

Clinical Cardiology

Critical analysis of the latest clinical research in cardiovascular medicine [ALERT]

ABSTRACT & COMMENTARY

CABANA Trial Reveals New Insights About Ablation for Atrial Fibrillation

By Joshua D. 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 Biosense Webster and Abbott.

SYNOPSIS: Ablation for atrial fibrillation did not reduce the composite endpoint of death, disabling stroke, serious bleeding, or cardiac arrest compared with drug therapy, although adverse events were infrequent and arrhythmia recurrence was reduced significantly.

SOURCE: Packer DL, Mark DB, Robb RA, for the CABANA Investigators. Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) trial: Study rationale and design. Presented at the 39th Heart Rhythm Scientific Sessions, Boston, May 10, 2018. Results published in *Am Heart J* 2018;199:192-199.

The long-awaited results of the Catheter Ablation vs. Antiarrhythmic Drug Therapy in Atrial Fibrillation (CABANA) trial were presented as a late-breaking session at this year's Heart Rhythm Scientific Sessions. The goal of the randomized study, which began enrolling patients in 2009, was to compare catheter ablation to state-of-the-art drug therapy for patients with new onset or "undertreated" paroxysmal or persistent atrial fibrillation (AF) that warranted therapy. Patients < 65 years of age also were required to exhibit at least one cardiovascular or stroke risk factor to be eligible. Patients in the ablation arm underwent pulmonary vein isolation at a minimum, and patients

in the drug therapy arm could be treated with rate or rhythm control. Originally, the primary endpoint was defined as mortality. However, partway through the trial, investigators changed this to a composite endpoint of all-cause mortality, disabling stroke, serious bleeding, or cardiac arrest due to difficulty with enrollment and low mortality.

A total of 1,108 patients were randomized to ablation therapy, 1,006 of whom underwent ablation and 102 of whom crossed over to the drug therapy arm. A total of 1,096 patients were randomized to drug therapy, 301 of whom crossed over to receive catheter ablation.

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Approximately one-third of patients in both arms were < 65 years of age, and approximately 37% were female. Baseline cardiomyopathy was slightly more prevalent in the drug therapy arm, although rates of congestive heart failure were similar. About 10% of patients had a history of prior stroke or transient ischemic attack. Overall, about 90% of patients completed a mean follow-up around four years. Complications in the ablation group were rare; hematoma at the catheter insertion site (2.3%) was most common. There were eight episodes of perforation and cardiac tamponade, but no atrioesophageal fistulas. In the drug therapy arm, hypo- or hyperthyroidism occurred in 1.6% of patients.

Over 60 months of follow-up, there was no statistically significant difference in the primary endpoint by an intention-to-treat analysis, although rates remained slightly lower in the ablation group throughout. Mortality alone also was not significantly different. There was a significant reduction in combined death or cardiovascular hospitalization in the ablation group, a secondary outcome, with a hazard ratio (HR) of 0.83. A subgroup analysis suggested a possibility of improved outcomes with ablation in younger patients and minorities. Freedom from recurrent AF was about 65% at one year in the ablation arm vs. only about 40% in the drug therapy arm. Rates of recurrent AF remained significantly lower in the ablation arm throughout follow-up (HR, 0.53; 95% confidence interval, 0.46-0.61). When groups were compared based on treatment received, there were significant reductions in the primary combined endpoint (HR, 0.67) and all-cause mortality (HR, 0.60) in the ablation arm compared with drug therapy.

■ COMMENTARY

The presentation of CABANA was highly anticipated, and electrophysiologists and cardiologists alike continue hotly debating the meaning and results. Many held up the “negative” result, with no significant difference in the combined primary endpoint, as proof that catheter ablation was overused compared with antiarrhythmic drugs. One prominent commentator even suggested that any alternate interpretations were evidence that electrophysiologists must be hopelessly conflicted by the financial rewards of a

complex procedure. By contrast, many others pointed to the dramatic reduction in recurrent AF in the patients randomized to ablation, with minimal cost in terms of procedural risk and no cost in terms of stroke, mortality, or bleeding.

