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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

Vol. 40, Issue 3, March 2021
ReliasMedia.com

ABSTRACT & COMMENTARY

Is Effective Transcatheter Tricuspid Repair Becoming a Reality?

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 two trials of transcatheter devices treating tricuspid regurgitation, the authors observed high efficacy and low adverse event rates.

SOURCES: Lurz P, Stephan von Bardeleben R, Weber M, et al. Transcatheter edge-to-edge repair for treatment of tricuspid regurgitation. *J Am Coll Cardiol* 2021;77:229-239.

Kodali S, Hahn RT, Eleid MF, et al. Feasibility study of the transcatheter valve repair system for severe tricuspid regurgitation. *J Am Coll Cardiol* 2021;77:345-356.

It has been called the forgotten valve. In the past, the importance of marked tricuspid valve regurgitation (TR) has been downplayed or simply pushed aside, at least in part over a lack of good therapeutic options. The high morbidity and mortality rates associated with surgical repair or replacement of the tricuspid valve certainly has dampened the field. In recent years, the MitraClip edge-to-edge repair device has been used in an off-label fashion to treat the tricuspid valve. Multiple devices, all still investigational in the United States, seek to use the basic paradigm of the MitraClip platform for tricuspid repair.

One of these devices is called the TriClip Tricuspid Valve Repair System, conceived and manufactured by the same company that markets MitraClip (Abbott). The TriClip was studied in a prospective, multicenter, single-arm investigation known as TRILUMINATE. These authors sought to determine the safety and effectiveness of this device. Although the trial was modest in size (fewer than 100 enrolled subjects), the TRILUMINATE authors used an echo core laboratory to perform imaging assessments, and they formed a clinical events committee to adjudicate all events. The one-year results were published recently.

Financial Disclosure: None of the planners or authors for this educational activity have relevant financial relationships to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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

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The authors enrolled 85 subjects with significant TR and elevated surgical risk, all of whom underwent successful clip implantation. The mean age of participants was 78 years, with a mean EuroSCORE II of 8.7%. In the initial short-term analysis, 86% of patients showed improvement in TR by at least one grade. At 12 months, 63 of the original 85 patients underwent evaluable follow-up imaging to assess TR. Of the 22 patients with missing data, seven had died, nine had withdrawn from the study or missed visits, and six lacked a readable echocardiogram. There were unevaluable baseline data for one patient, leaving 62 patients for the one-year analysis. A total of 54 of 62 patients demonstrated a sustained reduction in TR by at least one grade, while 70% showed moderate-or-less TR at one year. A detailed assessment revealed patients experienced a significant improvement in right ventricular function, as well as reductions in right ventricular diameter and right atrial volume. Significant improvements in functional status also were recorded. Eighty-three percent of subjects at one year were classified as New York Heart Association (NYHA) class I or II, up from 31% at baseline. Performance on the six-minute walk test and the Kansas City Cardiomyopathy Questionnaire (KCCQ) also were significantly better vs. baseline.

Shortly after the publication of these TRILUMINATE data, a separate group published the results of a study of a different transcatheter option for TR, the PASCAL device in the CLASP TR EFS trial. PASCAL, which features a clasp with a spacer that is meant to bridge the coaptation gap, is functionally similar to the TriClip and is delivered via a procedure that also involves large-bore venous access, general anesthesia, and TEE and intracardiac echo guidance.

The authors enrolled 34 patients in this single-arm feasibility trial. Most patients (88%) presented with functional TR. An implant was delivered successfully in 29 of 34 patients, and 85% of patients recorded a reduction of at least one grade in TR at 30 days. The procedure was safe; the major adverse event rate of 5.9% was attributed almost entirely to post-procedure gastrointestinal bleeding. The authors also observed improvements in NYHA class, six-minute walk distance, and KCCQ scores.

■ COMMENTARY

The tricuspid valve has been forgotten by many until recently. One problem with all repair modalities, including surgery, is patients have been referred for intervention quite late in their disease course, when the right heart has started to dilate and fail, or when the extent of secondary liver dysfunction is markedly advanced. The lack of less-invasive therapeutic options has contributed to this referral delay. Transcatheter options for tricuspid repair have been limited. Lately, there has been interest in several less direct and clumsier options, such as implantation of a transcatheter valve in the inferior vena cava to protect the liver from the effects of torrential TR. Clinically, the growing experience with the MitraClip has led to more off-label use for the tricuspid position. The development of purpose-built devices for the tricuspid valve gives builds more momentum in this area.

