A Review On Clinicopathologic Aspects Of Sudden Cardiac Death

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ABSTRACT

Sudden death is an unexpected natural death within the one hour onset of a symptom or witnessed death that occurs within 24 hours. This definition is most often used to describe death caused by cardiac failure as it is one of the well-known causes of natural death. Myocardial infarction is the leading cause either due to coronary atherosclerosis and / or thrombosis. An autopsy is a procedure done by pathologist to determine the cause and manner of death which provides information such as demographic factors comprises gender, age, ethnic, and life style that were linked to sudden death. This article review will discuss an autopsy in sudden death as well as aetiology of sudden death associated with cardiac abnormalities. Further the contribution of demographic factors also be discussed and highlighted.

KEYWORDS: Autopsy, Atherosclerosis, Myocardial infarction, Sudden death, cardiac abnormalities.

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1.0 INTRODUCTION:

According to the world health organization it is stated that any natural death that occurred within 24 hours from onset symptoms is considered as sudden death. But some researchers shorten the duration of death between the onset of symptoms and time of death to less than 1 hour [2] or 2 hours [3] or even 6 hours. [4] In the same study 10.8% of cases died without any complications of painfulness on the body parts or any potential, fatal diseases. [1, 4] About 20.1% of cases in which patients found to have ischemic heart diseases but remain healthy before the sudden

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death (SD) occur. Some sudden death which occurred unpredictably on those look healthy whether from the aspect of time or health status especially considered as SD despite the patient may have been diagnosed for any cardiovascular disease such as coronary heart disease. [5] Cases would only be categorized as SD only if the person died by any other natural causes or manner than expected. [1]

Sudden cardiac death (SCD) is significantly caused by an unanticipated natural cardiac death within an hour onset of a symptom or unwitnessed death within 24 hours. [6] Autopsy, toxicology and evidence has to be collected and examined to determine the cause of death. The pathologists or forensic scientist place a significant role in determining the cause and manner of sudden death. [7, 8] This complex task was highlighted in books, professional guidelines and articles including the procedure for an autopsy performed by pathologist in the investigation of sudden death. Following a report on a sudden death case the doctor will notify the police officer to classify as natural death prior to an autopsy. [2] The forensic pathology will gather information such as age, gender, occupation, lifestyle, circumstances of death, medical and family health history to conclude the cause and manner of death. [8] Autopsy comprises external and internal examination. During an external examination the body will be examined to determine identity, cause and manner of death and collection of evidence. Blood samples and tissues collected from internal examination should be analyzed in the laboratory. The laboratory tests are histological, biochemical, toxicological analyses. In SD drugs and alcohol might be involved in triggering the death so toxicological analysis is vital.

1. Histopathology examination is primary diagnostic tool to determine histomorpho-logical changes in a normal or diseased organ such as lung, liver, brain and heart. The heart sample will be examined macroscopically by following standard procedure as shown in the table1. In the presence of abnormalities of the heart is detected either grossly and / or microscopically other causes that mighty contribute should also be evaluated. As demonstrated in table 3 specimens sampled for toxicology analysis include blood from heart 25ml, peripheral blood from femoral veins 10ml, bile (if urine is not available) 20 to 30 ml, strands of head hair 100 to 200 mg. If there is suspicions of toxicity the postmortem report will be reserved until the laboratory results are conformed.

Table 1: The standard procedure of gross heart examination during post-mortem

NUMBER	PROCEDURE
I	Make an incomplete, transverse slice through the ventricles at a point about 3cm from the apex, as this allows good demonstration of left ventricular myocardium. This slice should be hinged to the remaining heart by the epicardium, to retain continuity.
II	Separate the aorta and pulmonary trunk from their intervening connective tissue, to make the subsequent opening of the outflow tracts easier.
III	Open the right atrium by cutting anteriorly from the free end of the inferior vena cava to the tip of the atrial appendage. The superior vena cava is deliberately left intact to allow (if necessary) the later examination of the sinoatrial node
IV	Open the right ventricle along the free, lateral border, by cutting through the tricuspid ring and continuing the excision to the apex. It is customary to place this cut through a commissure of the tricuspid valve.
V	Open the pulmonary outflow tract via a cut in the anterior wall of the right ventricle which starts at the apex and continues up through the pulmonary conus, valve, and artery. It is preferable to cut through the centre of a cusp of the pulmonary valve. The cut should be kept close to the interventricular septum to leave the anterior papillary muscles intact.
VI	Open the left atrium by making a hole in the atrial appendage and then extending it into a cut in a line parallel with and above the atrioventricular groove. Then make a second incision, at a 90° angle to the first, between the orifice of the pulmonary veins.
VII	Open the left ventricle by making a cut along the free, lateral border, through the mitral valve ring and extending to the apex. As with the tricuspid valve, it is best to place this cut through a commissure of the mitral valve.
VIII	When the left ventricle has been opened along the lateral border, the outflow tract can be opened by cutting from the apex along the anterior wall as close to the septal wall as possible, and then through the aortic valve to the free end of the aorta.

