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ABSTRACT & COMMENTARY

Valve-in-Valve TAVR for Failed Surgical Prostheses: Short-Term Advantages, Long-Term Unknowns

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: This large retrospective study of patients undergoing reintervention for failed bioprosthetic aortic valves showed better short-term outcomes with valve-in-valve transcatheter aortic valve replacement vs. redo surgical aortic valve replacement.

SOURCE: Deharo P, Bisson A, Herbert J, et al. Transcatheter valve-in-valve aortic valve replacement as an alternative to surgical re-replacement. *J Am Coll Cardiol* 2020;76:489-499.

Over time, there has been a progression toward using more bioprosthetic valves instead of mechanical valves in surgical valve replacement. The main drawback of these valves is their limited lifespan, with most valves affected at some point by structural deterioration. The traditional approach to this problem, redo valve surgery, is hindered by complication rates that are consistently well in excess of a first cardiovascular surgery. With the advent of transcatheter aortic valve replacement (TAVR) came early interest in treating failed aortic bioprostheses with valve-in-valve (ViV) TAVR.

Several retrospective studies have demonstrated advantages of ViV TAVR over redo surgical aortic valve replacement (SAVR) regarding obvious early outcomes, including bleeding, post-procedural hospital stays, and early mortality. Accordingly, ViV procedures have become more common over time vs. redo SAVR, reflecting increasing enthusiasm for this technique among both cardiologists and surgeons.

Deharo et al reported the results of an analysis of ViV TAVR vs. redo SAVR from a large, administrative database that includes all TAVR

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and SAVR procedures performed in France. Between 2010 and mid-2019, 4,327 patients were identified as undergoing procedures for failure of aortic bioprostheses, including 1,773 undergoing redo SAVR and 2,554 with ViV TAVR. In the unmatched cohort, patients treated by ViV TAVR were older, were more frail, presented with more comorbidities, and recorded higher expected surgical mortality rates as estimated by EuroSCORE II. After propensity score matching, 717 patients were identified in each group for the comparison.

The 30-day outcomes clearly favored TAVR. All-cause mortality was reported in 26 matched TAVR patients vs. 52 patients undergoing redo SAVR, with cardiovascular death the largest contributor (2.9% vs. 6.6%). The odds ratio for 30-day mortality with TAVR vs. SAVR was 0.48, with a 95% confidence interval of 0.30-0.78. Rates of stroke, myocardial infarction (MI), and major bleeding were not statistically different between groups, while pacemaker rates were higher after TAVR.

Longer-term follow-up was available for a median of 794 days in the redo SAVR group and 786 days in the ViV TAVR group. For the matched sets, there was no significant difference between groups regarding cardiovascular mortality, stroke, MI, and new atrial fibrillation. However, both rehospitalization for heart failure and new pacemaker implantation were more frequent in the TAVR group. The authors summarized their findings by saying short-term outcomes were better with ViV TAVR vs. redo surgery, while major cardiovascular outcomes during longer-term follow-up were not significantly different.

■ COMMENTARY

Short-term outcomes are better for TAVR vs. redo open surgery. This is an obvious finding. Even in this analysis dating back to 2010, ViV TAVR outnumbered redo SAVR for the entire dataset, accounting for nearly 60% of all cases. The numbers certainly would be more skewed toward TAVR in more recent years. The outcomes as framed in this paper appear straightforward: ViV TAVR is associated with lower short-term mortality and cardiovascular complications, with long-term outcomes that are reported to be not different. However, this greatly oversimplifies the case.

Closer analysis of the current publication shows in the central illustration exhibiting combined events at long-term follow-up, the lines cross at around 1.5 years. The early advantage of TAVR transitions to a clearly lower event rate for redo SAVR at four years post-intervention, and a non-significant difference for all events reported in the paper.

Hemodynamic data are unavailable in this analysis. Prior publications have shown ViV TAVR is associated with greater degrees of patient-prosthesis mismatch than redo SAVR, with higher transvalvular gradients post-procedure. This may explain the consistent finding, also seen here, of fewer hospitalizations for heart failure among patients undergoing redo SAVR.

