Presence of a congenitally bicuspoid aortic valve among patients having combined mitral and aortic valve replacement

Roberts WC, Janning KG, Vowels TJ, Ko JM, Hamman BL, Hebeler RF Jr


Although bicuspid aortic valve occurs in an estimated 1% of adults and mitral valve prolapse in an estimated 5% of adults, occurrence of the 2 in the same patient is infrequent. During examination of operatively excised aortic and mitral valves because of dysfunction (stenosis and/or regurgitation), we encountered 16 patients who had congenitally bicuspid aortic valves associated with various types of dysfunctional mitral valves. Eleven of the 16 patients had aortic stenosis (AS): 5 of them also had mitral stenosis, of rheumatic origin in 4 and secondary to mitral annular calcium in 1; the other 6 with aortic stenosis had pure mitral regurgitation (MR) secondary to mitral valve prolapse in 3, to ischemia in 2, and to unclear origin in 1. Of the 5 patients with pure aortic regurgitation, each also had pure mitral regurgitation: in 1 secondary to mitral valve prolapse and in 4 secondary to infective endocarditis. In conclusion, various types of mitral dysfunction severe enough to warrant mitral valve replacement occurred in patients with bicuspid aortic valves. A proper search for mitral valve dysfunction in patients with bicuspid aortic valves appears warranted.

Aortic medial elastic fiber loss in acute ascending aortic dissection


The cause of acute aortic dissection continues to be debated. One school of thought suggests that underlying aortic medial cystic necrosis is the common denominator. The purpose of the present study was to determine if there was loss and, if so, how much loss of medial elastic fibers in the ascending aorta in patients with acute aortic dissection with the entrance tear in the ascending aorta. We examined operatively excised aortic valves in 69 patients having acute dissection with tears in the ascending aorta. Patients with previous aortotomy, healed dissection, and connective tissue disorders were excluded. The 69 patients' ages ranged from 31 to 88 years (mean 56); 49 were men and 20 were women. Loss of aortic medial elastic fibers was graded as 0 (no loss), 1+ (trace), 2+ (mild), 3+ (moderate), and 4+ (full thickness loss). Of these 69 patients, 56 (82%) had 0 or 1+ elastic fiber loss; 13 patients (18%), 2+ to 4+ loss including 4 with 2+, 6 with 3+, and 2 with 4+. Nearly all patients (97%) had a history of systemic hypertension and/or had received antihypertensive drug therapy. In conclusion, most patients (82% in this study) having acute aortic dissection with entrance tears in the ascending aorta have normal numbers or only trace loss of aortic medial elastic fibers. Thus, underlying abnormal ascending aortic structure uncommonly precedes acute dissection.

Accuracy of two-dimensional echocardiography in determining aortic valve structure in patients >50 years of age having aortic valve replacement for aortic stenosis

Ayad RF, Grayburn PA, Ko JM, Filardo G, Roberts WC


We sought to measure the accuracy of 2-dimensional transthoracic echocardiography in determining aortic valve structure in patients with aortic stenosis (AS) undergoing aortic valve replacement (AVR). Few studies have compared aortic valve structure determined by echocardiography to that determined by examination of the operatively excised aortic valve. Two-dimensional echocardiograms were reviewed and interpreted by an expert echocardiographer in blinded fashion in 100 patients >50 years of age (mean 70) who had undergone AVR for isolated AS ± aortic regurgitation and the aortic valve structure (unicuspid, bicuspid, tricuspid) was compared to that from examination of the operatively excised aortic valve. After excluding 14 cases in which echocardiograms were uninterpretable because of heavy calcium and/or poor image quality, congenitally malformed valves were present in 44 patients (51%) and tricuspid valves in 42 of the 86 patients (49%). Ten of the 14 patients (71%) with uninterpretable echocardiograms had congenitally malformed valves. Valve structure by echocardiography was concordant with morphologic interpretation in 57 of 86 patients (66% accuracy, kappa = 0.33). Accuracy trended toward improvement as degree of AS decreased. In patients with valve areas similar to those enrolled in the recent transcatheter aortic valve implantation trial (PARTNER; 0.7 ± 0.2 cm²), aortic valve structure was accurately determined by echocardiography in 21 of 35 patients (60%). In conclusion, aortic valve structure was interpretable by transthoracic echocardiogram in 86 of 100 patients and accurate in 57 of these 86 patients (66%).

