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ABSTRACT & COMMENTARY

Giving the Cold Shoulder to Drug Therapy for Atrial Fibrillation

By Joshua Moss, MD

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SYNOPSIS: In two randomized trials published simultaneously, cryoballoon ablation proved superior to drug therapy for prevention of arrhythmia recurrence in patients with paroxysmal atrial fibrillation.

SOURCES: Wazni OM, Dandamudi G, Sood N, et al. Cryoballoon ablation as initial therapy for atrial fibrillation. *N Engl J Med* 2020; Nov 16. doi: 10.1056/NEJMoa2029554. [Online ahead of print].

Andrade JG, Wells GA, Deyell MW, et al. Cryoablation or drug therapy for initial treatment of atrial fibrillation. *N Engl J Med* 2020; Nov 16. doi: 10.1056/NEJMoa2029980. [Online ahead of print].

Mounting evidence suggests there are better outcomes with a rhythm control strategy than a rate control strategy for many patients with atrial fibrillation (AF). An important question remains: Once selected, should clinicians attempt the rhythm control strategy first with antiarrhythmic drug (AAD) therapy, or with catheter ablation? Guidelines recommended ablation after a failed trial of at least one AAD, while gradually accepting there are circumstances in which starting with ablation might be preferred.

In STOP-AF (Wazni et al) and EARLY-AF (Andrade et al), investigators sought to compare cryoballoon ablation to AAD therapy as first-line treatment for paroxysmal AF. Wazni et al randomized 203 patients 1:1 to cryoablation or AAD (class I or III agent). Mean age was 61 years, mean ejection fraction (EF) was 61%, and mean left atrial (LA) diameter was 39 mm. Most patients recorded a CHA_2DS_2-VASc score of 1 or 2, and 27% had undergone electrical or pharmacologic cardioversion in the prior 12 months. In the ablation group, 101 of 104 patients underwent a "successful" procedure. In the AAD group, about half were treated with flecainide (100-200 mg daily), and 12 of 99 crossed over to ablation before a documented arrhythmia recurrence. The primary endpoint was freedom from atrial arrhythmia recurrence after a 90-day blanking period. Patients were monitored via ECG every three months, via patient-activated phone monitoring for symptoms weekly, and via 24-hour ambulatory monitoring at six and 12 months.

Andrade et al randomized 303 patients 1:1 to cryoablation or AAD. Patient profiles were similar to those in STOP-AF: mean age was 58 years, mean

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EF was 60%, and mean LA diameter was 39 mm. The mean CHA_2DS_2-VASc score was 1.9, and 39% had undergone prior cardioversion. In the ablation group, complete pulmonary vein isolation was confirmed in 152 of 154 patients (two patients did not undergo the procedure). In the AAD group, a prespecified protocol was used to up-titrate medications to the maximum dose associated with an "acceptable" side effect profile. Most were treated with flecainide (median dose of 200 mg daily). No patients crossed over to ablation before the occurrence of a primary endpoint event. The primary endpoint was freedom from atrial arrhythmia recurrence after a 90-day blanking period. Notably, all patients received a LINQ implantable loop recorder (ILR) for continuous cardiac monitoring, inserted no more than 24 hours after catheter ablation or initiation of AAD.

Although patient populations and treatment strategies were similar, EARLY-AF was designed with more sensitive arrhythmia monitoring via ILR. Andrade et al also used a more regimented protocol for drug titration. Flecainide was most commonly used in both trials, although at somewhat lower doses in STOP-AF.

The results of both trials also were similar. In STOP-AF, freedom from procedural failure or recurrent arrhythmia at 12 months was 75% in the ablation group and 45% in the AAD group ($P < 0.001$). There were two pericardial effusions, two phrenic nerve injuries, and a TIA in the ablation group. Adverse events in the AAD group included four episodes of syncope in three patients, bradycardia in two patients, and a variety of drug side effects. Quality of life in the ablation group as assessed with two different measures improved significantly from baseline to 12 months. Scores were not reported for patients in the AAD group.

