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Distinctive Profile of Sudden Cardiac Arrest in Middle-Aged vs. Older Adults: A Community-Based Study

Amit Noheria, MBBS, SM^{1,*}, Carmen Teodorescu, MD, PhD^{1,*}, Audrey Uy-Evanado, MD¹, Kyndaron Reinier, PhD, MPH¹, Ronald Mariani, EMT-P¹, Karen Gunson, MD², Jonathan Jui, MD, MPH³, and Sumeet S. Chugh, MD¹

¹The Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA

²Department of Pathology, Oregon Health and Science University, Portland OR

³Department of Emergency Medicine, Oregon Health and Science University, Portland OR

Abstract

Background—While sudden cardiac arrest (SCA) rates increase with age, middle-aged adults (35–59 years) may comprise a significant proportion of SCA cases in the community (30–40%). However, there is a lack of studies evaluating SCA risk factors specifically associated with this age-group of the population.

Methods—Using prospective multiple-source surveillance methodology we identified cases of SCA 35 years in the ongoing Oregon Sudden Unexpected Death Study (Portland, Oregon metropolitan area, population ≈1,000,000). Out-of-hospital SCA cases, aged 35–59 years were compared to older SCA cases (≥60 years) in a comprehensive analysis of clinical profile of SCA.

Results—The middle-aged (n=753) compared to older (n=1251) cases were *more* likely to be male, obese, have sleep apnea and seizure disorder (all p < 0.001); and were *less* likely to have a history of hypertension, diabetes mellitus, known coronary artery disease, congestive heart failure and syncope (all p < 0.01). In multivariable analyses the middle-aged group had higher likelihood of male sex (O.R. 1.67, 95% C.I. 1.29–2.18), obesity (2.20, 1.52–3.19), sleep apnea (2.30, 1.44–3.68) and seizure disorder (2.69, 1.64–4.42); and lower rates of known coronary artery disease (0.57, 0.43–0.74) and congestive heart failure (0.35, 0.25–0.48).

Conclusions—SCA in the middle-aged adult was distinguishable from older subjects by higher rates of obesity, sleep apnea and seizure disorder; and lower prevalence of traditional clinical risk markers. With the growing epidemic of obesity, these findings have implications for SCA burden; and suggest the need for a clinical and investigational focus on SCA prediction and prevention in the middle-aged adult, that is distinct from older adults.

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Address Correspondence to: Sumeet S. Chugh MD, The Heart Institute, Saperstein 2S46, Cedars-Sinai Medical Center, 8700 Beverly Blvd, Los Angeles, CA 90048; Fax 310-423-3522; sumeet.chugh@cshs.org.

*These authors contributed equally to this work

^{1,2,3}The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

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Keywords

sudden-death; obesity; coronary artery disease; middle-age; community

Introduction

There are approximately 300,000–350,000 cases of out-of-hospital sudden cardiac arrest/death (SCA) in the United States every year, imparting a substantial public health burden. [1–5] Community-based analyses indicate that up to one-third of the cases of SCA in adults are under age 60 years.[1, 2, 6–9]

Factors that have been most commonly associated with occurrence of SCA in the overall population include coronary artery disease (CAD) and associated markers such as diabetes mellitus, left ventricular hypertrophy, hyperlipidemia and cardiomyopathies.[1, 6, 10–14] Studies focusing on the youngest adults <35 years old have reported myocardial disease, primary coronary anomalies and primary arrhythmic disorders as playing a more important role, with a higher proportion of SCAs that remain unexplained.[15–17] We have previously reported that a substantial proportion of SCAs in the 35–44 year population also remain unexplained despite autopsy evaluation, especially in women.[18]

While the 35–59 year age-group of SCA cases has substantial societal effects due to the sudden and unexpected loss of actively working members, there is limited information on the clinical profile of this sub-group. Due to the inherent logistical challenges in studying SCA, a prospective, community-based multiple-source case surveillance and adjudication approach is a relevant and feasible methodology.[1, 14, 19] Therefore, we performed an analysis of the ongoing Oregon-SUDS and conducted comparisons of clinical characteristics of SCA cases in the 35–59 year vs. 60 year age category.

