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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Predictive Accuracy of the New Risk Equation

By Michael Crawford, MD, Editor

SYNOPSIS: An evaluation of the predictive accuracy of the new pooled Cohort Risk Equation in > 300,000 subjects without heart disease or diabetes and a low-density lipoprotein cholesterol level between 70-189 mg/dL followed for five years showed that the new equation markedly overestimated the observed risk of cardiovascular events.

SOURCES: Rana JS, Tabada GH, Solomon MD, et al. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. *J Am Coll Cardiol* 2016;67:2118-2130.

Blaha MJ. The critical importance of risk score calibration: Time for transformative approach to risk score validation? *J Am Coll Cardiol* 2016;67:2131-2134.

The 2013 American College of Cardiology/American Heart Association Pooled Cohort Risk Equation (PRE) has been criticized for its basis in study populations conducted in the 1990s with limited ethnic diversity and age range. Clinicians believe it has limited generalizability to contemporary patients seen in clinical practice. Thus, investigators evaluated the large, contemporary, multiethnic population of Kaiser Permanente Northern California comparing the risk equation-derived five-year risk of atherosclerotic cardiovascular (CV) events with the observed rate. The population selected was > 21 years of age and had an low-density lipoprotein (LDL) cholesterol level between 70 and 189 mg/dL. The study excluded patients with known CV disease, those who had received a statin prescription within five years of enrollment, and those who used statins for primary prevention during the follow-up period. CV events included myocardial infarction, ischemic stroke, and cardiac death. The subjects were subcategorized for diabetes status. More than 941,000 patients met the initial entry criteria and after applying the exclusion criteria, 311,833 patients between the ages of 40-75 years were enrolled — 307,591 without diabetes and 4,242 with diabetes. The main analysis focused on non-diabetics, of which 62% were women, 22,283 were black, 52,917 were Asian/Pacific Islander, and 18,745 were Hispanic. In this study group, there were 2,061 CV events during 1,515,142 person years of follow-up. At all levels of risk predicted, observed CV events were substan-

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tially lower and the difference was greater at higher calculated risk scores. For example, in those with a predicted risk of > 5% in five years, the mean predicted risk was 8.72% vs. an observed rate of 1.85%. The correlation between expected and observed rates was better in diabetics, but researchers observed overestimation, especially at higher predicted risk. In the high-risk group, predicted CV events were 13.38% vs. 5.5% observed. Similar results were noted in the ethnic subgroups. The authors concluded that in a large real-world population, the Pooled Cohort Risk Equation substantially overestimated five-year risk of CV events in adults without diabetes and that ethnicity did not affect this result.

■ COMMENTARY

Other investigators have evaluated the PRE in several research populations that were not used in the creation of the PRE and found conflicting results. Interestingly, in cohorts gathered in the 1990s, the correlation between observed and predicted CV events by the PRE was better than in more contemporary populations. Some have argued that more contemporary populations include more patients on aspirin and statins, less smoking, and generally better lifestyles. Consequently, for this study, investigators excluded patients on statins before or during the study period. One could argue that this removed the higher-risk patients, but sensitivity analyses did not support this idea. Also, this study enrolled patients and followed them from 2008 until 2013, so it was not influenced by the new PRE. Other strengths included the large population (> 300,000) and the inclusion of reasonable numbers of all four major ethnic or racial groups in the United States. In addition, the patients were part of an integrated health system in which clinical data collection was of high quality.

One potential weakness of this study was the assumption that patients with health insurance are of higher socio-economic status and probably engage in better health habits than other populations. This may be true, but these are the majority of patients practitioners see. Additionally, data on diabetics were inadequate because researchers excluded diabetics from the main analysis. This was necessary because in their system, most diabetics were receiving statins. However, researchers' analysis of a diabetic subgroup that was not on statins confirmed overestimation of events by the PRE, but less so than observed in non-diabetics. An accompanying editorial noted that event rates were very low in this study in part because softer endpoints, such as revascularization, were not included.

