

## REVIEW

# Sudden cardiac death in elderly: the post-mortem examination of senile myocardium and myocardial infarction

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Cardiovascular diseases are the main cause of death globally. From a pathological perspective, the causes of sudden cardiac death (SCD) are different in young individuals compared with older ones where chronic degenerative diseases predominate. Most patients with heart disease are elderly, but aging is not synonymous of disease. Many people live past the age of 65 up to 90 and over without evidence of cardiac diseases and in many autopsies of elderly individuals, no specific lesions can be discovered that provide a clear cause of cardiac death. Where age-related changes are observed and no other cardiovascular findings can be related to an arrhythmic or mechanical mechanism of SCD or to myocardial infarction (MI), the senile myocardial degeneration is an inappropriate diagnosis although it is a common expression used by public health physicians and pathologists as cause of death. Age-associated changes in senile myocardium predispose to pathophysiological disease mechanisms and they can be a substantial substrate causing SCD even after acute emotional or physical stress as triggers of myocardial ischemia or arrhythmia. However, distinguishing the age-related physiological processes from the associated pathological changes and their role in a case of SCD is not always possible, since a heart failure (HF) can be the final cardiovascular aging pathway especially in elderly victims. Furthermore, unnatural deaths can be erroneously reported as natural deaths, leaving accidents or homicides undetected. The differentiation between sudden death and fatal elderly abuse is a difficult and critical diagnostic decision that needs a careful post-mortem investigation also in SCDs. To the best of our knowledge, there is no protocol for distinguishing SCD from elderly abuse fatalities. A specific protocol for sudden deaths also in elderly (similar to those already available for infant and child) could enhance the public and professional awareness on elder abuse fatalities as well as on the underlying mechanisms of cardiac deaths. In cases of sudden, unexpected deaths in healthy elderly, it is strongly suggested an accurate post-mortem investigation including a complete examination of clinical signs and medical history, toxicological and/or chemical laboratory tests, circumstantial data related also to the scene-of-the event.

**Key words:** Sudden cardiac death, Senile myocardium, Myocardial infarction, Elder abuse

## INTRODUCTION

Since the middle of the XX century, life expectancy has dramatically increased in developed countries, and for the first time in history most people can actually expect to live past the age of 65<sup>1,2</sup>. The principal causes of death have changed over time mainly due to changing environmental and social conditions and population's disease status<sup>3,4</sup>. Although death rates dropped at all

ages, it has been calculated that three-fourths of all deaths occur at elder age 65 and older. In this regard, data provided by the Center for Disease Control and Prevention (CDC) report that Heart Failure (HF), including heart attacks and chronic ischemic heart disease, is the leading cause of death followed by cancer and other chronic conditions<sup>5</sup>. Although death from atherosclerosis has dropped over 2 decades for all ages and sex, recent trends in elderly mortality suggest that heart

■ Received: September 3, 2016 - Accepted: May 3, 2017

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disease is still the most common cause of death <sup>5</sup>. However, in many autopsies on elderly, no specific lesions can be discovered that provide a clear cause of death <sup>6</sup>. Many old people even of age over 80 can show still healthy vessels with no coronary artery disease or evidence of other cardiac diseases. There are no traceable morphologic signs of the lethal cardiac event, and there is no correlation between autopsy cardiac findings and what we can call a suspected Sudden Cardiac Death (SCD). In fact, SCD can occur even in very old people since ageing is not synonymous of disease.

SCD has been recently defined in 2015 by the Task Force of the European Society of Cardiology (ESC) a “non-traumatic, unexpected fatal event occurring within 1 hour of the onset of symptoms in an apparently healthy subject. If death is not witnessed, the definition applies when the victim was in good health 24 hours before the event” <sup>7</sup>. The risk of SCD is higher in men than in women, and it increases with age due to the higher prevalence of Coronary Artery Disease (CAD) and, therefore, of myocardial infarction (MI) in older age <sup>8</sup>. In fact, atherosclerosis of the coronary arteries is the most prevalent cause of SCD in adults. Atherosclerotic CAD, commonly asymptomatic or unrecognized, is known to be extremely variable in “quantitative” terms, and findings raising the suspicion of coronary vasospasm (eg, localized or non-occlusive luminal narrowing, typically present in young and adult subjects) are often lacking even in elderly population <sup>9</sup>.