Buried in the discussion, with data shown only in the supplemental appendix, is the finding that among lower-risk patients (EuroSCORE < 5), redo SAVR was associated with a strong trend toward lower long-term cardiovascular mortality (2.9% vs. 4.5%; $P = 0.06$). Notably, these lower-risk patients outnumbered the high-risk patients in the dataset (959 vs. 475). Although the higher-risk patients clearly drove the negative outcomes, lower-risk patients were not rare.

Although ViV TAVR may be the procedure of choice for elderly patients with high surgical risk, the question remains as to whether redo surgery may result in better long-term outcomes for younger patients with fewer comorbidities. The authors of an accompanying editorial argued a randomized trial comparing these two therapies is in order; for now, no such trial is on the horizon. ViV TAVR will continue to grow in use. However, these results provide a note of caution, and should prompt us to consider all options in those patients who would be expected to handle surgery well. ■

ABSTRACT & COMMENTARY

Who Benefits from Primary Prevention ICDs?

By Jamie L. W. Kennedy, MD, FACC

Associate Professor, Division of Cardiology, Advanced Heart Failure & Transplant Cardiology, University of California, San Francisco

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

SYNOPSIS: Long-term follow-up of SCD-HeFT did not show any benefit in installing implantable cardioverter-defibrillator devices in patients with New York Heart Association class III symptoms or nonischemic cardiomyopathy.

SOURCE: JE Poole, B Olshansky, DB Mark, et al. Long-term outcomes of implantable cardioverter-defibrillator therapy in the SCD-HeFT. *J Am Coll Cardiol* 2020;76:405-415.

Most heart failure deaths fall into two categories: sudden death caused by ventricular arrhythmias and pump failure. The landmark Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), in combination with the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II), established the role of implantable cardioverter-defibrillators (ICDs) for primary prevention of sudden cardiac death.

The authors of SCD-HeFT enrolled 2,521 patients with New York Heart Association (NYHA) class II-III symptoms and left ventricular ejection fraction ≤ 35% between 1997 and 2001. Patients were randomized to placebo, amiodarone, or single-lead ICD. Medical management in all arms was similar. On enrollment, nearly 100% of subjects received angiotensin-modulating drugs, although only 69% were prescribed beta-blockers. There were slightly more ischemic than nonischemic patients (52% vs. 48%). Over a median follow-up of 45.5 months, the mortality in the ICD group was 22%, significantly lower than both amiodarone (29%) and placebo (28%) groups ($P = 0.007$). There were two prespecified subgroup analyses: functional class and cardiomyopathy etiology. NYHA class II patients clearly exhibited a mortality benefit (hazard ratio [HR], 0.54; $P < 0.001$) while NYHA class III patients did not (HR, 1.16; $P = 0.30$). The mortality benefit of ICD was similar in ischemic (HR, 0.79; $P = 0.05$) and nonischemic (HR, 0.73; $P = 0.06$) patients. Eleven percent of patients in the placebo and amiodarone arms underwent ICD implant during the study, one-third as part of a cardiac resynchronization device. In the ICD arm, 31% of patients received an ICD shock, only 68% of which were appropriate, and 2.5% underwent upgrade to a biventricular pacemaker (CRT-D).

In a long-term follow-up study, Poole et al collected data between 2010 and 2011 for a median follow-up of 11 years. Vital status was known for 91% of the 2,521 originally enrolled patients. Medical management patients were offered ICDs at the end of the original trial (59% of amiodarone and 55% of placebo patients are known to have undergone implantation). About 40% of implanted devices were CRT-Ds. In the ICD arm, 27% are known to have undergone CRT-D upgrades.

Overall, mortality in the ICD arm was 52.5%, amiodarone 52.7%, and placebo 57.2%. The difference between ICD and placebo was statistically significant ($P = 0.028$). Ischemic patients demonstrated improved survival in the ICD arm compared to placebo (mortality, 59.4% vs. 68%; $P = 0.009$). However, in the nonischemic patients, mortality was similar between the ICD and placebo groups (45.1% vs. 44.0%; $P = 0.802$). NYHA class II patients in the ICD group demonstrated improved survival compared to placebo (44.6% vs. 52.1%; $P = 0.001$). However, NYHA class III patients did not derive benefit from ICD implant (mortality, 69.7% vs. 68.9% in the placebo arm; $P = 0.575$). In an as-treated analysis, ICD implantation resulted in reduced mortality (HR, 0.82; 95% confidence interval [CI], 0.72-0.96; $P = 0.008$). In a time-based analysis, the benefit of ICD implantation was unclear more than six years after enrollment. The authors concluded the long-term follow-up of SCD-HeFT-enrolled patients failed to show ICD implantation was beneficial in patients with NYHA class III symptoms or nonischemic cardiomyopathy.

