

Clinical Cardiology

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

ABSTRACT & COMMENTARY

Outcome of PCSK9 Inhibitor-treated Patients

By Michael Crawford, MD, Editor

SYNOPSIS: In a meta-analysis of 17 studies, proprotein convertase subtilisin-kexin type 9 serine protease inhibitors markedly reduced low-density lipoprotein cholesterol levels and all-cause mortality, but was associated with a significant increase in neurocognitive adverse events.

SOURCE: Lipinski MJ, et al. The impact of proprotein convertase subtilisin-kexin type 9 serine protease inhibitors on lipid levels and outcomes in patients with primary hypercholesterolaemia: A network meta-analysis. *Eur Heart J* 2016;37:536-545.

Studies of proprotein convertase subtilisin-kexin type 9 serine protease (PCSK9) inhibitors demonstrate markedly reduced low-density lipoprotein (LDL) cholesterol and possibly improved outcomes. To further investigate potential outcomes, investigators from the United States, United Kingdom, and Italy performed a network meta-analysis of 17 trials of PCSK9 inhibitors vs placebo or ezetimibe to assess whether PCSK9 inhibitors reduced all-cause mortality or cardiovascular (CV) events. They excluded studies involving patients homozygous for familial hypercholesterolemia. The outcomes analyzed included all-cause mortality, CV death, CV events, adverse events, and serious adverse events. The 17 randomized, controlled trials included 13,083 patients: 8250 randomized to PCSK9 inhibitors, 3957 to placebo, 846 to ezetimibe, and 30 to PCSK9 plus ezetimibe. The subjects' mean age was 59 years and

52% were male, most of the subjects were Caucasian, and many had known coronary artery disease or risk factors for it. PCSK9 inhibitors reduced LDL cholesterol 57% from a mean baseline of 122 to 51 mg/dL, and increased HDL cholesterol 6%. PCSK9 inhibitors significantly reduced all-cause mortality (hazard ratio [HR], 0.43; 95% confidence interval [CI], 0.22-0.82; $P = 0.01$) but not CV death (HR, 0.50; CI, 0.22-1.13; $P = 0.10$) or CV events (HR, 0.67; CI, 0.43-1.04; $P = 0.07$) compared to placebo. PCSK9 inhibitors significantly increased neurocognitive events (HR, 2.31; CI, 1.11-4.93; $P = 0.02$). Other adverse events were not different on PCSK9 inhibitors compared to placebo. The authors concluded that PCSK9 inhibitors significantly improved lipid profiles and reduced all-cause mortality, but were associated with more neurocognitive adverse events than placebo.

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■ COMMENTARY

Last year, the FDA approved PCSK9 inhibitors for patients with homozygous familial hypercholesterolemia and those intolerant to statins or statin failures who have compelling reasons to lower cholesterol. These drugs are monoclonal antibodies, which must be administered by subcutaneous injection every 2-4 weeks. They are very effective at lowering LDL cholesterol, even on top of other therapy, and many trial patients were found to have at least one LDL value below 25mg/dL. Naturally, there has been concern about potential neurocognitive adverse effects. The individual trials did not demonstrate an increase in neurocognitive adverse effects, but they were clearly apparent in this meta-analysis.

The significant reduction in all-cause mortality was mainly due to two large studies (ODYSSEY LONGTERM and OSLER 2), which had long follow-up periods. Although there was a trend toward reduced CV death and events, it was not statistically significant. Since the individual studies were not powered for outcomes, these results are hypothesis generating, and we must await the results of larger studies to confirm any outcome benefits.

This study fuels the debate about prescribing statins (or other LDL-lowering drugs) based on risk of vascular disease alone or treating to certain targeted LDL values. Proponents of the latter approach espouse that aggregating statin studies shows the lower the LDL, the better the outcomes. This also occurred in the recent IMPROVE IT study of adding ezetimibe to simvastatin. However, prior studies did not achieve the LDL levels that are possible with PCSK9 inhibitors, especially if they are added to statin plus ezetimibe therapy. Thus, many believe there is a lower limit to LDL lowering beyond which neurological adverse effects occur more commonly. The Cholesterol Treatment Trialists' Collaboration has suggested that this may be 50 mg/dL. Since PCSK9 studies often achieved LDL levels below that in many patients, this may explain the meta-analysis results of more neurocognitive adverse events with PCSK9 inhibitors.

