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Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Early vs. Delayed Cardioversion: A Nonshocking Result

By Joshua Moss, MD

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Dr. Moss reports he is a consultant for Abbott, Boston Scientific, and Medtronic.

SYNOPSIS: For patients presenting to an ED with recent-onset atrial fibrillation, using rate control and outpatient cardioversion only as needed was associated with a high rate of spontaneous conversion within 48 hours of arrhythmia onset and noninferior short-term outcomes compared to immediate cardioversion in the ED.

SOURCE: Pluymaekers NAHA, Dudink EAMP, Luermans JGLM, et al. Early or delayed cardioversion in recent-onset atrial fibrillation. *N Engl J Med* 2019;380:1499-1508.

Symptomatic atrial fibrillation (AF) is a common reason for ED visits and referrals, both for first-time and recurrent episodes. Often, the treatment of choice is immediate pharmacologic or electrical cardioversion. Investigators sought to determine whether such early intervention is superior to a more conservative approach of outpatient observation and delayed cardioversion only as needed.

Pluymaekers et al randomized 437 adult patients from 15 hospitals in the Netherlands at the time of their ED visit to early or delayed cardioversion. Patients had to have hemodynamically stable, symptomatic AF with onset < 36 hours before, with no signs of myocardial ischemia or history of AF lasting > 48 hours. For early cardioversion, a pharmacologic approach was used initially in most patients, with electrical cardioversion as a backup. At enrollment, 40% of patients already were taking oral anticoagulant drugs; otherwise, anticoagulation was initiated before or immediately after cardioversion in patients with high stroke risk. Transesophageal echocardiography was not performed in any patients. For delayed cardioversion, patients were treated in the ED with beta-blockers, calcium channel blockers, or digoxin to achieve symptom relief and a heart rate of ≤ 110 beats per minute. Patients were discharged when stable and returned for an outpatient clinic visit as

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close as possible to 48 hours after onset of symptoms. If AF still was present on ECG, those patients were referred back to the ED for cardioversion. The mean age of patients was 65 ± 11 years; 60% of patients were male. Hypertension was common, and most registered a CHA_2DS_2-VASc score ≥ 2. The predominant symptom of AF was palpitations, although many patients also reported exercise-induced fatigue, dyspnea, and/or chest pain. About 23% of patients already were on an antiarrhythmic drug. The median duration of the index ED visit was 158 minutes in the early cardioversion group and 120 minutes in the delayed cardioversion group. In the early cardioversion group, conversion to sinus rhythm occurred spontaneously in 16% of patients before the actual cardioversion, and 94% left the ED in sinus rhythm. In the delayed cardioversion group, conversion to sinus rhythm within 48 hours occurred spontaneously in 69% of patients; an additional 28% underwent actual cardioversion.

During four weeks of follow-up, recurrence of AF documented via intermittent monitoring in a subset of patients occurred in 29% of the early cardioversion group and 30% of the delayed cardioversion group, with similar time to recurrence (median, 8 days vs. 12 days). At a four-week visit, 94% of patients in the early cardioversion group and 91% of patients in the delayed cardioversion group were in sinus rhythm, a noninferior outcome for delayed cardioversion per prespecified criteria. One patient in the early cardioversion group suffered a transient ischemic attack (TIA) within four weeks of randomization, and one patient in the delayed cardioversion group experienced an ischemic stroke. Other cardiovascular complications were uncommon and not significantly different between groups. Quality of life (QOL) scores via survey at the four-week visit also were not significantly different between groups. The authors concluded that in patients with recent onset AF, delayed cardioversion was not inferior to early cardioversion in restoring sinus rhythm at four weeks.

■ COMMENTARY

Several conclusions can be drawn from this study. First, episodes of AF starting < 36 hours before evaluation often terminate spontaneously. In this cohort, 16% of patients randomized to the early cardioversion group converted to sinus rhythm before cardioversion, and 69% of patients randomized to the delayed cardioversion group converted to sinus rhythm by 48 hours.

