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ABSTRACT & COMMENTARY

TAVR in Lower-risk Patients: How Low Should We Go?

By Jeffrey Zimmet, MD, PhD

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Dr. Zimmet reports no financial relationships relevant to this field of study.

SYNOPSIS: A meta-analysis of studies comparing transcatheter aortic valve replacement (TAVR) to surgical aortic valve replacement over a two-year follow-up in low surgical risk patients exhibits a higher mortality in the TAVR group, prompting the authors to recommend caution in applying TAVR to low-risk patients until randomized trials are completed.

SOURCE: Witberg G, Lador A, Yahav D, Kornowski R. Transcatheter versus surgical aortic valve replacement in patients at low surgical risk: A meta-analysis of randomized trials and propensity score matched observational studies. *Catheter Cardiovasc Interv* 2018 Feb 1. doi: 10.1002/ccd.27518. [Epub ahead of print].

The use of transcatheter aortic valve replacement (TAVR), which first gained commercial approval in the United States in late 2011, has been growing. Although the initial indication was reserved for patients at prohibitive risk for surgical AVR, the approval expanded quickly to include high-risk patients, and then more-recently to intermediate-risk patients. The most recent data suggest that more than 24,000 TAVR procedures are performed in the United States annually. Can approval for low-risk patients be far behind? Although interest in the less-invasive TAVR option is keen among patients and referring providers, data on outcomes in the low-risk population (generally defined as a Society for Thoracic Surgery [STS] score < 4%) have been sparse. Witberg et al published a meta-analysis that included seven studies (five were randomized, controlled trials) published between 2012 and 2017. A total of 3,484 patients in this risk category were enrolled in these trials. Mean age of the included patients was 80 years, and the average STS score was 3.

In the whole data set, short-term mortality was similar between TAVR and surgical aortic valve replacement (SAVR; 2.2% vs. 2.6%; relative risk [RR], 0.89; 95% confidence interval [CI], 0.56-1.41; $P = 0.62$). However, intermediate-term data with a median follow-up of two

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years showed a higher mortality rate for TAVR than for SAVR (17.2% vs. 12.7%; RR, 1.45; 95% CI, 1.11-1.89; $P = 0.006$).

Essentially, comparative procedural complication rates mirrored those reported by earlier studies of intermediate and high-risk groups. Importantly, there was no significant difference in rates of stroke or myocardial infarction between TAVR and SAVR groups (1.4 vs. 1.5%, and 0.75 vs. 1.26%, respectively). However, TAVR showed an expected advantage regarding major bleeding and acute kidney injury. The authors concluded that although TAVR and SAVR produce similar short-term mortality, their data suggest a higher mortality for TAVR beyond the short term. They suggested that expansion of TAVR to the low-risk population should be restricted, at least until data from dedicated randomized, controlled trials become available.

■ COMMENTARY

Since its commercial introduction in the United States, TAVR has become more common and straightforward, with all-percutaneous access serving as the norm, along with shorter lengths of stay and improved outcomes. Use of this technology has continued to increase year over year with the inclusion of lower-risk patients. At our center we are asked on a regular basis to consider TAVR in patients who do not fit the typical elevated risk profile. Of course, patients are interested in options that are less invasive and result in shorter recovery times (so are their physicians, for that matter). Are we properly serving these patients if we steer them toward TAVR as opposed to SAVR?

This meta-analysis sounds a cautionary note in the otherwise seemingly inevitable march toward the less-invasive procedure, suggesting that TAVR in low-risk patients may be associated with greater mortality at a median follow-up of two years. The authors are correct to counsel caution, and to recommend waiting for the randomized trials of low-risk TAVR before reaching firm conclusions. However, there is reason to doubt the mortality conclusion. Individual randomized, controlled trials of intermediate-risk patients have been published in the past two years: PARTNER 2 (2,032 patients) and SURTAVI (1,660 patients). The authors of both reported no significant mortality differences between TAVR and surgery at two years of follow-up, with a similar total number of patients. The possibility of a mortality hazard specific to low-risk patients as opposed to intermediate-risk patients at the still-short two-year mark is not very plausible. Notably, the longer-term outcomes that will be of particular interest for lower-risk patients are lacking and may remain so for quite a few years.

