic component separation. There were 4 males and 3 females with a mean age of 54 years (34-84), ASA 3.2 (3-4), and BMI of 37 kg/m² (30-45). The reason for contamination included exposed nonhealing mesh (6) and contaminated fluid collection around mesh (1). Residual defect size following removal of all prosthetic was 338 cm² (187-450). Mean operative time was 185 min (155-220). Laparoscopic component separation enabled tension-free primary fascial reapproximation in all patients. Three postoperative complications occurred including superficial surgical site infection (1), respiratory failure (1), and hematoma (1). There was no mortality in this series. During an average follow up period of 4.5 months, no recurrences were identified.

CONCLUSIONS: This study shows that a minimally invasive component separation is feasible and can result in minimal postoperative wound morbidity in these complex patients. Long term follow up is necessary to evaluate the outcomes with respect to recurrence rates.

LAPAROSCOPIC VERSUS OPEN COMPONENT SEPARATION: A COMPARATIVE ANALYSIS IN A PORCINE MODEL

Michael J. Rosen, MD, Christina Williams, MD, Judy Jin, MD, Michael F. McGee, MD, Steve Schomisch, BS, Jeffrey Marks, MD, Jeffrey Ponsky MD

BACKGROUND: The ideal surgical treatment for complicated ventral hernias remains elusive. Traditional component separation provides local advancement of native tissue for tension free closure without prosthetic materials. This technique requires an extensive subcutaneous dissection with division of perforating vessels predisposing to skin flap necrosis and complicated wound infections. A minimally invasive component separation may decrease wound complication rates, however the adequacy of the myofascial advancement has not been studied.

METHODS: Five, 25 kg pigs underwent bilateral laparoscopic component separation. A 10 mm incision was made lateral to the rectus abdominus muscle. The external oblique fascia was incised, and a dissecting balloon was inflated between the internal and external oblique muscles. Two additional ports were placed in the intermuscular space. The external oblique was incised from the costal margin to the inguinal ligament. The maximal abdominal wall advancement was recorded. A formal open component separation was performed and maximal advancement 5cm superior and 5cm inferior to the umbilicus was recorded for comparison. Groups were compared using standard statistical analysis.

RESULTS: The laparoscopic component separation was completed successfully in all animals in a mean of 22 minutes per side. Laparoscopic component separation yielded 3.9cm (sd 1.1) of fascial advancement above the umbilicus, while 4.4cm (1.2) was obtained after open release ($p=0.24$). Below the umbilicus, laparoscopic release achieved 5.0cm (1.0) of advancement while 5.8cm (1.2) was gained after open release ($p=0.13$).

CONCLUSIONS: The minimally invasive component separation achieved an average of 86% of the myofascial advancement as compared to a formal open release. The laparoscopic approach does not require extensive subcutaneous dissection and might theoretically result in a decreased incidence or reduced complexity of postoperative wound infections or skin flap necrosis. Based on our preliminary data in this porcine model, further comparative studies of laparoscopic versus open component separation in complex ventral hernia repair is warranted to evaluate the postoperative morbidity and long term hernia recurrence rate.

A NOVEL LIGHT WEIGHT MACROPOROUS PTFE MESH (MotifMESH): IN VIVO EFFECT ON ADHESION FORMATION AND TISSUE INTEGRATION

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INTRODUCTION: Expanded PTFE mesh is widely utilized for the repair of ventral hernias based on the reduction of adhesion formation as compared to most other prosthetic materials. Unfortunately, this material has displayed poor tissue integration profiles and significant in situ shrinkage. We propose to optimize the tissue integration and mesh shrinkage of this material by condensing the PTFE and introducing a patterned macroporosity to the condensed film.

METHOD: An acute hernia was created in 10 rats by excising a fascial defect of 3 x 1 cm. The defect was repaired in an underlay fashion using either MotifMESH (a light weight macroporous condensed PTFE (cPTFE)) or GoreTex DualMesh (ePTFE) with an overlap of 0.5mm. At 5 weeks, we evaluated mesh shrinkage, tenacity of adhesion, and abdominal tissue integration force.

RESULT: Five rat hernia defects were repaired with DualMesh and five with MotifMESH. The mesh shrinkage was $72 \pm 8\%$ in the DualMesh group and $31 \pm 5\%$ in the MotifMESH group ($p=0.004$). Adhesion to DualMesh covered 50-80% of the surface area and included both omentum and small bowel while the adhesion to MotifMESH covered 10-40% and included mostly omentum. The tenacity of adhesion was 6.6 ± 1.6 N in the case of DualMesh and 7.3 ± 0.9 N for the MotifMESH ($p=0.69$). The strength of tissue integration at the fascia/mesh interface was 7.4 ± 2.6 N for the DualMesh and 25.0 ± 4.9 N for the MotifMESH ($p=0.02$).

CONCLUSION: The new cPTFE MotifMESH demonstrated superiority in terms of reduction in mesh shrinkage and improved tissue integration force without increased adhesion formation as compared to the expanded PTFE DualMesh by displaying comparatively different mesh surface characteristics.

LAPAROSCOPIC VENTRAL HERNIA REPAIR; PARIETEX COMPOSITE MESH VERSUS GORE-TEX DUAL MESH. A COMPARATIVE ANALYSIS

Michael J. Rosen MD

INTRODUCTION: The ideal mesh for laparoscopic ventral hernia repair has not been defined. Despite the mechanical advantages of polyester based mesh in reduced shrinkage and better tissue ingrowth when compared to Gore-tex Dual mesh, American surgeons have not adopted this mesh given concerns of increased infection rates. We reviewed our experience with Parietex Composite mesh and Gore-tex dual mesh at our institution.

METHODS: All patients undergoing laparoscopic ventral hernia repair at Case Medical Center by a single surgeon were enrolled in a prospectively collected database. Patient demographics, operative details, postoperative outcomes, and long term follow up were recorded.

RESULTS: From August 2005 to November 2006, 39 laparoscopic ventral hernia repairs were performed. Twenty patients had Gore-tex dual mesh and 19 patients had Parietex Composite mesh. The patients were similar based on demographic characteristics including age (60 v 58 yrs; $p=0.67$), ASA (2.6 v 2.7; $p=0.45$), recurrent hernias (25% v 36%), and number of prior repairs (0.32 v 0.63; $p=0.23$). The operative details were similar between the two groups with regards to operative time (187 v 160 min; $p=0.27$), defect size (153 v 95 cm²; $p=0.18$), number of trocars (4 v 4; $p=0.32$), and size of mesh (403 v 332cm²; $p=0.33$). No postoperative infectious complications occurred in either group. During postoperative follow up two postoperative seromas developed in the Gore-tex group requiring repeated drainage, and no postoperative complications occurred in the Parietex group. There have been no hernia recurrences in either group.

CONCLUSIONS: Based on our experience polyester based mesh appears to perform in a favorable manner when compared to Gore-tex Dual mesh. There was no increased risk of infectious complications and potentially given the increased tissue ingrowth of polyester mesh, no postoperative seromas required intervention. Given the inherent advantages of less shrinkage and better tissue ingrowth, coated polyester mesh might be the ideal mesh product for laparoscopic ventral hernia repair.

MECHANICAL AND BIOCOMPATIBILITY TESTING OF HERNIA REPAIR PROSTHETICS: A PLEA FOR STANDARDIZATION

Michael F. McGee MD, Judy Jin MD, Christina P. Williams MD, David T. Matteson BA, Michael J. Rosen MD

INTRODUCTION: Currently, no standardized mechanical and biocompatibility testing algorithm exists to allow comparative testing for the myriad of prosthetic materials available for hernia repair. A unified, evidence-based, standardized testing algorithm would allow thorough testing of contemporary mesh prosthetics enabling more consistent performance comparisons for future meshes.

METHODS: A systematic literature review was performed within the MEDLINE electronic database for all articles pertaining to mechanical testing and biocompatibility of hernia repair prosthetics. Mesh type, study endpoints, mechanical testing protocols, and histological methods were recorded from all appropriate articles. Mechanical and biocompatibility testing protocols were determined to be qualitative or quantitative and were deconstructed into descriptive steps. Testing methods were compared across all eligible studies. Mechanical testing techniques were compared to those published by the American Society for Testing and Material Standards (ASTM).

RESULTS: Over 30 articles were eligible for review spanning from 1952 to 2006. In studies sharing similar quantitative mechanical endpoints, no consensus exists for proper testing technique. Histological endpoints intended to serve as surrogates of biocompatibility are widely varied, and offer no standardization and little quantitative data. Often, non-validated, qualitative, subjective grading systems are utilized as surrogates for both mechanical and biocompatibility quantitative testing. Study definitions of mechanical terms, material properties, and mechanical testing protocols were frequently mislabeled with inappropriate ASTM standardized testing techniques.

CONCLUSION: Despite nearly five decades of use, a lack of standardization for material testing methods of hernia repair prosthetics confounds performance-related comparisons between commercially available prosthetics. Often, mechanical testing is done inconsistently with semi-qualitative results in a non-standardized fashion. The majority of histological analysis relies on qualitative data using non-validated scoring systems. We propose a standardized, evidence-based, quantitative testing technique based on the literature review and ASTM standards.

PREOPERATIVE FINDINGS PREDICT CONVERSION FROM LAPAROSCOPIC TO OPEN CHOLECYSTECTOMY

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BACKGROUND: Previous studies evaluating predictive factors for conversion from laparoscopic to open cholecystectomy have drawn conflicting conclusions. We evaluated objective pre-operative variables to create an accurate, accessible risk score for conversion.

METHODS: A retrospective review was performed of laparoscopic cholecystectomy patients at an urban tertiary-care center. Data were collected on 70 characteristics and subjected to bi-variate and multivariate logistic regression analysis to identify parameters which independently predict conversion to open cholecystectomy. A model was created based on this analysis.

RESULTS: Laparoscopic cholecystectomy was performed on 1377 patients for benign gallbladder disease over 71 months. There were 112 (8.1%) conversions to open cholecystectomy. Multivariate analysis identified male sex, elevated white blood cell count, low serum albumin, ultrasound findings of pericholecystic fluid, diabetes mellitus, and elevated total bilirubin as independent predictors of conversion. A model to calculate risk for conversion was created with an area under the ROC of 0.83. Risk for conversion can be calculated using this model or estimated based on the number of factors identified: no factors, 2%; one factor, 5%; two factors, 13%; three factors, 28%, four factors, 51%; five factors, 74% and six factors, 89%.

CONCLUSIONS: Conversion to open cholecystectomy can be accurately predicted based on parameters available pre-operatively leading to triage to an appropriately experienced surgical team, optimized resource allocation and limited time to conversion minimizing risk for injury

TERTIARY HYPERPARATHYROIDISM ATTRIBUTABLE TO LONG-TERM ORAL PHOSPHATE THERAPY

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OBJECTIVE: To report a rare case of tertiary hyperparathyroidism (HPT) as a result of long-term oral phosphate therapy.

METHODS: We present a case report, with a focus on clinical manifestations and biochemical findings during the course of tertiary HPT, and discuss the pathophysiologic features of this disorder and the therapeutic strategies.

RESULTS: A 35-year-old woman, 22 years after the initial diagnosis of familial hypophosphatemic rickets and initiation of treatment with phosphate and vitamin D, underwent assessment for recurrent symptomatic kidney stones, bone pain, and fatigue. Laboratory studies performed 10 months before this presentation showed findings consistent with secondary HPT. Examination was notable for short stature, and pertinent laboratory results were as follows: intact parathyroid hormone 602 pg/mL, calcium 10.9 mg/dL, and phosphorus 3.6 mg/dL. Tertiary HPT was diagnosed, and she underwent subtotal parathyroidectomy and transcervical thymectomy. Postoperatively, she had hypocalcemia and was treated with calcitriol, phosphate, and calcium carbonate: the last agent was discontinued with the serum calcium normalized. Despite multiple dosage alterations in the phosphate and calcitriol therapy, the patient had recurrent tertiary HPT and another kidney stone (treated by lithotripsy). Three years after the subtotal parathyroidectomy, treatment consisted of cinacalcet, calcitriol, and elemental phosphate.

CONCLUSION: Long-term follow-up of patients with tertiary HPT is critical, with careful dosage adjustments in phosphate and vitamin D therapy and monitoring of serum levels of phosphorus, calcium, and parathyroid hormone.

INCIDENCE AND LOCATION OF ECTOPIC ABNORMAL PARATHYROID GLANDS

R. Phitayakorn, MD and C.R. McHenry, MD.

BACKGROUND: Ectopic parathyroid glands are a common cause for failed parathyroid exploration.

METHODS: Patients with hyperparathyroidism and ectopic parathyroid glands were identified from a parathyroid database. Epidemiologic and laboratory data, results of Tc-99m sestamibi imaging, gland weights, and surgical outcomes were obtained. The locations of the ectopic glands were correlated with results of sestamibi imaging.

RESULTS: Of the 231 patients operated on for hyperparathyroidism, 37 (16%) had an ectopic parathyroid gland, 23 (62%) inferior, and 14 (38%) superior glands. Ectopic inferior glands weighed 1.3 ± 1.9 g and were: intrathyroidic 7 (30%), anterosuperior mediastinal 5 (22%), intrathyroidal 5 (22%), within the thyrothymic ligament 4 (17%), and submandibular 2 (9%). Ectopic superior glands weighed 3.2 ± 4.7 g and were: in the tracheoesophageal groove 6 (43%), retroesophageal 3 (22%), posterosuperior mediastinal 2 (14%), intrathyroidal 1 (7%), in the carotid sheath 1 (7%), and paraesophageal 1 (7%).

Sestamibi imaging was true-positive in 81% of patients, including 13 of 16 with retrosternal glands, and a false-negative in 19% of patients. A 100% cure rate was achieved.

CONCLUSIONS: A 16% incidence of ectopic parathyroid glands and a 100% positive predictive value of sestamibi scintigraphy underscore the necessity and value of preoperative sestamibi imaging for achieving cure in patients with primary hyperparathyroidism and ectopic parathyroid glands.

AN INVESTIGATION OF EPIDEMIOLOGIC FACTORS ASSOCIATED WITH LARGE NODULAR GOITER

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BACKGROUND: Sporadic nodular goiter is a common problem in the United States and significant compressive symptoms may occur with progression to a critical size.

METHODS: Potential epidemiological variables associated with the development of large unilateral (≥ 50 g) and bilateral (≥ 100 g) nodular goiter were investigated including: age, gender, race, body mass index (BMI), family history of thyroid disease, pregnancy at time of diagnosis, insurance status, and tobacco or alcohol use. Data were obtained from an IRB-approved thyroid database and retrospective chart review of consecutive patients operated on for nodular goiter from 1990 through 2005. A univariate and multivariate analysis of epidemiological variables in patients with "large" versus "small" nodular goiter was completed.

RESULTS: Of the 488 patients operated on for nodular goiter, 113 (23%) were classified as "large," 43 with unilateral (mean 106 ± 72 g) and 70 with bilateral enlargement (mean 173 ± 92 g) and 375 (77%) were classified as "small," 179 with unilateral (18 ± 10 g) and 196 with bilateral (37 ± 24 g) enlargement. Based on univariate analysis, African-American race, age ≥ 40 years, BMI ≥ 30 kg/m², and lack of insurance were associated with an increased risk of large nodular goiter ($P \leq 0.001$), whereas alcohol use was protective ($P = 0.002$). A multivariate analysis revealed that African-American race [adjusted odds ratio (adj. OR) 3.3, 95% CI = 2.0-5.4], age ≥ 40 years (adj. OR 2.1, 95% CI = 1.2-3.8), and BMI ≥ 30 kg/m² (adj. OR 2.5, 95% CI = 1.5-4.0) were independently associated with large nodular goiter. No significant differences were observed in gender, family history of thyroid disease, pregnancy, or tobacco use ($P > 0.1$).

CONCLUSIONS: African-American race, obesity, and increasing age are independent risk factors for the development of large nodular goiter. These results may be helpful in determining how best to monitor patients with nodular goiter, with earlier intervention to help prevent progressive enlargement and its sequelae.

PERITONITIS – THE WESTERN EXPERIENCE

Mark A. Malangoni, Tazo Inui

Peritonitis is a common surgical emergency. This manuscript will provide an overview of recent developments in the management of peritonitis in the Western world. Emphasis is placed on the emergence of new treatments and their impact of outcomes.

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IMPROVING OPERATING ROOM EFFICIENCY THROUGH PROCESS REDESIGN

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BACKGROUND: Operating rooms (ORs) are important resources for patient care and revenue, yet a significant portion of OR time is taken up by nonoperative activities. We hypothesized that redesigning the process that occurs between operations would lead to a decrease in nonoperative time (NOT= room turnover time plus anesthesia induction and emergence time).

METHODS: Following a 3-month multidisciplinary planning process, a prospective study to reduce NOT was initiated in 2 of 17 ORs at a tertiary care academic medical center. Unlike previous reports, which have limited the number of participants, we constructed a process that was restricted only by case duration. The plan focused on minimizing nonoperative tasks in the OR, effecting parallel performance of activities, and reducing nonclinical disruptions. Eligible cases were those with an estimated operative time of 2 hours or less. A target NOT of 35 minutes was established. Cases of similar duration in the remaining ORs served as a concurrent control group.

