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ABSTRACT & COMMENTARY

Alcohol Consumption and Atrial Fibrillation

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of the UK Biobank database revealed low levels of alcohol consumption, especially with wine and spirits, is associated with the lowest incidence of atrial fibrillation.

SOURCE: Tu SJ, Gallagher C, Elliott AD, et al. Risk thresholds for total and beverage-specific alcohol consumption and incident atrial fibrillation. *JACC Clin Electrophysiol* 2021 Jul 19;S2405-500X(21)00524-7. doi: 10.1016/j.jacep.2021.05.013. [Online ahead of print].

Binge drinking alcohol can precipitate atrial fibrillation (AF), but little is known about low to moderate consumption, the importance of the beverage type, or sex of the drinker. Tu et al analyzed the UK Biobank database to provide information on these uncertainties.

The UK Biobank contains information about more than 500,000 subjects age 40-69 years who were enrolled between 2006 and 2010. Alcohol consumption data were obtained from questionnaires and corrected for variable consumption over time in the 12% of the population who provided repeat questionnaires during the study period. Investigators excluded subjects with a history of AF and those who had quit drinking alcohol to reduce the effect of reverse causality. Alcohol consumption was measured as standard U.K. drinks/week (standard U.K. drink is 8 g of alcohol; the standard U.S. drink is 14 g of alcohol). Binge drinking was defined as ≥ 6 drinks per day for women and ≥ 8 drinks/day for men. Frequent drinking was defined as ≥ 3 days/week. The primary outcome was incident AF (atrial flutter was included). Various covariates or comorbidities detected on the initial questionnaire or hospital records were used to adjust the data. Sensitivity analyses were conducted for those who developed AF in the first two years by excluding those with known heart disease, including ex-drinkers, and the consumption of other beverages. Exploratory analyses were conducted on the effect of sex, binge drinking, and frequent drinking.

The final population included 403,281 subjects (mean age = 58 years), of whom 52% were women and 94% were white. Median alcohol consumption was eight standard U.K. drinks/week, and 5.5% did not drink alcoholic beverages. After dividing alcohol consumption into quartiles, the higher the number of drinks, the lower the percentage of women and the higher the percentage of smokers. The highest quartile (> 28 drinks/week) included more men and more comorbidities.

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Over the 11-year follow-up, 21,312 people developed AF over 4.5 million person-years. The primary outcome of incident AF exhibited a J-shaped curve, with a nadir at five drinks/week. The lowest quartile (one to seven drinks/week) exhibited a lower risk of AF than that observed in non-drinkers (HR, 0.91; 95% CI, 0.86-0.96).

Higher consumption was associated with increasing risk of AF, but it varied with the type of alcoholic beverage. The lowest risk in beer drinkers was at zero drinks/week, whereas in red wine, white wine, and spirits drinkers, the lowest risk was at less than 10 drinks/week, 8 drinks/week, and four drinks/week, respectively, with a nadir at five drinks/week, four drinks/week, and one drink/week, respectively. In the low consumption quartile (one to seven drinks/week), of 70,683 subjects, 18,550 drank beer, 28,220 drank red wine, and 16,934 drank white wine. Compared to beer drinkers, wine drinkers were at lower risk for AF (HR, 0.83; 95% CI, 0.75-0.92 for red wine and HR, 0.89; 95% CI, 0.79-1.0 for white wine).

Sensitivity analyses did not alter the results. Higher risk was observed in binge drinkers and frequent drinkers. Analysis by sex only showed an increased risk with women who drank spirits. The authors concluded low levels of alcohol consumption were associated with the lowest AF risk, and low levels of wine and spirits may not be associated with increased AF risk. Any consumption of beer may increase risk.

■ COMMENTARY

When considering heart disease in general, a J-shaped curve relationship between alcohol consumption and risk has been demonstrated and an upper limit of alcohol consumption to realize this heart disease risk reduction has been proposed (14 drinks/week). Regarding AF specifically, there has been controversy with some studies showing a linear relationship between alcohol consumption and the risk of incident AF.[1] This UK Biobank study was designed to address this controversy and examine the importance of the type of beverage and sex on the risk of AF. The authors confirmed previous data showing binge drinking is associated with AF. However, at the low to moderate drinking level, there is a J-shaped curve, with low levels exhibiting lower risk, but at an alcohol consumption level lower than for heart disease protection generally (< 7 drinks/week vs. < 14 drinks/week). In addition, in their exploratory analyses, Tu et al demonstrated that at low levels of wine or spirit consumption, there was almost no increased risk of AF, but any beer consumption raised the risk. Since the beverage type analyses were not adjusted for multiple testing, these results should be considered exploratory. Finally, these results were not related to sex.