Even though this study seems like a step in the direction of adjusting the risk equation to reflect contemporary practice, this issue remains highly controversial because of the treatment implication of a "high" risk score. Using the PRE will probably result in over-treatment with statins, which will lead to high costs for any health system. Using other considerations, such as a CT calcium score, family history, or high-sensitivity C-reactive protein, have their proponents, but these practices have not been well validated. It would be nice to use this study to calibrate the PRE, but this study evaluated five-year risk, and the PRE predicts 10-year risk. At this time, we are back to using physicians' judgment considering all the data we have at our disposal, including the PRE and perhaps even the old LDL-cholesterol targets. ■

ABSTRACT & COMMENTARY

Management of Mixed Aortic Valve Disease

By Michael Crawford, MD, Editor

SYNOPSIS: Asymptomatic patients suffering from moderate aortic stenosis and regurgitation with preserved left ventricular function have the same prognosis as asymptomatic patients with severe aortic stenosis and normal left ventricular function and should be followed closely for the development of symptoms.

SOURCES: Egbe AC, Luis SA, Padang R, Warnes CA. Outcomes in moderate mixed aortic valve disease: Is it time for a paradigm shift? *J Am Coll Cardiol* 2016;67:2321-2329.

Parker MW, Aurigemma GP. The simple arithmetic of mixed aortic valve disease: LVH + volume load = trouble. *J Am Coll Cardiol* 2016;67:2330-2333.

There are few guidelines and little data on the management of mixed aortic valve disease. Investigators from the Mayo Clinic performed a retrospective observational study of 251 patients with moderate aortic stenosis and moderate aortic regurgitation for an average follow-up of nine years. Inclusion criteria were age > 18 years, asymptomatic, normal left ventricular (LV) ejection fraction (> 50%), and at least two years of follow-up. Exclusion criteria included radiation valve disease, prior endocarditis, prior aortic valve intervention, and concomitant moderate or more disease of other valves. The mixed aortic valve disease patients were compared to three matched control groups: isolated moderate aortic regurgitation, isolated moderate aortic stenosis, and isolated severe aortic stenosis. All the control groups also were asymptomatic and presented with normal LV systolic function. After matching for age and sex, there were 117 patients in each group for comparative analysis. Bicuspid valves made up 31% of the mixed group and 18-32% of the other three groups. The primary endpoint was composite adverse events: New York Heart Association class III-IV symptoms, aortic valve replacement, or cardiac death. The mean age of the mixed patients was 63 years, 73% were men, 38% featured a bicuspid valve, and 16% suffered from coronary artery disease. During follow-up, the composite endpoint occurred in 77% of patients. Sixty-nine percent developed symptoms, 62% underwent aortic valve replacement, and 4% died. At the time of aortic valve replacement, 75% had progressed to severe aortic stenosis and 14% had progressed to severe aortic regurgitation. The composite adverse event rate in the mixed group was similar to the severe aortic stenosis group (71% vs. 68% at five years), but higher than the moderate aortic stenosis group (31%) and the moderate regurgitation group (22%, both $P < 0.0001$). The authors concluded that moderate asymptomatic mixed aortic valve disease with preserved LV function has a similar prognosis as asymptomatic severe aortic stenosis with preserved LV function. Additionally, the authors noted that these patients should be monitored closely for the development of symptoms.

■ COMMENTARY

One of my clinical mentors told me that in valve disease two moderates equaled severe, and that is how you manage mixed valve disease. At that time, this was largely based on clinical experience, but sometimes clinical observations prove to be correct, and it is nice to see this one validated by a large observational study. In this study, the prognosis of moderate mixed aortic valve disease was similar to that of severe aortic stenosis. This knowledge should inform our management of those patients. The authors recommended close follow-up to detect the onset of symptoms. This seems straightforward enough, but are there objective criteria for valve replacement that would trump symptom development? Unfortunately, this study does not answer the question definitively, and there are no existing guidelines to help. However, this study suggests some parameters worth considering in borderline cases.

During follow-up, 19 patients in the mixed group developed symptoms without any change in the measured severity of aortic stenosis or regurgitation. These patients presented with advanced diastolic dysfunction and concentric LV hypertrophy. Interestingly, mixed patients demonstrated the largest measured LV mass of all four groups (138 g/m^2) compared to moderate aortic regurgitation (94 g/m^2), moderate stenosis (103 g/m^2), and severe stenosis (123 g/m^2, all $P < 0.02$). Also, the mixed group produced the highest prevalence of advance diastolic dysfunction (32% vs. 5% vs. 12% vs. 22%, respectively, all $P < 0.03$). Thus, the combination of a pressure and volume load results in a markedly hypertrophied left ventricle, which often develops diastolic dysfunction. The latter may result in symptoms before the individual valve lesions have progressed to severe. In the multivariate analysis, only age and relative wall thickness > 0.42 (thickness/diameter), which reflects mass and concentric hypertrophy, predicted adverse events. Also, among those in the group with progressive regurgitation leading to symptoms, none reached an end-systolic dimension of 50 mL, which is a replacement criterion for aortic regurgitation in the guidelines. Thus, LV dimensions may not be useful for decision-making in mixed patients.

