RELIAS MEDIA

Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

Vol. 37, Issue 9, September 2018
ReliasMedia.com

ABSTRACT & COMMENTARY

Canagliflozin Reduces Risk of Heart Failure Hospitalizations for Diabetic Patients

By Van Selby, MD

Assistant Professor of Medicine, University of California, San Francisco Cardiology Division, Advanced Heart Failure Section

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

SYNOPSIS: In type 2 diabetes mellitus patients with a higher risk of cardiovascular disease, canagliflozin lowered the risk of cardiovascular death or heart failure hospitalization. Patients with pre-existing heart failure may experience even greater benefit.

SOURCE: Rådholm K, Figtree G, Perkovic V, et al. Canagliflozin and heart failure in type 2 diabetes mellitus: Results from the CANVAS program (Canagliflozin Cardiovascular Assessment Study). *Circulation* 2018 Mar 11. pii: CIRCULATIONAHA.118.034222. doi: 10.1161/CIRCULATIONAHA.118.034222. [Epub ahead of print].

There is growing evidence of an association between sodium-glucose cotransporter 2 (SGLT2) inhibitors and improved cardiovascular outcomes in diabetic patients. These benefits may be even more pronounced for patients with pre-existing cardiovascular conditions such as heart failure (HF) in whom the risk of adverse cardiovascular events is particularly high. However, few investigators have compared the relationship between SGLT2 inhibitors and cardiovascular events in patients with pre-existing HF vs. those without HF.

The authors of the Canagliflozin Cardiovascular Assessment Study (CANVAS) randomized 10,142 patients with type 2 diabetes mellitus (T2DM) to the SGLT2 inhibitor canagliflozin vs. placebo. During a mean follow-up of 188 weeks, canagliflozin was associated with reduced risk of HF hospitalization. In this secondary analysis, Rådholm et al evaluated the association between canagliflozin and the combined outcome of cardiovascular death or hospitalized HF. Also, they compared the effects of canagliflozin in the 14.4% of patients with pre-existing HF to those without HF.

In the overall population, canagliflozin was associated with reduced risk of cardiovascular death or hospitalized HF (hazard ratio [HR], 0.78; 95%

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 Jill Drachenberg, and Editorial Group Manager Terrey L. Hatcher report no financial relationships relevant to this field of study.

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

Clinical Cardiology Alert,
ISSN 0741-4218, is published 12 times annually by Relias LLC
111 Corning Road, Suite 250
Cary, NC 27518-9238

GST Registration Number: R128870672. Periodicals Postage Paid at Cary, NC, and additional mailing offices.

POSTMASTER: Send all address changes to *Clinical Cardiology Alert*, Relias LLC, 111 Corning Road, Suite 250, Cary, NC 27518-9238.

SUBSCRIBER INFORMATION
(800) 688-2421
ReliasMediaSupport@Relias.com
ReliasMedia.com

Subscription Prices
United States
Print: 1 year with ***free*** *AMA PRA Category 1 Credits™*: $349
Add $19.99 for shipping & handling.
Online only, single user: with ***free*** *AMA PRA Category 1 Credits™*: $299

Back issues: $42. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Canada: Add 7% GST and $30 shipping.
Elsewhere: Add $30 shipping.

ACCREDITATION
Relias LLC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Relias LLC designates this enduring material for a maximum of 2.25 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only credit commensurate with the extent of their participation in the activity.

Relias LLC is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Contact hours [2.25] will be awarded to participants who meet the criteria for successful completion. California Board of Registered Nursing, Provider CEP#13791.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.25 MOC Medical Knowledge points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

This activity is intended for the cardiologist. It is in effect for 36 months from the date of the publication.

confidence interval [CI], 0.67-0.91). The observed benefit was even greater among patients with a history of HF (HR, 0.61; 95% CI, 0.46-0.8; *P* = 0.021 for the comparison to those without HF). Canagliflozin is associated with increased risks of amputation, fracture, and volume depletion. However, this risk was not higher in patients with HF compared to those without. The authors concluded that among patients with T2DM and elevated risk of cardiovascular disease, canagliflozin reduces the risk of cardiovascular death or HF hospitalization. Further, the benefits may be greatest in patients with baseline HF.