RESULTS: Twenty-three surgeons, 13 anesthesiologists, and 11 nurses worked in the project ORs over a 3-month period. Residents participated in all cases. There was a significant reduction in NOT (42.2 ± 12.9 vs 65 ± 21.7 minutes), turnover time (26.4 ± 11.2 vs 42.8 ± 21.7 minutes), and anesthesia-related time (16.9 vs 21.9 minutes, all $P < .001$) in the project rooms compared with cases of similar duration in control ORs. Process-related delays were identified in 70% of cases when NOT exceeded the 35-minute target.

CONCLUSIONS: These results demonstrate that a coordinated multidisciplinary process redesign can significantly reduce NOT. This process is applicable to most ORs and has optimal benefit for cases of 2 hours or less in duration. The high percentage of residual process-related delays suggests that further improvements can be anticipated. (Surgery 2006;140:509-516)

SAFETY OF MOXIFLOXACIN IN TRIALS OF COMPLICATED INTRA-ABDOMINAL INFECTIONS

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OBJECTIVES: A pooled analysis of data from two moxifloxacin (MXF) Phase III studies of sequential – intravenous (IV) followed by oral (PO) therapy – in complicated intra-abdominal infections (cIAIs) was conducted to determine the safety profile of MXF vs comparator (COMP) treatments.

METHODS: Study 1 – a prospective, randomized, double blind, active-control, multicenter Phase IIIB clinical study in patients with cIAIs in 71 centers in N. America and Israel. Treatments were MXF 400 mg IV then PO q24h or piperacillin/tazobactam (PIP/TAZ) 3.0/0.375 g IV q6h followed by AMOX/CLAV 800/114 mg PO q12h 681 patients were enrolled (MXF: 339, COMP: 342). Study 2 – a prospective, randomized, non-blind, comparative, parallel group, multicenter, multinational, Phase III clinical study in 58 centers worldwide. Treatments were MXF 400mg IV then PO q24h or ceftriaxone 2g q24h plus metronidazole 500mg q8h followed by AMOX/CLAV 500/125mg q8h. 595 patients were enrolled (MXF: 293, COMP: 302). Patients in both studies received a minimum of 3 days IV therapy and total treatment duration of 5-14 days (means \pm SD: Study 1: 9.1 \pm 3.9 days, Study 2: 9.3 \pm 3.7 days). In Study 1, there were 656 patients valid for safety analysis (MXF:329, COMP:327). In Study 2, there were 584 patients valid for safety (MXF: 289, COMP: 295).

RESULTS: In the pooled analysis 618 MXF and 622 COMP patients were evaluable for safety. Demographics were similar between groups. Safety data were as follows (some patients had > 1 event). Any adverse event (AE) – MXF: 456 (73.8%), COMP: 430 (69.1%). Any drug-related AE – MXF: 137 (22.3%), COMP: 127 (20.4%). Any serious AE – MXF: 134 (21.7%), COMP: 112 (18.0%). Any discontinuation due to drug-related AE – MXF: 22 (3.6%), COMP: 18 (2.9%). Total deaths – MXF: 18 (2.9%), COMP: 22 (3.5%). Death or AE considered to be a clinically relevant outcome of QTc prolongation - MXF: 1 (0.2%), COMP: 6 (1.0%). There were no clinically significant between-group differences in event rates. AEs were generally mild or moderate.

CONCLUSIONS: In this population pooled from two large Phase III clinical trials in patients with cIAIs, MXF treatment was associated with a favorable overall safety and cardiac safety profile vs standard comparators. The observed safety profile of MXF cIAIs is comparable to that in other indications.

Section 4

Pediatric Surgery

GASTRIC SCHWANNOMA

Sundeep Arora, Jonathan Gisser, Samra Blanchard, Raymond Redline, Robert Parry, Gisela Chelimsky

Case A: 16-year old female presented with anemia, palpitations and suffered a pre-syncopal event while jogging. She had 1 episode of melena, but denied abdominal pain or diarrhea. She was not taking any medications. On admission, she was pale and orthostatic. Hemoglobin and hematocrit were 6.1g/dl and 18.2%, respectively. Stool was positive for occult blood. Gastric lavage yielded clear fluid. Upper endoscopy showed a 5 cm antral mass with solitary ulcer. Endoscopic ultrasound showed a heterogeneous mass in the greater curvature of the stomach arising from submucosa. A PET scan and CT scan did not show any other lesions. She underwent endoscopic/laparoscopic visualization followed by partial gastrectomy and biopsies revealed a 7.5 cm hypocellular tumor arising from the muscularis with multiple areas of ischemic necrosis and hyalinization. Focal nuclear enlargement and hyperchromasia were also noted. Immunohistochemically, the tumor was negative for CD117, CD34 and desmin/muscle specific antigen, but positive for S100. This was consistent with the diagnosis of Schwannoma

Discussion: Schwannomas are common mesenchymal tumors, but represent only 2.9% of the gastrointestinal mesenchymal tumors. They occur most commonly in the stomach as a single nodular mass in the muscularis propria. They do not have any age or sex predilection. In contrast to Gastrointestinal Stromal Tumors (GISTs), which often present with hemorrhage and necrosis, Schwannomas are homogenous, well-defined mural masses. They are un-encapsulated (unlike soft tissue & CNS tumors), thus sometimes misdiagnosed as neurofibromas. Histologically, they have prominent peripheral lymphocytic aggregates with or without a germinal center. They are mainly composed of spindle cells, but epithelioid and rare plexiform variants have also been described. Immunohistochemically, they stain positive for vimentin and S100 protein, but negative for CD117. Gastrointestinal Schwannomas are benign tumors and have a good prognosis even when treated with enucleation.

INFLAMMATORY BOWEL DISEASE ASSOCIATED WITH A SIGMOID NEOVAGINA IN A PEDIATRIC PATIENT

Jonathan Gisser, Rebekah Slocum, Robert Parry, Raymond Redline, Gisela Chelimsky, Reinaldo Garcia-Naveiro

Case: A 2 year-old Caucasian girl presented with a one week history of abdominal pain, fever, hematochezia and vaginal discharge. She had a congenital cloacal malformation that was repaired in infancy with construction of a neorectum (rectal pull-thru) and neovagina (segment of descending colon). On admission, she was passing frequent bloody stools from her neorectum and had a bloody discharge from her partially prolapsed neovagina. She had hypoalbuminemia, leukocytosis and a markedly elevated inflammatory bowel disease (IBD) serological marker (pANCA 192 EU/ml). Endoscopic examination revealed gastritis, duodenitis and colitis consistent with IBD. Her neovaginal inflammation, however, was more severe than her colonic disease. After a prolonged remitting-relapsing course, complicated by *C. difficile* neovaginitis and a poor response to immunomodulator therapy with azathioprine, she stabilized on a regimen of subcutaneous methotrexate, intravenous infliximab, and topical metronidazole to her neovagina.

Discussion: This is an unusual case of diversion colitis (DC) -associated with IBD. DC involves a segment of bowel that has been diverted from the alimentary tract and fecal stream, such as a neovagina, and is typically treated by restoring bowel continuity. It is a relatively common occurrence in patients with sigmoid neovaginas. However, there are only five reported cases of patients with DC developing inflammation in the in-stream bowel. All of these cases were in adults and were deemed to be ulcerative colitis. This is the youngest case of DC-associated IBD, and the only one involving the stomach and small bowel, in addition to the colon. Furthermore, based on her clinical picture, histological findings, and serological markers, the patient's colitis is indeterminate. Although no patient with DC-associated IBD has ever been treated with infliximab, the patient has shown significant improvement on this regimen. This case has significant implications for the role of the fecal stream in the pathogenesis of IBD, and also illustrates the systemic dimensions of a presumably local disease.

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FECALITH: SOURCE OF AN EXAGGERATED INFLAMMATORY RESPONSE IN PEDIATRIC PATIENTS WITH ACUTE APPENDICITIS

Diya I. Alaadeen, MD and Walter J. Chwals, MD

INTRODUCTION: A fecalith (appendicalith) is a fecal concretion that can obstruct the appendix leading to acute appendicitis. The presence of a fecalith may predict a more severe progression of appendiceal inflammation and perforation.

METHODS: The charts of all pediatric patients who were diagnosed with appendicitis, and underwent an appendectomy by a single surgeon between 1/1/2005 and 12/31/2005 were reviewed. The presence of fecalith was confirmed on review of initial computed tomography or final postoperative pathology. Initial white cell count (WCC) and evidence of microperforation on final pathology were compared between patients with a fecalith and those without.

RESULTS: There were thirty-seven patients who had had an appendectomy for diagnosis of appendicitis. Twenty percent of the patients had fecalith. Twenty nine percent of the patients with a fecalith had evidence of microperforation on final pathology, versus seven percent of the patients without a fecalith. The average presenting WCC was significantly higher in patients with a fecalith versus those without a fecalith ($21.3 \pm 4.3K$ vs. $14 \pm 3.8K$ $p=0.005$).

CONCLUSIONS: There is a higher rate of appendiceal microperforation in patients with a fecalith. There was an elevated inflammatory response, as evidenced by the statistically significant higher WCC in patients with a fecalith. The presence of a fecalith on initial radiological studies, without evidence of gross perforation, should prompt an early appendectomy.

Section 5

**Pediatric Cardiothoracic
Surgery**

THE EXTRACARDIAC FONTAN PROCEDURE USING A HOMOGRAFT CONDUIT – ADVANTAGES, OUTCOMES AND RISK FACTORS

Ahmed Farouk, Kenneth Zahka, Ernest Siwik, Francine Erenberg, Yasser Al-Khatib, Wali Gauvin, Alex Golden, Mohsen Karimi, Minhaz Uddin, John Stork, Hani Hennen

BACKGROUND: Arrhythmias and pleural effusion remain the main causes of morbidity after the Fontan operation. The extracardiac Fontan (ECF) procedure may have significant advantages by maximizing pulmonary blood flow velocity, eliminating intra-atrial suture lines, and avoiding exposure to the circuit oxygenator. Use of a homograft eliminates long-term use of anti-coagulation.

METHODS: From 1997 to 2005, 128 consecutive patients (mean age 4.8 ± 2.0 yrs) underwent the ECF operation using a homograft conduit. Full CPB was used in 84 patients (66%), extracorporeal support without an oxygenator in 9 (7%), and no support in 35 (27%). No patient was anti-coagulated for greater than three months.

RESULTS: 124 patients (97%) survived to hospital discharge. Risk factors for death included atrioventricular valve regurgitation (AVVR, $p=0.001$), preoperative arrhythmias ($p=0.005$), and high end-diastolic pressure (EDP, $p=0.04$). Risk factors for arrhythmias included low Nakata index ($p=0.01$), single right ventricle ($p=0.04$), and high EDP ($p=0.04$). Risk factors for pleural effusions included closed or no fenestration ($p<0.001$), low Nakata index ($p=0.001$), and high EDP ($p=0.001$). At 5.6 ± 1.3 years follow-up there was no Fontan takedowns, conduit replacement, or thromboembolic complications.

CONCLUSION: The extracardiac Fontan operation using a homograft conduit is a safe and effective procedure that is applicable to virtually all forms of cardiac morphologies. The ECF operation avoids exposure to an oxygenator in many cases, and eliminates the need for long-term anti-coagulation. Right ventricular morphology, low Nakata index, high EDP, and AVVR are the principal risk factors for early and mid-term morbidity and mortality.

SURGICAL MANAGEMENT OF TRANSPOSITION OF GREAT ARTERIES WITH LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION IN A 2-YEAR OLD

Ahmed Farouk, MD; Hani Hennein, MD

Transposition of great arteries (TGA) with left ventricular outflow tract obstruction (LVOTO) is an extremely challenging substrate for primary arterial switch repair. We report a two years old patient with D-TGA, a ventricular septal defect, and a gradient of 36 mmHg across the LVOT, who undergone successful primary arterial switch repair. We describe the surgical options for this group of patients as well as the technique and advantages of this kind of repair.

INDIVIDUALIZED APPROACH TO THE INITIAL TREATMENT OF PULMONARY ATRESIA AND VENTRICULAR SEPTAL DEFECT

Ahmed Farouk, Kenneth Zahka, Ernest Siwik, Francine Erenberg, Yasser Al-Khatib, Wali Gauvin, Alex Golden, Mohsen Karimi, Minhaz Uddin, John Stork, Hani Hennein

BACKGROUND: Pulmonary atresia with ventricular septal defect (VSD) is a heterogeneous group of congenital heart defects characterized by diverse sources of pulmonary blood flow originating from both the native pulmonary arteries and aorto-pulmonary collateral (APC) vessels. Various operative strategies have been described for the treatment of this group of defects, ranging from single-stage unifocalization and intracardiac repair, to planned multi-stage reconstruction of the pulmonary vascular tree followed by intracardiac repair. We describe an individualized approach to this group of defects utilizing the aforementioned strategies, but basing the particular procedure on the presenting morphology.

METHODS: Over a consecutive 10 year period, 66 patients presenting with pulmonary atresia with VSD were treated utilizing an approach that individualized the management on the presenting morphology. Patients were initially classified into three groups according to their native pulmonary artery morphology and number of major APC arteries. Group A (favorable morphology) had confluent branch pulmonary arteries, a Nakata index of $> 150 \text{ mm}^2/\text{m}^2$, and no major APC arteries; Group B (intermediate) had either nonconfluent or moderately hypoplastic pulmonary arteries (Nakata index $90 - 150 \text{ mm}^2/\text{m}^2$) and ≤ 2 APC arteries; Group C (severe) had severely diminutive branch pulmonary arteries (Nakata index $< 90 \text{ mm}^2/\text{m}^2$) and ≥ 3 APC arteries. Our philosophy is to base pulmonary blood flow on the native pulmonary circulation whenever possible and to unifocalized collateral vessels only when necessary. All Group A patients ($n=29$) underwent a single-stage complete intracardiac repair and RVOT reconstruction utilizing either a transannular patch (TAP, $n=18$) or an RVPA conduit ($n=11$). All Group B patients ($n=9$) underwent an initial palliative procedure (modified Blalock-Taussig shunt (MBTS) in 7, TAP in 2), followed by intracardiac repair, all without unifocalization. All Group C patients ($n=28$) underwent an initial palliative procedure (RVPA conduit in 16, single-stage unifocalization and RVPA conduit in 5, MBTS in 6, and direct aorto-pulmonary anastomosis in 1), followed by intracardiac repair with ($n=15$) or without surgical unifocalization ($n=8$).

RESULTS: There were two deaths, one in Group A following an intracardiac repair, and one in Group C following placement of an RV-PA conduit. In all, 86 percent of the patient population achieved a complete biventricular repair, 42 (64 percent) based solely on the native pulmonary circulation without unifocalization. In Group C patients (severe morphology), 23/28 patients (82 percent) achieved a complete repair, 8 patients (28 percent) without unifocalization. The number of procedures per patient before complete repair was $0, 1.2 \pm 0.1$, and 3.8 ± 1.3 for Groups A, B, and C respectively. The post-repair PRV/PLV pressure ratio was $0.42 \pm 0.09, 0.38 \pm 0.27$, and 0.52 ± 0.14 in Groups A, B, and C, respectively. Kaplan-Meier 10-year freedom from reoperation rates were 46%, 0%, and 0%, and 10-year freedom from mortality rates were 96%, 100%, and 96% for Groups A, B, and C, respectively.

CONCLUSIONS: A high level of complete intracardiac repair (86 percent) can be achieved with a low mortality (3 percent overall) in a heterogeneous group of patients presenting with pulmonary atresia and VSD through a management strategy that individualizes the initial procedure to the presenting pulmonary arterial and APC morphology. In all, only 23 percent of the entire patient population but 75 percent of patients in Group C (severe morphology) required unifocalization. An individualized approach based on the presenting morphology maximizes the rate of complete intracardiac repairs, bases pulmonary blood flow on the native pulmonary arteries in the great majority of cases, and is achieved with acceptable rates of reoperation and mortality.

Section 6
Plastic and
Reconstructive
Surgery

SOFT TISSUE FUNCTIONAL ANATOMY OF THE NOSE

Guyuron, Bahman M.D.

The author discusses the role of soft tissues in aesthetic and functional rhinoplasty outcomes, stressing the dynamic function of the nasal muscles. These muscles are thin and difficult to visualize, but their preservation is vital to nasal function and appearance.

SEPTAL CARTILAGE DEFINED: IMPLICATIONS FOR NASAL DYNAMICS AND RHINOPLASTY

Mowlavi, Arian M.D.; Masouem, Shahryar B.S.; Kalkanis, James M.D.; Guyuron, Bahman M.D.

BACKGROUND: Although the septal cartilage is integral to structural nasal stability, it is routinely violated during septorhinoplasty. This occurs during dorsal hump reduction, caudal septal reduction, submucoperichondrial resection of a deviated septum, or harvesting of cartilage graft material. Despite such routine alteration and/or use, the characteristics of septal cartilage have not been adequately defined.

METHODS: By measuring septal length, height, and cartilage thickness mapped out at 5-mm intervals over the entire nasal septum in 11 fresh cadaver specimens, the characteristics of septal cartilage were determined.

RESULTS: Septal thickness measurements demonstrated significant differences along the nasal septum, with the greatest thickness along the septal base (2.7 +/- 0.1 mm), followed by intermediate thickness along the septal dorsum (2.0 +/- 0.2 mm) and the least thickness along the central portion (1.3 +/- 0.2 mm) and at the anterior septal angle (1.2 +/- 0.1 mm) ($p < 0.001$).

