

Clinical Cardiology

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

ABSTRACT & COMMENTARY

Complete Revascularization After STEMI: Do We Finally Know the Answer?

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: In this largest trial to date, patients who were randomized to complete revascularization by percutaneous coronary intervention (PCI) following successful intervention at the time of ST-elevation myocardial infarction (STEMI) had a lower risk of cardiovascular death, myocardial infarction, and ischemia-driven revascularization vs. patients who underwent culprit lesion-only PCI.

SOURCE: Mehta SR, Wood DA, Storey RF, et al. Complete revascularization with multivessel PCI for myocardial infarction. *N Engl J Med* 2019; Sep 1. doi: 10.1056/NEJMoa1907775. [Epub ahead of print].

Patients presenting with STEMI often exhibit significant disease of the noninfarct-related vessels. For years, one question was whether PCI of nonculprit vessels could or should be undertaken at the time of the initial STEMI procedure. For example, in the Preventive Angioplasty in Myocardial Infarction (PRAMI) trial, the authors focused attention on the value of PCI in noninfarct coronary vessels. However, the trial was relatively small in size and required additional angioplasty be performed at the time of primary PCI.¹ By far, the more common paradigm is that only the infarct-related vessel is treated at the time of STEMI presentation. Cardiologists are left to decide whether to recommend further elective PCI to achieve

complete revascularization. Enter the COMPLETE study, a trial designed to answer this question once and for all. Mehta et al enrolled 4,041 patients from 140 unique centers in 31 countries, randomizing 1:1 to either complete revascularization or culprit lesion-only PCI. Patients were randomized within 72 hours of successful culprit lesion PCI. Subjects assigned to the complete revascularization group were to undergo a staged PCI procedure either during the index hospitalization or after discharge, but no more than 45 days after group assignment. All eligible lesions (those judged to be at least 70% angiographically or 50-69% with a positive fractional flow reserve [FFR] measurement) were to be intervened on regardless

Financial Disclosure: *Clinical Cardiology Alert's* Physician Editor Michael H. Crawford, MD, Peer Reviewer Susan Zhao, MD, Nurse Planner Aurelia Macabasco-O'Connell, PhD, ACNP-BC, RN, PHN, FAHA, Editor Jonathan Springston, Editor Jason Schneider, Editorial Group Manager Leslie Coplin, and Accreditations Manager Amy M. Johnson, MSN, RN, CPN, report no financial relationships relevant to this field of study.

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Clinical Cardiology Alert (ISSN 0741-4218) is published monthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Clinical Cardiology Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

GST Registration Number: R128870672.

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of subsequent symptoms or noninvasive testing. Conversely, patients assigned to the culprit-only group received medical therapy alone. Within the first 45 days, 96 patients in the culprit-only group crossed over to complete revascularization, while 78 patients in the complete revascularization group crossed over to culprit lesion-only PCI.

At a median of three years follow-up, patients assigned to the complete revascularization group demonstrated a lower risk of cardiac death or new myocardial infarction (MI; 7.8% vs. 10.5%; hazard ratio [HR], 0.74; 95% confidence interval, 0.6-0.91; $P = 0.004$). This difference was driven by a reduced risk for new MI (5.4% vs. 7.9%). Death from cardiovascular causes was not significantly different (approximately 3% in each group). Among other secondary outcomes, ischemia-driven revascularization (1.4% vs. 7.9%; HR, 0.18; 95% CI, 0.12-0.26) and unstable angina (3.5% vs. 6.4%; HR, 0.53; 95% CI, 0.40-0.71) also were significantly lower in the complete revascularization group.

In this study of patients with STEMI and multivessel disease, the authors concluded that complete revascularization by staged PCI was superior to culprit lesion-only PCI, with outcomes driven by reductions in MI and ischemia-driven revascularization.

