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## Sudden Out-of-Hospital Coronary Death in Patients with No Previous Cardiac History. An Analysis of 221 Patients Studied at Autopsy

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**ABSTRACT:** Many epidemiological, clinical, and autopsy studies have demonstrated that the risk of sudden coronary death (SCD) is linked to the severity of coronary atherosclerotic lesions and to their thrombotic potential. However it remains unknown why some individuals manifest no clinical evidence of coronary disease until the onset of sudden death. The aim of this autopsy study has been to analyze the sociodemographic, clinical, and pathological features in case of sudden out-of-hospital coronary death where the death was the first manifestation of coronary disease. The results have been compared with those obtained from victims of SCD with known cardiac history. A total of 377 autopsies of sudden out-of-hospital cardiovascular deaths were performed at the Forensic Institute of Paris between 1989 and 1991. A total of 221 were SCD. A total of 160 of these subjects (72.4%) had no cardiac history (group A). The other 61 victims of SCD had cardiac antecedents (group B). Men account for 63% and 77% of the SCD in groups A and B respectively and are 12 years younger than women at the onset of SCD in both groups (65/77 years). Our study showed that in both groups SCD occurs in 83% of cases at home (and at rest) and in 30% of these cases while sleeping. Autopsy showed that SCD be it with or without antecedent occurs on a background of severe coronary disease with multivessels stenoses but coronary thrombosis was rarely observed (15%). SCD occurred in the context of underlying cardiomegaly. The increase in heart weight was significantly less marked in subjects of group A than in those of group B whereas the average age at the onset of SCD was the same in both groups. In conclusion it appears from our results that more than 70% of victims of SCD have no cardiac history and thus are unknown to cardiologists and to hospital statistics. The present study carried out in Paris over a three-year period is of interest and use not only to forensic pathologists but also to epidemiologists and cardiologists concerned with the problem of sudden death.

**KEYWORDS:** pathology and biology, sudden coronary death, epidemiology, autopsy study

Even though cardiovascular mortality has been declining over the last two decades, sudden cardiac death remains a major unresolved clinical and public health problem accounting for more than 300 000 of the deaths in the United States annually (50% of all cardiovascular deaths) [1]. Although cardiovascular causes of sudden death are varied

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and numerous, coronary artery disease accounts for the overwhelming majority (about 80%) of cardiovascular sudden deaths [1]. In France, while the true incidence of sudden cardiac death has not been determined, it can be estimated from studies in other countries [1-7] that 30 to 60 000 people die from sudden cardiovascular death each year.

Many epidemiological studies [1-7] have provided much valuable information concerning the risk factors of sudden coronary death (SCD). However in these studies the cause of death is based only on the death certificates, without further investigations, and therefore cannot be proven. Moreover, these studies provide no pathological information.

Autopsy studies allow one to describe the cardiac lesions found in SCD [8-22]. However the majority of these autopsy studies have concerned sudden in-hospital death. Sudden out-of-hospital coronary death has been studied most often in patients with known coronary artery disease, for example, in myocardial infarction survivors after discharge from hospital [22].

However it remains unknown why some individuals manifest no clinical evidence of coronary disease until the onset of sudden death.

The aim of our autopsy study has been to analyze the sociodemographic, clinical, and pathological features in case of sudden out-of-hospital coronary death where the death was the first manifestation of coronary artery disease. The results have been compared with those obtained from victims of SCD with known cardiac history.

### Study Patients and Methods

A total of 377 autopsies of victims of sudden-out-of-hospital cardiovascular death were performed at the Forensic Institute of Paris between 1989 and 1991. Table 1 lists the causes of these sudden deaths. Sudden death in this study has been defined as a death occurring within 1 hour of the onset of symptoms [25]. Included in the study were only those cases in which the death was witnessed or there was sufficient circumstantial evidence of SCD. Thus the type of clothing worn, the activity in which the decedent was engaged when he died, the position or posture of the body, the possible contusions received by the body on falling unconscious were investigated in order to determine whether the death had been sudden.

### Autopsy Procedure

The body of each subject whose heart was used in this study was submitted to a complete autopsy. In addition toxicological analyses were performed in all subjects in which the cause of death was not discerned on gross examination of the body.

TABLE 1—Causes of sudden cardiovascular death found at autopsy during the study period (1989-1991) at the Institute of Forensic Sciences of Paris. Number of patients (%).

