EPIDEMIOLOGY

Sudden arrhythmic death syndrome: a national survey of sudden unexplained cardiac death

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Objective: To describe the characteristics of sudden arrhythmic death syndrome (SADS) and compare its incidence with official national mortality statistics for unascertained deaths.

Design and setting: Sudden unexplained deaths were prospectively surveyed through 117 coroners' jurisdictions in England. Consecutive cases meeting the following criteria were included: white Caucasian, aged 4–64 years, no history of cardiac disease, last seen alive within 12 h of death, normal coroner's autopsy, cardiac pathologist's confirmation of a normal heart and negative toxicology.

Main outcome measures: The estimated mortality from SADS was calculated and the official mortality statistics for unascertained causes of deaths in 4–64-year-olds was identified for the same time period.

Results: 115 coroner's cases were reported and 56 (49%) SADS victims were identified: mean age 32 years, range 7–64 years and 35 (63%) male. 7 of 39 cases (18%) had a family history of other premature sudden deaths (<45). The estimated mortality from SADS was 0.16/100 000 per annum (95% CI 0.12 to 0.21), compared with an official mortality of 0.10/100 000 per annum for International Classification of Diseases 798.1 (sudden death, cause unknown—instantaneous death) or 1.34/100 000 per annum for unascertained causes of death.

Conclusions: Deaths from SADS occur predominantly in young males. When compared with official mortality, the incidence of SADS may be up to eight times higher than estimated: more than 500 potential SADS cases per annum in England. Families with SADS carry genetic cardiac disease, placing them at risk of further sudden deaths. SADS should therefore be a certifiable cause of death prompting specialised cardiological evaluation of families.

Sudden unexpected cardiac death in the community for which no cause can be found at the coroner's postmortem is recognised,[1] and a category of sudden unexpected death syndrome has been advocated.[2] We conducted a national prospective survey of sudden cardiac death through English coroners in white Caucasians aged 16–64 years without a history of cardiac disease and last seen alive within 12 h of death. In all, 23 (4.1%) cases were identified, with no clear cause of death despite a full coroner's autopsy and expert examination of the heart by a cardiac pathologist.[3] This finding was consistent with comparable population-based surveys such as the Wandsworth survey (4.7%)[1] as well as a study of sudden and unexpected young adult deaths in Olmstead County (7%).[4] Series of autopsy cases of sudden death have shown similar findings: Drory *et al*'s[5] retrospective study of sudden and unexpected deaths in 9–39-year-olds found no ascertainable cause in 12%; and an Italian study of sudden deaths in under 36-year-olds identified 6% as being unexplained.[6]

We proposed that unexplained cases be labelled as sudden adult death syndrome (SADS) to study their aetiology systematically. Since the early 1990s, this term has been increasingly used in death certification. We have undertaken a second prospective survey in England, focusing only on these sudden unexplained cardiac deaths with a normal postmortem and cardiac pathology. We have already reported a 22% frequency of underlying inheritable cardiac disease, principally long QT syndrome,[7–9] after cardiological evaluation of the surviving first-degree relatives of 32 of these 56 victims.[10] In this paper, we describe the mortality for all 56 ascertained SADS cases, their sociodemographic characteristics, and medical and family history, and compare the estimated annual death rate for this syndrome with contemporaneous Office of National Statistics (ONS) mortality for unascertained causes of death.

METHODS

SADS cases were identified prospectively through HM Coroners in England over a 20-month period (October 1997–May 1999), each coroner participating for 12 months.