Second, focusing on anticoagulation as well as symptom and rate control at the time of the index ED visit (while deferring cardioversion to the outpatient setting) shortened the time spent in the ED. This obviated the need for cardioversion in more than half of patients, with no rhythm or quality of life disadvantages four weeks later.

Third, regardless of cardioversion approach, AF recurrence in this population is common — at least 30% over four weeks, undoubtedly an underestimate given the use of intermittent monitoring. Finally, the risk of stroke or TIA, known to be higher after both active and spontaneous cardioversion from AF, is not completely eliminated even when therapeutic anticoagulation is used appropriately. One patient experienced a TIA 10 days after early electrical cardioversion despite rivaroxaban therapy, and one suffered a stroke five days after spontaneous conversion despite dabigatran therapy.

The authors noted another pragmatic difference between the two approaches: patients in the delayed cardioversion group who went on to convert spontaneously would thereafter be classified as having "paroxysmal" AF rather than "persistent" AF. This semantic distinction has no particular bearing on an individual patient's symptoms or outcome at four weeks, but it could have important consequences for how future treatment options are considered. For example, catheter ablation is a class IIa recommendation for symptomatic persistent AF refractory to at least one antiarrhythmic drug, but class I for paroxysmal AF.

It is difficult to know what psychological effect an early vs. delayed approach might have on individual patients. On one hand, discharge from the ED in AF could reassure some patients that the arrhythmia is not acutely dangerous and does not necessarily require urgent

medical attention. On the other hand, symptoms that originally were mild could be exacerbated after discharge by the new diagnostic knowledge for some patients. Perhaps QOL questionnaires administered after the index ED visit may have revealed a difference that faded by four weeks. Ultimately, the study revealed no clear disadvantage of a wait-and-see approach to recent onset of AF. Whether such an approach has advantages in overall resource use or long-term outcomes remains to be seen. ■

ABSTRACT & COMMENTARY

Is Earlier Better With Oral P2Y12 Inhibition in STEMI Patients?

By Jeffrey Zimmet, MD, PhD

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

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

SYNOPSIS: In a large retrospective analysis of patients in Sweden treated with primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction, a propensity-matched group of patients who received oral P2Y12 inhibitors at initial medical contact did not show improved outcomes vs. those receiving these agents at the time of PCI.

SOURCE: Redfors B, Dworeck C, Haraldsson I, et al. Pretreatment with P2Y12 receptor antagonists in ST-elevation myocardial infarction: A report from the Swedish Coronary Angiography and Angioplasty Registry. *Eur Heart J* 2019;40:1202-1210.

Both current European and U.S. guidelines recommend that patients presenting with ST-elevation myocardial infarction (STEMI) receive aspirin and a P2Y12 receptor antagonist as soon as practical after diagnosis, on the way to percutaneous revascularization. However, the data supporting this practice are limited.

Using the prospective Swedish Coronary Angiography and Angioplasty Registry (SCAAR) database, Redfors et al set out to compare outcomes in STEMI patients who were treated with clopidogrel, prasugrel, or ticagrelor at the time of first medical contact and diagnosis ("pretreated" patients) with those who received these medications later in the cardiac catheterization laboratory. During the study period (early 2005 to late 2016), 53,146 patients who received primary percutaneous coronary intervention (PCI) for STEMI were identified. After excluding patients who did not receive aspirin early, those who were treated with thrombolytics, and those with incomplete or missing data, 44,804 patients remained for analysis. Overall, 84.5% of patients were *pretreated* with these medications. Pretreated patients were significantly different from non-pretreated patients. They were on average younger, were more likely to be smokers, and had lower prevalence of other diagnoses (including diabetes, hypertension, hyperlipidemia, prior MI or stroke, congestive heart failure, and prior coronary revascularization). Furthermore, during the PCI procedure, pretreated patients were more likely to have radial artery access and were less likely to receive a GII2b/IIIa receptor antagonist or to have complex coronary disease. Pretreated patients were more likely to undergo complete revascularization during the index procedure and were less likely to develop cardiogenic shock. The median time from first medical contact to start of PCI was 74 minutes.