Many cardiovascular diseases can cause SCD, either through an arrhythmic mechanism (electrical SCD) or by compromising the heart's mechanical function (mechanical SCD), and might affect not only the coronary arteries and the myocardium, but also the cardiac valves, the conducting system, the intra-pericardial aorta or the pulmonary artery, the integrity of which is essential for a regular heart function <sup>10</sup>.

However, cardiac diseases associated with SCD also differ in young versus older individuals <sup>7</sup>. In the young, there is a predominance of channelopathies and cardiomyopathies, myocarditis and drug abuse-induced arrhythmias. In elderly, chronic degenerative diseases, such as CAD, valvular heart disease and HF, predominate. Furthermore, elderly decedents frequently suffer from more than one disorder (the so-called comorbidity) at time of death and, therefore, it is difficult for physicians to identify the originating cause among several pathological conditions <sup>11</sup>. Cardiovascular comorbidity in the elderly can produce serious health consequences so that it becomes difficult to determine which contributed most to SCD. In old people age-related changes in cardiovascular structure and function may lower the threshold for clinically significant signs and symptoms, sometimes occurred as SCD <sup>12</sup>. In these cases, SCD

generally follows arrhythmia (hyperkinetic or hypokinetic) of so severe degree to impair cardiac output and hence cerebral perfusion. In this respect, the main goal of this review is to focus on the difficulties still present in the diagnosis of SCD and its post-mortem examination as well as death certification.

## POST-MORTEM EXAMINATION AND DEATH CERTIFICATION

An accurate diagnosis of SCD is crucial and requires a complete autopsy, investigation of the circumstances of death, and exclusion of other potential cause of deaths. In fact, the incorrect assessment of cause and manner of death can have serious implications for public health and the judicial system. Unnatural deaths can be erroneously reported as natural deaths, leaving accidents or homicides undetected <sup>13</sup>. Negative autopsy can occur in deaths caused by toxic or illicit drug abuse, for example, in case of suicide and/or medical malpractice <sup>14</sup> or by asphyxia suffocation homicides and other types of elder abuse fatalities <sup>15 16</sup>.

There is also considerable variation in the way in which public health physicians and pathologists approach the complex task of the diagnosis of cause of SCD. A uniform method of investigation has been proposed since 2008 by the Association for European Cardiovascular Pathology, in order to improve the minimum standards of practice <sup>10</sup>. The role of the autopsy in SCD has been emphasized to distinguish not only between natural from unnatural deaths but also to establish: 1) whether the death can be referred to cardiac or to other non-cardiac causes of sudden death; 2) the nature of the cardiac disease, and whether the mechanism was arrhythmic or mechanical; 3) whether the cardiac condition causing sudden death may be inherited, requiring screening and counselling of the next of kin.

Unfortunately, the accuracy of death certificates can be questionable for various reasons, including level of expertise and training of the medical practitioner involved in the death investigation, lack of medical records related to the deceased, lack of circumstantial information related to the fatal event, and the perceived lack of importance of the death certificate <sup>13 17</sup>. In the tenth version of the World Health Organization's International Statistical Classification of Diseases and Related Health Problems (WHO's ICD-10) <sup>18</sup>, diseases of the circulatory system are inserted in chapter IX. In this section ischemic heart diseases are listed including angina pectoris, acute MI (due to coronary occlusion, thromboembolism, coronary failure, etc.) but also chronic ischemic heart disease mainly related to atherosclerosis and other forms of heart disease among which senile myocardial

