
Selected published abstracts of Baylor researchers

AMERICAN JOURNAL OF CARDIOLOGY

Cardiac transplantation for cardiac sarcoidosis with initial diagnosis by examination of the left ventricular apical “core” excised for insertion of a left ventricular assist device for severe chronic heart failure

Roberts WC, Vowels TJ, Ko JM, Capehart JE, Hall SA

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Three quinquagenarians who underwent insertion of a left ventricular assist device (LVAD) because of severe heart failure and for whom histologic examination of the left ventricular apical “core” (removed to insert the device) showed noncaseating giant cell granulomas typical of sarcoidosis are described. Later, cardiac transplantation showed widespread sarcoid granulomas in the walls of the right and left ventricles and ventricular septum in 2 patients and extensive scarring in the third patient in the absence of coronary narrowing. Previously, 11 patients who underwent cardiac transplantation because of cardiac sarcoidosis had been reported, and in 1 of these patients, diagnosis was also initially made by examination of the left ventricular core excised at the time of insertion of an LVAD. In conclusion, excision of a portion of left ventricular wall to enable insertion of a therapeutic device (LVAD) can also serve as the means of definitive diagnosis of the underlying cardiac condition.

AMERICAN JOURNAL OF MEDICAL QUALITY

Challenges in conducting a hospital-randomized trial of an educational quality improvement intervention in rural and small community hospitals

Filardo G, Nicewander D, Herrin J, Galimberti P, Tietze M, McBride S, Gunderson J, Collinworth A, Haydar Z, Williams J, Ballard DJ

Am J Med Qual 2008;23(6):440–447. Copyright © 2008 by the American College of Medical Quality. Reprinted by permission of SAGE Publications.

The study design for this hospital-randomized controlled trial of an educational quality improvement intervention in rural and small community hospitals, following the implementation of a Web-based quality benchmarking and case review tool, specified a control group and a rapid-cycle quality improvement education group of ≥ 30 hospitals each. Of the 64 hospitals initially interested in participating, 7 could not produce the required quality data and 10 refused consent to randomization. Of the 23 hospitals randomized to the educational intervention, 16 completed the educational program, 1 attended the didactic sessions but did not complete the required quality improvement project, 3 enrolled in “make-up” sessions, and 3 were unable to attend. Of the 42 individuals who attended educational sessions, 5 (12%) have left their positions. Quality improvement interventions require several different approaches to engage participating organizations and should include plans to train new staff given the high turnover of health care quality improvement personnel.

CANCER GENE THERAPY

Transcription factors: their potential as targets for an individualized therapeutic approach to cancer

Mees C, Nemunaitis J, Senzer N

Cancer Gene Ther 2009;16(2):103–112. Reprinted by permission from Macmillan Publishers Ltd.

Pro-cancer signals are controlled by the expression and transcription of oncogenes. Transcription of DNA is dependent on the spatially and temporally coordinated interaction between transcriptional machinery (RNA polymerase II, transcription factors [TFs]) and transcriptional regulatory components (promoter elements, enhancers, silencers and locus control regions). Unique TFs have been identified in association with cancer. This review summarizes key oncogene-related TFs and organizes their pro-cancer activity according to the six hallmark functions (self-sufficiency in growth signals, insensitivity to growth-inhibitory signals, evasion of programmed cell death, limitless replicative potential, sustained angiogenesis and metastatic spread) proposed as constituting the infrastructure of the malignant process.

CLINICAL THERAPEUTICS

A 52-week, multinational, open-label, parallel-group, noninferiority, treat-to-target trial comparing insulin detemir with insulin glargine in a basal-bolus regimen with mealtime insulin aspart in patients with type 2 diabetes

Hollander P, Cooper J, Bregnhøj J, Pedersen CB

Clin Ther 2008;30(11):1976–1987. Reprinted with permission from Excerpta Medica Inc.

Objective: This trial compared the efficacy and safety profiles of the insulin analogues detemir and glargine as the basal insulin component of a basal-bolus regimen in patients with type 2 diabetes mellitus (T2DM) who were being treated with oral antidiabetic drugs (OADs) or insulin with or without OADs.