I drew the following conclusions from the available data:

- 1. Ablation for atrial fibrillation is at least as good as medical therapy.** Many electrophysiologists hoped to see superior results with ablation. They were either disappointed in the actual results, or eager to focus on the on-treatment analysis, which is scientifically dubious. Researchers use randomization for a reason, and we do not know how patients who crossed over to ablation were different from other patients in the medical therapy arm. However, many of us were pleased to receive confirmation that outcomes such as mortality, disabling stroke, and serious bleeding were, at worst, equivalent in an intention-to-treat analysis. In general, crossover in a randomized trial tends to bias outcomes toward the null-hypothesis (i.e., toward no difference in treatment effect). Ablation proved to be as good as medical therapy despite that crossover.
- 2. Clearly, ablation is more effective than medical therapy at preventing AF.** Reduction in arrhythmia burden was not in the primary combined endpoint, and it often was overlooked during ensuing debates about intention-to-treat vs. on-treatment results. However, the likelihood of recurrent AF was reduced almost 50% with ablation compared with medical therapy — again, despite the crossover. Cardiovascular hospitalization also declined. Our primary objective in treating AF in patients without heart failure always has been to reduce symptoms and improve quality of life. It will be interesting to see the full impact of ablation in the final published results.
- 3. Ablation is safe.** Overall rates of complications were low, a finding that was important to confirm for a complex procedure performed electively.
- 4. A double-blinded trial of ablation is likely to follow.** Despite the clear reduction in AF with ablation, and the undisputable correlation between symptoms and arrhythmia in some patients, the true vs. placebo effect of ablation on symptoms in the broader population of patients with AF is unknown. Particularly after the successful

completion of the ORBITA trial and its intriguing results, we probably can expect a similar trial of ablation with a sham procedure control in the near future. The

ethics and comparability of such a sham procedure, depending on how it is performed, undoubtedly will be the subject of more debate. ■

ABSTRACT & COMMENTARY

Drug-eluting Stents Fare No Better Than Bare-metal Stents in Vein Graft Lesions

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco; Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

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

SYNOPSIS: The two largest randomized trials to date have shown no advantage to drug-eluting stents compared to bare-metal stents in saphenous vein graft percutaneous interventions.

SOURCE: Colleran R, Kufner S, Mehilli J, et al. Efficacy over time with drug-eluting stents in saphenous vein graft lesions. *J Am Coll Cardiol* 2018;71:1973-1982.

In treatment of obstructive disease involving saphenous vein grafts (SVGs), percutaneous intervention (PCI) is a common element of management, with high rates of upfront technical success. Generally, drug-eluting stents (DES) perform better than bare-metal stents (BMS) in native coronary vessels, with lower rates of target vessel revascularization and higher rates of primary patency in complex lesions. Multiple studies comparing BMS with DES in SVGs have been performed, with the majority comprised of relatively small populations. The authors of most of those older trials have reported an advantage to DES in terms of short- and intermediate-term events. Based on those results, current guidelines in both the United States and Europe recommend DES as a first-line option for SVG lesions.

The largest of these studies is the ISAR-CABG trial, which enrolled 610 patients who were randomized to treatment with DES (303) or BMS (307). In 2011, the 12-month results from this trial were published. Major adverse cardiac events (MACE) at one year were significantly lower in the DES group compared with BMS (15.0% vs. 22.1%; relative risk, 0.64; $P = 0.02$), a difference that was driven almost entirely by a reduction in ischemia-driven target lesion revascularization (TLR) (6.8% vs. 13.1%; $P = 0.01$). There were no differences in death (5.1% vs. 4.7%; $P = 0.83$), myocardial infarction (MI; 4.2% vs. 6.0%; $P = 0.27$), or stent thrombosis (0.7% vs. 0.7%; $P = 0.99$).