CONCLUSIONS: These observations clarify several nuances regarding septal structural stability, septal deformities, and the effects of septal alteration during rhinoplasty. The findings of this study reinforce several principles, including recognition of factors contributing to the high propensity of acquired central septal perforations; preservation of a generous L-strut width, especially at the anterior septal angle, or if planning dorsal hump reduction, prudent allocation of harvested septal cartilage; and clarifying the proclivity for supratip deformity following rhinoplasty.

MANAGEMENT OF THE BLACK HOLE IN VELOPHARYNGEAL INCOMPETENCE: COMBINED USE OF A FURLOW PALATOPLASTY AND SPHINCTER PHARYNGOPLASTY

Gosain, Arun K. M.D.; Arneja, Jugpal S. M.D.

BACKGROUND: Patients with velopharyngeal incompetence may have a combination of a large velopharyngeal gap and poor lateral wall motion on phonation, simulating a "black hole" on nasendoscopy. Pharyngeal flaps for treatment of velopharyngeal incompetence in these patients are of questionable efficacy, because poor lateral wall motion necessitates such a wide flap that nasal airway obstruction is likely.

METHODS: Thirteen patients with velopharyngeal incompetence were managed between 1994 and 2003 with a combined Furlow palatoplasty and sphincter pharyngoplasty by a single surgeon. A diagnosis of velopharyngeal incompetence was established by means of perceptual speech evaluation performed by a trained speech pathologist using a standardized speech/voice rating scale (0 to 13); scores of 4 or higher indicated an incompetent velopharyngeal valving mechanism. Surgical inclusion criteria were a large velopharyngeal gap (≥ 7 mm) and poor lateral wall motion (1 or 2 of 5, with 3 being rated as average) measured by multiview videofluoroscopy and nasendoscopy.

RESULTS: The mean preoperative score on the speech and voice rating scale was 10.5 (range, 4 to 13), with a mean postoperative score of 1.9 (range, 0 to 8) following Furlow palatoplasty and sphincter pharyngoplasty in 13 patients. Two patients required an additional surgical procedure to achieve complete correction of velopharyngeal incompetence without nasal airway obstruction, to achieve a final mean score of 0.8 (range, 0 to 2) among the 12 patients who completed surgical management, achieving a highly significant reduction in nasality ($p < 0.0001$).

CONCLUSIONS: Patients with velopharyngeal incompetence who have a black hole on nasendoscopy consisting of a large velopharyngeal gap and poor lateral wall motion are at high risk for recurrent velopharyngeal incompetence or nasal airway obstruction following surgical management. Initial treatment with a Furlow palatoplasty and sphincter pharyngoplasty has a high rate of success in these patients and does not preclude further surgical correction if needed, with minimal risk of nasal airway compromise.

A REINVESTIGATION OF MURINE CRANIAL SUTURE BIOLOGY: MICROCOMPUTED TOMOGRAPHY VERSUS HISTOLOGIC TECHNIQUE

Stadler, James A. III B.S.; Cortes, Wilberto M.D.; Zhang, Lin-Ling M.D.; Hanger, Christopher C. M.D.; Gosain, Arun K. M.D.

BACKGROUND: Histology remains the standard form to analyze cranial suture in murine models, but this technique provides only limited “snapshots” of the entire suture and requires animal euthanasia with tissue destruction. Because of the bone complex microarchitecture, better methods are required to study the behavior of the cranial suture and its surrounding environment. The authors compared microcomputed tomography and histology as techniques to evaluate murine cranial sutures.

METHODS: A total of 360 microcomputed tomography images and 160 to 170 histologic sections were processed from a mouse at postnatal days 22 and 45, respectively. After euthanasia, the posterior frontal and sagittal sutures were imaged with a microcomputed tomography system and subsequently processed for histologic analysis. Quantitative analysis of two-dimensional images was performed to determine the percentage of bone in a 1-mm² sample.

RESULTS: Quantitative analysis of the percentage of bone within the sutures showed identical patterns by microcomputed tomography and histology techniques. Both methods demonstrated the posterior frontal suture to have heavier fusion patterns in the anterior and endocranial portions, with variable skip areas of complete patency on the endocranial surface, ectocranial surface, or both at day 45.

CONCLUSIONS: Cranial suture fusion in the murine model is not an “all-or-none” phenomenon. The posterior frontal suture, previously thought to be completely fused on day 45 by histological analysis, showed variable fusion along the length of the suture by both methods. Quantitative assessment of the percentage of bone within the posterior frontal and sagittal sutures and morphologic assessment of these sutures demonstrated similar findings by both methods. Whereas thorough histologic evaluation of an entire suture would be extremely labor intensive and impractical, these findings help to validate microcomputed tomography as a rapid and reliable method of examining the entire suture in murine models.

BIOLOGIC BRACHYTHERAPY: EX VIVO TRANSDUCTION OF MICROVASCULAR BEDS FOR EFFICIENT, TARGETED GENE THERAPY

Michaels, Joseph V M.D.; Levine, Jamie P. M.D.; Hazen, Alexes M.D.; Ceradini, Daniel J. M.D.; Galiano, Robert D. M.D.; Soltanian, Hooman M.D.; Gurtner, Geoffrey C. M.D.

BACKGROUND: Gene therapy for cancer holds enormous therapeutic promise, but its clinical application has been limited by the inability to achieve targeted, high-level transgene expression with limited systemic toxicity. The authors have developed a novel method for delivering genes to microvascular free flaps (commonly used during reconstructive surgery) to avoid these problems.

METHODS: During the finite period in which a free flap is separated from the host (ex vivo), it can be perfused with extremely high titers of genetic material through the afferent artery, resulting in efficient transduction of the tissue. Before reanastomosis, unincorporated genetic material is flushed from the flap, minimizing systemic toxicity.

RESULTS: In a rodent model using an adenoviral vector containing the lacZ reporter gene, high regional expression of [beta]-galactosidase was achieved in all the different cells in a microvascular free flap. Moreover, no [beta]-galactosidase staining was observed outside of the transduced flap, and viral sequence was undetectable by polymerase chain reaction analysis in other tissues. Further analysis confirmed that high-level transgene expression was precisely localized to the explanted tissue, with no collateral transduction.

CONCLUSIONS: Targeting gene delivery with minimal systemic toxicity is essential for successful gene therapy. This form of "biological brachytherapy" provides a new opportunity to deliver targeted therapeutic transgenes to patients undergoing reconstructive surgery and allows microvascular free flaps to perform therapeutic and reconstructive functions.

REAL-TIME REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION: AN IMPROVEMENT IN DETECTING mRNA LEVEL IN MOUSE CRANIAL TISSUE

Singh, Rashmi M.S.; Recinos, Rene F. M.D., Ph.D.; Agresti, Michael M.S.; Schaefer, Richard B. M.D.; Bosbous, Mark B.S.; Gosain, Arun K. M.D.

BACKGROUND: Quantitation of messenger RNA levels has traditionally been carried out by Northern blot analysis. While this is regarded as the standard method, it is time-consuming and requires large quantities of RNA. Reverse-transcriptase polymerase chain reaction is a semiquantitative method that has been used as a more rapid and sensitive alternative to Northern blotting. Real-time reverse-transcriptase polymerase chain reaction is a quantitative technique that is gaining widespread acceptance as a rapid and reliable way of quantifying mRNA. Since both techniques are currently being used to evaluate gene expression in the murine cranial suture model, the present study was performed to compare the sensitivity and variability of real-time to conventional reverse-transcriptase polymerase chain reaction in this model.

METHODS: Mouse brain RNA was isolated and amplified using real-time and conventional methods. For the real-time method, a serial 10-fold dilution of RNA, ranging from 1 fg to 100 ng, was performed. For the conventional method, the minimum amount of RNA needed for consistent polymerase chain reaction amplification was determined. Transforming growth factor beta-1 and [beta]-actin RNA transcripts were measured using both techniques.

RESULTS: One femtogram of RNA could be detected by the real-time method, although 10 fg were required to reliably detect differences; 500 ng of RNA was required for consistent polymerase chain reaction amplification using the conventional method. The variability of real-time reverse-transcriptase polymerase chain reaction when expressed as a coefficient of variation (SD as a percentage of the mean) ranged from 0.23 to 2.6 percent for all genes tested, as compared with 9 to 70 percent for conventional reverse-transcriptase polymerase chain reaction.

CONCLUSIONS: Real-time reverse-transcriptase polymerase chain reaction was used successfully to detect mRNA from different mouse genes. The real-time method is much more sensitive in detecting small amounts of mRNA than both Northern blot analysis and conventional polymerase chain reaction. The variability of the real-time method is more than 10-fold lower compared with the conventional method performed in the authors' laboratory for all genes tested.

6

FOLLICULAR ANATOMY OF THE ANTERIOR TEMPORAL HAIRLINE AND IMPLICATIONS FOR RHYTIDECTOMY

Mowlavi, Arian M.D.; Majzoub, Ramsey K. M.D.; Cooney, Damon S. M.D.; Wilhelmi, Bradon J. M.D.; Guyuron, Bahman M.D.

BACKGROUND: Incisions made perpendicular to the hair follicles during anterior frontal hairline brow lifts or forehead shortening procedures help produce an inconspicuous forehead scar. The success of this "hidden" incision relies on the anteriorly directed frontal hairline follicles and their growth vector. The authors hypothesized that a similar incision could be made perpendicular to the hair follicles in the temple region during rhytidectomy. A well-designed anterior hairline beveled incision over the temple would allow for improved leverage during soft-tissue repositioning and a concealed hairline incision in the temple region.

METHODS: Anterior temporal hairline strips 4 cm in length at the level of the lateral canthus were excised from 16 fresh cadavers. Hairline follicles (n = 227) were assessed for direction and angle of growth after appropriate tissue preparation and staining (hematoxylin and eosin). The hair follicle angle was analyzed microscopically as it approached the epidermis.

RESULTS: The anterior temporal hairline follicles were oriented at a mean angle with the epidermis of 16 +/- 3 degrees anteriorly and inferiorly.

CONCLUSIONS: The anterior temporal hairline follicles of the scalp are oriented anteriorly and inferiorly with the epidermis, providing the surgical rationale for using a beveled hairline incision angled 30 to 45 degrees to the external skin surface to undercut the distal flap. This incision is perpendicular to and transects the temporal hair follicles during rhytidectomy, permitting hair growth through and anterior to the scar. This modified anterior temporal hairline incision reduces visibility of the scar at the hairline for patients in whom scar show and hairstyle versatility are important concerns.

Section 7

Surgical Oncology

EARLY EXPERIENCE WITH INTRAOPERATIVE RADIOTHERAPY IN RESECTED PANCREATIC ADENOCARCINOMA

Messick CA, Hardacre JM, Siegel CT, Stellato TA, Sanabria JR, Kinsella TJ, McGee MF, Schulak JA.

BACKGROUND: The use of intraoperative radiotherapy (IORT) in patients with resected pancreatic adenocarcinoma (PA) has not been clearly defined. This study assesses complications, recurrence, and survival in patients undergoing IORT for resected PA.

METHODS: The medical records of our first 22 patients receiving IORT for resected PA (2001-2006) were reviewed and compared to a group of 27 consecutive patients not receiving IORT (2004-2006). IORT (median dose 1200cGy) was administered in a dedicated operating room using a mobile linear accelerator.

RESULTS: The mean age of patients receiving IORT differed from that of patients not receiving IORT, 63 vs. 71 years, $p = 0.012$. A similar distribution of patients in both groups underwent proximal, distal, and total pancreatectomies. Mean estimated blood loss was greater in the IORT group (1159 ml) than in the no IORT group (696 ml), $p = 0.049$. Mean operative time tended to be greater in the IORT group than the no IORT group, 474 vs. 405 minutes, $p = 0.06$. There were no 30-day deaths in either group. At least one complication occurred in 50% (11/22) of patients

DO ALL ADRENAL MASSES NEED A FUNCTIONAL EVALUATION?

Juan M Proano, Martin I Resnick, Raymond P Onders, Scott M Wilhelm

INTRODUCTION: In 2002 the NIH issued a consensus statement on the evaluation of incidentally discovered adrenal masses. Current data suggest that all adrenal masses should undergo a biochemical evaluation for hormone excess. We hypothesize that patients with a hormone secreting adrenal mass will have clinical symptoms to guide functional testing. Patients without clinical symptoms or a history of hypertension may not need a biochemical evaluation.

MATERIALS AND METHODS: With IRB approval, patients who had an adrenal mass referred to either the surgery or the urology department at our tertiary care institution were retrospectively evaluated. Patients (n=205) were identified from billing records from 1997 to 2006 with potential adrenal masses. Fifteen patients had no available records, 9 patients did not have an adrenal mass, leaving 181 patients for review. Patients were divided into three groups based on symptoms at presentation: Group 1 - clinical symptoms consistent with a possible functional adrenal mass, Group 2 - no clinical symptoms suggestive of a functional adrenal mass but only a history of controlled hypertension, group 3 - no symptoms suggestive of functional adrenal mass and no history of hypertension.

RESULTS: 181 patients presented with an adrenal mass (average size 3.63cm, 0.3 - 20cm) at our institution. Biochemical evaluation for a functional adrenal mass was completed in 138 patients. Stratified according to the patients' symptoms, the result of the biochemical evaluation is seen in the chart.

Biochemical test	Positive	Negative	Total	P value
Group 1 (symptomatic)	53 (72.6%)	20	73	0.001
Group 2 (only hypertension)	9 (30.0%)	30	39	0.001
Group 3 (asymptomatic)	0 (0 %)	26	26	0.001

An adrenalectomy (n=101) was performed for various indications, size (28%), functional tumor (57%), growth (2%), and suspicious imaging or malignancy (13%). Of the functional tumors there were 33 aldosteronomas, 14 pheochromocytomas, 6 cortisol secreting tumors, 1 estradiol secreting tumor and 1 androgen secreting tumor. Hypertension was the most common clinical finding documented in 97%(32/33) of the aldosteronomas, 86%(12/14) of the pheochromocytomas, and 100%(6/6) of the patients with Cushing's syndrome.

CONCLUSIONS: Patients who present with an asymptomatic adrenal mass which does not meet the indication for adrenalectomy based on size or imaging, and who do not have a history of hypertension, may not require a biochemical evaluation.

MOLECULAR CLASSIFICATION OF THYROID NODULES BY CYTOLOGY

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OBJECTIVES: Fine needle aspiration (FNA) biopsy of thyroid nodules provides cytologic specimens whose interpretation can direct patients toward either thyroidectomy or observation. About 20% of FNA specimens yield an indeterminate result. Recent studies have characterized differences in gene expression between benign and malignant conditions, most often using whole tissue. Our goal was to determine feasibility of quantitative PCR (qPCR)-based gene expression analysis in cytologic samples. For five genes shown to be overexpressed in thyroid carcinomas (fibronectin, galectin-3, Met/HGFR, MUC1, and GA733-precursor) we compared expression between pathologic states.

STUDY DESIGN: Prospective laboratory analysis of twenty thyroidectomy specimens.

METHODS: Routine microscopy was performed. Cytologic samples were obtained from the dominant nodules and RNA was extracted. Preliminary analysis using fluorometry and reverse-transcriptase PCR (RT-PCR) was performed. Expression levels of the test genes in nodules and from control samples were measured by real-time qPCR. Fold-changes in gene expression were compared.

RESULTS: One specimen did not yield sufficient intact RNA; another consisted of Hurthle cell adenoma adjacent to papillary carcinoma; these were eliminated from consideration. RT-PCR revealed satisfactory RNA recovery. qPCR showed significant overexpression of fibronectin in the four papillary carcinomas compared with the five goiters and seven follicular adenomas. Differences in fibronectin and MUC1 expression between the two follicular carcinomas and the follicular adenomas approached significance. No other differences were statistically significant.

CONCLUSIONS: FNA specimens were a satisfactory source of tissue for qPCR-based gene expression analysis. Fibronectin was overexpressed in papillary carcinoma specimens compared with goiters and follicular adenomas. The other studied genes did not reliably classify the samples.

EVALUATION AND MANAGEMENT OF INCIDENTAL THYROID NODULES IN PATIENTS WITH ANOTHER PRIMARY MALIGNANCY

SM Wilhelm, AV Robinson, SA Krishnamurthi, HL Reynolds, (TA Stellato)

BACKGROUND: Some studies indicate that incidentally discovered thyroid nodules may have a higher rate of malignancy (7-12%) than traditionally discovered nodules (5%). Biopsy of incidental nodules ≥ 1 cm is indicated, but measurement accuracy of imaging modalities is not clear. We sought: 1) to determine the rate of malignancy in incidental thyroid nodules in patients with other malignancies, and 2) to examine the accuracy of ultrasound (U/S) vs. CT scan in determining nodule size.

METHODS: We did a retrospective review of 41 patients with history of another known malignancy (Gastrointestinal-23, breast- 11, others- 16) referred for evaluation of an incidental thyroid nodule found on various imaging modalities (CT, U/S, and others). All patients underwent office based U/S and biopsy of nodules ≥ 1 cm. Surgical intervention was based on biopsy results. Pearson correlation test was done to compare nodule size at pathology to size seen on CT or U/S. R2 and P values were calculated. $P < 0.05$ was considered significant.

RESULTS: 35 patients met criteria for biopsy. 19/35 (54%) patients had atypical biopsy results warranting resection. 16/19 underwent surgery. Pathology yielded 5 papillary thyroid cancers (PTC), 2 (microPTC), 2 metastatic cancers, and 7 benign lesions. Ultrasound measurement of nodules compared to size measured at pathology had an R2 correlation value of 0.90 with P value < 0.0001 . CT scan had an R2 value of 0.83 and P value of 0.005.

