1) AUTOMATIC QUANTIFICATION OF CORONARY ARTERY CALCIFICATIONS ON RADIOTHERAPY PLANNING CT IN PATIENTS WITH BREAST CANCER

Abstract

Importance Cardiovascular disease (CVD) is common in patients treated for breast cancer, especially in patients treated with systemic treatment and radiotherapy and in those with preexisting CVD risk factors. Coronary artery calcium (CAC), a strong independent CVD risk factor, can be automatically quantified on radiotherapy planning computed tomography (CT) scans and may help identify patients at increased CVD risk.

Objective To evaluate the association of CAC with CVD and coronary artery disease (CAD) in patients with breast cancer.

Design, Setting, and Participants In this multicenter cohort study of 15,915 patients with breast cancer receiving radiotherapy between 2005 and 2016 who were followed until December 31, 2018, age, calendar year, and treatment-adjusted Cox proportional hazard models were used to evaluate the association of CAC with CVD and CAD.

Exposures Overall CAC scores were automatically extracted from planning CT scans using a deep learning algorithm. Patients were classified into Agatston risk categories (0, 1-10, 11-100, 101-399, >400 units).

Main Outcomes and Measures Occurrence of fatal and nonfatal CVD and CAD were obtained from national registries.

Results Of the 15,915 participants included in this study, the mean (SD) age at CT scan was 59.0 (11.2; range, 22-95) years, and 15,879 (99.8%) were women. Seventy percent (n = 11,179) had no CAC. Coronary artery calcium scores of 1 to 10, 11 to 100, 101 to 400, and greater than 400 were present in 10.0% (n = 1,584), 11.5% (n = 1,825), 5.2% (n = 830), and 3.1% (n = 497) respectively. After a median follow-up of 51.2 months, CVD risks increased from 5.2% in patients with no CAC to 28.2% in patients with CAC scores higher than 400. After adjustment, CVD risk increased with higher CAC score (hazard ratio [HR] CAC<1-10 = 1.1; 95% CI, 0.9-1.4; HR CAC=11-100 = 1.8; 95% CI, 1.5-2.1; HR CAC=101-400 = 2.1; 95% CI, 1.7-2.6; and HR CAC>400 = 3.4; 95% CI, 2.8-4.2). Coronary artery calcium was particularly strongly associated with CAD (HR CAC>400 = 7.8; 95% CI, 5.5-11.2). The association between CAC and CVD was strongest in patients treated with anthracyclines (HR CAC=400 = 5.8; 95% CI, 3.0-11.4) and patients who received a radiation boost (HR CAC=400 = 6.1; 95% CI, 3.8-9.7).

Conclusions and Relevance This cohort study found that coronary artery calcium on breast cancer radiotherapy planning CT scan results was associated with CVD, especially CAD. Automated CAC scoring on radiotherapy planning CT scans may be used as a fast and low-cost tool to identify patients with breast cancer at increased risk of CVD, allowing implementing CVD risk-mitigating strategies with the aim to reduce the risk of CVD burden after breast cancer.

2) WOMEN AND TOBACCO, A GENDER PERSPECTIVE

Epidemiology

Globally, 942 million men and 175 million women aged 15 or older are current smokers. Nearly three quarters of male daily smokers live in countries with a medium or high human development index (HDI), whereas half of female daily smokers live in countries with a very high HDI [1].

Among the World Health Organization (WHO) regions, Europe has the highest prevalence of tobacco smoking among adults (28%) and some of the highest prevalence of tobacco use by adolescents. Moreover, Europe has one of the highest proportions of deaths attributable to tobacco use. The WHO has estimated that 16% of all deaths in adults over 30 in Europe are related to tobacco consumption. Even though tobacco use has been a predominantly male phenomenon for decades, the prevalence of cigarette smoking among women has increased worldwide in recent years and the gender gap has been substantially reduced in countries such as Greece, Denmark, Ireland, the Netherlands, Norway, Sweden and the United Kingdom. Although tobacco use among women is now decreasing overall, it is dropping at a much slower rate than in men and is still increasing in some areas of the European region.
Based on the WHO global report on trends in prevalence of tobacco use 2000-2025, in 2018 the prevalence for European women was 19%, the highest in the world, whereas the global rate was 9%. Even if women’s prevalence has declined in Europe from 23% in 2000, it is expected to sit at around 18% in 2025 [2], which is still a concerning picture. Tobacco consumption in women is very influenced by the socioeconomic status, with a higher prevalence in high-income countries.

According to the World Bank Report, the prevalence of smoking among women in countries with high income is 16.1%, compared to 2% in low-income countries. The lower prevalence of tobacco use in women in regions with a low HDI has offered a window of opportunity to the tobacco industry to tailor its marketing efforts in this direction. Of the 8.71 million annual tobacco deaths, 2.15 million are women (2019) [3], 71% of whom live in low- and middle-income countries [4].


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All= sum of regional totals; Differences are due to rounding.

There is a 30-year gap between peak tobacco use and peak tobacco-related mortality. As women’s uptake of tobacco has occurred later in the tobacco epidemic, the surge in tobacco-related female deaths has also occurred later than for male deaths. This perspective offers a relevant public health concern in many societies where the prevalence of female smoking is still rising [5].

Health effects of smoking in women

Tobacco use promotes exposure to a lethal mixture of more than 7,000 toxic chemicals, including at least 70 known carcinogens which can cause damage to nearly every organ system in the human body [1]. The risk of death and disease rises with the number of cigarettes smoked, but even low consumption can also cause significant damage.

Beyond increasing the risk of the same diseases as in men, smoking in women carries the risk of several gender-specific conditions such as cervical cancer, osteoporosis, fertility impairment, and premature menopause. The risk of preterm birth is increased in women who smoke before and during pregnancy, as is the risk of abnormal foetal growth, low birth weight, miscarriage, and foetal death [6]. Despite these well-known risks, smoking during pregnancy remains the leading cause of poor pregnancy outcome and prenatal death.

Globally, more than 50% of women who smoke daily continue doing so during pregnancy [7]. Persistent smoking behaviour in pregnant women is strongly associated with social health factors such as a young age, a lower socioeconomic status or a lower level of education [8].

An important body of evidence shows that smoking does not affect men and women equally when considering cardiovascular and lung diseases. The relative risk of lung cancer is significantly higher in women who smoke compared to male smokers [9]. Lung cancer is the leading cause of cancer death among men and, in many countries, it has also become the leading cause of cancer death in women, exceeding breast cancer [1].

Women who smoke also have a markedly increased risk of cancers of the mouth, pharynx, oesophagus, larynx, bladder, pancreas, and kidney. The risk of cervical cancer has also been shown to be higher in female smokers than in female non-smokers [10].
The worldwide prevalence of chronic obstructive pulmonary disease (COPD) has increased steadily in recent decades, with a greater rise in women than in men. A growing body of evidence suggests that female smokers are more likely to develop COPD than male smokers [11]. Women seem to be more vulnerable to lung function impairment and develop COPD at a younger age for a given amount of tobacco consumption [12].

Smoking is a more potent risk factor for cardiovascular disease in women. In a meta-analysis of 2.4 million subjects, cigarette smoking was found to confer a 25% increase in the risk for coronary artery disease in women compared with men [13]. Furthermore, oral contraceptive users who are current smokers have a tenfold increased risk of myocardial infarction and a threefold increased risk of stroke [14].

