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Sudden cardiac death-an Indian perspective

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Summary Coronary artery disease (CAD) is by far the commonest cause of sudden cardiac death (SCD), with the prevalence of CAD paralleling the incidence of SCD in epidemiological studies. With the alarming increase in prevalence of CAD, diabetes and hypertension in India, the incidence of SCD is also on the rise, especially in the urban regions. While the mortality of CAD in the West has decreased, it has reached epidemic proportions in India. Consequently, there is a need for implementing preventive cardiovascular health measures to meaningfully reduce the incidence of SCD.

Introduction

Sudden cardiac death (SCD) is defined as death due to cardiac causes, in which the time and mode of death is unexpected, in an individual with or without pre-existing cardiac diseases which occurs within 1 h of the onset of the heralding symptoms [1]. This definition is a modified combination of the various definitions of sudden cardiac death, which differ according to clinical, scientific and medico-legal requirements.

Epidemiology of SCD — difficulties in estimating its incidence

Estimating the overall incidence of SCD is difficult, partly due to the varying definitions of SCD used in epidemiological studies. Moreover, the etiological categorization of SCD, on the basis of clinical circumstances, is an estimate considering that 40% of sudden deaths are un-witnessed at the time of the event [2]. Even the reported incidence of SCD in the United States varies depending upon the source of information, with emergency rescue data giving an estimate of 200 thousand sudden deaths per year and retrospective analysis of vital statistic mortality data estimating more than 450 thousand sudden deaths per year [3,4]. Consequently, it is difficult to estimate, with fair approximation, the overall incidence of SCD in different countries.

The most recent estimates of SCD account for 300,000 to 350,000 deaths annually in the United

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States, which corresponds to about 50% of cardiac deaths [6—8]. The incidence of SCD ranges from 36 to 128 per 100,000 inhabitants per year in different studies [7]. These figures suggest an overall incidence between one and two deaths per 1000 persons among the general population [7].

Risk factors for SCD

The assessment of the risk factors of SCD is of importance for a reasonable assessment of its incidence when direct epidemiological measures are deficient; as well as in identifying 'population sub-groups at risk' while considering strategies for the prevention of SCD. The population subgroups can be broadly identified according to their cardiac disease profiles, age, gender and lifestyles.

Cardiac disease profiles

The major cardiovascular diseases which result in a significantly greater risk of SCD are as follows:

- Coronary artery disease (CAD) — the single largest causative risk factor.
- Cardiomyopathies:
  - o Idiopathic dilated cardiomyopathy — heart failure.
  - o Hypertrophic cardiomyopathy.
  - o Arrhythmogenic right ventricular dysplasia.
- Electrophysiologic abnormalities:
  - o Long QT syndrome.
  - o Brugada syndrome.
  - o Sudden Infant death syndrome (SIDS).
  - o Pre-excitation syndromes.
  - o Conduction system abnormalities.
- Valvular heart disease:
  - o Aortic stenosis.
- Congenital cardiac abnormalities.

Amongst these, CAD is, by far, the largest causative factor for SCD. In a review by Gillum, on the data for deaths occurring out of hospital and in the emergency room from 1980 to 1985 in 40 states in USA, the incidence of SCD paralleled the prevalence of coronary artery disease (CAD) [9].

Age and gender

There are two ages of peak incidence of sudden death: between birth and 6 months of age (SIDS) and between 45 and 75 years of age. The Gillum study showed that the incidence of SCD increases with age as the prevalence of CAD increases with age [9]. In the study, the cause of death varied for the 35—64 years and $\geqslant$65 years age group. Acute CAD, unspecified cardiovascular disease, cardiomyopathy and arrhythmias were more common in the younger age group. Chronic CAD and heart failure, in contrast, were more common in the older age group. In a study of vital statistics mortality data in United States, CAD was listed as the underlying cause of 62.2% of the death certificates, with successive age groups showing increased SCD rates [6].

The annual incidence of SCD is three to four times higher in men than in women, with approximately 75% of SCD in men. The reason for this difference is surmised by the gender difference in the incidence of CAD and the protection from atherosclerosis in women before menopause [6].