In these small trials, success rates were encouragingly high, with real improvements seen in terms of TR severity, right heart remodeling, and clinical assessments. The evidence so far suggests these procedures are safe, despite relatively long times under general anesthesia, with large-bore femoral venous access. Single-leaflet device attachment (where the clip lets go of one leaflet after deployment) occurred in 7% of patients, which is marginally higher than what has been seen with MitraClip.

Not every patient with tricuspid valve disease will be a candidate for these therapies. Imaging guidance for tricuspid interventions can be challenging, with a significant minority of cases showing poor imaging by transesophageal echo. A full one-third of screening failures in the PASCAL trial were excluded over suboptimal imaging. As this field progresses, expect to see growing options for transcatheter therapeutics for the tricuspid valve. Future trials will have to inform which patients will benefit from these therapies, and when in their disease course they are most likely to benefit. ■

ABSTRACT & COMMENTARY

Statins and Muscle Symptoms: Cause and Effect?

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of three large simvastatin trials revealed muscle symptoms on simvastatin are common, but true myopathy is rare and can be predicted by evaluating certain risk factors for its development, which can help guide patient management.

SOURCE: Hopewell JC, Offer A, Haynes R, et al. Independent risk factors for simvastatin-related myopathy and relevance to different types of muscle symptom. *Eur Heart J* 2020;41:3336-3342.

Myopathy caused by statins is rare, but muscle symptoms are common. Hopewell et al sought to identify independent risk factors for myopathy based on a study of 171 diagnosed cases among 58,390 subjects treated with simvastatin in three large trials. Subjects were followed at least every six months for an average of 3.4 years. Alanine transaminase (ALT) was measured at each visit, and creatine kinase (CK) was measured if there were any muscle symptoms or if the ALT was 1.5 times the upper limit of normal (ULN). Myopathy was diagnosed if the subject reported muscle pain or weakness and recorded a CK > 10 times the ULN. In one study, subjects with muscle symptoms and CK values between five and 10 times the ULN were evaluated, too.

In addition to analyzing common clinical characteristics of the subjects, the authors studied concomitant drug use, especially strong CYP34A inhibitors. Researchers created a subgroup of 9,239 subjects pulled from all three studies for whom genetic data were available. There were 196,521 person-years of exposure to simvastatin for a mean of 3.4 years of therapy. Among the 171 cases of myopathy, there were 14 with severe myopathy, with CK > 40 times the ULN and evidence of rhabdomyolysis. Among those with myopathy, 73% reported no muscle symptoms before the onset of myopathy. The mean time to myopathy was 18 months, with 36% within the first six months. The rate of myopathy was nine in 10,000 patient-years and was higher in the first year vs. later (19 vs. 5 per 10,000 patient-years). In those of Chinese ethnicity, it was 26 vs. 2 per 10,000 patient-years in European subjects. Myopathy also was more common on simvastatin 80 mg/day vs. 20 mg/day (13 vs. 1 per 10,000 patient-years). In the group with muscle symptoms and CKs between five and 10 times the ULN, the incidence was 0.2% vs. 0.1% in those with no symptoms.

Muscle symptoms without CK elevation were extremely common, occurring at least once in 26% of the subjects, or 981/10,000 patient-years. Simvastatin at the 80 mg/day dose was the highest independent risk factor for myopathy, followed by Chinese ancestry (10 times the rate of Europeans). Others included older age, smaller body mass index (BMI), female sex, and diabetics on hypoglycemic agents. Culprit drugs included verapamil (8x), niacin or diltiazem (3x), and beta-blockers or diuretics (0.67-0.75x). The odds ratio (OR) for the genetic variant SLCO1B1rs4149056 was 3.1. The OR for other muscle symptoms (no CK elevation) was 0.97. The authors calculated a risk score based on these factors, which averaged 7.2 in myopathy cases vs. 4.2 with other muscle symptoms. Dividing the scores into tertials, the OR for myopathy increased from 1.0 at the bottom tertial to 34 at the top in those with myopathy, but did not change in those without myopathy (1.0 at all levels). In those with symptoms and CK between five and 10 times the ULN, the ORs went from 1.0 to 3.5 at the top. The authors concluded the risk of statin myopathy is low, but higher-risk individuals can be detected by evaluating risk factors associated with myopathy.