Most patients who developed symptoms progressed to severe aortic stenosis, so the valve area by the continuity equation should be useful to follow. However, peak velocity alone may not be, as regurgitation can increase it as well. Ejection fraction decreased modestly during follow-up in patients who underwent valve replacement, but still was largely in the normal range, so it doesn't appear to be useful in this group either.

Follow closely asymptomatic patients with moderate mixed aortic valve disease and monitor them for symptom development. Pay special attention to those with marked increases in LV mass, concentric hypertrophy, and advanced diastolic dysfunction. ■

ABSTRACT & COMMENTARY

TAVR Without On-site Cardiac Surgical Backup: Fringe Procedure, or Wave of the Future?

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: Data from transcatheter aortic valve replacement procedures performed at German hospitals without on-site cardiac surgery shows relatively low rates of major complications and mortality similar to hospitals with full surgical programs.

SOURCE: Eggebrecht H, Bestehorn M, Haude M, et al. Outcomes of transfemoral transcatheter aortic valve implantation at hospitals with and without on-site cardiac surgery department: Insights from the prospective German aortic valve replacement quality assurance registry (AQUA) in 17,919 patients. *Eur Heart J* 2016 May 17 [Epub ahead of print].

Since its commercial introduction just a few years ago, transcatheter aortic valve replacement (TAVR) has become rapidly integrated into the standard of care for aortic stenosis patients at elevated risk for surgery. The early model encouraged performance of the procedure in a cath lab or hybrid operating room, with full cath lab and surgical teams, and with cardiopulmonary bypass and cardiac surgical equipment at the ready should an emergency arise requiring open surgical intervention. Guidelines from the European Society of Cardiology recommend performing TAVR procedures only at hospitals with cardiac surgery available on site. The situation in the United States is even more restrictive, limiting TAVR to a subset of cardiac surgical centers that meet particular operator- and institution-specific requirements. In Germany, regulations requiring on-site cardiac surgical backup for TAVR have been relaxed as part of an effort to increase access to this procedure. As a prerequisite for performing TAVR, these hospitals were required to evaluate patients as part of a heart team with visiting cardiac surgical specialists from external, collaborating hospitals. The data from 2013-2014 have been published, comparing transfemoral TAVR procedures at institutions with and without cardiac surgery.

Between the beginning of 2013 and the end of 2014, 17,919 patients in Germany underwent transfemoral TAVR. By 2014, 22 hospitals were performing this procedure without on-site surgical backup vs. 75 with surgery. Of these, 1,332 underwent TAVR at hospitals without on-site cardiac surgery. One concern has been that performance of TAVR at non-cardiac surgery centers would lead to a detrimental change in patient selection. Patients undergoing TAVR at non-cardiac surgical hospitals were significantly older (82.1 vs. 81.1 years; $P < 0.001$), belonged to higher NYHA CHF class, and were more likely to present with a history of coronary disease, peripheral arterial disease, COPD, and neurologic events. As a result, patients undergoing TAVR at non-cardiac surgical hospitals had a higher calculated risk of surgical mortality according to both the GAV-score and the logistic EuroSCORE. Nearly 84% of patients underwent TAVR as elective procedures.

Procedure times were longer in hospitals without on-site cardiac surgery (110.3 ± 48.2 vs. 79.3 ± 44.8 min; $P < 0.001$), although fluoroscopy times were similar. Total procedural complications were lower in non-cardiac surgery centers (8.4% vs. 11%; $P = 0.004$), while catastrophic complications, including annular rupture, aortic dissection, and device embolization, were similarly rare (all < 1%) in both groups. While the composite of complications that could potentially benefit from open cardiac surgery were similar between groups (3.4% vs. 3.9%), conversion to open sternotomy was less likely at non-cardiac surgical sites (0.3 vs. 0.7%). In-hospital mortality (3.8 vs. 4.2%; $P = 0.396$), myocardial infarction, stroke, and vascular complications were all similar between groups.

It is worth noting that, similar to prior reports, in-hospital mortality was very high for all patients requiring emergent cardiac surgery for TAVR complications (50% in non-cardiac surgery hospitals and 62.5% in hospitals with on-site surgery; $P = 0.694$).