degeneration. According to most of the forensic pathology community<sup>6</sup>, where nothing other than general senile atrophy of most organs is found and the history is unhelpful as to a specific manner of death, as long as the physician/pathologist can exclude any unnatural cause and non-cardiac causes of sudden death, then it is quite legitimate to ascribe the death to an acute cardiac death due to senile myocardial degeneration. That means to ascribe the death to a final HF caused by the aging-associated decline of cardiovascular structure and function. In fact, in contrast to other cardiovascular disorders, the prevalence of chronic HF is rapidly growing<sup>19</sup> along with the increasing longevity. The actual version of WHO's ICD-10<sup>18</sup> provides a specific code for such aging-related cardiac changes ("Degeneration of heart or myocardium: senile" – I.51.5), but geriatricians and some pathologists do not totally agree with such expression as cause of death in elderly, preferring the one of an acute cardiac death even when more specific lesions and signs of an ischemic heart disease or MI are not always detected. Under the section of other heart disease, ICD-10 also provides a specific code for SCD ("sudden cardiac death" – I-46.1) with conduction disorder or MI that seem more appropriate to be used also in elderly. In fact, distinguishing the age-related physiological processes from the associated pathological changes is not easy. In this respect, the main macroscopic and microscopic changes of the myocardial degeneration due to senility and to ischemia according to their main functional consequences are discussed as follows.

## THE SENILE MYOCARDIUM

Age-associated changes in senile myocardium can be usually concomitant with pathophysiological disease mechanisms determining the threshold, severity, and prognosis of cardiovascular disease in elderly<sup>20</sup>. Aging cardiovascular changes can be considered the effect of declining cardio-protective systems and increasing disease processes that are the substantial substrate for the development of HF<sup>19</sup>. Therefore, physicians must consider the frailty of the senile myocardium from a structural and functional perspective.

Atherosclerosis, left ventricular hypertrophy, interstitial myocardial fibrosis, atrial fibrillation and cardiac amyloidosis increase dramatically with age. But none of these conditions can be considered an ageing process, as they can be also the sequelae of cardiac adaptation<sup>21</sup> to functional stress or, better, the effect of cardiac structural remodeling<sup>19</sup>.

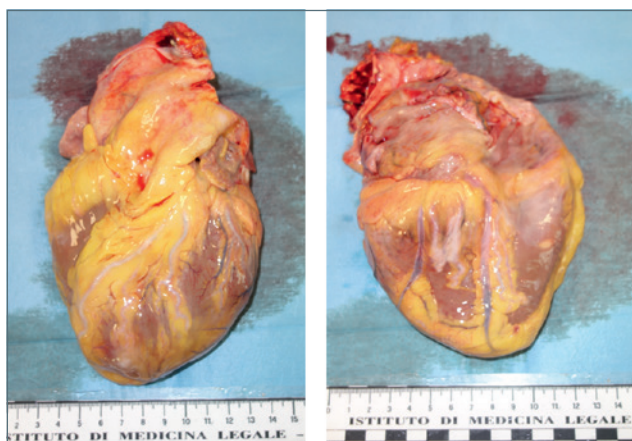
Senile heart changes its overall shape from elliptical to spheroid with an asymmetric increase in the

interventricular septum, more than free wall<sup>22 23</sup>. These structural changes in thickness and shape can have important implications for cardiac wall stress and overall contractile efficacy (Fig. 1). Senile hearts are also usually small, but hypertension may have enlarged the ventricles long ago and the effect of this process may be to sustain the heart at a normal weight<sup>6</sup>. Although in the past a relevant increase of cardiac mass with aging has been illustrated<sup>24</sup>, more recent autopsy-based studies show that the weight may be down to 300 g or even 250 g, if no previous hypertrophy has occurred<sup>6</sup>. Sometimes senile hearts can be brown on the surface. Such appearance (which is also called *brown atrophy* of the myocardium) is mainly related to the gradual increase in lipofuscin pigment and it is considered a true manifestation of biological ageing<sup>21</sup>. On a structural level, the senile heart can also be flabby and soft, the epicardial surface vessels tortuous as a sign of cardiac atrophy and the thumb can be pushed into myocardium without difficulty<sup>6</sup>.