■ COMMENTARY

Multivessel disease in patients presenting with STEMI is extremely common, affecting up to an estimated half of all subjects. To date, four smaller trials have addressed the question of pursuing nonculprit lesions, primarily at the time of the initial procedure. In real-world practice, primary PCI can occur at any time and can be complicated. Although the prior prohibition against nonculprit PCI at the time of STEMI has been removed, patients in most cases are best served by addressing the culprit lesion only at the index procedure, taking the time to achieve an optimal result. Therefore, Mehta et al sought to address this everyday question in clinical cardiology: For the patient who has undergone successful primary PCI, is it reasonable and advantageous to recommend further PCI, even in the absence of further symptoms or tests confirming ischemia?

The results are quite compelling. In addition to reducing the incidence of repeat revascularization (in relative terms, a “soft” outcome), complete revascularization by PCI in this trial also led to a significant decline in new MI. The fact that no decrease was seen in the low rate of cardiovascular or overall mortality is not surprising and should not reduce our enthusiasm for the overall outcome.

[I suspect that we will see increasing referrals for complete percutaneous revascularization after STEMI, at least in patients with suitable anatomy.]

Some people may criticize the trialists for not requiring FFR assessment of lesion severity before committing to revascularization. The fact that lesions could qualify for intervention with a visual estimate of 70% suggests that some lesions might not have required intervention had they been subjected to functional assessment. Available trial evidence suggests that the use of FFR in the general case decreases the use of PCI while improving clinical outcomes compared to the use of visual estimates alone. Therefore, the fact that FFR was not mandated in this trial for lesions estimated to be 70% or greater would, if anything, dilute the positive result of the study. In no way should this omission dissuade cardiologists from using functional studies such as FFR in suitable patients and lesions.

It is relatively uncommon that the results of a single trial change practice guidelines. However, in this case, I suspect that we will see increasing referrals for complete percutaneous revascularization after STEMI, at least in patients with suitable anatomy. ■

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Is It Safe to Stop Digoxin for Heart Failure?

By Michael Crawford, MD, Editor

SYNOPSIS: In a large older patient heart failure with reduced ejection fraction hospitalizations database, the outcome of withdrawing digoxin vs. continuing digoxin was examined at 30 days and up to four years of follow-up. Withdrawing preadmission digoxin in hospital resulted in higher mortality at 30 days and more readmissions at six months, one year, and four years.

SOURCES: Malik A, Masson R, Singh S, et al. Digoxin discontinuation and outcomes in patients with heart failure with reduced ejection fraction. *J Am Coll Cardiol* 2019;74:617-627.

Uretsky BF, Vallurupalli S. Is the digitalis leaf still withering? *J Am Coll Cardiol* 2019;74:628-630.

Digoxin therapy in heart failure with reduced left ventricular ejection fraction (HFrEF) is indicated to prevent recurrent hospitalizations. Discontinuation has been shown to increase the risk of adverse outcomes in certain patients. The objective of this study was to examine the effects of discontinuing digoxin in patients hospitalized for an episode of HFrEF.

Malik et al used the OPTIMIZE-HF registry, which includes information about more than 48,000 HF hospitalizations in 259 hospitals in 48 U.S. states, and the corresponding Medicare database to identify 3,499 patients with an EF \leq 45% who received digoxin before hospitalization. Among these patients, 721 discontinued digoxin during hospitalization. The authors used propensity score matching to derive a cohort who discontinued digoxin and a cohort; these subjects were balanced on 50 key baseline characteristics. The final study population included 698 in each group. Also, the authors conducted a sensitivity analysis on acute kidney injury, a common reason for digoxin discontinuation. The 1,396 matched patients averaged 76 years of age and LVEF of 28%; 41% were women.

At four years after discharge, the digoxin discontinuation group exhibited significantly higher rates of HF readmission (HR, 1.2; 95% CI, 1.05-1.39; $P = 0.007$) and the combined endpoint of HF readmission or all-cause mortality (HR, 1.2; 95% CI, 1.07-1.34; $P = 0.002$), but not all cause mortality alone. These results were evident at six months and one year after discharge. At 30 days after discharge, the digoxin discontinuation group showed a greater risk of all-cause mortality (HR, 1.8; 95% CI, 1.26-1.57; $P = 0.001$) but not HF readmission. The authors concluded that in older patients admitted for a HFrEF episode, discontinuing preadmission digoxin therapy was associated with poor outcomes.

