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Comprehensive statistical analysis of causes of death and histopathological diagnosis in medico-legal investigations of sudden cardiac deaths

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ABSTRACT

Background and objectives. Sudden cardiac deaths (SCDs) have a significant impact worldwide. Its distribution trends may vary across different communities globally. Consequently, investigating sudden cardiac deaths necessitates a regional, multi-faceted approach. This study aims to ascertain the pathological background of the patients who died in the context of sudden cardiac death and analyze it statistically to generate some trends and define the occurrence of disease.

Materials and methods. We conducted a retrospective analysis of the causes of death for cases from the Legal-Medicine Department of Maramures County, Romania, between 2021 and 2023. From this cohort, we identified and selected cases of SCD and conducted a statistical analysis of the number of cases, gender distribution, age group distribution, and the underlying cardiac pathology that led to this outcome.

Results. 276 sudden cardiac deaths (SCD) were identified from 1,186 autopsies. Males accounted for 75% of SCD cases, with a mean age of 58.8 years. Advanced myocardial fibrosis (41.6%) was the most frequent cause, followed by coronary artery disease (18.12%) and acute myocardial infarction (17.4%). Males had significantly more AMI cases ($p = 0.045$), while females had more coronary artery disease and advanced myocardial fibrosis, though not statistically significant.

Conclusions. Sudden cardiac death predominantly affects males, particularly those aged 51–60, with advanced myocardial fibrosis being the most common cause. The gender difference in AMI prevalence was significant, highlighting the need for targeted prevention and diagnostic improvements. Further research in liaison with experts in all fields is required.

Keywords: sudden cardiac death, histopathology, advanced myocardial fibrosis, coronary artery disease, acute myocardial infarction

Abbreviations (in alphabetical order):

AMF	– advanced myocardial fibrosis
AMI	– acute myocardial infarction
CAD	– coronary artery disease
CH	– cardiac hypertrophy
DCM	– dilated cardiomyopathy
Old MI	– old myocardial infarction

INTRODUCTION

Sudden cardiac deaths are increasing in the whole world, which is associated with multiple factors. Annually, approximately 350,000 individuals in Europe and between 300,000 to 400,000 individuals in the United States experience sudden and unexpected death and most of them are from sudden cardiac death [1,2]. There are various causes of sudden cardiac deaths, which include advanced coronary atherosclerosis, myocardial infarction, arrhythmias, cardiomyopathies, coronary artery spasms, and electrolyte