In EARLY-AF, freedom from recurrent arrhythmia at 12 months was 57% in the ablation group and 32% in the AAD group ($P < 0.001$). Symptomatic recurrence was documented in 11% of the ablation group and 26% of the AAD group. Overall arrhythmia burden was low. Median time in AF was 0% in the ablation group vs. 0.13% in the AAD group. There were two patients who required a pacemaker, one episode of syncope, and three persistent phrenic nerve palsies in the ablation group. Adverse events in the AAD group included one episode of tamponade (in a patient who underwent ablation after arrhythmia recurrence), two episodes of syncope and five episodes of presyncope, two wide complex tachycardia or proarrhythmic events, two patients who required a pacemaker, and one TIA event. Quality of life scores improved significantly in both groups.

The authors of both studies concluded that in patients with paroxysmal AF, cryoablation was superior to AAD therapy for preventing recurrent AF.

■ COMMENTARY

To cardiologists and electrophysiologists treating paroxysmal AF, the top line results of these two trials come as little surprise: Ablation is superior to AAD therapy in preventing recurrence of atrial arrhythmias. However, there are several additional important findings, with a few caveats to remember.

First, the benefit of intensive arrhythmia monitoring for accurate reporting in AF trials is demonstrated in EARLY-AF. There were higher overall rates of documented arrhythmia recurrence compared with STOP-AF, but with outcomes that were similarly superior for catheter ablation. In other words, more sensitive monitoring detected more asymptomatic episodes but did not "falsely" improve outcomes in one arm over the other.

The restricted crossover in EARLY-AF also was notable and helps increase confidence in the results. Patients with paroxysmal AF clearly experience asymptomatic arrhythmia episodes despite ablation and/or AAD therapy, affirming the need for continuous anticoagulation when risk factors are present.

On the other hand, these trial authors used cryoballoon ablation. Although similar outcomes might be expected with radiofrequency ablation (preferred by many operators), this was not part of either trial. Procedural complications were infrequent but not absent, particularly phrenic nerve palsy, an injury that often heals with time but can be associated with uncomfortable shortness of breath. The

trials likely were underpowered and follow-up too brief to detect differences in "hard" outcomes, such as stroke or death. Critics also point to the lack of a "true control" observation (and presumably risk factor modification). Nevertheless, for many patients who feel unwell with AF, in whom AF is likely to progress, and for whom recent data support earlier rhythm control to improve cardiovascular outcomes, ablation by an experienced operator after thorough discussion of risks is a reasonable first-line strategy. ■

ABSTRACT & COMMENTARY

How to Record Reliable Blood Pressure Measurements

By Michael H. Crawford, MD, Editor

SYNOPSIS: A small, community-based study to detect hypertension revealed one week of twice-daily home blood pressure (BP) measurements are more reliable and more accurately predict increased left ventricular mass than clinic or 24-hour ambulatory BP monitoring.

SOURCE: Schwartz JE, Muntner P, Kronish IM, et al. Reliability of office, home and ambulatory blood pressure measurements and correlation with left ventricular mass. *J Am Coll Cardiol* 2020;76:2911-2922.

Controversy exists about which method of diagnosing and monitoring high blood pressure (BP) is best for guiding therapy to prevent end-organ damage. Schwartz et al investigated the reliability and predictive accuracy of office BP (OBP) measurements vs. home BP (HBP) vs. ambulatory BP (ABP) for predicting left ventricular mass index (LVMi) measured by echocardiography.

The study population included participants from the Detection of Hypertension (IDH) study, a community-based sample of 400 subjects without known cardiovascular disease recruited between 2011 and 2013 in New York City.[1] Exclusion criteria included BP > 160/105 mmHg, evidence of secondary hypertension, pregnancy, or on medications that would affect BP. The study consisted of five visits over one month with OBP, 24-hour ABP twice, HBP over three weeks, and an echo on the last visit. OBPs were attended and performed three times with three different devices (mercury, clinic oscillometric, and home oscillometric). Complete ABP studies were obtained in 91% of subjects. HBP was conducted twice one minute apart in the morning and evening, and 96% recorded at least 12 out of 28 expected readings in a week for all three weeks. All measurements were corrected for regression dilution bias, and adjustments were made for clinical features of the subjects for estimating associations with LVMi. Mean age was 41 years, 60% were women, 26% were Black, and 64% were Hispanic.