The authors argued that serious complications from TAVR have declined markedly over time with increased experience and better devices, and that their data support the safety of performing this procedure

at sites without on-site cardiac surgical backup.

■ COMMENTARY

It is remarkable to note that more than 1,300 TAVR procedures were performed in German hospitals without on-site cardiac surgery over the short period from 2013 to 2014. Figures for mortality and life-threatening complications were low and were similar when compared to centers with cardiac surgery. The authors claimed their data support the feasibility and safety of this approach. Does this mean expanding TAVR to non-cardiac surgical centers is a good idea?

To explore this further, let's look at the data closely. Compared to centers with cardiac surgery, those without had significantly lower institutional procedure volumes. This translated to longer procedure times, as well as higher rates of at-least-moderate aortic insufficiency and higher rates of permanent pacemakers, both of which can be affected by operator and institutional experience. Mortality did not significantly increase, and this is undoubtedly positive. Although the number of procedures analyzed here was substantial, it is likely not large enough to show a difference in low-frequency outcomes such as mortality and emergent cardiac surgery. It should also concern clinicians that patient selection was significantly different at non-cardiac surgery centers, compared with the more experienced hospitals with both cardiology and cardiac surgery on site. Although this did not translate into a statistical difference in mortality, one could wonder whether the heart team model is consistently applied within this paradigm. Although the rates of emergent cardiac surgery with TAVR have fallen to below 1%, and the odds of surviving such a complication — even in a center with on-site surgery — are low, it is difficult to discount the notion that small numbers of lives might be saved by the immediate availability of cardiac surgery. I am not yet convinced that the issue of access to these mainly elective procedures is compelling enough to expand outside of established cardiac surgical centers. In the United States, we might expect steady expansion of TAVR procedures to more hospitals that currently offer cardiac surgery; however, the inclusion of hospitals without cardiac surgery on-site is most likely not on the immediate horizon. ■

ABSTRACT & COMMENTARY

Searching for Heyde's Syndrome in Prosthetic Valve Patients

By Michael Crawford, MD, Editor

SYNOPSIS: In a recent analysis, abnormalities of von Willebrand factor were much more common in dysfunctional prostheses and were associated with gastrointestinal bleeding and angiodysplasia.

SOURCES: Blackshear JL, McRee CW, Safford RE, et al. von Willebrand factor abnormalities and Heyde's syndrome in dysfunctional heart valve prostheses. *JAMA Cardiol* 2016;1:198-204.

Hillegass WB, Limdi NA. Valvular heart disease and acquired type 2A von Willebrand syndrome — The "hemostatic" Waring Blender syndrome. *JAMA Cardiol* 2016;1:205-206.

The association of severe aortic stenosis and gastrointestinal (GI) bleeding due to angiodysplasia (Heyde's syndrome), is thought to be due to intravascular shear-induced changes in von Willebrand factor (VWF). Sporadic reports of similar VWF abnormalities and GI bleeding in other dysfunctional valves led researchers to prospectively study 136 patients: 26 presenting with normally functioning surgical or transcatheter aortic prosthetic valves, 24 containing dysfunctional aortic prostheses, 36 enjoying normally functioning mitral valve prostheses or repairs; 19 suffering from dysfunctional mitral prostheses or repairs; and 31 patients featuring native isolated aortic regurgitation. A dysfunctional prosthesis was one with at-least-moderate stenosis or regurgitation. Several tests of VWF and platelet function were measured. In patients with native isolated aortic regurgitation (AR), abnormal VWF multimers were present in 77% of those with moderate-to-severe AR and regurgitant volume correlated with platelet dysfunction ($r = 0.74$; $P < 0.001$). Abnormal VWF multimers were more common in patients with dysfunctional aortic prostheses compared to those with normal function (83% vs. 4%; $P < 0.001$). Researchers observed similar findings with dysfunctional vs. normally functioning mitral valves (74% vs. 6%; $P < 0.001$). GI bleeding occurred in two of 21 patients with at-least-moderate native AR, but in six of 24 patients with dysfunctional aortic prosthesis and five of 19 with mitral prosthesis dysfunction. Among those with aortic prostheses dysfunction and GI bleeding, five of six demonstrated angiodysplasia. In those with mitral prosthesis dysfunction with GI bleeding, three of five experienced angiodysplasia and the other two

did not undergo endoscopy. The authors concluded that in patients with dysfunctional aortic and mitral valve prostheses, acquired abnormalities in VWF are associated with GI bleeding and angiodysplasia. They suggested that measuring VWF multimers may provide additional diagnostic and prognostic information in patients with dysfunctional valve prostheses.