Sudden cardiovascular death	377	(100)
Sudden cardiac death	313	(83)
Coronary artery disease	230	(73.5)
Cardiomyopathy	46	(14.7)
Valvular heart disease	18	(5.7)
Pericarditis	12	(3.8)
Right ventricular dysplasia	3	(1)
Myocarditis	3	(1)
Congenital Cardiopathy	1	(0.3)
Non cardiac sudden death	64	(17)
Rupture of aortic aneurysm	11	(17.2)
Pulmonary embolism	12	(18.8)
Stroke	41	(64)

*Heart Weight*—Before the heart was weighed (fresh) it was cleaned of postmortem intracavitary clot. A heart weighing >350 g in women and >400 g in men was considered increased in weight [11,15,16,20].

*Coronary Arteries*—The four main epicardial coronary arteries were cut at 0.5 cm intervals to their distal tributaries. Coronary artery narrowing was grossly evaluated. We selected for the purpose of this study only those hearts that bore evidence of sufficient coronary artery disease either acute or chronic to support the assumption that the death of these subjects had been due to coronary artery disease. Thus any subjects whose death was considered to be due to coronary artery disease possessed a heart that had at least one of its four coronary arteries occluded 75% or more either by an old or an acute process (thrombosis). In addition no other cause of death could be postulated.

The valves were inspected and the myocardium was studied by the bread-loafing method at intervals of 1 to 1.5 cm below the level of the atrioventricular valves.

Of the 377 cardiovascular sudden deaths, 230 were considered to be due to coronary artery disease. Nine of these subjects died as a result of cardiac rupture following myocardial infarction. These cases were excluded from our study, the cause of death being hemopericardium in which the mechanism of death differs from that of the other cases included in both groups A and B namely an electric event. Of the 221 included patients, 160 had no cardiac history (group A). The 61 others had cardiac antecedents (angina pectoris, myocardial infarction, cardiac insufficiency) (group B).

### *Statistical Analysis*

All results are expressed as mean  $\pm$  SEM. For each parameter mean values obtained in group A and in group B were compared using an analysis of variance.

## **Results**

### *Causes of Death*

Table 1 lists the causes of sudden cardiovascular death found at autopsy during the study period. Sudden cardiac death accounts for 83% of sudden cardiovascular deaths. A total of 73.5% of the cases of sudden cardiac deaths are coronary in origin. Cardiomyopathies accounted for 14.7% of sudden cardiac deaths. The other causes of sudden cardiac death made up the remaining 11.8%.

### *Age and Sex (Table 2)*

The percent of men were 62.5% and 77% in group A and group B respectively.

In group A the 160 patients ranged in age from 30 to 93 years (mean  $68.81 \pm 1.29$ ); the 100 men ranged from 30 to 93 (mean  $64.08 \pm 1.66$ ) and the 60 women from 46 to 93 (mean  $76.49 \pm 1.61$ ) ( $P < 0.001$ ). In group B the 61 patients ranged in age from 33 to 91 years (mean  $68.55 \pm 1.89$ ); the 47 men ranged from 33 to 91 (mean  $65.74 \pm 2.19$ ) and the 14 women from 70 to 88 (mean  $78.59 \pm 1.69$ ) ( $P < 0.01$ ). No significant difference was found between mean age in group A and in group B, in both sexes.

### *Resuscitation (Table 2)*

Attempts at resuscitation were applied in only 11.25% and 12.67% of the cases of group A and group B, respectively.

TABLE 2—Clinical and morphological features in sudden coronary death.

	Sudden coronary death			
	No previous cardiac disease (group A)		Known previous cardiac disease (group B)	
	Males	Females	Males	Females
Number of cases (%)	100 (62.5)	60 (37.5)	47 (77)	14 (23)
Average age (years) (Range)	64.08 ± 1.66 (30-93)	76.49 ± 1.61 <sup>a</sup> (46-93)	65.74 ± 2.19 (33-91)	78.59 ± 1.69 <sup>a</sup> (70-88)
Resuscitation (%)		11.25		12.67
Place of SCD:				
Home[sleeping (%)]	134 [38 (28.36)]			50 [16 (32)]
In the street (%)	26 (16.25)			11 (18)
Heart weight (g) (Range)	446.45 ± 11.58 (320-730)	381.54 ± 17 <sup>a</sup> (220-650)	513.78 ± 24.2 <sup>b</sup> (350-1100)	397 ± 28.4 <sup>a</sup> (350-505)
% thrombosis		13		15
Number of severely narrowed (>75%) coronary arteries:				
1 (%)		23 (14.2)		8 (13)
2 (%)		43 (26.8)		16 (26)
3 (%)		94 (59)		37 (62)

Values are mean ± SEM.

