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The magnitude of sudden cardiac death in the young: a death certificate-based review in England and Wales

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Aims In the UK, the true impact of cardiac and sudden death in the young (≤35 years) is speculative. The authors critically appraised the office of national statistics (ONS) data for causes of death in the 1–34 years age group in England and Wales in an attempt to present an estimate of the incidence of such deaths and their underlying causes.

Methods and results The investigators analysed the ONS mortality data for 2002–2005, inclusive. International classification of diseases-10 codes representing possible cardiac deaths were selected and divided into four classes; A1: definite cardiac deaths with no structural heart disease identified at post-mortem, A2: definite cardiac deaths with structural heart disease identified at post-mortem, A3: definite cardiac deaths with indeterminate cause, and B: possible cardiac deaths. Analysis of the data revealed an average of 419 (SD 16.5) definite cardiac deaths per annum (Class A1 + A2 + A3) equating to 1.8 per 100 000 per year (SD 0.08) or 8 deaths/week. There were also 433 (SD 6.2) deaths per year in class B which comprised primarily of deaths from drowning and epileptic seizures. The most prevalent causes were ischaemic heart disease (33.5%), cardiomyopathies (27%), sudden arrhythmic death syndrome (14%), myocarditis (11%), valvular heart disease (5%), and hypertensive cardiomyopathy (2%).

Conclusion Our findings suggest that the number of cardiac and sudden deaths in the young identified is sufficiently high to command attention even without the inclusion of potential misclassifications (Class B). Awareness of such deaths among primary-care physicians, pathologists, and coroners should be raised to ensure that those at risk are identified and further tragedies are avoided.

Keywords Sudden cardiac death • Sudden arrhythmic death syndrome • Death certificates • Epidemiology

Introduction

Sudden cardiac death accounts for 50% of cardiovascular mortality with an estimated annual toll of 300 000 deaths in the USA and 60 000 deaths in the UK.[1,2] The majority of sudden cardiac deaths are of ischaemic aetiology secondary to atherosclerotic coronary artery disease and affect the older section (>35 years) of the population.[3] In a significant proportion of sudden deaths, no specific cause is identified despite detailed histopathological examination and toxicology screen, and a diagnosis of sudden arrhythmic death syndrome (SADS) is advocated.[3,4] The recognition of such deaths is of utmost importance since evaluation of first-degree blood relatives of the deceased commonly results in the identification of an ion-channel disorder and less frequently a cardiomyopathy in just over half of families evaluated, thereby providing a potential cause of death and identifying surviving relatives at risk.[5,6]

The epidemiology of sudden cardiac death in the young (≤35 years) is less well established. A population-based study in Minnesota reported an incidence of 6.2 per 100 000 per year among residents aged 20–40, whereas an autopsy review of US military recruits aged 18–35 revealed a rate of 13 per 100 000

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recruit-years.[7,8] Studies in the young athletic population in Italy and the USA have suggested much lower rates of sudden cardiac death with an incidence of 2.1 per 100 000 per year and 0.5 per 100 000 per year, respectively.[9,10] Inherited cardiomyopathies are the commonest cause of sudden cardiac death in athletes, whereas coronary artery pathology including coronary artery anomalies and atherosclerotic disease predominate in the non-athletic population.[7–9,11] The reported frequency of structurally normal hearts (SADS) varies widely, ranging from 3% in American young athletes to 35% in US military recruits.[8–12]

In the absence of a systematic national registry documenting sudden cardiac deaths in the young, the true impact of such fatalities in the UK is speculative. The objective of this study was to examine and critically appraise the office of national statistics (ONS) data for causes of death in the 1–34 years age group in England and Wales in an attempt to present an estimate of the incidence of sudden cardiac death and underlying cardiac causes.

Methods

The ONS is the government agency responsible for compiling, analysing, and disseminating many of the UK statistics including periodic census of the population and health statistics.[13] The data used in the mortality statistics are derived from information obtained by the doctor certifying the death, the coroner, and details supplied by the informant to the Registrar. The deaths in males and females are reported at 5-yearly age intervals. The causes of death are registered according to the International Classification of Diseases-10 (ICD-10).[14]

