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ABSTRACT & COMMENTARY

Intensive Monitoring for Asymptomatic Atrial Fibrillation Did Not Prevent Strokes

By Joshua D. Moss, MD

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SYNOPSIS: Screening with an implantable loop recorder resulted in dramatically higher rates of atrial fibrillation detection and ensuing anticoagulation, but without a significant decrease in risk of stroke or systemic embolism by six years of follow-up.

SOURCE: Svendsen JH, Diederichsen SZ, Højberg S, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): A randomised controlled trial. *Lancet* 2021;398:1507-1516.

Anticoagulation lowers the risk of stroke in patients with clinically diagnosed atrial fibrillation (AF). Further, more-intensive ambulatory monitoring helps clinicians detect more asymptomatic or "subclinical" AF better than conducting periodic ECGs or short-term Holter monitoring. Svendsen et al sought to investigate whether anticoagulation guided by intensive AF screening with an implantable loop recorder (ILR) could prevent strokes.

At four centers in Denmark, 6,004 patients (mean age = 74.7 years; 47.3% women) with at least one risk factor for stroke (other than age) but no previously diagnosed AF or indication for anticoagulation were randomized in a 1:3 ratio to ILR monitoring or usual care. Required risk factors for stroke included hypertension (90.7%), diabetes (28.5%), prior stroke (17.6%), or heart failure (4.4%). Most patients recorded a CHA_2DS_2-VASc score of 3 or higher. In the ILR group, automated remote transmissions were reviewed daily, and oral anticoagulation was recommended if AF lasting at least six minutes was detected. In the usual care control group, patients were followed per routine with their general practitioner and participated in an annual interview with a study nurse. The primary outcome was the combined endpoint of stroke or systemic arterial embolism, with multiple secondary outcomes, including cardiovascular and all-cause mortality. No patients in the control arm crossed over to the ILR group, and 81 patients in the ILR group did not receive an ILR. The median duration of ILR monitoring was 39.3 months, with 11.7% of

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ILR patients prematurely discontinuing monitoring (before three years without outcome, AF, or death). Total median follow-up was 64.5 months.

AF was diagnosed at significantly higher rates in the ILR group compared with the control group (31.8% vs. 12.2%), and oral anticoagulation was initiated at similarly higher rates (29.7% vs. 13.1%), most within the first month of AF diagnosis. More ILR patients who started anticoagulation for AF eventually discontinued anticoagulation (5.8% vs. 3.6%).The primary outcome of stroke or systemic embolism occurred less frequently in the ILR group (0.88 events per 100 person-years) than the control group (1.09 events per 100 person-years), but these differences were not statistically significant. Neither cardiovascular death rates nor all-cause mortality rates were significantly different between groups. In subgroup analyses, ILR patients with systolic blood pressure in the highest tertial (≥ 157 mmHg) demonstrated significantly lower rates of stroke or systemic embolism than control patients (3.46% vs. 6.74%; HR, 0.51; 95% CI, 0.31-0.83). Similar differences were not seen for patients with lower blood pressure. Rates of major bleeding, hemorrhagic stroke, and traumatic intracranial hemorrhage were not significantly different between groups. The authors concluded long-term ECG monitoring with an ILR resulted in significantly higher rates of AF detection and ensuing anticoagulation, but no significant decrease in the risk of stroke or systemic embolism by 5.4 years of follow-up.

■ COMMENTARY

The relationship between AF and risk of stroke or systemic embolism is well established but complex. Longer episodes of AF (> 23.5 hours) have been shown to be associated with higher risk than shorter episodes, although even shorter episodes may portend significant risk in patients with higher CHA_2DS_2-VASc scores. Not all cardioembolic strokes occur at or near the time of an AF episode, and not all strokes in patients with AF are caused by cardiac thromboembolism. Anticoagulation to prevent thromboembolism might increase the risk of hemorrhagic stroke. All these factors make it difficult to predict the benefits of intensive arrhythmia monitoring in asymptomatic patients, or when anticoagulation is warranted, questions that may become increasingly important as more patients turn to commercially available wearable monitoring devices like smartwatches. However, the LOOP study offers both a great deal of useful information and new hypotheses to test.

Loop recorders are a safe way to continuously monitor for AF long-term. In 1,420 patients with the device implanted, the ILR was explanted for complications in only nine (eight of whom received a new device). Higher rates of anticoagulation in this patient population were not associated with significantly more bleeding complications over almost six years. That is not to say therapeutic anticoagulation could not have led to some episodes of intracranial bleeding, but that feared event did not occur more often in the ILR group.