After propensity score adjustment, the authors found no difference in 30-day mortality between the pretreated and non-pretreated groups (odds ratio [OR], 1.08; 95% confidence interval [CI], 0.95-1.24; $P = 0.313$). Similarly, patency of the infarct-related artery (IRA) at first angiography was not significantly higher in pretreated patients, with approximately 68% found to have IRA occlusion. Likewise, there was not

a significant difference in definite stent thrombosis (0.6% of each group), in-hospital bleeding, or neurologic complications. Although cardiogenic shock was more frequent among patients without pretreatment (5.3% vs. 2.7%; unadjusted OR, 0.50; 95% CI, 0.45-0.57; $P < 0.001$), this difference was no longer statistically significant after propensity score adjustment. The authors concluded that pretreatment of STEMI patients at initial patient contact and diagnosis with P2Y12 inhibitors was not associated with improvement in clinical outcomes, including 30-day mortality, IRA patency, or stent thrombosis compared to treatment at the time of PCI.

■ COMMENTARY

Prior to this study, the major work examining early P2Y12 inhibition in STEMI was the 2014 ATLANTIC trial. Those authors randomized more than 1,800 STEMI patients to receive ticagrelor either in the prehospital setting or in the cardiac cath lab. It is well known that ATLANTIC showed no difference between the groups in its two coprimary endpoints, which were ST-segment resolution and Thrombolysis In Myocardial Infarction flow in the IRA at initial angiography. Notably, early administration of ticagrelor showed a significant risk reduction in the secondary endpoint of stent thrombosis (ST), although due to small numbers (21 ST events within 30 days), this did not affect the overall statistics regarding death and MI. This difference in ST was found despite an average difference of only 31 minutes in the timing of loading doses between the two groups.

The strengths of the SCAAR analysis lie in the enormous size of the cohort in combination with remarkably complete data collection. However, this remains a retrospective study, with all its attendant weaknesses. One major issue is that guidelines recommended prehospital administration of P2Y12 agents and a large majority of patients (85.3%) in this study received these drugs drugs at first medical contact and diagnosis. Something about the patients who were not treated at initial presentation prevented early administration in contradiction to guidelines. Among the measured variables (age, diabetes, and coronary artery disease history), the two groups were quite different. Thus, despite the propensity analysis, residual confounding is highly likely here.

However, even assuming relatively well-matched groups, is it reasonable to expect a difference in outcomes referable to timing of oral P2Y12 inhibitor administration? Although the time difference between first medical contact and start of PCI was longer (average, 72 minutes) in this study compared with ATLANTIC, the precise medication administration times are not recorded, such that the actual time between medication administration and first angiography likely is shorter than this value. While the ATLANTIC authors used the relatively faster-onset agent ticagrelor exclusively, the SCAAR cohort received clopidogrel in 58.3% of cases, with ticagrelor and prasugrel representing 35.3% and 5.3% of the total, respectively. With oral agents whose time to peak effect is measured in multiple hours, it is unlikely that a difference of scarcely over an hour in administration of the oral loading dose would affect IRA patency at first angiography. The result we see is precisely what one would expect empirically.

From a practical perspective, giving an upstream loading dose of P2Y12 inhibitors has little downside in patients presenting with STEMI. There is no added cost, as one is giving the same agent at an earlier time, and the risk of requiring urgent surgery in the current era is minimal. Furthermore, it is easier to administer oral pills to an upright patient during transport vs. when the patient is lying flat on a cath lab table. Thus, for the average STEMI patient, the negative result of this study should not affect practice. ■

ABSTRACT & COMMENTARY

Mildly Elevated Pulmonary Arterial Pressure Associated With Higher Mortality Rate

By Van Selby, MD

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

Dr. Selby reports he is a consultant for Alnylam Pharmaceuticals and Akcea Therapeutics.

SYNOPSIS: In a large cohort of patients referred for echocardiography, an estimated right ventricular systolic pressure > 30 mmHg was associated with higher mortality rates.