The strengths of this study include the large database with beverage-specific information. Also, the authors excluded ex-drinkers and those with a history of AF to mitigate any reverse causality. In addition, Tu et al corrected for regression dilution bias by adjusting for measurement error and long-term variability in the data.

There also were some weaknesses. Although the data were collected prospectively, it was analyzed retrospectively and there could have been residual confounding and reverse causality despite the measures taken to reduce these biases. For example, beer and spirit drinkers were more morbid than wine drinkers. Self-reporting is likely to underestimate alcohol consumption, although adjustment based on the subgroup that was questioned a second time should have helped abrogate this concern.

There were no data on the type of AF (i.e., paroxysmal, persistent, permanent) and no outpatient data were captured. All the disease-specific data were based on hospital ICD codes. The population studied was almost all white, and the UK Biobank may suffer from the healthy volunteer bias. Finally, there were no data on prevalent AF since patients with known AF were excluded.

Considering the size and strengths of this study, it would seem that advising against all alcohol consumption to prevent AF probably is not warranted. Given the other potential heart disease preventive

effects of alcohol, low to moderate consumption could be safe and might be beneficial. However, the data are not strong enough to recommend non-drinkers start drinking. ■

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ABSTRACT & COMMENTARY

Coffee Consumption and Tachyarrhythmias

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis demonstrated an inverse association of coffee consumption and cardiac arrhythmias, which was not altered by genetic variations in caffeine metabolism, age, or sex.

SOURCE: Kim EJ, Hoffmann TJ, Nah G, et al. Coffee consumption and incident tachyarrhythmias: Reported behavior, mendelian randomization, and their interactions. *JAMA Intern Med* 2021; Jul 19. doi: 10.1001/jamainternmed.2021.3616. [Online ahead of print].

There are conflicting data about the potential risks and benefits of coffee consumption. Kim et al studied the association of coffee intake with the risk of tachyarrhythmias in the UK Biobank, a population of more than 500,000 subjects recruited between 2006 and 2010.

Coffee consumption was measured from enrollment questionnaires and grouped into eight categories based on cups consumed per day (< 1 cup, one cup, two cups, three cups, four cups, five cups, and six or more cups). The primary outcome was incident tachyarrhythmias during follow up (2006-2018). Those with previous diagnoses of tachyarrhythmia before enrollment were excluded from the primary analysis. Potential mediators and confounders were obtained from the entry questionnaires or subsequent in- or outpatient diagnoses (ICD codes). Genetic analyses for variants in the major metabolic pathway for caffeine were used to construct a polygenic score wherein a higher score reflected slower caffeine metabolism.

The authors performed a Mendelian randomization analysis on only those who self-identified as white British and were not closely related. Kim et al performed sensitivity analyses for such variables as decaffeinated coffee consumption only, sex, and age. Smoking status was used as a positive control. They excluded those who were pregnant on enrollment, those who dropped out, and those for whom data were missing

UK Biobank participants consumed a median of two cups per day; 22% did not consume coffee. After exclusion criteria were applied, 386,258 subjects were included in the primary analyses. Mean age was 56 years, 52% were women, and almost all were white. During the mean follow-up of 4.5 years, 12,881 had atrial fibrillation (AF), 1,920 had other supraventricular tachyarrhythmias (SVT), 909 had ventricular tachycardias (VT), 97 had premature atrial complexes (PAC), 632 had premature ventricular complexes, and 610 had unspecified arrhythmias. After adjustment for potential mediators and confounders, each one-cup increase in coffee consumption was associated with a 3% lower risk of an incident arrhythmia (HR, 0.97; 95% CI, 0.96-0.98; $P < 0.001$), which was of a similar magnitude and statistical significance when considering AF and SVT individually. Although point estimates for VT and PAC were similar, they did not achieve statistical significance.

The positive control of smoking showed a higher incidence of arrhythmias (HR, 1.09; 95% CI, 0.03-1.15; $P = 0.002$). Those with genetic variants associated with slower caffeine metabolism consumed less coffee but did not exhibit any association with arrhythmia risk. There were no differences in these results in the Mendelian randomization sensitivity analyses. Also, the authors did not observe any interactions by age or sex. The authors concluded the habitual consumption of greater amounts of coffee was associated with progressively lower rates of arrhythmias and was not altered by genetic variants in caffeine metabolism.