■ COMMENTARY

I learned the hard way as a trainee not to stop drugs prescribed by another physician before admission unless you thought the drug was harming the patient. Soon after discontinuing the drug, one may learn quickly why the patient was taking the drug in the first place.

The results of this study were not a surprise to me, but rather reinforced my prior experiential learning. What is interesting about this study was that in the face of modern pharmacologic and device therapy for HFrEF, we may have stopped using digoxin prematurely. Recently, I treated two elderly women with a HFrEF exacerbation in the hospital who either could not tolerate all our modern pharmacologic therapy or it just did not work. A resident asked about digoxin; after a couple of days of digoxin therapy, the patients started to improve and were discharged shortly thereafter. In the 1990s, we learned from the work of the Digitalis Investigation Group (DIG) that digoxin in HFrEF patients can reduce readmissions but does not increase longevity.¹ Although not currently listed as a first-line therapy option, digoxin still may play a role in HFrEF treatment — and not just for atrial fibrillation. The results of the Malik et al study suggest who might benefit most.

Why this retrospective propensity score-matched study when we have seen results from two randomized, controlled digoxin withdrawal studies (RADIANCE and PROVED)?^{2,3} These were small studies published in the early 1990s that showed that discontinuing digoxin in stable outpatients was associated with reduced functional class and EF and an increase in symptoms. Thus, there was a perceived need for a withdrawal study in hospitalized patients on modern neurohormonal-blocking therapy. Malik et al showed that digoxin withdrawal was associated with increased mortality for 30 days to one year and more readmissions from six months to four years. The subgroup analyses shed some light on the possible reason for these results. The adverse effects of digoxin withdrawal were most evident in those not on beta-blockers, with an EF $>$ 25%, with coronary artery disease, and with a heart rate \geq 70 bpm. These data suggest that the known suppression of sympathetic activity by digoxin may be important in certain patients, such as those with ischemic heart disease or those intolerant to beta-blockers.

The strengths of this study were its large size, use of contemporary therapy, and matching for 50 baseline variables. Some weaknesses included its retrospective,

observational design where not all potential confounders were measured. Further, there were no data on digoxin or other drugs after hospitalization. Also, the OPTIMIZE-HF data are from the early 2000s; there have been a few advances in HF therapy since then. Perhaps appropriately, the use of digoxin in HFrEF today has decreased to 10% of patients; it was about 33% in the OPTIMIZE-HF database. However, for those on digoxin when admitted to the hospital, it may not be a good idea to stop the therapy, especially in patients with coronary artery disease or who are intolerant to beta-blockers. This was the case in both my recent elderly women with HFrEF who responded to digoxin.

If one decides to initiate digoxin in HFrEF patients, it is important to remember that in the DIG trial, adverse effects of digoxin were minimized if the serum level was

kept < 1.0 ng/mL. In the Malik et al study, reduced renal function did not diminish the benefits of digoxin. Thus, digoxin can be used in patients with reduced renal function with proper dose adjustment. ■

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ABSTRACT & COMMENTARY

Is There a Role for Surgery in Isolated Severe Tricuspid Regurgitation?

By *Jamie L.W. Kennedy, MD, FACC*

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

SYNOPSIS: A retrospective single-center analysis of patients with isolated severe tricuspid regurgitation revealed no survival benefit from tricuspid surgery.

SOURCE: Axtell AL, Bhambhani V, Moonsamy P, et al. Surgery does not improve survival in patients with isolated severe tricuspid regurgitation. *J Am Coll Cardiol* 2019;74:715-725.

The presence of significant tricuspid regurgitation (TR) carries a poor prognosis; however, the benefit of intervention has not been studied rigorously. Most TR is secondary to left-sided heart disease, either valvular or myopathic, or pulmonary vascular disease. Primary TR from leaflet pathology is less common. Current expert consensus guidelines recommend tricuspid intervention for patients undergoing left-sided valve surgery and for patients with severe primary TR with either symptoms or progressive right heart dilation/dysfunction. Intervention for secondary TR in the setting of left heart failure, either systolic or diastolic, or pulmonary vascular disease is not addressed in the guidelines. Isolated tricuspid surgery, either repair or replacement, is a surprisingly high-risk procedure, with the in-hospital mortality rate ranging from 8% to 10%. Volumes are low, and there is not a Society of Thoracic Surgeons risk model for either repair or replacement.