Effect of body mass index on survival in patients having aortic valve replacement for aortic stenosis with or without concomitant coronary artery bypass grafting

Roberts WC, Roberts CC, Vowels TJ, Ko JM, Filardo G, Hamman BL, Matter GJ, Henry AC, Hebeler RF Jr


The purpose of this report is to describe the effect of body mass index (BMI) on 30-day and late outcome in patients having aortic valve replacement (AVR) for aortic stenosis (AS) with or without concomitant coronary artery bypass grafting. From January 2002 through June 2010 (8.5 years), 1,040 operatively excised stenotic aortic valves were submitted to the cardiovascular laboratory at Baylor University Medical Center at Dallas. Of the 1,040 cases 175 were eliminated because they had a previous cardiac operation. The present study included 865 adults whose AVR for AS was their first cardiac operation. Propensity-adjusted analysis showed that 30-day and late morality were strongly
and significantly associated with BMI. Decreased risk of 30-day and long-term mortality was observed for patients with BMI in the low 30s compared to patients with BMI in the mid 20s or >40 kg/m². In conclusion, the findings in this study indicate a strong and significant adjusted association between BMI and 30-day and long-term mortality in patients having AVF for AS with or without concomitant coronary artery bypass grafting. Better survival was observed in patients with BMIs in the low 30s compared to patients with BMIs in the mid 20s and >40 kg/m².

**ANNALS OF ALLERGY, ASTHMA, AND IMMUNOLOGY**

Randomized placebo-controlled trial of the bradykinin B₂ receptor antagonist icatibant for the treatment of acute attacks of hereditary angioedema: the FAST-3 trial

Lumry WR, Li HH, Levy RJ, Potter PC, Farkas H, Moldovan D, Riedl M, Li H, Craig T, Bloom BJ, Reshef A


**Background:** The For Angioedema Subcutaneous Treatment (FAST)-3 study was a phase III, randomized, double-blind, placebo-controlled study of icatibant (bradykinin B₂ receptor antagonist) in subjects with hereditary angioedema (HAE) resulting from C1-INH deficiency or dysfunction (type I/II).

**Objective:** To investigate icatibant efficacy and safety in subjects with acute HAE attacks.

**Methods:** Subjects with moderate to very severe cutaneous or abdominal symptoms received icatibant (n = 43) or placebo (n = 45). Five subjects with laryngeal (mild-to-moderate) first attacks received icatibant (n = 3) or placebo (n = 2), and 5 subjects with severe laryngeal first attacks received open-label icatibant.

**Results:** Cutaneous or abdominal attacks: icatibant significantly reduced median times (vs placebo) to 50% or more reduction in symptom severity (2.0 vs 19.8 hours; \( P < .001 \), primary y endpoint), onset of primary y symptom relief (1.5 vs 18.5 hours; \( P < .001 \), key secondary y endpoint), or almost complete symptom relief (8.0 vs 36.0 hours; \( P = .012 \)) and provided a shorter time to initial symptom relief (0.8 vs 3.5 hours; \( P < .001 \)). For laryngeal attacks, median time to 50% or more reduction in symptom severity was 2.5 hours (icatibant) and 3.2 hours (placebo). No icatibant-treated subject required rescue medication before symptom relief occurred. The incidence of adverse events (AEs) was similar in icatibant- and placebo-treated subjects (41% and 52%, respectively). All icatibant-treated subjects experienced injection site reactions, but none reported clinically relevant changes in safety parameters or serious AEs.

**Conclusions:** FAST-3 demonstrated that icatibant was effective and generally well tolerated in subjects with acute HAE attacks.