Other associated factors such as a sedentary lifestyle and obesity can increase the cardiovascular impact of smoking in women.

**Electronic cigarettes and novel tobacco products**

The rapidly evolving marketplace of vaping products has represented a challenge to the regulation capacity of different countries. The popularity of these products has been supported by strong marketing, targeted particularly to women and adolescents [15]. Flavourings that are currently banned in conventional cigarettes may be used to attract new young consumers who are prone to experimentation and risk-taking behaviour, facilitating the progression to regular use of e-cigarettes or other tobacco-related products.

While there is still a burning debate concerning the role of electronic nicotine delivery systems (ENDS) as a harm reduction strategy in adult smokers, from the public health perspective the main concern is that ENDS could be a gateway to nicotine addiction, particularly in adolescents [16,17]. E-cigarette use has recently been associated with the outbreak of e-cigarette or vaping product use-associated lung injury (EVALI) in the USA in 2019, with a particular impact on young e-cigarette users [18]. In any case, the long-term effects of e-cigarettes have not been established, while these products lack strict regulation in many countries and are often promoted as “socially acceptable” and “reduced-risk alternatives”.

Different “heat-not-burn” tobacco products have rapidly gained a market in recent years as the result of an aggressive promotion campaign from the tobacco industry, targeting particularly women and young consumers, and trying to evade conventional tobacco regulation. The devices heat processed tobacco in a controlled fashion instead of combusting it. As they contain tobacco, these products are hazardous and likely to be more harmful than e-cigarettes, and they lack reliable evidence of any harm reduction effect. Nevertheless, they are marketed as “less harmful”, a strategy fraught with dangers of youth uptake, unproven long-term impact, and the potential to mislead their potential users [19].

**Second-hand smoke**

Second-hand smoke (SHS) is the combination of smoke from the burning end of a cigarette and the smoke breathed out by smokers. SHS contains more than 7,000 chemicals, of which hundreds are toxic and about 70 can cause cancer [10]. Exposure to SHS is associated with a large number of adverse health effects and causes substantial mortality and morbidity globally.

SHS causes the death of 600,000 women every year, and 64% of annual SHS-related deaths are of women [3]. SHS can cause coronary disease, stroke, lung cancer, COPD, and reproductive effects in women such as low birth weight. SHS has also been related to sudden infant death syndrome, asthma, impaired lung function, lower respiratory illness and middle ear disease in children [10].

Lower socioeconomic groups and non-smoking women show higher exposure to SHS. It is estimated that SHS causes more deaths in women than in men globally (573,000 vs 311,000 in 2016). Homes are the main place of exposure to SHS for women and children in many populations. Therefore, regulation and preventive campaigns focusing on exposure inside the home are of paramount importance in order to reduce the burden of SHS [1].

**Barriers to smoking cessation in women**

One of the reasons for smoking in women has been the aggressive explicit or implicit promotion of tobacco products focused particularly on women over the past century. Despite the regulatory efforts in high-income countries, advertising continues in low-income countries, where female smoking rates are still low.

Stereotypical attractive qualities such as freedom, sophistication, self-determination, glamour, or slimness have been widely used to attract women or adolescent girls. Trying to elude the tobacco
marketing and promotion regulation in developed countries, tobacco companies still use other platforms available such as social media, cinema or women influencers. Exposure to tobacco in films is strongly related to tobacco uptake among young people, and it is a subtle and difficult to combat means of promotion of tobacco use [20]. Female characters who smoke are often shown as attractive, fashionable, provocative, cool and of high social status. This form of promotion is particularly concerning as it contributes to normalise smoking in different situations of daily life. Packaging and cigarette design can also be considered as marketing tools that have been widely used by the tobacco industry to target particular profiles of consumers. Super-slim and lipstick-style cigarette packs created a misleading perception of harm reduction in female smokers [21]. The adoption of plain packaging offers a relevant opportunity to remove this promotional strategy.

The strong addictive capacity of nicotine and the faster capacity to metabolise nicotine in women make women more prone to becoming hooked on tobacco [22]. Moreover, risk awareness is lower in women than in men and women have less success at quitting [23]. Women are likely to continue smoking due to a fear of weight gain.

The solutions

Effective tobacco control is of paramount importance in order to improve health and reduce disparities at the population level in all countries. Tobacco product taxation is an effective way to reduce tobacco use rates, and one of the most powerful measures in preventing tobacco consumption by adolescents [24].

Creating smoke-free environments is also vital in tobacco control.

Smoking bans protect non-smokers from the harmful effects of SHS and facilitate the progressive denormalisation of tobacco consumption, by reinforcing the idea of non-smoking as a societal norm.

Electronic cigarettes and novel tobacco products should not undermine tobacco control efforts, and thus require an updated and proper regulation.

Public health campaigns with a focus on preventing smoking among young people should be gender-sensitive, as the reasons for starting smoking differ between boys and girls, girls being more affected by the desire to control weight or by a positive image of smoking.

Tobacco cessation is a cost-effective healthcare intervention [10]. More quitting and less initiation of tobacco use contributes to greater individual and societal well-being. Governments and healthcare providers should make available more and accessible resources to help tobacco users stop. These interventions should be able to tackle women and adolescents from a specific perspective, taking into account the particular characteristics of nicotine addiction in these populations.

The younger someone is when he/she stops smoking, the greater the benefit in terms of health gains and mortality reduction. Pregnancy is a particular teachable moment to start a smoking cessation intervention in women and their partners. Smoking cessation in pregnant women has been associated with improvements in outcomes including better foetal growth and fewer preterm deliveries, and it can avoid subsequent risks to the child. Quitting smoking is also one of the best natural ways to boost fertility in both women and men [8, 10].

Conclusions

Tobacco causes an enormous health, social, economic, and developmental burden. Consistent with lower female smoking prevalence in many countries, the tobacco-related burden in women is lower than in men globally. However, recent increases in smoking prevalence among females, particularly in developing countries, might change this pattern.

- Female smokers are more vulnerable to some smoking-related pathologies than their counterparts.
- In addition to the harm caused directly by smoking, many women die because of involuntary exposure to second-hand smoke.
- Gender-specific action is needed to raise awareness of the impact of tobacco on women’s health and to tackle smoking cessation in women.

Tobacco control needs to counteract the gender-specific messaging transmitted by the tobacco industry that still tries to promote the use of tobacco and tobacco-related products by women.
3) PREVENTION OF CARDIAC DYSFUNCTION DURING ADJUVANT BREAST CANCER THERAPY

Abstract

Background:

Adjuvant breast cancer therapy containing anthracyclines with or without anti-human epidermal growth factor receptor-2 antibodies and radiotherapy is associated with cancer treatment–related cardiac dysfunction. In the PRADA trial (Prevention of Cardiac Dysfunction During Adjuvant Breast Cancer Therapy), concomitant treatment with the angiotensin receptor blocker candesartan attenuated the reduction in left ventricular ejection fraction (LVEF) in women receiving treatment for breast cancer, whereas the β-blocker metoprolol attenuated the increase in cardiac troponins. This study aimed to assess the long-term effects of candesartan and metoprolol or their combination to prevent a reduction in cardiac function and myocardial injury.