Methods

Study Population

The Oregon-SUDS is an ongoing prospective study of out-of-hospital SCA in the Portland, Oregon, metropolitan area (population ≈1,000,000).[1] Detailed methods have been published elsewhere.[1, 8, 19] Briefly, emergency medical services (EMS) for the metropolitan area are provided by a 2-tier, advanced life support first-response system. Incident cases of SCA were identified through EMS, the Medical Examiner's office, and the 16 local hospitals, and all available medical records were obtained for each subject. Subjects aged 35 years or older who were determined to have had SCA between February 1, 2002 and January 31, 2010 were included in this analysis. A detailed review of pre-arrest medical records and autopsy data was performed to identify demographic and clinical characteristics for each case and compared between the middle-aged (35–59 years) and the older (> 60 years) age groups. Informed consent was obtained from study participants. The institutional review boards of Oregon Health and Science University, Cedars-Sinai Medical Center, and all participating hospitals and health systems approved the study.

Definitions

SCA was defined as sudden unexpected death or resuscitation from a pulseless cardiac arrest that occurred either within 1 hour of witnessed symptom onset or within 24 hours of being observed alive and symptom free.[1, 20] Sudden deaths in patients that had a non-cardiac chronic terminal illness like malignancy that was not in remission, were excluded. In

addition, cases with an identifiable non-cardiac etiology, including deaths associated with trauma, violence, drug overdose, drowning, and suicide were also excluded.

EMS response time was calculated from the 911 dispatch time to time of arrival at patient's side. Return of spontaneous circulation was defined as return of a palpable pulse in conjunction with a systolic blood pressure ≥ 60 mm-Hg.

Diabetes mellitus was defined as a clinical history of diabetes mellitus or use of insulin or oral hypoglycemic agent. CAD by clinical history was defined as history of myocardial infarction, coronary revascularization, or at least 50% stenosis on coronary angiography. Hypertension, congestive heart failure, cerebral vascular accident, peripheral vascular disease, obstructive pulmonary disease, liver disease, sleep apnea, syncope and seizures were also identified from the documented clinical history prior to arrest.

Baseline ECG parameters were determined from any available pre-arrest resting 12-lead ECG that was closest to and unrelated to the cardiac arrest (median 10.8 months before cardiac arrest). In addition, a subset of cases had cardiac evaluation performed prior and unrelated to the cardiac arrest. Left ventricular systolic function was assessed by LVEF from echocardiogram, ventriculogram or multigated acquisition scan. Left ventricular mass was calculated from quantitative values on echocardiograms (median 12.9 months before cardiac arrest) using the American Society of Echocardiography modified equation, indexed to body surface area. Left ventricular hypertrophy was defined as left ventricular mass / body surface area >134 g/m² for men and >110 g/m² for women.[21]

Statistical Analysis

The differences in demographics, clinical characteristics, arrest circumstances, presenting arrhythmia, and resuscitation outcomes in cases of SCA between those 35–59 years old and those ≥ 60 years old were evaluated with the use of Pearson's χ^2 -tests (categorical variables) or independent sample *t*-tests (continuous variables). A multivariable logistic regression model was used to assess associations with pre-arrest clinical characteristics independent of other covariates. Clinical predictors with $p < 0.05$ on univariate analyses were included in this multivariate model. Further multivariate sensitivity analyses were performed adjusting for pre-arrest ECG variables. Two-tailed $\alpha = 0.05$ was considered the threshold for statistical significance for all comparisons. All statistical analyses were performed with SAS version 9.1 (Cary, NC). Distributions of categorical variables are expressed as number (percent) and of continuous variables are expressed as mean $\pm$ standard deviation.

Results

A total of 2004 incident cases of SCA were identified among the Oregon-SUDS population that were aged ≥ 35 years and occurred between February 1, 2002 and January 31, 2010. Of these, 753 (37.6%) were 35–59 years and 1251 (62.4%) were ≥ 60 years. Cases of SCA in the middle-age group compared to the older group had a larger proportion of males (75.8% vs. 60.7%, $p < 0.0001$). Middle-aged adults also had a larger proportion contributed by non-white minorities (17.0% vs. 11.0%, $p = 0.0004$). Middle-aged SCA cases were more likely to have been unwitnessed (51.9% vs. 44.0%, $p = 0.002$) and occur in public locations (22.7% vs. 11.8%); but less likely to occur in an outpatient/care facility (9.6% vs. 16.6%; $p < 0.0001$). The middle-aged group were more likely to present with ventricular tachycardia/ventricular fibrillation (VT/VF, 49.1% vs. 39.0%) and less pulseless electrical activity (PEA)/asystole (50.3% vs. 57.4%, $p < 0.0001$) as the first recorded rhythm. When resuscitation was attempted, the middle-aged group had a higher rate of survival to hospital discharge (14.1% vs. 9.9%, $p = 0.02$) [Table 1].