The mean awake systolic (SBP) by ABP was 8-9 mmHg higher than the mean OBP and HBP SBPs, which were almost identical. The reliability of the first visit OBP with the subsequent visits was 0.89 and 0.85 for SBP and DBP, respectively. For the first week of HBP vs. the second week, it was 0.94/0.92. For the first 24-hour ABP vs. the second, it was 0.85/0.84. The corrected correlations between the three measurement techniques ranged from 0.74 to 0.89. The multivariate adjusted correlation between SBP by HBP and LVMi of 0.50 was significantly higher than those of ABP and OBP (0.43 for both; $P < 0.001$). Correlations between DBP and LVMi all were weaker, but the HBP value of 0.33 was significantly higher than the awake ABP value of 0.26 ($P < 0.05$). The three OBP equipment types produced similar adjusted correlations between SBP and LVMi (0.32 mercury, 0.39 office oscillometric, and 0.43 home oscillometric). The authors concluded HBP measurements were more reliable and more strongly associated with LVMi than OBP or ABP measurements and suggested that one week of HBP monitoring may be the best way to diagnose hypertension.

■ COMMENTARY

These results are somewhat surprising since prior studies have shown ABP is superior to OBP for predicting cardiovascular events and all-cause mortality. However, those studies used one OBP measurement as the comparator. Also, HBP has not been well studied, especially in comparison to other methods. In addition, ABP does not account for resting awake BP and usually is performed for only one 24-hour period. In the Schwartz et al study, HBP involved twice-daily measurements, averaged for a week. This would tend to average out day-to-day variation and arguably would be the best estimate of basal resting BP in the subject's natural environment. OBP is well known to be problematic for several reasons. It occurs in an artificial environment. White coat hypertension is an issue. The SPRINT[2] authors worked around some of these office issues by designating a mandatory five-minute unattended (in most cases) delay before an automatic oscillometric machine measured BP. These

BP measures were lower than random home measures. However, the realities of clinic practice make such measurements impractical, and this technique has not gained widespread acceptance. The availability of ABP is limited, it is poorly reimbursed, and is used rarely. Thus, the one-week HBP approach is attractive, but there are barriers to widespread use of HBP. The daily schedule will not work for everyone, although in the Schwartz et al study, 96% of subjects recorded at least 12 of the expected 28 BP readings in a week. The cost of the device is not trivial, and there is no provider reimbursement for the data review. Also, there is no infrastructure to handle the data and provide the five minutes of training required to ensure accurate data.

There were weaknesses to this study. The population studied was small, young, and had few comorbidities. Whether HBP would work as well in an older population with more comorbidities and on medications is unknown. Also, although LVMi is a valid target organ abnormality to validate the technique's utility, Schwartz et al did not pursue long-term clinical outcomes. Current guidelines recommend two or three OBP measurements to diagnose hypertension. Surely, HBP would be more cost-effective than two or three office visits. At this point, I believe HBP is a good technique for diagnosing hypertension, but more data are needed before using it exclusively for the management of patients with known hypertension and other comorbidities. ■

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ABSTRACT & COMMENTARY

Is There an Ideal Time to Administer Antihypertension Medications?

By Michael H. Crawford, MD, Editor

SYNOPSIS: Taking all antihypertensive agents before bed vs. upon awakening in hypertensive patients showed there was less hypertension during sleep and few cardiovascular events over a six-year follow-up.

SOURCE: Hermida RC, Crespo JJ, Domínguez-Sardiña M, et al. Bedtime hypertension treatment improves cardiovascular risk reduction: The Hygia Chronotherapy Trial. *Eur Heart J* 2020;41:4565-4576.