Axtell et al used a single-center echocardiography database to identify patients with severe TR between November 2001 and March 2016. Patients with

moderate or worse aortic, mitral, and pulmonic valve disease were excluded, leaving 3,276 patients with “isolated” TR. These patients were followed through April 2018; median follow-up was 2.6 years. Patient care decisions, such as frequency of echocardiograms, medications, and surgery, were made by clinicians independent of the study. Over the course of the study, 171 patients underwent surgery (143 repair and 28 replacement) and 29 underwent concomitant coronary artery bypass grafting. Not surprisingly, compared to those medically treated, patients undergoing tricuspid surgery were younger, with higher average ejection fraction (52% vs. 57%) and lower rates of coronary disease (31% vs. 16%), heart failure (83% vs. 72%), diabetes (4% vs. 1%), and chronic kidney disease (39% vs. 20%). Interestingly, 15 patients in the medical management group underwent coronary artery bypass grafting without tricuspid intervention. From the isolated TR patient panel, a propensity-matched sample was selected. The sample consisted of pairs of similar patients managed medically and surgically. It is unclear from the paper which variables were used for matching.

Interestingly, there was substantially more secondary TR in the medical group and primary TR in the surgical group. The medical and surgical groups were similar in terms of right ventricular dilation and estimated right ventricular systolic pressure (RVSP). There was an apparent survival benefit with surgery at this point of the analysis; however, the authors adjusted for the time between diagnosis of severe TR and surgery (median, 3.7 months), the immortal time bias. Following this adjustment, there was no difference in survival between the two groups. Among patients who did undergo surgery, there was no difference in survival between repair vs. replacement.

As expected, surgical outcomes were worse for older patients and those with heart failure. There may have been significant clinical changes in the time between diagnosis and surgery. The authors performed a second analysis using clinical parameters at the time of surgery and found no difference in the outcome. The authors repeated the propensity matching analysis, including echo-derived RVSP. They found no difference in survival between medically and surgically managed patients. Finally, Axtell et al attempted to correct for those lost to follow-up by studying a “loyalty cohort” of patients who received most of their care at the study institution. Again, there was no difference between medical and surgical groups. The authors concluded that surgery for isolated TR does not improve survival. They mentioned the possibility that delayed intervention allows progressive right heart dysfunction and end-organ dysfunction, thereby limiting the benefit of intervention. However, the median time between echo diagnosis of severe TR and surgery was only 2.9 months in the overall cohort and 3.7 months in the propensity-matched sample.

■ COMMENTARY

A significant limitation in many studies of TR is the combined analysis of primary and secondary (or organic

and functional) etiologies. The study by Axtell et al was no exception. Patients with moderate or severe aortic, mitral, or pulmonic valve disease were excluded, but patients with secondary TR due to left ventricular systolic or diastolic dysfunction were included, as were patients with pulmonary vascular disease. The clinicians caring for these patients clearly took etiology into account in their management decisions. Only 39% of patients in the surgical arm of the propensity-matched group had secondary TR vs. 79% in the medically managed arm. Unfortunately, the rate of secondary TR for the entire cohort was not reported. Despite the preponderance of primary TR in the surgical patients, there was no survival benefit to surgery, an intriguing finding as current guidelines advocate for intervention in primary TR.

I am puzzled by the lack of information on hepatic function in these patients. Congestive hepatopathy and cardiac cirrhosis are well-recognized complications of long-standing TR. Liver disease is a powerful predictor of outcomes for patients undergoing cardiac surgery. Perioperative mortality for Child-Pugh class A is reasonable at 5%, marginal at 35% for class B, and likely prohibitive at 70% for class C. For this study, I imagine patients with significant hepatic impairment were medically managed. In light of this, it is again intriguing that surgery was not beneficial.