Physician records were available and were reviewed in 1523 (76%) cases of SCA, and these comprise the subjects for subsequent analyses. The 35–59-year group of SCA cases as compared to the ≥60-year group were less likely to have hypertension (52.2% vs. 70.9%, $p<0.0001$) or diabetes mellitus (29.1% vs. 37.2%, $p=0.002$); and were less likely to have known coronary artery disease (21.8% vs. 46.3%, $p<0.0001$), history of congestive heart failure (17.3% vs. 40.4%, $p<0.0001$) or syncope (4.8% vs. 8.6%, $p=0.008$). In addition, the middle-aged cases had lower prevalence of cerebrovascular accident, peripheral vascular disease and obstructive lung disease (all $p=0.001$). Notably however, the 35–59 year SCA cases had a higher prevalence of obesity (BMI ≥ 30 kg/m²; 48.1% vs. 33.0%, $p<0.0001$), sleep apnea (10.8% vs. 6.1%, $p=0.001$), and seizure disorder (9.4% vs. 4.2%, $p<0.0001$) [Table 2]. Autopsy information was available in 257/753 (34.1%) middle-aged but only 30/1251 (2.4%) older cases. Amongst these, CAD was established on autopsy examination in 178/257 (69.3%) vs. 24/30 (80%) patients respectively ($p=0.22$) [Table 3]. Among the subpopulation with CAD diagnosed on autopsy the clinical diagnosis of CAD was noted previously in the medical history in only 3/178 (1.7%) middle-aged vs. 5/24 (20.8%) older cases.

For the middle-aged and older groups, baseline assessment of left ventricular hypertrophy was available in 84/519 (16.2%) and 286/1004 (28.5%) respectively, and information on LVEF was available in 122/519 (23.5%) and 421/1004 (42.1%) cases. Amongst these subgroups, the distributions of left ventricular hypertrophy (35.7% vs. 46.8%, $p=0.07$) or severe systolic dysfunction (23.8% vs. 31.1%, $p=0.12$) were not statistically different between the two age categories. Similarly, when baseline ECG information was available, we did not find any statistical differences in the heart-rate corrected QT-interval (452.1 ± 38.9 ms vs. 453.5 ± 41.0 ms, $p=0.72$) or the $T_{\text{peak}}-T_{\text{end}}$ interval [14] (97.5 ± 20.8 ms vs. 99.7 ± 22.3 ms, $p=0.25$) between the two age categories. However, the middle-aged group had a narrower mean QRS duration (94.6 ± 19.1 vs. 104.6 ± 26.2 , $p<0.0001$) and a slightly higher mean heart rate (81.5 ± 18.5 vs. 77.9 ± 18.8 , $p=0.02$) [Table 2].

In logistic regression analyses, the following characteristics remained significantly associated with the 35–59 year group: male sex, non-white minorities, obesity, sleep apnea, and seizures; and absence of hypertension, known CAD, congestive heart failure, cerebrovascular accident, peripheral vascular disease or obstructive lung disease. There were no substantial changes in the multivariable results on sensitivity analyses performed by additional adjustments for ECG parameters – heart rate and QRS duration [Table 4].

Discussion

In this population-based study, well over a third of SCA cases in ≥35 year-old adults were in the middle-aged (35–59 year) category with a higher proportion of men as compared to the older group. The middle-aged group had fewer co-morbidities, including traditional risk markers for SCA: hypertension, diabetes mellitus, and clinical history of CAD, congestive heart failure or syncope. Moreover, among the subgroup of the middle-aged SCA cases that had historical information on LVEF available, half had normal pre-arrest LVEF and less than a quarter had severe left ventricular systolic dysfunction. Regardless, among the middle-aged cardiac arrest cases that had an autopsy evaluation performed, over two-thirds had CAD. A diagnosis of CAD made at autopsy was almost never (98.3%) observed by health care providers prior to the cardiac arrest. Remarkably, the middle-aged SCA victims had a higher prevalence of obesity than their older counterparts, and were more likely to have sleep apnea and history of prior seizure disorder. Additionally, the middle-aged SCAs had a higher likelihood of presenting with VT/VF but were more likely to be unwitnessed and not resuscitated. Nonetheless, when resuscitation was attempted the middle-aged group had a higher survival to hospital discharge.