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imbalances [1,3,4]. Sudden cardiac death (SCD) is defined as death presumed to be of cardiac origin, occurring within one hour of the onset of cardiac symptoms or within twenty-four hours of the individual being last seen in a healthy and alive state. While autopsies can sometimes determine a cardiac etiology, not all cases of SCD present an identifiable cause [5, 6]. This issue predominantly affects low- and middle-income countries, where delayed diagnoses often result in the premature deaths of young individuals [7]. These statistics highlight the significant impact of sudden cardiac death and the need for effective prevention and emergency response strategies. The incidence of sudden cardiac deaths has increased in all parts of the world. This can be attributed to multiple factors, including modifiable and non-modifiable factors. The dietary habits of people have changed drastically over the years; the sleep cycle has been disturbed, there is a decrease in the levels of physical activity, and a sedentary lifestyle, stressed-out routines, and mental disturbances are a few of the notable causes of the disease [1]. After the SARS-CoV-2 pandemic, there was an observed increase in sudden cardiac deaths [8,9]. Due to legislative requirements, the majority of autopsies for sudden cardiac deaths are conducted in legal-medicine departments. Some of these causes of death are difficult to determine through post-mortem gross and microscopic analysis of the cardiac tissue. For example, cases of sudden cardiac death; it is difficult to determine the cause of death when patients die from coronary artery spasms because the arteries may relax by the time an autopsy is performed. As a result, the cardiac muscle can show only signs of ischemia in coronary artery spasms and other various heart conditions. These changes are often missed during the microscopic examination if the individual does not survive long enough for the characteristic alterations to become visible on myocardium tissue using standard light microscopy. Therefore, it becomes necessary to use additional examinations, such as immunohistochemistry, to demonstrate the extent of ischemia or diagnose myocarditis that can lead to sudden cardiac death. It is widely accepted all over the world that many cardiac lesions are occult and are accidentally found on autopsy reports. There is a dire need for the evaluation of such cases to create a predictive model containing preventive measures, risk factors for the disease and pathological assessment. The risk of sudden cardiac death increases with age, but at any age, the risk for men is greater than for women. There are also significant racial differences in the incidence of sudden cardiac deaths, which cannot be specified to any known factors [10]. Multiple studies have been conducted over the years to have a better understanding of the causes that lead to sudden cardiac deaths, including extensive studies of the genome [11,12]. Research indicated that there could be a genetic predisposition to the people who die due to sudden cardiac arrests in addition to the modifiable factors. Some papers show intrinsic defects of channels involved in the transportation of electrolytes that can cause sudden cardiac arrests at any level. Most cases of sudden cardiac death (SCD) are reported to result from coronary artery disease [13]. Considering these facts, research is being conducted to analyze the causes of death and histopathological findings in the autopsy reports of patients who died from sudden cardiac death in order to generate conclusive evidence. The study aims to ascertain the pathological background of the patients who died in the context of sudden cardiac death and analyze it statistically to generate some trends and define the occurrence of disease. An accurate pathological background will help in reaching the clinical diagnosis and in determining the factors that lead to SCD. From our knowledge, it is the first statistical study done in this region regarding sudden cardiac death.

MATERIALS AND METHODS

Data collection, inclusion, and exclusion criteria

This study was a descriptive cross-sectional study exploring causes of SCD from 2021 to 2023 across various regions within Maramures County, Romania. The study was approved by the local ethics committee, ensuring adherence to ethical standards. The study cohort comprised patients who died from sudden cardiac death, defined as unexpected cardiac death occurring within 24 hours of symptom onset in individuals without prior significant symptoms or diagnoses. Cases involving traumatic cardiac injuries, positive toxicological findings, or deaths attributed to non-cardiac causes were excluded from this study.

Autopsy data and sample size

In total, 1,186 autopsies were performed over the study period. The breakdown of autopsies by year is as follows: 417 in 2021, 394 in 2022, and 375 in 2023. Among these, 126 cases in 2021, 89 cases in 2022, and 61 cases in 2023 were identified as sudden cardiac deaths. Thus, the study sample consisted of 276 cases of sudden cardiac death, which forms the basis of this analysis.

Histopathological examination

Each case was subjected to a detailed microscopic histopathological examination of cardiac tissues. A forensic histopathologist conducted these examinations in a controlled laboratory setting, ensuring diagnostic accuracy. Features of histopathology included different terms; myocardial stasis, cardiosclerosis,

cardiomyopathy, myocardial injury, hypertrophy, lipomatosis, atherosclerosis, and coronary issues.

Histopathological diagnoses were categorized in five distinct groups for statistical analysis:

Myocardial injury: This group includes acute coronary thrombosis, acute myocardial infarction, myocardial infarction in the phase of connective tissue organization, and old myocardial infarction.

Advanced myocardial fibrosis (AMF): Encompassing all cases with observed cardiosclerosis.

Lipomatosis: Characterized by an abnormal accumulation of fat cells within the myocardium.

Atherosclerosis and coronary issues: Includes cases with advanced coronary sclerosis.

Cardiomyopathy: Incorporates cases of both dilated and hypertrophic cardiomyopathy.

The final diagnosis of the SCD cause may fall in six categories based on the histopathology findings: acute myocardial infarction (AMI), coronary artery disease (CAD), advanced myocardial fibrosis (AMF), old myocardial infarction (Old MI), dilated cardiomyopathy (DCM), or cardiac hypertrophy (CH).