At this point, PCSK9 inhibitors are a reasonable alternative or additional therapy to those intolerant to statins or those in whom LDL cholesterol remains elevated despite statins plus ezetimibe. However, perhaps adjusting the dosage to keep the LDL in the 50-70 mg/dL range is prudent until further studies produce more data. ■

ABSTRACT & COMMENTARY

TAVR Still a Viable Option for Many Left Main Disease Patients

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: Performing planned left main percutaneous intervention before or during transcatheter aortic valve replacement does not confer increased risk of short- or intermediate-term adverse outcomes.

SOURCE: Chakravarty T, et al. Outcomes in patients with transcatheter aortic valve replacement and left main stenting: The TAVR-LM Registry. *J Am Coll Cardiol* 2016;67:951-960.

Severe aortic stenosis is often coincident with obstructive coronary artery disease, and cases involving significant left main (LM) coronary disease are not uncommon. For such patients, surgical aortic valve replacement with coronary artery bypass is clearly the gold standard treatment. However, for patients with

advanced age or extensive comorbidities that support transcatheter aortic valve replacement (TAVR), the combination of valve replacement and bypass typically involves a more-involved procedure and prohibitive surgical risk. Although percutaneous intervention (PCI) prior to TAVR has become commonplace for branch-

vessel disease, combining LM stenting with TAVR comes with some unique objections. Generally, surgeons perform revascularization by PCI in advance of TAVR to improve the safety of the valve procedure. However, the baseline higher risk of the LM PCI procedure itself is clearly elevated in the setting of severe aortic stenosis (AS), with a very real possibility of hemodynamic compromise. Additionally, the possibility exists of a negative interaction between the TAVR valve frame and a stent at the LM ostium. The initial randomized trials of TAVR did not include significant numbers of patients with LM disease. More recently, randomized trials of intermediate-risk patients, including SURTAVI and PARTNER II, have specifically excluded patients with untreated LM disease.

Recently published initial results from the TAVR-LM registry address this issue. This registry retrospectively collected information on patients who underwent TAVR and LM stenting from 11 high-volume centers in North America and Canada between January 2007 and December 2014. Full clinical and imaging data were collected for each patient, and angiograms and CT scans were evaluated by a core laboratory. Procedural, 30-day, and 1-year outcomes were collected for each patient.

From a pool of 6405 patients undergoing TAVR at the participating centers during the 8-year span, 204 patients (3.2%) were identified who also underwent LM PCI. Of these, 176 patients underwent planned LM PCI before ($n = 167$) or during ($n = 9$) TAVR. An additional 19 patients underwent emergent LM PCI due to complications from TAVR, either during the procedure itself or within 24 hours. The final nine patients underwent PCI after TAVR, due to routine progression of coronary disease. These nine patients all underwent uncomplicated PCI procedures, without reported hindrance from the valve frame. One hundred sixty-seven patients with LM stents who underwent TAVR (of whom 102 were unprotected LM stents) were compared with patients without LM revascularization, leading to 128 matched pairs for comparison and analysis.

Baseline characteristics of the matched groups were similar, including age, major comorbidities, and Society of Thoracic Surgeons risk scores. With regard to procedural outcomes, patients with LM PCI were more likely to experience major vascular complications (16.4% vs 3.9%; $P < 0.01$) and require permanent pacemakers (26.6% vs 14.1%; $P = 0.02$). Mortality at 30 days (3.1% vs 2.3%; $P = 0.67$) and at 1 year (9.4% vs 10.2%; $P = 0.83$) was not statistically different between the groups. Other 30-day and 1-year outcomes also were not statistically significant, although there was a trend toward higher target

vessel revascularization in the LM PCI group (5.5% vs 1.6%; $P = 0.06$).