Although known to reduce sleeping blood pressure (BP), there are few data on the effect of bedtime administration of the entire daily dose of antihypertensive medications vs. administration upon awakening in the morning on BP control and cardiovascular (CV) outcomes. The Hygia Chronotherapy Trial was a randomized, multicenter, controlled, open-label, blinded, endpoint study of whether bedtime administration is superior.

Hermida et al conducted this work in 40 primary care practices in Northern Spain, using 24-hour ambulatory BP (ABP) measurements to diagnose and manage hypertension. They recruited more than 22,000 patients with hypertension. Each participant underwent confirmatory 48-hour ABP measurements. After excluding those with an invalid study or normotension in untreated subjects, the authors randomized 19,168 subjects to all antihypertensive pharmacologic treatment at awakening or at bedtime. Pregnant patients, rotating shift workers, those with secondary hypertension, those with known CV disease, and those with renal failure all were excluded. A minimum follow-up of one year was required, with a target of five years. Eighty-four subjects were excluded for failing to follow up at one year. In the final study population (19,084), the mean age was 61 years, and 56% were men. Each of the 292 physicians involved chose the antihypertensive drugs. At each outpatient visit (at least annually), 48-hour ABP was performed, with the subject noting in a diary when he or she retired and awakened. The primary outcome was a combination of myocardial infarction, coronary revascularization, heart failure, ischemic stroke, or CV death. The bedtime group achieved lower sleeping BP readings than the morning group, but there was no difference in awake BP measurements. Sleep hypotension was rare (0.3% of participants), and there was no difference between groups. Poor drug compliance was about 3% for both groups. CV events occurred in 1,752 subjects over the median six-year follow-up. The adjusted hazard ratio (HR) for the combined primary endpoint in the bedtime group vs. the morning group was 0.55 (95% CI, 0.50-0.61; $P < 0.001$). The HR for CV death was 0.44 (95% CI, 0.34-0.56; $P < 0.001$). The HR for hemorrhagic stroke was 0.39 (95% CI, 0.23-0.65; $P < 0.001$). The HR for the heart failure was 0.58 (95% CI, 0.49-0.70; $P < 0.001$). Total adverse events were not different between groups (6.7% morning, 6% bedtime). No subgroup demonstrated better outcomes

with morning drug administration. The authors concluded bedtime administration of all antihypertensive medications resulted in lower sleeping BP control and markedly reduced CV events compared to taking all BP medications upon awakening.

■ COMMENTARY

Prior studies have shown ABP is superior for predicting outcomes in hypertensive patients, especially if blunted nocturnal BP reduction is detected (non-dipper pattern). Also, studies have demonstrated that bedtime administration of at least one antihypertensive medication abrogates the non-dipper pattern of sleep BP and lowers CV disease risk, but these studies did not include a control arm. In a randomized, controlled study, the authors observed 2,000 patients who experienced fewer CV events with bedtime drug administration compared to awakening.[1] The strengths of the Hygia trial include its large size (almost 20,000 patients) and the use of primary care centers. Asking patients to keep diaries to establish the circadian pattern of sleep and awake periods was helpful. The 48-hour ABP tactic improved reproducibility. In addition, there was a long follow-up period, with a robust number of CV events. The Hygia study showed there was better sleeping BP control with bedtime drug administration without loss of awake BP control. There was less non-dipping observed in the bedtime group and markedly fewer CV events. Finally, bedtime administration was safe, and patient adherence was excellent. But there were some weaknesses. First, the subjects were all Spanish Caucasians. Transferability to other ethnic groups is unknown. Second, the medication regimens used were not prescribed by the study protocol; rather, each participating physician devised his or her own treatment program. They were given the Spanish government's documents on selecting drugs for BP control, but how much they applied these recommendations is unknown. Third, the authors could not separate the effects of bedtime administration in dippers and non-dippers. Interestingly, there were other positive results of bedtime administration. Serum creatine and LDL cholesterol levels were lower, and HDL cholesterol levels were higher in the bedtime group. How do cardiologists translate these finding into practice? Not all medications may be well-tolerated taken at bedtime (e.g., diuretics). In the Hygia study, there was less diuretic use in the bedtime group. However, there are studies that showed changing one medication to bedtime produced similar results as Hygia, and the medications shifted usually were calcium blockers or ACEI/ARBs. Culling one medication would thwart the triple-drug combination pills that are so popular with patients, but would solve the diuretic-before-bed issue. The authors of other studies have suggested ACEI/ARBs would work best if taken at bedtime since the renin-angiotensin-aldosterone system is more active during sleep. The asleep mean SBP was 115 mmHg in the Hygia study, and hypotension during sleep was rare (0.3%). Still, the medications used here were calibrated by ABP, which usually would not be the case in U.S. clinical practice. Finally splitting the antihypertensive agents might reduce compliance if no other medication were taken twice a day. Thus, there are advantages to taking all the BP medications at once. I have moved at least one medication to the evening when patients note early morning hypertension, but may have to rethink my usual all-in-the-morning routine advice. Further trials that include more diverse populations would help me change my practice. ■