The lower prevalence of traditional risk markers of SCA in the middle aged group including clinical history of CAD, congestive heart failure or syncope is a novel finding and suggests the existence of SCA prevention challenges in middle age, that were not previously recognized. The significant and independent association of middle-aged SCA with obesity and sleep apnea has implications for future burden of SCA. The National Health and Nutrition Examination Survey (NHANES) has reported that the national obesity (BMI ≥ 30 kg/m²) prevalence among 40–59 year-old men has increased from 12.6% (1960–1962) to 34.3% (2007–2008). The prevalence of obesity in 40–59 year-old women has similarly increased from 18.5% (1960–1962) to 38.2% (2007–2008).[22, 23] Obesity is a known risk factor for SCA[10, 13, 24] and is a major risk factor for sleep apnea, a condition that has been associated with night-time SCA.[25] Therefore, obesity may potentially be a mechanistic link for SCA in the middle-aged adult population. Plausible mechanisms for SCA in the obese include obesity related ventricular remodeling (left ventricular systolic and diastolic dysfunction), pro-arrhythmic epicardial fat, metabolic derangements and accelerated coronary atherosclerosis.[24, 26, 27] While history of seizure disorder is a known risk factor for sudden unexpected death the higher prevalence in the middle-aged group warrants further investigation. Mechanistically, sudden death in epilepsy could be due to hypoxia and cardiac dysrhythmias with generalized seizure activity or possibly related to an increased propensity for cardiac arrhythmias.[28] From a public health standpoint, these findings highlight the need for a special risk-prediction focus in this age-group combined with a continued effort at primary prevention of obesity at younger ages.

The baseline QRS duration was shorter and the heart rate higher in middle-aged SCA cases, and whether these reflect generic age-related changes or have mechanistic implications for SCA in the middle-aged age group also warrants further evaluation. Middle-aged patients with sudden death had a higher proportion of VT/VF and less PEA/asystole as compared to the older population.[29] Since VT/VF are more likely to be associated with coronary disease (as compared to PEA/asystole), this may indicate that a higher proportion of SCAs in the 35–59-year group occur in association with a primary coronary event.

To the best of our knowledge this study is the first analysis focusing on the risk profile of SCA in the 35–59 year general population, and distinguishing it from ≥ 60 year patients. We show that middle-age SCA patients are more likely to be male, obese, and have history of sleep apnea or seizures when compared to the older SCA population. They are also less likely to have known CAD or structural heart disease, though undiagnosed CAD may play an important role. There are significant advantages to studying SCA in the general community and including all comers instead of just focusing on defibrillator implant patients, especially since defibrillator therapies are unlikely to be effective surrogates for sudden cardiac arrest.[20] Given the overall incidence of SCD (60/100,000) population-based analyses provide the only feasible way to obtain numbers that are large enough to conduct such analyses.[9] Therefore, the strengths of this study relate to its design, with prospective multiple-source surveillance methodology for identification all incident cases of SCA. This is a more robust method as compared to retrospective death-certificate based review, which overestimates SCA by nearly two-fold and has an unacceptably low positive predictive value.[1] In addition, the detailed review of pre-arrest medical records is a strength of this study.

Limitations

There are inherent limitations of community-based analyses of SCA. These include lack of documented clinical history for some cases. In subgroups of patients such as those with sleep apnea and seizure disorder, while clinical information is available, it may not be comprehensive. Physician records were available for only three-quarters of the case-population, and only a subgroup had baseline ECG and echocardiographic data; however,

since 40–50% cases may present with SCA as the first manifestation of illness, the lack of prior clinical data is not unexpected. Furthermore, since molecular autopsies were not performed as part of this study, it is possible that a small minority of 35-year-old SCA cases were related to genetic channelopathies, though these are quite rare even among younger subjects.[30, 31]

Conclusions

SCA in the middle-aged adult (35–59 years) demographic was independently and significantly associated with a higher prevalence of obesity, sleep apnea and seizure disorder compared to the older population. These findings may have mechanistic and public health implications, especially in light of the growing, global epidemic of obesity. It is likely that the nature of SCA prediction and prevention will be distinct for middle-aged vs. older adults and ongoing clinical and investigational efforts should take this into consideration.