■ COMMENTARY

T2DM and HF coexist frequently. No previous class of glucose-lowering therapy has been shown to reduce the risk of HF hospitalization in this population. The EMPA-REG OUTCOME trial was the first to show a reduction in HF hospitalization with an SGLT2 inhibitor (empagliflozin). The magnitude of the observed benefit was surprising to many observers, but data from CANVAS and a recent large retrospective study have added support for the HF-related benefits of SGLT2 inhibitors.

Using data from a large, rigorous, international, clinical trial, Rådholm et al have shown that canagliflozin substantially lowers the risk of a meaningful outcome (cardiovascular death or hospitalized HF). Furthermore, patients with pre-existing HF may derive even greater benefit. The observed HR of 0.61 among patients with pre-existing HF is comparable to long-standing, guideline-recommended therapies for chronic HF. SGLT2 inhibitors produce many cardiovascular effects. The exact mechanism by which they improve outcomes is not understood fully. In CANVAS, the benefits of canagliflozin were observed early, suggesting a hemodynamic or volume-related effect. SGLT2 inhibitors induce natriuresis and osmotic diuresis, lower blood pressure, and reduce arterial stiffness. Longer-term, SGLT2 inhibitors produce anti-atherosclerotic effects and affect cardiac metabolism favorably.

It is important to note that adverse events were no more frequent in HF patients compared to the general population. With everything considered, the growing evidence supporting HF-related benefits of SGLT2 inhibitors make this a compelling therapy to offer patients with HF and diabetes. There was no left ventricular ejection fraction criteria for defining the HF population within CANVAS. Therefore, it is reasonable to consider SGLT2 inhibitors in patients with HF and preserved ejection fraction (in whom diabetes is common and few effective therapies exist) in addition to those with systolic HF.

The story of SGLT2 inhibitors for reducing cardiovascular outcomes still is in its early stages. The Rådholm et al study was a secondary analysis; therefore, it must be interpreted with caution. With only 14% of the total study population in the HF group, we cannot draw firm conclusions regarding the increased benefit among HF patients. There are multiple ongoing trials that will help us understand the mechanism by which these agents exert their benefit and to identify the patients who will benefit most. There are even trials underway evaluating the benefit of SGLT2 inhibitors in patients with HF, but no diabetes. For now, these agents should be strongly considered in diabetic patients with HF (or other cardiovascular disease). Cardiovascular practitioners who are not comfortable prescribing drugs for treatment of diabetes can suggest these agents to their patients' primary care providers or endocrinologists, highlighting the cardiovascular benefits. ■

ABSTRACT & COMMENTARY

Home-based Detection of Undiagnosed Atrial Fibrillation

By Joshua D. Moss, MD

Associate Professor of Clinical Medicine, Cardiac Electrophysiology, Division of Cardiology, University of California, San Francisco

Dr. Moss reports he is a consultant for Biosense Webster and Abbott.

SYNOPSIS: In patients with risk factors for atrial fibrillation, screening with a self-applied wearable ECG patch resulted in significantly increased rates of new atrial fibrillation diagnoses within four months, along with greater use of anticoagulants and healthcare resources.

SOURCE: Steinhubl SR, Waalen J, Edwards AM, et al. Effect of a home-based wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation: The mSToPS randomized clinical trial. *JAMA* 2018;320:146-155.

Current screening for atrial fibrillation (AF) in high-risk populations generally is limited to auscultation, pulse palpation, and "spot" 12-lead ECGs during routine visits. Steinhubl et al sought to study the effect of a more aggressive but practical method of screening, using a self-applied, two-week, continuous ECG monitoring patch at home during routine activities.