SOURCE: Strange G, Stewart S, Celermajer DS, et al. Threshold of pulmonary hypertension associated with increased mortality. *J Am Coll Cardiol* 2019;73:2660-2672.

Pulmonary hypertension (PH) is associated with a poor prognosis, regardless of etiology. The results of several studies have suggested the traditional criteria for PH, a mean pulmonary arterial (mPA) pressure ≥ 25 mmHg measured by right heart catheterization, may fail to identify all patients at risk for adverse events. Echocardiography is the most common initial diagnostic test in the evaluation of PH, and it is helpful to identify clinically meaningful echo-measured thresholds.

To determine the prognostic significance of increasing pulmonary pressures, Strange et al evaluated the National Echo Database Australia (NEDA), which contains data on more than 300,000 patients referred for echocardiography at 12 centers across Australia. The estimated right ventricular systolic pressure (eRVSP, which approximates the pulmonary artery systolic pressure) was calculated using the modified Bernoulli equation based on the tricuspid regurgitant velocity (TRV) and assuming a right atrial pressure of 5 mmHg ($eRVSP = 4 \times TRV^2 + 5$ mmHg). The authors examined the underlying distribution of RVSP among patients referred for echocardiography and the prognostic significance of incremental increases in eRVSP. The primary endpoints were all-cause and cardiovascular-specific mortality, with a median follow up of 4.2 years.

The authors included echocardiograms from 157,842 patients with adequate TR jets in the analysis. The average age was 65.7 years, 52.9% were women, and the median eRVSP was 25 mmHg. Using a criterion of eRVSP > 40 mmHg, 18.7% of all patients had at least mild PH, and the authors confirmed that patients with PH exhibited worse survival rates compared to those without PH. To evaluate the effects of incremental increases in pulmonary pressures, the cohort was divided into quintiles based on eRVSP and analyzed for one- and five-year mortality after adjusting for factors including age and presence of left heart disease.

The authors found that even patients in the third quintile (corresponding to an eRVSP of approximately 30 mmHg) experienced significantly higher mortality rates than those in the lowest quintile (hazard ratio [HR], 1.41; 95% confidence interval, 1.31-1.52). Patients in the fourth (HR, 1.98) and fifth (HR, 4.04) quintiles of eRVSP were at an even higher risk of mortality compared to the lowest quintile ($P < 0.001$). The authors concluded that a threshold of eRVSP greater than 30 mmHg by echocardiography can be used to identify patients at a higher risk of mortality.

■ COMMENTARY

PH develops because of several causes, including intrinsic disease of the pulmonary arteries (as occurs in pulmonary arterial hypertension) or (more commonly) left heart or pulmonary disease. Regardless of the etiology, PH is a hemodynamic diagnosis based on an elevated mean pulmonary arterial pressure measured by right heart catheterization. Traditionally, the threshold to diagnose PH has been a mean pressure ≥ 25 mmHg. However, the authors of multiple studies have shown that patients with even milder elevations in mean pulmonary arterial pressure are associated with worse outcomes. Acknowledging the traditional threshold of 25 mmHg may be too high, the 6th World Symposium on Pulmonary Hypertension recently changed the diagnostic criteria for PH from an mPA ≥ 25 mmHg to a lower threshold of 20 mmHg. This change will lead to a marked increase in the number of patients diagnosed with PH. It is important to determine how this change will be incorporated into clinical practice.

Strange et al used echocardiography rather than right heart catheterization to identify patients with elevated pulmonary arterial pressures. When it comes to diagnosing PH using echocardiography, there are multiple limitations, including the inability to directly measure mPA pressure. Echocardiographic estimates of RVSP rely on the presence of a tricuspid regurgitant jet, which is not always present and is prone to measurement error. For these reasons and more, it is important to remember that echocardiography cannot diagnose PH. However, despite these limitations, it remains the most common initial test in the evaluation of PH; thus, it is helpful to have a clear idea how to interpret the eRVSP.