Methods: This was a multinational, 52-week, open-label, parallel-group, noninferiority, treat-to-target trial. Patients with a diagnosis of T2DM for ≥ 12 months who had been receiving an OAD or insulin, with or without OADs, for >4 months were randomized in a 2:1 ratio to receive detemir or glargine. According to the approved labeling, detemir could be administered once or twice daily, and glargine was administered once daily. Insulin aspart was given at mealtimes. Insulin secretagogues and α -glucosidase inhibitors were discontinued at study entry, and existing OADs were continued. Doses of detemir and glargine were titrated to achieve a prebreakfast (and predinner for detemir administered twice daily) plasma glucose target of ≤ 6.0 mmol/L. Patients monitored their plasma glucose levels before breakfast and dinner on the 3 days before each of 13 scheduled visits, recorded their insulin doses on 1 of these 3 days, and recorded their 10-point self-monitored plasma glucose (SMPG) at baseline and after 24 and 52 weeks. The primary efficacy end point was glycosylated hemoglobin (HbA_{1c}) at 52 weeks; secondary efficacy end points included changes

in fasting plasma glucose (FPG), postprandial plasma glucose, insulin doses, and weight change at 52 weeks. Safety end points included the frequency of hypoglycemia and adverse events (AEs).

Results: The intention-to-treat population included 319 patients (58.0% male, 42.0% female; 78.4% white; mean age, 58 years; mean weight, 92.8 kg; mean duration of diabetes, 13.6 years). At study entry, 46.1% of patients were receiving insulin and ≥ 1 OAD, 35.4% were receiving insulin only, and 18.5% were receiving ≥ 1 OAD only. At 52 weeks, there was no significant difference between detemir and glargine in terms of mean HbA_{1c} (7.19% and 7.03%, respectively; mean difference, 0.17% [95% CI, -0.07 to 0.40]) or the mean decrease in HbA_{1c} from baseline (-1.52% and -1.68%). The reduction in HbA_{1c} was not significantly affected by whether detemir was administered once or twice daily. There were no significant differences between groups in terms of mean FPG (7.05 and 6.68 mmol/L) or the mean change in FPG from baseline (-2.56 and -2.92 mmol/L; mean difference, 0.36; 95% CI, -0.26 to 0.99). The overall shape of the 10-point SMPG profiles was not significantly different between groups. Mean weight gain at 52 weeks was significantly lower with detemir than with glargine (2.8 vs 3.8 kg; mean difference, -1.04; 95% CI, -2.08 to -0.01; $P < 0.05$). Doses of basal and prandial insulins at the end of the study were not significantly different between groups. Major hypoglycemic episodes were reported by 4.7% and 5.7% of patients in the respective treatment groups. There was no significant difference in the risk of hypoglycemia between groups. The proportion of patients with AEs and the number of AEs per patient were comparable between groups (185/214 patients [86.4%] reporting 743 AEs and 88/105 patients [83.8%] reporting 377 AEs).

Conclusions: When used as indicated as part of a basal-bolus regimen in patients with T2DM who had previously received other insulin and/or OAD regimens, detemir was noninferior to glargine in its effects on overall glycemic control. Both basal insulins were associated with clinically relevant reductions in hyperglycemia. Both were well tolerated, with no significant difference in the frequency of hypoglycemia or AEs.

EXPERT REVIEWS IN ANTICANCER THERAPY

Sunitinib (SUTENT) for the treatment of metastatic renal cell carcinoma

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Expert Rev Anticancer Ther 2008;8(11):1723-1731. Reprinted with permission from Expert Reviews Ltd.

Kidney cancer accounts for approximately 2% of new cancers and conventional treatment with nephrectomy followed by IL-2 or IFN- α treatment does not provide long-term survival benefit in many patients. Increased understanding of the pathophysiology of renal cell carcinoma has prompted the development of targeted therapies for patients with this disease, including sunitinib. This paper reviews the most recent efficacy and safety data for sunitinib, as well as currently ongoing and planned studies for this receptor tyrosine kinase inhibitor. Results from a large-scale, long-term, Phase III trial have established sunitinib as the standard of care for first-line treatment of patients with advanced renal cell carcinoma, and it is now the reference standard against which other therapies for this cancer should be evaluated.