Microscopically, the myocardial fibers generally increase in size and the nuclei of the myocytes can have prominent clumps of lipofuscin pigment at their poles. There may be a fine, diffuse fibrosis, which is not ischemic in origin, because of the loss of cardiomyocytes with aging. However, none of these features is diagnostic of a cardiac cause of death, as other old persons dying of quite unrelated causes, such as trauma, might have equally "poor" heart muscle<sup>6</sup>. On a cellular level, remodeling process involves changes also in the composition of the heart fibrous skeleton and composition of the extracellular matrix. In particular, in the elderly, it has been noted also a partial loss of sinoatrial node pacemaker cells<sup>25</sup>, with formation of fibrous connective tissue in the cardiac conduction system and in LV tissue<sup>26 27</sup>.

Other age related changes concern cusps thickening because of fibrosis both atrial surface of the atrio-ventricular valves and ventricular surface of the aortic valves. Moreover, the line of closure could be eccentrically accentuated and, particularly on the aortic and mitralic valves, the so-called Lambl's excrescences develop. These changes could play an important role in predisposing to some pathological conditions such as infective endocarditis, raised pressure and regurgitant flow<sup>28</sup>. Mitral insufficiency can be a common clinical feature under these circumstances. However, sometimes in elderly aortic valve sclerosis develops usually without much hemodynamic consequences although the term "senile aortic stenosis" is often used in this context<sup>21</sup>.

In old individuals, the most important phenomenon to be considered is also the left ventricular (LV) structural remodeling because of an increase in the thickness of



**Figure 1.** Senile myocardium of a man 94 years old.

the wall as results of the fibrosis due to loss of myocardial fibers and increased cardiomyocyte size<sup>22</sup>. However, LV resulting from age-related remodeling must be differentiated from LV hypertrophy associated with hypertension. In the first one, LV remodeling begins with an increase in the relative wall thickness (wall thickness/LV radius ratio)<sup>29</sup> within normal limits, explaining the lack of effect on total cardiac mass. In fact, autopsies on subjects free from hypertension, CAD and cardiovascular disease did not show an increase in cardiac mass with aging<sup>30</sup>. Therefore, against previous findings<sup>24</sup>, total cardiac mass does not increase significantly with aging as also supported by autopsy-based and echocardiographic studies<sup>31</sup>.

A progressive decline in LV compliance with age has been also observed and the heart has been found to fill with blood more slowly in older compared with young individuals<sup>19</sup>. Such decline in LV compliance may go unnoticed for many years, but with the occurrence of an acute stress, the subclinical dysfunction can become acutely evident producing a fatal HF<sup>12</sup>. For example, during exercise a mismatch in loading can occur in older individuals because of a failure of LV elastance to increase in proportion to the increase in vascular elastance<sup>12</sup>.

Although LV hypertrophy has been associated with increased risk for CAD and SCD, another interesting aging-related heart remodeling concerns atrial hypertrophy and dilation. In the elderly, atrial contraction can assume a more pronounced role in LV filling during diastole than in the young people<sup>21</sup>, as this structural change can favor the development of atrial fibrillation<sup>32</sup>. Furthermore ageing changes in the right heart are less pronounced than the left sided changes, although they can be enhanced by the presence of other diseases.

At last, another aging-related change in cardiac tissue

is amyloid deposition derived from atrial natriuretic peptide (ANP). The incidence and severity of isolated atrial amyloid deposits increase with age, from 75% incidence in patients aged 51-60 years, to 86% incidence in those aged 81-90 years<sup>33,34</sup>.

In summary, autopsy findings of senile myocardium can show age-associated changes as adaptive pathophysiological mechanisms with unpredictable myocardial functional sequelae. However, distinguishing the age-related physiological processes from the associated pathological changes and their role in a case of SCD is not always possible.