CONCLUSION: After evaluation, incidental thyroid nodules found in patients with another primary malignancy warranted resection in 54%. The rate of malignancy (including well differentiated thyroid cancer and metastatic disease) in incidental thyroid nodules in our study was 22%, which is well above the expected rate of 5% seen in traditionally discovered nodules. U/S correlation with nodule size at pathology was excellent and superior to CT scan measurements. Thyroid U/S is essential to determine accurate lesion size if we are to use size as a criterion for which lesions warrant biopsy. All incidental thyroid nodules ≥ 1 cm seen in patients with another malignancy warrant further evaluation.

EARLY EXPERIENCE WITH INTRAOPERATIVE RADIOTHERAPY IN RESECTED PANCREATIC ADENOCARCINOMA

Messick CA, Hardacre JM, Siegel CT, Stellato TA, Sanabria JR, Kinsella TJ, McGee MF, Schulak JA.

BACKGROUND: The use of intraoperative radiotherapy (IORT) in patients with resected pancreatic adenocarcinoma (PA) has not been clearly defined. This study assesses complications, recurrence, and survival in patients undergoing IORT for resected PA.

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LAPAROSCOPIC ILEOSTOMY AS PALLIATIVE CARE FOR MALIGNANT SMALL BOWEL OBSTRUCTION

S.M. Wilhelm and V. von Gruenigen

BACKGROUND: In 2005, The American College of Surgeons (ACS) issued a statement, ST-50, outlining guiding principles of palliative care for surgeons. This defined an evolving role for surgeons to assist patients with terminal conditions. Carcinomatosis can result in intestinal obstructions; patients in this situation have limited if any treatment options. They are often discharged to hospice with nasogastric tubes and abdominal pain. Our purpose was to determine if laparoscopic ileostomy if feasible and useful in this challenging patient population.

METHODS: 2 patients with Stage IV cancers (Colon and Cervical) were identified with distal small bowel obstructions (SBO) presumed secondary to carcinomatosis. Patients were deemed inoperable by prior evaluations. Patients were offered and underwent diagnostic laparoscopy and palliative laparoscopic ileostomy.

RESULTS: Both patients were found to have diffuse carcinomatosis, omental caking, and distal ileum obstruction due to tumor burden. Laparoscopic ileostomy was created in both pts with only three ports, one of which was converted to the stoma. Average operative time was 43 minutes, EBL < 10cc. Pre-op pain scores (Wong-Baker faces scale) ranged 3-7/10, post-op scores decreased to 0-2/10 within 24 hours: significant improvement in pain score ($p=0.003$). Both patients had return of bowel function via the stoma in 48 hrs, tolerated diet on POD#2, and were discharged home with a length of stay (LOS) of 4.2 days. Pt #1 lived 7 mos, Pt #2 lived 2.5 mos and created a video diary for her 2 yr old child to view in the future.

DISCUSSION: This is the first report of laparoscopic ileostomy creation for the management of malignant SBO. Although it represents a preliminary study, this technique follows the ACS ST-50 guidelines and represents a new role that we as surgeons must take the lead on. Palliative care surgery should become a part of our mission. Laparoscopic ileostomy for malignant SBO is feasible, and as seen with traditional laparoscopic procedures: decreases LOS, post-op pain, and postoperative ileus.

INTRATUMORAL NATURAL KILLER CELL AND LYMPHOCYTE INFILTRATION: IMPACT AND OUTCOMES FOR PANCREATIC ADENOCARCINOMA

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INTRODUCTION: Natural Killer (NK) cells and lymphocytes are involved in cancer immunosurveillance. The extent of intratumoral NK and lymphocyte infiltration has been shown to affect prognosis for gastric, colorectal, and ovarian cancer. We sought to determine if intratumoral NK or lymphocyte infiltration have prognostic significance for pancreatic adenocarcinoma.

METHODS: Tumors from 45 patients who underwent surgical resection for pancreatic cancer were analyzed. Immunohistochemistry was performed with CD-57, a monoclonal antibody, to assess NK infiltration. Slides were reviewed and classified as "high" NK infiltration ≥ 25 NK/HPF or "low" < 25 NK/HPF. Specimens were also reviewed for lymphocyte infiltration. "High" infiltration was classified as ≥ 150 lymphocytes/HPF and "low" as < 150 lymphocytes/HPF. Patient demographics, tumor characteristics, disease staging, and patient length of survival (LOS) were determined. Statistical analysis was performed using Student's T-test for comparison of means and regression analysis for correlations with significance of $p < 0.05$.

RESULTS: Of our 45 patients, 21 were female and 24 male, ages (40-81). By AJCC staging, Stage I (n=7), Stage II (n=8), Stage III (n=23), and Stage IV (n=7). LOS for all stages ranged 1-49 months. LOS (months \pm SEM) by stage was: Stage I- 20.5 \pm 7.5, II- 20.6 \pm 12.1, III- 12.2 \pm 2.1, IV- 8 \pm 3.7. LOS correlated well with tumor stage ($p = 0.04$), and tumor size ($p = 0.03$). As seen in Table 1- high levels of NK cell or lymphocyte infiltration did not statistically affect patient survival, or reduce tumor size. There was also no improvement in tumor stage or nodal metastases based on NK cell/lymphocyte infiltration.

CONCLUSION: There is evidence that intratumoral NK cell and lymphocyte infiltration can improve patient outcomes for some cancers. Based on our study, these cells do not improve any prognostic indicators we studied for pancreatic adenocarcinoma. The lack of impact of the innate and cellular immune systems on pancreatic cancer may highlight another reason why this tumor is so uniformly lethal and why recent IL-2 trials in pancreatic cancer yield limited benefit.

Table 1

	NK ≥ 25 /HPF	NK < 25	Lymph ≥ 150	Lymph < 150
LOS (months)	15.9 \pm 2.1 *	13.5 \pm 3.0 *	14.1 \pm 2.8 †	14.4 \pm 1.8 †
Tumor size (cm)	4.1 \pm 0.4	3.3 \pm 0.3	4.0 \pm 0.5	3.6 \pm 0.3
P value	* = 0.55		† = 0.54	

PRIMARY SQUAMOUS CELL CARCINOMA OF THE MAIN HEPATIC BILE DUCT

Rime Abbas,1 M.D., Joseph Willis, 2 M.D. F.A.C.P., Timothy Kinsella,3 M.D., Christopher Siegel,1 M.D. Ph.D., and Juan Sanabria,1 M.D. M.Sc. F.R.C.S.C. F.A.C.S. From the 1Department of Surgery, Division of Transplant and Hepatobiliary Surgery, the 2Department of Pathology and the 3Department of Radiation Oncology, Ireland Cancer Center, University Hospitals - Case Medical Center, Case Western Reserve University, Cleveland, OH.

Biliary malignancies represent less than 1% of all neoplastic processes in North America. The vast majority of them correspond to an adenocarcinoma type; only 2% of biliary neoplasms account for squamous cell origin. The case on hand may be the second presentation of a primary squamous cell carcinoma at the bifurcation level. We describe its clinical presentation, current forms of imaging modalities and additional recommended therapy to the surgical procedure. A 28-year-old Caucasian female was referred with 4 weeks history of continuous moderate RUQ pain associated with jaundice, weight loss (10kg over the last three months) and a liver mass at US. Pain sensation seemed different from previous colicky attacks the patient had experienced prior to a laparoscopic cholecystectomy she had 7 years ago. At physical examination she was obese (BMI=37.8) with icterus noted over the conjunctivae, oral mucosa and skin. Patient underwent exploratory laparotomy with intra-operative ultrasound revealing a 3.5 x 2.5cms cystic lesion within the central portion of the liver, anterior to the Porta Hepatis. Intra-operative cholangiogram demonstrated an extensive stricture obliterating the left hepatic duct with partial occlusion of the right hepatic duct. An extended left lobectomy en bloc with the biliary confluence was performed. At frozen section all margins were clear of malignancy. Reconstruction was performed with a Roux-Y cholangio-jejunostomy to three second radical bile ducts in the right side. Intra-operative radiotherapy was applied to the surgical margins. The patient completed treatment by 6 weeks of image guided external beam radiation centered at the resection field labeled at surgery. Final pathology described this tumor as infiltrating moderately differentiated squamous cell carcinoma associated with severe dysplasia of the bile duct epithelium. Patient recovered uneventfully and she is currently doing well 18 months from the initial surgical procedure with an unremarkable CT scan. We advocate primary surgical treatment with intra-operative radiation therapy of the resection margins followed by postoperative external radiation for the treatment of Squamous Cell carcinoma of the MHBD.

THE DEVELOPMENT OF A SWINE MODEL OF SECONDARY LIVER TUMORS FROM A GENETICALLY INDUCED SWINE FIBROBLASTS CELL LINE

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Swine models of secondary liver tumors may demonstrate to be an ideal model to study the efficacy of surgical and ablative treatment options available for liver tumors. The purpose of the present studies was to develop a secondary liver tumor in a large animal model. Fibroblasts from swine were isolated from ear lobule; cells then were transfected with amphotropic retroviruses encoded with human genetic (hTERT, p5300, cyclinD-1, CDK4R24C, Myc T58A, RASG12V) material. Transformed cell lines were inoculated into swine under tacrolimus based immunosuppression (n=4). Isolates from first pass were cultured and then inoculated as a second pass into 1) nude immunodeficient mice (n=5), 2) immune intact wild mice (n=2) and, 3) porcine animals without immunosuppression (n=2). Tumor growth was evident in 75% of immunosuppressed swines. One animal die with diarrhea and failure to thrive before the completion of experiment (3weeks). Growth of tumors was slow in two animals while in one animal tumor was larger with a peak growth of 42mm at three weeks. All growths showed to be malignant on histology. Cell morphology changed from initial cell line as compared with cell isolates after first pass. Tumor growth was evident in 100% of the nude immunodeficient mice with a peak size of 22mm (17+5mm, Mean+SD) at the time of sacrifice (3weeks). Tumor growth was evident in all wild mice with a peak size of 8.9mm at the end of the third week. Tumor growth in swine was characterized for slow growth with a peak size of 8mm at three weeks. Characterization of new mutations in cell lines after first pass is the matter of current studies. Further changes may produce a more rapid growth of genetically induced tumorigenic cells in the immune-intact swine.

DISCOVERY PROTEOMICS IN HUMAN COLORECTAL CANCERS

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Colorectal cancers (CRC) are the second leading cause of cancer and cancer death in adult Americans. A number of research efforts are ongoing trying to elucidate the cellular and molecular mechanism that causes the onset of CRC, and its progression through increasingly more severe pathological stages (0-IV). We are using a proteomics approach to further our understanding of the mechanistic cause of CRC, and to potentially identify biomarkers that indicate the stage, severity, and prognosis of the disease. A pathologic database at the Case Cancer Center contains matched (normal/tumor) tissue samples collected during surgery from an extensive variety of patients diagnosed with varying stages of CRC. As an initial attempt to use discovery proteomics to examine CRC, we obtained twelve matched tissue samples (normal/stage IV) and performed differential gel electrophoresis (2D-DIGE) to evaluate significant changes in the expression of proteins common to both the normal and diseased tissues. 58 spots are differentially expressed ($\pm 50\%$) between normal and cancer tissue with statistical significance ($p \leq 0.05$). These proteins have been identified by mass spectrometry, and the involved metabolic and cell signaling pathways will be reported. Such pathways may present new targets for adjuvant chemotherapy. Using the protein abundance values on the gels, a supervised learning technique is under development to train a support vector machine (SVM), which in turn could be used to classify an electrophoretic gel pattern as "cancer" or "no-cancer."

WHEN FINE-NEEDLE ASPIRATION BIOPSY CANNOT EXCLUDE PAPILLARY THYROID CANCER: A THERAPEUTIC DILEMMA

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HYPOTHESIS: Clinical or cytology factors predictive of malignancy can be identified and incorporated into a treatment algorithm for patients with a fine-needle aspiration biopsy (FNAB) specimen interpreted as "suspicious for" papillary thyroid cancer (PTC).

DESIGN: Retrospective review of a prospectively maintained database.

SETTING: University-affiliated tertiary care hospital.

PATIENTS: Seven hundred thirty-eight patients with nodular thyroid disease evaluated between 1990 and 2004.

INTERVENTIONS: Patients with a FNAB specimen suspicious for PTC were identified. The frequency of carcinoma was determined. Clinical features were reviewed. The FNAB specimens suspicious for PTC were examined in a blinded fashion to determine if specific cytologic features were important in distinguishing benign vs malignant disease.

MAIN OUTCOME MEASURES: The presence of specific clinical and cytologic features was correlated with the incidence of carcinoma. A secondary outcome measure was to determine the value of frozen section examination in establishing the extent of thyroidectomy.

RESULTS: Forty-five patients (7%) had an FNAB specimen suspicious for PTC; 18 (40%) of these patients had carcinoma. Prominent nuclear inclusions and/or grooves, papillary formations, and the absence of colloid were features associated with PTC ($P < .05$). No clinical features reliably identified malignant disease. Frozen section examination results altered treatment in 15 (56%) of 27 patients.

CONCLUSIONS: An FNAB specimen suspicious for PTC is associated with a 40% incidence of carcinoma. Extensive nuclear inclusions and/or grooves, papillary formations, and the absence of colloid are predictive of carcinoma. Rare intranuclear inclusions and/or grooves alone in an otherwise benign-appearing specimen are uniformly associated with benign disease. Frozen section examination is of value in determining the extent of thyroidectomy.

Section 8

**Transplantation and
Hepatobiliary Surgery**

TOWARDS INDIVIDUALIZED TREATMENT OF KIDNEY TRANSPLANT RECIPIENTS: PRETRANSPLANT ANTI DONOR CELLULAR IMMUNITY BY IFN- γ ELISPOT IDENTIFIES CANDIDATES THAT CAN MOST BENEFIT FROM INDUCTION THERAPY

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Indications for induction therapy in rena transplantation remain controversial and are often stratified by perceived immunologic risk. We hypothesized that measuring the strength of anti-donor cellular immunity pretransplant would identify a subgroup of patients who would benefit most from induction therapy. We analyzed outcomes of 131 consecutive kidney (n=119) and kidney-pancreas (KP) (n=12) recipients in which we performed pre-transplant, donor-reactive IFN-SPOT assays. Thirty-three of 131 (25%) were IFN-SPOT (+) (> 25 spots/300K pbIs). Acute rejection (AR) occurred in 33% of IFN-SPOT (+) vs. 13% of IFN-SPOT (-) patients (p=0.01), and IFN-SPOT (+) status remained a correlate for AR by multivariable analysis (odds ratio 4.8, p=0.02). We next analyzed the impact of induction therapy. Indications for induction included KP protocol (n=12), multicenter study protocol (n=9), or patients with either positive B cell flow crossmatch or previous transplant (n=12). Among IFN-SPOT (+) patients, 8 received induction therapy with antithymocyte globulin (ATG) (n=3) or basiliximab (n=5), while 25 IFN-SPOT (-) patients received induction with ATG (n=6) or basiliximab (n=19). Outcomes stratified by induction and IFN-SPOT status are shown below.

	Induction	No Induction	p Value
IFN-SPOT (+)	n=8	n=25	
AR, %	0	44	0.02
GFR 12 mos	65±22	39±17	0.001
IFN-SPOT (-)	n=25	n=73	
AR, %	16	12	ns
GFR 12 mos	53±23	53±17	ns

In 27 IFN-SPOT (+) patients who had subsequent postransplant IFN-SPOT analysis, conversion to IFN-SPOT (-) in the absence of AR occurred in 6/7 patients who received induction vs. 4/20 patients with no induction therapy (p=0.001).

CONCLUSIONS: In addition to providing an independent predictor of postransplant outcome, this observational study suggests that pretransplant assessment of donorreactive cellular immunity by IFN-SPOTs can identify patients who will most benefit from induction therapy. The findings support the need for a prospective randomized trial to address individualization of immunosuppression based on this functional measure of cellular immunity.

TIME ON HEMODIALYSIS INCREASES T CELL ALLOREACTIVITY MEASURED BY A DONOR-REACTIVE ELISPOT ASSAY FOR IFN- γ

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Duration of dialysis prior to kidney transplantation is an independent correlate of subsequent allograft failure, but mechanisms underlying this observation are unknown. We hypothesized that increasing time on dialysis enhances cellular alloimmune reactivity, potentially by increasing cumulative exposure to environmental antigens. To test this, we quantified anti-donor cellular immunity prior to transplantation by IFN- γ ELISPOT (IFN-SPOTS) and correlated the results with duration of dialysis in 111 renal transplant candidates (102 maintained on hemodialysis and 9 transplanted preemptively). A positive anti-donor ELISPOT was defined as ≥ 25 spots/300,000 recipient peripheral mononuclear blood cells. Because African Americans (AAs) generally exhibit higher rates of allure activity with this assay, results are stratified by ethnicity. Median time on dialysis was 15 months in non-AA patients vs 53 months in AAs ($p < 0.001$). There was a significant correlation between the number of IFN-SPOTS and time on dialysis ($r = 0.248$, $p = 0.009$). Median duration of dialysis was 24 months in 81 IFN-SPOT (-) patients vs 46 months in 30 IFN-SPOT (+) patients ($p = 0.003$). Only 1 of 9 patients transplanted preemptively was IFN-SPOT (+). Mean number of IFN-SPOTS and percentage of patients with (+) IFN-SPOTS in those on dialysis for less or more than 3 years are shown below:

Duration of Dialysis	< 3 years	≥ 3 years	p
All Patients	n=55	n=56	
Mean IFN-SPOTS	10 \pm 21	32 \pm 57	0.01
% IFN-SPOT (+)	13	41	<0.001
Non-AA Patients	n=37	n=20	
Mean IFN-SPOTS	10 \pm 23	41 \pm 76	0.03
% IFN-SPOT (+)	13	40	0.02
AA Patients	n=18	n=36	
Mean IFN-SPOTS	10 \pm 18	26 \pm 42	0.13
% IFN-SPOT (+)	11	42	0.02

Results of this analysis support the hypothesis that donor-reactive cellular alloimmunity increases with time on dialysis, possibly accounting for the observed correlation between lower graft survival with increased duration of dialysis. The phenomenon is observed in both AA and non-AA patients, suggesting that T cell reactivity is more closely associated with duration of dialysis than with ethnicity. Whether the findings are due to repeated specific environmental exposures and/or to enhanced immunity from prolonged dialysis itself will require further study.