As expected, patients experiencing unplanned LM PCI due to complications during or directly after TAVR fared worse than those with planned PCI. Eighteen of 19 patients with unplanned LM PCI experienced LM occlusion during valve deployment, while one experienced LM dissection. These patients were more likely to develop cardiogenic shock (21.1% vs 3.4%; $P < 0.001$), to need CPR (15.8% vs 0.6%; $P < 0.001$), and to develop renal failure (26.3% vs 5.8%; $P = 0.002$). Thirty-day (15.8% vs 3.4%; $P = 0.013$) and 1-year (21.1% vs 8.0%; $P = 0.071$) mortality also greatly increased in this group.

The authors concluded performing planned LM PCI before or during TAVR does not confer increased risk of short- or intermediate-term adverse outcomes, and argue that coexisting LM disease and AS should not prevent evaluation for TAVR.

■ COMMENTARY

This is a significant study in several respects. Data on this important subset of TAVR patients have been in short supply, and it is essential that going forward clinical decisions be made on the basis of good evidence rather than anecdotal information. Clearly, some early fears about combining LM stenting and TAVR are unfounded, and the safety of implanting TAVR valves, even with ostial LM stents, is no longer in doubt. The data also support the ability to perform PCI following TAVR, although the numbers are much smaller.

This is not to say physicians should regard unrevascularized LM disease in potential TAVR patients as a minor issue. Rather, physicians should remember that this is a registry and not a randomized trial. Patients with highly complex LM disease and critically severe AS are undoubtedly at very high risk for intervention. Physicians have no information on patients who were deemed too high risk for intervention or who never made it to a TAVR procedure.

The issue of unplanned LM intervention during TAVR is an important one to recognize, although it addresses a different question from the main cohort of planned LM PCI. Patients with low LM ostia, effaced aortic sinuses, heavily calcified cusps, and LM stents that protrude far into the aorta are at increased risk of coronary occlusion at the time of the TAVR procedure. Mostly, ECG-gated CT scans recognize these risk factors pre-procedure. However, do not underestimate the risk for adverse outcomes in this population. ■

ABSTRACT & COMMENTARY

Prognostic Value of Coronary Calcium on Standard Chest CT Scans

By Michael H. Crawford, MD, Editor

SYNOPSIS: Coronary calcium scan on standard CT scans performed for other indications is of equivalent prognostic value to that seen on ECG-gated coronary studies and should be included in radiology test reports.

SOURCES: Hughes-Austin JM, et al. Relationship of coronary calcium on standard chest CT scans with mortality. *JACC Cardiovasc Imaging* 2016;9:152-159.

Hecht HS. "See No Evil." *JACC Cardiovasc Imaging* 2016;9:160-162.

Coronary artery calcium (CAC) scores performed on ECG-gated, 3 mm sliced CT scans are strong predictors of coronary artery disease (CAD), cardiac events, and mortality. Physicians perform standard 6 mm sliced chest CT scans much more often for a variety of reasons. A study by Hughes-Austin et al is a case-controlled analysis of patients who underwent both scan types between 2000 and 2003 and were followed for 8 years to assess whether CAC observed on a standard CT scan was as useful as that on a coronary-specific CT scan. Among 4544 community living subjects who underwent whole body CT scans, which included both types of chest CT imaging, 157 subjects who died were matched with 494 controls by sex and age. Subjects with known CAD were excluded. Researchers calculated a CAC score on all CT scans using the Agatston method. They read the 3 mm gated scans at the time of acquisition. Readers blinded to the 3 mm results later studied the 6 mm scans. The group collected clinical data as well, and the primary endpoint was all-cause mortality. The mean age of the 651 subjects was 68 years, and 63% were men. The mortality cases had higher median CAC scores on both scan types. The correlation between the two was excellent ($r = 0.93$), but the median Agatston score on the 6 mm scans was 22 vs 104 on the gated 3 mm scans. CAC scores adjusted for traditional CAD risk factors showed identical risk ratios (RR) for mortality on the two scan types (RR, 1.5). The authors concluded standard chest CT scans performed for other reasons can provide useful information on CAD risk.