The study population consisted of participants in a single large national health insurance plan, with eligible patients chosen from more than 1 million candidates based on risk factors for AF: age ≥ 75 years of age, or men > 55 years of age, or women > 65 years of age with one or more comorbidities (including prior stroke, heart failure, or the combination of diabetes and hypertension, among others). Patients with any current or prior diagnosis of atrial arrhythmia who already were on anticoagulation therapy or who had an implantable pacemaker or defibrillator were excluded. More than 100,000 eligible patients were contacted, with most eventual enrollees contacted by email. Individuals who chose to enroll were consented remotely. A total of 2,659 patients were randomized: 1,366 received an ECG patch and instructions for self-application within two weeks (immediate group), and 1,293 received their patches four months later (delayed group). Additionally, 5,318 matched observational controls who were eligible for the study but not contacted for participation in the randomized trial were identified, two for each patient randomized.

The primary endpoint in the intention-to-treat analysis of randomized patients was incidence of newly diagnosed AF (defined as ≥ 30 seconds of AF, flutter detected by device, or a new clinical diagnosis recorded in claims data at the end of the initial four-month monitoring period). In the immediate monitoring group, 908 of 1,366 participants wore an ECG patch, and incidence of new AF was 3.9%. In the delayed monitoring group, incidence of new AF was 0.9% in the first four months (before those participants received their patch). In the observational study with one year follow-up, new AF was detected at a rate of 6.7 per 100 person-years in the actively monitored cohort (the two arms of the randomized trial) vs. 2.6 per 100 person-years in the matched observational controls.

Patients who were actively monitored were more likely to start both anticoagulation and antiarrhythmic medications. Further, there were more office visits as well as cardioversion and ablation procedures for these patients. However, the actively monitored group experienced a slightly lower incidence of hospitalizations or ED visits.

■ COMMENTARY

Improvements in digital technology for cardiac rhythm monitoring and AF diagnosis have made wearable devices that patients can use to send data to their physicians, or even self-diagnose, more accessible. Data from the mSToPS trial corroborate the work of other investigators who have evaluated more frequent or continuous monitoring and found a higher incidence of AF than would have been realized otherwise, including the REHEARSE-AF and CRYSTAL-AF studies. Uniquely, patients in the mSToPS trial were approached mostly via email, consented remotely, and applied and removed their own monitoring devices. In an ongoing trial, researchers are enrolling patients to use Apple Watch-based photoplethysmography to monitor for AF.

The increased rate of AF detection is not surprising. However, the absolute difference in detection rates between those monitored (for a median total monitoring time of about 25 days over a four-month period) and those not monitored still is impressive

(considering 458 of 1,366 patients randomized to immediate monitoring never wore a patch). Also unsurprising is the resultant increase in healthcare resource use in the actively monitored cohort, with an increase in office visits, more prescriptions for anticoagulation therapy, and additional cardioversions and ablation procedures. The results may not be completely generalizable to a broader population. Patients who were invited to participate and enrolled were more likely to have been invited by email rather than direct mail, were slightly younger, more often male, and exhibited less hypertension and diabetes but more obesity and sleep apnea than those who declined. Additionally, patients who participated in randomization but never wore a monitor had some different characteristics than those who wore the patch.

The larger question raised is whether more aggressive screening for AF in asymptomatic patients will translate to real long-term health benefits, and at what cost. The primary goal of detection for many patients would be stroke prevention via anticoagulation, but such a benefit has not yet been demonstrated. Additionally, more anticoagulation inevitably will lead to more bleeding events. The recently published NAVIGATE ESUS study ended early because patients empirically anticoagulated after a presumed embolic stroke without a clear source experienced more bleeding events and no apparent change in recurrent stroke risk at 11 months follow-up.