THE NATIONAL OPTN POLICY FOR SHARING OF ALL ZERO ANTIGEN MISMATCHED (OMM) KIDNEYS: ANALYSIS OF ALLOCATION OUTCOMES

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Mandatory national sharing of 6 antigen matched (1987) and OMM (1995) kidneys has been a key component of OPTN allocation policy. OPOs accepting a OMM kidney incur a debt and are required to payback (PB) a kidney to the national pool. This study analyzed the distribution of deceased donor (DD) kidneys and its effect on the distribution to candidates (CAND) on the wait list (WL).

METHODS: All DD kidney alone transplants (Tx) during 2003-2004 were included. Txs were grouped by allocation type: OMM (n=2611), PB (n=724) or Points (n=14,082) (allocated by the standard OPTN points system) and stratified by donor and recipient characteristics. DD were categorized as standard (SCD), expanded (ECD) and donation after cardiac death (DCD) by OPTN criteria.

RESULTS: 2611 (14.1%) of all DDTx were OMM, of which 2260 (86.6%) were shared with another OPO. Because a PB debt is repaid by shipping a OMM kidney, only 4.2% were returned as PB to the national pool. Points kidneys were primarily Tx locally.

	SCD	DD White	Recip White	Recip AA	PRA <20%	PRA >20%	Wait Time >3yrs
OMM	90.7%	80.4%	69.9%	10.9%	64.1%	14.2%	11.8%
PB	96.5%	62.0%	45.2%	34.3%	79.7%	7.7%	18.6%
Points	76.5%	69.9%	44.9%	33.2%	77.9%	7.5%	31.6%

The distribution of ethnicity among points and PB kidney recipients approximates the ethnicity of WL CAND (40% white and 34.5% black(AA)). However, OMM kidneys are distributed to white recipients at a nearly 7:1 ratio compared to AA. Highly sensitized (PRA>80%) CAND are Tx twice as frequently with OMM kidneys indicating a benefit of the national share to this group (p<0.0001). Allocation of 14.1% of all DD kidneys, 90.7% from SCD (17.1% of all SCD donors) disproportionately to white CAND while 86% of kidneys are Tx by points allocation (with a lower proportion of SCD kidneys), places AA WL CAND at a potential disadvantage. Additionally, 49.8% of OMM recipients were Tx with <1 year of wait time.

CONCLUSION: The OMM sharing policy succeeds in providing kidneys for highly sensitized recipients but also results in the preferential Tx of white CAND with better quality kidneys and shorter wait times. This may partially account for the longer wait times and poorer graft survival seen in AA recipients. Based on these data, the OMM sharing algorithm should be reevaluated to optimize benefit to all CAND.

SURVIVAL AND FUNCTION OF ZERO ANTIGEN MISMATCHED (OMM) KIDNEYS: IS HLA THE PRIMARY DETERMINANT?

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Mandatory national sharing of 6 antigen matched donor kidneys has been an OPTN policy since the inception of UNOS. The policy was subsequently amended to include the mandatory sharing of OMM kidneys and the payback (PB) of a kidney to the national pool. This was justified by the improved graft survival (GS) in the OMM recipients. With the continuing improvement in graft outcomes, it has been proposed that the degree of HLA match is not as important a factor in GS as it once was. Recent reports have also shown that graft function at 1 year portends long term graft survival.

METHODS: All deceased donor kidney alone transplants during 2003-2004 were included in the study. Transplants were grouped based on allocation type: OMM (n=2611), PB (n=724) or Points (n=14,082) (allocated by the standard OPTN points system) and donor type: standard (SCD), expanded (ECD) and donation after cardiac death (DCD). Kaplan Meier GS rates and median serum creatinine Cr at 6 and 12 months were calculated for each group. The logrank test was used to compare survival rates, the Wilcoxon test was used to compare Cr, and cold ischemic time (CIT) was compared using the chi-square test.

RESULTS:

	Donor SCD	GS 6 mo	GS 12 mo	GS 24 mo	Median Cr 6 mo	Median Cr 12 mo	CIT >24hr
OMM n=2611	90.7%	95.0%	92.4%	86.9%	1.3	1.3	29.9%
PB n=724	96.5%	94.0%	91.9%	87.0%	1.3	1.3	51.7%
Points n=14082	76.5%	91.8%	88.7%	82.1%	1.4	1.4	22.0%

The 12 month median Cr ($p=0.13$) and GS rates ($p=0.31$) were not statistically different between the OMM and the PB kidney recipients despite the fact that 77.3% of the PB recipients had 4 or greater HLA antigens MM (comparable to the 77.7% of the points recipients with 4-6 HLA MM). The points kidneys included 17.6% from ECD donors and 5.9% from DCD donors (compared to 6.2% ECD and 3.1% DCD for OMM recipients and 1.9% ECD and 1.5% DCD for PB recipients). Additionally, PB kidneys had a significantly higher percentage of organs with a CIT > 24 hours compared to the OMM kidneys ($p<0.001$).

CONCLUSION: The similar outcomes of OMM and PB kidneys (despite the poor match level of PB kidneys) compared to the relatively poorer outcomes of points kidneys seem to be more a result of the quality of the donor organ (SCD) than the degree of HLA match. A reevaluation of the mandatory share policy of all OMM kidney may be necessary to define which recipient populations (e.g. highly sensitized) may achieve the most benefit.

PROGRESS IN ESTABLISHMENT OF A NATIONAL PAIRED DONATION NETWORK IN THE UNITED STATES

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Recent modeling studies and clinical experiences with paired kidney donation have indicated that large regional paired donation programs (PDPs) are necessary to enroll the substantial numbers of donor/recipient pairs needed for effective matching. The purpose of this report is to describe experience with regional PDP establishment and the progress in linking these PDPs in a national paired donation network in the United States.

METHODS: A complete package was developed for establishing and linking regional PDPs. Regional PDPs were established by first identifying level of interest amongst kidney transplant program leaders in PDPs. An informational presentation was made to program leaders that described the paired donation process and PDP development package (web-based matching software, patient educational brochures, policy and procedure manual, educational web pages). If substantial interest existed amongst program leaders, an organizational meeting was held. A few weeks later, a training meeting was conducted for transplant program personnel. A conference call was held for program leaders and a formal vote taken to form a regional PDP. Matching software websites were activated, patients enrolled, and match runs conducted.

RESULTS: To date, 7 regions have had initial presentations, 6 have held organizational meetings, and four have held educational meetings. Four regions have voted to form regional PDPs, and two have registered patients, conducted match runs, and transplanted patients. The four regions that have formed PDPs include 77 kidney transplant programs in 18 states (population exceeding 163,000,000). Progress in establishment of regional PDPs is outlined in the table.

	States Represented	#Kidney Tx Programs	Informational Presentation	Organizational Meeting Held	Educational Meeting Held	Voted to Establish PDP	Pts Enrolled/ Match Run Conducted
Paired Donation Consortium	OH, MI, IN, KY, WV, PA, NY, IL, WI	30	Yes	Yes	Yes	Yes	Yes
New Jersey PDC	NJ	6	Yes	Yes	Yes	Yes	Yes
Southeast PDC	FL, ALA, GA, SC	20	Yes	Yes	Yes	Yes	
Southwest PDC	TX, OK, ARK, LA	21	Yes	Yes	Yes	Yes	
Great Plains	KA, MO, IA, NEB		Yes	Yes			
Northern California	CA		Yes	Yes			
Southern California	CA		Yes				
Totals	18	77	6 presentations	5 PDP org mtgs	4 PDP educ mtgs	4 regional PDP votes	2 PDPs with match runs

CONCLUSIONS: In conclusion, considerable progress has been made in establishing a national paired donation network. For the first time, two large regional PDPs have been established using identical matching software and programmatic rules.

NETWORKING OF REGIONAL PAIRED DONATION PROGRAMS: A STEP TOWARD NATIONALIZATION

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Modeling studies and clinical experience with paired donation (PD) have demonstrated that large numbers of donor/recipient (D/R) pairs are needed to achieve effective matching. A primary strategy for generating large pools of D/R pairs is to create large multicenter paired donation programs (PDPs). A nationalized PD system in the US will likely consist of several regional PDPs. Herein we describe establishment of two multicenter regional PDPs that utilize a common protocol and computer matching software, and matching results.

METHODS: An inexpensive, easily portable set of instruments for establishing new PDPs were created (policy/procedure manual, web-based computer matching software, pt education brochures). Two large multicenter, regional PDPs were created using these instruments. D/R pairs were registered, and computer match runs generated immunologically feasible matches (ABO compatible matches that did not involve transplantation of unacceptable HLA antigens).

RESULTS:

	PDN Total	PDP One	PDP Two	p value
# Transplant Centers	36	30	6	
# States	11	10	1	
Population served	91,600,000	83,000,000	8,600,000	
# D/R pairs registered	108	83	36	
# Match runs conducted	17	16	1	
# Immunologically feasible matches	41	40	1	
# Pts transplanted	14	12	2	
# Transplants pending	4	4	0	
Characteristics of Registered Pts				
% Male	48	49	45	NS
% Caucasian	80	88	47	0.0001
% African American	11	8	19	NS
% Other race	14	4	34	0.0001
% O BG	56	51	64	NS
% A BG	26	28	20	NS
% B BG	16	15	16	NS
% with PRA 0-10	33	33	34	NS
% with PRA 11-49	13	16	6	NS
% with PRA 50-100	53	50	60	NS

The second PDP was created and a paired donation completed in 8 mos. Pt registration and match results from the 2 PDPs are presented in the table.

CONCLUSIONS: This experience demonstrates substantial similarities in blood group and PRA distributions between the two PDPs, with the only significant difference being racial distribution. This experience demonstrates that: 1) PDPs can be established rapidly using pre-developed tools and web-based computer matching, and 2) large pools of D/R pairs can be generated using this approach. This experience represents the first linkage of large, multicenter PDPs and the first multiregional PD network. This accomplishment is an important step toward creation of a nationalized PD network.

MULTIPLE DONOR REGISTRATIONS FOR INDIVIDUAL RECIPIENTS IN PAIRED DONATION PROGRAMS: INCIDENCE, TRANSPLANT RATES, AND NEED FOR EDUCATION

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Modeling and clinical experiences have indicated that O blood group and high PRA recipients will be disadvantaged in their matching opportunities in paired donation programs (PDPs). One strategy for increasing transplant rates in these patients is to allow registration with multiple recipients. The purpose of this study was to analyze match rates in a multicenter paired donation program for recipients registered with single or with multiple donors.

METHODS: Computer-based matching was employed in a multicenter paired donation program. The matching software was coded to allow registration of recipients with one or more donors. Recipients with multiple donors were entered and treated as unique donor/recipient (D/R) pairs by the matching software. Transplant centers were encouraged to list patients with multiple donors whenever possible to enhance matching probability.

RESULTS: A total of 83 D/R pairs were entered for 72 recipients over a 22 month period from 9 individual transplant programs. Of these 72 recipients, 2 (2.7%) were listed with three potential donors, 7 (9.8%) with 2 potential donors, and 63 (87.5%) with one potential donor. Demographic comparisons and transplant rates for recipients registered with multiple or single donors are presented in the table.

	Recipients with Multiple Donors	Recipients with One Donor	p value
# Recipients	9	63	
% of registered recips	12.5	87.5	
Female (% of recips)	67	55	NS
Caucasian (% of recips)	100	89	NS
O blood group(% of recips)	55	51	NS
A blood group (%of recips)	33	30	NS
B blood group (% of recips)	11	16.6	NS
PRA 0-10 (% of recips)	0	38	0.02
PRA 11-49 (% of recips)	11	17.5	NS
PRA 50-100 (% of recips)	89	44.4	0.01
% Transplanted	22	15.9	NS

CONCLUSIONS: These data indicate that: 1) multiple donor registration rates in PDP are relatively low (12.5%), 2) match rates were numerically, but not statistically higher for recipients registered with multiple donors, 3) O blood group recipients were not listed with a higher proportion of multiple donors, but 4) high PRA recipients were listed with a higher proportion of multiple donors. This experience emphasizes the need for improved educational approaches for paired donation participants and transplant professionals about the benefits of multiple donor registrations in PDPs, especially amongst O blood group recipients.

INABILITY TO PREDICT POSITIVE CROSS-MATCHES UNDERSCORES THE NEED FOR HISTOCOMPATIBILITY EXPERTISE IN PAIRED DONATION PROGRAMS (PDP)

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BACKGROUND: Paired donation has the potential to increase transplantation rates for patients with ABO or cross-match(XM) incompatibility with a living donor. In an 18 month period, 40 feasible paired donations were defined using computer-based matching. The outcome of the XM testing and final evaluations of these screened matches were examined.

METHODS: Data regarding HLA and unacceptable HLA antigens were entered for each donor and recipient. The computer based matching algorithm first considered all possible donor recipient combinations and excluded all matches that were ABO incompatible or involved unacceptable HLA antigens. All XMs were performed at recipient transplant centers using each center's cross matching techniques.

RESULTS: 40 feasible matches were identified. 19 feasible matched pairs were referred for cross-match testing (XM). 11 matched pairs (58%) had negative XMs and were referred for final evaluations. 8 matched pairs had a +XM (42%) and were returned to the pool (4 matches(21%) had 1 pair with a +XM, 4 matches(21%) had both pairs with a +XM). Mean PRA of the negative XM pairs is 23%, while the mean PRA of the +XM pairs was 54%. There were 4 matches excluded during the final evaluation process, 2 due to patient withdrawal, 2 due to interval development of medical problems prohibiting transplantation. 6 paired donations were completed for a total of 12 transplants. 1 transplant is pending final evaluation.

CONCLUSION: Our initial 18 month experience shows that while 58% of matching pairs had mutually negative XMs, 42% had +XMs. Furthermore 36% of negative XM pairs did not culminate in transplants owing to patient withdrawal or final stage medical exclusion. This high rate of exclusion will disrupt optimized match results. Enhanced ability to predict cross-matching would greatly facilitate the logistics of PDPs. This underscores the need for histocompatibility expertise within PDPs.

EXPECTATIONS FOR SUCCESSFUL MATCHING IN A PAIRED DONATION CONSORTIUM (PDC): EFFECT OF ABO AND SENSITIZATION.

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The PDC originated as an Ohio consortium of 9 transplant programs and the first PDC transplant (TX) was in late 2004. It is now a database of immunologically incompatible donor recipient (D/R) pairs available to 23 transplant programs in 7 states. Match runs are performed every 8 weeks with the results discussed by representatives of each participating program. This study evaluated our immunologically compatible match (ICM) and transplant rates to define the expectations each D/R pair can have for a success. Methods: All immunologically incompatible D/R pairs (by ABO or + crossmatch) entered into the database were available for study and were stratified by D/R characteristics. Results: Of 83 registered pairs, 42 (50.6%) have been included in an ICM. Of these, 12 patients (28.6%) have undergone successful TX. A patient may be included in >1 ICM on any given run. Allocations are approved on a total points basis, the D/R pairs receiving the most points are preferentially evaluated, and if not suitable, the allocation would pass to the next ICM.