■ COMMENTARY

It seems like a no brainer that radiologists reading standard chest CT scans should report on coronary calcium the way they do lung nodules and other incidentalomas. This knowledge would help clinicians with primary prevention decisions without having to order other tests, some of which would add radiation exposure. However, scant available data suggest that clinicians report less than half of observed CAC and infrequently conduct formal scoring. Dr. Hecht plays the devil's advocate in an accompanying editorial, noting there is no evidence that reporting CAC on a standard CT scan results in better outcomes. Also, it takes time, especially if a physician performs a formal CAC score, adding more time to an already-crowded schedule. Additionally, there are downstream effects of reporting. The ordering physician, who may have little understanding of the issues involved, has to deal with information that no one requested. This could start a test cascade that could lead to cardiac catheterization and an unnecessary percutaneous intervention. To prevent this, physicians may need education. As Dr. Hecht points out, this occurs in the radiology report for nodules, etc. and could be templated in the electronic medical record for coronary calcium.

Standard CT scans are performed 8 times more frequently than coronary CT scans, and this is rising with the 2014 lung cancer screening guidelines. A semi-quantitative (mild, moderate, severe) coronary calcium reporting dictum would make a lot of sense and not cause excessive extra work. ■

ABSTRACT & COMMENTARY

Cardiopulmonary Exercise Testing and Survival in Systolic Heart Failure

By Van Selby, MD

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

SYNOPSIS: A large study of patients with chronic systolic heart failure undergoing cardiopulmonary exercise testing found peak oxygen uptake (VO_2), exercise duration, and percent predicted peak VO_2 were the strongest predictors of survival. The association between peak VO_2 and survival varied substantially by sex.

SOURCE: Keteyian SJ, et al. Variables measured during cardiopulmonary exercise testing as predictors of mortality in chronic systolic heart failure. *J Am Coll Cardiol* 2016;67:780-789.

Cardiopulmonary exercise (CPX) testing is commonly used to measure functional capacity and determine prognosis in heart failure with reduced ejection fraction (HFrEF). Although several individual CPX-derived variables have been shown to correlate with survival, no study has compared the relative predictive strengths of many CPX-derived variables and the effect of patient sex on these associations.

In a post-hoc analysis of the HF-A Controlled Trial Investigating Outcomes of exercise trainiNg (HF-ACTION) trial, Keteyian et al compared the ability of 10 different CPX-derived parameters to predict clinical outcomes. Two thousand one hundred patients with chronic HFrEF and New York Heart Association (NYHA) functional class II-IV symptoms underwent CPX using a modified Naughton treadmill protocol. The primary outcome was all-cause survival.

During a median follow-up of 32 months, 357 subjects died. Nearly all 10 of the measured variables were predictive of mortality; only the respiratory exchange ratio (RER) was not significantly associated with survival. After adjusting for age and sex, the strongest predictors were peak oxygen uptake (VO_2), percent predicted peak VO_2 (%pp VO_2), and exercise duration. In men, peak VO_2 was the single strongest predictor of mortality ($P < 0.0001$), with a peak VO_2 cutpoint of 10.9 mL/kg/min identifying those with a 10% 1-year mortality rate. In women, exercise duration was the strongest predictor ($P < 0.0001$). Peak VO_2 was a strong predictor as well, though with a cutpoint of 5.3 mL/kg/min identifying those with 10% 1-year mortality. When the analysis was stratified according to the RER (the ratio between CO_2 production and O_2 uptake), the peak VO_2 predicted survival in patients with $\text{RER} > 0.95$.

The authors concluded peak VO_2 , exercise duration, and %pp VO_2 are the strongest predictors of outcomes in patients with HFrEF, peak VO_2 cutpoints vary by gender, and RER has little effect on the ability of peak VO_2 to predict mortality.

■ COMMENTARY

CPX testing has been used for decades in the evaluation of chronic heart failure (HF). Using either a treadmill or cycle, CPX identifies impairments in aerobic capacity, providing valuable information regarding functional capacity and severity of HF. CPX testing is particularly important in the evaluation of candidates for heart transplantation. A landmark study found a

peak $\text{VO}_2 < 14$ mL/kg/min identified HF patients with increased mortality compared to heart transplantation, and this cutpoint is now commonly used to identify transplant candidates (although a cutpoint of 12 mL/kg/min is often used in patients on beta-blockers). The Keteyian et al study contributes substantially to the understanding of CPX by confirming the utility of CPX-derived variables in a large, contemporary HF cohort.