The investigators analysed the ONS mortality data stating the cause of death for England and Wales for four consecutive years 2002–2005, inclusive. Five of the ICD-10 chapters were included in the analysis (*Table 1*). Within these chapters, two of the senior authors (E.R.B. and M.N.S.) scrutinized the ICD-10 classification codes to identify codes that may represent cardiac deaths. Data were then summed from the existing age subgroups to include deaths of individuals from the age of 1 year to the age of 34 years. The selected ICD-10 codes were subsequently divided into four classes as deemed relevant by the investigators (*Table 2*): Class A1: definite cardiac deaths with no structural heart disease identified at post-mortem representing SADS; Class A2: definite cardiac deaths with structural heart disease identified at post-mortem comprising sudden and non-sudden deaths with likely causation by structural heart disease; Class A3: definite cardiac deaths with indeterminate cause comprising sudden and non-sudden deaths where the presence or absence of underlying heart disease was either not recorded or ill defined; and Class B: possible cardiac deaths since a proportion of these deaths may represent misclassifications of cardiac deaths and in particular SADS as epilepsy or drowning. Where there was disagreement relating to the class of an ICD-10 code, a third senior author (S.S.) was consulted. Although the great majority of deaths referred to 'natural causes' (non-accidental, non-malicious), a small proportion of the total cohort is likely to represent accidental deaths since ICD-10 codes W65–W74 from Chapter XX representing accidental drowning and submersion were included in Class B.

Incidence rates were calculated based on the ONS census data of the resident population for individuals aged 1–35 years in England and Wales. Data were further analysed according to age subgroup and gender in order to identify potential trends or gender differences.

Table 1 List of the World Health Organisation international classification of diseases-10 chapters included in the analysis[16]

Chapter VI	Diseases of the nervous system
Chapter IX	Diseases of the circulatory system
Chapter X	Diseases of the respiratory system
Chapter XVIII	Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified
Chapter XX	External causes of morbidity and mortality

Table 2 Examples of the most frequent International Classification of Diseases-10 codes included in each class (presented in order of frequency)

Class	ICD-10 code
Class A1	R96: other sudden death, cause unknown I49.9: cardiac arrhythmia, unspecified I46.1: sudden cardiac death, so described I45.6: pre-excitation syndrome (WPW)
Class A2	I21.9: acute myocardial infarction, unspecified I25.1: atherosclerotic heart disease I42.0: dilated cardiomyopathy I42.9: cardiomyopathy, unspecified
Class A3	I50.9: heart failure, unspecified I51.9: heart disease, unspecified I50.1: left ventricular failure I50.0: congestive heart failure
Class B	G40.9: epilepsy, unspecified G41.9: status epileptics, unspecified W69: drowning and submersion while in natural water J46: status asthmatics

Statistical analysis

Data manipulation and analysis were undertaken using SPSS software, version 14 (SPSS Inc., Chicago, IL, USA). Data are expressed in means and standard deviations. Annual mortality incidence per 100 000 was calculated as the mean of the 4 years using the following type: (100 000 × number of deaths)/population size. χ^2 or Fisher's exact test was used to test group differences of proportions.

Results

The number of deaths in the 1–34 years age group is reported in *Table 3* according to class and year of death. Analysis of the ONS data revealed an average of 419 (SD 16.5) definite cardiac deaths per annum (Class A1 + A2 + A3) equating to eight young cardiac deaths per week in England and Wales. On the basis of the average estimated size of the resident population of 23 564 050, these data indicate an incidence of young cardiac death of 1.8 (SD 0.08) per 100 000 per year. There were also an average of 433 (SD 6.2) deaths per year, corresponding to more than 8 deaths/week, in Class B which comprised primarily deaths from drowning, epileptic seizures, and other ill-defined causes of

Table 3 Number of deaths according to class per year

Class	Number of deaths per year				Total number of deaths	Mean deaths per annum (SD)	Mean mortality rate per 100 000 per annum (SD)
	2002	2003	2004	2005			
A1	60	50	57	61	228	57.00 (4.97)	0.24 (0.02)
A2	363	358	324	324	1369	342.25 (21.17)	1.45 (0.09)
A3	19	20	21	20	80	20.00 (0.82)	0.09 (0.00)
A1 + A2 + A3	442	428	402	405	1677	419.25 (19.10)	1.78 (0.08)
B	438	424	434	436	1732	433.00 (6.22)	1.84 (0.03)
Total (A1 + A2 + A3 + B)	880	852	836	841	3409	852.25 (19.67)	3.62 (0.08)