Practically speaking, there are two major concerns limiting TAVR uptake in the low-risk population. First, the longevity of TAVR valves is still an unknown. These valves simply have not been in use long enough to develop longer-term data, and there is reason to think that the process of crimping valves for transcatheter delivery may affect lifespan. Obviously, this is of more concern to a low-risk patient at age 70 compared to a patient at age 85 with similar comorbidities. Second, pacemaker rates remain significantly higher with TAVR than with SAVR, even with the latest-generation devices. Again, this is of greater concern to younger patients for whom a permanent pacemaker will mean more years of surveillance and generator changes, not to mention the potential deleterious effects of right ventricular pacing. For providers considering the choice between TAVR and SAVR for low-risk patients, age may be a better discriminator than low-risk status alone, at least today. For the future, at least three large trials of low-risk TAVR are ongoing (PARTNER 3, Medtronic Transcatheter Aortic Valve Replacement in Low Risk Patients, and NOTION 2), so more definitive answers can be expected in the coming years. ■

ABSTRACT & COMMENTARY

CABG vs. PCI in Diabetes With Multivessel Coronary Artery Disease and LV Dysfunction

By Michael H. Crawford, MD, Editor

SYNOPSIS: A propensity score-matching analysis of all patients undergoing coronary angiography in Alberta, Canada identified a subgroup with diabetes, multivessel coronary artery disease, and left ventricular ejection fraction < 50% who were undergoing revascularization and could be separated into a group undergoing percutaneous coronary intervention (PCI) and another coronary artery bypass grafting (CABG). At five years follow-up, the CABG group experienced significantly fewer major cardiac or cerebral vascular events compared to PCI and a low risk of stroke that was similar to that observed with PCI.

SOURCES: Nagendran J, Bozso SJ, Norris CM, et al. Coronary artery bypass surgery improves outcomes in patients with diabetes and left ventricular dysfunction. *J Am Coll Cardiol* 2018;71:819-827.

Velazquez EJ, Petrie MC. CABG or PCI for diabetic patients with left ventricular dysfunction. *J Am Coll Cardiol* 2018;71:828-831.

There are no randomized trials or sufficiently powered subgroup analyses of trials that have compared coronary artery bypass grafting (CABG) to percutaneous coronary intervention (PCI) in diabetic patients with systolic left ventricular (LV) dysfunction. Thus, investigators from Canada performed a propensity score-matching analysis of the database of all patients undergoing cardiac catheterization in the province of Alberta between 2004 and 2016. Of the more than 110,000 patients identified, non-diabetics, single-vessel disease patients, those with LV ejection fraction (EF) > 50%, and those not undergoing revascularization were excluded. This left almost 3,000 patients, of whom 1,738 could be propensity matched for important clinical variables, with 869 undergoing PCI and 869 undergoing CABG. The primary outcome was major adverse coronary and cerebral events (MACCE). Secondary outcomes included mortality, stroke, myocardial infarction (MI), or repeat revascularization.

PCI resulted in higher MACCE at five years compared to CABG in those with EF 35-49% (51% vs. 28%; $P < 0.001$) and EF < 35% (61% vs. 29%; $P < 0.001$). Mortality followed the same pattern (26% vs. 16%; $P < 0.001$) in those with higher EFs (35% vs. 19%; $P < 0.002$) and in those with lower EFs. Stroke rates were all < 5% and did not differ between the two treatment groups. Repeat revascularization was consistently higher after PCI, but MI was only higher with PCI in the EF < 35% group. A sensitivity analysis of time during the trial showed similar results over the years of the study. The authors concluded that in patients with multivessel coronary artery disease, diabetes, and reduced systolic LV performance, CABG resulted in significantly fewer MACCE than PCI over long-term follow-up, without a higher risk of stroke.