Methods:

In this 2×2 factorial, randomized, placebo-controlled, double-blind, single-center trial, patients with early breast cancer were assigned to concomitant treatment with candesartan cilexetil, metoprolol succinate, or matching placebos. Target doses were 32 and 100 mg, respectively. Study drugs were discontinued after adjuvant therapy. All 120 validly randomized patients were included in the intention-to-treat analysis. The primary outcome measure was change in LVEF assessed by cardiovascular magnetic resonance imaging from baseline to extended follow-up. Secondary outcome measures included changes in left ventricular volumes, echocardiographic peak global longitudinal strain, and circulating cardiac troponin concentrations.

Results:

A small decline in LVEF but no significant between-group differences were observed from baseline to extended follow-up, at a median of 23 months (interquartile range, 21 to 28 months) after randomization (candesartan, 1.7% [95% CI, 0.5 to 2.8]; no candesartan, 1.8% [95% CI, 0.6 to 3.0]; metoprolol, 1.6% [95% CI, 0.4 to 2.7]; no metoprolol, 1.9% [95% CI, 0.7 to 3.0]). Candesartan treatment during adjuvant therapy was associated with a significant reduction in left ventricular end-diastolic volume compared with the noncandesartan group (P=0.021) and attenuated decline in global longitudinal strain (P=0.046) at 2 years. No between-group differences in change in cardiac troponin I and T concentrations were observed.

Conclusions:

Anthracycline-containing adjuvant therapy for early breast cancer was associated with a decline in LVEF during extended follow-up. Candesartan during adjuvant therapy did not prevent reduction in LVEF at 2 years, but was associated with modest reduction in left ventricular end-diastolic volume and preserved global longitudinal strain. These results suggest that a broadly administered cardioprotective approach may not be required in most patients with early breast cancer without preexisting cardiovascular disease.

4) CAREER ADVICE FOR NURSING PROFESSIONALS

PracticeUpdate: What advice would you give nurses just starting their careers from your perspective as an oncology nurse?

Lillie Shockney: I think that television shows have steered nurses toward the emergency room and the ICU—what people will sometimes refer to as the "sexy" areas of a hospital. The ER is considered a very sexy area. Everything's fast, and life-threatening, and what I see on these TV shows is usually just that. A young woman in nursing school will think, "That's what I want to do." And I say, broaden your horizons, broaden them, because, quite frankly, when you're in the ER or you're in the ICU, you see a patient for a snapshot of time, and to really get the full experience of nursing, as I have, you need to pick up the patient at the point of diagnosis. I am with the patient across every phase of treatment into short- and long-term survivorship or into the end of life. That is incredibly rewarding.

People think that oncology is a sad area to work in. Maybe they don’t know that the majority of people are going to survive their cancer. (I personally am 29 years out from my first cancer.) It’s very satisfying to be able to celebrate with patients when they have finished their treatment, to be part of their extended family. To keep them on track for the milestones in their lives. To make sure that cancer takes away no more of them than is absolutely necessary.
We ask patients with advanced disease a series of questions. We may start with, "How much do you know about your cancer? How much do you want to know about your cancer?" Because, frankly, not everybody wants to know things. Some people want just-in-time information because it's just too overwhelming. And we ask, "What are you hoping for? What are you most worried about?" And, "Tell me three things that bring you joy." We want to preserve those three joys; that's really important. And, usually, we can in some way. Then, later, we ask her these questions again, because what she's hoping for and what she's most worried about are going to change over time.

I don't want people to see oncology as a depressing field because, believe you me, it's not. I would not ever have found as much joy as I have in my career if I had chosen to go into another field. I know it.

Practice Update: Why is work–life balance important to maintain for providers in this field?
Lillie Shockney: We do need work–life balance. I have a tendency to not practice what I preach, and I will admit that. However, we need to teach ourselves that we need to maintain a life outside of work. One of the ways to do that is to change clothes when you get home. If you’re going to stay in your scrubs, or whatever it is that you wear to work, you haven’t disconnected from work, you still look like you’re at work, and you might still feel like that you’re at work. Also set some boundaries on how available you think is realistic for you to be. If I give a patient my phone number, I say, "Please don’t call me on the weekends unless something really bad has happened and I need to get you into care somewhere. I try to hold my weekends for my family."

Also, it’s important that we find our own joy. I ask myself, “What am I hoping for today? What am I most worried about right now? And what are three things that bring me joy?” And I want to make sure that I am experiencing those three things. If I’m not, then I need to hit the pause button, “Okay, what am I doing that I’m losing those things?” It’s probably that I’m losing time, that I’ve shifted more time over to my patients and made less time for myself and my family. That doesn’t mean that the balance has to be 50/50, but you can’t devote all your time to work and have none for yourself and family because you’ll burn out, you will burn out, and then all those people who you could have helped and really done a phenomenal job in supporting will miss out.

Practice Update: You mentioned setting that boundary of emergency-only calls on the weekend. Do you have any other strategies for maintaining personal and professional commitments?
Lillie Shockney: I think it’s important that people have a calendar and plan events for themselves. "I want to go to the autumn festival." Make that happen. "I am going to take Tuesday off next week to go to school and see my grandson read a poem." If we don’t proactively add these things to our calendar, then we’ll let work take that time. We will; it happens. So, we have to be proactive for ourselves, and that’s not being selfish. I’m now 67 and, years ago, I thought it was being selfish; but, no, I’m preserving my mental health is what I’m doing. I cannot take good care of patients if I am not healthy, including emotionally healthy, myself. I’m going to let them down, and that’s not right; I have control over that.

5) MORE BLEEDING EVENTS AFTER PCI IN WOMEN WITH BASELINE RISK FACTORS

Baseline factors, such as older age and kidney impairment, increased bleeding risk for women compared with men who underwent percutaneous coronary intervention (PCI) and were treated with ticagrelor. Withdrawal of aspirin while continuing treatment with ticagrelor reduced bleeding events in both women and men, according to study results published in JAMA Cardiology.

In a prespecified secondary analysis of TWILIGHT, a placebo-controlled, randomized multicenter trial, the investigators sought to evaluate treatment outcomes associated with sex among patients treated with ticagrelor plus aspirin vs ticagrelor monotherapy. The primary endpoint for bleeding events was Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding; the primary endpoint for ischemic events was a composite of death, myocardial infarction, or stroke.

Researchers analyzed data from 7119 patients who underwent successful PCI with drug-eluting stents from 187 sites across 11 countries. Study participants had at least 1 clinical and 1 angiographic feature associated with a high risk of bleeding or ischemic events and were adherent to ticagrelor plus aspirin for 3 months postintervention.

Participants without any major adverse events were then randomly assigned to receive ticagrelor with aspirin (852 women, 2712 men) or ticagrelor with placebo (846 women, 2709 men) for 12 more months. Models were adjusted for baseline risk factors and confounding conditions, including age, race, region, smoking status, diabetes, anemia, hypertension, chronic kidney disease, previous PCI, and more.
Women made up 23.9% (1698) of the study population, and participants’ mean [SD] age was 63.9 [10.2] years. Compared with men, women were older (65.5 [9.6] years vs 63.4 [10.3] years) and more likely to be non-White. Women had a higher prevalence of insulin-dependent diabetes, anemia, hypertension, and chronic kidney disease (21.2% vs 14.7%). On the other hand, women were less likely to be smokers or to report previous myocardial infarction, PCI, or coronary artery bypass graft surgery.