■ COMMENTARY

Since caffeine is a stimulant that increases serum catecholamine levels and promotes wakefulness, it could cause or exacerbate cardiac arrhythmias. I have advised patients with arrhythmias to cut back or eliminate caffeine intake. Coffee is the main source of caffeine for most people, so this meant reducing or eliminating coffee intake or switching to decaffeinated coffee. However, many have touted the antioxidant and anti-inflammatory properties of coffee. Also, recent studies have either not supported an arrhythmogenic role for coffee or actually have shown a decrease in arrhythmias.[1] This study supports the latter conclusion. However,

observational research cannot explore the reason people drink coffee and the amount they drink. Such decisions may be related to unmeasured confounders, which always makes this type of research problematic compared to a randomized, controlled trial.

There were several strengths of the Kim et al study. It was a large, prospective, community-based study of unprecedented sample size. The results were adjusted for a comprehensive array of confounders. A Mendelian randomization sub-study strongly supported the results by showing a genetic propensity to coffee consumption also was not related to arrhythmias. Also, consideration of the variants in the genes that regulate caffeine metabolism did not support an arrhythmogenic effect of coffee.

In addition to its observational nature, there were other limitations to this work, with the potential for unmeasured confounders. Coffee consumption was self-reported at enrollment; investigators assumed what was reported did not change over the follow-up period. There was no information on the type of coffee (i.e., drip, espresso) or the intake of other caffeinated beverages — except for tea, whose consumption averaged about three cups a day in the study population. Also, the diagnosis of arrhythmias was based on ICD codes, which can be inaccurate. In addition, the follow-up period was relatively short for a group whose mean age was in the mid-50s. AF in particular is more prevalent in older individuals.

The authors believe advising against coffee consumption or reducing its intake to reduce the risk of arrhythmias is not warranted. Considering there is no compelling research to refute this advice, I am inclined to agree with them. However, they excluded patients with known arrhythmias at enrollment, so an exacerbating role of caffeine intake in these patients has not been disproven. ■

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ABSTRACT & COMMENTARY

The Difficulty of Showing Benefit of Cerebral Protection Devices During TAVR

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: In this trial of cerebral protection in transcatheter aortic valve replacement, the TriGUARD device was safe vs. historical controls, but failed to meet its primary efficacy endpoint.

SOURCE: Lansky AJ, Makkar R, Nazif T, et al. A randomized evaluation of the TriGuard™ HDH cerebral embolic protection device to Reduce the Impact of Cerebral Embolic LEsions after TransCatheter Aortic Valve ImplanTation: The REFLECT I trial. *Eur Heart J* 2021;42:2670-2679.

Despite significant advances over the past decade, stroke remains the most common ischemic complication of transcatheter aortic valve replacement (TAVR) and certainly is one of the most feared.[1] Imaging studies have demonstrated an overwhelming majority of TAVR patients develop new ischemic lesions in the brain after the procedure.[2] Clinically evident stoke occurs more selectively and unpredictably in many cases, affecting somewhere in the range of 2% to 6% of patients.[1] These strokes are thought to result from embolization of particulates from the calcified valve itself and from manipulation of atheromatous disease in the ascending aorta and aortic arch. The concept of cerebral embolic protection (CEP) devices that can capture such debris before it reaches the brain has considerable intuitive appeal. To date, a single device, the Sentinel, has received FDA approval.[3] This device is deployed from the right radial artery and places filters in the brachiocephalic trunk and left carotid artery. A competing device that has thus far only been available in Europe, TriGUARD, is deployed from the femoral approach and could protect each arch vessel. The REFLECT 1 trial was designed to prospectively evaluate the efficacy of this device in TAVR patients.

To this end, the authors recruited patients to be randomized 2:1 to the TriGUARD device or to standard care without CEP. The trial included a composite safety endpoint (all-cause death and stroke), as well as outcomes including bleeding, acute kidney injury, vascular complications, coronary obstruction, and major valve dysfunction. The

primary endpoint was a hierarchical composite of all-cause mortality or any stroke at 30 days, NIH Stroke Scale score worsening from baseline to two to five days after procedure or MoCA cognitive function test worsening at 30 days, and total volume of cerebral ischemic lesions detected by MRI performed two to five days after procedure.