■ COMMENTARY

Previous trials have shown that CABG is preferable to PCI in patients with multivessel disease and diabetes, but these trials provided insufficient data about those with reduced LV function to assume that the same holds for them. There are reasons to believe that the results could be different. Reduced LVEF could increase surgical mortality more than PCI mortality, neutralizing any advantage to surgery. Conversely, CABG may lead to better improvement in LVEF due to more complete revascularization than PCI, leading to better long-term outcomes. Thus, a study such as this one is important for clinical decision-making.

This study also was more real world in that about two-thirds of the patients studied exhibited an acute coronary syndrome on their index admission. One important finding was that there was no difference in stroke rates between the two treatment groups (3% for both). This is in contrast to other studies such as FREEDOM, which showed stroke rates at five years of 5.2% for CABG and 2.4% for PCI. Perhaps the low LVEFs in this study leveled the playing field in comparison to other studies. The editorial accompanying this article noted the tremendous public health implications of the study. Picking CABG instead of PCI in these patients effected a 16% reduction in

mortality over five years. Compare that to the 2.8% reduction in mortality observed through randomization to sacubitril/valsartan vs. enalapril to put things in perspective.

Of course, this isn't a randomized trial, so it will not produce the same effect that a double-blinded, randomized, drug comparison study would. Propensity matching can't eliminate all sources of bias. Another criticism is the 12-year span of the study, since significant changes in revascularization techniques may have occurred. However, by 2004, drug-eluting stents were in widespread use in Canada, so only refinements in the further generations of these stents would be operant. Also, a time-based sensitivity analysis didn't show any difference in the results. It would have been interesting to know how the 3,000 patients who received medical therapy only performed. In addition, the operative or procedural mortality was not given; rather, these data were included in the overall five-year results. Finally, the authors provided very little other clinical data, such as brain natriuretic peptide levels, mitral regurgitation, LV hypertrophy, or the concomitant medical therapy the patients received. Despite these flaws, the clinical message is clear and consistent with previous studies: CABG should be the first-line treatment for patients with symptomatic multivessel coronary artery disease, diabetes, and reduced systolic LV function — unless predicted operative mortality is excessive. ■

ABSTRACT & COMMENTARY

Are Beta-blockers Indicated for Heart Failure at all LVEF Levels?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A meta-analysis of 11 trials of beta-blockers for heart failure showed that beta-blockers increased left ventricular ejection fraction and reduced cardiovascular mortality in patients in sinus rhythm with baseline ejection fractions < 50%, including those in the 40-49% range.

SOURCES: Cleland JGF, Bunting KV, Flather MD, et al. Beta-blockers for heart failure with reduced, mid-range, and preserved ejection fraction: An individual patient-level analysis of double-blind randomized trials. *Eur Heart J* 2018;39:26-35.

Wilcox JE, Mann DL. Beta-blockers for the treatment of heart failure with a mid-range ejection fraction: Deja-vu all over again? *Eur Heart J* 2018;39:36-38.

Randomized, controlled trials of beta-blockers in patients with heart failure associated with reduced left ventricular ejection fraction (HFrEF) have shown improvement in EF and reductions in morbidity and mortality. More recently, heart failure with preserved EF (HFpEF) has received considerable attention, but no therapy to date has improved mortality in these patients. HFpEF has been defined as EFs > 40%, > 45%, or > 50%. Thus, uncertainty exists as to the EF above which beta-blocker therapy is futile. Also, beta-blocker therapy has not reduced mortality in HF patients with atrial fibrillation (AF), but the relation of this observation to EF is unclear.