## MYOCARDIAL INFARCTION

A consensus document by an International Joint ESC/ACC Committee defined in 2000 the myocardial infarction (MI) as “myocardial cell death due to prolonged ischemia”, emphasizing that any necrosis in the setting of myocardial ischemia should be labeled as MI<sup>35</sup>.

In 2007, this definition was revised in the light of different conditions that may lead to a MI<sup>36</sup>. But, the development of more sensitive assays for markers of myocardial necrosis pushed the scientific community to an up-dated position. In 2012, the Third Universal Definition of MI consensus document redefined acute MI as “a condition in which there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia”<sup>9</sup>. The new definition recognizes that very small amount of myocardial necrosis can be detected by biochemical markers and/or imaging supporting better the final diagnosis of MI. Therefore in case of MI, a rise and/or fall of a cardiac biomarker values (preferably cardiac troponin – cTn) should be observed, with at least one value above the 99<sup>th</sup> percentile upper reference limit, and with at least one of the following: 1) ischemic symptoms; 2) new or presumed new significant ST-segment or T-wave changes or new left bundle-branch block; 3) development of pathological Q waves in the electrocardiogram (ECG); 4) imaging evidence of new loss of viable myocardium such as a new regional wall motion abnormality; 5) identification of an intracoronary thrombus by means of coronary angiography or autopsy.

Autopsy case studies have suggested that in subjects with CAD, the factor triggering the fatal arrhythmic event causing SCD can be transitory (coronary spasm) or prolonged (occlusive coronary stenosis) myocardial ischemia. However, although most of the elderly people show underlying severe CAD, on occasion they may also have non-obstructive or no CAD at all. Many very old people have excellent coronary arteries and no sign of myocardial ischemia, so that the erroneous clinical



diagnosis of CAD is much over-used by physicians.

In this respect, various types of acute MI have been defined based on pathological and clinical differences<sup>7</sup>: type 1 (spontaneous MI related to atherosclerotic plaque rupture, ulceration or coronary thrombosis), type 2 (MI secondary to an ischemic imbalance where a condition other than CAD can contribute to an imbalance between myocardial oxygen supply and/or demand such as in a coronary artery spasm, coronary endothelial dysfunction, hypotension etc.), type 3 (MI resulting in death when biomarker values are unavailable), type 4 and 5 (MI related to percutaneous coronary intervention or coronary artery bypass grafting, respectively).

At autopsy, some doubts and difficulties persist mainly concerning the minimum level of lesion compatible with MI and the condition of coronary arteries<sup>37</sup>. In fact, applying the proposed diagnostic criteria, any amount of myocardial necrosis caused by ischemia should be labeled as an infarct. In this respect, there should be continuity from minimal myocardial ischemic damage to classic large MI. In cases of SCD it is therefore extremely important to identify even a small area of myocardial necrosis demonstrating previous ischemia, based on clinical and autopsy findings. In a post-mortem examination, the signs of early myocardial damage must be accurately searched for and documented by all available means including histologic and histochemical stains: *in vivo*<sup>7</sup> by electrocardiograms tracing ischemic modifications, for example, and blood tests studying serologically the level of myocardial necrosis indicators (among them the preferred biomarker is cTn which has high myocardial tissues specificity, as well as high clinical sensitivity).

However, public health professionals must keep in mind that myocardial cell death does not occur instantaneously at the onset of ischemia. It takes several hours (at least 4-6 h) before myocardial necrosis can be identified by standard macroscopic or microscopic post-mortem examination depending on the sensitivity of the myocytes, the presence of collateral circulation to the ischemic zone, persistent or intermittent coronary arterial occlusion, individual demand for oxygen and nutrients<sup>36</sup>. The entire process leading to a healed infarction usually takes at least 5-6 weeks and the reperfusion may alter the macroscopic and microscopic appearance.