	Recip A	Recip B	Recip O	Donor A	Donor B	Donor O	PRA >50%
Registered (83)	28 (34%)	13 (16%)	42 (51%)	38 (46%)	11 (13%)	30 (36%)	46 (55%)
ICM (42)	20 (48%)	8 (19%)	14 (33%)	18 (43%)	8 (19%)	16 (38%)	19 (45%)
Transplant (12)*	6 (50%)	2 (17%)	4 (33%)	4 (33%)	2 (17%)	6 (50%)	4 (33%)

DECREASED ALBUMIN EXCRETION AFTER CONVERSION FROM SIROLIMUS TO ENTERIC-COATED MYCOPHENOLIC SODIUM IN PATIENTS MAINTAINED ON CNI THERAPY

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Recent cases of proteinuria have been reported in conjunction with sirolimus (SRL) therapy in kidney transplant recipients, often after conversion from CNIs. The pathophysiology of such proteinuria is poorly understood. In an ongoing study, we investigated the mechanism of SRL-related proteinuria. Glomerular and tubular proteins were measured in the urine before and after conversion from SRL to enteric-coated mycophenolic sodium (EC-MPS). Three month follow-up data is available in 9 kidney transplant recipients who converted at a median of 16 months post-transplant (range 4-59 months). EC-MPS was initiated at 720 mg BID in all patients after abrupt discontinuation of SRL. All patients remained on tacrolimus and prednisone. Four of 9 were on angiotensin blocking agents, but there was no change in dosage during the study interval, and blood pressure regimen in general was not altered during the study. Pre-conversion, the median level of spot urine albumin/creatinine ratio (ACR) was 52 $\mu\text{g}/\text{mg}$ (range 17-508). Four patients had microalbuminuria (30-300 $\mu\text{g}/\text{mg}$), and two had overt proteinuria ($> 300 \mu\text{g}/\text{mg}$). Post-conversion, median ACR fell to 23 $\mu\text{g}/\text{mg}$ (range 5-211), ($p=0.025$ by Wilcoxon test). ACR fell into the normal range in three patients with previous microalbuminuria, and fell to levels consistent with microalbuminuria in the two patients with previous overt proteinuria. To directly assess tubular dysfunction, we measured the ratio of N-acetyl-beta-D-glucosaminidase (NAG) to creatinine in the urine. This ratio trended downward from pre-conversion (7.1 U/g, range 2.8-23.9 U/g) to post-conversion (4.3 U/g, range 1.3-12.3 U/g), ($p=0.08$), and fell in 7/9 patients. We also measured alpha 1-microglobulin (A1M), a marker of tubular proteinuria. In patients with abnormal ACR, median A1M:creatinine was 20.2 $\mu\text{g}/\text{mg}$ (range 3-92) pre-conversion, and 7.6 $\mu\text{g}/\text{mg}$ (range 2-33) post-conversion ($p=0.12$). Conclusion: Preliminary results from this ongoing study demonstrate that conversion from SRL to EC-MPS is associated with reduced ACR in the face of stable therapy with tacrolimus. Urinary markers of tubular injury and tubular proteinuria also tended to drop after conversion. These results suggest that SRL increases urinary albumin excretion, perhaps secondary to a defect in tubular reabsorption of filtered protein.

DECREASED ERYTHROPOIETIN RESISTANCE AFTER CONVERSION FROM SIROLIMUS TO ENTERIC-COATED MYCOPHENOLATE SODIUM

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Blockade of p70S6 kinase activity by mTOR inhibitors may inhibit the actions of erythropoietin (EPO) and lead to EPO resistance and anemia. We previously reported that anemia was more frequent and more severe in sirolimus-treated kidney transplant recipients than in those receiving mycophenolate mofetil-based immunosuppression. In an ongoing study, we are testing the hypothesis that conversion from sirolimus to enteric-coated mycophenolate sodium (EC-MPS) will result in decreased EPO resistance (as measured by serum EPO/hemoglobin ratio) and increased concentrations of hemoglobin. Three month follow-up data is available in 9 kidney transplant recipients who were converted from sirolimus to EC-MPS 23+19 months posttransplant (range 4-59 months) because of intractable edema (n=6), rising serum creatinine (n=2), or severe hyperlipidemia (n=1). None of the patients was selected for conversion based on anemia per se. All patients remained on concomitant, unchanged doses of tacrolimus and prednisone. Four of 9 patients were receiving angiotensin inhibitors but doses were not changed during the 3 month follow-up period. At the time of conversion, mean sirolimus dose and trough blood level were 3.4+1.7 mg/day and 10.5+2.2 ng/ml, respectively. EC-MPS was initiated at 720 mg BID in all patients after abrupt discontinuation of sirolimus. The dose of EC-MPS remained unchanged after 3 months in each patient. Only 1 of 9 patients was receiving exogenous EPO at the time of enrollment. After 3 months, hemoglobin concentrations increased in 8 of 9 patients. The sole patient receiving exogenous EPO was weaned off the agent at last follow-up. Mean data for hemoglobin and other parameters are shown below:

	Baseline	3 month follow-up	p
Hemoglobin (gm/dl)	11.1±1.5	12.8±1.5	0.004
Serum EPO (mIU/ml)*	27.2±13.4	16.7±7.6	0.05
EPO/hemoglobin ratio*	2.5±1.4	1.3±.05	<0.001
Serum creatinine (mg/dl)	1.61±.43	1.65±.52	NS

*excluding patient receiving exogenous EPO

Preliminary results from this ongoing study suggest that sirolimus induces a state of EPO resistance. Conversion from sirolimus to EC-MPS reduces EPO resistance and leads to increased erythropoiesis and increased concentrations of hemoglobin in kidney transplant recipients.

A TWO YEAR EXPERIENCE WITH A REGIONAL, MULTICENTER PAIRED DONATION PROGRAM

E Steve Woodle, David Goldfarb, Mark Aeder, Michael Rees, Tanmay Lal, for the Paired Donation Consortium

The future of paired donation programs (PDPs) is based on development of large regional consortia and computer-based matching programs. Actual clinical experience with computer-based matching is essential to provide data necessary to properly develop paired donation policies. A two year experience with computer based matching in a large PDP is reported.

METHODS: A web-based computer matching algorithm was created to facilitate patient registration and matching for a regional PDP. Computer match runs were performed monthly for 14 months, then every other month. ABO blood group and unacceptable HLA antigens were entered for each recipient. All potential 2 pair matches were first screened by the computer matching program to assure ABO blood group compatibility, and in a second step, to assure that unacceptable HLA antigen barriers were not violated. These screened 2 pair matches are termed "feasible matches". Feasible matches then underwent crossmatching and final medical evaluations prior to transplantation.

RESULTS: 83 donor/recipient (D/R) pairs were registered, with 42 feasible matches were generated and 12 pairs transplanted (14%). The computer match runs generated a total of 3487 potential 2 pair matches, of which 3393 (97.3%) were excluded because they violated ABO or HLA barriers: 2463 (70.6%) matches for ABO incompatibility, and 930 (26.7%) for unacceptable HLA barriers. 54 (1.5%) matches were excluded for other reasons, usually because a D/R pair was already involved in another tentative match. Of the 40 feasible matches, 19 (47.5%) were referred for crossmatching: 8 (20%) were excluded for positive crossmatches, 7 (17.5%) had negative crossmatches (6 underwent paired donation, and 1 is awaiting paired donation), and 2 are pending final crossmatches. 21 matches (52.5%) were excluded for medical reasons or because the matches involved a pair who were transplanted in another paired donation. The 83 pairs were entered by a total of 9 transplant centers.

CONCLUSIONS: 1) Paired donation programs require entry of a substantial number of D/R pairs in order to achieve matching and subsequent paired donation, 2) the great majority (97.3%) of potential 2 pair matches are excluded due to unacceptable ABO and HLA barriers, 3) actual transplantation rates may be smaller than predicted by proposed models, and 4) positive crossmatches and mutual exclusions are the most common reasons that preclude feasible matches from going on to paired donation.

A CLINICALLY PROVEN, WEB-BASED, KIDNEY PAIRED DONATION REGISTRY

Michael A Rees, E Steve Woodle, Jonathan Kopke, Audrey B Bohnengel, Alan R Rees, Annette Blair, Mitchell L Henry, David A Goldfarb, Jens Goebel, Scott Johnson, Tanmay Lal, Mark I Aeder. Paired Donation Consortium; Institute for the Study of Health, University of Cincinnati; Ohio Solid Organ Transplantation Consortium; Anchor Enterprises, Atlanta, GA; Medical University of Ohio

To be effective, paired donation (PD) programs must draw from a large collection of patients. As the number of pairs increases, the number of possible donor/recipient (D/R) pair combinations increases exponentially. Therefore, several transplant (Tx) programs pooled their efforts to create a web-based PD registry with a computerized matching algorithm.

METHODS: A prototype computer matching program was developed using Visual Basic to provide a ranked list of all potential D/R pair matches in an algorithm analogous but distinct from the UNOS system for cadaveric kidney allocation. This approach was further developed in ColdFusion into a web-based system and the underlying database was stored in Oracle. Data is shared securely over the internet by each Tx center. The program assigns points for each potential match of two D/R pairs based on the following parameters: D/R wait time, distance between D and R hospitals, age disparity of proposed D and R, age disparity of donors, pediatric bonus, HLA mismatch, PRA, and CMV/EBV mismatch. Pairs are excluded based on blood type or known HLA incompatibilities in sensitized recipients. The program limits access to the data based on permission encoded into each login ID and mandates strict adherence to a mutually agreed upon policies and procedures manual. Final identification of suitable pairs is determined by a medical review committee composed of members from each Tx center. Suitable matches that subsequently fail (positive crossmatch, etc.), returning the involved D/R pairs to the pool, are excluded on future match runs.

RESULTS: A web-based software package was developed that has been successfully used to support a clinical PD program since March 2004. As of September 2005, 68 pairs had been registered, among whom the computer program has identified 36 immunologically feasible matches. Six of these matches have successfully completed the entire PD process, resulting in 12 (18%) living donor kidney transplants.

CONCLUSIONS: The computer system described here represents the first large-scale trial of a web-based registry to match immunologically incompatible D/R pairs in a kidney PD program. This approach overcomes many issues of equity in the matching of D/R pairs.

SEQUENTIAL STEROID-FREE, CALCINEURIN INHIBITOR-FREE IMMUNOSUPPRESSION AFTER KIDNEY TRANSPLANTATION: OUTCOMES AND BARRIERS

Padiyar A, Augustine JJ, Bodziak KA, Siegel C, Sanabria J, Aeder M, Schulak JA, Hricik DE

Steroids (STR) and calcineurin inhibitors (CNIs) exhibit many toxicities that have prompted withdrawal trials. Since 1/06, we have treated kidney transplant recipients (KTRs) with a protocol consisting of induction antibody therapy (rabbit ATG for deceased-, basiliximab for live-donor KTRs) and initial STR, tacrolimus (FK, target levels 8-10 ng/ml), and mycophenolate mofetil (MMF, 2 gm/d). STR are stopped on day 5, sirolimus (SLR) started on day 60, and FK stopped once SLR levels are 8-12 ng/ml. 50 KTRs (age 50±24; 24 females; 28 blacks; 30 live donor) have been enrolled. 3 early graft losses resulted from thrombosis (n=2) or death (n=1). Of the remaining 47 KTRs, 32 (68%) were withdrawn from STR. Reasons for not withdrawing STR included delayed graft function (DGF) (n=9), MMF intolerance (n=2), prior transplant (n=3), and prior STR therapy (n=1). Acute rejection (AR) occurred after STR withdrawal in 5 of 47 KTRs (11%). 10 KTRs are awaiting FK to SLR conversion. 23 of the remaining 37 KTRs have been converted. Timing of conversion was 91±39 days and was postponed most often because of leukopenia. In 14 KTRs, conversion was postponed indefinitely because of AR (n=4), leukopenia/anemia (n=3), wound healing problems (n=3), noncompliance (n=2), or AR in prior transplants (n=2). 4 of 23 KTRs were converted back from SLR to FK for AR (n=1) or SLR side effects (n=3). To date, 18 of 37 KTRs (49%) completing the protocol remain STR-free and CNI-free. Comparison of parameters before and 1 month after FK to SLR conversion indicate trends toward increased urine protein/creatinine ratio (.236±.12 to .417±.31; p=0.16) and increased GFR (62±14 to 65±17 ml/min; p=0.35). WBC (4,400±1700 to 3,700±1100 /mm³; p=0.031) and MMF dose (1.64±.5 to 1.44±.61 gm/d; p=0.027) decreased significantly. Our early experience indicates that STR-free, CNI-free immunosuppression can be achieved in KTRs treated with induction antibodies and maintained on SLR and MMF, with low rates of AR and good short-term graft function. However, DGF, AR, leukopenia/anemia and other side effects of SLR often prevent successful completion of the protocol. Long-term studies are needed to determine whether elimination of CNIs and MMF dose reductions driven by leukopenia/anemia will influence graft function and survival.

METHOXYPOLYETHYLENE GLYCOL MODIFIED-ALBUMIN (PEG-Alb) ENHANCED THE COLD PRESERVATION PROPERTIES OF UW SOLUTION IN RAT LIVER GRAFTS

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Liver grafts preserved in cold undergo changes mainly manifested by morphological changes of the sinusoidal endothelium. Swollen and fragmented cytoplasm translates into poor portal blood flow, increase release of liver enzymes and low bile production upon liver reperfusion. Studies were performed to determine if the addition of higher molecular weight polyethylene glycol modified albumin to the University of Wisconsin (UW) preservation solution ameliorates the cold preservation injury of liver grafts. Methoxypolyethylene glycol 5000 activated with cyanuric chloride was covalently coupled to human albumin (Peg-Alb) at multiple sites. The Isolated Perfused Rat Liver model was used (IPRL). Human and Rat hepatocytes cell lines were preserved in cold under similar preservation solutions. Effects were studied after rewarming of cells on Glutathione turn over by mass spectrometry. Apoptosis of SLC's on liver tissue and cell lines were evaluated by Tunel assay and flowcytometer techniques.

Table 1. IPRL results of grafts preserved with UW solution and UW solution plus PEG- Alb. Values are given after 60minutes of perfusion with a sanguineous perfusate.

Group (n=4) *(preservation time in hours)	Portal Blood flow ml/g of liver/minute	AST Units/g of liver	Bile production l/g of liver
Control neg UW *(1h) Mean±SD	0.93±0.033**	2.1±1.08*	10.5±5.97
Control pos UW *(30h)	0.19±0.010	14.4±0.34	0±0
PEG-Alb & UW *(30h)	0.98±0.005**	28.4±1.03	3.5±7.54
Alb & UW *(30h)	0.05±0.007	26.9±2.45	0±0

** p<0.05 by ANOVA

Preliminary results showed Glutathione turnover was significantly decreased in all groups compared to negative controls. In contrast, apoptosis of SLC was similar in the PEG-Alb group when compared to the negative control group but significantly decreased in the PEG-Alb group when compared to other groups.

CONCLUSIONS: The addition of high molecular albumin to UW preservation solution appears to ameliorate endothelial injury of cold preserved liver grafts as judged by better portal vein blood flow, increased bile production and decreased SLC apoptosis. PEG-Alb appears to have no effect on hepatocytes preservation.

ESTABLISHMENT OF A NATIONALIZED, MULTIREGIONAL PAIRED DONATION NETWORK

Woodle ES, Goldfarb D, Aeder M, Lal T, Rike A, Weimert N, Waterman A.

Over the past few years, significant progress has been made in the science and development of paired donation. With increasing awareness of paired donation and ready availability of the tools necessary to establish new consortia, paired donation can be made available to transplant programs and patients with increasing alacrity. Increasing registration of recipients and their donors for paired donation will lead to larger pools for matching and to transplantation of increasing numbers of patients via paired donation. As paired donation becomes common practice throughout the US and the international transplant community, its role in facilitating transplantation of sensitized patients will be better defined. Presently, paired donation remains an attractive alternative to desensitization and wait list paired donation for a majority of patients with preexisting humoral immunity to their donors.

HEMODIALYSIS VINTAGE, BLACK ETHNICITY, AND PRETRANSPLANTATION ANTIDONOR CELLULAR IMMUNITY IN KIDNEY TRANSPLANT RECIPIENTS

Augustine JJ, Poggio ED, Clemente M, Aeder MI, Bodziak KA, Schulak JA, Heeger PS, Hricik DE.

Prolonged exposure to dialysis before transplantation and black ethnicity are known risk factors for acute rejection and graft loss in kidney transplant recipients. Because the strength of the primed antidonor T cell repertoire before transplantation also is associated with rejection and graft dysfunction, this study sought to determine whether hemodialysis (HD) vintage and/or black ethnicity affected donor-directed T cell immunity. An enzyme-linked immunosorbent spot (ELISPOT) assay was used to measure the frequency of peripheral T cells that expressed IFN-gamma in response to donor stimulator cells before transplantation in 100 kidney recipients. Acute rejection occurred in 38% of ELISPOT (+) patients versus 14% of ELISPOT (-) patients ($P = 0.008$). The median (HD) vintage was 46 mo (0 to 125 mo) in ELISPOT (+) patients versus 24 mo (0 to 276 mo) in ELISPOT (-) patients ($P = 0.009$). Black recipients had a greater median HD vintage (55 versus 14 mo in nonblack recipients; $P < 0.001$). Black recipients with less HD exposure had a low incidence of an ELISPOT (+) test, similar to nonblack recipients. Among variables examined, only HD vintage remained a significant positive correlate with an ELISPOT (+) result (odds ratio per year of HD 1.3; $P = 0.003$). These data suggest that the risk for developing cross-reactive antidonor T cell immunity increases with longer HD vintage, providing an explanation for the previously observed relationship between increased dialysis exposure and worse posttransplantation outcome. Longer HD vintage may also explain the increased T cell alloreactivity that previously was observed in black kidney recipients.

LONG-TERM GRAFT OUTCOMES AFTER STEROID WITHDRAWAL IN AFRICAN AMERICAN KIDNEY TRANSPLANT RECIPIENTS RECEIVING SIROLIMUS AND TACROLIMUS

Hricik, DE, Augustine JJ, Knauss TC, Bodziak KA, Aeder M, Siegel C, Schulak JA

BACKGROUND: We previously reported excellent short-term outcomes in African American kidney transplant patients receiving tacrolimus/sirolimus and withdrawn from corticosteroid therapy three months after transplantation. We now report the long-term outcomes of patients subjected to this protocol.

METHODS: In all, 47 African American kidney transplant recipients were enrolled in an uncontrolled trial in which they were initially treated with sirolimus, tacrolimus, and corticosteroids, without antibody induction therapy. Eligible patients were withdrawn from prednisone between three and five months posttransplant, and followed for acute rejection and changes in renal function. Outcomes (group 1, n=32) were compared to those of patients deemed not to be candidates for steroid withdrawal (group 2, n=15).