■ COMMENTARY

The results of this long-term analysis are limited by incomplete follow-up and a high crossover rate. Medical management has continued to improve. In the period of this analysis, beta-blocker use increased, and the use of aldosterone antagonists and cardiac resynchronization therapy have become widespread. The observed loss of benefit of ICD implantation six years after enrollment is not unexpected considering these factors. The lack of benefit in NYHA class III patients was seen at the conclusion of the initial trial and persisted through the long-term follow-up phase. Similarly, a meta-analysis of

SCD-HeFT, the Multicenter Automatic Defibrillator Trial I (MADIT-I), MADIT-II, and the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) revealed statistically significant reduction in mortality in NYHA class II patients, but not in NYHA class III patients. Attempts at risk stratification in heart failure have been limited, but some common themes have emerged. Older age, hyponatremia, renal dysfunction, hypotension, frequent hospitalizations, poor functional status, and inability to tolerate guideline-directed medical therapy all convey poor prognosis. In clinical practice, patients with one or more of these features warrant a thorough assessment. If patients do not improve with medical optimization (e.g., adequate diuresis or transition from angiotensin-converting enzyme inhibitors to sacubitril/valsartan), then ICD implantation seems reasonable. If not, then it seems unlikely that a primary prevention ICD will be beneficial. The benefit of ICD implantation in patients with nonischemic cardiomyopathy has been unclear despite several clinical trials. The DEFINITE trial concerned nonischemic cardiomyopathy patients with non-sustained ventricular tachycardia or frequent premature ventricular contractions, the reduction in mortality with ICD implantation was not considered statistically significant at two years of follow-up (14.1% control vs. 7.9% ICD; $P = 0.08$). The DANISH trial authors enrolled patients with nonischemic cardiomyopathy and similarly found no statistically significant reduction in mortality at a mean 67.6 months of follow-up (HR, 0.87; 95% CI, 0.68-1.12; $P = 0.28$).

Part of this uncertainty may be the heterogeneity of the nonischemic population. Some genetic cardiomyopathies, like arrhythmogenic right ventricular cardiomyopathy, lamin A/C, and sarcoidosis, carry substantial arrhythmic risks. More detailed characterization of nonischemic patients enrolled in clinical trials, and in practice, is long overdue to facilitate the next generation of tailored therapy. ■

ABSTRACT & COMMENTARY

Achieving AV Synchrony Without Wires

By Joshua Moss, MD

Associate Professor of Clinical Medicine, Cardiac Electrophysiology, Division of Cardiology, University of California, San Francisco

Dr. Moss reports he is a consultant for Abbott, Biosense Webster, and Boston Scientific.

SYNOPSIS: In the MARVEL 2 prospective study of patients with atrioventricular block treated with a leadless ventricular pacemaker, atrial sensing via an accelerometer-based algorithm was largely successful in establishing atrioventricular synchronous pacing.

SOURCE: Steinwender C, Khelae SK, Garweg C, et al. Atrioventricular synchronous pacing using a leadless ventricular pacemaker: Results from the MARVEL 2 study. *JACC Clin Electrophysiol* 2020;6:94-106.

Leadless pacemakers, implanted in the right ventricle via femoral venous access, and integrating both pacing circuitry and pacing electrodes in a single small capsule, have proven effective in several clinical scenarios. The initial iteration of these devices, which the Food and Drug Administration (FDA) approved in 2016, provide asynchronous (VOO mode) or demand-based ventricular pacing based on ventricular sensing only (VVI mode), without the benefit of atrioventricular (AV) synchrony.