Therefore, at autopsy the recognition of early myocardial damage using routine histologic techniques such as hematoxylin and eosin staining is possible only if death has occurred at least 4-6 hours after the onset of the ischemic injury. This means that an individual with an ischemic insult has to live for at least 4-6 hours to have detectable histological changes in the myocardium such as necrotic clotting, multifocal patches of wavy

fibers, contraction band lesions, hyper-eosinophilic enucleated myocytes, and marginal rearrangement reactions with early inflammatory infiltrate<sup>38,39</sup>. A period of 1-hour interval or less from the angina attack is not usually enough to produce such histological findings, commonly known as classic morphologic alterations of the MI. In fact, the timing of appearance of the above alterations is strongly affected by various factors such as the efficacy of any collateral blood flow in compensating perfusion of the ischemic area, the duration of the vessel occlusion (persistent or intermittent coronary artery disease or when the vessel lumen could recanalize and regular blood flow resume), and the sensitivity of the myocardial fibers themselves<sup>7,35</sup>.

Furthermore, in cases of suspected SCD, whether the autopsy findings deal with "coronary" or "myocardial" lesions, there may be a variety of possible combinations that need to be still investigated before the final diagnosis of MI can be formulated. It is essential to apply adequate study methods of the myocardial morphology, including not only an examination of the various coronary branches but also histologic analysis of the myocardium of both ventricles, by standard and targeted sampling of evident or suspicious lesions<sup>37</sup>. In several cases, scarring of some myocardial areas can cause arrhythmia as well as in cases of MI, the loss of myocytes usually follows prolonged ischemia resulting in cell death (necrosis) as a result of oncosis, and only to a lesser extent of apoptosis<sup>35</sup>. For example, histological evidence of myocardial necrosis may be detectable in clinical conditions associated with predominantly non-ischemic myocardial injury<sup>7</sup>. Small amounts of myocardial injury with necrosis may be detected, which are associated with HF, tachy-brady-arrhythmia, myocarditis, arrhythmias, renal failure, even pulmonary embolism or otherwise uneventful percutaneous or surgical coronary procedures. According to the Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology<sup>7</sup>, these entities can also be associated with MI in case of clinical evidence of acute myocardial ischemia with rise and/or fall of cTn. They should not be labeled as MI or a complication of the procedures, but rather as myocardial injury. In fact, elevated cTn values, indicative of myocardial injury with necrosis, may be also observed in cases of non-ischemic HF syndrome<sup>7,40</sup>.

In summary, in cases of SCD it is not always easy to differentiate between arrhythmic and non-arrhythmic mechanism of death, as often the pathologists have not enough body of evidence to determine the cardiac cause of death.

## DISCUSSION

Cardiovascular disease is a global health problem and the leading cause of death in elderly <sup>41</sup>. Most patients with HF are elderly, constituting up to 80% of patients suffering from this disease with both incidence and prevalence increasing with age <sup>42</sup>. This can explain the growing interest of the cardiac disease in geriatric medicine as SCD can occur also in elderly individuals without previous symptoms of heart disorders and with excellent coronary arteries.

In this regard, the certification of cause and manner of death is fundamental for legal and epidemiological purposes <sup>13</sup>. In medico-legal setting the incorrect assessment of cause and manner of death can affect not only statistics of mortality but may allow unnatural deaths to go undetected which is an increasing problem in elderly abuse fatalities <sup>16 43 44</sup>. Forgoing forensic autopsies in sudden unexplained deaths is a violation of Recommendation No. R 99 of the Committee of Ministers (Council of Europe) adopted in 1999 <sup>36 37</sup> and partially applied in several European countries <sup>45 46</sup>.

It is recommended that all unexplained sudden death victims undergo post-mortem examination to investigate first whether a cardiac origin should be the leading cause, or other non-cardiac causes are involved.

