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Cardiac Enlargement in US Firefighters: Prevalence Estimates by Echocardiography, Cardiac Magnetic Resonance and Autopsies

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Abstract

Background: Cardiovascular Disease (CVD) accounts for 45% of on-duty deaths in US fire service; cardiac enlargement is common among US firefighters; and plays a major role in firefighter Sudden Cardiac Death (SCD).

Objective: To estimate the prevalence of cardiac enlargement in US Firefighters by autopsies, echocardiography (ECHO) and Cardiac Magnetic Resonance (CMR).

Methods: In the present cross-sectional study, the prevalence of Left Ventricular Hypertrophy (LVH)/cardiomegaly was a) estimated non-invasively among active career firefighters and b) examined by reviewing autopsies of firefighters who suffered a non-cardiac, on-duty fatality. Left ventricular mass (LVM) among active career firefighters was assessed by ECHO and CMR, and normalized (indexed) for body surface area (BSA) and height. Autopsy estimates were based on cardiac weights and other forensic parameters.

Results: LVH prevalence estimates among active career firefighters presented a range from 3.3% to 32.8% among ECHO; and 0.0% to 5.3% among CMR criteria. LVH was present in 17.5% and 0.4% of the active firefighters as defined by LVM indexed to height 1.7 (by ECHO and CMR, respectively). LVM indexed to BSA as measured by CMR indicated zero prevalence of LVH. Among non-cardiac traumatic autopsies, prevalence estimates of cardiomegaly and LVH were 39.5% (95% CI 33.7–45.3) and 45.4% (95% CI 39.5–51.4) respectively, even after adjustment for age and BMI.

Conclusions: The prevalence of cardiac enlargement varied widely depending on the imaging assessment, the cutoffs and the normalization techniques. For autopsy data, BMI was a major determinant of heart weight. Future CVD-outcome based studies are needed to provide evidence for the most accurate clinical cutoffs, while standardization of autopsies is needed across protocols and jurisdictions.

Keywords: Cardiomegaly; Hypertrophy; Echocardiography; Cardiac magnetic resonance; Autopsies; Fire service

Introduction

Cardiovascular disease (CVD) is the leading cause of duty related fatalities among firefighters (45% of on-duty fatalities) [1-4]. Moreover, for every fatal on-duty CVD event, there are an estimated 25 additional nonfatal CVD events [5,6]. Therefore, CVD events are a problem of paramount importance in the US fire service.

The risk of on-duty CVD events is not evenly distributed among all firefighters, but is highly concentrated among the most susceptible individuals [1,7]. On-duty CVD events and heart disease retirements occur primarily in firefighters with underlying disease (known or subclinical) or excess cardiovascular risk factors [8-10]. Increasingly, evidence from the general population points a major role of left ventricular hypertrophy (LVH)/cardiomegaly in the risk of sudden cardiac death (SCD), either alone or together with co-morbid Coronary Heart Disease (CHD) [11-13]. Moreover, evidence from studies based on autopsy reports from formerly active career firefighters, indicates that LVH/cardiomegaly is common among US firefighters and plays a major role in on-duty CVD events and SCD risk in the fire service [8,14].

Notwithstanding, the known significance of LVH/cardiomegaly as a clinical and epidemiologic marker of CVD and SCD, its definition demonstrates wide variability among imaging modalities, technicians,

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normalization processes and algorithms [15-17]. The two most frequently used imaging modalities for the non-invasive identification of LVH, are echocardiography (ECHO) and cardiac magnetic resonance (CMR), with CMR considered the gold standard [18]. The aim of this paper is to estimate the prevalence of cardiac enlargement (including LVH) in US firefighters and determine how these prevalence estimates vary according to different methods of assessment.

Materials and Methods

We derived prevalence estimates for LVH among active career firefighters by two imaging techniques (ECHO and CMR). We also compared these with prevalence estimates from direct measures of heart weight and LV wall thickness at autopsy among formerly active firefighters who suffered a non-cardiac fatality while on-duty.