These findings refine the ability to apply CPX results when making clinical decisions, and tailor interpretations of the results to a particular patient. One of the most important findings from this study is the sex-related differences. Exercise capacity appears to be a particularly important predictor in women. Peak VO_2 is a strong predictor as well; however, the cutpoint used to identify women at increased risk of mortality appears to be much lower than current values. A peak VO_2 of approximately 5 mL/kg/min identified women with 1-year expected mortality of 10% (the approximate cutoff at which transplant is indicated). The exact reason for the observed male-female discrepancy is unknown, but others have hypothesized that it may be due to higher body fat in women. Currently, a peak VO_2 of 14 mL/kg/min is generally used regardless of sex.

Another important issue is the utility of peak VO_2 regardless of the RER. An $\text{RER} \geq 1.1$ is generally recommended to confirm maximal exercise effort, with variables such as peak VO_2 losing their prognostic ability at $\text{RER} < 1.1$. As a result, clinicians dismiss many CPX results due to inadequate effort. In the Keteyian et al study, peak VO_2 discriminated mortality in all patients with $\text{RER} > 0.95$, and a peak $\text{VO}_2 < 12$ was associated with poor survival regardless of RER. Clinicians should not dismiss the significance of a low peak VO_2 just because a patient did not meet traditional criteria for maximal exercise effort.

There are limitations worth noting. The cohort studied only included HFrEF, and the findings cannot be extrapolated to HF with preserved ejection fraction. All patients exercised according to a modified Naughton protocol. While this is the most commonly used protocol in the United States, the data may not be generalizable to CPX performed using alternative protocols. Despite these limitations, the Keteyian et al study confirms the prognostic utility of CPX in the evaluation of HFrEF, and demonstrates that a lower peak VO_2 cutpoint may be necessary in female patients. ■

Ventricular Tachycardia Ablation for Recurrent Arrhythmia and Coronary Artery Disease

By *Cara Pellegrini, MD*

Assistant Professor of Medicine, University of California San Francisco; Cardiology Division, Electrophysiology Section, San Francisco VA Medical Center

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

SYNOPSIS: Acute and long-term success rates with ventricular tachycardia ablation in patients with coronary artery disease are relatively high with an acceptably low complication rate.

SOURCE: Marchlinski FE, et al. Long-term success of irrigated radiofrequency catheter ablation of sustained ventricular tachycardia. *J Am Coll Cardiol* 2016;67:674-683.

The role of ablation in the management of sustained monomorphic ventricular tachycardia (VT) has been somewhat unclear. Should clinicians perform it prophylactically in those with coronary heart disease, as the SMASH-VT or VTACH studies might advocate? Or is it a treatment of last resort — the classic practice? Perhaps its role is somewhere in between. Does it have a lasting effect, maybe even a mortality benefit, or are any salutatory effects transient in nature? What objective evidence exists demonstrating that it affects quality of life, hospitalizations, or other intermediate outcomes?

The multicenter NaviStar ThermoCool Catheter for Endocardial RF Ablation in Patients With Ventricular Tachycardia (THERMOCOOL VT) trial evaluated the use of irrigated radiofrequency catheter ablation for recurrent VT in drug-refractory post-myocardial infarction (MI) patients, and gained FDA approval for the open-irrigation ablation catheter for this purpose. This prospective, non-randomized, single-arm, post-approval study furthered those findings, examining long-term safety and effectiveness of ablation among patients with ≥ 4 sustained VT episodes, two episodes within 2 months, incessant VT, or spontaneous symptomatic VT despite antiarrhythmic medications or implantable cardioverter defibrillator (ICD) intervention. There were 249 patients. They were overwhelmingly male and Caucasian, with a mean age of 67.4 years. The vast majority had coronary artery disease and a previous MI and 95% had an ICD in place, with 25% sporting a biventricular pacemaker defibrillator. One-quarter had VT ablation performed previously. Operators were given a fair bit of flexibility in how they conducted the ablation and in the management of medications and ICD settings thereafter. The acute procedural endpoint was assessment of inducibility of the targeted VT, but other efficacy outcomes, including

mortality, were collected for 3 years post-ablation. The primary safety endpoint was cardiovascular-specific adverse events within 7 days of the ablation.