Steinwender et al assessed an enhanced pacing algorithm for providing AV synchronous pacing with a standard Medtronic Micra leadless pacemaker. The software is designed to detect atrial contraction, using the built-in accelerometer to assess movement of the device within the right ventricle during the cardiac cycle. The authors enrolled 77 patients with leadless ventricular pacemakers from 12 centers, including 40 patients with a predominant rhythm of underlying sinus with complete AV block.

The novel algorithm was downloaded onto the implanted device of 75 patients and optimized individually for each. Pacing was tested in a VVI mode (ventricular pacing without atrial sensing), at a lower rate of 50 beats per minute (bpm), then in a VDD mode (ventricular pacing synchronized to atrial contraction based on the accelerometer data). Holter ECG monitoring data were collected in a series of postures at rest, as well as during walking at two different paces.

The primary safety endpoint was based on freedom from atrial undersensing (leading to pauses lasting more than two cycles of the programmed lower rate) and atrial oversensing (leading to tachycardia faster than 100 bpm at rest for more than three minutes). In the 75 patients with the algorithm

downloaded, there were no instances of ventricular pauses or oversensing-induced tachycardia in more than 600,000 cardiac cycles analyzed. There were no adverse events believed to be related to the algorithm.

The primary efficacy endpoint was defined as a paced or sensed ventricular beat within 300 msec of at least 70% of ECG-confirmed P-waves, as assessed in the 40 patients with complete AV block. No patients experienced > 70% AV synchrony during VVI pacing at 50 bpm (median, 26.9%). In contrast, 38 of 40 recorded > 70% AV synchrony during VDD pacing using the accelerometer-based algorithm (median, 94.3% AV synchrony). One patient with only 69% AV synchrony as a result of atypical accelerometer signals presented with a history of repaired tetralogy of Fallot. Results were better when resting in sitting or lying positions vs. standing.

Additionally, echocardiograms were collected during both VVI and VDD pacing, with blinded measurement of left ventricular outflow velocity-time integral (VTI) as a secondary endpoint. The VTI, a proxy for stroke volume, increased by an average of 9% during VDD pacing vs. baseline VVI pacing. Sinus rate slowed from an average of 73 bpm during VVI pacing to 66 bpm during VDD pacing. The device also successfully mode switched from VVI to VDD pacing in patients with intermittent AV block, facilitating minimization of ventricular pacing. The authors concluded atrial sensing via an accelerometer-based algorithm was largely successful in establishing AV synchronous pacing with the available leadless right ventricular apical pacemaker.

■ COMMENTARY

Leadless pacemakers, currently limited clinically to the Medtronic Micra device, have become an important tool in our pacing armamentarium. A principal disadvantage of these single-chamber devices has been the lack of ability to provide AV synchronous pacing. Without electrodes in the atrium to sense atrial depolarization, ventricular pacing can be delivered based only on timing from a previous sensed or paced ventricular depolarization. In patients with prior device infections, difficult subclavian venous access, limited functional status, or permanent atrial fibrillation, ventricular-only pacing can be adequate or even advantageous. AV pacing has not been shown to improve survival or clearly reduce the risk of heart failure.

However, it is well established that AV pacing provides superior cardiac output, reduces the risk of atrial fibrillation, and minimizes the incidence of pacemaker syndrome. Additionally, for patients with intact sinus node function, faster ventricular pacing rates in response to native chronotropic response may be superior to that afforded by hardware-based activity sensors.

The MARVEL 2 study showed that despite the lack of implanted electrodes in the atrium, atrial activity can be reliably identified via analysis of the device accelerometer data (normally used to drive activity-based pacing rate changes). The hemodynamic impact of atrial contraction creates a signature movement of the device within the right ventricle that can be leveraged to enable ventricular pacing with AV synchrony. Implementation of such an algorithm represents a significant step toward substantially expanding the patient population in which a leadless device may be practical or even preferred.

[Atrial sensing via an accelerometer-based algorithm was largely successful in establishing AV synchronous pacing with the available leadless right ventricular apical pacemaker.]