Case definition

Sudden unexpected deaths were defined as white Caucasian, aged 4–64 years, with no medical history of cardiac disease, last seen alive within 12 h of being found dead and a coroner's postmortem required to issue a death certificate, a requirement for all sudden unexpected deaths in the UK. If the coroner's pathologist could not identify a cause of death despite a full autopsy, including pulmonary and neurological evaluation, then the whole heart was referred for a thorough assessment by a cardiac pathologist at the Royal Brompton and Harefield Hospital, National Heart & Lung Institute, Imperial College, London or St George's University of London, London, UK. The cardiac pathologists reported their findings directly to the coroner. For each case, a panel reviewed reports from the coroner's officer, the coroner's pathologist and the expert cardiac pathologist, together with the results of an independent toxicological screen (tricyclic antidepressants, anticonvulsant drugs, benzodiazepines, amphetamines, barbiturates, cannabis, cocaine, opiates, methadone, alcohol, volatile hypnotics and solvents) undertaken by the Medical Toxicology Unit at Guy's Hospital, London, UK. If the cardiac pathologist could find no macroscopic or microscopic evidence of cardiac disease and the toxicological screen was negative, the case was defined as SADS. The word ''arrhythmic'' was substituted for ''adult''

Abbreviations: ICD, International Classification of Diseases; LREC, local research ethics committee; ONS, Office of National Statistics; SADS, sudden arrhythmic death syndrome

Table 1 Sociodemographic and lifestyle characteristics of sudden arrhythmic death syndrome cases derived from the coroner's officers reports (n = 56)

Mean age in years (range, median)	32 (7–64, 29)
Males	31 (16–56, 29)
Females	34 (7–64, 41)
<16 years (%)	5 (9%)
Male/female (%)	35 (63)/21 (37)
Social class*	
I+II	15 (27%)
III	17 (31%)
IV+V	11 (19%)
Armed forces	2 (4%)
Other	11 (20%)

*Social class coded by the Office of National Statistics from the occupation given on the death certificate.

because the lower age limit included children as young as 4 years in this survey. For each SADS case, the general practitioner of the coroner's informant (usually next of kin) was approached by a research nurse (AC) for permission to contact the informant directly. Once permission was given, AC wrote to informants requesting a home interview to obtain information about the SADS victim, including demographic characteristics, reported symptoms, and medical and family history. General practitioner and hospital records were also examined where appropriate.

ONS mortality figures were identified for certified causes of death in 4–64-year-olds in England over the study period for the following codes in the International Classification of Diseases—ninth edition (ICD9): 798.1 sudden deaths, cause unknown—instantaneous death; 799.9 other ill-defined and unknown causes of morbidity and mortality—other unknown and unspecified cause; 427.8 and 9 cardiac arrhythmias (0.8, other; 0.9, unspecified); 428.9 heart failures—unspecified; 429.9 ill-defined diseases and complications of heart disease—unspecified. The ICD codes 427.8/9, 428.9 and 429.9 were only included when no other cause was mentioned on the death certificate. The denominator population was calculated from local authority populations that matched participating coroners' jurisdictions based on ONS 1998 age-specific mid-year population estimates. This denominator was reduced to 92.7% of its total to correspond with the proportion of the total population estimated to be white Caucasian. Annual mortality per 100 000 with 95% confidence intervals (CIs) were calculated for SADS cases identified by the survey and for ONS-certified causes of death for the specified ICD codes.

Ethical approval

Local research ethics committee (LREC) approval was initially granted by the Royal Brompton and Harefield Hospitals NHS Trust and St Georges Hospital NHS Trust. The Multicentre Research Ethics Committee approved the study on condition that all LRECs in districts in which relatives of the deceased lived also be approached for their approval. It was necessary for this national study to submit applications to all 239 English LRECs, of which 234 gave ethical approval. Five LRECs refused. Only 179 LRECs were ultimately relevant to the survey because of a SADS case or relative in their domain.

RESULTS

In all, 117 of 122 (96%) HM Coroners in England agreed to participate in the study; 115 coroners' cases meeting the study's entry criteria were referred from 57 coroners' jurisdictions. Of these 57 coroners, 27 (47%) referred more than one case (range 2–6 per coroner). The panel confirmed 56 of the 115 (49%) cases as SADS. Table 1 shows the coroners' officers reported demographic and lifestyle characteristics of these SADS cases. Mean age (range) was 32 (7–64) years. The male:female ratio was 1.7:1. Social class was obtained for all cases through ONS (table 1). Social class of the father was given for those aged <16 years.