Statistical analysis

Using Excel software, descriptive trends in the data were determined. To assess statistical differences between various groups, the Chi-Square test was employed. This test was particularly useful for analyzing categorical data, such as differences in pathological findings between genders. Additionally, one way analysis of variance (ANOVA) was utilized to examine mean age differences across the different diagnostic groups, helping to determine if age variations had a significant impact on the prevalence of different cardiac pathologies [14,15].

RESULTS

During the years 2021, 2022, and 2023, the legal-medicine department of Maramures County conducted a total of 1,186 autopsies, encompassing both traumatic and non-traumatic deaths. Out of these, 276 cases were attributed to sudden cardiac death. It is evident that nearly 23% of all autopsies, which include both traumatic and non-traumatic deaths, were due to sudden cardiac death. 75% of sudden cardiac deaths were found in males. The mean age and standard deviation of the included sample is 58.8 (10.8) with a median value of 58 with a range from 35 to 86 years. The data shows a consistent spread, with the majority of individuals being in their 50s to 60s (35%) (Figure 1). Most SCD cases, whatever the cause, were more frequent in age group 51-60; AMF (33%), AMI (39.6%), CAD (40%), CH (32%), DCM (34.3%), and old MI (33.3%). The most common cause of death observed in autopsies in sudden cardiac death was advanced myocardial fibrosis (AMF) (41.6%). Coronary artery disease (CAD) ranks second (18.12%), closely followed by acute myocardial infarction (AMI) (17.4%). Other significant conditions include dilated cardiomyopathy (DCM) (12.7%), cardiac hypertrophy (CH) (7.9%), and old myocardial infarction (old MI)