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References

1. Chugh SS, Jui J, Gunson K, Stecker EC, John BT, Thompson B, et al. Current burden of sudden cardiac death: multiple source surveillance versus retrospective death certificate-based review in a large U.S. community. *J Am Coll Cardiol.* 2004;1268–1275. [PubMed: 15364331]
2. Chugh SS, Reinier K, Teodorescu C, Evanado A, Kehr E, Al Samara M, et al. Epidemiology of sudden cardiac death: clinical and research implications. *Progress in cardiovascular diseases.* 2008;213–228. [PubMed: 19026856]
3. Cobb LA, Fahrenbruch CE, Olsufka M, Copass MK. Changing incidence of out-of-hospital ventricular fibrillation, 1980–2000. *JAMA : the journal of the American Medical Association.* 2002; 288:3008–3013. [PubMed: 12479765]
4. Myerburg RJ, Interian A Jr, Mitrani RM, Kessler KM, Castellanos A. Frequency of sudden cardiac death and profiles of risk. *Am J Cardiol.* 1997; 80:10F-9F.
5. Escobedo LG, Zack MM. Comparison of sudden and nonsudden coronary deaths in the United States. *Circulation.* 1996; 93:2033–2036. [PubMed: 8640979]
6. Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. *Circulation.* 2001;2158–2163. [PubMed: 11684624]
7. de Vreede-Swagemakers JJ, Gorgels AP, Dubois-Arbouw WI, van Ree JW, Daemen MJ, Houben LG, et al. Out-of-hospital cardiac arrest in the 1990's: a population-based study in the Maastricht area on incidence, characteristics and survival. *J Am Coll Cardiol.* 1997;1500–1505. [PubMed: 9362408]
8. Chugh SS, Reinier K, Singh T, Uy-Evanado A, Socoteanu C, Peters D, et al. Determinants of prolonged QT interval and their contribution to sudden death risk in coronary artery disease: the Oregon Sudden Unexpected Death Study. *Circulation.* 2009; 119:663–670. [PubMed: 19171855]
9. Havmoeller R, Reinier K, Teodorescu C, Uy-Evanado A, Mariani R, Gunson K, et al. Low Rate of Secondary Prevention ICDs in the General Population: Multiple-Year Multiple-Source Surveillance of Sudden Cardiac Death in the Oregon Sudden Unexpected Death Study. *Journal of cardiovascular electrophysiology.* 2013; 24:60–65. [PubMed: 22860692]
10. Jouven X, Desnos M, Guerot C, Ducimetiere P. Predicting sudden death in the population: the Paris Prospective Study I. *Circulation.* 1999; 99:1978–1983. [PubMed: 10209001]