The informants' general practitioners of four SADS cases could not be approached because LREC approval for these districts was not granted. Of the 52 general practitioners contacted, 48 agreed to the informant of the SADS case being approached. Five informants refused to be interviewed, three did not respond and one family was already under cardiological investigation. Interviews of informants took place for 39 of 56 (70%) cases (three subjects aged <16 years). Table 2 shows the educational, employment, smoking status and alcohol consumption of these 39 SADS cases, as well as reported symptoms and medical and family history. Although there was no personal history of cardiac disease in the SADS cases, two thirds were reported by informants to have had one or more cardiac symptoms at some time in the past. In the 48 h before death, four cases had reported cardiac symptoms. In one case, there was reported epilepsy but this was not the cause of death. Three cases had a psychiatric history, but toxicological screens

Table 2 Sociodemographic and lifestyle characteristics, reported symptoms, and medical and family history of sudden arrhythmic death syndrome cases as reported by informants during interviews (n = 39)

Education*	
Primary school	3 (8%)
Secondary school	22 (61%)
College of further education	6 (17%)
University	5 (14%)
Employment*	
Self-employed	4 (13%)
Employed	22 (61%)
Unemployed	4 (11%)
House-person	1 (3%)
Full-time education	5 (14%)
Smoking status*	
Current smoker	12 (33%)
Ex-smoker	6 (17%)
Non-smoker	18 (50%)
Alcohol consumption*	
Teetotaller	2 (6%)
Occasional	24 (67%)
Regular	10 (28%)
Symptoms†	
Dizzy spells	11 (28%)
Fainting/blackouts	7 (18%)
Palpitations	7 (18%)
Shortness of breath	10 (26%)
Chest pain	7 (18%)
Indigestion	13 (33%)
Medical history†	
Hypertension	1 (3%)
Epilepsy	1 (3%)
Psychiatric history	3 (8%)
Family history†	
Miscarriage	8 (21%)
Cot death	2 (5%)
Childhood death	3 (7%)
Unexplained accident	2 (5%)
Sudden death	7 (18%)

SADS, sudden arrhythmic death syndrome.
*3 SADS cases <16 years, all of whom were in full-time education, are not included.
†SADS cases appear more than once under these table subheadings.

Table 3 Office of National Statistics-coded causes of death recorded for the 56 SADS cases

ONS classification (ICD9)		Number of SADS cases
345.9	Epilepsy—unspecified	1
410.0	Acute myocardial infarction	1
422.9	Other and unspecified acute myocarditis	1
425.4	Cardiomyopathy—other primary cardiomyopathy	2
427.8	Cardiac dysrhythmias: 0.8 = other	1
427.9	Cardiac dysrhythmias: 0.9 = unspecified	5
428.9	Heart failure—unspecified	2
429.9	Ill-defined diseases and complications of heart disease —unspecified	1
518.5	Other diseases of lung—pulmonary insufficiency after trauma	1
571.0	Chronic liver disease and cirrhosis—alcoholic fatty liver	1
798.1	Sudden death, cause unknown—instantaneous death	18
799.9	Other ill-defined and unknown causes of morbidity and mortality—other unknown and unspecified cause	20
E9102	Accidental drowning and submersion while engaged in other sport or recreational activity without diving equipment	1
E911	Inhalation or ingestion of food causing obstruction of respiratory tract or suffocation	1

ICD, International Classification of Diseases; ONS, Office of National Statistics; SADS, sudden arrhythmic death syndrome.

were negative. There was a family history of other premature sudden deaths (<45 years), including unexplained accidents and childhood deaths in seven (18%) cases.

Table 3 describes the ONS-coded causes of death as officially recorded for the 56 SADS cases. Only 18 of 56 (32%) cases were categorised most appropriately as ICD code 798.1 (sudden death cause unknown—instantaneous death) and the rest were attributed to other codes, including some pathologies that were incorrect. The survey's ascertainment of SADS cases, and the estimated annual death rates based on these cases, are shown in table 4. Table 4 also shows the numbers of registered causes of death at ONS for ICD9 codes 798.1, 799.9, 427.8/9, 428.9 and 429.9 (unascertained causes of death) for the entire study period from October 1997 to May 1999, and the calculated annual incidence rates excluding local authorities for HM Coroners jurisdictions not participating in the survey. The survey's estimated annual death rate for SADS of 0.16/100 000 was higher than the ONS registered rate of 0.10/100 000 for sudden death cause unknown—instantaneous death (798.1). However, the ONS rate for all ICD codes to which SADS could be attributed (unascertained causes of death: 798.1, 799.9, 427.8/9, 428.9 and 429.9) was 1.34/100 000; more than eight times higher than the survey's estimated rate for SADS. Table 5 gives the estimated number of potential SADS cases over a 1-year period in residents aged 4–64 years for all of England.