Table 2: Evolution of Morphologic changes in Myocardial Infarction

TIME	GROSS FEATURES	LIGHT MICROSCOPE	ELECTRON MICROSCOPE
REVERSIBLE INJURY			
0-1/2 hour	None	None	Relaxation of myofibrils; glycogen loss; mitochondrial swelling
IRREVERSIBLE INJURY			
½-4 hour	None	Usually none; variable waviness of fibers at border	Sarcolemmal disruption; mitochondrial amorphous densities
4-12 hour	Dark mottling (occasional)	Early coagulative necrosis; edema; hemorrhage	

12-24 hour	Dark mottling	Ongoing coagulative necrosis; pyknosis of nuclei; myocyte hypereosinophilia; marginal contraction band necrosis; early neutrophilic infiltrate	
1-3 days	Mottling with yellow-tan infarct center	Coagulative necrosis, withloss of nuclei and striations; brisk interstitial infiltrate of neutrophils	
3-7 days	Hyperemic border; central yellow-tan softening	Beginning disintegration of dead myofibers, with dying neutrophilis; early phagocytosis of dead cells by macrophages at infarct border	
7-10 days	Maximally yellow-tan and soft, with depressed red-tan margins	Well-developed phagocytosis of dead cells; granulation tissue at margins	
10-14 days	Red-gray depressed infarct borders	Well-established granulation tissue with new blood vessels and collagen deposition	
2-8 weeks	Gray-white scar, progressive from border toward core of infarct	Increased collagen deposition, with decreased cellularity	
>2 months	Scarring complete	Dense collagenous scar	

Table 3: Types and quantity of samples according to the Guidelines of the Society of Forensic Toxicologists and the American Academy of Forensic Sciences

NUMBER	TYPES OF SAMPLES	QUANTITY
I	blood from heart	25ml
II	peripheral blood from femoral veins	10ml
II	Urine	30 to 50 ml
V	bile (if urine is not available)	20 to 30 ml
V	strands of head hair	100-200mg

2.0 OVERVIEW OF SUDDEN DEATH:

2.1 EPIDEMIOLOGY OF SUDDEN DEATH

Epidemiological reports revealed that both sudden death and sudden cardiac death were strongly associated with age, gender, lifestyle, ethnicity, and family medical history. [9] Hence all the demographic factors should be taken into consideration in an autopsy to assist in the determination of cause of death. Approximately 30% of all global mortality is caused by cardiovascular diseases (CVD). Among them 40 to 50% is sudden cardiac death (SCD). The causes are formation of atheroma and thrombus in the coronary artery occlusion resulting in myocardial infraction (MI). [11] In developing countries 80% of SCD are due to ventricular tachyarrhythmia. [10] The number of cardiac cases had increased among female at the age of 45 to 54 years. [12]

SCD among youngsters has a more significant impact than cancer and other deadly diseases which create an impact and burden to the public health system. [13] The ratio among male and female is 10.5:1. About 90% are SD due to cardiovascular diseases. [15] In addition patients with metabolic syndrome (METS) exhibited a higher risk of developing CVD. METS is a condition comprising obesity , elevated blood pressure atherogenic, dyslitidaemia and high plasma glucose or insulin resistance as defined by WHO.

2.2 ETIOLOGY OF A SUDDEN CARDIAC DEATH:

Disease like myocardial infarction (MI) cardio myopathy, myocarditis and congenital disabilities are linked to the etiology of SCD.

2.2.1 MYOCARDIAL INFRACTION

Approximately 90% of the cases of SCD developed from MI the most frequent cause of coronary artery disease (CAD). [26] MI has significant contribution to morbidity and mortality globally. [25] MI is characterized by irreversible necrosis of myocardium resulting from decreased blood flow in arteries which leads to lack of oxygen supply. This condition is due to formation of atheroma and/or coronary thrombosis in an artery [11] that leads to ischemia and death of myocardial tissue.