The principal limitation of the study is the duration of the observational period — only about 30 minutes in various positions at rest and four minutes while walking for patients without new devices. Additionally, the sample size was small, including only 40 patients with sinus rhythm and complete AV block. Additional longer-term data in a larger and more diverse population of patients will be necessary to fully assess the effect of the VDD pacing algorithm. However, the safety data certainly suggest a favorable risk-benefit ratio, especially considering the ability to use an established physical device design and implant procedure.

Some may consider > 70% AV synchrony to be a relatively low bar for success, considering a rate closer to 100% would be expected for a standard dual-chamber pacemaker with atrial and ventricular leads. However, when combined with the algorithm for minimizing ventricular pacing in patients with intermittently intact AV conduction, that degree of AV synchrony may be more than adequate to achieve the benefits associated with dual-chamber devices. Longer-term studies are needed to determine the effect of upgraded software. Based in part on results of the MARVEL 2 study, the FDA approved the Medtronic "Micra AV" device with the necessary algorithms for clinical use in January. ■

ABSTRACT & COMMENTARY

What to Do with Large Pericardial Effusions

By Michael H. Crawford, MD, Editor

SYNOPSIS: An observational study of patients with chronic, large, hemodynamically insignificant, C-reactive protein-negative, idiopathic pericarditis in which the majority were treated by pericardiocentesis or surgical drainage showed most patients treated conservatively remained stable. The invasive approach did not reveal an etiology for the effusions.

SOURCE: Lazaros G, Antonopoulos AS, Lazarou E, et al. Long-term outcome of pericardial drainage in cases of chronic, large, hemodynamically insignificant, C-reactive protein negative, idiopathic pericardial effusions. *Am J Cardiol* 2020;126:89-93.

Current guidelines recommend drainage of large chronic idiopathic pericardial effusions, even if they are not of hemodynamic significance and the patient is asymptomatic. However, there is a paucity of data supporting this practice.

Lazaros et al studied such patients who were seen at one pericardial disease referral center and three other clinics in Greece from 2013 to 2018. Inclusion criteria were that the effusions were large (> 2 cm diastolic echo-free space), chronic (> 3 months), idiopathic, hemodynamically insignificant, and that the patients were asymptomatic and had normal serum C-reactive protein (CRP) levels. These criteria excluded 304 of 378 patients with pericardial effusions identified, leaving a study population of 74 patients.

Among these 74 patients, 52 chose drainage of the effusion. The attending physician and patient decided whether this was accomplished by pericardiocentesis or pericardial window. This resulted in 39 patients who chose pericardiocentesis, 13 a pericardial window, and 22 who were conservatively treated. The primary endpoint was re-accumulation of fluid over a median follow-up of 24 months. Complications of drainage and other clinical events also were recorded.

At baseline, there were no significant differences in the demographics or pericardial disease characteristics among the three groups. An analysis of the pericardial fluid and pericardial biopsies taken in those undergoing surgery all failed to reveal a specific fluid etiology. Re-accumulation of fluid occurred in 32 of 52 patients drained (30 in the pericardiocentesis group and two in the surgical group; $P < 0.001$). Those who re-accumulated experienced longer disease duration and larger effusions compared to those who did not re-accumulate. Among conservatively treated patients, most remained stable over time (77%), some regressed (14%), and a few developed impending tamponade and were drained (9%). Procedural complications occurred in 13% of patients undergoing pericardiocentesis and 15% of surgical drainage patients (P = not significant). There were seven deaths during follow-up and all were non-cardiac. No one developed constrictive pericarditis. The authors concluded a conservative approach is reasonable in patients with chronic, large, hemodynamically insignificant, CRP-negative, idiopathic pericardial effusion.

■ COMMENTARY

There is an old clinical adage that large pericardial effusions should be drained because they are more likely to result in cardiac tamponade. This may be true, but probably only in the acute or early phase of pericarditis. Draining the fluid may be associated with less tamponade, but usually other therapies (e.g., anti-inflammatory drugs) are given at the same time, so the effect of pericardial drainage per se is difficult to discern. Lazaros et al, in their interesting observational study, assessed the value of pericardial drainage in large, chronic, idiopathic, asymptomatic, hemodynamically insignificant, and CRP-negative effusions. Thus, these are patients with no clear indication for any therapy. They found pericardiocentesis did not prevent re-accumulation, since almost two-thirds re-accumulated. Although surgical pericardial window was superior at preventing re-accumulation, 15% experienced significant complications from the procedure. Also, routine biopsy of the pericardial tissue uncovered no occult diagnoses. Paradoxically, re-accumulation was associated with longer disease duration and larger effusions, two factors that might be thought to favor drainage. There appears to be little advantage to draining the fluid in this small asymptomatic subgroup of patients.