■ COMMENTARY

Interestingly, the authors did not present the risk score algorithm in the paper, only in the supplementary online material. I believe they did not think physicians were going to use the score, partly because the risk concepts presented are so straightforward, and they did not test all possible risk factors because the trials they examined did not include the data. Despite several hypotheses, the actual mechanism of statin myopathy is unknown. What is clear is that it is related to blood levels. Thus, the most potent predictor of myopathy was the simvastatin dose.

Other risk predictors were those that would be expected to raise blood levels: Chinese ethnicity, concomitant drug therapy, small BMI, and female sex because of sexual dimorphism. The association with the genetic variant SLCO1B1 certainly is because it is known to raise the blood levels of patients on statins.

Although not assessed in the Hopewell et al study, the genetic variant raises different statins by varying amounts. For example, it raises simvastatin 40 mg per day levels by 221%, atorvastatin 20 mg per day by 144%, and rosuvastatin 40 mg per day by 117%. Thus, the risk of myopathy varies with the statin and explains why simvastatin 80 mg was withdrawn from the U.S. market. The association with diabetics treated with hypoglycemic agents is unclear, but since it was not seen in diabetics not on drug treatment, it likely also is a drug interaction.

One weakness of the study was the authors did not investigate other CYP34A inhibitors, such as amiodarone, probably because there were not enough data on these drugs in the trials. Also, the authors did not examine thyroid disease or grapefruit juice ingestion, probably for the same reason. Although renal dysfunction would be expected to raise blood statin levels, no association was observed in the Hopewell et al study. This probably is because the average GFR in the studies examined was marked at 90 mL/min/1.73 m^2, and less than 3% of subjects recorded GFR levels less than 45 mL/min/1.73 m^2. Therefore, the more factors that could raise the blood levels of patients on statins, the higher the risk of myopathy.

As the Hopewell et al study shows, most muscle symptoms are not caused by the statin. The authors suggested checking a CK level for any muscle symptoms. If normal, try to convince the patients to continue the statin. With a CK in the borderline range of five to 10 times the ULN, Hopewell et al suggested carefully following the patient while trying to keep him or her on the statin.

When initially considering therapy with a statin, the authors recommended considering the risk factors listed in this article and perhaps using non-statin therapy for high-risk patients. However, even in vulnerable patients, the risk of statin myopathy is much lower than that of a major cardiovascular event if they do not lower their LDL cholesterol. ■

ABSTRACT & COMMENTARY

Are Beta-Blockers Still Relevant After a Myocardial Infarction?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A large, contemporary, nationwide, observational study of post-myocardial infarction beta-blocker administration shows that after three months, there were no beneficial effects on adverse cardiovascular events to continued beta-blocker use.

SOURCE: Holt A, Blanche P, Zareini B, et al. Effect of long-term beta-blocker treatment following myocardial infarction among stable, optimally treated patients without heart failure in the reperfusion era: A Danish, nationwide cohort study. *Eur Heart J* 2021 Jan 11;ehaa1058. doi: 10.1093/eurheartj/ehaa1058. [Online ahead of print].

The long-term use of beta-blockers following myocardial infarction (MI) is based on older trials conducted before the widespread use of reperfusion, statins, and antiplatelet drugs beyond aspirin. Investigators from Denmark tested the hypothesis that beta-blocker use after three months post-MI in patients without heart failure was of no benefit.

Using the Danish National Patient Register, Holt et al identified patients age 30 to 85 years with a first MI admission who underwent a percutaneous coronary intervention (PCI) or coronary angiography between 2003 and 2018 and had never used beta-blockers. The study population included those patients who survived for 90 days and were prescribed statins and aspirin. The authors excluded patients with a contraindication for beta-blockers; another indication for beta-blockers; and those who had undergone a cardiac procedure or surgery beyond the initial PCI, before MI, or during the first 90 days after MI. Beta-blocker use was defined as beta-blockers started within the first 30 days post-MI. The primary outcomes were cardiovascular (CV) death, recurrent MI, and a composite of CV events. Secondary outcomes were potential beta-blocker adverse events. Those who received beta-blockers and those who did not were compared after adjustment for potential confounding.