An eRVSP of 40 mmHg is used often to identify patients with PH (correlating roughly to a mPA pressure of 25 mmHg). Here, Strange et al have used one of the largest echocardiography databases available to confirm that patients with an eRVSP > 40 mmHg are at a higher risk for mortality vs. those with no PH. However, they also found that a threshold of 40 mmHg misses a significant proportion of patients at a higher risk for mortality; an eRVSP threshold of 30 mmHg may be more appropriate. This is an important finding, since 28.6% of all patients in the cohort had an eRVSP of 30-39 mmHg and would be reclassified as higher risk using this lower threshold.

Although the authors demonstrated that an eRVSP > 30 mmHg is associated with higher mortality rates, it is unclear whether the elevated pulmonary pressure contributes to this, or if it is a marker of comorbidities. For example, is an eRVSP of 30 mmHg really enough to cause RV dysfunction and failure, or is the mildly elevated RVSP a marker of other disease? The authors found a sequential increase in the prevalence of right heart dilation and RV dysfunction with increasing eRVSP, starting with 30 mmHg. This suggests, but does not necessarily prove, that even a mild increase in pulmonary artery pressure may be

sufficient to affect RV function. Therefore, mild PH may contribute to the observed relationship between eRVSP and mortality.

Identifying patients with elevated pulmonary pressures will not always lead to direct changes in medical therapy. Most patients in this cohort (and most patients with PH in general) exhibited associated left heart or lung disease. These patients have not been shown to benefit from pulmonary vasodilator therapy. Even in patients without these associated conditions, treating those with a mean pulmonary arterial pressure < 25 mmHg has not yet been shown to improve outcomes. For now, identifying optimal pressure thresholds is important for earlier diagnosis, earlier focus on treating factors that contribute to PH, and perhaps closer follow-up. Through earlier detection, we can move toward a more preventive approach to managing PH that aims to avoid right heart dysfunction before it develops. ■

ABSTRACT & COMMENTARY

Are Calcium Channel Blockers Needed for Radial Artery Grafts?

By Michael H. Crawford, MD, Editor

SYNOPSIS: A combined analysis of six trials comparing radial artery grafts vs. saphenous vein grafts for coronary bypass surgery revealed that patients taking calcium channel blockers for at least one year experienced fewer major cardiac events and fewer radial graft occlusions than those not so treated.

SOURCE: Gaudino M, Benedetto U, Fremes SE, et al. Effect of calcium-channel blocker therapy on radial artery grafts after coronary bypass surgery. *J Am Coll Cardiol* 2019;73:2299-2306.

The use of radial artery (RA) grafts as conduits for coronary artery bypass graft surgery (CABG) likely will increase now that the results of randomized, controlled trials (RCTs) have shown that they are superior to saphenous vein grafts for reducing subsequent coronary events. However, the role of calcium channel blocker (CCB) therapy and its duration after RA graft placement are unclear.

Investigators pulled data from six RCTs to address this issue. The authors of each trial recommended CCBs postoperatively, although with different agents for different time periods. The primary outcome was a major adverse cardiac event (MACE) at maximum follow-up. The main secondary outcome was RA graft occlusion. The final study population included 732 patients, of whom 502 received CCBs. Angiographic information by protocol was available for 243 patients treated with CCBs, and 200 of those who were not so treated. Median clinical follow-up was 60 months, and angiographic follow-up was 55 months.

Comparing the treated vs. not treated groups, the MACE rate at 36 months was 3.7% vs. 9.3%; at 72 months, 13.4% vs. 17.6%; and at 108 months, 16.8% vs. 20.5% ($P = 0.003$.). The incidence of RA graft occlusion was 0.9% vs. 8.6% at 36 months, 9.6% vs. 21.4% at 72 months, and 14.3% vs. 38.9% at 108 months ($P = 0.001$). An adjusted multivariate analysis revealed a significantly lower risk of MACE on CCBs (hazard ratio [HR], 0.52; 95% confidence interval [CI], 0.31-0.89; $P = 0.02$) and lower RA graft occlusion (HR, 0.20; 95% CI, 0.08-0.49; $P < 0.001$). When specific CCBs were analyzed separately, both diltiazem and amlodipine significantly lowered MACE and increased RA graft patency compared to no CCB therapy. Finally, the use of CCB therapy for one year was associated with lower MACE rates than therapy for less than one year ($P = 0.001$). Therapy for more than one year was not significant ($P = 0.08$). Similar results were found for RA patency. The authors concluded that CCB therapy for the first year after RA graft placement was associated with better clinical and angiographic outcomes.