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ABSTRACT & COMMENTARY

Paclitaxel-Eluting Devices: Is It Time to Stop Worrying?

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: Paclitaxel-eluting devices vs. bare metal stents in peripheral arterial disease showed no significant difference in all-cause mortality, contradicting the results of a controversial meta-analysis.

SOURCE: Nordanstig J, James S, Andersson M, et al. Mortality with paclitaxel-coated devices in peripheral artery disease. *N Engl J Med* 2020;383:2538-2546.

In late 2018, the authors of a meta-analysis of trials of paclitaxel-eluting balloons and stents in peripheral arterial disease (PAD) reported a surprising finding.[1] Using pooled data from 28 randomized, controlled trials (RCTs; 4,663 total patients), researchers studied all-cause mortality at one, two, and five years. In the entire cohort, mortality at one year was not different between the paclitaxel and control arms. However, in

the subsets of studies with available two-year data (12 RCTs; 2,316 patients) and five-year data (three RCTs; 863 cases), the authors reported an increased risk of all-cause mortality among patients treated with the paclitaxel-coated devices. This news led to a flurry of further investigations and produced a chilling effect on clinical use of these tools. Part of the fallout of this resulted in the halting of ongoing research into the efficacy of these devices.

One of the affected clinical trials was SWEDEPAD, a large, multicenter, randomized study of drug-eluting technology in lower limb PAD in Sweden. Investigators explored whether paclitaxel-coated devices can affect amputation rates in patients with limb-threatening ischemia, and to better quality of life measures in claudicants. The authors began enrolling in late 2014, but temporarily stopped in December 2018 over safety concerns raised in the 2018 meta-analysis. The data and safety monitoring committee recommended the unusual step of performing an unplanned analysis of all-cause mortality with the available data. Up until the point of the temporary hiatus, 2,289 patients had been enrolled in SWEDEPAD. The authors had randomized these patients 1:1 to paclitaxel-coated or uncoated devices. Of these, the authors noted chronic limb-threatening ischemia in 1,480. The remaining 809 had intermittent claudication. The average age of included patients was 75 years, and approximately 55% were men. Twenty-three patients in the drug-coated device group and 25 patients in the uncoated device group had undergone intervention with paclitaxel devices before the index procedure. The interim analysis was carried out through March 2020, at which time the mean follow-up period was 2.5 years, with a range of approximately one to four years.

At the time of analysis, 574 patients had died. This included 293 of 1,149 patients in the paclitaxel group and 281 of 1,140 patients in the uncoated device group (HR, 1.06; 95% CI, 0.92-1.22). Similarly, there was no significant difference in mortality for paclitaxel vs. no-drug patients with critical limb ischemia (33.4% vs. 33.1%; HR, 1.04; 95% CI, 0.90-1.21) or for those with intermittent claudication (10.9% vs. 9.4%; HR, 1.18; 95% CI, 0.72-1.93). The authors concluded their analysis did not show an excess mortality hazard among PAD patients treated with paclitaxel-coated devices. Enrollment of patients in the original randomized trial has resumed.