Of the 30,177 patients included in the study, 58% underwent a primary PCI, 26% a subacute PCI, and 16% coronary angiography without intervention. At baseline, 82% were on beta-blockers (75% male; median age, 61 years) and 18% were not (68% male; median age, 62 years). Patients on beta-blockers were more likely to have undergone primary PCI, but other differences were not clinically significant. The proportion of patients on beta-blockers declined throughout the study period (92% in 2003-2005

to 67% in 2015-2018). Over the study period, 405 subjects died from CV causes, 1,859 experienced a recurrent MI, and 7,768 reached the composite endpoint. There was no difference in outcomes between those on beta-blockers compared to those not. Also, no association was found between beta-blockers and the risk of an adverse event requiring a hospital visit. As a negative control, the effect of beta-blockers on pneumonia was analyzed, and no association was found. Also, beta-blocker use did not affect all-cause mortality. The authors concluded there was no effect of beta-blocker treatment on long-term CV prognosis in optimally treated MI patients without heart failure who survived at least three months post-MI.

■ COMMENTARY

The most recent American College of Cardiology/American Heart Association guidelines recommend giving beta-blockers to MI patients after the first 24 hours, unless there are contraindications to their use, and continue those for at least three years.[1] This recommendation is based on trials conducted in the era before reperfusion therapy, statin use, and advanced antiplatelet agents were available. Since reperfusion rapidly reduces sympathetic drive, beta-blocker therapy may not be as necessary as originally thought.

The Danish study was conducted in the reperfusion era. Patients with indications or contraindications for beta-blockers were excluded. Also, these authors optimized the use of other therapies of known value. Ninety-five percent of the Danish patients were taking aspirin and statins. In addition, Holt et al argued their work was a real-world experience, which complements randomized trial data. The guidelines recommend titrating metoprolol up to 200 mg/day, if possible, based on older, randomized trial data.[1] The median metoprolol dose in the Holt et al study was 50 mg/day. Thus, one could argue subjects were underdosed. However, these high doses are used rarely, at least in my experience. In the Holt et al study, there was no association between beta-blockers and adverse events that required going to the hospital. They did not study less significant nuisance adverse effects, but compliance with beta-blocker use was excellent. It is unknown why some patients were not treated with beta-blockers, but the data were not confounded by indication, since patients with indications for beta-blockers were excluded. It is likely the absence of more recent data supporting their use explains why some patients were not treated. The authors noted the use of beta-blockers declined during the 15-year study period from 92% to 67%.

There were other strengths, such as the inclusion of a positive control analysis of the association between statins and the primary outcomes, which showed significant reductions. Also, there was a negative control analysis of pneumonia where no association with beta-blocker use was shown. However, in observational studies, one can never completely exclude the influence of unmeasured confounders and selection biases. The authors believe their results should help inform future updates to the acute MI guidelines. For now, they recommend giving beta-blockers early after an MI to those without contraindications, but re-evaluate this use at three months. ■

REFERENCE

1. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;61:e78-e140.

ABSTRACT & COMMENTARY

Can Antioxidant Intake Prevent Coronary Artery Disease?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A study of single nucleotide polymorphisms (SNP) that increase blood levels of diet-derived antioxidants in three large individual subject genetic databases did not demonstrate a relationship between SNPs and coronary artery disease.

SOURCE: Luo J, le Cessie S, van Heemst D, Noordam R. Diet-derived circulating antioxidants and risk of coronary heart disease: A Mendelian randomization study. *J Am Coll Cardiol* 2021;77:45-54.

Oxidative stress is thought to cause endothelial damage and dysfunction, and to accelerate the development of atherosclerosis. Thus, there has been considerable interest in antioxidants derived from diet or supplements. Luo et al explored the relationship between dietary-derived circulating antioxidants and primary coronary artery disease (CAD) using Mendelian randomization (MR).

The authors retrieved the single-nucleotide polymorphisms (SNP) for five circulating diet-derived antioxidants from published genome-wide association studies (GWAS) data: vitamins E and C, retinol, beta-carotene, and lycopene. Researchers derived the associations of these SNPs with CAD from three large genetic databases: CARDIoGRAMplusC4D, UK Biobank, and FinnGen, encompassing 93,230 CAD cases out of 768,121 subjects.