More aggressive monitoring, and the ensuing increase in anticoagulation rates, did not result in significantly lower rates of stroke or systemic embolism over six years. However, the event curves did appear to start separating at two to three years follow-up, and they continued to separate thereafter. Only 16.4% of participants were followed for the primary outcome at year 6, necessitating caution in interpretation. But it is not unreasonable to think a larger study or longer follow-up could have led to a different conclusion. Additionally, several factors may have biased outcomes against the ILR group. First, it is possible there was a lower average burden of AF (and lower overall stroke risk) in anticoagulated patients in the ILR group, if longer and/or more frequent episodes were required for AF detection in the control group. It also is possible AF was detected more often with "usual care" than might otherwise be expected, given participation in a clinical trial and higher awareness of AF.

AF is a cause of stroke and a marker of stroke risk. Of the 67 patients in the ILR group who recorded a primary outcome,

only 17 experienced an event after AF was first detected, 15 of whom were on anticoagulation. There was no temporal relationship between AF episodes and stroke. More severe hypertension may warrant higher vigilance for AF and more aggressive initiation of anticoagulation, a hypothesis generated from the compelling subgroup data. Anticoagulation for AF will warrant a risk-benefit discussion and shared decision-making with patients. In my own practice, I still recommend anticoagulation for AF episodes longer than six minutes with higher CHA_2DS_2-VASc scores when a direct-acting oral anticoagulant is an option. In the absence of symptoms, I would not advocate for routine ILR monitoring. However, I may suggest a higher level of vigilance for patients with more severe hypertension. ■

ABSTRACT & COMMENTARY

Coronary CT Angiography in the General Population

By Michael H. Crawford, MD, Editor

SYNOPSIS: Coronary artery CT angiography in asymptomatic, middle-aged subjects without known coronary artery disease showed coronary atherosclerosis is common but mostly mild and appears in women after a 10-year delay.

SOURCE: Bergström G, Persson M, Adiels M, et al. Prevalence of subclinical coronary artery atherosclerosis in the general population. *Circulation* 2021;144:916-929.

The prevalence of coronary artery atherosclerosis (CAA) in the general population without suggestive symptoms or apparent disease is unknown. Still, determining this status is important for prevention. Coronary artery calcium (CAC) scores often are used to detect CAA, but for symptomatic patients, coronary artery CT angiography (CCTA) could provide a more accurate assessment of CAA. The authors of the Swedish CArdioPulmonary BioImage Study (SCAPIS) sought to determine if this is true for an asymptomatic general population without known coronary artery disease (CAD).

Between 2013 and 2018, Bergström et al randomly recruited more than 30,000 participants ages 50-64 years. Subjects were excluded if there was known CAD or if CT exams were technically insufficient. Researchers obtained Agatston CAC scores and CCTAs. The main challenge to CCTA is defining the level of obstruction of calcified plaques. When investigators encountered so-called calcium blooming artifact, the lesion was graded as 1% to 49% stenosis, since calcium blooming tends to overestimate the severity of obstruction. The authors assessed each patient's risk factor burden and calculated various risk scores. After applying the exclusion criteria, 25,182 subjects were included in the initial analysis: 49% men, mean age 57 years.

Researchers found detectable CAA in 42% of subjects, and 5% had a significant stenosis (> 50%). Severe CAA of the left main, proximal left anterior descending (LAD), or three-vessel, disease was less common (2%). The proximal LAD was the most commonly affected vessel. The delay in disease onset between men and women was about 10 years. The prevalence of CAA increased with higher risk factor scores. Subjects with only non-calcified plaques were unusual (2.4%). A mix of calcified and non-calcified plaques occurred in 8%. CAC-positive subjects followed a similar pattern, with 40% of the subjects testing positive and the severity paralleling the CAC score.

Among subjects with a CAC score > 400, 46% showed significant stenoses. In those with a CAC of 0, 5.5% exhibited CAA and 0.4% significant stenoses. In those with CAC scores of 0 and an intermediate risk profile, 9% showed CAA. A few patients with low CAC scores (1-10) did not exhibit CAA on CCTA. The authors concluded that in this random sample of the general population of Sweden, silent CAD by CCTA was common. Those with high CAC scores carried a high probability of significant stenoses. A CAC score of 0 did not exclude CAA, especially if subjects were at higher clinical risk.