Recently, investigators reported five-year outcomes from this trial. In the final analysis, the combined endpoint of death, MI, or TLR occurred in 159 patients in the DES group vs. 157 patients in the BMS group. While the event rate was lower in the DES group at the end of

the first year, there was a “catch up” phenomenon over the subsequent time in the study, such that TLR actually was higher in the DES group after the first year, and not significantly different at five years.

The authors concluded that in patients undergoing PCI for treatment of SVG lesions, the initial advantage of DES over BMS is subsequently lost, such that there is no significant difference in efficacy by five years.

■ COMMENTARY

The first learning point from this trial is the obvious one — namely, that BMS can be used in vein grafts with similar efficacy to DES. In support of this finding, the recently published DIVA study showed no significant difference in outcomes between DES and BMS among 597 patients followed for a median of 2.7 years.¹ The main implication of this result pertains to cost, as there remains a significant (although shrinking as the cost of DES comes down) price differential between these devices. One should not be too quick to conclude that a shorter length of dual antiplatelet therapy (DAPT) also is indicated, however, as all patients in the ISAR CABG trial were prescribed six months of DAPT, regardless of stent type.

What else can we learn from these data? We know that SVGs, compared with native coronaries, exhibit different pathophysiology, leading to higher rates of adverse outcomes. Additional lesions often form after treatment of an initial SVG stenosis, leading to recurrent SVG failure. In this regard, the numbers reported in the trial still are striking. At the five-year mark, the primary outcome (a composite of death, MI, and TLR) had occurred in *more than half* of all patients in the trial, regardless of

treatment strategy. This sobering statistic reminds us that SVG failure, even after successful PCI, is a marker for adverse outcomes in a majority of patients, and should prompt us to optimize therapy in every possible way.

One strategy for dealing with this dismal record is to examine each individual case for the optimal revascularization strategy. Redo CABG often is not the best choice, but should be considered when the left internal thoracic artery has not been grafted, and when multiple lesions require treatment. Because PCI of the native coronary vessels is likely to demonstrate superior longevity to treatment of the graft, native vessel alternatives to SVG PCI also should be examined. For situations in which

PCI of the native coronary is not overly complex, some authors have advocated approaching the native vessel first, even when PCI of the graft also is straightforward.

The two largest trials to date have shown no advantage of DES compared with BMS in PCI of SVG lesions. The high subsequent event rates in patients with SVG lesions should, in each case, prompt a global evaluation of optimal medical therapy and revascularization strategies. ■

REFERENCE

1. Brilakis ES, Edson R, Bhatt DL, et al. Drug-eluting stents versus bare-metal stents in saphenous vein grafts: A double-blind, randomised trial. *Lancet* 2018;391:1997-2007.

ABSTRACT & COMMENTARY

Long-term Risk of Transient Atrial Fibrillation After Coronary Artery Bypass Graft Surgery

By Michael H. Crawford, MD, Editor

SYNOPSIS: Investigators compared post-coronary artery bypass graft (CABG) atrial fibrillation (AF) to non-surgical, non-valvular AF in a large cohort derived from the Danish health system database. Despite a lower rate of oral anticoagulant use compared to non-valvular AF patients and equivalent CHA₂DS₂-VASc scores, post-CABG AF demonstrated a lower risk of thromboembolism, death, and recurrent AF. These data do not support the concept that post-CABG AF is the same as traditional non-valvular AF regarding thromboembolic risk.

SOURCES: Butt JH, Xian Y, Peterson ED, et al. Long-term thromboembolic risk in patients with postoperative atrial fibrillation after coronary artery bypass graft surgery and patients with nonvalvular atrial fibrillation. *JAMA Cardiol* 2018;3:417-424.

Healey JS, McIntyre WF, Whitlock RP. Late stroke after coronary artery bypass grafting. *JAMA Cardiol* 2018;3:425-426.

New onset post-operative atrial fibrillation (POAF) is a common, but usually self-limiting, complication of coronary artery bypass graft surgery (CABG). Although generally thought to be relatively benign, there are few data on its long-term implications. Current guidelines give little guidance on the role of oral anticoagulants (OAC) in POAF.