<sup>a</sup>P < 0.05 or better for the comparisons between male and female values.

<sup>b</sup>P < 0.05 or better for the comparisons between group A and group B values.

*Place and activity at the moment of SCD (Table 2)*

In group A, 83.75% of SCD occurred at home (28.36% of these in bed). In group B, 82% occurred at home (32% in bed). In cases of SCD occurring outside the home the victims were not involved in strenuous activity. In both groups victims never experienced acute symptoms or exhibited acute signs before death.

*Pathological Findings (Table 2)*

**Heart weight**—In group A heart weight in the 160 patients ranged from 220 to 730 g (mean  $425.7 \pm 9.92$ ); the heart weight ranged from 320 to 730 g (mean  $446.45 \pm 11.58$ ) in the 100 men and from 220 to 650 g (mean  $381.54 \pm 17$ ) in the 60 women. In group B heart weight in the 61 patients ranged from 288 to 1100 g (mean  $472.23 \pm 23.21$ ). The mean heart weight in group B was significantly greater than in group A ( $P < 0.05$ ); the heart weight ranged from 350 to 1100 g (mean  $513.78 \pm 24.2$ ) in men and from 350 to 505 g (mean  $397 \pm 28.4$ ) in women. In men the mean heart weight in group B was greater than in group A ( $P < 0.01$ ). This difference was not found in women. In group A, 66% of the 100 men and 63% of the 60 women had a heart of increased weight. In group B, 69% of men and 67% of women had a heart increased in weight.

**Coronary Artery Narrowing**—In group A, of the 160 patients only one artery was so narrowed by plaque in 23 patients (14.2%) and in group B, of the 61 patients, in eight patients (13%) (NS); two arteries were so narrowed in 43 patients (26.8%) in group A and in 16 patients (26%) in group B (NS); three arteries were so narrowed in 94 patients (59%) in group A and in 37 patients in group B (62%) (NS).

An occlusive coronary artery thrombosis was found in 13% of the cases in group A and in 15% of the cases in group B.

**Discussion**

Our autopsy study provided sociodemographic, clinical and pathological information regarding 221 victims of sudden out-of-hospital coronary death and compared the results obtained from those cases (160 patients) with no cardiac history, with those (61 patients) with known cardiac disease. Our results confirm that coronary artery disease is numerically the single most common cause of sudden death and are in this regard in accord with other necropsy studies [8–22] and data obtained from large epidemiological studies using death certification [1–7]. Since diagnoses, in these epidemiological studies, are based only on the death certificates without further investigation, and therefore cannot be proven, true incidence of SCD, as the first manifestation of coronary artery disease, cannot be established and candidates profile cannot be surely determined. Moreover these studies provide no pathological information. In our study 72.4% of all victims of SCD manifested no evidence of coronary artery disease until the onset of sudden death.

Autopsy studies allow one to describe the cardiac lesions found in SCD. However the majority of these autopsy studies have concerned sudden-in-hospital death. Sudden out-of-hospital coronary death has been studied most often in patients with known coronary disease, for example, in myocardial infarction survivors after discharge from hospital [22].

SCD occurring in patients with no previous cardiac history, as the first manifestation of coronary artery disease has not been thoroughly investigated. The data obtained from morphological studies in SCD have often been difficult to compare because of the use of different temporal definition and because of the different technique used to examine the heart. The temporal definition of SCD range from death within a few seconds of the acute onset of symptoms [9] to death within 24 h of the acute onset of symptoms [24]. In our study the 1 hour definition has been utilized as in other studies such as in the

Framingham study [7]. After a few hours established infarction is commonly present with complications such as cardiogenic shock.

In group A men accounted for 62.5% of SCD and were on average 12 years younger than women at the onset of SD (64/76 years). The percent of men in group B was higher (77%). Men were also in group B 12 years younger than women (66/78). From these results it appears that whereas the difference in age at the onset of SD between men and women is the same in both groups, the percent of men who suffer clinical manifestations of their coronary artery disease is higher. Our results show that in both groups SCD occurs in 83% of cases at home and in 30% of these cases while sleeping, confirming previous data from other studies [8]. In cases of SCD occurring outside the home the victims were not in general involved in strenuous activity.