There are secondary benefits to earlier AF detection, such as a higher likelihood of aggressive risk factor modification, but also other ill effects, such as anxiety for some and complications of therapy for others. Whether patients should screen and diagnose themselves with AF is the subject of active debate in the cardiology and EP communities. However, one thing is certain: Our methods for educating patients about AF and all the potential benefits and risks of early diagnosis and treatment must evolve at the same pace as the technology for detection. ■

ABSTRACT & COMMENTARY

Risk of Infective Endocarditis Revisited

By Michael H. Crawford, MD, Editor

SYNOPSIS: In a comparison of patients with infective endocarditis (IE) and either bicuspid aortic valve (BAV) or mitral valve prolapse (MVP) vs. other IE patients at high or low to moderate risk of IE, BAV and MVP patients were more likely to exhibit viridans streptococci group infections of suspected odontogenic origin and cardiac complications at similar rates to high-risk patients.

SOURCES: Zegri-Reiriz I, de Alarcón A, Muñoz P, et al. Infective endocarditis in patients with bicuspid aortic valve or mitral valve prolapse. *J Am Coll Cardiol* 2018;71:2731-2740.

Chambers JB. Antibiotic prophylaxis against infective endocarditis: Widening the net? *J Am Coll Cardiol* 2018;71:2741-2743.

There are growing data regarding an increase in infective endocarditis (IE) in those at moderate risk who are excluded from antibiotic prophylaxis (AP) prior to nonsterile procedures. Zegri-Reiriz et al evaluated patients with bicuspid aortic valve (BAV) and mitral valve prolapse (MVP) with IE to learn more about the potential use of AP in patients with these intermediate risk conditions.

Patients with IE from 31 Spanish hospitals were entered into a registry from 2008-2016 (n = 3,524; a total of 316 patients with isolated device-related IE eventually were excluded). After exclusion, 3,208 patients remained, of whom 1,226 were high risk and 1,982 were low to moderate risk. Among the 1,982 low to moderate risk patients remaining, Zegri-Reiriz et al considered an additional 143 patients from this group separately (n = 54 BAV patients and n = 89 MVP patients). Major adverse IE events were heart failure, embolism, persistent bacteremia, and intracardiac complications. The likely portal of bacteria entry was identified prospectively. The main analysis was a comparison of the clinical features of BAV and MVP IE patients to those at high risk and low to intermediate risk of IE. In patients with BAV or MVP, the most common organism detected was viridans streptococci group, which was about three times more common than that observed in the high-risk and remaining low to intermediate risk groups (39% vs. 13%; $P < 0.01$).

An odontological portal of entry also was more common in the BAV/MVP group than in the remaining patients (17% vs. 6%; $P < 0.01$). By contrast, staphylococci were the most frequently detected organisms in the high-risk and the remainder of the low to intermediate risk groups ($P < 0.01$) and was more likely nosocomial in these groups. BAV and MVP patients demonstrated similar rates of intracardiac complications as the high-risk patients, both of which were higher than in the low to intermediate risk patients (50% BAV/MVP and 47% high risk vs. 31% low to moderate risk; $P < 0.01$). The authors concluded that IE patients with BAV or MVP have more viridans group infections from odontologic sources than other

IE patients and a clinical profile similar to high-risk IE patients. These data suggest that these two lesions should be considered high risk for AP consideration.

■ COMMENTARY

As more data accumulate, the controversy over the 2007 antibiotic prophylaxis guidelines to prevent IE intensifies. A recently published study from the United Kingdom showed that during a five-year follow-up, many patients considered at moderate risk for IE developed IE at a similar frequency or higher than those considered at high risk by the guidelines.[1] Those authors concluded that the guidelines should be changed to recommend IE prophylaxis for patients with electrophysiology devices, hypertrophic cardiomyopathy, congenital valve disease, and nonrheumatic valve disease. As this U.K. study was based on administrative data, few clinical details were available. BAV and MVP patients were included in the congenital and nonrheumatic valve disease categories, respectively, but there were no specific details on these common conditions. Thus, the Zegri-Reiriz et al study of BAV and MVP patients is of interest.