Investigators from the Beta-blockers in Heart Failure Collaborative Group studied the effect of beta-blockers on EF and outcomes stratified by baseline EF and rhythm. They selected 11 randomized, controlled trials of beta-blockers in HF and obtained original patient data to perform a meta-analysis. The primary outcomes selected were all-cause mortality and cardiovascular death. EF was analyzed as a continuous variable and categorized into groups based on EF ranges. Statistical analysis was based on the intention-to-treat principle. Individual data from the 11 trials were obtained on more than 18,000 patients. Those with missing data, rhythm other than sinus, or AF were excluded, leaving 14,262 with sinus rhythm and 3,050 with AF who were followed for a mean of 1.5 years. The median age was 65 years, 24% were women, and 66% exhibited ischemic heart disease. Median EF was 27%, and 721 patients registered an EF between 40-49%, while 317 demonstrated an EF > 50%. Patient characteristics between those randomized to beta-blockers vs. placebo were well matched. As expected, baseline EF was inversely associated with mortality. This association was stronger for those in sinus rhythm. Mortality was predominantly cardiovascular (CV), with sudden death and worsening HF the most common. Beta-blockers reduced mortality compared to placebo in those with sinus rhythm that was consistent across all EF groups, except for the small group with EF > 50%. For those in the 40-49% group, CV mortality in the beta-blocker group compared to placebo was 4.5% vs. 9.2% (hazard ratio, 0.48; 95% confidence interval, 0.24-0.97). Also, EF increased on beta-blockers in all with sinus rhythm except for those with EF > 50%. In those with AF, beta-blockers increased LVEF in those in whom it was < 50% at baseline, but did not improve outcomes. The authors concluded that beta-blockers increase EF

and reduce CV mortality in patients with HF in sinus rhythm with baseline EF < 50%.

■ COMMENTARY

This study addressed an important issue that is confusing if one looks at the various HF guidelines; namely, those with an EF of 40-49%. Studies of HFpEF have used cutoffs of > 40% and > 45%, recognizing up to a 10% error in EF measurements and the desire to increase enrollment. However, patients in the 40-49% range often represent patients with HFrEF in whom EF has improved.

This distinction is critical because beta-blockers would be indicated in this group. Some have called this group "HF improved" or "recovered EF." The European Society of Cardiology has labelled it "HF with mid-range EF," and suggested it be treated as HFpEF, which would contraindicate beta-blockers. Thus, this analysis of 11 randomized, controlled beta-blocker trials is important because it suggests that this group should be treated with beta-blockers.

To be fair, these 11 trials were designed to treat HF due to reduced EF, but, for several reasons, some patients with EFs > 50% were included. However, this provided the opportunity to study the effect of beta-blockers in those with EFs near 50%.

An explanation for the results of this analysis was suggested in the editorial accompanying the paper. Those editorialists noted that most of the patients in the 40-49% EF group registered EFs < 43%. Accordingly, they emphasized that the 40-49% group is heterogeneous; some may be those with initial EFs < 40% in whom EF recovered somewhat, and some may be HFpEF patients in whom EF deteriorated somewhat. They recommended that in this group, EF must be examined in the overall context of the patient and their course up to that point to classify these patients properly. Of course, this is not always possible, so treatment with beta-blockers in this group should be attempted since this meta-analysis did not show any harm in doing this.

The authors also noted that both the TOPCAT study (spironolactone) and the CHARM study (candesartan) in HFpEF patients showed a trend toward mortality reduction in the 40-49% EF subgroups, but not those with higher EFs, which would lend further support to this recommendation. ■

ABSTRACT & COMMENTARY

Age-stratified NT-proBNP Thresholds Identify Acute Heart Failure

By Van Selby, MD

Assistant Professor of Medicine, University of California, San Francisco Cardiology Division, Advanced Heart Failure Section

Dr. Selby reports no financial relationships relevant to this field of study.

SYNOPSIS: In patients presenting to the ED with acute dyspnea, age-based NT-proBNP cutpoints help diagnose acute heart failure.