Investigators from Denmark performed a retrospective cohort study of stroke prophylaxis and the long-term risk of thromboembolism (TE) in 2,108 patients undergoing first isolated CABG who developed new POAF. These patients were matched by age, sex, and CHA₂DS₂-VASc scores with 8,432 patients with non-surgical, non-valvular AF (NVAF). Inclusion criteria for the POAF patients included no prior history of AF, no prescription for OAC \leq 6 months prior to surgery, no history of deep venous thrombosis or pulmonary embolism, and survival until discharge from the hospital. The NVAF comparison group met similar criteria. The primary outcome was any TE. Secondary endpoints included death and recurrent AF requiring hospitalization. The mean age of the POAF group was 69 years, and 82% were men. Their mean CHA₂DS₂-VASc score was 3.1, which was the same as the NVAF group. However, there were significant differences in many co-morbidities between

the two groups. OAC therapy was started within 30 days in 8.4% of POAC subjects and 43% of NVAF subjects. Anti-platelet therapy was employed in 79% of the POAF group and a little over half of NVAF patients. Median follow-up was five years in the POAF group and 3.5 years in the NVAF group. The incidence of TE was 18.3 per 1,000 person years in POAF patients and 29.7 in NVAF patients.

By multivariate analysis, the incidence of TE was significantly lower in the POAF group (adjusted hazard ratio [HR], 0.67; 95% confidence interval [CI], 0.55-0.81; $P < 0.001$). OAC therapy was associated with a significantly lower risk of TE in both groups compared to those not treated with OAC. POAF was associated with a lower risk of death compared to NVAF (HR, 0.55; 95% CI, 0.49-0.61; $P < 0.001$). However, OAC use was only associated with a lower risk of death in the NVAF group. Also, in POAF patients, the risk of recurrent AF was significantly lower than in the NVAF patients (HR, 0.29; 95% CI, 0.25-0.34; $P < 0.001$), but higher than in those post-operative patients who did not develop AF (HR, 2.27; 95% CI, 1.84-2.80; $P < 0.001$). Additionally, mortality was higher in POAF patients compared to post-operative patients without AF (HR, 1.32; 95% CI, 1.18-1.47; $P < 0.001$). The authors concluded that these

data do not support the concept that POAF is equivalent to NVAF regarding long-term TE risks.

■ COMMENTARY

Previous studies have shown that POAF in CABG patients usually disappears by six weeks post-operation, no matter what therapy is given, which supports the notion that it is largely due to the systemic inflammatory response to surgery. Also, prior studies have shown a higher incidence of TE in the first 30 days in those with POAF compared to those without, but the incidence of long-term TE has been unclear, and few studies have contained data about long-term OAC use. In this observational study, only 8% of POAF patients received OAC compared to 43% of NVAF patients. Yet, POAF patients demonstrated a much lower incidence of TE despite equivalent CHA₂DS₂-VASc scores. Also, death and recurrent hospitalization for AF was lower in POAF subjects vs. NVAF subjects. The authors concluded that POAF is more benign than typical NVAF, but stopped short of making OAC recommendations.

Both the U.S. and European guidelines state that it is reasonable to consider OAC therapy in POAF patients, but don't elaborate further. The critical issue is that most POAF probably is a transient phenomenon that does not necessitate long-term OAC therapy, but some of these patients may resemble NVAF patients who

happen to have received the diagnosis of AF after CABG. How do we identify these higher-risk POAF patients? Unfortunately, this study does not address that issue and the authors recommended conducting a randomized, controlled trial. Until such a trial is performed, how should we proceed? It appears that short-term OAC should be given, if feasible post-operatively, since it reduces TE compared to those with POAF, who did not receive it in this study and in others. The decision about long-term OAC should be made after considering other risk factors for recurrent AF or TE. Perhaps those with very large atria or very high CHA₂DS₂-VASc scores should receive OACs long term. Certainly those with persistent AF or recurrent AF should. Perhaps an ambulatory ECG monitor should be employed after the return of sinus rhythm, but within 8-12 weeks post-operatively.