11. Kannel WB, Plehn JF, Cupples LA. Cardiac failure and sudden death in the Framingham Study. *American heart journal*. 1988;869–875. [PubMed: 3354416]
12. Kannel WB, McGee DL, Schatzkin A. An epidemiological perspective of sudden death. 26-year follow-up in the Framingham Study. *Drugs*. 1984;1–16. [PubMed: 6499693]
13. Albert CM, Chae CU, Grodstein F, Rose LM, Rexrode KM, Ruskin JN, et al. Prospective study of sudden cardiac death among women in the United States. *Circulation*. 2003;2096–2101. [PubMed: 12695299]
14. Panikkath R, Reinier K, Uy-Evanado A, Teodorescu C, Hattenhauer J, Mariani R, et al. Prolonged Tpeak to Tend Interval on the Resting Electrocardiogram Is Associated with Increased Risk of Sudden Cardiac Death. *Circ Arrhythm Electrophysiol*. 2011
15. Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Annals of internal medicine*. 2004;829–834. [PubMed: 15583223]
16. Corrado D, Basso C, Thiene G. Sudden cardiac death in young people with apparently normal heart. *Cardiovasc Res*. 2001;399–408. [PubMed: 11334844]
17. Shen WK, Edwards WD, Hammill SC, Bailey KR, Ballard DJ, Gersh BJ. Sudden unexpected nontraumatic death in 54 young adults: a 30-year population-based study. *The American journal of cardiology*. 1995;148–152. [PubMed: 7611149]
18. Chugh SS, Chung K, Zheng Z-J, John B, Titus JL. Cardiac pathologic findings reveal a high rate of sudden cardiac death of undetermined etiology in younger women. *American heart journal*. 2003;635–639. [PubMed: 14564316]
19. Stecker EC, Vickers C, Waltz J, Socoteanu C, John BT, Mariani R, et al. Population-based analysis of sudden cardiac death with and without left ventricular systolic dysfunction: two-year findings from the Oregon Sudden Unexpected Death Study. *J Am Coll Cardiol*. 2006;1161–1166. [PubMed: 16545646]
20. Fishman GI, Chugh SS, Dimarco JP, Albert CM, Anderson ME, Bonow RO, et al. Sudden cardiac death prediction and prevention: report from a National Heart, Lung, and Blood Institute and Heart Rhythm Society Workshop. *Circulation*. 2010; 122:2335–2348. [PubMed: 21147730]
21. Devereux RB, Lutas EM, Casale PN, Kligfield P, Eisenberg RR, Hammond IW, et al. Standardization of M-mode echocardiographic left ventricular anatomic measurements. *J Am Coll Cardiol*. 1984; 4:1222–1230. [PubMed: 6238987]
22. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. *JAMA : the journal of the American Medical Association*. 2002; 288:1723–1727. [PubMed: 12365955]
23. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. *JAMA : the journal of the American Medical Association*. 2010; 303:235–241. [PubMed: 20071471]
24. Hookana E, Junttila MJ, Puurunen VP, Tikkanen JT, Kaikkonen KS, Kortelainen ML, et al. Causes of nonischemic sudden cardiac death in the current era. *Heart rhythm : the official journal of the Heart Rhythm Society*. 2011; 8:1570–1575. [PubMed: 21740887]
25. Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. *The New England journal of medicine*. 2005; 352:1206–1214. [PubMed: 15788497]
26. Duflou J, Virmani R, Rabin I, Burke A, Farb A, Smialek J. Sudden death as a result of heart disease in morbid obesity. *American heart journal*. 1995; 130:306–313. [PubMed: 7631612]
27. Tavora F, Zhang Y, Zhang M, Li L, Ripple M, Fowler D, et al. Cardiomegaly is a common arrhythmogenic substrate in adult sudden cardiac deaths, and is associated with obesity. *Pathology*. 2012; 44:187–191. [PubMed: 22406485]
28. Shorvon S, Tomson T. Sudden unexpected death in epilepsy. *Lancet*. 2011
29. Teodorescu C, Reinier K, Dervan C, Uy-Evanado A, Samara M, Mariani R, et al. Factors associated with pulseless electric activity versus ventricular fibrillation: the Oregon sudden unexpected death study. *Circulation*. 2010; 122:2116–2122. [PubMed: 21060069]
30. Chugh SS, Senashova O, Watts A, Tran PT, Zhou Z, Gong Q, et al. Postmortem molecular screening in unexplained sudden death. *J Am Coll Cardiol*. 2004; 43:1625–1629. [PubMed: 15120823]

31. Doolan A, Langlois N, Chiu C, Ingles J, Lind JM, Semsarian C. Postmortem molecular analysis of KCNQ1 and SCN5A genes in sudden unexplained death in young Australians. *International journal of cardiology*. 2008; 127:138–141. [PubMed: 17544529]

Table 1

Demographics and arrest circumstances of middle-aged and older cases with sudden cardiac arrest, Portland, Oregon metropolitan area, 2/2002–1/2010 (n=2004)