SOURCE: Januzzi JL, Chen-Tournoux AA, Christenson RH, et al. N-terminal pro-b-type natriuretic peptide in the emergency department: The ICON RELOADED study. *J Am Coll Cardiol* 2018;71:1191-1200.

Natriuretic peptides, including N-terminal prohormone of brain natriuretic peptide (NT-proBNP), are used commonly in the evaluation of acute dyspnea and receive a strong class Ia recommendation in clinical practice guidelines. However, there is not universal agreement regarding the appropriate cutoff values for identifying acute heart failure (HF). The authors of previous studies have proposed specific cutoffs based on the patient's age. To evaluate whether these criteria are still valid in contemporary practice, patients presenting to 19 EDs in North America for dyspnea underwent blood draws for measurement of serum NT-proBNP. A clinical events committee that was blinded to the NT-proBNP level independently reviewed each case to determine whether the patient had acute HF. The authors evaluated the ability of NT-proBNP to diagnose HF, using a cutoff of > 450 pg/mL in patients < 50 years of age, > 900 pg/mL in patients aged 50-75 years, and > 1,800 pg/mL in patients > 75 years of age. Of 1,461 patients enrolled, 277 were diagnosed with HF. The average age of all patients was 56 years, and half were female. NT-proBNP levels predicted acute HF in the overall study population, with an area under the receiver operating curve of 0.9 ($P < 0.001$, with 1.0 representing a perfect test). Using the age-specific cutoffs of 450 pg/mL, 900 pg/mL, and 1,800 pg/mL to diagnose acute HF yielded sensitivities of 85.7%, 79.3%, and 75.9% in their respective age groups. Specificity also

was strong at 93.9%, 84.0%, and 75.0%. An NT-proBNP level < 300 pg/mL was very useful for ruling out HF in all age groups, with a sensitivity of 93.9% and specificity of 98.0%. The authors concluded that in patients presenting to the ED with dyspnea, age-based NT-proBNP cutoffs aid in the diagnosis of acute HF, and a value < 300 pg/mL strongly rules out acute HF in all age groups.

■ COMMENTARY

Recommended cutoff values for the diagnosis of acute HF using NT-proBNP vary substantially. NT-proBNP is renally cleared; therefore, serum levels are affected by age-related declines in renal function. The authors of previous studies found that using age-based NT-proBNP cutoffs improved the accuracy of NT-proBNP for diagnosing acute HF. Since the publication of these studies, there has been significant change in both the demographics and treatment of HF. Here, in a large prospective cohort, Januzzi et al showed that age-based NT-proBNP cutpoints remain useful for the diagnosis of acute HF and improve diagnostic accuracy compared to any single age-independent cutoff. NT-proBNP is particularly useful for "ruling in" HF among patients < 50 years of age. Among these patients, an NT-proBNP level > 450 pg/mL predicts a diagnosis of acute HF with an impressive specificity of 93.9% and a positive likelihood ratio of 14.08. NT-proBNP also was excellent at ruling out HF when the level was < 300 pg/mL, a useful tool when evaluating patients for causes of acute dyspnea. Unfortunately, this study cannot solve a well-known limitation of both NT-proBNP and BNP: the "gray zone" of values that can neither rule in or out a diagnosis of HF. Using the cutoffs recommended in this study, the gray zone varies from 300-450 pg/mL in patients < 50 years of age to 300-1,800 pg/mL in patients > 75 years of age. In these cases, other diagnostic tools must be used to diagnose or exclude acute HF.