JOURNAL OF NEUROSURGERY

Virtual framing: the feasibility of frameless radiosurgical planning for the Gamma Knife

Giller CA, Fiedler JA

J Neurosurg 2008;109(Suppl):25-33. Reprinted with permission.

Object: Gamma Knife (GK) treatments are typically delivered in 1 day with little opportunity to test different planning strategies. The authors demonstrate 2 methods for imposing GK coordinate systems upon imaging datasets without frame attachment to allow leisurely preprocedural planning, and discuss potential applications.

Methods: A "virtual framing" is constructed by coregistering a CT scan of a Leksell frame with a patient dataset using the GammaPlan (Multi-view) module. Equations for skull radii are derived by approximating the skull as an ellipsoid. No proprietary software other than that of the GK system is required. In a second method, images of fiducial markers are directly superimposed on the patient dataset. Validation of the first method was achieved by comparing the lengths of 75 line segments and 60 single shot diameters measured in the virtual coordinates with those measured in real coordinates. In addition to preplanning, 2 applications are discussed. The first is the use of GK software to aid radiosurgical planning for other devices. The second is the use of virtual framing to enhance automatic optimization algorithms.

Results: Mean (\pm standard deviation) and root-mean-square differences in lengths were 0.18 ± 0.32 and 0.37 mm. Mean and root-mean-square differences in diameters of single-shot plans were 0.01 ± 0.18 and 0.18 mm.

Conclusions: Virtual framing allows exploration of radiosurgical planning strategies prior to the day of treatment using only the GK software. Other applications include enhancement of radiosurgical planning for other systems and enhancement of optimization algorithms.

JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY

Orthognathic surgery in the young cleft patient: preliminary study on subsequent facial growth

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J Oral Maxillofac Surg 2008;66(12):2524-2536. Reprinted with permission from Elsevier.

Purpose: This study evaluated the long-term effects of orthognathic surgery on subsequent growth of the maxillomandibular complex in the young cleft patient.

Patients and methods: We evaluated 12 young cleft patients (9 male and 3 female patients), with a mean age of 12 years 6 months (range, 9 years 8 months to 15 years 4 months), who underwent Le Fort I osteotomies, with maxillary advancement, expansion, and/or downgrafting, by use of autogenous bone or hydroxyapatite grafts, when indicated, for maxillary stabilization. Five patients had concomitant osteotomies of the mandibular ramus. All patients had presurgical and postsurgical orthodontic treatment to control the occlusion. Radiographs taken at initial evaluation (T1) and presurgery (T2) were compared to establish the facial growth vector before surgery, whereas radiographs taken immediately postsurgery (T3) and at longest follow-up (T4) were used to determine postsurgical growth. Each patient's lateral cephalograms

were traced, and 16 landmarks were identified and used to compute 11 measurements describing presurgical and postsurgical growth.

Results: Before surgery, all patients had relatively normal growth. After surgery, cephalograms showed statistically significant growth changes from T3 to T4, with the maxillary depth decreasing by $-3.3^\circ \pm 1.8^\circ$, Sella-nasion-point A by $-3.3^\circ \pm 1.8^\circ$, and point A-nasion-point B by $-3.6^\circ \pm 2.8^\circ$. The angulation of the maxillary incisors increased by $9.2^\circ \pm 11.7^\circ$. Of 12 patients, 11 showed disproportionate postsurgical jaw growth. Maxillary growth occurred predominantly in a vertical vector with no anteroposterior growth, even though most patients had shown anteroposterior growth before surgery. The distance increased in the linear measurement from nasion to gnathion by 10.3 ± 7.9 mm. Four of 5 patients operated on during the mixed dentition phase had teeth that erupted through the cleft area. A variable impairment of postoperative growth was seen with the 2 types of grafting material used. No significant difference was noted in the effect on growth in patients with unilateral clefts versus those with bilateral clefts. The presence of a pharyngeal flap was noted to adversely affect growth, whereas simultaneous mandibular surgery did not. After surgery, 11 of 12 patients tended toward a Class III end-on occlusal relation.

Conclusions: Orthognathic surgery may be performed on growing cleft patients when mandated by psychological and/or functional concerns. The surgeon must be cognizant of the adverse postsurgical growth outcomes when performing orthognathic surgery on growing cleft patients with the possibility for further surgery requirements. Performing maxillary osteotomies on cleft patients would be more predictable after completion of facial growth.