Study population (Imaging assessment)

Male career firefighters, aged 18 years and older were recruited from the Indianapolis Fire Department (IFD). Eligible firefighters had no restrictions on duty and had a recorded fire department-sponsored medical exam in the last two years that included a submaximal exercise tolerance test.

From those eligible (n=1059), we selected a total of 400 participants, utilizing an "enriched" randomization strategy based on age at randomization, obesity, hypertension (HTN) and cardio-respiratory fitness (CRF) status at last examination, so that a larger number of higher risk participants would be selected. Thus, we randomly selected: 100 participants from the entire eligible population; 75 low-risk participants (age <40, non-obese, free of HTN and high CRF) and 225 higher risk participants (at least 2 of the following: age ≥ 40, obese, HTN or low CRF) for further LVH/cardiomegaly screening and imaging tests. Obesity was defined by standard criteria (BMI ≥ 30 kg/m^2). Hypertension was considered present if resting blood pressure is ≥ 140/90 mm Hg. Low CRF was defined as the bottom tertile, as measured by the recorded treadmill time and the estimated maximal VO_2 during the last exercise test. Those selected were included in the study if they had no contraindication to CMR and had signed informed consent to participate. Out of the 400 active career firefighters, we excluded 7 participants with missing measurements of LVM, as assessed by CMR.

Definitions of cardiac enlargement by imaging assessment

LVM was assessed by both ECHO and CMR imaging. First, a transthoracic cardiac echocardiogram was done as a simple two-dimensional (2-D) study with limited m-mode recordings. An abbreviated cardiac MRI (CMR) was performed as "function only" immediately after the ECHO. Images were obtained using a retrospectively ECG-gated steady-state free precession cine sequence. In this fashion, a contiguous short axis stack of 8 mm slices was obtained parallel to the atrioventricular groove to cover the entire length of the LV. Then, manual tracing of end-diastolic epicardial and endocardial borders was performed. Standard long axis views were also obtained including horizontal long axis, vertical long axis, and 3-chamber views, facilitating the interpretation of ventricular function. Board certified specialists performed the clinical interpretation of imaging.

LVM indices were derived by dividing LVM in grams with either body surface area (in meters^2) or height to the allometric powers of 1.7 and 2.7 (in meters 1.7 and meters 2.7, respectively). Body surface area was estimated with the Mosteller formula. LVH/cardiomegaly was defined based on the cutoff values presented in Table 1, for posterior and septal wall thickness, LVM and LVM indices.

Cutoff Values for Cardiomegaly/Left Ventricular Hypertrophy		
ECHO/CMR	Posterior wall thickness (cm)	≥ 1.2
	Septal thickness (cm)	≥ 1.2
ECHO	LVMi _BSA (g/m^2)	>115
	LVMi _Height$^{1.7}$ (g/m$^{1.7}$)	>81
	LVMi _Height$^{2.7}$ (g/m$^{2.7}$)	>50
	LVM (g)	>225
CMR	LVMi _BSA (g/m^2)	>106.2
	LVMi _Height$^{1.7}$ (g/m$^{1.7}$)	>80
	LVMi _Height$^{2.7}$ (g/m$^{2.7}$)	>45.1
	LVM (g)	>203.5
Autopsy Reports	**Quantitative Definitions**	
	Heart Weight (g)	≥ 450
	LV wall thickness (cm)	≥ 1.2
	Qualitative Definitions	
	Heart size abnormality noted	YES
	Increased Wall Thickness noted	YES
	Comprehensive definitions	
	Cardiomegaly	≥ 450 and/or YES
	Left Ventricular Hypertrophy	≥ 1.2 and/or YES

LVMi: Left Ventricular Mass index; LVM: Left Ventricular Mass; ECHO: Echocardiography; CMR: Cardiac Magnetic Resonance

Table 1: Definition of Cardiomegaly/Left Ventricular Hypertrophy, by both Imaging Modalities (echocardiography and cardiac magnetic resonance) and Autopsies.

