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IP International Journal of Forensic Medicine and Toxicological Sciences

Journal homepage: <http://www.ijfmts.com/>

Review Article

A review on role of autopsy in the diagnosis of sudden arrhythmic deaths

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ARTICLE INFO

Article history:

Received 11-03-2022

Accepted 30-03-2022

Available online 19-07-2022

Keywords:

Sudden death

Sudden cardiac death

Sudden arrhythmic death

ABSTRACT

Sudden death (SD) is described as “death within 24 hours from the earliest manifestation, without any proof of violence and with no pre-existing disease, where no cause of death can be identified clinically”. In about 5%–10% of cases of sudden cardiac death (SCD), no underlying heart disease can be found at autopsy. Mostly these are the arrhythmic SCD and have a morphologically normal heart. There is a scope for uncertainty among relatives and/or investigating authorities regarding the cause & manner of death specifically in unattended sudden cardiac death. The postmortem examination must include detailed history or clinically relevant information of the deceased, his/her family members, macroscopic, microscopic, toxicological & molecular examination.

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1. Introduction

Sudden death (SD) is described as “death within 24 hours from the earliest manifestation, without any proof of violence and with no pre-existing disease, where no cause of death can be identified clinically”.

Causes of SD include cardiac conduction abnormalities, acute myocardial infarction, intracranial haemorrhage, pulmonary embolism and acute aortic catastrophe. Majority of SDs are due to cardiovascular diseases (40-50%).¹ Sudden Cardiac Death (SCD) is a term describing an unforeseen death of a person as a consequence of a cardiovascular event, with or without a pre-existing cardiac pathology.² SCD is a major international public health problem with an estimated incidence of 15%-20% of all deaths worldwide.³

Studies of SCD, show the following gender differences, the SCD rate has been lower among women than among men, 85%, and 83% of SCDs were witnessed in men & women respectively.^{4,5}

SCD occurred indoors & during night more often in women than men respectively. SCD occurred during exercise more frequently in men than in women (11% versus 2%, $P < 0.001$, respectively).

Men show more of non-arrhythmic SCD when compared with women. Women were considerably older when SCD occurred, and ECG's of female subjects were more likely to be normal than male subjects. The above data suggests that it is relatively more difficult to diagnose SCD in women.⁶

Hinkle-Thaler classifies SCD into arrhythmic and non-arrhythmic.⁷ Coronary heart disease is the most frequent cause of non-arrhythmic SCD with acute coronary lesions (ruptured plaque, coronary thrombosis) detected at autopsy in 20–80% cases.⁸

In about 5%–10% of cases of SCD, no underlying heart disease can be found at autopsy. Mostly these are the arrhythmic SCD and have a morphologically normal heart.⁹

There is a scope for uncertainty among relatives and/or investigating authorities regarding the cause & manner of death specifically in unattended sudden cardiac death. Generally such deaths are subjected to complete

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postmortem examination. Hence, this article has been compiled after reviewing the available literature for addressing samples and procedures required to conclude the cause of death in case of arrhythmic SCD.

2. Discussion

2.1. Objectives of medicolegal autopsy in sudden cardiac death

1. Whether the death is natural or unnatural.
2. If natural, whether the death is attributable to a cardiac disease or non-cardiac causes of sudden death.
3. The type of the cardiac disease.
4. Arrhythmic or non-arrhythmic type of SCD.
5. The possibility of toxic or illicit drug abuse and other unnatural deaths.

The postmortem examination must include detailed history or clinically relevant information of the deceased, his/her family members, macroscopic, microscopic, toxicological & molecular examination.

Non-cardiac causes of sudden death should be first excluded.¹⁰

2.2. Information required before starting autopsy (if available)

1. Age, gender, physical build, occupation, food habits, addictions and physical activity
2. Complaints before the death, if involved in any activity at the time of death, mental status at the time of death, if medical care is given, the inference of the medical caregiver.
3. Previous similar complaints, undergoing any treatment.
4. Any ECG tracings and chest X-rays, results of cardiovascular examination, laboratory investigations (especially lipid profiles, serum enzyme and troponin measurements).
5. Prescription and non-prescription medications.
6. Family cardiac history: ischaemic heart disease and premature sudden death, arrhythmias, inherited cardiac diseases.
7. Witnessed or unwitnessed death

2.3. External examination of the body

In most of the guidelines it is suggested to record body weight and height, to correlate with heart weight and wall thickness. But, body weight is a less reliable parameter than body length in correlating with the corresponding pre-mortem measurement. Autopsy body weights are elevated in part due to peripheral edema /anasarca. Alterations in body weight at autopsy can confound the interpretation of organ weight measurements.¹¹