It is important to keep in mind the clinical context when interpreting an NT-proBNP level. Januzzi et al performed their study in patients presenting to the ED with acute dyspnea. The cutpoints identified are different from what should be used in other settings. For example, the FDA recommends much lower NT-proBNP cutoff values of 125 pg/mL and 450 pg/mL for patients < 75 years of age and ≥ 75 years of age, respectively. These values were developed for identifying chronic HF in stable outpatients. Applying the FDA criteria to an ED setting would lead to significant misdiagnosis of acute HF. Similarly, applying the cutoffs from the Januzzi et al study to an outpatient setting would lead to missed diagnoses of chronic HF. Natriuretic peptides, including NT-proBNP, remain an easy, useful aid for the diagnosis of acute HF in patients presenting with dyspnea. To use them appropriately, it is imperative to set clear cutoffs. Januzzi et al have shown that an age-stratified set of NT-proBNP cutoffs can identify acute HF in patients presenting to the ED with dyspnea. ■

ABSTRACT & COMMENTARY

Permanent His-bundle Pacing Cardiac Resynchronization: The Way Nature Intended

By Joshua D. Moss, MD

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Dr. Moss reports no financial relationships relevant to this field of study.

SYNOPSIS: When used as either a primary alternative to biventricular pacing or a rescue therapy for failed biventricular pacing, permanent His-bundle pacing was associated with significant QRS narrowing, an increase in left ventricular ejection fraction, and an improvement in New York Heart Association functional class.

SOURCE: Sharma PS, Dandamudi G, Herweg B, et al. Permanent His-bundle pacing as an alternative to biventricular pacing for cardiac resynchronization therapy: A multicenter experience. *Heart Rhythm* 2018;15:413-420.

Although the concept of permanent His-bundle pacing (HBP) is not new, the last several years have seen rapidly growing interest in and research on its potential clinical applications. Sharma et al sought to assess the feasibility of and outcomes related to HBP in various patients for whom biventricular pacing traditionally has been used as first-line therapy.

A total of 106 patients with baseline LV ejection fraction less than or equal to 50% and New York Heart

Association (NYHA) class II-IV heart failure symptoms at five centers underwent attempted HBP for cardiac resynchronization therapy (CRT). In 33 patients, traditional biventricular pacing (BVP) for CRT had failed already, either due to unsuccessful LV lead implantation (n = 25) or lack of clinical response to BVP (n = 8). In the remaining 73 patients, HBP was used as first-line CRT instead of BVP for elevated right ventricular (RV) pacing burden (n = 31), bundle branch block (n = 27), or AV block or AV junction ablation (n = 15). The same pacing lead was used for all patients, with the implant procedure limited to either five attempts or 20 minutes of fluoroscopy for successful lead positioning for HBP. In patients for whom HBP was unsuccessful, an LV lead was implanted via traditional coronary venous approach (if not attempted previously).

"Selective" HBP was defined as ventricular activation achieved exclusively via the His-Purkinje system, with an isoelectric segment between the pacing stimulus and QRS onset. "Nonselective" HBP was achieved when pacing resulted in capture of both the His-bundle and the basal ventricular septum.

Successful HBP was achieved in 95 patients, with half classified as selective HBP and half nonselective. Mean baseline QRS duration (either native or via RV pacing) decreased significantly, from 157 msec to 118 msec with HBP; narrowing of at least 20% was achieved in 44 of 48 patients with underlying bundle branch block. There was significant improvement in LV function with HBP, with 73% of patients demonstrating a > 5% improvement in LV ejection fraction.

Among 72 patients with baseline EF less than or equal to 35%, mean EF improved from 25% to 40%, and 27 of those patients were "super-responders," with absolute improvement in EF ≥ 20%. Six of eight patients who were prior non-responders to BVP demonstrated a mean increase in EF of 30% to 38% (an improvement that did not reach statistical significance), and seven of eight exhibited a clinical response (with significant improvement in NYHA class from 2.8 to 1.8). No immediate procedure-related complications were noted, although one patient required system explant for pocket infection at six months.

The authors concluded that HBP used as either a primary alternative to BVP or a rescue therapy for failed BVP was associated with significant QRS narrowing, an increase in left ventricular ejection fraction, and an improvement in NYHA functional class.