Assessment of cardiovascular risk factors

Height was measured in the standing position with a clinical stadiometer. Body weight was measured with bare feet and in light clothes on a calibrated scale. BMI was calculated as the weight in kilograms divided by the square of height in meters. Blood pressure was measured using an appropriately sized cuff with the subject in the seated position. Heart rate and blood pressure were obtained in a resting state from the physical examination (and were not measured prior to the exercise test). Medical exam data were further supplemented by a pre-imaging questionnaire, which collected comprehensive information on smoking status, personal history of heart rhythm problems, family history of cardiac problems and moderate to vigorous physical activity level in minutes per week. High risk of obstructive sleep apnea (OSA) was assessed using the validated Berlin Questionnaire [19].

Direct measures of heart weight and wall thickness based on autopsy reports

Male non-cardiac traumatic fatalities (deaths due to blunt trauma, burns, or asphyxiation) were identified for 2006 to 2012 from a firefighter autopsy research data bank maintained by the National Fallen Firefighters Foundation. The inclusion criteria for the non-cardiac trauma controls were (1) age ≤ 65 years, (2) duty-related death, and (3) cause of death determined by autopsy to be due to blunt trauma, burns, or asphyxiation and not related to any cardiovascular pathologic entity.

Definitions of cardiac enlargement based on autopsy reports

We defined LVH and cardiomegaly from autopsy data, based on both qualitative and quantitative criteria; with qualitative definitions based on the narrative conclusions of the autopsy report (Table 1).

Data from 353 autopsy reports were available. We conducted our main analysis with data from 293 autopsy records, excluding those with missing information on BMI. Under the assumption that the pathologists would have reported the weight in the autopsies if this was in the obesity range, we also performed a series of sensitivity analyses with data from all 353 autopsy records, where the prevalence rates of LVH and cardiomegaly were estimated assuming a BMI of 25 kg/m^2 and then 27 kg/m^2 for all records with missing information.

Statistical analysis

We performed a weighted analysis regarding the imaging data so as to account for our enriched randomization sampling strategy. Weights were calculated based on the total number of risk factors per subject with the technique of inverse probability weighting. Baseline characteristics were described using the mean (SD) for quantitative variables and the frequency (%) for categorical variables. Prevalence estimates for LVH based on ECHO and CMR assessments were calculated as percentages (95%). Comparisons of prevalence estimates between paired data were performed with the McNemar's test.

Prevalence estimates of LVH and cardiomegaly based on autopsy records were adjusted for age and BMI according to the age and BMI distributions of the active career firefighter population using the method of direct standardization. Age was classified in 10-years classes (26-35, 36-45, 46-55, 56-65) while BMI was categorized as normal (BMI<25 kg/m^2), overweight (25<BMI <29 kg/m^2), obesity class I (30<BMI<34 kg/m^2), obesity class II/III (BMI ≥ 35 kg/m^2). Agreement between the qualitative and the quantitative definitions applied to detect cardiomegaly and LVH among autopsy records was evaluated using the Cohen's kappa. The significance of the trend across ordered groups of ages or BMI was evaluated with the use of the score test under a linear trend of odds.

Analyses were performed using SPSS, version 21.0 (IBM, Armonk, New York) and Stata, version 14.0 (StataCorp, College Station, Texas). A p-value<0.05 was considered statistically significant and all tests performed were two-sided.

Results

The baseline characteristics are summarized in Table 2. After adjusting for the weighted sampling strategy, the mean age of active career firefighters was 45.3 years (SD 8.1); 45% were obese; 32% had high risk of OSA and 34% had low CRF.

The prevalence estimates of LVH by both ECHO and CMR assessment based on different criteria are summarized in Table 3. Great variability was observed within ECHO based on different definitions/ indices applied. Normalization by BSA using CMR measurements was the only criterion to deliver zero prevalence of cardiac enlargement.

LVH and cardiomegaly distributions by age and BMI categories and based on quantitative definitions among the non-cardiac traumatic autopsies are presented in table 4. Prevalence rates steadily increased with increasing age and BMI.