Between June 2016 and July 2017, 258 patients were enrolled from 20 centers in the United States and six in Europe. A total of 54 of these patients were in a predesigned roll-in phase, leaving 141 patients randomized to the CEP device and 63 to control. The balloon-expandable SAPIEN valve was used in approximately 60% of study patients, with the self-expanding CoreValve accounting for most of the remainder. Among patients assigned to the device arm, the device was deployed successfully across all three great vessels for 93.4%, while it remained fully in place throughout the TAVR surgery in just 57.3% of procedures. The operators reported the device interfered significantly with the TAVR system in 8.8% of cases.

The primary safety endpoint occurred in 21.8% of patients in the device group by 30 days. Although this met the safety endpoint by beating the prespecified performance goal of 34.4%, it was significantly higher than the 8.5% event rate observed in the control group. This was driven primarily by a higher rate of major vascular complications in the TriGUARD group (7.1% vs. 0%). The other components of the safety endpoint were not significantly different. The primary efficacy endpoint was not significantly different between groups. This was true for the entire set, as well as for the subset of patients who achieved full cerebral coverage with the device for the duration of the procedure. The rates of stroke at 30 days were numerically higher in the device arm (10%) vs. controls (6.8%), although this difference was not statistically significant. Among patients who underwent brain imaging with diffusion-weighted MRI, the number of ischemic lesions and the total volume of lesions were not different between the groups. The authors reported the TriGUARD device was safe when compared with a performance goal based on historical data, but failed to meet its efficacy endpoint in the primary hierarchical composite of death, stroke, NIH Stroke Scale score worsening, or total ischemic lesion volume.

■ COMMENTARY

In a world where positive publication bias is a reality, a negative trial like this one seems rare. Seemingly hidden in the text is the fact the authors paused the study early at the recommendation of the Data Safety and Monitoring Board, although the reasons for this are not included in the publication. The sponsor elected not to resume the trial, instead focusing its attention on its next-generation device, TriGUARD 3. What can we learn from this relatively underpowered trial, with an older-generation device, that ended prematurely?

Even the assertion the device met its safety endpoint is somewhat suspect. Using a prespecified historical event rate of 35%, seemingly high by current standards, as a comparator should rate some notice. The fact the safety composite was significantly lower in the actual control group should raise some eyebrows, especially with a device that requires a relatively large second (in addition to the TAVR sheath) femoral access site.

Stroke rates in REFLECT were higher than what usually is reported in clinical registries. This seems to reflect a general finding that stroke rates are higher when all patients are subjected to formal neurologic assessment. The disconnect between the appearance of ischemic lesions on MRI, seen in 85% of participants, and clinical stroke is well-known and is demonstrated here. Whether the post hoc observation indicating the device reduced larger lesions and carries clinical relevance remains to be seen.

Usually, medical devices continue to improve with further iterations. The TriGUARD device studied here was successful in protecting the great vessels throughout the TAVR procedure in just over half of patients and interacted negatively with the TAVR system itself in nearly 10%. The device is relatively large and requires femoral access. We can expect the devices and outcomes to improve, especially when we can learn from negative trials such as this one.

Much larger trials using the Sentinel device are in the works, including PROTECTED TAVR (3,000 patients) and British Heart Foundation PROTECT-TAVI (7,730 patients).[4,5] However, despite a compelling backstory, the routine use of CEP devices in TAVR continues to lack robust data showing unequivocal benefit in reducing the clinically important strokes that matter most. We will continue to watch this space with keen interest as future trials are presented. ■

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ABSTRACT & COMMENTARY

Early Physical Rehabilitation in Acutely Hospitalized Heart Failure Patients

By Michael H. Crawford, MD, Editor

SYNOPSIS: A tailored, progressive physical rehabilitation program started in the hospital and continued for three months in older, relatively frail acute heart failure admissions resulted in significantly improved physical function vs. usual care but did not reduce six-month readmission rates.

SOURCE: Kitzman DW, Whellan DJ, Duncan P, et al. Physical rehabilitation for older patients hospitalized for heart failure. *N Engl J Med* 2021;385:203-216.

Physical limitations are common in patients admitted for acute heart failure and are exacerbated by hospital bed rest, leading to a vicious cycle that often ends in readmission. Whether an early transitional, tailored, progressive rehabilitation program would improve physical function and reduce readmissions was the subject of this multicenter, randomized, single-blind, controlled study. Patients at least age 60 years who could walk 4 meters (13 feet) with or without a support device, who were living independently before admission, and for whom discharge home was planned were enrolled. They were randomized to the tailored rehabilitation intervention or usual care, which could include standard cardiac rehabilitation or physical therapy programs. The tailored program started in the hospital and continued on for three 60-minute one-on-one outpatient visits per week for four weeks and home exercises on the off days, which included walking for 30 minutes and strength exercises. The outpatient visits focused on strength, balance, mobility, and endurance.