■ COMMENTARY

This is the first article published about SCAPIS, a nationwide, randomized, population-based cohort where half the people asked to participate enrolled. Although one cannot exclude some selection bias, their characteristics were close to those of the general population and similar to other developed countries with largely white populations. Thus, the findings likely are widely applicable. SCAPIS consisted of an asymptomatic, middle-aged population, with the expected slight predominance of women and no history of CAD.

Overall, there were three major findings. First, 42% of subjects showed evidence of silent CAD. Significant stenoses (> 50%) were found in 5% of subjects (2% of cases were severe). Second, there was a 10-year delay in the onset and severity of CAA in women compared to men. Also, the distribution of CAA was identical between the sexes after accounting for the delay in women. Third, CAA detected by CCTA was associated with risk factor scores and the CAC score, but there were significant subgroups where CAC and risk scores were inaccurate. For example, among those with low risk-based scores, one-third of men and one-quarter of women had CAA. Likewise, in those with CAC scores of 0 to 10, 22% of women and 30% of men had CAA. Thus, using risk equations or CAC to determine whom among those with intermediate risk should start statin therapy is problematic, especially since the benefit of statins in such patients is uncertain.

There were some limitations to this investigation. This was a cross-sectional study, so there are no data on the progression of disease or outcomes. Also, those interpreting the CT scans saw both the CAC scores and the CCTA results, which could have biased their interpretations. Determining percent obstruction in heavily calcified lesions is problematic, too. Their assumption that heavy calcification overestimates the degree of obstruction may not be justified in all cases. The big issue with a study like this is whether CCTA is worth the expense for screening populations. The answer to this question may be forthcoming, since trials to assess the value of risk formulae vs. CCTA on outcomes are in progress. ■

ABSTRACT & COMMENTARY

Importance of Age in the Application of Coronary Artery Calcium Detection

By Michael H. Crawford, MD, Editor

SYNOPSIS: Using coronary CT strategy as a diagnostic first line in patients with symptoms suggestive of coronary artery obstruction revealed relying on the coronary calcium score alone is inadequate for younger patients with a higher frequency of non-calcified obstructions.

SOURCE: Mortensen MB, Gaur S, Frimmer A, et al. Association of age with the diagnostic value of coronary artery calcium score for ruling out coronary stenosis in symptomatic patients. *JAMA Cardiol* 2021; Oct 27. doi: 10.1001/jamacardio.2021.4406. [Online ahead of print].

Although a coronary artery calcium (CAC) score of 0 is associated with a low likelihood of obstructive coronary artery disease (CAD), that does not mean risk is nonexistent. Since early coronary plaques may not be calcified, the relationship between CAC and obstructive disease may be age-related. Investigators from the Western Denmark Heart Registry used data about consecutive real-world patients who exhibited symptoms suggestive of CAD and underwent coronary calcium scoring followed by CT angiography (CTA) to test this association.

In Western Denmark, CTA is a first-line diagnostic test for non-emergency patients with suspected obstructive CAD. For this analysis, Mortensen et al included all patients older than age 18 years who underwent CTA between 2008 and 2017. Only patients with inconclusive test results, missing results, or a history of known CAD were excluded. The authors obtained clinical data from the Danish National Patient Registry. They categorized the severity of CAD as none (0% luminal stenosis and Agatston score of 0), nonobstructive (1% to 49% stenosis), or obstructive (> 49%). The primary endpoint was myocardial infarction and all-cause death. All analyses were corrected either for age and sex or age, sex, smoking, diabetes, and symptom characteristics.

Among the study cohort of 23,759 patients (45% men, mean age = 58 years), 54% recorded a CAC score of 0. The prevalence of obstructive CAD in patients with a CAC score of 0 in the overall population was 6%. In those younger than age 40 years, it was 3%; age 40-49 years, it was 5%; age 50-59 years, it was 6%; age 60-69 years, it was 6%; and older than age 70 years, it was 8%. Overall, 14% of patients with obstructive CAD recorded a CAC score of 0; percentages declined with age: 58% in those younger than age 40 years, 34% in those age 40-49 years, 18% in those age 50-59 years, 9% in those age 60-69 years, and 5% in those age 70 years or older. Although the distribution by age was similar, overall women with obstructive CAD more often recorded a CAC of 0.