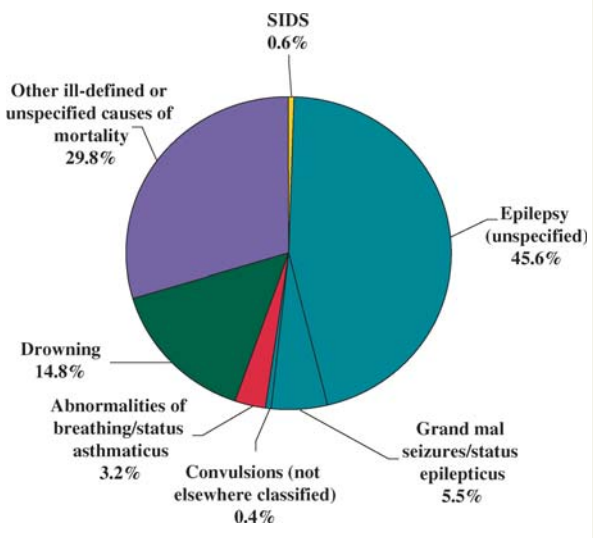

Figure 1 Causes of death in the young expressed as percentage of the total number of deaths in Class B (possible cardiac deaths). SIDS, sudden infant death syndrome.

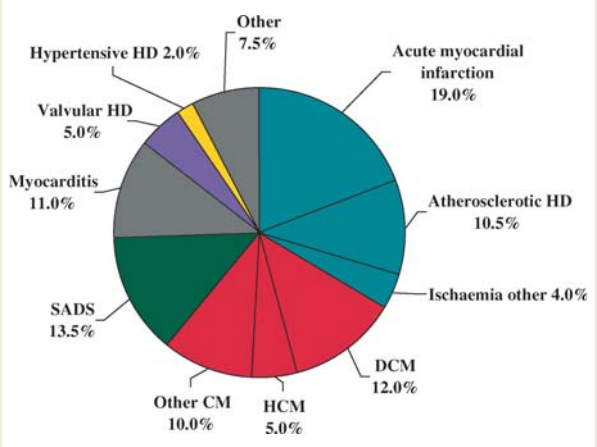

Figure 2 Causes of cardiac death in the young expressed as percentage of the total number of definite cardiac deaths (A1 + A2 + A3). CM, cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; HD, heart disease; SADS, sudden arrhythmic death syndrome.

mortality (*Figure 1*). There was no significant variation in the number of the resident population or the number of deaths per year.

The most prevalent causal cardiovascular pathology was ischaemic heart disease comprising one-third (33.5%) of the definite cardiac deaths (A1 + A2 + A3). Although the majority of ischaemic deaths (56%) were attributed to acute myocardial infarction (ICD-10 code: I21.9), in a significant proportion (32%), the presence of atherosclerotic heart disease alone (ICD-10 code: I25.1) was documented as the principal cause of death, comprising 19% and 11% of the definite cardiac deaths, respectively (*Figure 2*). Cardiomyopathies were the second commonest cause of cardiac death corresponding to 27% of definite cardiac deaths in the cohort with dilated and hypertrophic cardiomyopathies accounting for 12% and 5% of the deaths, respectively. Sudden arrhythmic death syndrome accounted for 14% of definite cardiac deaths followed by myocarditis (11%), valvular heart disease (5%), and hypertensive cardiomyopathy (2%) (*Figure 2*).

Causes of death by gender and age

Definite cardiac deaths (Class A1 + A2 + A3) were more prevalent among males with a male to female ratio of 2.4 : 1. The only pathology associated with a statistically significant difference between the male and female gender was ischaemic or potentially ischaemic causes which accounted for 22% of all deaths in males but only 13% in females ($P < 0.001$). The same gender difference was also observed for possible cardiac deaths (Class B) with a male to female ratio of 2.0 : 1. Deaths attributed to epilepsy comprised a greater proportion of female deaths (male vs. female; 22% vs. 31%, $P < 0.001$), whereas drowning-related deaths were more prevalent among males (9% vs. 4%, $P < 0.001$) (*Figure 3*).