■ COMMENTARY

Frank hemolysis with schistocytes on the blood smear due to prosthetic valve dysfunction is rare, but VWF syndrome with angiodysplasia and GI bleeding is common. This syndrome has been described in moderate-to-severe aortic stenosis, severe AR, severe mitral regurgitation, hypertrophic obstructive cardiomyopathy, various congenital heart defects, and left ventricular assist devices. VWF is a large, multimerized protein that contains binding sites for collagen, platelet glycoprotein, and factor VIII. When the arterial wall is breached, VWF adheres to the site of injury, recruits platelets, and binds factor VIII, leading to the blood clotting cascade. Increased blood shear forces as seen in the disorders listed above results in cleavage of the multimers and a reduction in the number of multimers. Too few multimers leads to bleeding, especially at high shear points such as angiodysplasia in the gut. Too much VWF leads to abnormal clotting.

This paper analyzed VWF function parameters and clinical events in a series of patients with native and prosthetic valve disease and showed that abnormalities of VWF are found in about 80% of dysfunctional aortic valve prostheses, whether placed surgically or by transcatheter; dysfunctional mitral valve repairs and prostheses; and moderate-to-severe native valve AR. More importantly, about one-fourth of prosthetic valve dysfunction patients experienced GI bleeding that was almost always associated with angiodysplasia. GI bleeding occurred in only 10% of the moderate-to-severe native AR patients, probably because shear forces are lower in AR due to lower pressure gradients in AR as compared to aortic stenosis or mitral regurgitation.

The authors suggested two potential clinical uses of this information. First, VWF measures could be used as a biomarker for the severity of native valve AR and prosthetic valve dysfunction. Interestingly, they also measured brain natriuretic peptide levels in this study and they were not discriminatory. Second, reduced VMF multimers may identify patients at risk for GI bleeding. Unfortunately, there is only one way to fix increased shear stress: fix or replace the valve. This is not always a straightforward decision for someone who just underwent valve surgery. Also, many valve disease patients are on warfarin, especially if they also suffer from atrial fibrillation. Bleeding often is mistakenly attributed to anticoagulation. Measure VWF in any of these patients with bleeding.

There are several limitations to this study. First, the incidence of VWF abnormalities and bleeding may be exaggerated due to referral bias. Also, there were only four patients in this series with severe native AR. In addition, due to the relatively low number of patients overall, information about specific prosthetic valve malfunctions and their outcomes, especially after corrective procedures, is too small to analyze meaningfully. Patients in the series featured patient-prosthesis mismatches, prosthetic stenosis, and perivalvular leaks. Despite these limitations, this study clearly identified the potential importance of measuring VWF function in patients with suspected left-sided valve prosthesis dysfunction and those with abnormal bleeding. At this point, there are no agreed-upon cutpoints for decision-making, but the information may push the need for a corrective procedure one way or another. ■

ABSTRACT & COMMENTARY

Reduced Cardiac Index Is Not Correlated with Renal Function in Heart Failure Patients

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 a retrospective analysis of patients with acute decompensated heart failure who received a pulmonary artery catheter, there was no significant correlation between cardiac index and markers of renal function, contradicting the importance of cardiac output in renal dysfunction among patients with heart failure.

SOURCE: Hanberg JS, Sury K, Wilson FP, et al. Reduced cardiac index is not the dominant driver of renal dysfunction in heart failure. *J Am Coll Cardiol* 2016;67:2199-2208.

Renal dysfunction is common among patients hospitalized for heart failure (HF) and associated with a worse prognosis. Many believe reduced cardiac index (CI) is the primary cause of worsening renal function. However, several small studies have suggested CI is not correlated with renal function in HF. No study has thoroughly evaluated the relationship between CI and markers of renal dysfunction in a large, heterogeneous, acute HF population.

Investigators analyzed data from 575 patients enrolled in the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) study who received a pulmonary artery catheter (PAC) to guide management of acute decompensated HF. Patients were included whether they were enrolled through the randomized ESCAPE trial or the concurrent PAC registry. The mean ejection fraction was 23%, mean CI was 2.3 L/min/m^2, and mean estimated glomerular filtration rate (eGFR) at baseline was 52.4 mL/min/1.73 m^2. Researchers measured the correlation between CI and eGFR at baseline and evaluated the relationship between changes in CI and eGFR over time.