The standard gross examination of the heart should be carried out, and the macroscopic examination findings may range from, plaque rupture, stenosis of the arterial lumen, hypertrophic cardiomyopathy (HCM) shows left ventricular (LV) wall thickness, asymmetrical septal hypertrophy and mid-ventricular obstruction, dilated cardiomyopathy (DCM) shows dilation of the left and right ventricles, thrombi in the cardiac chambers, and wall thickness may be increased or decreased, arrhythmogenic right ventricular dysplasia where history of exercise prior to death gives a clue as exercise is a common trigger of arrhythmia, myocarditis shows ventricular dilation with a mottled appearance along with scarring, fibrosis and minor coronary occlusion, infective endocarditis shows the presence of a vegetation on the infected valve, erosion of the underlying tissue, the chordae tendineae may be disrupted resulting in their rupture, congenital heart diseases in children with coarctation of the aorta (CoA), stenosis is observed proximal to the ductus arteriosus and distal to the left subclavian artery.

2.4. Standard histological examination of the heart

Coronary arteries stained with haematoxylin-eosin and special stains and immunohistochemistry should be performed as deemed necessary.

For histological examination of myocardium take samples of the left ventricle, right ventricle from anterior, lateral, and posterior sides, the ventricular septum anterior and posterior sides, and from each atria. In addition, any area with macroscopic abnormalities should be sampled. Haematoxylin-eosin and a connective tissue stain are standard. Special stains and immunohistochemistry should be performed as required. If there is the suspicion of rare cardiomyopathies a small sample of myocardium (1 mm³) should be fixed in 2.5 % glutaraldehyde for electron microscopy examination.

2.5. Histologic study of the conduction system

If the clinical history and ECG suggest of arrhythmic sudden death then the conduction system should be histologically examined in the following way.

Two block specimens of the heart to be obtained for paraffin embedding.

1. The first block contained the sino-atrial node (SAN), its atrial approaches, and the SAN gangliar plexus. At heart sampling, two longitudinal cuts are driven, parallel to the sulcus-crista line, through the atrial wall with a medial prolongation on the right side to encompass the anterior aspect of the inlet of the superior vena cava. On the left side, the cava-cava bridge is sectioned medially, prolonging the cut on the superior vena cava wall.

2. The second block contained the atrio-ventricular junction (AVJ) including the atrio-ventricular node (AVN), the His bundle (HB), the bifurcation (BIF), the left bundle branch (LBB) and the right bundle branch (RBB). At heart sampling, the following cuts are driven: an inferior, longitudinal incision through the posterior part of the septum, across the AV annulus fibrous and up to the superior margin of the coronary sinus ostium; an anterior longitudinal incision parallel to the former, through the superior part of the septum, extending to the aortic valvular ring; and two cuts perpendicular to the previous two cuts. The two blocks were routinely fixed in 10% buffered formalin and embedded in paraffin. The sections were cut at intervals of 20–40 μm (levels). For each level, three 8- μm sections are retained, mounted, and, at alternate levels, stained with HE and Azan. All intervening sections are kept and stained as deemed necessary.

Precise interpretation of the ECG facilitates the topographic identification of the abnormal conduction pathway, pointing where to remove the tissue block and make histologic serial sectioning.¹²

2.6. Molecular autopsy

For molecular autopsy 10 ml of EDTA blood and 5 g of myocardium (from the left ventricular free wall) and spleen and/or liver should be taken, frozen, and stored at -80°C or and nucleic acid extraction accomplished through thermocycler and gene sequencing done.

2.7. Toxicological investigation

For toxicology, blood from heart (25 ml), femoral veins (10 ml), urine (30–50 ml), or bile (20–30 ml), should be stored at 4°C .

2.8. Drafting a cause of death in SCD

In most of the SD, a gross pathological / histological lesion can be identified. But the diagnosis of SCD is with varying degree of accuracy and is classified as certain, highly probable, or uncertain. All cardiac lesions showing frank gross lesions are certain. But lesions like coronary artery atherosclerosis with or without the coronary stenosis exceeding 75% degree, in the absence of other causes of death, may be considered highly probable.

Identification of some coronary artery congenital anomalies, should be regarded as uncertain. Non-structural arrhythmic diseases also fall under uncertain degree.

3. Conclusion

Preserving the entire heart in formalin 10%, for future examinations is ideal. The examination should be complete, exclude all other causes of death, collect the required

or relevant information and samples before fixing the heart. Each case should be concluded based on clinical history, circumstances, autopsy findings and ancillary investigations.

4. Conflicts of Interest

The authors have no conflict of interest to declare.


5. Source of Funding

None.

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Cite this article: Mada P, Parmar P, Yadukul S, Pannala DR. A review on role of autopsy in the diagnosis of sudden arrhythmic deaths. *IP Int J Forensic Med Toxicol Sci* 2022;7(2):39-42.