RESULTS: After a mean follow-up of 48.5 months, 13 of 32 patients (41%) in group 1 developed acute rejection; only 13 patients (41%) remain steroid-free. Nine of 13 rejection episodes were associated with noncompliance. Graft loss occurred in 8 of 32 patients (25%) in group 1 and in 5 of 15 patients (33%) in group 2 (P=NS). Serum creatinine rose from 1.4+/-0.41 to 2.45+/-1.7 mg/dL in group 1 (P=0.004) and from 2.1+/-0.45 to 2.62+/-1.2 mg/dL (P=NS) in group 2. Among 13 patients in group 1 who remain steroid-free, creatinine concentration has risen from 1.28+/-0.37 prior to steroid withdrawal to 1.64+0.54 at last follow-up (P=0.027).

CONCLUSIONS: Late noncompliance and/or rejection in African Americans withdrawn from steroids have a negative impact on long-term graft function and survival. Steroid withdrawal may be associated with long-term deterioration of renal function, even in the absence of overt acute rejection.

SUCCESSFUL RENAL TRANSPLANTATION DESPITE LOW LEVELS OF DONOR-SPECIFIC HLA CLASS I ANTIBODY WITHOUT IVIg OR PLASMAPHERESIS

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We prospectively transplanted 10 primary kidney recipients with deceased donor organs (nine kidney and one pancreas/kidney) when their flow cytometric T-cell IgG, HLA class I donor-specific crossmatch was positive but the AHG T-cell crossmatch was negative, with a median follow-up of 1.8 yr. No pre- or peri-operative IVIg or plasmapheresis was administered to any patient. All but one of the 11 organs transplanted into patients with a flow T(+)/AHG(-) crossmatch is currently functioning despite the continued presence of circulating low levels of HLA class I antibody. Flow HLA class I antigen-coated beads showed the presence of at least one donor-specific HLA class I antibody at transplantation in each of the 10 cases. No rejections were observed in seven of the 10 cases (70%). Six rejection episodes, four cellular and two humoral, occurred in three patients. Each rejection was successfully treated. The only graft loss occurred in a kidney recipient on day 667 secondary to ischemia to the kidney because of cardiac surgery. Thus, short-term (one to two years) graft survival in primary transplants was not influenced by low levels of donor-specific HLA class I antibody present at transplantation and no prophylactic treatment such as IVIg, plasmapheresis, anti-CD20 or splenectomy was needed peri-operatively.

IMPROVED RENAL FUNCTION AFTER CONVERSION FROM TACROLIMUS/SIROLIMUS TO TACROLIMUS/MYCOPHENOLATE MOFETIL IN KIDNEY TRANSPLANT RECIPIENTS

Augustine JJ, Chang PC, Knauss TC, Aeder MI, Bodziak KA, Schulak JA, Hricik DE.

BACKGROUND: There is limited data on the potential nephrotoxicity of sirolimus (SRL) and tacrolimus (TAC) in combination.

METHODS: We reviewed the course of 97 kidney transplant patients treated with SRL and reduced-dose TAC. Conversion from SRL to mycophenolate mofetil (MMF) was prescribed in a minority (n = 19) for various nonrenal side effects. We compared outcomes of converted patients to those remaining on TAC/SRL (n = 78).

RESULTS: TAC levels were increased in converters (P = 0.009). Rejection rates were similar between groups over 18 months (21% vs. 16%, p = ns). Serum creatinine (Cr) and MDRD glomerular filtration rate (GFR) were similar between groups at nadir and six-months, but at 18 months the percent change from six-month Cr was +17% in non-converters vs. -10% in converters (P = 0.004 for the difference). The difference in GFR between groups at 18 months was also significant (P = 0.01). By multivariate analysis, only conversion to MMF was associated with a greater percent change in Cr from 6 to 18 months (P = 0.015). Conversion to MMF also correlated with higher GFR at 18 months independent of rejection, delayed graft function, and ethnicity.

CONCLUSIONS: Conversion from TAC/SRL to TAC/MMF led to improved renal function despite increased TAC exposure after conversion.

Section 9
Trauma

AEROSOLIZED CEFTAZIDIME PROPHYLAXIS AGAINST VENTILATOR-ASSOCIATED PNEUMONIA IN HIGH-RISK TRAUMA PATIENTS: RESULTS OF A DOUBLE-BLIND RANDOMIZED STUDY

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BACKGROUND: Ventilator-associated pneumonia (VAP) is a frequent complication during recovery of severely traumatized patients. The primary objective of this study was to determine if prophylactic administration of aerosolized ceftazidime reduced the incidence of VAP in high-risk injured patients without altering the incidence of other infectious complications.

PATIENTS AND METHODS: This was a single-institution double-blind, randomized trial that compared a seven-day course of aerosolized ceftazidime with placebo. Intubated high-risk patients admitted to the trauma intensive care unit at a large regional trauma center between February 2003 and September 2005 were eligible for enrollment. The main outcome evaluated was the incidence of VAP at two weeks and 30 days. The incidences of multi-drug-resistant infections and other infectious complications were secondary outcomes.

RESULTS: A total of 105 patients were randomized, resulting in 52 patients in the placebo arm and 53 patients in the ceftazidime arm. There was no statistical difference between the groups with regard to demographic data, injury severity, calculated risk of VAP, or the number of doses received. In the intention-to-treat analysis, the incidence of VAP at two weeks was 24/52 (46%) in the placebo group and 21/53 (40%) in the ceftazidime group. The number of patients with VAP at 30 days was 26/52 (50%) in the placebo group and 26/53 (49%) in the ceftazidime group. There was no statistical difference in the development of multi-drug-resistant VAP or other infectious complications in the two groups.

CONCLUSION: The use of aerosolized ceftazidime did not reduce the rate of VAP in high-risk patients admitted after traumatic injury, but neither did it increase the incidence of other infectious complications. Routine use of prophylactic aerosolized ceftazidime to prevent VAP in trauma patients cannot be recommended.

ANTITHROMBOTIC THERAPY AND ENDOVASCULAR STENTS ARE EFFECTIVE TREATMENT FOR BLUNT CAROTID INJURIES: RESULTS FROM LONGTERM FOLLOWUP

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Shelly D Timmons, MD, PhD, Peter E Fischer, MD, Martin A Croce, MD, FACS

BACKGROUND: Significant confusion exists about management of blunt carotid injuries (BCI). Currently, three common treatments are being used without significant longterm followup data to demonstrate efficacy. Although heparin has been shown to reduce in-hospital stroke rates, antiplatelet therapy (aspirin and clopidogrel) has emerged as an alternate therapy without proved efficacy; carotid stenting has also been implemented for pseudoaneurysms (13% BCI), but its utility has recently been challenged. This is the first study to assess longterm efficacy of various therapeutic approaches.

STUDY DESIGN: Consecutive patients treated and followed at a single regional trauma center over 10 years (1996 to 2005) were reviewed. Outcomes evaluated included stroke, functional status, and angiographic evolution.

RESULTS: One hundred ten patients (11/year) were diagnosed with 133 injuries (23 bilateral). Overall mortality was 26%, with 6% directly attributable to BCI. Angiographic followup was available on 67 injuries (in 50 patients) at a mean of 6 months (range 0.25 to 67 months); 75% remained the same or improved. Clinical followup was available in 55 of 81 patients (68%) who survived to discharge (mean, 34.4 months [range 1 to 109 months]). Of surviving patients receiving antithrombotic therapy, 44% were treated with antiplatelet therapy, 49% with anticoagulation, and 7% with both. No patients experienced stroke after discharge, and there was no difference in functional outcomes based on the therapy received. Twenty-two endovascular stents were placed (18 for pseudoaneurysms, 4 for extensive dissection). Mean followup on these patients was 29.7 months (range 3 to 94 months). No patients receiving stents experienced periprocedural complications, and one patient with an associated head injury had a stroke.

CONCLUSIONS: Longterm followup of BCI demonstrates that antithrombotic therapy prevents stroke; antiplatelet therapy and anticoagulation are equally effective; and carotid stents appear to be safe and effective for lesions that develop pseudoaneurysms or extensive dissections.

“AWAKE” LAPAROSCOPY FOR THE EVALUATION OF EQUIVOCAL PENETRATING ABDOMINAL WOUNDS

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BACKGROUND: Diagnostic laparoscopy is useful for the assessment of equivocal penetrating abdominal wounds, and has become the modality of choice for the evaluation of such wounds at our institution. We hypothesized that, in appropriate patients, diagnostic “awake” laparoscopy (AL) could be performed under local anesthesia in the emergency department (ED), allowing for expedited discharge and potential cost savings.

METHODS: Selected haemodynamically stable patients with penetrating abdominal injury underwent AL. Suitability for AL was at the discretion of the attending surgeon. Identification of peritoneal penetration by AL led to exploratory laparotomy in the operating room. Patients with no evidence of peritoneal penetration were discharged from the ED (ALneg). These patients were matched to a cohort of 24 patients who underwent diagnostic laparoscopy in the OR which was negative for peritoneal penetration (DLneg). Length of stay and hospital charges were compared.

RESULTS: Over a 30-month period, 15 patients underwent AL without complication. No peritoneal penetration was found in 11 patients. The remaining four patients underwent exploratory laparotomy, of which two were positive for intra-abdominal injury. Mean time to discharge was 7 h in the ALneg group versus 18 h in the DLneg group ($p = 0.0003$). Cost savings on hospital charges averaged US\$ 2227 per patient in the ALneg group compared with the DLneg group.

IMPROVED OUTCOME OF ADULT BLUNT SPLENIC INJURY: A COHORT ANALYSIS

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BACKGROUND: The purpose of this study was to review our 15-year experience in the treatment of blunt splenic injury in adults. Our hypothesis was that the implementation of a change in practice, with stress on splenic preservation and splenic artery embolization for the management of splenic injury, would result in improved splenic salvage rates without negatively affecting mortality rates.

METHODS: A retrospective cohort analysis was performed on all consecutive adults with blunt splenic injury who were admitted to a Level One Trauma Center. The cohorts were defined by 2 separate 7.5-year periods (1991-1998 and 1998-2005).

RESULTS: Six hundred twenty-five patients with blunt splenic trauma were identified; 403 patients who were treated from 1998 to 2005 were compared with 222 patients whose cases had been reviewed previously (1991 to 1998). The present cohort differed in age (35 vs 40 years; $P < .001$) and injury severity score (27 vs 21; $P < .0001$). Nonoperative treatment was implemented in 136 patients (61%) in the initial cohort and 344 patients (85%) in the present cohort. The frequency of splenic artery embolization increased from 2.7% to 22.6% ($P < .001$). The success of nonoperative management increased from 77% to 96% ($P < .001$); the splenic salvage rate for all patients improved from 57% to 88% ($P < .0001$). Hospital mortality rates decreased from 12% to 6% ($P < .001$), and the mean hospital length of stay decreased from 15 to 9 days ($P < .001$).

CONCLUSION: These results demonstrate that the success of nonoperative management and the splenic preservation for blunt injury has improved over time. This improvement correlated with a greater use of splenic artery embolization.

IMPROVING THE MONITORING OF NOSOCOMIAL INFECTIONS IN THE INTENSIVE CARE UNIT WITH REAL-TIME MEDICAL INFORMATICS

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Nosocomial infections in the surgical and trauma intensive care unit (STICU) are responsible for significant morbidity and mortality. We developed the Surgical Intensive Care – Infection Registry (SIC-IR), to monitor all infections and record mandatory Joint Commission on the Accreditation of Healthcare Organization’s (JCAHO) core measures in an easy to use application; which will enable us to easily undertake STICU quality of care improvement initiatives to enhance the diagnosis and treatment of these important infections.

INTRODUCTION: Infections in the intensive care unit are extremely common with approximately two million nosocomial infections occurring annually¹. The diagnosis and treatment of nosocomial infections has been estimated to cost 4.5 billion dollars each year¹. Most of these costs occur in the intensive care unit. Therefore, effective and efficient diagnosis of infections in the STICU becomes paramount both to patient outcome and health care expenditure.

The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) recognizes the importance of nosocomial infections and enforces ICU core measures that are aimed at reducing infections such as ventilator associated pneumonias and catheter-related blood-stream infections³. Tracking these core measures helps ICU teams to pursue quality improvement programs.

Developing, implementing, evaluating, and sustaining such quality of care improvement programs in the STICU is critical to combat nosocomial infections. A recent report by the Critical Care Medicine’s Outcomes Task Force outlined a “how-to” guide for ICU quality improvement. Two of the seven key components dealt with development of data collection and reporting systems⁴. We developed SIC-IR as such a system to document, report, and research our STICU infections with the goal to improve their diagnosis and treatment.

Surgical Intensive Care Infection Registry

SIC-IR is a relational database application which includes components for data capturing, reporting, and clinical decision support. SIC-IR was developed to: improve patient care through real-time monitoring of STICU infections; improve house staff time utilization, documentation, and transfer of care; and to provide a quality data repository for STICU infection-related research and modeling.

SIC-IR is directly linked with our laboratory and microbiology systems to allow it to report infection results in a concise, user friendly format. SIC-IR also offers the ability to write initial patient history and physicals, daily progress notes and consolidates data to generate a resident sign-out for transfer of care. It also provides many metrics as decision support aids.

CONCLUSION: Infections in the STICU are a critical problem recognized by JCAHO. SIC-IR was developed to improve overall patient care through assisting in the diagnosis and treatment of these often deadly infections.

FEVER AND LEUKOCYTOSIS IN CRITICALLY ILL TRAUMA PATIENTS: IT'S NOT THE URINE

Joseph F. Golob MD, Mark J. Sando BS, Charles J. Yowler MD, Mark A. Malangoni MD, William R Phipps MD, and Jeffrey A. Claridge, MD

BACKGROUND: Because infectious complications are a major cause of morbidity and mortality in critically ill trauma patients, fever and leukocytosis often trigger an extensive laboratory workup. This “fever-workup” often includes a urinalysis (UA) and urine culture (UCx) since urinary tract infections (UTIs) are the most common nosocomial infection. The purpose of this study was to: 1) define the current practice for obtaining a UA and UCx in trauma patients admitted to our surgical and trauma intensive care unit (STICU), and 2) test our hypothesis that there is no association between UTIs and fever or leukocytosis during the initial 14 hospital days.

METHODS: An 18-month retrospective cohort analysis was performed on consecutive trauma patients admitted for ≥ 2 days to the STICU at a level I trauma center. Data collected included: demographics, injuries, and the first 14 days of daily maximal temperature (TMax), leukocyte count, UA, and UCx if obtained. Fever and leukocytosis were defined as TMax $\geq 38.5^{\circ}\text{C}$ and leukocyte count $\geq 12,000 / \text{mm}^3$, respectively. Positive UA was defined as a positive urine nitrite and/or a positive urine leukocyte count ($\geq 10/\text{HPF}$). UTIs were diagnosed with a positive UCx (≥ 105 organisms).

RESULTS: 510 patients were evaluated for a total of 3839 patient-days. The mean patient age was 49 ± 1 years and injury severity score was 19 ± 1 . 72% were males and 91% had blunt injuries. The population had a Foley catheter in place for 97% of the patient-days. 470 UAs and 407 UCx were obtained. 42 (8%) patients had 60 UTIs. Our practice pattern demonstrated a significant association between obtaining UCx with fever and fever+leukocytosis ($p < 0.0001$), but no association with leukocytosis alone. However, there was no association of UTI with fever, leukocytosis, or fever+leukocytosis. Furthermore, regression analysis demonstrated no association between any temperature and a positive UCx ($p = 0.49$, CI = 0.59 – 1.3), and an inverse association was observed between an increasing white blood cell count and a positive UCx ($p = 0.04$, CI = 0.88 – 0.997). In the patients with a UA and UCx done concomitantly, the sensitivity and specificity was 54% and 80%, respectively for a UA predicting UTI (PPV=35% and NPV=90%).

CONCLUSIONS: Our practice for obtaining UA and UCx was related to fever and fever+leukocytosis. However fever, leukocytosis, or both were not associated with UTIs. These data suggest that there is an unnecessary emphasis on attributing the urine as a source of fever and leukocytosis in injured patients during their first 14 STICU days. This study indicates that the “fever-workup” paradigm for evaluating UTI should be reevaluated in critically ill trauma patients.

TRAUMA TEAM ACTIVATION CAN BE TAILORED BY PREHOSPITAL CRITERIA

BACKGROUND: Responses to trauma activations are triggered by predetermined criteria at individual trauma centers and utilize a large amount of resources to provide care for injured patients. The purpose of this study was to identify and evaluate which prehospital criteria did not require full trauma team activation and resources while maintaining or improving current standards of patient care.

	Phase I (n = 852)	Phase II (n = 306)	P value
Age	35	35	
%admitted	46	23	< 0.001
Hours in ER	3.9	4.2	NS
# of blood tests	3.8	3.2	0.01
# of CT scans	2.4	3.3	< 0.001
Charges	8589	6432	< 0.001

METHODS: A two phase prospective study was carried out at a regional urban Level I trauma center over one year. Phase I involved collecting observational data to determine which trauma criteria could potentially be used to identify patients that could be evaluated by a lower level trauma activation (LowAct). LowAct involved a smaller response team with priority access to imaging. Phase II involved implementing a LowAct and prospectively evaluating the outcomes related to resources and patient care.