After three months, the intervention group received an exercise prescription they were to continue indefinitely, and they were phoned every month for six months to assess their progress. The control group received a phone call at two weeks and follow-up visits at one and three months. The primary outcome was the Short Physical Performance Battery (SPPB) at three months, which included standing balance, gait speed, and a strength test. Each were scored 0-4 points, where 4 is best, for a total possible score of 12. The secondary endpoint was rehospitalization rate at six months. Between 2014 and 2019, 349 patients were randomized (average age = 73 years, 52% women, 46% Black, 53% with heart failure with preserved ejection fraction). In addition, 97% were either frail or pre-frail. The SPPB score at three months was 8.3 in the intervention group and 6.9 in the control group ($P < 0.001$), and all three measures increased significantly. Specifically, walking endurance increased from 11 minutes to 22 minutes. The rehospitalization rate at six months was 1.2% vs. 1.3%, which was not significant, nor was mortality (21% vs. 16%). Adherence to the intervention at six months was 78%. The authors concluded a tailored, progressive physical rehabilitation intervention started in the hospital in older patients admitted for acute heart failure and continued for three months exhibited greater improvement in physical function vs. usual care.

■ COMMENTARY

Physical limitations are common in heart failure patients because of multiple comorbidities and reduced left ventricular function. Hospitalization often improves their heart failure but does not necessarily improve their physical functioning. This study by Kitzman et al is unique in that they applied their intervention to relatively frail elderly patients with multiple comorbidities, starting in the hospital and continuing as outpatients. Also, the study was multicentered, blinded, controlled, and involved a diverse population. In addition, the beneficial results of the intervention occurred despite 43% of the control group undergoing some form of physical therapy or cardiac rehabilitation after discharge as part of usual care. Remarkably, 83% of the intervention group was engaging in regular exercise at home six months after discharge. On the negative side, there was no change in clinical events, such as rehospitalization. Although not significant, mortality was higher in the intervention group. Also, 30 patients in the intervention group dropped out. Finally, the long-term benefits of the intervention are unknown.

Although clearly of some benefit to the patients, initiation of such a program in the hospital and

continuing on an outpatient basis would be costly. This was a one-on-one intervention, which was tailored to each patient's rehabilitation needs. The outpatient sessions lasted 60 minutes each and were conducted three times a week for a duration of three months, with periodic phone calls for up to six months. Considering the resources expended, the results are good but not spectacular. However, exploratory endpoints, such as six-minute walk test, frailty index, cognitive assessment, and depression, improved, and there were no subgroups where the intervention was not effective. Until your hospital system has the resources to start such a program, ensuring that all heart failure discharges are at least referred for cardiac rehabilitation would be a good start. ■

ABSTRACT & COMMENTARY

Value of Optimal Medical Therapy After Revascularization

By Michael H. Crawford, MD, Editor

SYNOPSIS: Patients with three-vessel or left main coronary artery disease randomized to coronary bypass surgery vs. percutaneous therapy on optimal medical therapy at five years with three or four of the recommended drugs recorded a lower 10-year all-cause mortality rate vs. those on ≤ 2 drugs.

SOURCE: Kawashima H, Serruys PW, Ono M, et al. Impact of optimal medical therapy on 10-year mortality after coronary revascularization. *J Am Coll Cardiol* 2021;78:27-38.

The SYNergy between percutaneous coronary intervention with TAXus (paclitaxel eluting stent) and cardiac surgery (SYNTAX) study demonstrated reduced mortality at five years in patients treated with optimal medical therapy following coronary artery revascularization.[1] The SYNTAXES substudy extended the follow-up to 10 years. SYNTAXES was a multicenter, randomized, controlled trial of percutaneous coronary intervention (PCI) vs. coronary artery bypass surgery (CABG) in patients with left main or three-vessel disease with stable or unstable myocardial ischemia, but not myocardial infarction. It was conducted in 83 hospitals in 18 countries in North America and Europe.