■ COMMENTARY

The original paper from this compilation of six RCTs showed a significant reduction in MACE and repeat revascularization when the RA was used as the second conduit compared to saphenous veins (Gaudino M, et al. *N Engl J Med* 2018;378:2069-2077) and certainly influenced the European Society of Cardiology 2018 guidelines on myocardial revascularization, which gave it a class I indication (Neumann FJ, et al. *Eur Heart J* 2019;40:87-165). Since the six RCTs were randomized on conduit use, this post-hoc analysis of CCB use must be considered observational and hypothesis-generating. Two earlier randomized trials of CCBs vs. placebo in patients with RA grafts failed to demonstrate improved outcomes at one year, but each included ≤ 115 patients and used diltiazem at ≤ 180 mg/day. Consequently, the authors of the current study claim that they were underpowered. Also, most surgeons have empirically prescribed CCBs for

patients with RA grafts based on the known enhanced muscularity and vasospastic properties of RAs. One could argue that only those without contraindications to CCB use received them. Indeed, the no CCB group in this combined study was markedly different from the CCB therapy group; they were older and had lower left ventricular function. Perhaps the authors believed this group needed other therapies such as beta-blockers and renin angiotensin system modulators more than they needed CCBs and were not likely to tolerate CCBs. The authors used statistical methods to adjust for these and other differences, but there could be unmeasured confounders that influenced the results.

Ideally, a large randomized trial would answer the controversy over CCB use after RA grafting and its optimal duration. However, because the effect size in this combined observational study was so large, it is unlikely to ever happen. Another strength is that both diltiazem and amlodipine were used in large numbers and showed equivalent effects. Also, the beneficial effects of the CCB were only realized in therapy lasting ≥ 1 year. However, the authors did not provide data on doses or adverse effects of CCB therapy. The authors of other studies have shown peripheral edema in up to 25% of patients on CCBs and headaches in up to 9%. In my experience, most of the adverse effects of CCBs are dose-related. Theoretically, the dose could be adjusted to eliminate adverse effects, but it would be useful to know the least effective dose. At this time, it appears prudent to prescribe a CCB at the highest tolerated dose for at least one year after RA grafting for CABG. ■

ABSTRACT & COMMENTARY

Workplace Violence, Bullying Associated With Cardiovascular Disease Risk

By Michael H. Crawford, MD, Editor

SYNOPSIS: In a 12-year follow-up of surveyed Scandinavian employees, reported workplace violence and bullying increased the risk of future cardiovascular disease of a magnitude similar to other recognized cardiovascular disease risk factors.

SOURCES: Xu T, Magnusson Hanson LL, Lange T, et al. Workplace bullying and workplace violence as risk factors for cardiovascular disease: A multi-cohort study. *Eur Heart J* 2019;40:1124-1134.

Herrmann-Lingen C. Victimization in the workplace: A new target for cardiovascular prevention? *Eur Heart J* 2019;40:1135-1137.

Workplace stressors such as bullying and violence are associated with a higher risk of type 2 diabetes, but their role in cardiovascular (CV) disease is unclear. From three large Scandinavian longitudinal studies of working men and women, Xu et al studied four cohorts based on enrollment years ranging from 1995 to 2011. Employees aged 18-65 years with no prior CV disease and information available on workplace bullying and violence were identified. This resulted in a study population of more than 79,000 people.

Workplace bullying and exposure to or threat of violence were obtained from self-administered questionnaires. CV disease was defined as first hospitalization for coronary or cerebral vascular disease. Other biographical data were obtained to assess confounders and other stressors at work that could influence the results. The subjects' mean age was 43 years; 53% of subjects were women.