A meta-analysis of these data demonstrated that genetically predicted circulating antioxidants were not causally associated with CAD risk. Odds ratios ranged from 0.93 to 1.03 for each antioxidant, and none were significant. Sensitivity analyses detected no pleiotropy, and a leave out analysis did not reveal significant changes in the data by excluding individual SNPs. The authors concluded a genetic predisposition to higher levels of dietary-derived antioxidants did not protectively affect the development of CAD. They suggested increasing blood levels of antioxidants by diet or supplements was unlikely to prevent CAD.

■ COMMENTARY

The central concept of the antioxidant hypothesis is that for LDL cholesterol to enter the arterial wall, it must be oxidized. Thus, preventing or mitigating this oxidation would be expected to ameliorate or eliminate atherosclerosis. However, trying to study this hypothesis is complicated because those who regularly ingest antioxidant-rich foods or take supplements usually exercise more, eat better, and take better care of themselves generally. In fact, the much-touted Mediterranean diet is rich in antioxidants. However, randomized, controlled trials of antioxidant supplements have been largely negative. Thus, this study is of interest. Other MR studies of vitamin E have been negative, but the genetic variants those authors studied also beneficially affected lipids.[1,2] The Luo et al study of genetic variants that raise the blood levels of five antioxidants and does not effect lipids shows no association between these genetic variants and the development of CAD.

The circulating levels of antioxidants produced by the genetic variants that Luo et al studied approximate those achieved in antioxidant supplementation randomized trials. Of course, subjects with these genetic variants maintain these levels their entire life, not just during a randomized study period. In addition, the authors studied SNPs that increase circulating levels of antioxidants and their metabolites. In other words, the authors did not omit antioxidants that have short half-lives in the blood. Finally, they studied these genetic variants in three huge databases. Thus, small effects would be detected easier.

This probably is not the end of the story because there may be subgroups at especially high risk for CAD in whom antioxidants may be beneficial, such as diabetics with familial hypercholesterolemia. Also, it is possible that multiple antioxidants might be synergistic. I expect future MR studies will explore some of these nuances. For now, there does not seem to be any compelling reason to recommend antioxidant supplements broadly for CAD prevention. However, the Luo et al study does not negate the lipid hypothesis. Dietary interventions known to lower lipids, regardless of their effect on antioxidant blood levels, still should be recommended. ■

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ABSTRACT & COMMENTARY

New Risk Factors for Atherosclerosis

By Michael H. Crawford, MD, Editor

SYNOPSIS: An analysis of the Women's Health Study based on a recent questionnaire about adverse pregnancy outcomes showed hypertensive disorders of pregnancy and low birth weight are independent predictors of subsequent atherosclerotic cardiovascular disease.

SOURCE: Søndergaard MM, Hlatky MA, Stefanick ML, et al. Association of adverse pregnancy outcomes with risk of atherosclerotic cardiovascular (CV) disease in postmenopausal women. *JAMA Cardiol* 2020;5:1390-1398.

Adverse pregnancy events have been associated with the development of atherosclerosis risk factors and atherosclerotic cardiovascular (CV) disease later in life. However, it is unclear whether they are risk factors themselves or are just associated with risk factors for CV disease. Søndergaard et al sought to clarify this issue by analyzing data from the Women's Health Initiative (WHI), a large,

multiethnic cohort study with prospective follow-up and adjudicated CV disease outcomes.

The WHI authors enrolled postmenopausal women between 1994 and 1998, but no data on pregnancy outcomes were obtained at that time. In 2017, researchers sent a questionnaire on pregnancy outcomes to all surviving enrollees who were still participating in WHI. The questionnaire asked about five conditions requiring a yes or no answer: gestational diabetes, hypertensive disorders of pregnancy, low birth weight (< 2.5 kg), high birth weight (> 4.1 kg), and preterm delivery by > 3 weeks. The primary outcome was atherosclerotic CV disease, defined as myocardial infarction, stroke, peripheral artery disease, or coronary revascularization, all of which were collected during the study period up to 2017 and were adjudicated. The outcomes data were adjusted for other known risk factors, including hyperlipidemia, hypertension, diabetes not pregnancy-related, and smoking. All participants who were pregnant longer than six months were included. Subjects were excluded if they reported any CV disease at baseline.