The strength of this trial is the complete information available through the Danish health system, especially regarding OAC use. The weaknesses, in addition to its observational design, are that we have no information about the duration of POAF or the rhythm at discharge. Also, we don't know the type of AF the NVAF patients had. Despite these weaknesses, this study adds to our knowledge in this area and helps inform the clinical judgment required to manage patients with POAF after CABG. ■

ABSTRACT & COMMENTARY

Mortality Risk Score for Degenerative Mitral Regurgitation

By Michael H. Crawford, MD, Editor

SYNOPSIS: An international database of patients with significant degenerative mitral valve regurgitation was used to derive and test a score using clinical and echocardiographic data to estimate mortality with medical and surgical therapy. From seven weighted characteristics, investigators developed a 0-12 score that predicted medical and surgical long-term mortality with high discriminatory ability (C-statistic, 0.78 and 0.81, respectively). Investigators found the score added incremental information to surgical scores and believe that it will be useful for therapeutic decision-making.

SOURCES: Grigioni F, Clavel MA, Vanoverschelde JL, et al. The MIDA mortality risk score: Development and external validation of a prognostic model for early and late death in degenerative mitral regurgitation. *Eur Heart J* 2018;39:1281-1291.

Vahanian A, Lung B. Predicting the outcome of degenerative mitral regurgitation: A step forward but still a long way to go! *Eur Heart J* 2018;39:1292-1294.

Mitral valve regurgitation (MR) is the most frequent valve disease. Degeneration often with prolapse is the most common cause of MR. Although surgical risk scores exist, there is no non-surgical, long-term mortality score to help guide clinicians. Accordingly, investigators sought to develop and validate such a score from a large international degenerative MR database (MIDA). Prognostic markers from clinical data and echocardiography were selected from current guidelines

and assessed in the derivation cohort (2,472 patients with a flail leaflet), which established the weight of each marker. The resulting MIDA score was tested for predictive ability for one year mortality, regardless if the patient underwent subsequent surgery. The MIDA score was validated in the MIDA-BNP registry (1,194 patients with flail or prolapsed leaflets) over a 10-year follow-up. Since the results of the two cohorts were analogous in the prognostic ability of the MIDA score, they were

combined (n = 3666) for a more robust analysis. The weighted markers were age > 65 years (3 points), symptoms (3 points), right ventricular systolic pressure > 50 mmHg (2 points), atrial fibrillation (1 point), left atrial diameter > 5.5 cm (1 point), left ventricular (LV) end-systolic diameter > 4.0 cm (1 point), and LV ejection fraction (EF) < 60% (1 point), for a total possible score of 0-12. After a mean eight-year follow-up, 1,151 of the 3,666 patients died. Overall survival was 84% at five years and 69% at 10 years. During a mean medical follow-up of two years, 521 patients died. Eventually, surgery was performed in 2,659 patients (90% repair); 630 died during follow-up. The MIDA score accurately predicted mortality in both medical and surgical patients (see Table) and added incremental value to surgical scores such as the EuroScore II. The authors concluded that the MIDA score may represent an innovative tool to help manage degenerative MR patients, whether they are under medical or surgical care.

■ COMMENTARY

As soon as a patient with significant degenerative MR becomes symptomatic or develops one other criteria for mitral valve surgery, a surgical risk score is deployed, and decisions about surgery are made. This biases surgical therapy toward lower-risk patients, which many studies have demonstrated. Part of the problem is the lack of a good estimator of mortality on medical therapy; hence, the impetus for the development of the MIDA score, the use of which may help prevent leaving high-risk patients on medical therapy. This is especially important today because we have minimally invasive surgery and percutaneous approaches to mitral valve repair. The MIDA score robustly predicted early and late mortality in medical and surgical patients with good discrimination (C-statistic, 0.78 and 0.81, respectively).