Life-style and psychosocial risk factors

The present day urban lifestyle with its contributing psychosocial factors has been implicated in increased risk of SCD [10,11]. In a study of 2320 men who survived MI, social isolation and high-level psychological stress were associated with an increased risk of SCD. These factors were also directly associated with low educational levels [11]. Study of SCDs among women showed an increased risk for women who were not married, who had fewer or no children and who had greater educational discrepancy with their spouses. Type A personality has also been associated with an increased incidence of CAD and its manifestations, including SCD [10].

Other risk factors of SCD include a history of psychiatric treatment, greater alcohol consumption, obesity and cigarette smoking [10,12]. Cigarette smoking and obesity were amongst the few risk factors in the Framingham study which showed the proportion of sudden deaths due to CAD increased in association with the risk factor for SCD. The Framingham study also demonstrated that cigarette smokers have a twofold to threefold increase in SCD risk in each decade of life between 30 and 59 years [12].

Epidemiological observations have also shown the relationship between low levels of physical activity and increased CAD risk. In a case-controlled crossover study, a strong association between vigorous exercise and the onset of MI, particularly in persons who are habitually sedentary was observed [13]. It was suggested that the

acute bouts of exercises increase the sympathetic activity and decrease the vagal activity, leading to an acute increase in susceptibility to ventricular fibrillation [14]. In contrast, regular vigorous exertion increases the vasovagal tone, resulting in increased cardiac electrical stability and protection against ventricular fibrillation [15]. However, there is a dearth of studies on the effect of physical activity in various clinical settings.

Thus, the observations from the various population sub-groups clearly underline the importance of CAD as a causative factor of SCD.

The Indian perspective

In addition to the known difficulties in the estimation of SCD, in India the levels of coverage of vital registration and the reliability of the cause of death as stated on the death certificate is often low, especially in the rural areas which significantly adds to the estimation of SCD incidence. Consequently, the estimation of SCD incidence has to be done from surrogate endpoints. Therefore, the calculation is often done from the epidemiological estimates of cardiovascular disease profiles in the population.

By these estimates, the rates of SCD are considerably lower, paralleling the rates of CAD in developing countries. However, India as one amongst the ''newly industrialized country'' in Asia, has shown in recent years an increase in the rates of CAD and a corresponding increase in SCD incidence, as shown in Tables 1–3. This trend is similar to the increase in prevalence of the major cardiovascular diseases in the other South Asian countries like China, Pakistan, Thailand, etc. [16–18]

However, an estimation of SCD in the Indian subcontinent is skewed, with observations from studies indicating a rural–urban divide in the prevalence of CAD. In a study by Bahl et al. in 2001, the prevalence of CAD in urban areas ranged from 7.6% to 12% as compared to rural areas with a range of 3.1% to 7.4% [18]. These findings related to the rural–urban gradient in CAD may be attributed to the lower risk factors in rural areas – plausibly due to the socio-economic patterns.

Since autopsies are difficult to perform on a large scale, the exact cause of sudden death is often unclear. However, one can be definite about the commonest etiology (MI), if there is ECG documentation of the same. In the absence of this, classical symptoms of rest angina with sweating immediately preceding death would indicate a high probability of the same diagnosis. But often, the exact cause of sudden death goes down as ''unknown''. Death certificates world over have been found to be very deficient when making scientific analyses of the cause of death in general, leave alone sudden death. An interesting concept of a ''verbal autopsy'' (Tables 4 and 5) was undertaken on a large scale in South India [19]. Lay volunteers, who were graduates, were given brief training before they undertook a survey among family members of those who had died. This revealed a significant decrease in the category of ''unspecified'' medical causes as compared to the death certificate data. Such verbal autopsies have been scientifically validated. Such data are very meaningful for estimating the magnitude of SCD, since we know that SCD incidence parallels the incidence and mortality from CAD.

The prevalence of CAD in the urban areas in this study was already found to be comparable to the recent update on CAD prevalence in USA [20]. The Global Burden of Disease Study has also estimated that by the year 2020, India will have more individuals with CAD than any other region [8]. Nevertheless, this aspect must be judged in the context that the information on SCD incidence is usually obtained from secondary and tertiary care hospitals in various parts of the country. Therefore, extrapolation of the conclusions drawn from the available data to rural regions may not be entirely valid because of the ethnic, economic and cultural diversity, and the differing levels of literacy and awareness among the population, access to healthcare and standards of healthcare.