The overall diagnostic value of a CAC score of 0 for excluding obstructive CAD was a 63% lower

likelihood than expected based on other clinical characteristics. However, this varied across different age groups, ranging from 32% in those younger than age 40 years to 82% in those age 70 years and older. This effect was more pronounced in women younger than age 40 years (18% vs. 41% in men younger than age 40 years). During the mean follow-up of four years, the primary outcome occurred in 31% of patients with a CAC score of 0, with an adjusted multivariable hazard ratio (HR) of 1.51 (95% CI, 0.98-2.33). The HR varied with age, from 1.80 in those younger than age 60 years to 1.24 in those older than age 60 years. The authors concluded the diagnostic value of a CAC score of 0 varied with age. There was less value in younger patients with symptoms suggestive of obstructive CAD. Those younger than age 60 years with a CAC score of 0 made up a large proportion of those experiencing the primary endpoint.

■ COMMENTARY

Because of the logistical issues surrounding stress testing, many chest pain units have moved to using CTA to diagnose obstructive CAD. However, when coronary calcium is present, CTA becomes less accurate for detecting stenoses. Thus, CTA often is preferentially directed at younger patients who are less likely to exhibit significant calcium. In fact, many younger patients will show no detectable coronary calcium. The risk of obstructive CAD in such patients is low, but it is not zero.

Mortensen et al hypothesized the diagnostic value of the CAC score would be age-related, based on the pathophysiology of atherosclerosis wherein calcium deposition is a later manifestation of coronary plaques. In this study, a CAC score of 0 was more common in younger patients, especially women (55%). The prevalence of obstructive CAD in those with a CAC score of 0 was low, ranging from 3% in those younger than age 40 years to 8% in those older than age 70 years. However, in those with obstructive CAD, 14% overall recorded a CAC score of 0; the proportion was higher in younger patients (58% in those younger than age 40 years vs. 5% in those older than age 70 years). Consequently, the diagnostic value of a CAC score of 0 was less in younger patients and women. Although the overall risk of the combined primary outcome of myocardial infarction or all-cause mortality was low in patients with a CAC score of 0 (< 1%), one out of three events occurred in patients with a CAC score of 0. Thus, CTA is necessary in younger patients with symptoms suggestive of CAD, since relying on the CAC score alone is problematic.

There were weaknesses in this investigation. A referral bias to CT scan cannot be excluded, but this was the recommended approach in Denmark. This was a relatively low-risk population (less than 1% experienced the primary outcome). More importantly, the authors observed changes in management based on the CT scans, but those changes were not considered in the analyses. Also, researchers did not consider the severity of calcium deposition. Nevertheless, this was a large, real-world study, with baseline characteristics representative of everyday practice patients. ■

ABSTRACT & COMMENTARY

Long-Term Post-TAVR Survival and Permanent Pacemaker Implantation

By Jeffrey Zimmet, MD, PhD

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

SYNOPSIS: An analysis of a real-world database revealed 14% of patients undergoing routine transfemoral transcatheter aortic valve replacement required permanent pacemaker implantation within 30 days of the valve procedure. There was no difference in long-term survival between patients who did and did not undergo pacemaker implant.

SOURCE: Rück A, Saleh N, Glaser N. Outcomes following permanent pacemaker implantation after transcatheter aortic valve replacement: SWEDEHEART observational study. *JACC Cardiovasc Interv* 2021;14:2173-2181.

Transcatheter aortic valve replacement (TAVR) has expanded dramatically over the past decade. This procedure was limited to patients who were at prohibitive or high risk of surgical complications, and primarily involved patients of advanced age with significant comorbidities. As TAVR has expanded to younger and lower-risk patients, it has become increasingly important to understand the differences in outcomes between surgical AVR and TAVR. Mechanical pressure from

the TAVR valve itself, along with inflammation following valve deployment, results in an increased risk of high-grade atrioventricular block requiring permanent pacemaker implantation following TAVR. The ventricular desynchrony induced by right ventricular pacing has been associated with higher rates of atrial fibrillation, reduced ejection fraction, and clinical heart failure. The effect of this higher pacemaker risk on longer-term outcomes after valve replacement is uncertain. Rück et al examined the records of all patients who underwent transfemoral TAVR in Sweden between 2008 and 2018, using the SWEDEHEART registry. Of 4,750 TAVR patients during this period, the authors excluded those with non-transfemoral access (581 patients), those with preoperative permanent pacemakers (465 patients), and those who underwent valve-in-valve procedures (160 patients). A total of 124 patients who died within 30 days of the procedure also were excluded. This left 3,420 patients for analysis.