■ COMMENTARY

A signal for increased late mortality after treatment with paclitaxel-eluting balloons and stents was initially reported in a meta-analysis in late 2018. The FDA reiterated this using patient-level data from the same trials. The authors of other meta-analyses have come to different conclusions. To date, the results of observational studies have not suggested such excess mortality. The percutaneous interventional treatment of lower extremity PAD has been hampered by a high rate of restenosis, which is responsible for significant morbidity and repeat procedures. There is no mystery as to why there has been such enthusiasm for drug-eluting devices in this space, when most trials have reported improvements in primary patency and target-lesion revascularization vs. uncoated devices.

Importantly, no clear mechanism has been identified that would explain why paclitaxel, in doses far smaller than what is used systemically to treat cancer, would lead to excess mortality at points longer than one year. Explanations have been proposed, including the seemingly quixotic theory that by decreasing restenosis, paclitaxel-eluting devices decrease contact with the medical system, resulting in poorer downstream outcomes. The 574 deaths reported in this single trial exceeds the combined number reported in 36 prior randomized trials. The completeness of the data in this trial, performed within the Swedish health system, is remarkable, with no patients lost to follow-up. For now, the SWEDEPAD data should be reassuring to those who seek to resume related clinical research. Time will tell whether individual clinicians will be adequately reassured about reincorporating paclitaxel devices in routine practice. ■

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ABSTRACT & COMMENTARY

Transitioning Patients from ECLS to Durable MCS

By Jamie L. W. Kennedy, MD, FACC

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

SYNOPSIS: A registry of patients transitioned from extracorporeal life support to durable mechanical circulatory support was used to derive a tool predicting one-year survival.

SOURCE: Saeed D, Potapov E, Loforte A, et al. Transition from temporary to durable circulatory support systems. *J Am Coll Cardiol* 2020;76:2956-2964.

Using extracorporeal life support (ECLS) to rescue patients in cardiogenic shock has become more popular. Some patients can be weaned from ECLS successfully (e.g., after revascularization or valve intervention). However, patients with severe ventricular dysfunction often cannot be weaned. Thus, treatment options narrow to durable mechanical circulatory support (MCS), heart transplant, or comfort care. There are few data to guide the selection of patients supported by ECLS for durable MCS.

Saeed et al constructed a registry of 531 patients at 11 European centers who transitioned from ECLS to durable MCS between January 2010 and August 2018. There were no centralized protocols regarding ECLS weaning, patient selection for MCS, or timing of MCS implant. Patient data were collected before MCS implant and outcomes collected afterward, including patients who subsequently underwent heart transplantation or device explant.

One-third of patients had undergone CPR before ECLS, and one-third required renal replacement therapy while supported by ECLS. Similar to prior MCS studies, 82% of patients were men, and the average age was 53 years. Cardiomyopathy was ischemic in etiology for 57% of patients, 29% had atrial fibrillation, 25% had undergone cardiac surgery, and 23% had diabetes mellitus. ECLS cannulation was peripheral in 87% of patients, and 25% also had an intra-aortic balloon pump.

Patients were supported by ECLS a median of five days before undergoing MCS implant. Cardiopulmonary bypass was used for 61% of implants. HeartWare HVAD was implanted in 372 patients, HeartMate II LVAD in 81, HeartMate 3 in 44, and small numbers of a variety of other assist devices. The total artificial heart was used for 19 patients. Of those who underwent LVAD implant, 225 also required right ventricular mechanical support, although only seven durable RVADs were implanted. Other postoperative complications included respiratory failure in 48%, renal failure requiring dialysis in 61%, liver failure in 25%, and bleeding requiring re-exploration in 36%. Survival at 30 days was 77%, one year 53%, and three years 43%. Over a median follow-up of 1.27 years, 21% underwent transplant, and 5% of VADs were explanted for recovery. Stroke was the most common long-term complication at 0.13 events per patient year. There was no comment on the severity of neurological injury.