■ COMMENTARY

In permanent HBP, a pacemaker lead is fixated directly into or immediately adjacent to the penetrating bundle of His rather than other commonly used pacing sites in the right ventricle, such as the apex, septum, or outflow tract. By directly stimulating the bundle of His, depolarization of the ventricles can be achieved via the native conduction system, thereby reproducing a "normal" narrow-complex QRS. Narrow-paced QRS complexes often can be achieved even in patients with an underlying bundle branch block, effectively correcting the native wide-complex QRS. This somewhat counterintuitive phenomenon is most often explained by the concept of "longitudinal dissociation," whereby the bundle of His actually is composed of fibers already pre-destined for the right bundle and left bundle. If pacing capture can be achieved in the bundle of His distal to a site of block in these pre-destined fibers, a bundle branch block can be bypassed electrically.

Pacing capture thresholds often are higher for HBP, particularly when trying to overcome an underlying bundle branch block, resulting (on average) in shorter pacemaker battery life. In 7.4% of patients in this study, there also was significant late increase in HB capture threshold — three of those patients required a repeat procedure for HBP lead extraction and replacement with an LV lead, and the other four required high-pacing outputs to be programmed. Thus, the risk of unanticipated loss of HBP capture, plus the risks associated with more frequent operative procedures, is not trivial. Practically, some operators still prefer to implant a "backup" traditional RV pacing lead in addition to the HBP lead in patients who are pacemaker-dependent, although complete loss of RV pacing capture does not typically accompany loss of His-bundle capture.

Interest in using HBP as an alternative to both BVP for CRT and RV pacing for AV block is growing in the electrophysiology community, given the close reproduction of normal electrical physiology that apparently can be achieved. Sharma et al add substantial data to support that interest. HBP proved to be a successful "rescue" strategy in patients for whom BVP could not be achieved or who did not respond to BVP, with an overall success rate of 91%. It also was feasible, safe, and effective as first-line therapy in patients with cardiomyopathy, heart failure, and an indication for CRT (complete AV block, anticipated ventricular pacing burden > 40%, or bundle branch block).

Randomized studies comparing HBP to BVP for CRT, as well as HBP vs. RV pacing for standard pacing indications, are ongoing. Some degree of experience is required for operators to achieve consistently successful HBP, and procedural times are likely to remain longer on average, which may delay widespread adoption. However, HBP ultimately may become a standard of care in pacing therapy as efforts continue to restore physiology the way nature intended. ■

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CME/CE QUESTIONS

1. **For diagnosing heart failure in patients with acute dyspnea, natriuretic peptide levels perform better if adjusted for:**
   a. age.
   b. weight.
   c. height.
   d. sex.

2. **Symptomatic patients with multivessel coronary artery disease, diabetes, and reduced left ventricular ejection fraction experience the best outcomes with:**
   a. maximum medical therapy.
   b. cardiac rehabilitation.
   c. coronary artery bypass grafting.
   d. percutaneous coronary intervention.

3. **His-bundle pacing in heart failure with reduced LV function patients resulted in:**
   a. reduction in QRS duration.
   b. increase in LVEF.
   c. reduction in New York Heart Association functional class.
   d. All of the above

4. **Surgical aortic valve replacement (AVR) compared to transcutaneous AVR in low surgical risk patients over a two-year follow-up period showed:**
   a. less acute kidney injury.
   b. more strokes.
   c. lower mortality.
   d. more myocardial infarctions.

5. **Beta-blockers are indicated for heart failure patients in which EF range?**
   a. < 50%
   b. < 45%
   c. < 40%
   d. < 35%

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss the most current information related to cardiac illness and the treatment of cardiac disease;
- explain the advantages and disadvantages, as well as possible complications, of interventions to treat cardiac illness;
- discuss the advantages, disadvantages, and cost-effectiveness of new and traditional diagnostic tests in the treatment of cardiac illness; and
- discuss current data regarding outpatient care of cardiac patients.