From this group, 481 underwent permanent pacemaker implantation within 30 days after TAVR. The mean age of the study population was 81 years, and half were women. Patients who received pacemakers were more likely to be men and recorded a higher prevalence of atrial fibrillation, diabetes, prior MI, and prior cardiac surgery. Balloon-expandable valves were used less frequently in patients who received pacemakers vs. those who did not. During a median follow-up of 2.7 years (interquartile range = 2.5 years; maximum = 11.8 years), there was not a significant difference in survival between those patients who received pacemakers and those who did not. The survival rates at one, five, and 10 years were 90.1%, 52.7%, and 10.9% in the pacemaker group and 92.7%, 53.8%, and 15.3% in the non-pacemaker group, respectively. Similarly, there was no significant difference in cardiovascular death between groups.

The incidence of endocarditis was not different in the pacemaker and no pacemaker groups (2.9% and 2.6%, respectively). Heart failure hospitalization was numerically higher in the pacemaker group (15%) than in the non-pacemaker group (9.3%), but this did not meet statistical significance (HR, 1.23; 95% CI, 0.92-1.63; $P = 0.157$).

The authors did not find a difference in long-term survival between patients who did and did not require permanent pacemaker implantation after TAVR.

■ COMMENTARY

Much of the editorial commentary regarding this study centers on the term "reassuring." That is, the lack of a signal for higher long-term mortality rates among patients who required pacemaker implantation post-TAVR gives reassurance these patients are not experiencing harm.

One of the more illuminating comparisons comes from a previous publication from the same research group, which found permanent pacemaker implantation after surgical AVR was associated with a higher risk for heart failure hospitalization and all-cause mortality.[1] The major difference here, as Rück et al noted, is surgical AVR patients historically are younger and present with fewer comorbidities vs. TAVR patients. Those undergoing TAVR during the examined period likely died of other causes before the full detrimental effects of permanent pacing become fully evident, at least in terms of hard outcomes, including death and congestive heart failure hospitalization. For these patients, the results of the Rück et al study are reassuring.

There is no mystery when it comes to the negative effects of long-term right ventricular pacing. The question Rück et al hoped to answer concerned the potential deleterious effects of permanent pacing in patients who are younger and with longer life expectancy. For this group, the study adds little. These are the patients in whom TAVR is increasingly applied and for whom the decision between surgical AVR and TAVR will need to consider not only the relative morbidity of the surgery and longevity of

the implant, but also the persistent difference in post-implant pacemaker requirement that is likely to remain in surgery's favor. We are certain to see more discussion of this issue in the future, as more contemporary data become available. ■

REFERENCE

1. Glaser N, Persson M, Dalén M, Sartipy U. Long-term outcomes associated with permanent pacemaker implantation after surgical aortic valve replacement. *JAMA Netw Open* 2021;4:e2116564.

ABSTRACT & COMMENTARY

Left-Sided Breast Cancer Radiation Therapy and Coronary Artery Disease

By Michael H. Crawford, MD, Editor

SYNOPSIS: A study of breast cancer survivors revealed left breast radiation therapy doubles the subsequent risk of coronary heart disease vs. right-sided radiation.

SOURCE: Carlson LE, Watt GP, Tonorezos ES, et al. Coronary artery disease in young women after radiation therapy for breast cancer. *JACC CardioOncol* 2021;3:381-392.

Although radiation therapy is known to increase the risk of developing cardiovascular disease in older patients (older than age 50 years) with breast cancer, little is known about its effects in younger women. Researchers from the Women's Environmental Cancer and Radiation Epidemiology (WECARE) follow-up study described the self-reported incidence of cardiovascular disease in younger women diagnosed with breast cancer in relation to the treatment they received and lifestyle factors.

WECARE was a population-based study of women diagnosed with stage I or II breast cancer before age 55 years between 1985 and 2008 from five medical centers (three in in the United States and one each in Denmark and Canada). Data were collected from medical record abstraction and structured phone interviews conducted between 2013 and 2015 among living women from the study. From the total population of 2,342 women contacted, participants were excluded if they did not complete the questionnaire, declined to participate, did not undergo radiation therapy, or had a history of cardiovascular (CV) disease before breast cancer diagnosis, resulting in the final study population of 972 women. The follow-up time was defined as the time from breast cancer diagnosis until the diagnosis of a second primary cancer, breast cancer recurrence or metastasis, or the end of the prescribed follow-up. The average radiation dose was 55 Gy (range was 45 Gy to 65 Gy) and did not differ by laterality. The primary endpoint was the development of CV disease in right vs. left breast radiation therapy patients. Adjustments were made for baseline lifestyle and CV risk factors. Lifestyle and risk factors for CV disease were evenly distributed between the 48% who underwent left-sided radiation and the 52% who underwent right-sided treatment. The median age of breast cancer diagnosis was 46 years and the median follow-up was 14 years (range = one year to 29 years). Most patients were white, and two-thirds had stage I cancer. Adjuvant chemotherapy was administered in 60% (half of that was an anthracycline). Less than half underwent hormone therapy.