RESULTS: A total of 3104 patients were evaluated with 2076 patients enrolled over 6 months in phase I and 1037 enrolled in phase II. Three criteria out of the 36 studied were most commonly identified that were not associated with admission. These criteria were pedestrian struck by vehicle, high speed vehicular crash, and Glasgow Coma Score (GCS) 12-14. These were then used as triggers for LowAct in phase II. Comparisons of patients with these three identified criteria are illustrated in the table. Follow up (mean = 3.8 days) of discharged patients treated by the LowAct during phase II demonstrated that 78% of patients felt they had adequate treatment and 9% required additional unplanned health care.

CONCLUSION: LowAct is appropriate for the following three criteria: pedestrian struck by vehicle, high speed vehicular crash, and GCS 12-14. The utilization of LowAct resulted in a decrease utilization of many resources without sacrificing patient care.

Section 10

**Vascular and
Endovascular
Surgery**

SHORT TERM RESULTS OF SINGLE SITE INFRAINGUINAL SILVERHAWK ATHRECTOMY

Jessie Jean-Claude MD, Preet S Kang MD, Gilles Pinault MD, Mathew Eiseman RN, Elizabeth Kempe RN

AIM: Short term results and patient outcomes at a single VA center experience with infrainguinal athrectomy in 25 patients

METHODS: From Apr 2005 onwards 25 consecutive patients, who underwent infrainguinal athrectomy were included in this retrospective study. All patients were males with mean age 59 years, range (47-84), with athrectomy performed in 42 lesions (25 limbs). Lesion characteristics by TASC criteria A-D were 24, 9, 6 and 3 respectively. The lesions ranged from 1 -12 cm in length. There were 25 femoropopliteal lesions, 12 tibial lesions and 5 both femoropopliteal and tibial lesions. The indications for revascularization were severe claudication in 5 (20%), rest pain in 4 (16%) and tissue loss in 16 (64%) patients. The end points were vessel patency and patient outcomes in terms of symptom relief and limb salvage. The follow-up ranges from 8-18 months.

RESULTS: The procedure achieved successful revascularization in 23 patients with at least 50% or more luminal patency by angiography. There were two procedure failures due to inability to cross occlusions. Adjunctive therapy was used in 3 cases. Duplex and ABI follow up indicated vessel patency and improved flow in all successfully treated cases. Minor and major complications were 8 % and 4 % respectively. There were 2 reinterventions at 3 and 5 months after the original athrectomy.

CONCLUSION: Silverhawk plaque excision athrectomy is a safe and effective treatment of infrainguinal atherosclerotic disease in the short term. More data and longer follow-up is needed to define its status in the treatment of infrainguinal peripheral arterial disease.

USE OF ATHERECTOMY AND OTHER ENDOVASCULAR TECHNIQUES FOR SALVAGE FOLLOWING FAILED INFRA-INGUINAL BYPASS

Gilles Pinault MD, Preet Kang MD, Matt Eiseman RN, Elizabeth Kemp NP, Jessie Jean-Claude MD

BACKGROUND: Failing or failed infra-inguinal bypasses are dreaded complications faced by vascular surgeons. The mechanism of graft failure is multifactorial. Early failure is associated with intimal hyperplasia whereas late failure can be ascribed to progression of atherosclerotic disease. The surgical options to salvage failing bypasses, especially if the greater saphenous vein has been previously harvested, are less than optimal. They can be technically challenging secondary to dissection in previously scarred planes as well as chronic edema. The patients have multiple co-morbidities. The use of arm vein, cryopreserved vein, and synthetic conduit has been described with mixed results. Patients status post below knee /tibial bypasses typically present with recurrent rest pain and/or tissue loss and are at significant risk of subsequent amputation. Excisional atherectomy has been approved for the use in the primary treatment of claudication and critical limb ischemia. Its usefulness as a salvage technique has not been well described.

METHODS: A series of 6 patients are described where atherectomy was the primary technique used for salvage. Four patients were noted to have progression of atherosclerotic disease distal to their previous bypass. Two of these patients presented with rest pain/tissue loss. The other two presented with acute occlusion of bypasses. In these patients their bypasses were used to access their distal disease. Two patients presented with graft failure. Atherectomy was used to re-cannulate their previously occluded native SFA. All six patients were a technical success. Early follow-up was promising.

CONCLUSIONS: Atherectomy is a viable option for salvage of failed infra-inguinal bypass grafts. Advantages include lack of requirement of new conduit and avoidance of redo surgery in a previously operated field. The operative stress on high-risk patients is reduced. Early results are promising however, further study is required to evaluate long-term results.

THE EFFECT OF BACTERIAL CONTAMINATION ON NEOINTIMAL HYPERPLASIA IN VASCULAR GRAFTS

Norma M. Edwards, MD, * Jeffrey A. Claridge, MD., † Dan H. Shell IV, MD., * Charles R. Handorf, MD, PhD., * Martin A. Croce, MD., * Timothy C. Fabian, MD*

From the *Department of Surgery, University of Tennessee Health Science Center, Memphis, Tennessee and †MetroHealth Medical Center, Case Western Reserve University School of Medicine, Cleveland, Ohio

Neointimal hyperplasia (NH) is the most significant contributing factor to long-term vascular graft failure. Inflammation is known to be important in its development; however, the role of bacterial infection is unclear. We examined the effect of contamination with common organisms on the development of NH in expanded polytetrafluoroethylene grafts. Thirty adult pigs were randomized into one of four groups: no infection, contamination with *Staphylococcus aureus*, mucin-producing *Staphylococcus epidermidis*, or *Pseudomonas aeruginosa*. An expanded polytetrafluoroethylene graft (6 mm × 3 cm) was placed as a common iliac artery interposition graft and was inoculated with 1–2 × 10⁸ of the selected organism before closure. Grafts were explanted 6 weeks postoperatively. Microbiologic, histological, and morphometric evaluations were performed. All grafts were patent at the time of euthanasia. The mean areas of NH were 5.45 mm² in sterile grafts, 8.36 mm² in *S. aureus*, 7.63 mm² in *S. epidermidis*, and 11.52 mm² in *P. aeruginosa* grafts. Comparison of means via analysis of variance showed that *P. aeruginosa* grafts had significantly higher formation of NH than sterile grafts ($P = 0.025$). NH production in infected grafts appears to be organism specific and is significantly higher with *P. aeruginosa* than common Gram-positive organisms. Increased NH from subclinical infection may be a significant factor contributing to late graft failures.

Section 11
Clinical Trials

CARDIOTHORACIC SURGERY

“The Use Of Transmyocardial Revascularization As An Adjunct To Coronary Artery Surgery”

Arie Blitz, MD

“Jarvik Trial: Multicenter trial evaluating the use of the Jarvik 2000 pump as a bridge to transplant”

Arie Blitz, MD (at Case)

“Use of Jarvik Heart as Destination Therapy (Multicenter)”

Arie Blitz, MD (at Case)

“Methylene Blue to Protect Against Vasoplegic Syndrome”

Arie Blitz, MD

“Interagency Registry For Mechanically Assisted Circulatory Support (INTERMACS)” (Multicenter)

Arie Blitz, MD (at Case)

COLORECTAL SURGERY

CWRU 4201 – Response of Chemo and Radiation in Rectal Cancer

Conor Delaney, MD, Joseph Willis, MD

“Quality of Life / Post-Op Ileus Discharge Criteria Study”

Conor Delaney, MD

“Follow-up phone calls after colorectal surgery to assess patient satisfaction and post-operative outcomes”

Conor Delaney, MD, PhD. Primary contact: Michelle Briehl, RN.

“Enhancing the Safety of Surgical Technical Skills”

Conor Delaney, MD, PhD. Primary contact: Mary Ann Draves

“Impact of an Experienced Laparoscopic Colorectal Surgeon to an Existing Traditional Colorectal Practice in an Academic Medical Center”

Vince Obias, MD, Laparoscopic Fellow

“A randomized trial comparing outcomes for the Ligasure and disposable stapling instruments for laparoscopic colectomy”

Conor Delaney, MD, PhD. Primary contact: Bridget O'Brien-Ermlich, RN

Sponsor: Tyco Healthcare/Valley labs

“A Randomized, Double-blind, Placebo-controlled Study Evaluating Two Doses of Asimadoline on the Duration of Post-operative Ileus in Subjects Undergoing Laparoscopic/Hand-assisted Laparoscopic Segmental Colonic Resection Secondary to Colon Cancer or Polypectomy”

Conor Delaney, MD, PhD. Primary contact: Bridget O'Brien-Ermlich, RN

“STARR Registry”

Conor Delaney, MD, PhD. Primary contact: Bridget O'Brien-Ermlich, RN

Sponsor: Ethicon Endosurgery

“A Prospective, Observational, Multicenter Study Assessing Early Postoperative Recovery Following Laparoscopic Partial Large Bowel Resection”

Conor Delaney, MD, PhD. Primary contact: Bridget O'Brien-Ermlich, RN or Michelle Briehl, RN

Sponsor: Adolor Corporation

“Color II: A randomized Clinical Trial Comparing Laparoscopic and Open Surgery for Rectal Cancer”

Conor Delaney, MD, PhD

GENERAL SURGERY**“Laparoscopic Hernia Pain Pump Study”**

Michael Rosen, MD

“Intensive Communication System for Chronically Critically Ill” NIH RO1 NR 008941

Joel Peerles, MD

“Stimulation of the Diaphragm in Amyotrophic Lateral Sclerosis”Raymond Onders, MD, Bashar Katirji, MD, Robert Schilz, PhD, DO, Mary Jo Elmo, ACNP,
Jane E. Prasse, MA, CCC-SLP, Robert Gilkerson, MD**“Electrical Activation of the Diaphragm for Ventilatory Assist”**Raymond P. Onders, MD, Mary Jo Elmo, RN, ACNP, Robert Schilz, PhD, DO,
Subhalakshmi Sivashankara, MD, Bashar Katirji**“Electrical Activation of the Diaphragm for Ventilatory Assist in Spinal Cord Injured Who Have a Cardiac Pacemaker”**Raymond Onders, MD, Mary Joe Elmo, RN, ACNP, Robert Schilz, PhD, DO,
Subhalakshmi Sivashankara, MD, Bruce S. Stambler, MD, Judith A. Mackall**“Ongoing Study of GISTs”**Jeffrey M. Hardacre, MD, Julian Kim, MD, Judy Jin, MD, Robert Shenk, MD, Thomas Stellato, MD,
Joseph Willis, MD**“Initial Experience with IORT for Pancreatic Cancer”**Jeffrey M. Hardacre, MD, Timothy Kinsella, MD, Christoher Siegel, MD, PhD, Juan Sanabria, MD,
Julian Kim, MD, James Schulak, MD, Charles Kunos, MD, Melanie Lynch, MD, Michael McGee, MD**“Hyperthyroidism Crisis Revisited”**

Roy Phitayakorn, MD, Christopher McHenry, MD

“The Rate Of Conversion From a Laparoscopic to an Open Approach and Selective Open Resection for Adrenal and Extraadrenal Neuroendocrine Tumors”

Roy Phitayakorn, MD, Christopher McHenry, MD

“The Incidence of Thyroid Cancer in Patients with Graves Disease”

Roy Phitayakorn, MD, Christopher McHenry, MD

“Prospective Evaluation of the Intra-Operative use of Transluminal Flexible Endoscopes during Combined Flexible and Laparoscopic Foregut Surgery”

Jeffrey Marks, MD. Primary contact: Mike McGee, MD

“Development of An Assessment Tool to Measure Flexible Endoscopic Performance”

Jeffrey Marks, MD

“Prospective, Randomized, Double-Blind Trial of Continuous Infusion of 0.5% Bupivacaine by Elastomeric Pump for Postoperative Pain Management After Laparoscopic Ventral Hernia Repair”

Michael Rosen, MD. Primary contact: Michelle Briehl, RN

“NeuRx RA/4 Motor-point Stimulation for Conditioning the Diaphragm of Patients with Amyotrophic Lateral Sclerosis”

Raymond Onders, MD. Primary contact: Mary Jo Elmo, RN

“Ablation of Gastrointestinal Tissue in Patients Prior to Undergoing Planned Removal of Said Tissue-Bearing Organ Clinical Protocol B-400”

Jeff Marks, MD. Primary contact: Michelle Briehl, RN

Sponsor: BARRX

PEDIATRIC CARDIOVASCULAR SURGERY

“The Right Ventricle in Congenital Heart Diseases: Risk Factors and Outcomes”

Ahmed Farouk, MD, Hani Hennein, MD

“Effects of Cardiopulmonary Bypass on Cerebral Oxygenation”

Ahmed Farouk, Jake Ostrowsky, Mark Henderson, Steve Schomisch, Hani Hennein

“Arterio-Arterial Flow Augmentation: A Novel Approach With Particular Suitability In The Pediatric Heart Failure Population”

Ahmed Farouk, Jake Ostrowsky, Mark Henderson, Steve Schomisch, Yasuhiro Kamotani, Jaikrishnan Kadambi, John Stork, Mohsen Karimi, Hani Hennein

PLASTIC SURGERY

“Comprehensive surgical treatment of migraine headaches” (status: IRB approved—long-term patient follow-up underway)

Bahman Guyuron, MD

“Placebo-controlled surgical treatment of migraines” (status: IRB approved—data collection completed and data analysis underway)

Bahman Guyuron, MD

“Determinants of facial aging in identical twins” (status: IRB approved—data collection completed and data analysis underway)

Bahman Guyuron, MD

“Pretricheal incision and cessation of alopecia” (status: IRB approved—recruiting patients)

Bahman Guyuron, MD

“Turbinectomy vs. coblation for management of the airway in rhinoplasty” (status: IRB approved—recruiting patients)

Bahman Guyuron, MD

“Evaluation of scarring following different methods of facial rejuvenation incisions, intra-operative incision management, and post-operative incision dressing” (status: IRB approved—data analysis underway)

Bahman Guyuron, MD

“Regional differences gene expression in patients who have undergone bicoronal scalp incisions” (status: IRB approval pending)

Bahman Guyuron, MD

“Differences in genetic expression in human scalp following frontal hairline incisions and management of alopecia” (status: IRB approval pending)

Bahman Guyuron, MD

“Scalp vessel ligation to treat androgenic alopecia” (status: IRB approval pending)

Bahman Guyuron, MD

“Correlation between antidepressants and the use of DDAVP in patients undergoing rhytidectomies” (status: IRB approval pending)

Bahman Guyuron, MD

“Age-related lengthening and thinning of the earlobe and earlobe classification system” (status: IRB approval pending)

Bahman Guyuron, MD

“Collection of craniosynostosis specimens from human cranial sutures for growth factor analysis” (status: IRB approval pending)

Arun Gosain, MD

“Electron microscopic changes in zygomaticotemporal branch of trigeminal nerve in migraine patients” (status: IRB approval pending)

Bahman Guyuron, MD

SURGICAL ONCOLOGY

“A Phase 2, single Arm, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of Lymphoseek as a Lymphoid Tissue Targeting Agent in Patients With Known or Suspected Melanoma or Breast Cancer Who Are Undergoing Lymph Node Mapping. Clinical Study Protocol No. NEO-03-01”

Julian Kim, MD. Primary contact: Marla Sustin, RN

Sponsor: Neoprobe Corporation

“Molecular studies of T cell clones for adoptive therapy”

Julian Kim, MD

TRANSPLANTION AND HEPATOBILIARY SURGERY

“Comparison of the Efficacy of The Rita Device vs The Cool Tip switching controller Device for the Ablation of Primary and Secondary Liver Neoplasm's in the Porcine Model”

Juan Sanabria MD MSc, Chris Siegel MD PhD, Jim Schulack MD

“Islet Cell Transplant Initiative”

Juan Sanabria MD MSc*, Christopher Siegel MD PhD*, James Schulak MD*, Donald Hricik MD**, Faramarz Ismaeli-Beigi MD PhD***, Kathy Horowitz MD***, Henry Brunengraber MD PhD†, Michael Weiss MD PhD§

“Metabolomics & Isotopomer Analysis in Normal and Diseased Human Livers”

Juan Sanabria2 MD MSc, P.I., . Christopher Siegel2 MD PhD, Jeffrey Ponsky2 MD, Achilles Demetriou2 MD PhD, James Schulak2 MD, Thomas Stellato2 MD, Peter Holloway2MD, Anthony Post8 MD, Pierre Gholam8 MD, Jackson Wright8 MD, Anthony Tavill7,8 MD

“Determinants of Access to Liver Transplantation in Ohio”

Juan Sanabra MD, Robert S. O'Shea MD, MSCE, Gregory Olds MD

“Cost- effective analysis of the determination of the intravascular volume status in patients with End Stage Renal Disease by the BVA-100 system”

Juan Sanabria, MD

VASCULAR and ENDOVASCULAR SURGERY

“The incidence of Deep Venous Thrombosis in Patients with Thermal Injury”

Jeffrey Alexander, MD, Charles Yowler, MD

“A Prospective, Randomized, Multi-Center, Two Arm Study to Evaluate the Safety and Effectiveness of the Vascular Sealant Compared With Gelfoam/Thrombin for Control of Anastomosis Suture Lines Bleeding in Patients Undergoing Peripheral Vascular Reconstructive Surgery with PTFE Grafts”

Jerry Goldstone, MD. Primary contact: Bridget O'Brien-Ermlich, RN, or Mary Ann Draves

Sponsor: Confluent Surgical

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