Also based on the 2015 guidelines published recently by the ESC Task Force, an autopsy is recommended to investigate the causes of sudden death and to define whether SCD is secondary to arrhythmic or non-arrhythmic mechanisms (e.g. rupture of an aortic aneurysm or cardiac rupture). Standard histological examination of the heart and the analysis of the blood for toxicology and molecular pathology are also requested. In the elderly, unlike the young, the causes of SCD are mostly related to chronic degenerative disease (CAD, valvular heart disease and HF). However, in most of the SCDs, a clear evidence of the pathological cause cannot be always found. The postmortem diagnosis of acute MI represents still a current challenge for pathologists, particularly when death occurs within minutes to a few hours after the ischemic insult. Unfortunately, despite of the autopsy protocols available and the attention raised in this issue, a proportion of sudden deaths, ranging from 2 to 54%, remain still unexplained <sup>47</sup>. Many elderlies may die suddenly for the so many cardiac and non-cardiac causes. In fact, it is worth of mentioning that aging does not itself cause HF but in elderly, a HF can be the final cardiovascular aging pathway <sup>19</sup> representing the convergence of age-associated changes in cardiovascular structure and function, aging changes in other organ systems, and the progressive increase in cardiovascular diseases <sup>19</sup>.

In this regard, all health professionals should realize

that different degrees of certainty exist in defining the cause-effect relationship between the cardiovascular clinical and pathological findings and the sudden death event. Since 2008 the Association for European Cardiovascular Pathology <sup>10</sup> has summarized the pathological changes related to SCD grouped in three main categories of reliability. Among the certain post-mortem findings of SCD there are of course massive pulmonary embolism, haemopericardium due to aortic or cardiac rupture, mitral valve papillary muscle or chordae tendineae rupture with acute mitral valve incompetence and pulmonary edema, acute coronary occlusion due to thrombosis or embolism, anomalous origin of the coronary artery from the pulmonary trunk, massive acute. Among the highly probable post-mortem findings of SCD there are stable atherosclerotic plaque with luminal stenosis > 75% with or without healed MI, anomalous origin of the left coronary artery, cardiomyopathies (hypertrophic, arrhythmogenic right ventricular etc.), aortic stenosis with left ventricular hypertrophy, ECG anomalies (consistent with a Wolff-Parkinson-White syndrome, Brugada syndrome etc.). Other common post-mortem cardiac findings (such as patent or moderate coronary disease, small foci of inflammatory cells or fatty infiltration of the right ventricle) are considered uncertain cause of SCD. However, both in high probable, and especially in the uncertain categories, it is recommended that each case should be considered unique in its clinical and circumstantial peculiarity. In this regard, the clinical history and the circumstances of death can deeply affect the decision-making process of the diagnosis of cause and manner of death.

In SCDs, doubts and suspects persist mainly concerning the manner of death: natural or unnatural (accidental, homicide, suicide etc.). In elderly, the suspect of unnatural death should always be considered as most of the cases related to elder maltreatment are not reported due to the difficulties and obstacles of identifying the different types of elder abuse (physical, sexual, emotional or psychological, self-neglect etc). Elder abuse is an alarming social problem and a growing public health concern because of the complex area of investigation. Signs of abuse may overlap with symptoms and outcomes of various diseases or side effects of medications <sup>15 16 48</sup>. For example, it is well known that acute emotional stress can have significant adverse effects on the heart and sometimes these latter are fatal even in young adults <sup>49 50</sup>.

An intense emotion can produce left ventricular dysfunction, myocardial ischemia, or cardiac arrhythmia and, therefore, it is widely recognized as trigger of SCD. An acute coronary syndrome can also be the result of such severe stress. From the pathophysiological point of view, an acute emotional stress can cause a

sudden adrenergic discharge, which can also lead to MI by causing plaque destabilization and then coronary thrombosis (type 1 pathophysiology), or by inducing a spasm of epicardial coronary vessels and/or coronary microcirculation (type 2 pathophysiology)<sup>51</sup>. The disequilibrium in the myocardial supply and demand caused by the intense emotional/physical stress related can determine the fatal myocardial ischemia.