After a five-year latency period, the incidence of coronary artery disease (CAD) increased more in those who underwent left-sided vs. right-sided radiation therapy (adjusted HR, 2.5; 95% CI, 1.3-4.7; $P = 0.01$). The overall cumulative incidence of CAD after 27.5 years was 10.5% for left-sided radiation and 5.8% for right-sided ($P = 0.01$). There was no interaction with baseline risk factors or lifestyle that reached statistical significance. Also, CAD risk was not modified by chemotherapy or hormone therapy. The authors concluded the risk of CAD in women with breast cancer who underwent left-sided radiation therapy was twice that of women who underwent right-sided therapy. This risk was independent of other risk factors and should be considered in the management of breast cancer survivors.

■ COMMENTARY

About half of women with breast cancer receive radiation therapy as part of a breast-conserving strategy. For women younger than age 50 years with stage I or II breast cancer, there is ample time to develop CV disease. Any treatments that affect the development of CV disease would be of importance, especially in younger women who generally are at low risk for CV disease. Thus, this study of the

effects of radiation therapy on the risk of CAD in younger women with breast cancer is of interest. Rather than studying women who did or did not receive radiation therapy, which could have led to selection bias, Carlson et al chose to study the laterality of therapy in those who did undergo radiation. Left-sided breast radiation delivers an average of 3.7 Gy more radiation to the heart compared to right-sided therapy, creating a natural randomized experiment. The authors demonstrated that left-sided radiation therapy was an independent risk factor for CAD in women with breast cancer diagnosed before age 55 years.

In the WECARE study, the incidence of CAD in those ages 25-39 years who received right-sided radiation therapy was zero. In those ages 40-54 years, the incidence was 5.9% over 28 years of follow-up. Also, at less than five years of follow-up in WECARE, the incidence of CAD was 9%. This is a long-term concern for breast cancer survivors. In addition, lifestyle, other CAD risk factors, and adjuvant therapies did not alter the results, which emphasizes the fact radiation therapy is an independent factor.

WECARE included a relatively large study population, and the follow-up period was long. However, there was no cardiac dosimetry, so the authors used laterality as a substitute, which is reasonable. Also, there are no data on the use of heart-sparing techniques, such as prone positioning. CAD was self-reported and not verified, but the Danish group conducted a validation study, finding 80% agreement between self-reporting and the clinical record. In addition, laterality would not affect any reporting errors. Finally, there may be a selection bias in those who agreed to the study vs. those who did not. Left-sided radiation therapy should be added to the risk factors when it comes to protecting the CV health of breast cancer patients. ■

CME/CE QUESTIONS

1. **What raises the risk of coronary artery disease in survivors of breast cancer?**
   a. Anthracycline chemotherapy
   b. Radiation therapy to the left breast
   c. Hormone therapy
   d. Breast removal surgery

2. **Transcatheter aortic valve replacement patients who received a pacemaker recorded a higher prevalence of:**
   a. happiness.
   b. balloon-expandable valves deployed.
   c. mortality.
   d. atrial fibrillation.

3. **Deploying an implantable loop recorder in patients at risk for atrial fibrillation compared to a control group showed:**
   a. more atrial fibrillation detection.
   b. lower mortality.
   c. fewer strokes.
   d. more major bleeding.

4. **A study of coronary CT studies as a first-line approach in patients with non-emergency symptoms suggestive of coronary artery disease showed that a coronary artery calcium score of 0:**
   a. completely excluded obstructive disease.
   b. was less common in younger patients.
   c. was of less diagnostic value in younger patients.
   d. was less common in women.

5. **A study of coronary CT angiography in middle-aged asymptomatic subjects showed coronary atherosclerotic lesions were present in about what percentage?**
   a. 10%
   b. 20%
   c. 40%
   d. 60%