	Age 35–59 yrs (n=753)	Age 60 yrs (n=1251)	P-value *
Male	571 (75.8%)	759 (60.7%)	<0.0001
Race-ethnicity			0.0004
Non-Hispanic White	615 (83.0%)	1097 (89.0%)	
African American	65 (8.8%)	70 (5.7%)	
Asian	23 (3.1%)	39 (3.2%)	
Hispanic	22 (3.0%)	16 (1.3%)	
Other [†]	16 (2.2%)	11 (0.9%)	
Unknown [‡]	12	18	
Arrest location			<0.0001
Home	482 (64.4%)	842 (67.7%)	
Public	170 (22.7%)	146 (11.8%)	
Outpatient/care facility	72 (9.6%)	207 (16.6%)	
Other	24 (3.2%)	48 (3.9%)	
Unknown [‡]	5	8	
Witnessed status			0.002
Bystander witnessed	328 (43.8%)	632 (51.8%)	
EMS witnessed	32 (4.3%)	51 (4.2%)	
Not witnessed	388 (51.9%)	537 (44.0%)	
Unknown [‡]	5	31	
Response time (min)	6.8 ± 3.5 (n=461)	6.7 ± 3.5 (n=970)	0.78
Presenting arrhythmia			<0.0001
VF/VT	251 (49.1%)	374 (39.0%)	
PEA	116 (22.7%)	273 (28.5%)	
Asystole	141 (27.6%)	277 (28.9%)	
Other [§]	3 (0.6%)	35 (3.6%)	
Unknown [‡]	242	292	
Resuscitation attempted	519 (68.9%)	926 (74.0%)	0.01
Survival to hospital discharge	73 (9.7%)	92 (7.4%)	0.07
Outcome among subjects with resuscitation attempted (n=1445)			
Return of spontaneous circulation	165 (32.6%)	339 (37.6%)	0.06
Unknown [‡]	13	24	

	Age 35–59 yrs (n=753)	Age 60 yrs (n=1251)	P-value *
Survival to hospital discharge	73 (14.1%)	92 (9.9%)	0.02

* P value from Pearson chi-square test for categorical variables and *t*-test for continuous variables.

[†] Other race category includes: American Indian, Alaskan Native, Pacific Islander, and Native Hawaiian.

[‡] For variables with missing values, proportions and p-values are calculated using the non-missing data as the denominator.

[§] Other presenting rhythms include: paced rhythm, third degree heart block, and bradycardia.

EMS= emergency medical services; PEA= pulseless electrical activity; VF/VT= ventricular fibrillation/ ventricular tachycardia.

Table 2

Baseline clinical characteristics of middle-aged and older cases with sudden cardiac arrest and physician records available, (n=1523)

	Age 35–59 yrs (n=519)	Age 60 yrs (n=1004)	P-value*
BMI	31.7±9.8 (n=391)	28.4±7.7 (n=655)	<0.0001
BMI categories [‡]			<0.0001
Underweight	8 (2.0%)	28 (4.3%)	
Normal	90 (23.0%)	206 (31.4%)	
Overweight	105 (26.9%)	205 (31.3%)	
Obese	188 (48.1%)	216 (33.0%)	
Unknown [‡]	128	349	
Hypertension	271 (52.2%)	712 (70.9%)	<0.0001
Hyperlipidemia	175 (33.7%)	428 (42.6%)	0.0008
Diabetes mellitus	151 (29.1%)	373 (37.2%)	0.002
Clinical history of CAD	113/519 (21.8%)	465/1004 (46.3%)	<0.0001
Congestive heart failure	90 (17.3%)	406 (40.4%)	<0.0001
Cerebral vascular accident	36 (6.9%)	207 (20.6%)	<0.0001
Peripheral vascular disease	26 (5.0%)	163 (16.2%)	<0.0001
Chronic renal insufficiency	72 (13.9%)	214 (21.3%)	0.0004
COPD/asthma	119 (22.9%)	316 (31.5%)	0.0005
Liver disease	15 (2.9%)	15 (1.5%)	0.06
Sleep apnea	56 (10.8%)	61 (6.1%)	0.001
Syncope	25 (4.8%)	86 (8.6%)	0.008
Seizure	49 (9.4%)	42 (4.2%)	<0.0001
Left ventricular hypertrophy	30 (35.7%)	134 (46.8%)	0.07
Unknown [‡]	435	718	
Severe left ventricular systolic dysfunction [§]	29 (23.8%)	131 (31.1%)	0.12
Unknown [‡]	397	583	
Heart rate (bpm)	81.5±18.5 (n=215)	77.9±18.8 (n=543)	0.02
QRS duration (ms)	94.6±19.1 (n=215)	104.6 ±26.2 (n=548)	<0.0001
QTc (ms)	452.1±38.9 (n=172)	453.5±41.0 (n=313)	0.72

	Age 35–59 yrs (n=519)	Age 60 yrs (n=1004)	P-value*
Gender-specific QTc categories			0.13
Normal	57 (33.1%)	127 (40.6%)	
Borderline	46 (26.7%)	62 (19.8%)	
Abnormal	69 (40.1%)	124 (39.6%)	
Unknown [‡]	347	691	
Tpeak-Tend (ms)	97.5±20.8 (n=190)	99.7±22.3 (n=473)	0.25

* P value from Pearson chi-square test for categorical variables and *t*-test for continuous variables.