At 12 months, BARC 2, 3, or 5 bleeding occurred more often in women than in men (6.8% vs 5.2%; hazard ratio [HR], 1.32; 95% CI, 1.06-1.64; P = .01). After multivariate adjustment, associated bleeding risk for women was no longer significant (adjusted HR [aHR], 1.20; 95% CI, 0.95-1.52; P = .12). No significant differences in ischemic endpoints were reported between women and men.

In comparing treatments, ticagrelor monotherapy vs ticagrelor plus aspirin was associated with lower risk of bleeding in women (5% vs 8.6%; aHR, 0.62; 95% CI, 0.42-0.92; P = .02) and in men (3.7% vs 6.6%; aHR, 0.57; 95% CI, 0.44-0.73; P < .001). In fact, aspirin withdrawal was associated with an absolute reduction of bleeding risk for women (-3.6%; 95% CI, -6.0% to -1.2%) and in men (-2.9%; 95% CI, -4.1% to -1.7%). Rates of ischemic endpoints were similar for both aspirin and placebo groups in women (3.5% vs 3.5%; aHR, 1.04; 95% CI, 0.61-1.77; P = .88) and in men (4.0% vs 4.1%; aHR, 1.06; 95% CI, 0.80-1.39; P = .69).

The investigators suggested that differences in baseline characteristics between women and men place women who undergo PCI and receive ticagrelor at higher hemorrhagic risk. When adjusting for baseline factors, however, the risk of bleeding was similar between women and men. The researchers indicated that the benefits of continuing ticagrelor therapy without aspirin (namely, an absolute reduction in bleeding events) were comparable between women and men.

6) CARDIOVASCULAR PREVENTION AFTER HYPERTENSIVE DISORDERS OF PREGNANCY: DO NOT FORGET FETAL GROWTH RESTRICTION!

We read with great interest the paper by countouris et al (1) about long-term cardiovascular (CV) remodelling after a pregnancy complicated by hypertensive disorders of pregnancy (HDP). The authors should be applauded for several issues.

First, at long term, they definitely confirmed the association between hypertensive disorders of pregnancy and CV alterations later in life. This is also more relevant because it persists even in normotensive women, alterations later in life. This is also more relevant because it persists even in normotensive women, although at a lesser extent, extending our previous findings in women without CV risk factors (2, 3) and underlining the need for a closer CV follow-up for still-normotensive women.

Second, they analysed the independent evaluation of the role of placental hypoxic lesions regarding CV sequelae, finding neutral results. However, their data should not discourage future research in this field. Placental insufficiency is a hallmark of pre-eclampsia (PE) and is responsible for the development of fetal growth restriction (FGR), which confers high neonatal morbidity and mortality. Because FGR can be present independently from PE, to analyse its independent role, we recently studied, for the first time (to our knowledge), the cardiac consequences of PE, FGR, and their combination by means of strain echocardiography at 6 months to 4 years after birth in normotensive women without CV risk factors. Although the combination of PE and FGR was associated with the highest rate of myocardial dyssynchrony, FGR alone was as well (4). Notably, FGR and PE share the same pathophysiology, such as inflammation and oxidative stress (3, 4). It would be interesting if countouris et al. (1) had also analysed this subgroup in their paper. Therefore, we suggest also considering placental hypoxia and insufficiency in terms of FGR and not only of histological vascular malperfusion so as not to exclude from dedicated follow-up women previous normotensive FGR.

7) DELAYS AT EVERY STAGE OF STEMI ADD UP TO WORSE CARE FOR WOMEN

An examination of the individual time intervals that occur from initial STEMI symptoms to PCI shows a pattern of greater delays in women than men, both before and after hospital arrival. Total ischemic time also was longer, with women being less likely than men to have a first-medical-contact (FMC)-to-device time under 90 minutes.
“Although patient delays are important, we found that the largest component of time delay in women with STEMI was actually healthcare system delays (prehospital system and hospital delays),” write Julia Stehli, MD (Monash University, Melbourne, Australia), and colleagues in the paper, which was published online June 22, 2021, in the *Journal of the American Heart Association*. Delays in time from arrival at a PCI-capable hospital to reperfusion occurred despite similar numbers of men and women being transported to a PCI-capable, “from which we can infer that a STEMI or at least an acute coronary syndrome was suspected in all of these patients,” they add.

The delays correlated with worse outcomes for women in the form of higher 30-day all-cause mortality (OR 1.38; 95% CI 1.06-1.79) and more major bleeding (OR 1.54; 95% CI 1.08-2.20) compared with men.

Suzanne Steinbaum, MD (Mount Sinai Hospital, New York, NY), who commented on the study for TCTMD, said that seeing the delays broken down into time intervals is “staggering.”

“Across the board, there’s biases everywhere, from a woman acknowledging her symptoms to the ambulance evaluating her,” she observed. “There’s not one place where someone’s going to pick up the slack. It’s just not happening.”

Steinbaum added that regardless of how good the care being given is, delays of even just a few minutes matter and need to be eliminated. “We know that once women have a heart attack, they do significantly worse, and this is really one of those issues where you can say it’s really because of delay in care.”

**Delays Everywhere**

Stehli et al analyzed data on 6,330 STEMI patients (mean age 63 years; 21% women) who were included in a clinical-quality registry designed to monitor PCI performance and outcomes at 30 hospitals in Victoria, Australia. In general, women were older and had more comorbidities than men. Times were broken down into patient delays and healthcare system delays (prehospital and in-hospital), and then further broken down to include symptom onset, emergency medical services (EMS) call, first medical contact, ECG acquisition, departure to hospital, arrival at hospital, and reperfusion.

**There’s not one place where someone’s going to pick up the slack. It’s just not happening.** Suzanne Steinbaum

After adjustment, women experienced more delays than did men at every interval, including EMS call-to-door time, the primary endpoint. The total healthcare delay, calculated as the time from the EMS call-to-device time, was 10 minutes longer for women than men, while the total ischemic time was 17 minutes longer.

**Delays According to Sex: Adjusted Geometric Mean**

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom-to-Call, min</td>
<td>47</td>
<td>44</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Call-to-Door, min</td>
<td>58.1</td>
<td>55.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Call-to-FMC, min</td>
<td>11.6</td>
<td>11.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Hospital Delay, min</td>
<td>58.8</td>
<td>54.9</td>
<td>&lt; 0.006</td>
</tr>
<tr>
<td>Total Healthcare Delay, min</td>
<td>137.2</td>
<td>127.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total Ischemic Time, min</td>
<td>207</td>
<td>190.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

The percentage of women who achieved a FMC-to-device time of 90 minutes or less was 20.2% versus 27.6% for men (*P* < 0.001). Ascertainment of an ECG within 10 minutes of FMC was the only variable with no differences between women and men (*P* = 0.62).

According to Stehli and colleagues the data illustrate a complex series of differences in presentation and in patient and professional bias.

Some things specific to female STEMI presentation such as nausea, radiation of pain, and shortness of breath may “lead to an initial misdiagnosis at the time of EMS phone call and the delay in EMS call-to-FMC seen in women,” the researchers note. “However, longer healthcare delays have been described even in women with typical symptoms, suggesting a healthcare worker bias may still exist with women perceived as lower risk for STEMI.”

**Checklists and Calls to Action**
One potential way to combat gender disparity and bias, in addition to healthcare worker education, is systems-based approaches to STEMI care that include machine learning and checklists, Stehli and colleagues say.