Table 1 Estimated prevalence of major cardiovascular diseases in India and China – 2004.[a]

Country	Heart failure	Atrial fibrillation	Angina	Peripheral artery disease
China				
Prevalence (000s)	18,703	4546	42,862	68,839
Prevalence rate (%)	1.40	0.40	3.30	5.30
India				
Prevalence (000s)	15,763	4260	38,982	60,176
Prevalence rate (%)	1.50	0.40	3.70	5.70

[a] Data from: the Asian cardiovascular market outlook to 2010, business insights, 2006. By Nehru and Fox-Tucker [16].

Table 2 Estimated incidence of myocardial infarction in India and China — 2004.[a]

Country	Incidence (000s)	Incidence (%)	Share in 2004 (%)
China	4156	0.30	45.20
India	3728	0.40	40.50

[a] Data from: the Asian cardiovascular market outlook to 2010, business insights, 2006. By Nehru and Fox-Tucker [18].

Table 3 Distribution of acute myocardial infarction cases in South Asia.[a]

	Overall			Male			Female		
	No. of cases	Age, mean (SD), y	No. of cases < 40 y (%)	No. of cases	Age, mean (SD), y	No. of cases 40 y (%)	No. of cases	Age, mean (SD), y	No. of cases 40 y (%)
Worldwide	12,460	58.1 (12.2)	751 (6.0)	9458	56.3 (12.0)	683 (7.2)	3002	63.7 (11.4)	68 (2.3)
South Asia	1732	53.0 (11.4)	154 (8.9)	1480	53.0 (11.2)	143 (9.7)	252	58.6 (11.6)	11 (4.4)
India	470	53.0 (11.4)	55 (11.7)	411	51.0 (10.4)	52 (12.7)	59	57.3 (11.6)	7 (11.9)
Pakistan	637	53.3 (11.1)	57 (8.9)	543	52.4 (10.9)	54 (9.9)	94	58.3 (10.9)	0

[a] Data from Joshi et al. [17].

Table 4 Cause of death classified by Vital Statistics Department and based on verbal autopsy of 48,000 adult deaths (aged ⩾ 25) in Chennai (urban), south India: 1995—1997.[a]

Causes of death (ICD9 codes)	Cause of death in VSD	Cause of death based on verbal autopsy		
	M (%)	F (%)	M (%)	F (%)
Vascular disease (390—415, 418—459)	8319 (30)	5168 (25)	11,056 (41)	7435 (37)
Respiratory tuberculosis (TB) (011, 012, 018)	1399 (5)	372 (2)	2231 (8)	575 (3)
Other respiratory diseases (416, 417, 460—519)	1088 (4)	596 (3)	1597 (6)	855 (4)
Neoplasm (140—239)	1163 (4)	1002 (5)	2344 (9)	1999 (10)
Infection except respiratory & TB (rest of 1—139, 279.8 [HIV], 320-6, 590, 680-6)	584 (2)	303 (2)	1034 (4)	618 (3)
Unspecified medical causes (780-9, 797-9)	12,291 (44)	11,511 (56)	4367 (16)	5889 (29)
Other specified medical causes	1899 (7)	1045 (5)	4414 (16)	2804 (14)
No cause given in VSD (hence probably medical)	983 (4)	634 (3)	Nil	Nil
Total deaths — medical	27,726	20,631	27,043	20,175
Re-assigned by VA to external causes	Excluded from the study[a]		683	456
Total deaths (medical causes + external causes)	27,726	20,631	27,726	20,631

VSD, Vital Statistics Department.
[a] Data from Gajalakshmi and Peto [19].

Tertiary hospital statistics underestimate the incidence of SCD, since most of them occur outside hospital. Yet, an evaluation by Gupta et al. (November, 2007), of KEM Hospital in Mumbai for a period of 3 months showed a similarity in the trend of SCD in urban India and the West [21] (see Table 6).

In the study by Bahl et al., acute coronary syndromes were observed to be a significant cause of SCD, which if managed systematically can significantly reduce the incidence of SCD [18]. This includes improving the time from symptom onset to presentation at hospital and in-hospital care including management and drug treatment.