DISCUSSION

This national survey of SADS is the first to characterise victims through informant interviews and to compare the mortality for this syndrome with official ONS mortality statistics for unexplained deaths. Most are symptomatic, young male adults and adolescents. The social class distribution of those victims who were economically active is similar to that reported by the Health Survey for England (1996).

The estimated annual death rate (range) for SADS from this survey (0.16 (0.12–0.21) per 100 000 per annum) is up to twice that registered at ONS to ICD code 798.1 (0.10 per 100 000 per annum), the category that most closely approximates the inclusion criteria for a SADS case. The rates for this ICD code are also higher for males. It is important to emphasise that the survey excluded all other cardiac pathologies and non-cardiac causes of sudden death such as trauma, intracranial haemorrhage or pulmonary embolus by a full coroner's autopsy and a specialist examination of the heart by a cardiac pathologist. In addition, only 32% of the cases in our survey were correctly certified at ONS. The causes of death in several SADS cases had been incorrectly attributed by the coroner's pathologist to a cardiac cause such as myocardial infarction, myocarditis or cardiomyopathy, or to non-cardiac causes such as epilepsy or accidental drowning. Thus, the official ONS statistics for sudden unexpected death underestimate the real numbers of deaths due to SADS.

Table 4 Numbers and estimated annual mortality for sudden arrhythmic death syndrome survey cases and for Office of National Statistics registered causes of death under International Classification of Diseases—ninth edition

	Male		Female		Total	
	Number of deaths	Rate per 100 000 pa (95% CI)	Number of deaths	Rate per 100 000 pa (95% CI)	Number of deaths	Rate per 100 000 pa (95% CI)
SADS	35	0.20 (0.14 to 0.28)	21	0.13 (0.08 to 0.19)	56	0.16 (0.12 to 0.21)
ICD 9 code						
798.1	36	0.13	21	0.08	57	0.10
799.9	470	1.68	165	0.61	635	1.15
427.8/9	17	0.06	14	0.05	31	0.06
428.9	10	0.04	2	0.01	12	0.02
429.9	2	0.01	0	0	2	0.00
Total	535	1.91	202	0.74	737	1.34

ICD, International Classification of Diseases; pa, per annum; SADS, sudden arrhythmic death syndrome.
Values are for ages 4–64 years over entire study period (October 1997–May 1999) and calculated annual mortality in England excluding local authorities for HM Coroners' jurisdictions not participating in the survey.

Table 5 Number of potential sudden arrhythmic death syndrome cases* over a 1-year period and calculated rates in residents aged 4–64 years for all of England

	Male		Female		Total	
Age group (years)	Rate per 100 00 pa	Number of deaths pa	Rate per 100 000 pa	Number of deaths pa	Rate per 100 000 pa	Number of deaths pa
4–15	0.14	5	0.14	5	0.14	11
16–24	0.95	26	0.46	12	0.71	38
25–34	1.99	79	0.69	26	1.36	105
35–44	2.78	100	0.87	31	1.84	131
45–54	3.44	112	1.29	42	2.36	154
55–64	2.93	71	1.40	35	2.15	105
Total	1.97	393	0.78	151	1.38	544

ICD 9, International Classification of Diseases—ninth edition; pa, per annum.
*Unascertained causes of death—ICD9 codes 798.1, 799.9, 427.8/9, 428.9 and 429.9.