Immediate success was high, with 75% of patients showing noninducibility of the targeted VT at the end of the procedure. This occurred with a complication rate of 3.9%, which met the protocol-established performance criteria. There were no strokes, and the three early deaths that occurred were preceded by recurrent VT, suggesting the procedure was sometimes insufficient to prevent death, but likely not its direct cause. Nearly two-thirds of patients remained VT-free at 6-month follow-up. A significant decrease in ICD therapies (shocks and ATP), amiodarone use, and hospitalizations echoed this. There was a significant improvement in anxiety scores and a trend toward improvement in depression levels. The mortality rate at 3 years was 25.4%. The authors concluded that the acute and long-term success rates with ablation for VT associated with coronary artery disease are high, and that the complication rate is acceptably low.

■ COMMENTARY

This study is the first large-scale study of VT ablation to demonstrate quality of life improvements and a sustained decrease in cardiac-related hospitalizations. The immediate success rate, in terms of noninducibility of targeted VT, and the 6-month recurrence-free percentage are relatively high, particularly considering the disease burden pre-ablation. The complication rate compares at least equivalently, if not favorably, to the widely performed atrial fibrillation ablation procedure. The significant decline in amiodarone use and shock burden hints at a potential for downstream benefits. Yet, the 3-year mortality rate in this study is nearly identical to that from early reports of patients treated with ICD only.

When interpreting the results of this study, there are several cautions to consider, beyond its nonrandomized comparison design, that could explain why a “hard” outcome like mortality didn’t show the same positive trajectory as the “softer” outcomes. While nearly all patients had an ICD interrogated at the 6-month follow-up visit to assess VT burden, many study outcomes relied on patient self-reporting at yearly telephone interviews, which can be subject to recall bias and could certainly have underestimated asymptomatic VT events (including those treated with ATP therapy). There were many patients lost to follow-up (26% of patients were not part of the 6-month effectiveness cohort, and 43% did not contribute to 3-year data); if those lost to follow-up were more ill, the results could look better than reality. The relative homogeneity of the study population detracts from generalizability. Decline in amiodarone use over time may track with arrhythmia burden reduction, as suggested, but also could be partly due to development of intolerances or side effects over time, as commonly

occurs with this drug. Finally, carefully note that the study sponsor (the ablation catheter manufacturer) performed all statistical analyses and managed the data.

Despite these methodological weaknesses, this study is yet another addition to the literature supporting a more prominent role for VT ablation among those with coronary heart disease. Indeed, the beneficial effects of VT ablation just as easily might have been underestimated due to the biases above. Additionally, long-term effectiveness and survival may have been curtailed by the more advanced disease burden of the patients in this study. The relatively low procedural complication rate is remarkable and likely minimally affected by the concerns above. Notably, the operators in this multicenter study were highly experienced, and perhaps access to high volume centers and providers is the greatest obstacle to implementation of VT ablation earlier in the disease course. ■

ABSTRACT & COMMENTARY

The Current Outlook for Cardiac Tamponade

By Michael Crawford, MD, Editor

SYNOPSIS: In the modern era, cardiac tamponade is most commonly caused by malignancies with poor prognosis. As compared to older literature, iatrogenic causes have increased, most resulting from complications of percutaneous coronary intervention.

SOURCE: Sánchez-Enrique C, et al. Cause and long-term outcome of cardiac tamponade. *Am J Cardiol* 2016;117:664-669.