Based on the results of this study, tricuspid surgery may not improve survival and should be undertaken cautiously, after thorough preoperative evaluation (including a complete hemodynamic study and end organ assessment). I hope the authors of future studies differentiate primary and secondary TR and capture information on hepatic impairment. Similar to our experience with functional mitral regurgitation, we may need a well-conducted percutaneous intervention trial to truly assess the role of tricuspid intervention. ■

ABSTRACT & COMMENTARY

Blood Pressure Targets in the Elderly

By Michael Crawford, MD, Editor

SYNOPSIS: The authors of a large population study found that reducing blood pressure to < 140/90 mmHg is associated with increased mortality, and mortality was highest in those with previous cardiovascular events and age > 80 years.

SOURCES: Douros A, Tölle M, Ebert N, et al. Control of blood pressure and risk of mortality in a cohort of older adults: The Berlin Initiative Study. *Eur Heart J* 2019;40:2021-2028.

Ewen S, Mahfoud F, Böhm M. Blood pressure targets in the elderly: Many guidelines, much confusion. *Eur Heart J* 2019;40:2019-2031.

Optimal blood pressure (BP) in elderly hypertensive patients is controversial, partly because there are few randomized trials that have included subjects 75 years of age or older. Investigators from the Berlin Initiative Study (BIS), an ongoing prospective,

observational study of eligible Berlin residents ≥ 70 years of age, tested the hypothesis that BP values < 140/90 mmHg during treatment of hypertension would reduce all-cause mortality. Since the focus of the BIS was renal function, those with a kidney transplant or on dialysis

were excluded. Douros et al investigated a subgroup treated for hypertension from 2009 until 2011 and followed through 2016. BP values were the mean of two office measurements within 10 minutes after patients were seated quietly for five minutes. Among 2,069 BIS subjects, 79% were treated for hypertension at baseline. Of these, 39% registered BP values < 140/90 mmHg, and 61% registered higher pressures. Antihypertensive treatment consisted of diuretics in 60% of subjects, beta-blockers in 59%, ACE inhibitors in 50%, calcium antagonists in 34%, and ARBs in 30%. Combination therapy was noted in 69%.

After a median follow-up of 73 months, all-cause mortality was highest in the normalized BP group (lower than 140/90 mmHg): 60 vs. 49 per 1,000 person years; adjusted HR, 1.26; 95% CI, 1.04-1.54. A subgroup analysis showed that the mortality risk was highest in the normalized BP group, particularly for those with previous cardiovascular events vs. those without (98 vs. 64 per 1,000 person years; HR, 1.61; 95% CI, 1.14-2.27) and in those > 80 years of age (102 vs. 78 per 1,000 person years; HR, 1.40; 95% CI, 1.12-1.74). Using a BP cutoff of < 150 in the octogenarians attenuated the risk (HR, 1.21). Also, if normalized BP was changed to < 130, mortality risk increased further (HR, 1.42), which was statistically significant at all values < 125.

The authors concluded that reducing BP to lower than 140/90 mmHg in elderly patients or in those with previous cardiovascular (CV) disease is associated with increased mortality.

■ COMMENTARY

The SPRINT-Senior, the VALISH, and JATOS randomized, controlled trials of BP-lowering in elderly patients with hypertension all demonstrated the superiority of lower than 120 mmHg compared to < 140 mmHg.¹⁻³ However, the generalizability of the studies has been questioned due to their strict inclusion criteria. For example, SPRINT excluded patients with prior stroke, heart failure, diabetes, and dementia. It has been estimated that only about one-third of elderly Americans would qualify for the SPRINT trial. Also, these randomized, controlled trials included a relatively short follow-up period; SPRINT was three years.

In contrast, the BIS study was large, there were few exclusion criteria, and the median follow-up was six years. Also, in addition to adjusting for comorbidities, BIS was adjusted for terminal decline using a one-year lag. Of course, it was an observational study, and there could have been unmeasured confounders that affected the results. For example, other than prior myocardial infarction, Douros et al did not include specific data on coronary artery disease, nor did they include cause of death information. Perhaps the biggest weakness was that BP was only measured at intake into the study.