As previously established [9–23] our results showed that SCD be it with or without cardiac antecedent occurs on a background of severe coronary disease. In our study, 14.2%, 26.8%, and 59% of patients in group A had one, two, and three arteries narrowed > 75% in cross sectional area by atherosclerotic plaque respectively. The results obtained in group B were not significantly different (13%, 26%, 61%). In one study of 168 SCD Roberts et al. [16] reported 15% to have single vessel 27% to have double vessel and 47% to have triple vessel disease. Another study of 239 out-of-hospital SCD without previous infarction gave figures of 20, 32, and 48% [21] whereas a study of 118 SCD with previous infarction 12, 26, 62 for single, double and triple vessel disease, respectively [21]. In the Wandsworth study [6] Thomas et al. found figures of 26, 39, and 33% for single-, double-, and triple-vessel disease, respectively.

There is far less agreement on the role of the thrombosis in SCD. Plaque instability with local thrombus formation is now firmly established as the major factor precipitating unstable angina and acute myocardial infarction. Davies [13,15,19,22] found a high incidence of coronary thrombosis but other pathological studies [10,20,21,38] have however not found such a high incidence of coronary thrombosis. Figures vary from 4% [20] to 74% [22]. Our study discloses that the frequency of coronary arterial thrombus is low—15%—Comparison of data is difficult because of differing criteria for inclusion particularly differing definition of sudden (minutes to 24 hours). Inclusion of patients with acute myocardial infarction among patients with SCD increases the frequency of coronary thrombus. Likewise, the longer the interval from onset of symptoms of myocardial ischemia to death, the higher the frequency of coronary thrombus [10]. Our results are in accord with other necropsy studies in which the interval from onset of symptoms of myocardial ischemia to death was short and patients had no myocardial infarction [10]. From our study it appears that coronary artery thrombosis plays only a minor role in SCD occurring as the first manifestation of coronary disease, when the interval from onset of symptoms to death is < 1 hour.

The present data confirm that SCD occurs in the context of underlying cardiomegaly. A previous study from our laboratories [24] has shown that mean heart weight in normal age-matched adults were 336.5 g  $\pm$  2.4 (357.94 g  $\pm$  2.6 in men and 294.81 g  $\pm$  3.72 in women). Hence in the present study mean heart were significantly greater in both sexes and in both groups (in men: 446.45 g  $\pm$  11.58 (A)/513.78 g  $\pm$  24.2 (B) vs. 357.94 g  $\pm$  2.6,  $P$  < 0.001; in women 381.54 g  $\pm$  17 (A)/397 g  $\pm$  28.4 (B) vs. 294.81 g  $\pm$  3.72  $P$  < 0.001). Cardiomegaly (heart weight more than 400 g) has always been found at necropsy [8–22] in patients who died suddenly from coronary artery disease. Interestingly the present study shows that the increase in heart weight is significantly less marked in subjects without antecedent than in subjects with antecedents, whereas the average age at the onset of SCD is the same in both groups. The mean heart weight and the frequency of increased heart weight was similar among the patients with one, two, three coronary arteries narrowed >75% in cross sectional area by plaque. Thus there is not a close correlation between heart weight and extent of coronary artery stenoses in SCD victims. These results confirm data from previous studies [22].

## Conclusion

The present study analyzed the sociodemographic, and clinical features and autopsy findings in 160 cases of sudden out-of-hospital coronary death with no previous cardiac history and compared the results with those from 61 cases of sudden out-of-hospital coronary death with known cardiac disease. Our study showed no difference between the two groups in terms of age at death, or the circumstances surrounding the SCD. However the proportion of men in group B is higher than in group A. In both groups men died 12 years younger than women. SCD occurred most often at home and in 30% while sleeping. Heart examination showed that SCD occurred in both groups in the background of severe coronary artery disease. Heart weight was increased in both groups but interestingly less so in group A, than in group B. The frequency of coronary artery thrombosis was similar in both groups and low (15%).

Thus it appears from our study that the clinical profile of the candidate for SCD with no previous cardiac history strongly resembles that of the candidate for SCD with cardiac antecedents. At the present time these individuals present a major and near insuperable challenge to prospection identification. The present study carried out in Paris over a three-year period is of interest and use not only to forensic pathologists but also to epidemiologists and cardiologists concerned with the problem of sudden death.

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