JOURNAL OF VASCULAR AND INTERVENTIONAL RADIOLOGY

Left colic artery pseudoaneurysm from pancreatitis presenting as upper gastrointestinal hemorrhage

Marichal DA, Savage C, Meler JD, Kirsch D, Rees CR

J Vasc Interv Radiol 2009;20(1):133–136. Reprinted with permission from Elsevier.

Visceral pseudoaneurysms resulting from pancreatitis occur in approximately 10% of cases. The present report describes a left colic artery pseudoaneurysm from pancreatitis presenting with active duodenal bleeding. Based on the clinical and endoscopic demonstration of duodenal bleeding, celiac and superior mesenteric arteriograms were initially obtained, and their findings were negative. Repeat arteriography, including an inferior mesenteric artery injection, demonstrated a left colic pseudoaneurysm with rupture into the pancreatic duct and retrograde flow into the duodenum. Because of inconsistent diagnostic yields for arteriography performed for pancreatitis-related bleeding, the authors recommend disciplined interrogation of all three major mesenteric vessels, unbiased by initial endoscopic findings, to reduce false-negative examination results and empiric embolization.

JOURNAL OF VASCULAR SURGERY

Two-year randomized prospective comparison of percutaneous ePTFE/nitinol self-expanding stent graft vs prosthetic femoral-popliteal bypass in the treatment of superficial femoral artery occlusive disease

McQuade K, Gable D, Hohman S, Pearl G, Theune B

J Vasc Surg 2009;49(1):109–116. Reprinted with permission from Elsevier.

Background: A randomized prospective study comparing the treatment of superficial femoral artery occlusive disease percutaneously with an expanded polytetrafluoroethylene (ePTFE)/nitinol self-expanding stent graft (stent-graft) vs surgical femoral to above knee popliteal artery bypass with synthetic graft material.

Methods: One hundred limbs in 86 patients with superficial femoral artery occlusive disease were evaluated from March 2004 to May 2005. Patient symptoms included both claudication and limb threatening ischemia with or without tissue loss. The TransAtlantic InterSociety Consensus (TASC) II A (N = 18), B (N = 56), C (N = 11), and D (N = 15) lesions were included. Patients were randomized prospectively into one of two treatment groups: a percutaneous treatment group (group A; N = 50) with angioplasty and placement of one or more stent-grafts or a surgical treatment group (group B; N = 50) with a femoral to above knee popliteal artery bypass using synthetic conduit (Dacron graft or ePTFE). Patients were followed for a total of 24 months. Follow-up evaluation included clinical assessment and physical examination, ankle-brachial indices (ABI), and color flow duplex sonography at 3, 6, 9, 12, 18, and 24 months.

Results: The mean total lesion length of the treated arterial segment in the stent-graft group was 25.6 cm (SD \pm 15 cm). The stent-graft group demonstrated a primary patency of 81%, 72%, and 63% with a secondary patency of 86%, 83%, and 74% at 6, 12, and 24 months, respectively. The surgical femoral-popliteal group demonstrated a primary patency of 84%, 77%, and 64% with a secondary patency of 89%, 86%, and 76% at 6, 12, and 24 months, respectively. No statistical difference was found between the two groups with respect to primary ($P = .716$) or secondary patency ($P = .695$). Grouping of less severe (TASC II A/B) vs more severe (TASC II C/D) lesions demonstrated patency at 24 months for the femoral-popliteal arm of 63% and 67%, respectively while that of the stent-graft arm was 64% and 47%, respectively. Secondary patency was 76% in both TASC classifications for the femoral-popliteal arm with 78% and 47% patency found respectively in the stent-graft group. These resulted in no significant difference for primary ($P = .978$) or secondary ($P = .653$) patency overall, although there is a trend for decreased patency with higher TASC II lesions.

Conclusion: Management of superficial femoral artery occlusive disease with percutaneous stent-grafts exhibits similar primary patency at 24-month follow-up when compared with conventional femoral-popliteal artery bypass grafting with synthetic conduit. This treatment method may offer an alternative to treatment of the superficial femoral artery segment for revascularization when prosthetic bypass is being considered or when autologous conduit is unavailable.