MI is diagnosed by from the history and electro cardio graphy (ECG). Symptoms of chest pain, discomfort in thorax, epigastrium, dyspnoea and fatigue which will last about 20 minutes. There might be diaphoresis and nausea. Atypical symptoms of MI are palpitation or asymptomatic with increase or decrease of cardiac markers. MI may be classified as

Type 1- Spontaneous MI.
Type 2- MI with ischaemic imbalance.
Type 3- MI resulting in death
Type 4a-MI related to percutaneous coronary intervention (PCI)
Type 4b- MI related to stent thrombosis.

Type 5- MI related to coronary artery bypass grafting (CABG) All MI are classified based on the value of bio marker clinical history and angiographic result.

2.2.2 ATHEROSCLEROSIS

Atherosclerosis is a pathological and multifactorial chronic condition characterized by narrowing and hardening of arteries contributing to CVD. [4] The features are presence of plaque or fuel of fats, cholesterol, lipophages, leukocytes and deposition of calcium in arteries. [16, 17] Hardening of arteries is due to accumulation of cholesterol and fat in the blood vessel walls. When low density lipoprotein (LDL) is engulfed by macrophages it will turn to be foam cells which then form plaques. Overtime these plaques narrowing or completely obstruct the arteries which leads to various cardiovascular disorders. In adults and elderly [15] Atherosclerosis is the most common cause of SD due to CAD. Studies by Luqman *et al*. [18] stated that coronary atherosclerosis is the most common findings in the autopsy. Formation of plaque will block the blood flow, which then restricts blood supply to major organs such as brain, heart, arms, legs and kidney. A decrease in blood circulation to the major organs may be caused by peripheral artery disease, coronary heart disease, chronic kidney disease and angina. [9]

Chest pain sudden collapse dyspnoea, cold sweating and vomiting are the clinical features. Systemic indicators is elevation of cholesterol level in plasma. [19] Hypertension, diabetes and smoking contribute for the development of atherosclerosis. Presence of inflammatory markers (interleukin 8), low density lipoprotein (LDL) are the biomarkers. Apolipoprotein and apo A-1 are the protective factors against atherosclerosis which promotes the modification of LDL and to prevent atherogenic and induces reverse cholesterol transport. Concomitantly the progression of plaque will slow down and promote rapid regression. [20]

2.2.3 THROMBOSIS

Acute coronary syndrome is associated with athero-thrombosis which is the formation of blood clot in the artery and ischaemia. A healthy endothelium modulates vasodilation of vessel, inhibits platelet aggregation, activate clotting factors and defense against inflammation and repair mechanism. But endothelial dysfunction may culminate vasoconstriction, thrombus formation, inflammation and proliferation of smooth muscle may generate the formation of atherosclerotic plaque [21] a significant cause of mortality worldwide. [22] Formation of unstable plaque is prone to rupture will lead to exposure of injured epithelium to blood circulation which then trigger the activation of extrinsic coagulation pathway. Circulatory platelet will adhere to the sub-endothelial matrix and damaged endothelial cells. Activated platelet release intermediaries such as serotonin, adenosine diphosphate (ADP), thormboxaneA2, endothelin, free radicals and platelet activating factor will be released followed by platelet aggregation and vasoconstriction. The aggregated platelet named white thrombus will be formed but it is unstable, and it will cause reduced blood flow. [23] The activation of coagulation system will promote deposition of fibrin and strengthen the platelet aggregation thereby; vasoconstriction will produce impaired blood flow resulting in pooling of blood and formation of red thrombi. [24]

3.0 OTHER CARDIAC ABNORMALITIES

Moreover, cardiac abnormalities that are often reported in association with SD are ventricular tachycardia and fibrillation. According to a study, the fatal arrhythmia is caused by electric irritation of myocardium induced by ischaemia. [27] Ventricular tachycardia is a condition, where three or more consecutive ventricular beats at a rate of 120 beats/min that last for 30 seconds. [28] Besides, ventricular fibrillation can be defined as a heart contractile behavior on visual inspection [29], which is also known as primitive practice. [30] A well-defined post-mortem report will be helpful to determine the cause of death, especially in some cases that are complex to the forensic pathologist when the heart appears to be healthy to the naked eye. [31] Research by [30] stated that electrocardiogram is a primary test used to determine ventricular tachycardia and ventricular fibrillation. Other non-cardiac causes that contribute to sudden deaths are cerebral haemorrhage, bronchial asthma, Waterhouse–Friderichsen syndrome (WFS)

and acute haemorrhagic shock [7] as shown in Table 4.