Such kind of event (also known as scared to death) should be considered in elderly where the senile myocardial degeneration can represent, due to its structural frailty, the substantial substrate predisposing SCD. There are myocardial diseases where the border between physiological changes and pathological findings is not well defined such as the senile myocardial degeneration. A sort of grey zone where no other pathological evidence is available for a certain diagnosis of SCD even after a careful macroscopic and microscopic examination of the heart and laboratory analyses. In these unexplained cases, the death should be classified as arrhythmic death syndrome according to other authors as the main mechanism involved is the ability of the emotional stress to trigger myocardial ischemia and/or arrhythmia via sympathetic nervous system hyper-responsivity<sup>10 52</sup>.

In every SCD, pathologists and physicians are requested to find enough evidence of a specific cause of death, and in particular to establish whether SCD is secondary to arrhythmic or non-arrhythmic mechanisms or otherwise to HF. However, in elderly, it is not easy to distinguish the aging of the heart by the overlapping of old-age diseases. In the absence of any other cardiac and non-cardiac diseases, old people can eventually die few passing the age of 90 years. Therefore, where age-related changes are observed and no other cardiovascular findings can be related to a MI, it is also author's opinion that senile myocardial degeneration (code I.51.5 of the WHO's ICD-10) is an inappropriate diagnosis of cause of death. Unfortunately, it is a common expression still used by public health physicians and also pathologists. These professionals should realize that aging and senile myocardium is not an acceptable code in death certification just because SCD (code I-46.1 of the WHO's ICD-10) is an appropriate and more specific cause of death even in elderly. SCD should be used especially when there is exclusion of unnatural causes of deaths or no clear evidence of cardiac death has been found post-mortem as well as in the scenario of a fatal event such as scared to death<sup>53 55</sup>. Acute cardiac deaths precipitated by the stress of normal activities and events of daily life can be regarded as natural. But they are different from a scenario with the clear intent to scare of become alarmed which constitutes an assault and, therefore, can be classified as a homicide. In these

cases, it is strongly suggested an accurate post-mortem investigation including a complete examination of clinical signs and medical history, toxicological and/or chemical laboratory tests, circumstantial data related also to the scene-of-the event. The inaccuracy of cause of death determination without an autopsy is well known by the forensic pathology community<sup>56</sup>. The forensic autopsy examination is still a reliable form of quality control to be adopted with strong implications on the public health and judicial systems.

However, to the best of our knowledge, there is no protocol for distinguishing SCD from elderly abuse fatalities. There are several guidelines for distinguishing sudden infant death syndrome (SIDS) or sudden unexpected infant death (SUID) from child abuse fatalities<sup>57 58</sup>, but no one of such post-mortem procedures are dealing with the elderly. The differentiation between sudden death and fatal child/elderly abuse is a difficult and critical diagnostic decision that needs a careful post-mortem investigation. A specific protocol for sudden deaths in elderly could enhance the public and professional awareness on elder abuse fatalities as well as on the underlying mechanisms of cardiac deaths. This knowledge could be also of help for the treatment of the patient with cardiac diseases<sup>59</sup> and improving cardiovascular performance in the elderly<sup>60</sup>.

## CONCLUSIONS

Cardiovascular diseases are the main cause of death internationally. From a pathological perspective, the causes of SCD are different in young individuals compared with older ones where chronic degenerative diseases and CAD predominate.

The aging myocardial changes could predispose SCD. All public health professionals should change old behaviors in classifying elderly deaths as related to senile myocardium in favor of an appropriate diagnosis of cause of death such as SCD even in elderly. In this regard, the hope is that the upcoming revision of WHO's ICD-10 could delete the imprecise code of "Degeneration of heart or myocardium: senile" – I.51.5, according to the clinical and pathophysiological evidence on the physiological nature of senile myocardium. Guidelines for distinguishing SCD in elderly from elder abuse fatalities are needed, similar to those already available for infant and child for SUID and SIDS. It is the time that geriatricians and pathologists think about such a protocol for elderly victims, as aging is not a synonymous of fatal disease. A procedure for the post-mortem examination of elderly deaths could enhance the public and professional awareness on elder abuse fatalities as well as on the underlying mechanisms of cardiac deaths.

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