[†] BMI categories defined as: Underweight BMI <18.5, Normal BMI =18.5–24.9, Overweight BMI =25–29.9, Obese BMI ≥30.

[‡] For variables with missing values, proportions and p-values are calculated using the non-missing data as the denominator.

[§] Severe LV systolic dysfunction defined as EF <35%.

Corrected using Bazett's formula; QTc categories defined as: Males <430ms (normal), 431–450ms (borderline), >450ms (abnormal); Females <450ms (normal), 451–470ms (borderline), >470ms (abnormal).

BMI= body mass index; CAD= coronary artery disease; COPD= chronic obstructive pulmonary disease; QTc= corrected QT interval.

Table 3

Coronary artery disease in middle-aged and older cases with sudden cardiac arrest

	Age 35–59 years	Age 60 years	P-value *
History of CAD documented in medical records [†]	113/519 (21.8%)	465/1004 (46.3%)	<0.0001
Diagnosis of CAD on autopsy [‡]	178/257 (69.3%)	24/30 (80.0%)	0.22
Overall cases diagnosed with CAD	320/753 (42.5%)	501/1251 (40.0%)	0.28

Values listed as number/denominator (%).

* P value from Pearson chi-square test.

[†] Denominator is cases with physician records available.

[‡] Denominator is cases with detailed autopsy.

CAD= coronary artery disease.

Table 4

Multivariate odds ratio estimates of clinical predictors of middle-aged vs. older cases

Characteristics	Model 1* OR (95% CI) n=1505	Model 2* OR (95% CI) n=748
Male	1.67 (1.29–2.18) [†]	1.89 (1.27–2.81) [†]
Non-Hispanic White	0.44 (0.31–0.64) [†]	0.39 (0.24–0.63) [†]
BMI categories [‡]		
Underweight	0.83 (0.34–2.04)	0.85 (0.24–2.98)
Normal	1.0 (ref)	1.0 (ref)
Overweight	1.32 (0.90–1.94)	1.14 (0.66–1.96)
Obese	2.20 (1.52–3.19) [†]	2.05 (1.21–3.47) [†]
Unknown	0.70 (0.49–1.00)	0.93 (0.54–1.61)
Hypertension	0.57 (0.44–0.73) [†]	0.56 (0.37–0.84) [†]
Hyperlipidemia	1.12 (0.85–1.48)	1.32 (0.88–1.99)
Diabetes	0.84 (0.63–1.12)	0.97 (0.64–1.48)
Clinical history of CAD	0.57 (0.43–0.74) [†]	0.70 (0.47–1.05)
Congestive heart failure	0.35 (0.25–0.48) [†]	0.52 (0.34–0.80) [†]
Cerebral vascular accident	0.40 (0.26–0.60) [†]	0.29 (0.17–0.51) [†]
Peripheral vascular disease	0.45 (0.28–0.73) [†]	0.51 (0.27–0.97) [†]
Chronic renal insufficiency	1.08 (0.75–1.54)	1.61 (1.02–2.56) [†]
COPD/asthma	0.73 (0.55–0.97) [†]	0.81 (0.55–1.20)
Sleep apnea	2.30 (1.44–3.68) [†]	2.10 (1.15–3.81) [†]
Syncope	0.61 (0.36–1.02)	0.58 (0.30–1.11)
Seizure	2.69 (1.64–4.42) [†]	2.64 (1.37–5.12) [†]
Heart rate (10bpm increase)	-	1.05 (0.96–1.16)
QRS duration (10ms increase)	-	0.82 (0.75–0.90) [†]

* Multivariate logistic regression models to estimate the relative odds of middle-aged (35–59 year) as opposed to the older age group. Model 1 includes the significant comorbidities from the univariate analyses. Model 2 additionally adjusts for baseline ECG variables: heart rate and QRS duration.

[†] P < 0.05.

[‡] BMI categories defined as: Underweight BMI <18.5, Normal BMI =18.5–24.9, Overweight BMI =25–29.9, Obese BMI ≥30.

OR= odds ratio; CI= confidence interval; BMI= body mass index; CAD= coronary artery disease; COPD= chronic obstructive pulmonary disease.