Optimal medical therapy (OMT) consisted of an antiplatelet agent, a statin, an angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), and a beta-blocker. The authors strongly encouraged prescribing all four drugs as part of OMT. However, the final decisions about which drugs to prescribe and how many were left to the treating physician. The primary outcome was all-cause mortality at 10 years. Patients were stratified by the number of OMT agents they were taking. Various covariates, such as age, sex, and clinical characteristics, were used to construct propensity-matched cohorts. At the five-year follow-up, there was drug information available for 1,472 patients, of whom 46% were on OMT and 54% were not.

Patients on OMT were more likely to have experienced a myocardial infarction and been diagnosed with three-vessel disease (36% vs. 28% and 64% vs. 57%, respectively; both $P < 0.001$). Otherwise, the two groups were well matched. At 10 years, all-cause mortality in those on one or two of the four medications was 20% vs. 13% in those on three or four of the medications (adjusted HR, 0.47; 95% CI, 0.29-0.76; $P = 0.002$). An analysis of individual medications showed statistically significant differences in mortality if the patients were on antiplatelet drugs or statins, but not ACEI/ARB or beta-blockers. When the type of revascularization was considered, patients post-CABG benefitted more from OMT than those post-PCI. Again, this benefit was statistically significant only for antiplatelet drugs and statins. There was no effect of lesion characteristics and clinical presentation on the results. The authors concluded OMT at five years post-CABG or PCI for non-infarct-related three-vessel or left main coronary artery disease was associated with a significant reduction in all-cause mortality at 10 years vs. those not on OMT.

■ COMMENTARY

The main finding of this report is post-coronary artery revascularization patients on at least three of the four drugs considered OMT at five years have a better chance of survival at 10 years, with an absolute gain of 7%. Also, when individual drugs are considered, antiplatelet drugs and statins seem to be the most important, especially in post-CABG patients. Of course, this report is preaching to the choir. Antiplatelet drugs and statins are prescribed commonly to patients with coronary artery disease.

In this study, antiplatelet usage was 87% and statin usage was 85%. Angiotensin-inhibiting agents and beta-blockers are used less and most often for specific indications, such as hypertension or post-myocardial infarction. The message here is that for at least five years after revascularization, patients should be on an antiplatelet drug, a statin, and at least one of the other two drugs. In the five-year follow-up of the SYNTAX trial, antiplatelet drugs, statins, and beta-blockers had HRs < 0.50 for survival. However, for angiotensin inhibitors, the HR was 0.70.[1] Perhaps beta-blockers are the best choice for the third agent, unless there are specific reasons to use angiotensin inhibitors or contraindications to beta-blockers.

Although this was meticulously collected, randomized data, with a 10-year follow-up rate of 94%, it was a post hoc analysis of information collected for another purpose. There was no randomization of medication use, so there may be unmeasured confounders that biased drug selection. However, the biggest weakness of this study was the fact there was no assessment of drug adherence after five years. It was assumed drug use remained constant for the next five years. If a patient stuck with these drugs for five years after a procedure, would the patient remain compliant for another five years? We do not know this for sure. Another potential unmeasured confounder is a lack of information on lifestyle and other pharmacological interventions. Also, like any 10-year-old study, the current therapeutic milieu is markedly different. The stents used in the study were first generation. Now, there are more potent statins and other drugs for cholesterol-lowering. There are more potent antiplatelet drugs and new inhibitors of clotting (e.g., rivaroxaban). In addition, there are new diabetic drugs that also reduce mortality in coronary artery disease patients. Thus, these data, although encouraging, may be out of date. ■

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CME/CE QUESTIONS

1. A tailored, progressive physical rehabilitation program for acutely hospitalized heart failure patients resulted in what at six months?

a. Lower readmission rates
b. Lower mortality rates
c. Better physical functioning
d. Better diabetes control

2. Which technique did investigators use to demonstrate coffee consumption is inversely related to incident arrhythmias?

a. Bayesian analysis
b. Mendelian randomization
c. Meta-analysis
d. Propensity matching

3. A study of the association of alcohol consumption with incident atrial fibrillation showed:

a. a linear relationship.
b. no relationship.
c. a J-shaped curve.
d. a bimodal curve.

4. The absolute difference in 10-year survival in those on one or two vs. three or four optimal medical therapy agents at five years after coronary revascularization in the SYNTAXES study was:

a. 3%.
b. 7%.
c. 11%.
d. 15%.

5. A trial of the TriGUARD cerebral embolic protection device during transcatheter aortic valve replacement failed to:

a. achieve its efficacy endpoint.
b. achieve its safety endpoint.
c. reduce pacemaker need.
d. reduce transcatheter aortic valve thrombosis.