Little is known about the etiologies and prognosis of cardiac tamponade in the modern era. Thus, investigators from Madrid performed a retrospective observational study from 2003 to 2013 on 136 consecutive cases of cardiac tamponade. Patients with large pericardial effusions but no clinical signs of pericardial tamponade were not included. Pericardial fluid was evaluated. An exudative effusion was defined as a pericardial fluid protein to serum protein ratio of > 0.5, or was highly cellular, or had a glucose < 60 mg/dL. The patients were classified into seven groups: infective, neoplastic, uremic, iatrogenic, myocardial infarction (MI), other causes, and idiopathic. Researchers followed all patients for at least 1 year. The median age was 65 years, and 55% were men. Pericardiocentesis was required in 81%. Most had a transudate or hemorrhagic fluid. A positive cytology occurred in 15% and bacteria in 4%. Malignancy was the most common cause (32%), followed by infection (24%), idiopathic (16%), iatrogenic (15%), post-MI (7%), uremic (4%), and other (2%). The most common malignancies were lung (55%) and breast (18%). In the iatrogenic group, percutaneous coronary interventions (PCI) were the most common. Cardiac tamponade re-

curred in 10%, and 48% died. Malignancy carried the highest probability of both events (hazard ratio, 5.47; 95% confidence interval, 3.27-9.61; $P < 0.001$). The authors concluded the most common cause of cardiac tamponade is malignancy, and it has the worst prognosis. With aggressive management, other causes have a much better prognosis, especially iatrogenic causes.

■ COMMENTARY

Pericardial tamponade is infrequent, and much of our knowledge about its causes and prognosis is based on older literature. Thus, this contemporary 10-year experience in a modern urban hospital is of interest. Older literature suggested idiopathic was the most common diagnostic category, but now one-third of cases are due to malignancy. There are several possible reasons for this. Physicians may be better at diagnosing malignant effusions. Before, performing cytology on pericardial fluid was worthless; however, in this series it was positive in 46% of proven malignancy cases. Infection was common, whereas physicians once considered infective cardiac tamponade unusual. Surely the use of polymerase chain reaction and perhaps better culture techniques have increased the

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ability to diagnose infected fluid. However, the infective causes have changed. Tuberculosis is much less common, although not gone, and the viral causes are now likely to be cytomegalovirus and herpes, rather than coxsackie and echovirus. Although not in this series, other contemporary populations would have more HIV. Iatrogenic causes would have been unusual in the last century, but now share third place with idiopathic. Interestingly, most of the iatrogenic cases

were post-PCI, probably because more stents are deployed now than 10 years ago. Post-MI was next most frequent and it was most commonly free wall rupture. That seems unique to this series, as hospitals with ST elevation MI PCI teams on call rarely experience cardiac rupture. Finally, there were no cases of rheumatic diseases causing tamponade, which may be due to modern therapy with biologic agents. ■

CME/CE QUESTIONS

- Ventricular tachycardia ablation in post-myocardial infarction patients is associated with:**
 - > 90% initial success rate.
 - < 5% complication rate.
 - > 75% arrhythmia free at 6 months.
 - < 10% 3-year mortality.
- A meta-analysis of 17 proprotein convertase subtilisin-kexin type 9 serine protease-controlled treatment trials showed:**
 - a two-fold increase in neurocognitive adverse events.
 - a 90% decrease in low-density lipoprotein cholesterol.
 - a 25% increase in high-density lipoprotein cholesterol.
 - no difference in all-cause mortality.
- A long-term follow-up study of coronary CT imaging compared to standard chest CT observed coronary calcium showed:**
 - equal coronary calcium scores between the two methods.
 - poor correlation between methods for the detection of coronary calcium.
 - no difference in the reporting of calcium presence.
 - similar mortality prediction by both methods.
- In systolic heart failure subjects, the cardiopulmonary exercise test parameter with the highest predictive value for mortality was:**
 - respiratory exchange ratio.
 - exercise duration.
 - peak oxygen uptake.
 - percent predicted peak oxygen uptake.
- A registry study showed that compared to transcatheter aortic valve replacement (TAVR) alone, TAVR plus left main coronary disease displayed:**
 - higher mortality.
 - less target vessel revascularization.
 - equivalent vascular complications.
 - more frequent need for permanent pacemakers.
- Compared to the last century, the most common cause of pericardial tamponade is:**
 - malignancy.
 - infective.
 - iatrogenic.
 - uremic.

We Need Your Help!

The *Clinical Cardiology Alert* editors are planning topics for 2016 issues and would like your feedback on topics recently covered. Please help us by answering three questions at the following link:
<https://www.surveymonkey.com/r/CCASurvey2016>. Thank you!

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