The overall correlation between baseline CI and eGFR was weak, and higher CI was actually correlated with lower eGFR (r = -0.12; *P* = 0.02). There was no correlation between CI and eGFR in a broad range of subgroups, including patients with advanced symptoms, worse renal function, or inotrope dependence. Longitudinal changes in renal function were not associated with individual measurements of CI or change in CI over time. In a multivariate analysis, both higher right atrial pressure and higher CI were associated with lower GFR, although hemodynamic predictors accounted for a tiny amount of the observed eGFR variability. The authors concluded that low cardiac output is not the predominant driver for renal dysfunction in patients with decompensated HF.

■ COMMENTARY

The complex relationship between the heart and kidneys in HF patients remains incompletely understood. The concept of decreases in CI driving worsening renal function seems intuitive to many clinicians. The eGFR is related to the product of renal blood flow and the filtration fraction. Therefore, any factor that reduces overall perfusion (i.e., cardiac index) should reduce the eGFR. This is the largest and one of the most thorough studies to date evaluating the relationship between CI and renal dysfunction and demonstrates convincingly that CI is not the primary driver of renal dysfunction in HF. This is primarily due to renal autoregulation that maintains renal perfusion over a wide range of hemodynamic conditions. Changes in the CI do not have a strong effect on renal blood flow, therefore maintaining eGFR.

The authors impressively used subgroup analyses and longitudinal changes in CI to re-enforce the finding that low CI does not drive renal dysfunction. There was not a single clinical or hemodynamic subset of patients in whom CI and eGFR were positively correlated, including patients with very low CI. Additionally, it also is worth noting the lack of a relationship between CI and renal dysfunction observed in patients referred for PAC placement specifically to evaluate and manage oliguric renal failure. Furthermore, these researchers demonstrated that neither baseline nor changes in CI predicts worsening renal function during hospitalization for HF.

So which hemodynamic factors drive renal function in HF? Several studies have identified systolic blood pressure, an important determinant of renal blood flow, as the strongest predictor of renal dysfunction, with the relationship maintained independent of CI. Both the central venous pressure and intra-abdominal pressure contribute to renal venous pressure, and also have been identified as important determinants of GFR in HF. Therefore, factors that alter the perfusion pressure across the kidneys, whether it be lower arterial pressure or higher renal venous pressure, appear to be much more important than the CI in determining eGFR. Increased neurohormonal activation, particularly the sympathetic and renin-angiotensin systems, also plays a role.

There are several limitations to this study. Serum creatinine, which was used to estimate GFR for the primary outcome, is an imperfect measure of renal function. This may be true especially in the decompensated HF population. Creatinine also primarily reflects glomerular filtration and does not account for changes in other components of renal function, such as tubular function.

Although this was not a study of treatment strategies for acute HF, we can make several conclusions based on the findings. First, the practice of starting or uptitrating inotropes to correct renal dysfunction in HF may not be an effective strategy. Similarly, right heart catheterization should not be used indiscriminately to evaluate worsening renal function in patients with acute HF. Rather, efforts to avoid or minimize hypotension and decrease the central venous pressure are more likely to restore perfusion pressure and improve renal function. ■

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CME/CE QUESTIONS

1. **Patients with prosthetic left heart valves and gastrointestinal (GI) bleeding may feature which of the following?**
   a. Acquired von Willebrand syndrome
   b. An INR > 4.0 units
   c. GI pathology
   d. All of the above

2. **The major determinant of renal function in acute heart failure patients is:**
   a. cardiac index.
   b. renal perfusion pressure.
   c. atrial natriuretic protein levels.
   d. cardiac inotropic state.

3. **In a large, multiethnic, primary prevention population, the new Pooled Cohort Risk Equation:**
   a. accurately predicted observed risks in diabetics.
   b. accurately predicted observed risk in non-white subjects.
   c. overestimated observed risk in all subgroups.
   d. underestimated observed risk in white subgroups.

4. **Compared to on-site cardiac surgery centers, transcatheter aortic valve replacement performed at hospitals in Germany without cardiac surgery showed:**
   a. higher complication rates.
   b. longer procedure times.
   c. higher mortality.
   d. All of the above

5. **In asymptomatic patients with normal left ventricular systolic function, mixed-moderate aortic stenosis and regurgitation has the same prognosis as:**
   a. severe aortic stenosis.
   b. moderate aortic stenosis.
   c. moderate aortic regurgitation.
   d. All of the above