Steinbaum agreed, adding that checklists not only aid in consistency of care, but also reduce the potential for human error in all its forms. “I think it comes down to [the need for] this algorithmic process,” she said. “The checklist is a constant way of taking out someone’s impression of a given patient.”

According to Steinbaum, delays in female STEMI care coupled with the unknown health repercussions from the COVID-19 pandemic constitute an urgent call to action to fix the gender inequality in cardiovascular healthcare delivery. In a recent article in *Medicina*, she writes that the disproportionate stress on women—from losing or giving up jobs, to helping children with homeschooling, to having less time for self-care—raises serious concerns that those burdens will take a physical toll in the coming years in the form of an uptick in heart disease in women.

“We are going to see this having an effect,” she told TCTMD. “If we don’t figure this piece out—the fact that women will not be taken care of equally as well as men—then in 5 to 10 years from now, we’re in trouble.”

8) **EXPLORING THE REFRACTORY PERIOD OF AN ACTIVE STAND IN FEMALES WITH INITIAL ORTHOSTATIC HYPOTENSION**

Initial orthostatic hypotension (IOH) is a form of orthostatic defined by a transient decrease in systolic blood pressure (SBP) by >40 mm Hg or diastolic blood pressure by >20 mm Hg within 15s of an active stand, with rapid recovery in under 1 min (1).

Patients with IOH experience symptoms of pre-syncope with orthostatic secondary to the reduction in BP and often return to a sitting position to relieve symptoms. Subsequent orthostatic then does not elicit pre-syncope. This suggests that the muscle activation reflex underlying IOH (2) may have a refractory period, which could be exploited for treatment. To our knowledge, there are no published reports exploring the refractory period of this reflex in IOH (1, 3,4). The2 goals of this study were to: 1) determine if the reflex underlying IOH has a refractory period; and 2) determine the duration of the refractory period in IOH if one exists We hypothesized that a stand following a 30-s sit would result in a smaller SBP drop compared to a stand following a 20- min sit.

The study was approved by the Calgary conjoint Health Research Ethics Board (REB19-0792). All participants provided their written informed consent and refrained, and continuous heart rate (HR) and beat-to-beat blood pressure were measured. Stroke volume (SV) and systemic vascular resistance (SVR) were estimated using modelflow (BMEYE, Amsterdam, the Netherlands).

Each participant performed 8 sit – to – stand manueuvers of varying interim seated duration, starting with a 20-min sit (LONG) and then, in a random order, 30-s (SHORT) and 2-, 3-, 4-, 5-,7-, and 10-min sits, each followed by a 2-min stand.

The primary endpoint was to determine the existence of a refractory period by comparing the change in SBP from baseline (mean of each sit’s final 30 s) to nadir SBP during the stand following a SHORT sit to a LONG sit(figure 1). Changes in HR, SV, and SVR were also compared using paired t-tests. The secondary endpoint was to determine the drop in SBP between the sit-to-stand manueuvers of 8 sit durations. This compation was performed using a repeated measures analysis of variance with Bonferroni correction for 28 comparisons. Data are reported as mean ±SD.

A Total of 24 female participants (age: 32± 8 years, body mass index: 24 ± 6 kg/m2) completed the study protocol and had data analysed. The SBP drop following SHORT (-12 ± 6mm Hg) was reduced compared to LONG (-34 ± 16mm HG: P < 0.001). The increase in HR after SHORT (11 ± 6 beats/min) was reduced compared to LONG (24 ± 8 beat/min; p < 0.001). Compared to baseline, SV increased after SHORT (2 ± 9 mL) but decreased after LONG (-5 ± 15mL; p= 0.03). The drop in SVR after SHORT (-171 ± 16 dyne.s/cm5) was also significantly reduced compared to LONG (-459 ± 188 dyne – s/cm5;
p < 0.001). The drops in SBP following the remaining 6 sit durations were not significantly different than the LONG sit.

Study limitations include that the LONG sit was always performed first, which could have introduced an order effect. IOH participants were enrolled based on self-reported symptoms. There were no male participants in the study. Prior IOH studies have explored supine or squat to stand (1, 3), while we explored sit to stand.

The Key findings of this study are: 1) the SBP drop is significantly reduced following a SHORT sit compared to a LONG sit, indicating that the hemodynamic response underlying IOH in females has a refractory period; 2) the large drop in SBP returned following the 2-min sit, indicating that the refractory period lies between 30 s and 2 min sit, indicating that the refractory period lies between 30s and 2 min; and 3) the SBP drop in IOH is likely driven by a combination of a large, rapid decrease in both SV and SVR. These study data provide IOH patients with a simple symptom management option. Upon feeling faint after standing, a subsequent short sit will reduce symptoms of the next stand.

9) UNSEEN AND UNHEARD: IN THE CATH LAB, ANTIRACISM EFFORTS FALL SHORT

Yolanda Carter, RN, MSN, JD, began her career in the 1980s working as a trauma nurse in a Texas emergency department, where she would often accompany STEMI patients to the cath lab, and fell in love with the work being done there. Born to Native American and Black parents, Carter’s own childhood history of rheumatic fever convinced her that cardiovascular medicine was her calling. But years of frustration followed. Several times she says she tried to obtain a permanent position in the cath lab but was passed over in favor of less-skilled, less-educated white colleagues.

“There was a mentality that came from leadership and management that I wasn't allowed to do it, quite frankly, because my skin was brown,” she said. Once, at a California hospital where she was seeking a management position, a coworker told her that the CEO had referred to her using the N-word.

“I have been treated badly not because of my skills, but because of the color of my skin, and that’s sad,” Carter said. “But it exists, and it's real, and it’s real across this country.” Her husband, who is Black and also works in a cath lab, has relayed similar experiences.

Over the past year, cardiology societies, journals, academic departments, and meetings have issued position statements and road maps aimed at stamping out racism and increasing diversity and inclusion in cardiovascular medicine. But much of that call to arms has been led by physicians on behalf of physicians; the voices of nurses, techs, and other support staff have too often gone unheard.

Earlier in the pandemic, nurses and techs, both in the cath lab and beyond, were in the spotlight for leaving full-time positions to become high-paid travelers taking short-term posts around the United States. But for some it has never been an option to quit a full-time job for the allure of the road, and money was never the driver. In Carter’s case, the only way she felt should could even get a cath lab position was to become a traveler. “The people who are hiring you can’t see you. If they can’t see you, they can’t judge you; they just need the help and that’s what they get,” she explained.

“There are too many talented people of color who are just not being appreciated and who could bring so much to the cath lab environment,” Carter added.

Falling Through the Cracks

Triston Smith, MD (Trinity Health System, Steubenville, OH), a Black interventional cardiologist, agreed that stories like those of Carter and her husband are indeed real and all too common, both for short-term travelers and full-time staff.

“If you look at the workforce composition of most cath labs, you’ll see that there isn’t a fair representation of minorities . . . either as interventionists, or techs, or nurses,” he said. “Does that happen by chance? I doubt it.” Smith said his experience suggests that excuses are often made that certain groups—which tend to be all-white—work better together, and that if few people of color have been in leadership positions at a given institution, it’s likely to stay that way.

“When you break through that barrier, it’s just sheer willpower to get it done and not accept anything else [but] having your eye on the prize, so to speak,” he observed. “Many times, someone recognizes
your talents and gives you a leg up, but in my opinion, it’s always more difficult for that to happen when it comes to people of color.”

