ISSN 0735-1097/$36.00

Letters

Sexual Activity as a Trigger for Sudden Cardiac Arrest

Sexual activity is an important aspect of quality of life, and is associated with both health and mortality benefit (1). Nonetheless, it is not without risk. In a study from Germany, 0.2% of autopsied natural deaths were linked to sexual activity (2). It is also recognized that sexual activity may trigger nonfatal acute cardiac events such as myocardial infarction. Sudden cardiac arrest (SCA), which manifests as an unexpected collapse and loss of the pulse, is a mostly lethal condition that results in over 300,000 deaths annually in the United States. Physical activity, especially when nonhabituated, has been associated with increased risk of SCA (3). To our knowledge, there is no available information on sexual activity as a potential trigger for SCA in the general population.

The community-based Oregon SUDS (Sudden Unexpected Death Study) study, ongoing since 2002, uses multiple-source ascertainment to prospectively identify cases of SCA that occur in the Portland, Oregon, metropolitan area (catchment population approximately 1 million) (4). All SCA cases are adjudicated based on emergency medical services reports containing detailed circumstances of the cardiac arrest event, lifetime medical records, and autopsy data. Emergency medical services personnel record the individual's location, activity, and circumstances of SCA. We included all subjects over 18 years of age, ascertained between 2002 and 2015. All SCA cases that occurred during or within 1 h of sexual intercourse were considered as related to sexual activity (sex-SCA).

For comparisons between sex-SCA versus all other SCA cases, independent sample Student's *t*-test, Pearson's chi-square test and Fisher exact test were used. For calculation of SCA incidence rates, analysis was limited to the first 10 years from Multnomah County, the largest subset of the Portland metropolitan area (average population >18 years of age = 544,370).

A total of 4,557 SCAs were identified (mean 65.2 ± 16.3 years of age; 68.0% men). Of these, 4,525 (99.0%) had detailed information available to determine whether sexual activity preceded SCA. Overall, 34 (0.7%) of SCAs were linked to sexual activity, yielding an annual incidence of 0.28 per 100,000 adults. SCA occurred during sexual activity in 18 (55.0%) of these cases, and within minutes after cessation of sexual activity in 15 (45.0%) cases. For one case, exact timing could not be determined. Of the sex-SCA cases, 32 (94.0%) were men. Among men, sex-SCA was responsible for 1.0% of overall SCA burden, compared with 0.1% among women.

Individuals with sex-SCA were on average 5 years younger (range 34 to 83 years of age) and more likely to be African American than were the rest of the SCA cases (Table 1). Cardiac comorbidities were relatively common in both groups. Among those with sex-SCA, 29% of patients had a history of coronary artery disease, 26% had symptomatic heart failure, and the majority were taking cardiovascular medications.

Sex-SCA was more likely to present with ventricular fibrillation or tachycardia than other SCA (76% vs. 45%; $p < 0.001$), and this finding remained consistent in a sensitivity analysis of subjects with witnessed cardiac arrest. Only one-third of the sex-SCA cases received bystander cardiopulmonary resuscitation (CPR). There was a nominal difference

TABLE 1 Clinical Characteristics of Patients With SCA Related to Sexual Activity, Compared With SCA Occurring During Other Circumstances

	Sexual Activity–Related SCA (n = 34)	Other SCAs (n = 4,523)	p Value
Age, yrs	60.3 ± 10.6	65.2 ± 16.3	0.011
Male	32 (94.1)	3,068 (67.8)	0.001
Race			0.022
Black	6 (18.8)	330 (7.8)	
Other	26 (82.2)	3,896 (92.2)	
Medical history			
Heart failure	8 (25.8)	1,097 (26.0)	0.92
Coronary artery disease	9 (29.0)	1,016 (24.0)	0.58
Cardiac arrest characteristics and outcomes			
Ventricular fibrillation/tachycardia	25 (75.8)	1,567 (45.2)	<0.001
Bystander CPR	11 (32.4)	1,232 (27.2)	0.51
Return of spontaneous circulation	14 (41.2)	1,488 (33.4)	0.34
Survival to hospital discharge	6 (19.4)	555 (12.9)	0.29

Values are mean ± SD or n (%). Race available for 32 sex-related sudden cardiac arrests (SCAs) and 4,226 other SCAs; medical history available for 31 sex-related SCAs and 4,226 other SCAs; initial SCA rhythm available for 33 sex-related SCAs and 3,464 other SCAs; survival status available for 31 sex-related SCAs and 4,290 other SCAs.
CPR = cardiopulmonary resuscitation.

JACC VOL. 70, NO. 20, 2017
NOVEMBER 14/21, 2017:2599–604

in survival between the 2 groups (Table 1), likely explained by the differences in rates of shockable rhythms.

We observed a relatively low overall burden of SCA related to sexual activity in the community, with the vast majority of cases confined to men. Although sexual activity involves exertion, the mechanisms triggering SCA may be unique, and in some situations may also involve medications, stimulants, and alcohol use. The absolute risk of sex-SCA appears to be extremely low, even among subjects with clinical heart disease that have a prevalence of 7% to 10% in the community. However, we lacked information on the overall frequency of sexual activity and could not assess relative risk compared to rest and physical activity. These findings have implications for cardiac patients as well as health care professionals, advising them on the safety of engaging in sexual activity. Moreover, even though SCA during sexual activity was witnessed by a partner, bystander CPR was performed in only one-third of the cases. This likely explains the relatively low survival rates despite mostly shockable initial cardiac arrest rhythms. Therefore, these findings also highlight the importance of continued efforts to educate the public on the importance of bystander CPR for SCA, irrespective of the circumstance.

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http://dx.doi.org/10.1016/j.jacc.2017.09.025

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Myofilament Calcium-Buffering Dependent Action Potential Triangulation in Human-Induced Pluripotent Stem Cell Model of Hypertrophic Cardiomyopathy

Familial hypertrophic cardiomyopathy is caused by mutations in genes encoding sarcomere proteins. Among hypertrophic cardiomyopathy-linked disease genes, cardiac troponin T (TnT) mutations are associated with a high incidence of arrhythmic cardiac death (1), but the underlying mechanism has remained elusive. Studies in mice suggest that increased myofilament Calcium (Ca) buffering caused by pathogenic TnT mutations such as TnT-I79N generates susceptibility to ventricular arrhythmias by Ca-dependent action potential (AP) remodeling (2). As cardiac electrophysiological properties of mice differ substantially from humans, here we used cardiomyocytes (CMs) derived from human-induced pluripotent stem cells (hiPSCs) to study the effect of increasing myofilament Ca sensitivity on cytosolic Ca buffering and cardiac AP.

We first generated hiPSC lines from dermal fibroblasts of 3 healthy donors using standard approaches. One of the 3 hiPSC lines was edited using CRISPR/Cas9 and a heterozygous Ca-sensitizing TnT-I79N mutation introduced. Hence, the unedited line was the isogenic control line. The other 2 lines were named population controls. We then used the Matrigel mattress method (3) to generate single rod-shaped CMs for each iPSC line and studied TnT-I79N protein levels, cytosolic Ca buffering, and electrophysiology.

Analysis by nano-liquid chromatography mass spectrometry indicated that 43% of total TnT protein was mutant in I79N hiPSC-CMs. Cytosolic Ca buffering was quantified in voltage-clamped hiPSC-CMs as reported in Hwang et al. (4). Cytosolic Ca binding affinity was significantly higher (= lower K_d values) in I79N compared to both isogenic control and population control hiPSC-CMs (Figure 1A). Furthermore, application of the Ca sensitizer EMD57033 (EMD,