**ANTIVIRAL THERAPY**

Reactivated hepatitis B due to medical interventions: the clinical spectrum expands

Perrillo RP


Reactivated hepatitis B is a potentially serious disorder that can result in liver failure and death. It has been described with a wide variety of immunosuppressive interventions, such as cancer chemotherapy, anti-rejection drugs and the use of tumour necrosis factor-α inhibitors and monoclonal antibody to B-cell antigen. It now appears reasonable to consider transarterial chemoembolization (TAC) for hepatocellular carcinoma as an additional medical inter vention associated with hepatitis B reactivation. Pre-emptive antiviral treatment of hepatitis B surface antigen (HBsAg) carriers can prevent serious complications arising from immunosuppressive-induced viral reactivation. Specific recommendations for antiviral prophylaxis in HBsAg carriers undergoing TAC should be added to international management guidelines.

**CLINICAL REVIEWS IN BONE AND MINERAL METABOLISM**

Uric acid nephrolithiasis: a systemic metabolic disorder

Wiederkher MR, Moe OW


Uric acid nephrolithiasis is characteristically a manifestation of a systemic metabolic disorder. It has a prevalence of about 10% among all stone formers, the third most common type of kidney stone in the industrialized world. Uric acid stones form primarily due to an unduly acid urine; less deciding factors are hyperuricosuria and a low urine volume. The vast majority of uric acid stone formers have the metabolic syndrome, and not infrequently, clinical gout is present as well. A universal finding is a low baseline urine pH plus insufficient production of urinary ammonium buffer. Persons with gastrointestinal disorders, in particular chronic diarrhea or ostomies, and patients with malignancies with a large tumor mass and high cell turnover comprise a less common but nevertheless important subset. Pure uric acid stones are radiolucent but well visualized on renal ultrasound or computed tomography. A 24 h urine collection for stone risk analysis provides essential insight into the pathophysiology of stone formation and may guide therapy. Management includes a liberal fluid intake and dietary modification. Potassium citrate to alkalize the urine to a goal pH between 6 and 6.5 is essential, as undissociated uric acid deprotonates into its much more soluble urate form.

**ISLETS**

Establishment of a prolonged pancreas preservation model for islet isolation research in mice


Establishing a prolonged pancreas preservation model in a small animal is important for islet isolation research. Use of a rat pancreas model has been reported, but no published reports have used a mouse pancreas for prolonged cold preservation prior to islet isolation. For the model, a mouse is preferred over a rat because of its small size, well-known immune characterization, and variety of gene-modulated models. In the present study, we established a prolonged pancreas preservation model in a mouse for islet isolation research. The collagenase solution was injected successfully after 24 and 48 h cold preservation in University of Wisconsin solution, and islets could be isolated from both groups of preserved pancreata. The islet yields from the control, 24 h preserved, and 48 h preserved pancreata were 183.9 ± 13.9, 128.5 ± 15.5, and 24.6 ± 12.9 per pancreas, respectively. The propidium iodide-positive
area secretion was significantly increased in both preserved groups, and insulin secretion levels in response to 20.0 mM glucose and stimulation indices were significantly decreased in the 48 h preserved group. Inflammation-related gene mRNA levels were significantly upregulated in the 24 h preserved group, as previously shown in the human model. Thus, this model might be useful for the human islet isolation screening model, preserving research using human pancreata for the most promising approaches.

**JOURNAL OF BIOLOGICAL CHEMISTRY**

Early alterations of brain cellular energy homeostasis in Huntington disease models