Unadjusted prevalence estimates (based on comprehensive definitions) showed cardiomegaly to be present in 41.3% (n=121) of non-cardiac traumatic fatalities and LVH in 45.5% (n=135). The agreement between the unadjusted qualitative and quantitative definitions was low for both cardiomegaly and LVH (Cohen's kappa 0.35 and 0.18, respectively), while 28.3% of the autopsies reported both LVH and cardiomegaly, based on the comprehensive definitions (Appendix 1). Age- and BMI-adjusted prevalence estimates of cardiomegaly and LVH (based on comprehensive definition) as high as 39.5% (95%CI 33.7–45.3) and 45.4% (95%CI 39.5–51.4) respectively were documented. The prevalence estimates of cardiomegaly and LVH did not change considerably in either of the sensitivity analyses conducted with the missing BMI's imputed as 25 or 27 kg/m^2.

	Imaging	Imaging	Autopsy
Variables	**Study Sample**	**Study Sample Unweighted**	**Data**
	(N=393)		(N=293)
Age years †	46.5 ± 8.2	45.3 ± 8.1	42.7 ± 10.3
Height inches †	70.3 ± 2.5	70.3 ± 2.6	70.1 ± 3.9
Heart Rate bpm †	80.5 ± 13.4	79.5 ± 13.0	NA
Resting SBP mmHg †	126.3 ± 9.7	125.2 ± 9.4	NA
Resting DBP mmHg †	81.8 ± 8.1	81.3 ± 7.4	NA
High Risk of OSA *	112 (38.1)	254 (31.6)	NA
Body Mass Index kg/m^2 †	31.1 ± 4.6	30.3 ± 4.5	31.2 ± 6.9
Smoking *	50 (13.0)	135 (12.9)	NA
Personal History of Heart Rhythm Problems *	60 (15.7)	153 (14.7)	NA
Family History of cardiac problems*	153 (40.2)	426 (41.3)	NA
Age >=40 years *	301 (78.2)	770 (72.7)	172 (58.7)
BMI>=30 kg/m^2 *	260 (56.1)	474 (44.8)	142 (48.5)
Low CRF *	178 (46.7)	363 (34.3)	NA
MVPA Physical Activity min/week †	177.4 ± 117.3	187.3 ± 117.7	NA
Cardiac Measures			
LVM_ECHO g †	189.0 ± 38.1	186.9 ± 36.6	NA
LVM_CMR g †	139.2 ± 24.0	137.6 ± 23.4	NA
Heart weight g †	NA	NA	438 ±99 ‡
Posterior wall Thickness_CMR cm †	0.93 ± 0.2	0.92 ± 0.2	0.9 (0.4) §

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; OSA: Obstructive Sleep Apnea; BMI: Body Mass Index; CRF: Cardiorespiratory Fitness; MVPA: Moderate to Vigorous Physical Activity; LVM: Left Ventricular Mass; ECHO: Echocardiography; CMR: Cardiac Magnetic Resonance. † Mean (SD) for continuous variables; * n (%) for categorical variables. Low CRF was defined as the lowest tertile, as measured by the recorded treadmill time and the estimated maximal VO2 during the last exercise test. ‡Information available in 251 (85.7%) autopsy records. §Information available in 139 (47.4%) autopsy records, a value of 0.9 was imputed for missing data.

Table 2: Baseline descriptive characteristics.

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		LVH (n,%)	
		Study Sample (N=393)	**Study Sample Unweighted**
ECHO	LVM	58 (15.3)	146 (14.1)
	Posterior Wall Thickness	61 (16.0)	136 (13.1)
	Septal Wall Thickness	140 (36.7)	341 (32.8)
	LVM/BSA	13 (3.4)	34 (3.3)
	LVM/Height$^{1.7}$	70 (18.7)	181 (17.5)
	LVM/Height$^{2.7}$	34 (9.1)	90 (8.7)
CMR	LVM	4 (1.1)	9 (1.0)
	Posterior Wall Thickness	21 (6.0)	50 (5.3)
	LVM/BSA	0 (0.0)	0 (0.0)
	LVM/Height$^{1.7}$	2 (0.6)	3 (0.4)
	LVM/Height$^{2.7}$	1 (0.3)	2 (0.2)

LVM: Left Ventricular Mass; BSA: Body Surface Area; ECHO: Echocardiography; CMR: Cardiac Magnetic Resonance

Table 3: Prevalence estimates of left ventricular hypertrophy (LVH) by echocardiography and cardiac magnetic resonance.