Table. One-year Medical and Surgical Mortality vs. Five-year Medical and Surgical Survival

MIDA Score	One-year Mortality Medical %	One-year Mortality Surgical %	Five-year Survival Medical %	Five-year Survival Surgical %
0	0.4	1.0	98	99
7-8	17	7	57	82
11-12	48	14	21	57

Thus, the authors thought it could be a useful tool for decision-making in patients with significant MR.

The strengths of this study were that it is the largest study of degenerative MR to date, with more than 3,000 patients; it included clinical and echo parameters and is of incremental value over surgical scores. However, there were some weaknesses. There was a selection bias toward severe MR patients, but with low surgical risk (mean EuroScore, 1.2). The precise grading of MR was not specified, but was a combination of measures. Patients undergoing percutaneous repair were under-represented, and comorbidities were not considered. Consequently, Vahanian and Iung concluded in an accompanying editorial that one could not use this score alone to make decisions; rather, one must consider all available data and make a reasoned clinical judgment. They emphasized that directing the Heart Team to evaluate the patient, as recommended by the European Society of Cardiology Guidelines (2017), is the best approach. However, I don't think committees should make clinical decisions, but rather help inform the patients and their doctors' decisions. In this context, the MIDA score will be a useful adjunct to decision-making in degenerative MR patients. ■

ABSTRACT & COMMENTARY

Simple Prediction Tool Facilitates Diagnosis of Heart Failure With Preserved Ejection Fraction

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 with unexplained dyspnea, a score based on six noninvasive criteria can predict the likelihood of heart failure with preserved ejection fraction.

SOURCE: Reddy YNV, Carter RE, Obokata M, et al. A simple, evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction. *Circulation* 2018 May 23. pii: CIRCULATIONAHA.118.034646. doi: 10.1161/CIRCULATIONAHA.118.034646. [Epub ahead of print].

Exertional dyspnea is a frequent complaint among patients referred to cardiology clinics. Heart failure with preserved ejection fraction (HFpEF) is common among such patients, but the diagnosis can be challenging without invasive testing. Reddy et al sought to develop a simple risk prediction score based on readily available clinical data. They retrospectively analyzed a cohort of 414 consecutive patients with unexplained dyspnea who were referred for right heart catheterization with exercise testing at the Mayo Clinic. A diagnosis of HFpEF was confirmed if the patient demonstrated a pulmonary arterial wedge pressure ≥ 15 mmHg at rest or ≥ 25 mmHg during exercise. Multivariable logistic regression was used to identify clinical variables associated with the presence of HFpEF.

Of the 414 patients studied, 267 were diagnosed with HFpEF, and the rest were diagnosed with noncardiac dyspnea. The clinical predictors in the final model were obesity, atrial fibrillation, age > 60 years, treatment with two or more antihypertensive medications, an E/e' ratio > 9 on echocardiography, and a pulmonary artery systolic pressure > 35 mmHg on echocardiography. The authors developed a weighted composite (the H₂FPEF score) using these six predictors, with scores ranging from 0-9. The score was strongly associated with the likelihood of HFpEF, with the odds of HFpEF doubling for every one-unit increase in score (odds ratio, 1.98; $P < 0.0001$). The area under the curve (AUC) for predicting HFpEF was 0.841 ($P < 0.0001$), with a score of 1.0 representing a perfect test. The H₂FPEF score was validated in a separate cohort of 100 patients with similar performance (AUC, 0.886; $P < 0.0001$).

The authors concluded the H₂FPEF score enables discrimination of HFpEF from noncardiac causes of dyspnea and is useful in the evaluation of patients with unexplained exertional dyspnea.

■ COMMENTARY

HFpEF can be challenging to diagnose when obvious signs and symptoms are absent. Right heart catheterization with exercise is considered the gold standard for diagnosing HFpEF. However, given the invasive nature and required resources, it is not feasible to refer all patients with suspected HFpEF for such testing. Using data from patients referred to the Mayo Clinic catheterization laboratory for evaluation of unexplained dyspnea, Reddy et al developed an easy-to-use score that predicts the likelihood of HFpEF in such patients using data obtained during routine clinical evaluation.