LIVER TRANSPLANTATION

Twenty years of follow-up of aortohepatic conduits in liver transplantation

Nikitin D, Jennings LW, Khan T, Sanchez EQ, Chinnakotla S, Randall HB, McKenna GJ, Goldstein RM, Levy MF, Klintmalm GB

Liver Transpl 2008;14(10):1486–1490. Copyright © 2008, American Association for the Study of Liver Diseases. Reprinted with permission from Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

Arterial problems remain a formidable challenge in liver transplantation. In many situations, an aortohepatic conduit can provide a solution. No long-term results (over 5 years) have been reported. This study was designed to assess the impact of aortohepatic conduits on graft survival after liver transplantation and the safety of aortohepatic conduits and to establish the long-term results (up to 20 years) of aortohepatic conduits. Data from 2346 adult liver transplants were prospectively collected into the computerized database and analyzed. In the majority of cases, arterial conduits were constructed from the donor iliac artery obtained at the liver retrieval. Aortohepatic conduits were required in 149 (6.4%) first transplants. The long-term graft survival after liver transplantation using aortohepatic conduits was excellent and comparable to that of the control group. The graft survival was 59% with the conduit versus 67% without the conduit at 5 years of follow-up, 50% versus 52% at 10 years, and 33% versus 35% at 15 years. With up to 20 years of follow-up, there was no statistically significant difference in graft survival, patient survival, hepatic artery complications, or biliary complications. For the same time period, there was no statistically significant difference in graft survival or patient survival for the retransplants with and without aortohepatic conduits. In conclusion, in experienced hands, aortohepatic conduits can be used safely for liver transplantation with no negative impact on long-term graft survival, patient survival, hepatic artery complications, or biliary complications. Excellent long-term results can be obtained.

NATURE IMMUNOLOGY

Influence of the transcription factor ROR γ t on the development of NKp46⁺ cell populations in gut and skin

Luci C, Reynders A, Ivanov II, Cognet C, Chiche L, Chasson L, Hardwigsen J, Anguiano E, Banchereau J, Chaussabel D, Dalod M, Littman DR, Vivier E, Tomasello E

Nat Immunol 2009;10(1):75–82. Reprinted by permission from Macmillan Publishers Ltd.

NKp46⁺CD3⁻ natural killer lymphocytes isolated from blood, lymphoid organs, lung, liver and uterus can produce granule-dependent cytotoxicity and interferon- γ . Here we identify in dermis, gut lamina propria and cryptopatches distinct populations of NKp46⁺CD3⁻ cells with a diminished capacity to degranulate and produce interferon- γ . In the gut, expression of the transcription factor ROR γ t, which is involved in the development of lymphoid tissue-inducer cells, defined a previously unknown subset of NKp46⁺CD3⁻ lymphocytes. Unlike ROR γ t⁻ lamina propria and dermis natural killer cells, gut ROR γ t⁺NKp46⁺ cells produced interleukin 22. Our data show that lymphoid tissue-inducer cells and natural killer cells shared unanticipated similarities and emphasize the heterogeneity of NKp46⁺CD3⁻ cells in innate immunity, lymphoid organization and local tissue repair.

SOUTHERN MEDICAL JOURNAL

Concurrent primary hyperparathyroidism and humoral hypercalcemia of malignancy in a patient with clear cell endometrial cancer

Richey DS, Welch BJ

South Med J 2008;101(12):1266–1268. Reprinted with permission from Lippincott Williams & Wilkins.

A 65-year-old Caucasian woman with a known history of clear cell endometrial cancer presented with hypercalcemia. Further evaluation demonstrated that the patient had primary hyperparathyroidism due to a parathyroid adenoma, as well as an increased parathyroid hormone-related peptide secondary to her malignancy. To the best of our knowledge, this is the first reported case of a female patient with concurrent primary hyperparathyroidism and humoral hypercalcemia of malignancy. This case illustrates the importance of considering a broad differential when evaluating patients with hypercalcemia. It also emphasizes the importance of recognizing the biochemical interplay between parathyroid hormone and parathyroid hormone-related peptide.

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