	Heart weight ≥ 450g				LV wall thickness ≥ 1.2 cm				LV wall thickness ≥ 1.4 cm				LV wall thickness ≥ 1.7 cm			
	No	(%)	Yes	(%)	No	(%)	Yes	(%)	No	(%)	Yes	(%)	No	(%)	Yes	(%)
Age (years)																
26–35	56	(73)	21	(27)	49	(64)	28	(36)	56	(73)	21	(27)	69	(90)	8	(10)
36–45	75	(76)	27	(24)	68	(67)	34	(33)	78	(76)	24	(24)	94	(92)	8	(8)
46–55	42	(56)	33	(44)	35	(47)	40	(53)	42	(56)	33	(44)	60	(80)	15	(20)
56–65	17	(44)	22	(56)	20	(51)	19	(49)	2	(56)	17	(44)	32	(82)	7	(18)
P trend[a]				<0.001				0.026				0.007				0.051
Body mass index																
Normal	45	(94)	3	(6)	36	(75)	12	(25)	39	(81)	9	(19)	47	(98)	1	(2)
Overweight	80	(78)	23	(22)	66	(66)	37	(36)	73	(71)	30	(29)	91	(88)	12	(12)
Obesity, class I	37	(52)	34	(48)	39	(55)	32	(45)	46	(65)	25	(35)	65	(92)	6	(8)
Obesity, class II/III	28	(39)	43	(61)	31	(44)	40	(56)	40	(56)	31	(44)	52	(73)	19	(27)
P trend[a]				<0.001				<0.001				0.003				<0.001

Table 4: Distribution of LVH and cardiomegaly by age and body mass index by autopsy reports.

Discussion

The results from the present study in US firefighters demonstrate great variability of the prevalence estimates of LVH within and between ECHO and CMR, according to the different criteria utilized. Considerable variance was also observed using direct measures at autopsy, again, depending on the criteria used. Additionally, autopsy findings clearly indicated that BMI was a major determinant of heart weight. We have also found that BMI is the major determinant of LVM by ECHO and CMR [20]. Prevalence estimates of LVH were considerable when based on LVM indices and assessed by ECHO. Although CMR is considered to be the gold standard among imaging techniques, the prevalence estimates of cardiac enlargement observed in the present study seemed unrealistically low, especially when compared to direct measures at autopsy in a similar firefighter population. Given the great variance in LVM and LVH estimates, surprisingly, the average LV wall thickness was similar across both imaging techniques and at autopsies.

Taken together, our results reflect the lack of standardization among definitions of cardiac enlargement, and therefore, prevalence estimates were highly variable depending critically on the choice of the normalization technique, the imaging modality and the cutoff values. To the best of our knowledge, our study is the first to evaluate the prevalence of cardiac enlargement among active career firefighters by both ECHO and CMR measurements based on different criteria, as well as the first to compare these estimates to those derived from non-cardiac traumatic fatalities. We previously found the prevalence of cardiomegaly to be 22% in a smaller sample of non-cardiac, traumatic firefighter autopsies limited to those under the age of 45 years of age [21]. Our estimates for these age groups were similar, 27% and 24% for those under the age of 35 and 45 years of age respectively.

Prevalence estimates of LVH were substantially higher when ECHO measurements were considered as compared to CMR. Nonetheless, great variability was still observed among ECHO prevalence estimates. This could be explained by the fact that the measurement of LVM, which was the main and single variant component of calculating LVM indices was on average 49.3 grams higher by ECHO than by CMR. This wide range of prevalence estimates of cardiac enlargement that was observed among the same subjects, could be explained in large by the fact that the cut off values used by each criterion are very close between the ECHO and the CMR measurements, although current evidence suggests that CMR consistently yields lower average values compared to ECHO for the same subjects [22,23]. Given the large differences in mean LVM consistently observed between ECHO and CMR, it is puzzling that suggested LVH cutoff values are so close for the two different imaging techniques.