The prevalence of bullying ranged from 8-13% over 12 months in the four cohorts. Mainly, the perpetrators were from within the company (79%), and 21% were clients. The prevalence of violence ranged from 7-17% over 12 months in the cohorts, and the perpetrators were mainly clients (91%). Only 10-14% of employees experienced both stressors at the same time. After a mean follow-up of 12.4 years, 3,229 CV events occurred in these employees. After adjustment for various covariates, bullying increased the risk of CV disease (hazard ratio [HR], 1.59; 95% confidence interval [CI], 1.28-1.40).

Workplace violence also increased CV disease risk (HR, 1.25; 95% CI, 1.12-1.40). The frequency of bullying increased the risk (frequent HR, 2.22; 95% CI, 1.23- 4.01). Frequent violence increased risk of cerebrovascular disease by 36%. The authors concluded that bullying and violence in the workplace are common and associated with a greater risk of developing CV disease.

■ COMMENTARY

Previous studies have revealed that mental illnesses such as depression are independent risk factors for CV disease, as are certain personality traits, such as hostility and anger. Also, social risk factors, such as low socio-economic status and stress, have been identified.

Considering that workplace bullying and violence are related to some of the above risk factors, it is not surprising that they would be independent risk factors, too. In this study, the population-attributable risk was 5% for bullying and 3% for violence, which is similar to other well-established risk factors such as diabetes (4%). In addition, a dose response relationship was established for bullying, less so with violence. Sensitivity analyses with known confounders suggested these results were robust. Interestingly, there were no identified differences between the two sexes. Since such behavior potentially is modifiable, physicians and workplace managers need to be aware of these results.

There were limitations to this study. The authors relied on self-reporting on one day, and no further bullying or violence data were collected during follow-up. There is no information on underlying personality traits and behaviors, which could be important in understanding the results. It is possible that some victims may have exhibited negative behaviors that provoked inappropriate responses. Also, there may have been other stressors involved, such as marital conflict. The authors of these large studies did not provide data on clinical information such as blood pressure and cholesterol levels. Finally, this was a Scandinavian population, and the results may not be generalizable to other groups.

The main strengths of the study were the large population (> 79,000 people) and the long follow-up (mean = 12 years). Also, it is biologically feasible that these work stresses could lead to anxiety, depression, overeating, increased alcohol consumption, impaired sleep, and hypertension, all of which would explain an increased incidence of CV disease. The weaker association with violence compared to bullying may be due to the fact that almost all the violence was perpetrated by clients. The authors suggested that workers in these jobs may be self-selected for their ability to deal with irate clients better. In the final analysis, though, outcome studies that mitigate these behaviors need to be conducted to prove that eliminating bullying and violence would improve CV health. ■

CME/CE QUESTIONS

1. **In a report from Scandinavia, workplace violence almost always is perpetrated by:**
   a. coworkers.
   b. clients.
   c. management.
   d. security.

2. **In a study of new-onset atrial fibrillation (AF) comparing early ED cardioversion to delayed outpatient cardioversion, most of the early group demonstrated:**
   a. a shorter ED stay.
   b. spontaneous cardioversion.
   c. sinus rhythm upon discharge.
   d. recurrent AF within four weeks.

3. **The results of a recent large database study suggest that the upper limit of normal estimated right ventricular systolic pressure by echocardiography should be:**
   a. 25 mmHg.
   b. 30 mmHg.
   c. 35 mmHg.
   d. 40 mmHg.

4. **A large database analysis of first medical contact vs. at the cath lab administration of a P2Y12 inhibitor in STEMI showed:**
   a. less infarct-related artery occlusion.
   b. more bleeding complications.
   c. less in-stent restenosis.
   d. equivalent 30-day mortality.

5. **Following coronary artery bypass graft surgery, using the radial artery as a conduit, calcium channel blockers should be given for at least:**
   a. six weeks.
   b. three months.
   c. six months.
   d. one year.