Despite efforts to address diversity, equity, and inclusion, minority cath lab staffs are clearly falling through the cracks with no support structures to amplify their voices and experiences, noted Bailey Ann Estes, BSN (Hendrick Medical Center, Abilene, TX).

“Stories like Yolanda’s are something we need to address, and you sometimes wonder if issues like this even cross anyone’s mind,” she added. “We get caught up in our own little worlds, our own little cath labs . . . and we don’t have a great, strong society that connects us. The first step is that we have to create awareness that a problem exists.” Doing so increases the opportunity to garner support through a chorus of allied health voices, as well as physician leaders who are willing to step up. It also decreases the opportunity for excuses to not address what is going on, she added.

We have ‘he for her.’ Why not ‘doctors for nurses’ and ‘doctors for staff?’ Bailey Ann Estes

“One thing we know about cardiac cath lab people is they are there for the long haul. People fall in love with it and they become ‘cath lab-ers’ for life,” Estes noted. “That’s something that we need to foster and build on. Physicians don’t want baby nurses and baby techs coming in that don’t know what they’re doing. Turning away people who are highly experienced based on their race is a very, very big issue that we can’t ignore.”

For Smith, being judged on the color of his skin was far from his mind as a child growing up in multicultural Grenada, but he’s felt it firsthand in the United States. Having showed strong leadership ability and helped build a thriving structural heart program straight out of his fellowship, he was denied the director position and told he was too young despite seeing white colleagues with similar qualifications go into director positions out of fellowship.

“For me as a physician, it’s been tough, so I understand how difficult it would be for nurses and techs who are trying to navigate around all of these issues and trying to gain acceptance in the community,” he said.

A Reckoning on Racism in Medicine

The critical juncture of race and medicine was thrust into the spotlight following the 2020 police killing of George Floyd on top of the already stark disparities laid bare by the disproportionate effects COVID-19 was having on racial and ethnic minorities. In response to the Black Lives Matter movement, the Association of Black Cardiologists (ABC), the American Heart Association (AHA), and the American College of Cardiology (ACC) issued a joint statement calling on medical organizations, particularly cardiovascular ones, to speak out against racial discrimination given the role it plays in limiting access to cardiovascular health and quality care. The board of trustees of the American Medical Association (AMA) also urged physicians to “stand in opposition to racism because it truly is a public health emergency.”

Less than a year later, however, JAMA found itself apologizing and promising to do better after airing a tone-deaf podcast that suggested physicians can’t be racist and that the term “racism” may be harmful and should be replaced with something else. STAT subsequently reported that researchers had for years been asked by the journal’s editors to scrub the word racism and similar terms from their submitted articles, and confirmed with their own search that they couldn’t find any articles in either JAMA or the New England Journal of Medicine that had racism in their title or abstract.

Many times, someone recognizes your talents and gives you a leg up, but in my opinion, it’s always more difficult for that to happen when it comes to people of color. Triston Smith

Some journals have since stepped up and published articles aimed at addressing the need for collaborative work to improve racial diversity in the workplace. In a recent paper in the Journal of the American College of Cardiology, for example, Nina Williams, MD (Saint Francis Hospital, Tulsa, OK), and colleagues offered steps for building an antiracist culture in cardiology.

Speaking to TCTMD from her own experience as a Black woman who recently completed a fellowship in interventional cardiology, Williams said it’s important to speak out about the fact that racially directed microaggressions at work, either said or unsaid, are often simply accepted for the sake of professionalism, “and then we just keep moving.” For trainees, she said, “there are barriers that are not discussed or identified, and individuals are suffering in silence or suffering together, and just accepting it as a norm when it doesn’t need to be.”

Speaking, Listening, Changing

Manesh Patel, MD (Duke University Medical Center, Durham, NC), a former cath lab director and now chief of cardiology, said inequality in medicine is something everyone must work harder to address.
One way to combat structural racism in the healthcare environment, he noted, is with diversity in the workforce at all levels, from physician and nursing leadership to administration.

“For every position, for every job that we’re trying to fill, we need to ensure that we have an open and transparent process by which applicants know about the job, and have the opportunity to apply for the job,” he said. “Secondly, you have to have a culture where people feel comfortable wanting to do that and feel the value of having a diverse workforce, both at leadership levels and everywhere throughout the organization.”

There also have to be processes and supports for people reporting hostile behavior, microaggressions, or other harmful and racist conduct on the job.

“When white people say the same sort of things, they are called ‘passionate’ for speaking out,” Smith observed. “When you’re Black and you speak out, you’re ‘angry.’ Words like that are said to make you not speak out or speak up, which is unfortunate.”

Where some might choose to either ignore it or vent to spouses, family, or friends, Smith said those conversations won’t spark the changes needed for the people who care for patients while feeling mad, hurt, and unheard. As a voting member of the Society for Cardiovascular Angiography and Intervention’s recently formed Diversity, Equity, and Inclusion (DEI) Taskforce, he feels strongly that not addressing pervasive racism in medicine is not only demoralizing to healthcare workers, but also can cost some minority patients their lives and increase the chance that others will avoid getting the care they need.

Patel agreed. “Our patients are more likely to feel comfortable with us and more likely to consider recommendations and changes to their healthcare behaviors when they’re coming from people that they trust, and who look [like them], and feel and understand their cultural backgrounds,” he said.

As a nonphysician and a woman of color in nursing leadership, Elizabeth Perpetua, DNP, ACNP-BC (Empath Health, Seattle, WA), noted that giving voice to the pain caused by microaggressions and admitting to feeling powerless to change in the workplace are rarely encouraged in the healthcare arena. Yet she agreed that it is necessary, even if moving on—literally or figuratively—to avoid confrontation often seems, intuitively, to be the best option.

“Moving on from it hurts us more than it helps us,” she observed. “But giving voice to it and speaking up about it is really, really scary.” At different times in her career, Perpetua added, “I’ve told myself all kinds of different stories to not speak up, and then when I have spoken up, I have certainly been less effective than I had hoped or dreamed, or have suffered consequences from it, and it’s painful.”

I’ll gladly speak out about this, because there has to be a voice at some point who does, and maybe this is that point. Yolanda Carter

The silver lining, she added, is that by voicing these personal stories, there’s a high likelihood of them resonating and maybe even helping others be a little braver about speaking up for themselves or colleagues.

“I think people are listening a little bit more and [by listening to others] it becomes more normalized instead of something so scary,” Perpetua said, adding that it’s really the moving on that is more likely to result in nothing changing, even if it feels like the only way to take back power in that situation. Speaking truth to the pain, she added, can actually create more options than one might think. What concerns her most, though, is that without champions for the cause and organizations that extend to continuing and broadening the conversations, opportunities for change and support may be lost.

Estes said holding the organizations that collect professional dues from cath lab professionals to account is a good place to start. This then could become the hub where all cath lab team members can talk about racial issues that affect them and work on recommendations to leadership to make changes happen.

“I think having a big voice of allied health, in the form of cath lab staff, step up and say something is going to be a big thing,” she said. “Also, physician support, especially from cath lab directors, would go a long way. We have ‘he for she.’ Why not ‘doctors for nurses’ and ‘doctors for staff’?”

Carter said her love for cath lab work persists despite all she has experienced, although she said she will never again apply for a management job despite holding a master’s degree and a juris doctorate in addition to her RN education. So what makes her want to stay?
“Because that’s my gift, and you don't let someone steal your joy. You just don’t,” she said. “I'll gladly speak out about this, because there has to be a voice at some point who does, and maybe this is that point.”