Table 4: Etiology with example

ETIOLOGY	EXAMPLE
Cerebral or central nervous system	Sub-arachnoid or intra-cerebral haemorrhage
Respiratory system	Asthma, Anaphylaxis
Acute hemorrhagic shock	Ruptured aortic aneurysm, peptic ulcer
Septic shock (waterhouse – friderichsen syndrome)	Neisseria meningitides infection

4.0 DEMOGRAPHIC FACTORS AND SUDDEN DEATH

The demographic factors that include age, gender, and lifestyle, ethnic and family history are associated with sudden death due to cardiovascular disorders. The risk factors increase with age and that is dependent on gender. Selected groups of peoples are more susceptible to SCD.

4.1 GENDER

Cardiovascular disease is the leading cause of mortality in both male and female. After menopause female will have higher risk of MI compared to male. This is because of declining of estrogen level after menopause. They have higher risk of CVD compared to premenopausal. [32] The general function of estrogen in the vascular system includes the release of nitric oxide and vasodilation [33] regulation of prostaglandin production, which is a potent vasodilator [34] and inhibit smooth muscle proliferation.[35] It also protects the vascular endothelium by enhancing the release of vasodilators [45] hence the reduction of estrogen in menopause women is the primary cause of MI.[9] In both genders SCD is the most common cause of death compared to cancer and disease related death .[14]

4.2 AGE

As age increases there is higher risk of MI. It was evidenced that female with an average age 71.8 years posed a high risk of MI compared to a 65-year-old male. [9] This is due to physiological changes that occur in female such as hormonal changes, unhealthy lifestyle and reduction of body metabolic rate. [25, 36] Research exhibited that frequency of MI between different sexes was more prevalent among women in an age less than 55 years old based on hospital information.[37] Reports by the National Centre For Health Statistics in 2015 stated readmission due to cardiac disease in female was higher than male at the age of 65 and above. [12] The American Heart Association Statistics Committee and Stroke Statistics Subcommittee reported that the average age for women presenting with the first MI was 71.8 years old, while for men, it was 65 years old. [9]

4.3 ETHINICITY

Several researchers compare the risk of MI between distinctive ethnic (table 4) and it was documented. Studies have shown that CVD present differently across ethnics. [38] Black women have a higher number of incidences of SCD compared to white women. [39] According to the studies by INTERHEART Asian Indian have higher CVD risk factor with MI presentation compared to non-Hispanic white women, black and Hispanic women at the age as young as 69 years. [40] Indian women have diabetic from the clinical history are prone to SCD.[55] Studies in Singapore by Wong et al also concluded that Indians have a higher risk of developing MI before the age of 46 compared to Malays and Chinese. [25] Correspondingly, the researchers pointed out that Indians were most likely to present with new-onset diabetes with the highest HBA1C values for those with pre-existing diabetes compared to other ethnics. However, most Malays in the study were diagnosed with the new onset of hypertension compared to others.

Table 5

NATIONLITY	ETHINIC	HEALTH PROBLEM	REFERENCES
Indian	Indians	Hypertension	[42]
American	Whites, Blacks and Asian higher	Hypertension	[42]
American	Whites, Blacks and Asian higher	Obesity	[42]
Pennsylvania	White and Hispanic youth	Obesity	[43]
Malaysia	Malay	Obesity	[44]

4.4 LIFESTYLE

Healthy life style is known to have benefits over cardio vascular health.[42] Research in 2012 presented that unhealthy lifestyle such as smoking, unhealthy diet intake and obesity are contributors to CVD in males and females of all ethnicities. Wong *et al.* [25] stated that tobacco is the most critical risk factor in triggering MI.

[46] Prevalence of tobacco usage among men was higher compared to women, and studies showed a strong relationship of tobacco with MI development. [47]

Research has proven that regular sports activities and vigorous activities may contribute to some risk of SD. [43] Strenuous actives can have led to SD and MI [45] due to increase in the platelet adhesiveness and aggregation while moderate exercise may have the advantage to the heart by decrease platelet adhesiveness and aggregation. A study stated that male athletes have a high risk of SD than female athletes while black athletes also showed a higher risk than the white athletes. [46]

5. CONCLUSION

Sudden death (SD) is defined as natural death in which the duration between the onset of symptoms and the time of death is not more than 24 hours excluding poising and trauma. There is difference of opinion among the researches only in the duration which may be 1 hour, 2 hour, 6 hour or 8 hours. Cardio vascular diseases especially MI remains as the most common causes in men and women leading to SD worldwide apart from atherosclerosis and coronary thrombosis. Menopausal women have a higher risk of developing MI. The average age among women with MI is around 71.8 year and 65 years in men. Indians are more prone to developing MI due to the higher incidence of diabetes. Unhealthy life styles such as cigarette smoking and history of hypertension have a strong correlation with MI. Although the benefits of active physical activities are well established there is higher incidence of sudden death among athletes and vigorous activity that will contribute to MI and SD.

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