There was a rising incidence of definite cardiac deaths with advancing age, with individuals ≥30 years old having a 10-fold risk compared with children aged <10 years. The only underlying causes of definite cardiac deaths exhibiting a significant age trend were ischaemia and cardiomyopathies. Ischaemic deaths exhibited an increasing trend with advancing age, accounting for almost one-third (31%) of all deaths in the 30–34 years age group but

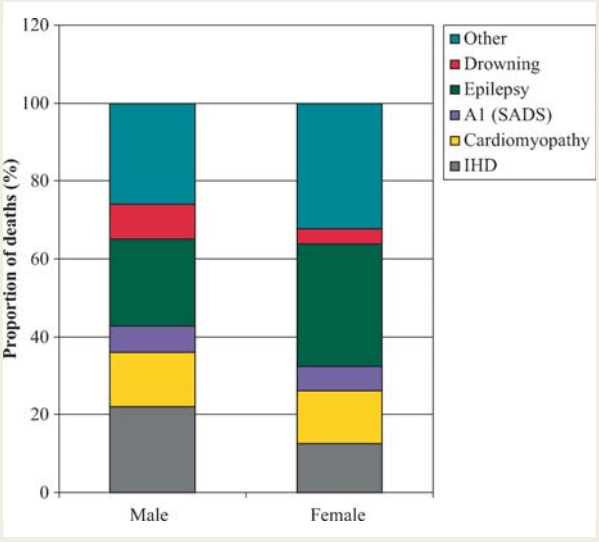

Figure 3 Proportional (%) distribution of underlying cause of death by gender. IHD, ischaemic heart disease; SADS, sudden arrhythmic death syndrome.

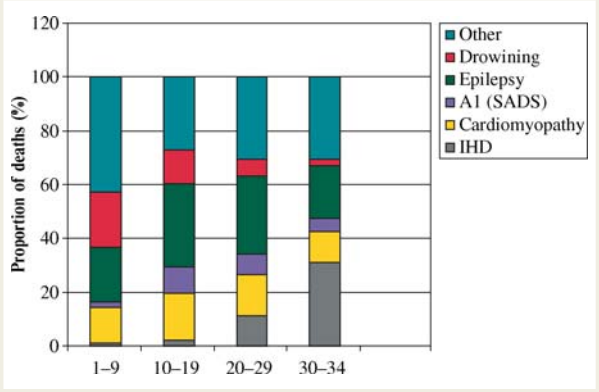

Figure 4 Proportional (%) distribution of underlying cause of death by age. IHD, ischaemic heart disease; SADS, sudden arrhythmic death syndrome.

only 1% in children aged <10 years ($P < 0.001$). In contrast, cardiomyopathy-related deaths peaked during adolescence, accounting for a greater proportion of deaths at the 10–19 years age group (18%) and accounting for only 11% of deaths in the 30–34 years age group ($P = 0.001$) (*Figure 4*).

A similar trend was observed with possible cardiac deaths in Class B, with individuals 30–34 years old having a five-fold risk compared with children aged <10 years old. Underlying causes exhibiting a statistically significant age trend included deaths attributed to epilepsy and drowning. Epilepsy-related deaths peaked in the second and third decades of life, accounting for almost one-third of deaths in the 10–19 and 20–29 years age groups ($P < 0.001$). In contrast, drowning exhibited a reverse trend with age, accounting for 21% of deaths in children aged <10 years but only 3% in individuals ≥30 years old ($P < 0.001$) (*Figure 4*).

Discussion

According to the ONS data, the incidence of cardiac death in the young in England and Wales is 1.8 per 100 000 per year, which corresponds to eight young lives per week. This figure is lower than those documented in retrospective studies of sudden death in the USA in young military recruits and young individuals in Minnesota, which relied on data such as death certificates and post-mortem reports[7,8] and more in keeping with prospective studies in Italy where the reported incidence of sudden cardiac death in young Italian athletes subjected to pre-participation cardiovascular evaluation is 2.1 per 100 000 per year.[9] Therefore, it is likely that our figure derived from the ONS data is a significant underestimate of the true incidence of cardiac death in the young, given the nature of our study and the absence of systematic screening in the UK.