10) STROKE RISK UP FOR OFFSPRING OF MOMS WITH HTN IN PREGNANCY

TUSSDAY, June 15, 2021 (Health Day News) -- Offspring of mothers with hypertensive disorders during pregnancy (HDP) may have an increased risk for developing stroke later in life, according to a study presented at ESC Heart & Stroke 2021, the International Conference of the European Society of Cardiology Council on Stroke, held virtually from June 2 to 4.

Fen Yang, from the Karolinska Institutet in Stockholm, and colleagues examined the associations between maternal HDP and the risk for ischemic heart disease (IHD) and stroke in offspring in a cohort study of 5,807,122 singleton live births in Sweden during 1973 to 2014 and Finland during 1987 to 2014.

The researchers found that 3.76 percent of mothers had maternal HDP. During follow-up of offspring up to 41 years, there were 5,360 strokes and 2,340 cases of IHD (0.09 and 0.04 percent, respectively). Offspring exposed to maternal HDP had increased risks for IHD and stroke of 29 and 33 percent, respectively. The associations persisted after adjustment for preterm birth and fetal growth restriction. In sibling analyses accounting for genetic/environmental factors, the association persisted with stroke, but not with IHD.

“The sibling analyses suggest that shared genetic or environmental factors were the main contributors to the association between hypertensive pregnancy disorders and the risk of ischemic heart disease. However, the increased risk of stroke persisted, indicating the possibility of direct intrauterine effects,” Yang said in a statement. “This was one of very few studies in this area and more research is needed. It was an observational study, and we cannot make any conclusions about causality.”

11) STRESSORS OF INTEGRATING WORK, LIFE HIGHER FOR FEMALE FACULTY

TUSSDAY, June 15, 2021 (Health Day News) -- The stressors of integrating work and life are higher among female than male faculty and were more noticeable since the COVID-19 pandemic, according to a study published online June 15 in JAMA Network Open.

Susan A. Matulevicius, M.D., from the University of Texas Southwestern in Dallas, and colleagues conducted an online survey among 1,186 faculty members at a large urban medical center between Sept. 1 and 25, 2020, to examine perceptions of work-life balance before and since COVID-19.

The researchers found that compared with before the pandemic, since COVID-19, faculty were more likely to consider leaving or reducing employment to part time (23 versus 14 percent and 29 versus 22 percent, respectively). Compared with men, women were more likely to reduce employment to part time before the pandemic (28 versus 12 percent) and to consider leaving or reducing employment to part time since the pandemic (28 versus 15 percent and 40 versus 13 percent, respectively). Compared with before the pandemic, faculty with children were more likely to consider leaving and reducing employment since the pandemic (29 versus 17 percent and 40 versus 24 percent, respectively); women with children were more likely to consider leaving compared with women without children (35 versus 17 percent). Both before and since the pandemic, working parent faculty and women were more likely to decline leadership opportunities.

"Without true change in the culture of medicine to support work-life integration and family-friendly work policies, further disillusionment in academic careers may occur and threaten the future of academic medicine as an institution," the authors write.

12) CLOSING THE GENDER GAP IN CARDIOLOGY CLINICAL TRIAL LEADERSHIP: A ROAD MAP

Women are conspicuously absent as leaders of cardiovascular clinical trials—now, an “actionable road map” aims to rectify this imbalance by itemizing the core competencies required to lead a clinical trial, and by offering concrete steps that institutions, professional societies, industry, and public funding agencies can take to ensure clinical trials get more female principal investigators and chairs.

“We must adopt transformative strategies to harness the strengths of women as CV clinical trial leaders and deconstruct the sexism that has been normalized in the clinical trial enterprise,” the
authors write. “For far too long, recruitment, advancement, mentorship, and sponsorship have followed gender lines, with decisions generally made by men for men.”

The document, led by Harriette Van Spall, MD (McMaster University/Population Health Research Institute, Hamilton, Canada), was published online this week in the Journal of the American College of Cardiology.

Cardiology’s gender gap has been highlighted in a range of recent studies looking at fellowships, first authors, senior authors, full professorships, and the choice to pursue cardiology or interventional cardiology as a specialty from the outset. Cardiology clinical trial leadership suffers from the same problem. As Van Spall and co-authors point out, research published last year covering a recent 4-year period indicates that more than half of cardiovascular clinical trials published in the big three medical journals (Lancet, JAMA, and New England Journal of Medicine) lacked women on their steering committees and only one in ten were led by female principal investigators.

The current viewpoint, Van Spall told TCTMD, “represents a move from calling out a problem to solving it in a very constructive way. What we lay out are checklists that institutions can use to track progress, to report progress, and to move to the next phase to completely close the gap.”

A Multipronged Approach
Van Spall and colleagues review the rationale for ending gender inequality in research, pointing out that diverse leadership in randomized clinical trials has been shown to benefit both professionals and patients. Notably, trials led by women tend to enroll more female, Black, Indigenous, and people of color, they note, leading to results that more accurately reflect the makeup of most physician practices.

The document goes on to describe the specific “competencies” required of physicians seeking to lead clinical trials in cardiology, itemized with an eye toward early career/physicians-in-training.

Next, the paper addresses the critical role played by academic institutions and, again, provides a checklist of steps universities and teaching hospitals can take to improve the representation of women as trial leaders.

“There are things that academic institutions need to do to close the gaps, through the purposeful recruitment, retention, and [provision of] internal opportunities that allow for advancement based on merit, rather than informal networks that are often the basis of career progression,” Van Spall explained. “Academic institutions are highly politically charged, and you can be exceptional but not belong to a network that is going to lift you.”

“Catalyzer” organizations are important advocates for female leaders, the document notes, but responsibility for ending gender inequality also falls to professional societies, trial leadership selection committees, funding bodies, medical journals, and ultimately individual scientists themselves, each of which are dealt with in turn by the paper, with itemized calls to action.

In recent years, professional societies and their affiliated meetings and medical journals have made strides in closing the gender gap, but industry—which funds the lion’s share of cardiovascular clinical trials—has a lot of ground to make up.

“We’ve seen through multiple studies of ours that industry-led trials are definitely less likely to have women and diverse representation among trial leadership, and the path to leading an industry-sponsored trial is quite unclear,” Van Spall said. “It relies heavily on being part of certain networks that are really not open. And so this is a call for our industry partners, who we value and we rely on for innovation and interventions that help our patients: we’re calling them to step up with us and to harness the energy and the potential and the enthusiasm and the skills that we have to diversify the face of leadership.” Several co-authors on the paper, she added, were from industry. Van Spall hopes that as industry boards increase the number of female members, this may ultimately help increase awareness about the lack of diversity among clinical trial leaders.
But the “wait-and-see” approach has not necessarily achieved what many had hoped, Van Spall cautioned: hence, the rationale for a paper like this one that sets out clear and concrete steps for individuals and groups to follow.

“We haven’t seen the trends change over the last 20 years, which is why this document is so focused on actually creating that change,” she stressed. “Because time alone, conversations alone, highlighting gaps alone will not bring that change [or tell us] what we need to do from here.”

Contacted for comment, a spokesperson for PhRMA, the trade group representing the US pharmaceutical industry, said the organization is actively working to improve gender, ethnic, and racial diversity in the drug development process.