At baseline, there were 161,808 participants (72,063 were excluded, mainly for death, and 42,940 did not respond to the survey). This left 46,805 responders (65% of those eligible) with a median age of 60 years at enrollment. Adverse pregnancy outcomes (APO) were reported in 13,482. CV disease was more common in these women than those without APO (7.6% vs. 5.8%). Each of the five APOs analyzed separately was significantly associated with CV disease in the univariate model. However, when adjusted for other CV disease risk factors, only gestational diabetes, hypertension, low birth weight, and preterm delivery remained significant.

When all five APOs were analyzed together in an adjusted model, only hypertensive disorders of pregnancy (OR = 1.34; 95% CI, 1.15-1.54) and low birth weight (OR = 1.18; 95% CI, 1.03-1.35) remained independently associated with CV disease. Adjustments for race/ethnicity, income, education, body mass index, breastfeeding, and parity did not materially change the results. The authors concluded hypertensive disorders of pregnancy and low birth weight were independently associated with the development of CV disease after adjustment for atherosclerosis risk factors and other APOs in this multiethnic cohort of postmenopausal women.

■ COMMENTARY

Current guidelines recommend considering APO in the CV disease risk estimation in women and for decision-making about prescribing cholesterol-lowering agents for primary prevention.[1] However, it is unclear whether APOs are risk factors in themselves or if they are associated with other risk factors. For example, gestational diabetes is known to be associated with the development of type 2 diabetes later in life, and gestational hypertension often is a precursor to later hypertension. In fact, some have suggested that pregnancy is a stress test that can bring out the predisposition to cardiometabolic abnormalities. Thus, this analysis of the WHI is of interest because Søndergaard et al parsed whether APOs are independent of other risk factors for CV disease. The authors showed that all APOs, except high birth weight, are independently associated with CV disease when adjusted for other risk factors. Some APOs often occur together in the same women. When those APOs were analyzed together with traditional risk factors, the results showed that only hypertensive disorders of pregnancy and low birth weight remained independently associated with CV disease. Low birth weight, prematurity, and gestational hypertension may share a common mechanism of placental dysfunction. Prematurity and low birth weight often occurred together and were not independent of one another.

There were limitations to this study. Gestational hypertension and pre-eclampsia were lumped together as hypertensive disorders of pregnancy. This may not be appropriate, but since they often occurred together, this seemed expedient to the investigators. Although touted as multiethnic, 90% of the subjects were white, 5% Black, 2.5% Hispanic, and 2.5% other. This disparity could be explained by the fact minorities in WHI died more often and were less likely to respond to the survey. Also, there was a survival bias in that the highest-risk subjects died before the APO survey was conducted. There may be a recall bias, too, in that it is easier to recall low birth weight than gestational diabetes. However, these biases would only serve to reduce the odds ratios. APOs are risk predictors for CV disease that are unique to women, but since about 85% of women experience at least one pregnancy, of which about 20% are complicated by an APO, these are important risk factors. This is especially true for hypertensive disorders of pregnancy, low birth weight, and gestational diabetes. It would be useful if at least these three APOs were included in electronic medical record templates. ■

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CME/CE QUESTIONS

1. A Mendelian randomization study of genetic variants that raise diet-derived antioxidant levels in the blood showed:

a. blood levels like those seen in randomized antioxidant administration trials.

b. a reduction in the development of coronary artery disease.

c. confounding effects on serum lipid levels.

d. lower mortality rates.

2. A large study of post-myocardial infarction patients in the Danish National Patient Register showed beta-blocker use after three months was associated with:

a. a lower all-cause mortality rate.

b. fewer adverse cardiovascular events.

c. more hospitalizations.

d. no change in the incidence of pneumonia.

3. Which pregnancy-related outcome is associated with the later development of atherosclerotic cardiovascular disease in an adjusted multivariate analysis?

a. Gestational diabetes

b. Hypertension

c. Preterm delivery

d. High birth weight

4. Which is the most important risk factor for statin myopathy?

a. History of muscle symptoms

b. European ancestry

c. Statin blood levels

d. Concomitant losartan use

5. New devices for transcatheter repair of the tricuspid valve for tricuspid regurgitation are based on:

a. the bioprosthetic valve used in the pulmonic area.

b. the MitraClip.

c. mitral annular cinching devices.

d. surgical repair.

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.