The Zegri-Reiriz et al study is the largest series to date regarding IE in BAV and MVP patients. Participants were relatively young, male, and had few comorbidities. However, these participants exhibited cardiovascular complications at rates similar to patients with high-risk conditions (BAV, 50%; MVP, 47%; high risk, 45%) and significantly higher than low to moderate risk IE patients. Also, the MVP/BAV patients had high rates of viridans streptococcal group IE and of suspected odontologic origin. In addition, the number of patients sent to surgery was high in BAV patients (68%). MVP patients were sent to surgery at rates similar to the low to moderate risk groups (39%), but 66% left the hospital with severe mitral regurgitation. Given the equivalent or worse outcomes of IE in BAV and MVP patients, the authors believed that this indirectly supports including these patients in the AP recommendations.

The major strengths of this study were the large number of patients and complete microbiologic data. There were weaknesses, though, including the lack of AP data. Since Zegri-Reiriz et al recruited patients after the 2007 guidelines were released, presumably the high-risk patients underwent AP and the low or moderate risk patients did not. Also, odontologic origin was not divided into subcategories such as dental procedures and poor dentition. Additionally, this was a study of hospitalized patients with IE. We do not know what the denominator is; thus, IE incidence or prevalence cannot be determined. However, we know from other studies that IE in BAV patients is 30 times higher than the general population, and MVP is the most common underlying condition for IE in developed countries.

If the AP guidelines are ever revised, perhaps patients with BAV and MVP (especially those with moderate or more valvular regurgitation) should be included in the high-risk group and considered candidates for AP. ■

REFERENCE

1. Thornhill MH, Jones S, Prendergast B, et al. Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur Heart J* 2018;39:586-595.

ABSTRACT & COMMENTARY

Substance Abuse and Myocardial Infarction

By Michael H. Crawford, MD, Editor

SYNOPSIS: Among patients ≤ 50 years of age with first myocardial infarctions, use of cocaine or marijuana increased the likelihood of an ST-segment elevation myocardial infarction and the subsequent risk of all-cause and cardiovascular mortality.

SOURCES: DeFilippis EM, Singh A, Divakaran S, et al. Cocaine and marijuana use among young adults with myocardial infection. *J Am Coll Cardiol* 2018:71:2540-2551.

Lee JD, Schatz D, Hochman J. Cannabis and heart disease: Forward into the great unknown? *J Am Coll Cardiol* 2018:71:2552-2554.

As more states legalize recreational marijuana, its use is on the rise, yet we know little about its health effects. Cocaine is well recognized as a risk factor for myocardial infarction (MI). DeFilippis et al studied the prevalence of substance abuse among patients ≤ 50 years of age with their first MI and its relation to outcomes. Investigators used chart review or toxicology screen on MI admission to determine if patients used cocaine or marijuana prior to MI. Patients who used both substances were put in the cocaine group for subanalyses. Opioid use was discovered but was not analyzed because there were insufficient data to distinguish prescription use from nonprescription use. Methamphetamine and other substances also were detected but constituted too few cases for analysis. The primary outcomes of interest were all-cause and cardiovascular mortality. Among 2,097 young MI patients, 11% used

cocaine or marijuana, one-third of whom used both substances. ST-segment elevation myocardial infarctions (STEMIs) were more common in the substance abuse patients (65% vs. 52%; $P < 0.001$). Diabetes and hyperlipidemia were less common in substance abuse patients (15% vs. 20%; $P = 0.05$ and 46% vs. 61%; $P < 0.001$, respectively). Tobacco use was more common in substance abuse patients (70% vs. 49%; $P < 0.001$). Substance abuse was associated with a higher cardiovascular mortality (hazard ratio [HR], 2.22; 95% confidence interval [CI], 1.27-3.70; $P = 0.005$) and all-cause mortality (HR, 1.99; 95% CI, 1.35-2.97; $P = 0.001$) after adjustment for baseline covariates over a mean follow-up of 11 years. The authors concluded these findings support the current guidelines, which recommend screening young adults with their first MI for substance use and counseling users about the importance of abstinence to prevent future events.