Brain energy deficit has been a suggested cause of Huntington disease (HD), but ATP depletion has not reliably been shown in preclinical models, possibly because of the immediate post-mortem changes in cellular energy metabolism. To examine a potential role of a low energy state in HD, we measured, for the first time in a neurodegenerative model, brain levels of high energy phosphates using micro-ovarian fixation, which instantaneously inactivates brain enzymatic activities and preserves in vivo levels of analytes. We studied HD transgenic R6/2 mice at ages 4, 8, and 12 weeks. We found significantly increased creatine and phosphocreatine, present as early as 4 weeks for phosphocreatine, preceding motor system deficits and decreased ATP levels in striatum, hippocampus, and frontal cortex of R6/2 mice. ATP and phosphocreatine concentrations were inversely correlated with the number of CAG repeats. Conversely, in mice injected with 3-nitropropionic acid, an acute model of brain energy deficit, both ATP and phosphocreatine were significantly reduced. Increased creatine and phosphocreatine in R6/2 mice was associated with decreased guanidinoacetate N-methyltransferase and creatine kinase, both at the protein and RNA levels, and increased phosphorylated AMP-dependent protein kinase (pAMPK) over AMPK ratio. In addition, in 4-month-old knock-in Hdh(Q111/+) mice, the earliest metabolic alterations consisted of increased phosphocreatine in the frontal cortex and increased the pAMPK/AMPK ratio. Altogether, this study provides the first direct evidence of chronic alteration in homeostasis of high energy phosphates in HD models in the earliest stages of the disease, indicating possible reduced utilization of the brain phosphocreatine pool.

**JOURNAL OF EXPERIMENTAL MEDICINE**

Targeting self- and foreign antigens to dendritic cells via DC-ASGPR generates IL-10–producing suppressive CD4+ T cells


Dendritic cells (DCs) can initiate and shape host immune responses toward either immunity or tolerance by their effects on antigen-specific CD4+ T cells. DC-asiaglycoprotein receptor (DC-ASGPR), a lectin-like receptor, is a known scavenger receptor. Here, we report that targeting antigens to human DCs via DC-ASGPR, but not lectin-like oxidized-LDL receptor, Dectin-1, or DC-specific ICAM-3-grabbing nonintegrin favors the generation of antigen-specific suppressive CD4+ T cells that produce interleukin 10 (IL-10). These findings apply to both self- and foreign antigens, as well as memory and naive CD4+ T cells. The generation of such IL-10–producing CD4+ T cells requires p38 extracellular signal-regulated kinase phosphorylation and IL-10 induction in DCs. We further demonstrate that immunization of nonhuman primates with antigens fused to anti-DC-ASGPR monoclonal antibody generates antigen-specific CD4+ T cells that produce IL-10 in vivo. This study provides a new strategy for the establishment of...
antigen-specific IL-10–producing suppressive T cells in vivo by targeting whole protein antigens to DCs via DC-ASGPR.

JOURNAL OF NURSING ADMINISTRATION

Lessons learned from implementation of postdischarge telephone calls at Baylor Health Care System

Cochran VY, Blair B, Wissinger L, Nuss TD

J Nurs Adm 2012;42(1):40–46. Reprinted with permission from Lippincott Williams & Wilkins.

Postdischarge telephone calls can enhance patient satisfaction, outcomes, and care continuity. The authors describe the Dallas–Fort Worth-based Baylor Health Care System standardized process for placing emergency department discharge telephone calls to patients. The metrics and guidelines related to the process as well as lessons learned, models of care, the future state of the postdischarge telephone calls, and findings are discussed.

LIVER TRANSPLANTATION

Implications of a positive crossmatch in liver transplantation: a 20-year review

Ruiz R, Tomiyama K, Campsen J, Goldstein RM, Levy MF, McKenna GJ, Onaca N, Susskind B, Tillery GW, Klintmalm GB

Liver Transpl 2011 Dec 5 [Epub ahead of print]. Reprinted with permission from the American Association for the Study of Liver Diseases and John Wiley and Sons.

Whether a positive crossmatch result has any relevance to liver transplantation (LT) outcomes remains controversial. The authors describe the Dallas–Fort Worth-based Baylor Health Care System standardized process for placing emergency department discharge telephone calls to patients. The metrics and guidelines related to the process as well as lessons learned, models of care, the future state of the postdischarge telephone calls, and findings are discussed.

If you are a Baylor researcher and would like your published abstract to be included in this section, please e-mail the PubMed citation to Cynthia.Orticio@BaylorHealth.edu.