The authors developed a model predicting survival at one year from patient characteristics available at the time of durable MCS implant, including demographics, comorbidities, lab values, pressor and inotrope doses, prior cardiac surgery, prior CPR, ECLS cannulation strategy, and duration of support. The final model incorporates age, sex, BMI > 30 kg/m^2, prior cardiac surgery, lactate level, history of atrial fibrillation, and MELD-XI (model of end-stage liver disease excluding INR) to predict one-year survival. The C index for the model was 0.72. The authors concluded that this model will be useful to help decide who should move from ECLS to durable MCS.

■ COMMENTARY

As with other registry studies, there were significant limitations. Only patients selected to undergo durable MCS implant were included. The authors did not provide information on patients deemed ineligible for implantation of durable MCS devices. I look forward to validation of the prediction tool in a second patient cohort.

The significantly worse outcomes women experienced in this registry are noteworthy. Using the risk equation, the predicted survival rate for women at one year is 7% less than men in the best of circumstances. The difference approaches 20% with additional risk factors. The data on sex differences in the MCS literature is mixed and limited, since sex-specified outcomes are not reported consistently. The HeartMate II bridge to transplant and HeartMate 3 clinical trials revealed no outcome differences between sexes.[1,2] A retrospective study of hospital administration data from seven states revealed significantly worse outcomes for women undergoing implantation of either temporary or durable

ventricular assist devices between 1994 and 2012. In-hospital mortality for women was 52.3% vs. 40.8% for men, and the difference remained significant after adjustment for other risk factors.[3] A subsequent analysis of the U.S. national inpatient sample between 2009 and 2014, which focused on durable LVADs, revealed similar inpatient mortality for men and women (13.42% and 12.85%, respectively).[4] Perhaps most relevant to the Saeed et al article, a recent analysis of the STS-INTERMACS database, which included patients transitioned from ECLS to durable MCS between 2008 and 2017, showed female sex conferred higher mortality.[5]

If women do experience worse outcomes than men, why? Is sex a surrogate for smaller blood vessels, smaller hearts, or lower muscle mass? Do hormonal differences lead to more thromboembolic complications in women? Do women present with more advanced disease that risk models do not capture adequately? In an environment of increasing financial pressures and scrutiny of outcomes, I fear this unvalidated prediction model will be used to decide candidacy for implantation of durable MCS devices to the detriment of women. ■

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CME/CE QUESTIONS

1. A study of antihypertension medication administration at bedtime vs. at awakening showed:

a. less blood pressure reduction during sleep.

b. fewer cardiovascular events.

c. more early morning hypotension.

d. reduced control of awake blood pressure.

2. A study of various methods of diagnosing high blood pressure revealed that which best predicted increases in left ventricular mass?

a. A week of home blood pressure monitoring

b. A 24-hour ambulatory blood pressure recording

c. SPRINT-style office blood pressure measurement

d. Ordinary clinic blood pressure measurement

3. An interim analysis of a large trial of paclitaxel-eluting stents vs. bare metal stents for peripheral artery disease revealed no difference in:

a. critical limb ischemia.

b. intermittent claudication.

c. in-stent restenosis.

d. all-cause mortality.

4. The most surprising factor to be a significant predictor of one-year mortality in patients transitioning from extra corporeal life support to durable mechanical support was:

a. age.

b. female sex.

c. BMI > 30 kg/m^2.

d. prior cardiac surgery.

5. In two studies of patients with paroxysmal atrial fibrillation comparing cryoablation to antiarrhythmic drug therapy, which serious adverse effect was most common with cryoablation?

a. Phrenic nerve injury

b. Pericardial tamponade

c. Stroke/TIA

d. Pacemaker requirement