There were study limitations. Although the data were collected prospectively, it was an observational study subject to the biases of this type of investigation. Also, most patients came from one pericardial disease referral center, which emphasizes the uniqueness of the observed population. Further, we cannot translate the findings of this study to other, more acute patients with large pericardial effusions. Nor can the results be applied to symptomatic patients or those with a known inflammatory condition. These results do support routine follow-up of similar patients. In the conservatively treated patients, 9% developed tamponade, but this low rate also does not justify routine drainage of large effusions in this type of patient. Current guidelines suggest follow-up every three to six months, which seems reasonable. ■

ABSTRACT & COMMENTARY

Is Isolated Diastolic Hypertension a Disease?

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of three large prospective databases showed the 2017 American College of Cardiology/American Heart Association revised definition of isolated diastolic hypertension as > 80 mmHg rather than the previous definition of > 90 mmHg resulted in a 5% higher prevalence of diastolic hypertension. This was not significantly associated with cardiovascular disease outcomes.

SOURCE: McEvoy JW, Daya N, Rahman F, et al. Association of isolated diastolic hypertension as defined by the 2017 ACC/AHA blood pressure guideline with incident cardiovascular outcomes. *JAMA* 2020;323:329-338.

In 2017, the American College of Cardiology/American Heart Association (ACC/AHA) hypertension guidelines redefined diastolic hypertension (DH) as > 80 mmHg based on expert opinion, not trials. McEvoy et al sought to establish the prevalence of DH under these revised guidelines and to assess the association between DH so defined with cardiovascular disease (CVD) outcomes.

To accomplish these goals, they analyzed cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) database from the 2013-2016 survey of U.S. adults and longitudinal data from the Atherosclerosis Risk in Communities (ARIC) study second examination in 1990-1992 with follow-up through 2017. The longitudinal results were validated in NHANES from 1988-1994, NHANES 1999-2014, and the Give Us a Clue to Cancer and Heart Disease (CLUE) II cohort from the 1989 baseline data. In NHANES and ARIC, blood pressure (BP) was measured after five minutes of sitting, and the mean of two to three measurements were used. In ARIC, high-sensitivity troponin and NT-proBNP also were measured. The prespecified cardiovascular disease (CVD) outcomes in ARIC were atherosclerotic (AS) CVD, heart failure (HF), and chronic kidney disease (CKD). ASCVD was a composite of myocardial infarction, ischemic stroke, or CVD death. Sensitivity analyses were performed for age, systolic BP, and antihypertensive treatment.

After excluding patients with missing data and age < 20 years, 9,590 NHANES patients were available, of which DH was present in 1.3% by JNC 7 criteria (> 90 mmHg) and 6.5% by 2017 ACC/AHA criteria. Few were recommended for drug therapy by either definition (1.6% and 2.2%, respectively). Among the > 14,000 ARIC patients aged 46-69 years, after excluding those with systolic hypertension, 2% met JNC 7 criteria for DH and 11% met ACC/AHA criteria. Those with isolated DH were more likely younger, male, Black, overweight, or had lipid abnormalities. During a median follow-up of 25 years, compared to normal BP, there were no statistically significant associations between DH and the composite outcome of ASCVD, HF, or CKD (hazard ratio [HR], 1.03; 95% confidence interval [CI], 0.93-1.15) or any of the individual endpoints. Sensitivity analyses did not change the results. In the NHANES validation cohort, DH was not associated with all-cause or CVD death (HRs, 0.92 and 1.17, respectively). Similar results were seen in the CLUE validation cohort (HR, 1.02 for both endpoints). Also, in ARIC, there were no significant associations between DH and cardiac biomarkers (troponin, BNP). The authors concluded that in this analysis of several populations of U.S. adults, isolated DH by the 2017 ACC/AHA definition was more prevalent than with the JNC 7 definition, but was not significantly associated with CVD outcomes.