■ COMMENTARY

This analysis exhibits that despite a generally lower incidence of traditional risk factors, those who used substances had a higher incidence of STEMIs than nonusers. This generates the hypothesis that substance abuse is a risk factor for early MI. Also, MIs in the substance abuse group were more likely to be discovered because of out-of-hospital cardiac arrest, which was driven by the marijuana users. Cocaine has long been recognized as a trigger for acute MI, probably because cocaine use increases heart rate, blood pressure, and coronary vasoconstriction. However, we know comparatively little about the effects of marijuana. Marijuana can be similar to tobacco smoking in that one inhales burning vegetable matter in both instances. Still, there probably are other effects that could be attributed to chemicals in marijuana, which would be more relevant to vaporized cannabis oil and edibles. There is evidence that tetrahydrocannabinol increases plasma catecholamines, impairs vascular endothelial function, and decreases myocardial contractility. Thus, marijuana may not be the benign recreational drug that it is touted to be.

The major limitation to the DeFilippis et al study was the potential effects of multiple confounders. The investigators adjusted the HR calculations for other known risk factors and showed about a two-fold increase in all-cause and cardiovascular mortality. However, cocaine and marijuana users also could smoke tobacco, drink alcohol, or take opioids. Also, substance users may be more likely to participate in other risky behaviors and have a higher prevalence of hepatitis C, HIV, and depression. These factors could affect mortality post-MI and were not assessed in this study. Also, the prevalence of substance abuse in the risk population (age < 50 years) could not be ascertained. Thus, the relative risk of substance abuse causing an MI is unknown. What is clear is that substance abuse patients are at higher risk for adverse events post-MI. When one encounters a patient with an MI who uses substances, it would be reasonable to counsel him or her that quitting would be in their best interest. ■

ABSTRACT & COMMENTARY

Instantaneous Wave-free Ratio vs. Fractional Flow Reserve: Defining Low-risk Population for Deferral of PCI

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: Researchers recently found that deferral of percutaneous coronary intervention based on fractional flow reserve and instantaneous wave-free ratio is equally safe, with a low one-year major adverse cardiac event rate of approximately 4%.

SOURCE: Escaned J, Ryan N, Mejía-Rentería H, et al. Safety of the deferral of coronary revascularization on the basis of instantaneous wave-free ratio and fractional flow reserve measurements in stable coronary artery disease and acute coronary syndromes. *JACC Cardiovasc Interv* 2018;11:1437-1449.

In the cardiac catheterization laboratory, clinicians recognize that visual estimates of lesion severity are limited, especially in cases of intermediate coronary stenoses. Physiologic measures have proven superior, with fractional flow reserve (FFR) taking the place as the default standard. Clinicians should recognize that the superiority of FFR-guided intervention (compared to guidance by angiography alone) demonstrated in investigations such as the FAME trial was based on the ability of the physiologic test to determine which lesions on which *not* to intervene. In general, the use of FFR results in fewer interventions compared to decision-making by angiography. The strategy of using a high FFR value to support conservative management of a lesion was based primarily on the outcomes of the 2001 DEFER trial, whose authors randomized 325 patients with FFR values > 0.75 to medical therapy or to percutaneous coronary intervention (PCI). DEFER was relatively small, included only patients with stable angina, and was performed in a different era of coronary intervention.