Our results are in line with current evidence, suggesting that when cardiac enlargement is assessed by imaging, anthropometric parameters should be accounted for in order to provide more accurate estimates and allow for comparisons among individuals [17,18,24]. In addition, indexing to height over an allometric power is suggested as a more optimal indexing method than BSA, being less variant among subjects with normal BMI and more accurate among those overweight or obese. Indexing to BSA leads to a gross underestimation of cardiac enlargement among obese and overweight individuals and this becomes apparent from our results where the prevalence estimates provided by indexing to BSA were null, which is difficult, if not impossible to believe given the population's risk profile [17,24].

Among traumatic deaths, where any possible contribution of cardiac pathology to the death was reasonably excluded, as many as 40% demonstrated cardiomegaly while up to 50% presented LVH. This can be explained in large by the high prevalence of obesity that was documented among those noncardiac traumatic controls, while in addition our results suggested the prevalence of cardiac enlargement to be steadily increasing as a function of BMI. Our findings are consistent with the literature, which finds obesity to be a significant risk factor for LVH and increased cardiac mass [1,14]. Furthermore, one could hypothesize that traumatic fatalities occur more frequently in obese firefighters as they could be more inclined to be physically trapped during a fire secondary to their body size and relative physical immobility [21]. In fact, the average BMI of the non-cardiac fatalities was higher than that of the active firefighter study base population (31.2 *vs.* 30.3) and that previously reported for representative, population-based firefighter samples (28.6 for career firefighters) [25].

One limitation of the data and therefore, of the current study is the fact that we were not able to conduct direct comparisons between heart mass or LVM in autopsies and clinical imaging, with imaging modalities focusing on the determination of cardiac enlargement via LVM assessment, and autopsies using total heart weight. None of the autopsies reviewed in the present study reported individual ventricular weights, but rather only reported total heart weight. However, total heart weight consists of many different components, such as the epicardial fat, the ventricular weight, and the atrial weight, and therefore, having only measurements for total heart weight makes it challenging to reach any firm conclusions about the proportional contribution of the LVM [26,27].

Another limitation of our study is the low correlation between the quantitative, qualitative and comprehensive definitions of LVH and cardiomegaly among autopsy reports, due to the fact that autopsies vary considerably based on different forms and protocols utilized across various jurisdictions. It seems from current data that values on LV wall thickness and heart weight were more likely to be reported if they were relatively high, while sometimes instead of the value itself the medical examiner/coroner only reported qualitatively for the presence of hypertrophy and/or enlargement without giving an actual value. Considering that heart weight and LV wall thickness are valuable criteria, it is critical to ensure that quantitative measurements would be reported for current and future comparisons.

A major strength of our study is the fact that we had access not only to data from active career firefighters, but also to autopsy reports from non-cardiac traumatic fatalities. In addition, our autopsy findings relied mostly on quantitative data, with heart weight measurement reported in almost 90% of the non-cardiac autopsy reports examined. Taken together, we were able to estimate the prevalence of cardiac enlargement in the US fire service via several different methods and get a more holistic picture.

Second, we made direct comparisons of prevalence estimates based on the same definitions within and between ECHO and CMR. This is critical since there are only a few direct comparisons of ECHO and CMR prevalence estimates of cardiac enlargement, and the methods used are currently not cross-standardized. Strength of our study is our age- and BMI- adjustment for the prevalence based on autopsies. In addition we used the definition of 1.2 cm for defining LVH based on LV wall thickness, considering a more conservative approach to avoid any overlap with physiologically enlarged hearts due to athletic training.

The present results, taken together reveal the large impact of the choices of the clinicians/ researchers on defining cardiac enlargement, affecting greatly estimates of cardiac enlargement in the US fire service. Irrespectively of the variability in prevalence estimates, our study clearly revealed BMI as a major driver of heart weight. Overall there is a great need for CVD-outcome based studies that will provide definite evidence about the most accurate normalization indices and cutoffs.

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