Sudden arrhythmic death syndrome

The incidence of Class A1 deaths that best correlate with SADS was 0.24 per 100 000 per year, with no significant gender or age predilection. This is significantly higher than the previous incidence of 0.10 per 100 000 per year obtained from the ONS statistics for 1997–1999 that used the ICD-9 classification, although an associated prospective national coroner survey would suggest that calculations based on ONS data continue to underestimate the true incidence of SADS.[4] The most plausible explanation for this discrepancy is that the ONS mortality statistics are derived largely from documentation on death certificates which may under-report the true incidence of cardiac arrhythmias. Indeed the classification of deaths by ONS does not differentiate sudden from non-sudden deaths clearly, although most of the pathologies reported as causes of deaths, such as atherosclerotic heart disease and cardiomyopathy, would be more likely to cause sudden rather than non-sudden death in this age group. Malignant cardiac arrhythmias secondary to ion channelopathies such as Brugada syndrome and long-QT syndrome may manifest as epileptiform seizures and collapse secondary to brain anoxia or drowning resulting in misclassification of genuine cases of SADS as epilepsy[15,16] or unexplained drowning.[17,18] The latter is particularly relevant since there is a well established association between the most common subtype of long-QT syndrome, LQT1, and sudden death in swimmers.[19,20] Conversely, post-mortem findings such as coronary atherosclerosis without significant narrowing of the arterial lumen or without macroscopic or microscopic evidence suggestive of acute or chronic ischaemia, as well as mitral valve prolapse and myocarditis,[21] are quite common and may be falsely attributed as the cause of death.

Mortality gender and age predilection in the young

Consistent with prior literature reports, ischaemic or potentially ischaemic causes contributed a greater proportion of deaths in males and with increasing age, in particular after the age of 30 years. Conversely, potentially inherited cardiomyopathies such as hypertrophic and dilated cardiomyopathies did not exhibit any gender predilection but there was a significant age trend,

contributing a greater proportion of deaths in the 10–19 age group with a gradual decrease thereafter.

Epilepsy appeared to exhibit a female predilection, accounting for a greater proportion of deaths during adolescence. These results should however be viewed with caution given the limited data available and the multiple factors which may influence epilepsy-related mortality, as established by a prior large, prospective study in the UK.[22] Finally, in accord with previous reports, drowning-associated deaths were more prevalent among males and children aged <10 years, with a reverse trend with increasing age.[23]

Clinical implications

Considering the devastating impact of sudden and cardiac death in the young and the potential number of life years lost our findings suggest that the number of deaths identified (8 deaths/week) is sufficiently high to command attention even without the inclusion of potential misclassifications (Class B). If consideration is given to the possibility that at least 20% of deaths attributed to epilepsy or drowning may actually be caused by a primary myocardial electrical disorder, then the estimate of sudden and cardiac death in the young is at least 10 per week.

It is imperative that awareness of young cardiac deaths and in particular SADS is raised among pathologists and coroners to ensure that accurate conclusions are derived from autopsies. If the autopsy identifies cardiomyopathy or a case of SADS, this should trigger the referral of families of victims for comprehensive cardiological screening and guide their assessment. This is important because a significant proportion of conditions implicated in young cardiac death and SADS, in particular, are inherited. Indeed, over half of families with SADS deaths demonstrate evidence of an ion-channel disorder or a cardiomyopathy.[5,6] Reforms and further tightening of procedures to address these issues have been proposed, and a national pathology registry has been launched in the UK.[24,25]

Increased awareness among primary care physicians is also vital to ensure recognition of cardiac conditions in young people with the propensity to cause sudden cardiac death since these deaths are often preceded by warning symptoms including syncope. Appropriate assessment may therefore prevent a proportion of these tragic deaths.[6]

Limitations

This epidemiological study exhibits some important limitations that warrant mention. The cause of death was ascertained from the ONS data and the authors did not examine death certificates or post-mortem reports on an individual basis in order to identify potential misclassifications. Although the ONS data do not provide information regarding the number of deceased individuals who underwent a post-mortem examination, it would be reasonable to assume that the majority of the victims were subjected to a post-mortem examination given their youth and the UK medico-legal implications.

The investigators concede that this study relied solely on information provided to the ONS from documentation on death certificates and post-mortem reports which may not always accurately reflect the true cause of death given the ambiguities related to the diagnosis of conditions associated with sudden cardiac death in the young. This may explain the absence of conditions such as arrhythmogenic right ventricular cardiomyopathy (ARVC) as a distinct entity, whereas minor manifestation of certain common disorders such as atherosclerosis may have been falsely attributed as the cause of death. In addition, ARVC does not have its own ICD-10 code and is classified currently as I42.8—other cardiomyopathies. The purpose of this study, however, was to provide an estimate of the incidence of cardiac death and underlying cardiac causes in the young in order to highlight the need to establish the scale and nature of the problem.

Contributors

M.P., S.S., S.C., M.N.S., V.F.P., and E.R.B. carried out the literature search, collected, analysed, and interpreted the data, drafted the article and revised it critically for scientific content, and approved the final version for publication. E.R.B. is the guarantor.

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