“As part of our effort toward better representation, our industry made a commitment to being part of this change through the PhRMA Equity Initiative, which seeks to build career opportunities for emerging talent, improve health equity, and enhance clinical trial diversity in Black and Brown communities,” Sarah Sutton, PhRMA’s director of public affairs, said in an email. “PhRMA’s member companies voluntarily adopted principles on enhancing clinical trial diversity in October that took effect in April. PhRMA also just hosted a large-scale stakeholder workshop intended to identify partnerships and actionable next steps for sustainable clinical trial diversity.”

And while men have an important role to play in advocating for diversity, Van Spall believes championing women as clinical trial leaders doesn’t have to mean stepping aside.

“We need to envision this not as any one group giving up their role, but on creating more roles and inviting more people to the table,” she said. “There are not a finite number of seats at the table. We need to create more seats so that we can make room for people who are capable, who have the skill set, and who can generate funds for research to lead the research.”

13) TYPE A AORTIC DISSECTION TIED TO GREATER MORTALITY IN WOMEN

While more common among men, type A aortic dissection (TAAD) is associated with substantially higher rates of in-hospital mortality among women, according to new data. Women also tend to present with more advanced disease with intramural hematoma, periaortic hematoma, or complete or partial false lumen thrombosis as well as hypotension or coma.

Similar to MI, “time is of the essence” with TAAD because “it carries a mortality rate of about 1-2% per hour for the first 48 hours,” senior author Thomas Gleason, MD (University of Maryland Medical Center School of Medicine, Baltimore), told TCTMD.

The sex discrepancies found in terms of presentation suggest “that there may be a difference in the time from onset of symptoms to definitive diagnosis in females compared to males,” he said. “If we can reduce the time to diagnosis and treatment, we will likely reduce mortality. That’s probably the most important point I take from this study. I hope that it can invoke a greater awareness among diagnosing physicians on the front lines . . . to have a lower threshold to rule out dissection in the context of symptoms that occur with dissection.”

The data also indicate a potentially “different trigger point” for women to seek medical care when they begin experiencing symptoms or for diagnosing physicians to respond to women compared with men with potential TAAD. “In other words, a woman may develop the same symptom as a man, but the presentation in the woman doesn’t trigger the same level of urgency by the patient or for a diagnostic workup to rule out dissection—thus creating the potential for delay in diagnosis,” Gleason said. “For such a lethal disease as aortic dissection, this is a concern.”

You come in with a primary complaint of chest pain, the first responding physician needs to be thinking, This could be an aortic dissection. Thomas Gleason
Commenting on the study for TCTMD, Benjamin Youdelman, MD (Maimonides Medical Center, Brooklyn, NY), who works with the aortic disease awareness campaign Think Aorta US, said, “I’m surprised that women are presenting so late, because I will tell you that the symptoms associated with aortic dissection are not subtle. These are often the most dramatic, the most overwhelming, and the most significant abnormal discomforts symptomatology that any patient has ever experienced. And yet the women are not presenting to the hospital. That’s shocking to me.”

Higher Mortality Among Women
For the study, published online last week ahead of print in the Journal of Thoracic Surgery, Lauren V. Huckaby, MD (University of Pittsburgh Medical Center, PA), Gleason, and colleagues looked at 2,823 TAAD patients (65.7% men) from the Interventional Cohort of the International Registry of Acute Aortic Dissection database who underwent either operative repair or a surgical approach as part of a hybrid repair between 1996 and 2018.

On average, women were older (65.4 vs 58.6 years; \( P < 0.001 \)) and more likely to present with intramural hematoma (19.4% vs 13.2%; \( P < 0.001 \)), complete false lumen thrombosis (17.2% vs 10.2%; \( P = 0.001 \)) or partial false lumen thrombosis (24.8% vs 19.4%; \( P = 0.039 \)), or pericardial (49.6% vs 39.8%; \( P < 0.001 \)) or pleural effusion (15.3% vs 9.2%; \( P = 0.007 \)). A higher prevalence of shock (31.3% vs 22.2%; \( P < 0.001 \)) and altered consciousness (11.5% vs 7.5%; \( P = 0.001 \)) also were identified in women compared with men.

Men more often underwent complete arch replacement, a Bentall procedure, and aortic valve replacement, while median times for cerebral perfusion and total cardiopulmonary bypass were longer compared with women.

In-hospital mortality was greater in women compared with men (16.7% vs 13.8%; \( P = 0.039 \)), but postoperative complications were comparable with the exception of acute renal failure, which was lower in women. At 5 years, Kaplan-Meier estimates were similar for survival (82.6% vs 85.9%) and freedom from reintervention (87.8% vs 87.6%).

Over the study period, procedural techniques like ascending aortic cross-clamping, aortic valve-sparing root replacement, and hemiarch replacement increased significantly in both sexes. Additionally, antegrade cerebral perfusion became more common, whereas use of retrograde cerebral perfusion lessened.

On multivariate analysis, there was a trend toward higher in-hospital mortality in women (OR 1.40; 95% CI 1.00-1.98), but this disappeared when only including patients in the last decade of enrollment (OR 0.93; 95% CI 0.54-1.62).

The results suggest “that progress in TAAD management has resulted in narrowing the previous mortality gap between the sexes,” Huckaby and colleagues write. “Nevertheless, sex-specific differences in TAAD presentation should prompt an individualized approach to make further strides in reducing perioperative mortality, which remains high.”

Bringing Aortic Disease to the Forefront
Gleason said the data were not able to illuminate why women show up with more-advanced presentations, suggesting that it could be due to factors related to patient stoicism as well as physicians not responding quickly enough.

“There’s a whole spectrum of presentation, but when a patient comes in with signs and symptoms that are within the spectrum of those seen with aortic dissection, somebody has to think of it,” he said. “You come in with a primary complaint of chest pain, the first responding physician needs to be thinking ‘This could be an aortic dissection’ and has to rule it out.”

Likewise, Youdelman said a physician encountering a patient with TAAD symptoms “should have lightbulbs, flashing lights, and all kinds of stuff going off. But unfortunately, . . . an emergency room physician over the course of 2-4 years might see one or maybe two patients who have an aortic dissection.”
Improvement in care for TAAD across the board needs to start with education, said Youdelman. “Number one, there is no patient type for an aortic dissection, except to say that it’s more common in men than women... The only consistent piece of information is that if someone has a family history of aortic dissection, aortic aneurysm, unexplained sudden death, or if they have a cerebral bleed, which is an indication of a cerebral aneurysm in the family and they have these strange symptoms, they need to be worked up for an aortic dissection.”

“If we could diagnose everyone quicker,” added Gleason, “we would save more lives, not just women.”

The next step will be figuring out why women are presenting further along in the disease course. “Is it because they are not seeking medical care early enough, or is the problem more on the receiving end in the emergency room?” he asked. “There may be other important factors to tease out.”

Youdelman also encouraged physicians to put aortic disease more at the forefront of their thinking when assessing patient histories. “I think the fact that aortic disease is probably underappreciated, underdiagnosed, and therefore aortic dissections continue to be a significant problem is something that needs to come up into people’s thinking when patients are in the office to ask these very pointed questions,” he said. “Because everybody usually asks heart disease, stroke, diabetes, and they stop there. But the other two are cancer and aortic disease, both of which kill people, so why stop at the three as opposed to asking all five?”