The time from symptom onset to presentation at hospital is also typically longer among patients in India than in the West. The mortality of MI showed that 60% of deaths occurred out of hospital, mostly sudden [3]. Thus hospital based treatment of MI, including high-tech primary angioplasty, would prevent only a small proportion of MI deaths. The time from symptom onset to emergency department arrival for patients with acute ST elevation myocardial infarction (STEMI) ranges between 110

Table 5 Cause of death classified by Vital Statistics Department and based on verbal autopsy of 48,000 adult deaths (aged ⩾ 25) in Chennai (rural), south India: 1995–1997.[a]

Causes of death (ICD9 codes)	Cause of death in VSD		Cause of death based on Verbal Autopsy	
	M (%)	F (%)	M (%)	F (%)
Vascular disease (390–415, 418–459)	3351 (20.3)	1614 (14.4)	3928 (24.6)	2404 (22.0)
Respiratory tuberculosis (TB) (011, 012, 018)	1659 (10.1)	686 (6.1)	1841 (11.5)	671 (6.1)
Other respiratory diseases (416, 417, 460–519)	717 (4.4)	471 (4.2)	1044 (6.5)	728 (6.6)
Neoplasm (140–239)	415 (2.5)	594 (5.3)	488 (3.1)	664 (6.1)
Infection except respiratory & TB (rest of 1–139, 279.8 [HIV], 320-6, 590, 680-6)	1818 (11.0)	1584 (14.1)	1954 (12.2)	1411 (12.9)
Unspecified medical causes (780-9, 797-9)	5829 (35.4)	4565 (40.7)	4173 (26.1)	2737 (25.0)
Other specified medical causes	2237 (13.6)	1346 (12.0)	2570 (16.1)	2334 (21.3)
No cause given in VSD (hence probably medical)	451 (2.7)	343 (3.1)	Nil	Nil
Total deaths – medical	16,477	11,203	15,998	10,949
Re-assigned by VA to external causes	2817	1291	3296	1545
Total deaths (medical causes + external causes)	19,294	12,494	19,294	12,494

[a] Data from Gajalakshmi and Peto [19].

Table 6 SCD incidence – hospital data.[a]

Evaluation period of 3 months King Edward Memorial Hospital, Mumbai, India	
Total no. of admissions	21,126
Total no. of deaths	1194
Total no. of sudden non-cardiac deaths	40 (3.4% of total deaths)
Total no. of cardiac deaths	126
Total no. of sudden cardiac deaths	55 (4.6% of total deaths)
Percentage of SCD	
SCD/total admissions	0.26%
SCD/ total deaths	4.6%
SCD/total sudden deaths	45.5%
SCD/total cardiac deaths	43.7%
SCDs confirmed on autopsy	27.3%

[a] Data from Gupta et al. [21].

and 140 min in North America, while in India, it is 180–330 min [20,22–24]. This delay in presentation is due to several factors such as lack of symptom awareness, longer distances travelled to reach hospital and problems of transportation. Only 5.4% of patients are brought to hospital in an ambulance, with the large majority using public transport (buses) and hired vehicles. Interestingly, consultation with the family doctor, local practitioner or local primary health centre has been found to be an important cause of delay. Thus, the true incidence in the general population remains to be determined.

In-hospital care is determined by the type of hospital that the patient attends. In prospectively collected data from 14 hospitals in three southern Indian states, George et al. found that government hospitals were least likely to follow guidelines for the treatment of acute STEMI compared with private hospitals or those run by voluntary organisations [25]. Patients treated at hospitals affiliated to medical colleges were more likely to receive fibrinolytic treatment and β blockers than those admitted to non-teaching hospitals [25].

Conclusion

Thus, the scenario in India as regards the epidemiology and management of SCD is one of striking heterogeneity. There is a need for correctly estimating the incidence and risk factors of SCD in the various regions. The urban areas of India are already showing a trend similar to the West with CAD being the commonest underlying cause of SCD.

With the alarming increase in prevalence of CAD, diabetes and hypertension in India, the incidence of

SCD is also on the rise, especially in the urban regions. While the prevalence of CAD in the West has decreased, it is reaching worrying proportions in India. Consequently, there is a need for implementing preventive cardiovascular health measures to meaningfully reduce the incidence of SCD. Guidelines incorporating evidence-based, cost-effective treatments should be formulated taking into consideration the resource-constraints of the region and widely disseminated for implementation.

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