The authors of the Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation (DEFINE-FLAIR) and iFR Versus FFR in Patients With Stable Angina Pectoris or Acute Coronary Syndrome (iFR-SWEDEHEART) randomized, clinical trials compared iFR to FFR in clinical decision-making for patients with coronary artery disease and intermediate-severity lesions. With instantaneous wave-free ratio (iFR), clinicians use a coronary pressure wire, similar to that used for FFR, to interrogate stenoses with a hyperemia-free (without adenosine) algorithm. Escaned et al used the combined data set from these two trials (4,486 patients total) to examine patients who deferred intervention based on the results of their invasive physiologic testing.

In the combined groups, 2,130 patients deferred PCI based on FFR values > 0.80 or iFR values > 0.89. Deferrals accounted for 50% of the iFR group and 45% of the FFR group. Of these, 1,675 patients presented with stable angina, while the remaining 440 patients had presented with acute coronary syndrome (ACS). Fewer lesions were deferred among patients with ACS compared to those presenting with stable angina (36% vs. 50%; $P < 0.001$).

Among deferred patients, major adverse cardiac events (MACE) at one year occurred in 46 of 1,117 patients in the iFR group and in 41 of 1,013 patients in the FFR group. Urgent revascularization accounted for most MACE events, occurring in approximately 3% of each group. Presentation with ACS was associated with a higher MACE rate compared to stable angina in deferred patients (5.91% vs. 3.64% in ACS and stable angina, respectively; hazard ratio, 0.61; 95% confidence interval, 0.38-0.99; $P = 0.04$).

The authors concluded that both iFR and FFR led to safe deferral of revascularization, with a low one-year MACE rate. Patients presenting with ACS experienced a higher event rate compared to those with stable angina.

■ COMMENTARY

It is a common misperception that the primary role of invasive physiologic tests such as iFR and FFR is to determine which lesions should be intervened on. The more important role of this technology is to demonstrate which lesions are not hemodynamically significant and should be managed medically.

The Escaned et al study included data from two large randomized studies, was performed with

up-to-date techniques and devices, and featured highly complete data collection. The historical DEFER trial, on which much of current practice is based, included only 92 patients randomized to medical management. Escaned et al included more than 2,000 such patients. Understanding the expected hazards for patients going forward can be important. A 4% MACE rate for patients with a negative FFR or iFR is a good fact to know. Even for the ACS population, for which MACE was closer to 6% in the Escaned et al study, these data are reassuring, and support the concept of invasive physiologic testing to guide deferral of intervention. ■

CME/CE QUESTIONS

1. **Acute myocardial patients who use cocaine and marijuana have a higher incidence of:**
   a. all-cause mortality.
   b. cardiovascular mortality.
   c. ST-segment elevation myocardial infarction.
   d. All of the above

2. **Patients with infective endocarditis with bicuspid aortic valve or mitral valve prolapse compared to those with high-risk underlying conditions exhibit:**
   a. fewer viridans streptococcal group infections.
   b. more staphylococcal infections.
   c. similar rates of cardiac complications.
   d. less suspicion for an odontologic origin.

3. **If a coronary artery intervention is deferred based on physiologic testing in the catheterization laboratory, the one-year cardiovascular event rate is about:**
   a. 2%.
   b. 4%.
   c. 8%.
   d. 10%.

4. **A large study of a new self-applied patch for atrial fibrillation detection compared to controls showed:**
   a. lower stroke rates.
   b. less drug therapy.
   c. more atrial fibrillation detected.
   d. fewer office visits.

5. **A secondary analysis of a recent trial of canagliflozin vs. placebo in diabetics showed reduced rates of:**
   a. cardiovascular death and hospitalization for heart failure.
   b. amputation.
   c. fractures.
   d. volume depletion.

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss the most current information related to cardiac illness and the treatment of cardiac disease;
- explain the advantages and disadvantages, as well as possible complications, of interventions to treat cardiac illness;
- discuss the advantages, disadvantages, and cost-effectiveness of new and traditional diagnostic tests in the treatment of cardiac illness; and
- discuss current data regarding outpatient care of cardiac patients.