■ COMMENTARY

The 2017 ACC/AHA guidelines for the treatment of hypertension caused quite a bit of controversy over the stricter definition of systolic hypertension to > 130 mmHg. Such measurements mainly revolved around older individuals in whom systolic BP naturally tends to increase with age and in patients with conditions such as coronary artery disease in whom higher pressures may be required to perfuse the myocardium. At the other end of the spectrum are subjects with isolated DH who more frequently tend to be young men. The new definition of DH raised the prevalence of it several-fold compared to the previous JNC 7 definition. This decision was based largely on older epidemiologic data that showed an increase in the risk of developing CVD at diastolic BPs > 75 mmHg and expert opinion. This carried psychological, social, and financial implications, so it is not a trivial matter.

However, this analysis of NHANES and ARIC data did not demonstrate an increase in CVD events or mortality. Perhaps more importantly there was no signal of subclinical organ damage, as evidenced by no significant changes in troponin and BNP. Prior studies have shown an association with DH and the development of later systolic hypertension, which was not analyzed in this study. Despite this possibility, there is no indication for drug treatment of isolated DH. This advice is consistent with the

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Hypertension Optimal Treatment (HOT) study, which did not show any benefit to reducing diastolic BP from 90 to 80 mmHg. Periodic surveillance for systolic hypertension would seem reasonable.

There were some limitations to the work of McEvoy et al. Although several sensitivity analyses and comparisons to other databases were conducted, there always is the possibility of residual confounding. Also, in ARIC, the lowest age for participation was cut off at 48 years, so these results may not apply to younger individuals. Still, the results were consistent with the NHANES data, where the lowest age was 20 years, and CLUE, where the median age was 42 years.

In addition, the studies used included patients on antihypertensive therapy. In such patients, any intervention would be escalation of therapy to further lower diastolic BP. Sensitivity analyses to adjust for this factor did not change the results. Finally, in ARIC, participants had to self-identify as either Black or white, so the results may not apply to other racial or ethnic groups. On the other hand, NHANES included all ethnicities in proportion to the U.S. population, and the results were the same in this population.

Despite all these potential weaknesses, this was a large study of three population cohorts that all demonstrated the same findings. Isolated DH does not seem to be a pathological entity, yet may represent about one-quarter of U.S. adults who have been recommended for BP therapy since the introduction of the 2017 ACC/AHA guidelines. It is time to re-examine the diastolic component of the controversy over these new guidelines. ■

CME/CE QUESTIONS

1. **An analysis of two large study databases has shown that moving to the new guideline definition of isolated diastolic hypertension as > 80 mmHg would result in:**

   a. a strong association with cardiovascular events.

   b. a strong association with cardiovascular mortality.

   c. a strong association with elevated cardiac biomarkers.

   d. a substantial increase in the number of individuals with this diagnosis.

2. **A recent observational study of patients with large pericardial effusions showed the best approach to patients with chronic, hemodynamically insignificant, C-reactive protein-negative, idiopathic effusions is:**

   a. conservative management.

   b. intense medical management with steroids and colchicine.

   c. pericardiocentesis.

   d. surgical pericardial window.

3. **The leadless right ventricular pacemaker reprogrammed to sense atrial mechanical activity resulted in:**

   a. pauses of > 2 cycle lengths.

   b. oversensing-induced tachycardia.

   c. atrioventricular synchronous pacing.

   d. reduced left ventricular outflow tract velocity time integral.

4. **In comparison to valve-in-valve transcatheter aortic valve replacement, redo surgery demonstrated a long-term reduction in:**

   a. mortality.

   b. rehospitalization for heart failure.

   c. stroke.

   d. myocardial infarction.

5. **Long-term follow-up of patients enrolled in SCD-HeFT showed which group randomized to implantable cardioverter-defibrillators vs. amiodarone or placebo showed reduced mortality?**

   a. Ischemic cardiomyopathy

   b. Nonischemic cardiomyopathy

   c. New York Heart Association (NYHA) class III symptoms

   d. NYHA class IV symptoms

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