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Letters

Association Between High Levels of Physical Exertion, Anger, and Anxiety Immediately Before Myocardial Infarction With Mortality During 10-Year Follow-Up

Transient episodes of heavy physical exertion (1) and psychological stressors, such as high levels of anger and anxiety (2), are associated with an immediately higher risk of myocardial infarction (MI) and other cardiovascular events, but little is known about the long-term prognosis of patients surviving an MI after these potential acute triggers. In this study, we evaluated whether high levels of physical exertion, anger, and anxiety in the 2 h before MI is associated with a higher rate of 10-year all-cause mortality.

As described previously (1,2), 3,886 MI patients were recruited between 1989 and 1996. Anger and anxiety data were available for 2,176 participants, comprising the present study population. Within a median of 4 days after MI admission, participants were interviewed about the time of symptom onset; the last time they experienced high levels of anger, anxiety, and exertion; and, for comparison purposes, their exposure 24 to 26 h before MI. High physical exertion was defined as self-reported exertion ≥6 metabolic equivalents. High anger and anxiety was defined as a State-Trait Personality Inventory score modified to assess the 2-h short-term exposures above the 90th percentile (2). The primary outcome was 10-year all-cause mortality based on the National Death Index, as described previously (3).

We used Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals (CI). Multivariable models were adjusted for covariates selected a priori including demographics (age, sex, age*sex, race, marital status, education, income), health behaviors (smoking status, alcohol consumption, body mass index, usual frequency of physical exertion), medical history (history of MI; congestive heart failure; angina; hypertension; diabetes mellitus; noncardiac comorbidities including stroke, cancer, respiratory disease, and renal failure), thrombolytic therapy, peak creatine kinase, and medication use.

Among 2,176 participants (mean 60.1 ± 12.5 years of age, 29.2% women, 89.0% white), 26% had a prior MI, and the peak creatine kinase level was 1.5 ± 1.9 U/l. In the 2 h before MI, high levels of physical exertion, anger, or anxiety were reported by 128 (6%), 205 (9%), and 204 (9%) patients, respectively.

Over 10 years of follow-up, 580 (27%) patients died. Compared to people reporting no anxiety before MI, the mortality rate was 44% higher (adjusted HR: 1.44; 95% CI: 1.09 to 1.91) for people reporting anxiety in the 2 h before MI. High levels of anger (adjusted HR: 1.34; 95% CI: 0.98 to 1.82) and physical exertion (HR: 1.15; 95% CI: 0.73 to 1.79) before MI were associated with higher mortality rates, but the associations did not reach statistical significance. After adjusting for anxiety in the 24 to 26 h before MI, anxiety during the 2 h before MI remained a statistically significant predictor of mortality (HR: 1.44; 95% CI: 1.01 to 2.06).

Prior research by Brodov et al. (4) found that among 662 MI patients there was no association between physical or emotional precipitants of MI and 1-year mortality, which may in part reflect low statistical power. Arnold et al. (5) found perceived stress at the time of MI was associated with a 42% (95% CI: 1.15 to 1.76) higher rate of 2-year mortality. However, the measure used did not evaluate acute stress before MI. We did not find an association between exposure to high levels of physical exertion before MI and subsequent mortality, possibly because patients with an MI preceded by physical exertion were relatively young with less comorbidity. There were also fewer participants who reported heavy physical exertion immediately before MI onset compared to the number who reported anger and anxiety. The analyses for anger and anxiety 0 to 2 h before MI did not change when adjusting for exposure 24 to 26 h before MI, but this does not rule out the potential role of trait levels of these psychological factors.

In conclusion, anxiety immediately before MI onset is associated with a higher 10-year all-cause

mortality rate. Future research is needed to determine the characteristics of patients who are at risk of MI immediately after emotional stressors and whether specific subgroups have a worse prognosis after MIs preceded by emotional stressors.

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Lifetime Risk of Pulmonary Hypertension for All Patients After Shunt Closure

Successful repair of shunts in patients with congenital heart disease (CHD) is often erroneously considered a cure, leading to a large number of patients lost to follow-up after discharge (1). The prevalence of pulmonary hypertension (PH) appears to be high after shunt closure (2) and is associated with increased morbidity and mortality (3). Until now, only limited data on the risk of PH after shunt closure were available, and these data were hampered by the use of database encoded analyses, single-center studies, or small cohort studies in specific cardiac defects. We aimed to identify the time course of the development of PH after shunt closure in adults with CHD to optimize monitoring intervals of these patients and to identify PH in an early stage.

We used the Dutch CONgenital CORvitia registry, containing 15,800 adult CHD patients, to identify all patients with a closed systemic-to-pulmonary shunt (n = 3,340), of which a randomized sample, stratified according to secondary or tertiary center, underwent thorough review of all medical records. In this nationwide cohort sample of 1,103 patients, we determined the cumulative incidence of PH after shunt closure. Subsequently, a nested case-control study was performed to analyze predictors associated with PH after shunt closure. All cases of PH were matched with up to 2 controls on age (±5 years), sex, and presence of Down syndrome. Presence of PH was defined as documented systolic pulmonary artery pressure >40 mm Hg on echocardiography. Patients with signs of left-sided valvular disease (moderate or severe mitral stenosis or regurgitation, moderate or severe aortic stenosis or regurgitation) or elevated diastolic filling pressures (early diastolic velocity ratio >15, left ventricular ejection fraction <40%, moderate or severe left atrial dilation) were excluded.

In the cohort of 1,103 shunt patients, closure was performed in year 1987 (median, interquartile range: 1977 to 1990) at a median age of 8.5 years (interquartile range: 2.9 to 27.6). The most common diagnoses were secundum atrial septal defect (ASD) (n = 382), ventricular septal defect (n = 283), and primum ASD (n = 92). In total, 72 cases with PH were identified during a mean period of 25 ± 14 years. The cumulative incidence of PH immediately after closure was 2.1% (95% confidence interval [CI]: 0.3 to 7.7) and >15% (95% CI: 2.6 to 23.8) 50 years after closure (**Figure 1A**). Remarkably, even patients with mild defects such as secundum ASD closed <25 years of age, were at risk of developing PH several decades after repair (6 of 141 patients, 4.3%). The incidence of PH, specified according to age at closure, is visualized in **Figure 1B**. In multivariate conditional logistic regression analysis of the case-control cohort, presence of PH pre-closure (rate ratio 5.7; 95% CI: 2.4 to 13.6; p <0.001) and New York Heart Association functional class >I pre-closure (rate ratio: 2.9; 95% CI: 1.3 to 6.8; p = 0.009) were the