When other ill-defined and unknown causes of mortality (ICD code 799.9, 427.8/9, 428.9 and 429.9) are considered, and to which SADS cases could be inaccurately attributed, the potential annual death rate for SADS increases almost eightfold (1.38 per 100 000 per annum). Therefore, our survey may also be underestimating the true number of SADS cases. As case ascertainment was dependent on coroners, their officers and pathologists maintaining active surveillance over the course of a year, it is inevitable that some cases meeting our inclusion criteria were not identified by our study. There was also inconsistency in referral patterns of SADS cases across England shown by most of the referred cases being supplied by a small minority of coroners. In addition, under-ascertainment of SADS cases may have been due to families not agreeing to further expert cardiac examination or to coroners' pathologists attributing the cause of death incorrectly. Using the combined ICD codes for unascertained causes of death as a surrogate for SADS, the potential number of victims in England could be as high as around 500 per annum.

The 18% prevalence of a family history of other premature sudden death and unexplained accidents raises the possibility of underlying heritable cardiac disease. We have already reported that approximately one fourth of families whose surviving first-degree relatives underwent cardiological evaluation[10] were affected by predominantly long QT syndrome and incompletely penetrant cardiomyopathy (hypertrophic[11 12] and dystrophica myotonica[13]). Another more recent study of families of a selected series of 44 unexplained sudden deaths[14] reported a 40% frequency of inheritable cardiac disease known to cause sudden death. This included non-structural disease such as catecholaminergic polymorphic ventricular tachycardia,[15–17] long QT[18] and the Brugada syndromes,[19–21] as well as structural diseases such as hypertrophic and arrhythmogenic right ventricular cardiomyopathy.[22 23] Autopsy studies of sudden unexpected death among athletes have also showed cardiomyopathy as the most common demonstrable cause,[6 24] although non-structural disease is also likely to have a role.[6] Other supporting evidence for the importance of heritable conditions in SADS comes from genetic screening. For example, KCNH2 mutations, supportive of diagnoses of either the LQT2 subtype of long QT syndrome[25] or short QT syndrome,[26 27] have been detected in autopsies on sudden unexplained death,[28] whereas catecholaminergic polymorphic ventricular tachycardia-associated Ryanodine receptor (hRyR2) mutations were present in 7 of 49 sudden unexpected deaths.[29] Other genetic non-structural cardiac diseases have also been associated with sudden unexpected death in case reports and pedigree studies: ankyrinB mutation-associated arrhythmia syndromes[30] and the LQT4 subtype of long QT syndrome[31]; Andersen's syndrome[32]; Timothy syndrome[33]; and Calsequestrin2 (CASQ2) mutation associated with autosomal recessive catecholaminergic polymorphic ventricular tachycardia.[17]

Limitations

The comparison between the SADS survey and ONS-certified causes of death is limited by several factors. ONS-registered deaths will not have met all the inclusion criteria of the SADS survey. The death certificate does not provide information on ethnicity or past medical history, and may not report other underlying causes. It is assumed there was no prior cardiac disease, but this may be incorrect. Also, it is impossible to establish from ONS data whether the victim was seen alive within 12 h of being found dead. So the ONS-registered unascertained causes of death will include victims who would not have been included in our survey. It is also possible that for some of these ONS-unascertained deaths, a specialist examination of the heart by a cardiac pathologist would have found cardiac disease. Finally, for some of the ONS cases, the time elapsed between death and postmortem would make the cause of death unascertainable because of the state of the body.

In summary, this national survey describes the demographic, social, medical and family history of sudden, unexpected and pathologically unexplained cardiac deaths in young people in the community. We recommend that these deaths are more appropriately termed ''sudden arrhythmic death syndrome'' rather than ''sudden adult death syndrome'', given that the age spectrum includes children and the probable underlying causes are arrhythmic. They are also likely to be genetic, and there is a real risk of further avoidable sudden deaths in families with identified SADS deaths.[10] In March 2005, the new National Service Framework chapter on arrhythmias and sudden cardiac death was published, stating that good practice requires the clear identification of SADS cases by coroners and their pathologists and the appropriate support, counselling and management of families through specialist cardiac centres. With an incidence of up to 500 potential SADS deaths per annum in England this guidance must be heeded.

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