The H₂FPEF score is simple to calculate: 3 points for atrial fibrillation, 2 points for obesity, and 1 point for each of the other criteria. A score of 0-1 was considered sufficient to eliminate HFpEF. High scores

(6-9) usually can establish the diagnosis of HFpEF with reasonable confidence. In patients with scores of 2-5, a diagnosis of HFpEF can neither be confirmed nor ruled out, and further testing (such as invasive exercise study) should be considered. The authors also provided a more sophisticated calculator (available in the supplementary material published with the article) that can be used if even more precise risk estimation is desired. The H₂FPEF score performed markedly better than other available algorithms for determining the likelihood of HFpEF. For example, when compared to criteria proposed in expert guidelines from the European Society of Cardiology (primarily based on natriuretic peptide levels and echocardiographic parameters), the H₂FPEF score performed substantially better in this Mayo cohort (increase in AUC of +0.169; $P < 0.0001$).

Although the test has advantages over other risk prediction tools, there are important considerations to keep in mind when using the test. Even in patients with a score of 1 (low risk), the prevalence of HFpEF was approximately 20%. When suspicion for HFpEF persists and an alternative explanation for a patient's exertional dyspnea cannot be identified, it is reasonable to consider invasive exercise hemodynamic testing. The test performs much better when the score is high; more than 90% of patients with scores above 5 were confirmed to have HFpEF by invasive testing.

The H₂FPEF score was derived only using data from patients treated at the Mayo Clinic, and it is unclear how the same test would perform outside of this highly specialized, tertiary referral setting. The final model contained multiple variables that are well-known predictors of HFpEF (i.e., echocardiographic evidence of diastolic dysfunction), but left out other predictors that are previously shown to predict HFpEF (such as natriuretic peptide levels). The authors did not find a strong enough association to include NTproBNP level in the final score, but NTproBNP data were missing for 24% of patients. Does this mean we should ignore NTproBNP levels when evaluating a patient for HFpEF? Probably not.

Tools like H₂FPEF cannot replace clinical judgment. In patients with clear signs and symptoms of vascular congestion, a diagnosis of HFpEF can be made regardless of the score. Similarly, in patients with a clear alternative etiology for dyspnea, the score should not distract from the obvious causes.

Despite its limitations, the H₂FPEF score provides a useful framework for estimating the likelihood of HFpEF in select patients with exertional dyspnea that remains unexplained despite appropriate initial evaluation. ■

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1. **Long-term mortality in patients with significant mitral valve regurgitation is heavily influenced by:**
 - a. age.
 - b. left ventricular ejection fraction.
 - c. symptoms.
 - d. Both a and c
2. **Post coronary artery bypass graft atrial fibrillation in comparison to traditional non-valvular atrial fibrillation is characterized by:**
 - a. a higher risk of death.
 - b. a higher risk of recurrent atrial fibrillation.
 - c. a lower risk of thromboembolism.
 - d. All of the above
3. **The CABANA study, which compared an ablation to a medical strategy for atrial fibrillation, showed which of the following in the ablation arm?**
 - a. Higher mortality
 - b. Less recurrent atrial fibrillation
 - c. More death or cardiac hospitalization
 - d. All of the above
4. **The five-year results of the ISAR-CABG trial (a comparison of drug-eluting vs. bare-metal stents for saphenous vein graft lesions) showed that drug-eluting stents:**
 - a. reduced major adverse cardiac events.
 - b. reduced mortality.
 - c. reduced myocardial infarction.
 - d. None of the above
5. **A clinical score for predicting that a patient has heart failure with preserved ejection fraction is heavily influenced by:**
 - a. atrial fibrillation.
 - b. hypertension on two medications.
 - c. age > 60 years.
 - d. an estimated pulmonary arterial wedge pressure on echo of > 35 mmHg.

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.

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