Nevertheless, the results of the BIS study are in line with other observational studies from the United Kingdom and China with shorter follow-up periods, as well as the older HYVET study, which showed that a target of < 150 mmHg was superior to < 160 mmHg after a short follow-up of 1.8 years.⁴ The main findings from the BIS study were that the 26% increase in the risk of all-cause mortality with BP < 140 mmHg was mainly driven by the BP < 130 mmHg subgroup, in addition to the increased risk in those age > 80 years and the 61% increase in those with known CV disease. There seems to be some equipoise in the 70 to 79-year-old group, where the < 140 mmHg target was neutral regarding mortality. When these nuances are considered, it may be reasonable to conclude that a BP target of < 140 mmHg is acceptable for those age 60 to 80 years. This would be in line with the recent European Society of Cardiology (ESC) guidelines (2018) but not the American Heart Association/American College of Cardiology (AHA/ACC) guidelines (2017).^{5,6} In those > 80 years of age, the ESC moves to < 160 mmHg, while the AHA/ACC stays at < 130 mmHg.

The real issue is discovering the driving pressure needed for optimal organ perfusion in the elderly. This probably depends on the individual. Ideally, one would consider the patient's biological age, comorbidities, and fitness to decide on what should be the optimal BP target. In those with clear vascular disease, higher thresholds for treatment makes sense, whereas healthy, fit elderly individuals may benefit from a lower target. Also, it is recommended that the introduction of antihypertensive medications and their uptitration should be handled more cautiously in the elderly, with particular attention paid to frailty. Frail individuals are going to be more prone to hypotension, syncope, and falls. Thus, in patients > 60 years of age, antihypertensive therapy should be more individualized rather than following strict BP targets. ■

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ABSTRACT & COMMENTARY

Size Matters Regarding Left Heart Valve Vegetations

By Michael Crawford, MD, Editor

SYNOPSIS: An international registry study of left-sided valvular infective endocarditis patients revealed that large vegetations (> 10 mm) are associated with increased mortality at six months, but not if early surgery is performed.

SOURCES: Fosbøl EL, Park LP, Chu VH, et al. The association between vegetation size and surgical treatment on 6-month mortality in left-sided infective endocarditis. *Eur Heart J* 2019;40:2243-2251.

Habib G. How do we reduce embolic risk and mortality in infective endocarditis? Measure the size of the vegetation and operate early in patients with large vegetations. *Eur Heart J* 2019;40:2252-2254.

There is conflicting evidence on the benefits of early surgery for large vegetations in patients with left heart valve infective endocarditis (IE). Investigators from the international collaboration on endocarditis (ICE) tested the hypothesis that early surgery before finishing antibiotic therapy in IE patients with vegetations > 10 mm would result in a lower six-month mortality compared to not operating. ICE is a prospective, multinational registry of consecutive IE, cases collected from 34 centers in 18 countries, hospitalized between 2008 and 2012, with at least six months of follow-up. Patients with device-related IE were excluded. In patients with multiple IE episodes, only the first episode was included. Fosbøl et al used transesophageal echo to determine vegetation size. The authors used a propensity score model to account for other reasons for surgery.

Among 2,124 patients in the ICE registry, 1,006 had left-sided IE with vegetation size recorded; 58% of these patients had large vegetations (> 10 mm). Operative risk in both groups was similar. Embolic events were more common in patients with large vegetations (44% vs. 28%; $P = 0.001$) as was six-month mortality (25% vs. 19%; $P = 0.001$). After propensity adjustment, the association with higher mortality for patients with larger vegetations was seen only with medical management (HR, 1.86; 95% CI, 1.48-2.34), not surgical management (HR, 1.01; 95% CI, 0.69-1.49). Patients with large vegetations more often had *Staphylococcus aureus* IE (26% vs. 20%; $P = 0.026$).

The authors concluded that in patients with left-sided IE and vegetation size > 10 mm, increased six-month mortality was observed, but it was treatment-dependent in that undergoing surgery eliminated the higher mortality of a large vegetation.

■ COMMENTARY

Left heart valve IE is extremely challenging for many reasons, but seeing on echo the impending disaster of a large vegetation (especially if it is mobile) takes the cake. Early operation always is a tough sell to surgeons, even if other indications for surgery are present. Still, large vegetations are known to increase the risk of emboli and mortality. On the other hand, the risk of systemic emboli decreases rapidly after a few days of antibiotics and is rare after two weeks of therapy. Surgeons often find reasons to delay, even though one randomized, controlled trial of 76 patients has shown that early surgery for large vegetations decreases the risk of emboli, but not six-month mortality.¹

However, in the Fosbøl et al study, many patients crossed over to surgery later in their hospital course, which could have improved the outcomes for the initial medical therapy group. Thus, this registry study is of interest because the authors focused on the issue of mortality at six months. Fosbøl et al showed that early surgery, a median seven days after admission, decreases the embolic rate and mortality at six months compared to medical therapy, after adjusting for surgical selection criteria and estimated operative risk. These adjustments are important because there were considerable baseline differences between the surgery and medical treatment groups. Surgical patients were younger and presented with more complications such as heart failure, paravalvular complications, and persistent bacteremia.

Although informative, there were limitations to the Fosbøl et al study. It was a retrospective analysis of observational data from selected tertiary care centers. Surgery was performed at the discretion of the local physicians. There was no core echo lab to confirm vegetation size, and there were no data on vegetation

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mobility. Also, the authors only examined all-cause mortality. The U.S. guidelines give a IIb recommendation to consider early surgery if vegetation size is > 10 mm and it is mobile.² The ESC guidelines give a class I indication for surgery if a left-sided valve vegetation is > 10 mm and if one or more systemic emboli have occurred despite antibiotic therapy.³ A class IIa recommendation is a large vegetation with hemodynamic effects, such as severe stenosis or regurgitation (also for a very large vegetation [> 30 mm]). A 15-29 mm vegetation receives a class IIb rating. At a measurement of 10-15 mm, with no other indications, surgery would not be recommended by either guideline. If the results of this ICE registry study are adopted into the guidelines, they probably would recommend early surgery for left-sided IE with vegetation size > 10 mm, regardless

of other characteristics or complications at level II. In addition, in practice a large vegetation plus other high-risk features would strengthen the recommendation for surgery. In an area with a paucity of data, this registry study adds important information. ■

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CME/CE QUESTIONS

1. **A large registry study of patients with infective endocarditis showed that those with large vegetations compared to those with small vegetations had:**
 - a. higher operative mortality.
 - b. more embolic events.
 - c. more streptococcal infections.
 - d. no benefit from surgery.
2. **In hospitalized patients with heart failure due to reduced ejection fraction, if prior digoxin therapy was stopped, what was noted?**
 - a. Lower readmission rates at four years
 - b. Higher readmission rates at 30 days
 - c. Higher mortality at four years
 - d. Higher mortality at 30 days
3. **A large observational study of hypertension treatment to < 140/90 mmHg in older patients showed that mortality was highest in:**
 - a. patients 70-79 years of age.
 - b. patients > age 80 years.
 - c. patients with no prior heart disease.
 - d. patients with systolic blood pressure lower than 160 mmHg.
4. **A recent study of isolated tricuspid regurgitation showed no survival advantage for surgery compared to medical therapy. Which subgroup undergoing surgery fared worse?**
 - a. Patients with heart failure
 - b. Patients with coronary artery disease
 - c. Patients < age 50 years
 - d. Patients with hepatic cirrhosis
5. **In the study of acute STEMI patients that compared those who received complete staged percutaneous coronary revascularization within 45 days to those treated medically after initial culprit vessel percutaneous intervention, those completely revascularized early at three years follow-up showed:**
 - a. lower mortality.
 - b. a higher risk of subsequent revascularization.
 - c. a lower rate of new myocardial infarction.
 - d. a higher rate of subsequent unstable angina.

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