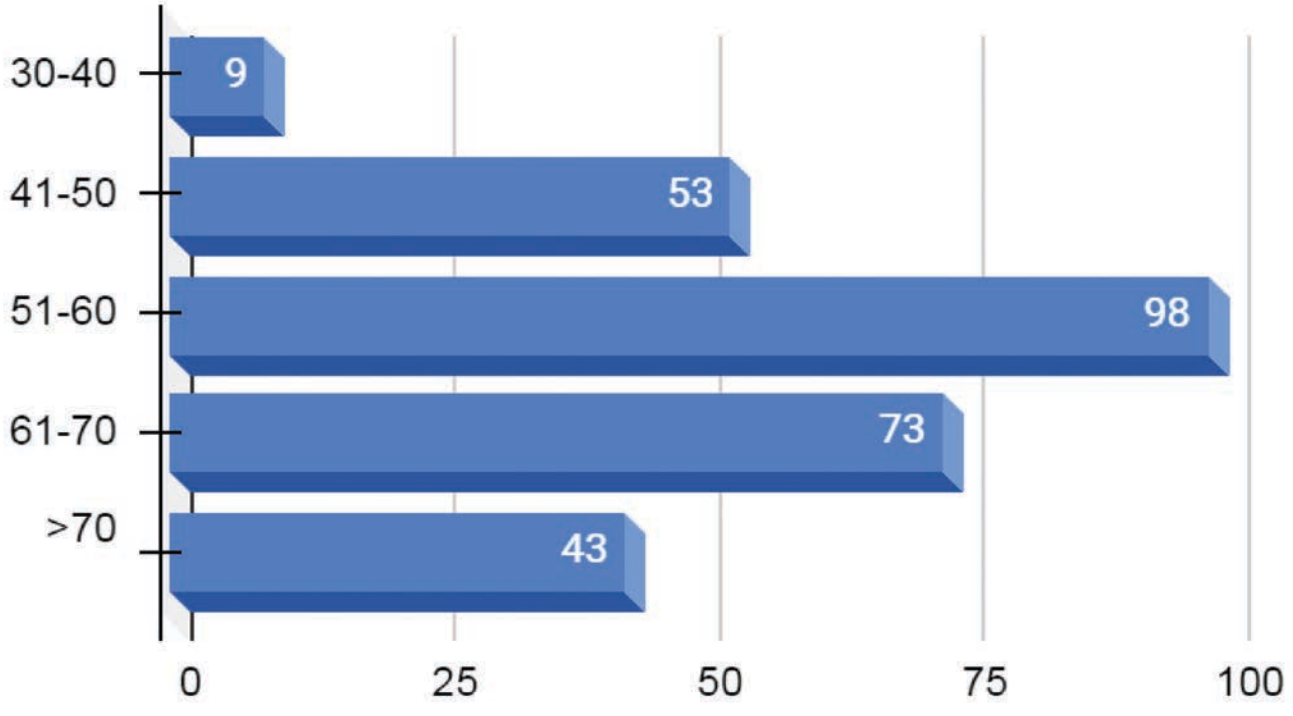

FIGURE 1. A bar chart showing the number of SCD cases per each age range

TABLE 1. Frequencies of different SCD causes per each age range

Age ranges	AMF	AMI	CAD	CH	DCM	Old MI	Total
>70	22 (51%)	5 (11.65%)	6 (14%)	5 (11.65%)	3 (7%)	2 (4.7%)	43
30-40	2 (22.3%	4 (44.4%)	1 (11.1%)	1 (11.11%)	0 (0%)	1 (11.1%)	9
41-50	21 (39.6%)	8 (15.1%)	9 (17%)	5 (9.4%)	10 (18.9%)	0 (0%)	53
51-60	38 (39%)	19 (19.2%)	20 (20.3%)	7 (7.2%)	12 (12.2%)	2 (2.1%)	98
61-70	32 (43.8%)	12 (16.4%)	14 (19.2%)	4 (5.5%)	10 (13.7%)	1 (1.4%)	73
Total	115	48	50	22	35	6	276

The % represents the percentage of each diagnosis in each age group.

being the least frequent cause (2.2%). Table 1 provides a breakdown of the frequencies of different causes of sudden cardiac death (SCD) across various age ranges. In the dataset, the most common cause of SCD for the >70 age group is AMF (51%). For individuals aged 51-60, AMF also predominates with 39% of the cases. The data indicates a shift in predominant SCD causes as age increases, with AMF being more prevalent among the older age groups. The total counts show that AMF is the most frequent cause overall, with 115 cases out of 276 (Figure 2).

The analysis highlights the importance of considering age-specific risk factors and prevention strategies for AMF, particularly in older populations where its impact is most pronounced.

As previously explained, sudden cardiac death can result from a variety of heart pathologies, some of which are difficult to detect in routine examinations. Microscopic diagnoses were categorized into five distinct groups for statistical evaluation. The first group, myocardial injury, includes acute coronary thrombosis, acute myocardial infarction, myocardial infarction in the phase of conjunctive tissue organization and old myocardial infarction. The second group, advanced diffuse myocardial fibrosis, encompasses all cases where cardiosclerosis was observed. The third group, lipomatosis, consists of cases with abnormal accumulation of fat cells within the myocardium, the muscle tissue of the heart. The fourth group, atherosclerosis and coronary issues comprises cases that are presented with advanced coronary sclerosis. The fifth group, cardiomyopathy, includes cases with dilated and hypertrophic cardiomyopathy. The majority of cases showed a combination of cardiac pathology with overlapping features among different causes of SCD. For instance, advanced myocardial fibrosis was present in 86% of all cases of sudden cardiac death analyzed over three years. The myocardial injury group included cases of acute myocardial infarctions, old myocardial infarctions, and acute coronary thrombosis since this is an indirect sign of myocardial infarction. Despite the expanded criteria for this group, these conditions were observed in microscopy hematoxylin-eosin staining in only 28% of all cases. Coro-

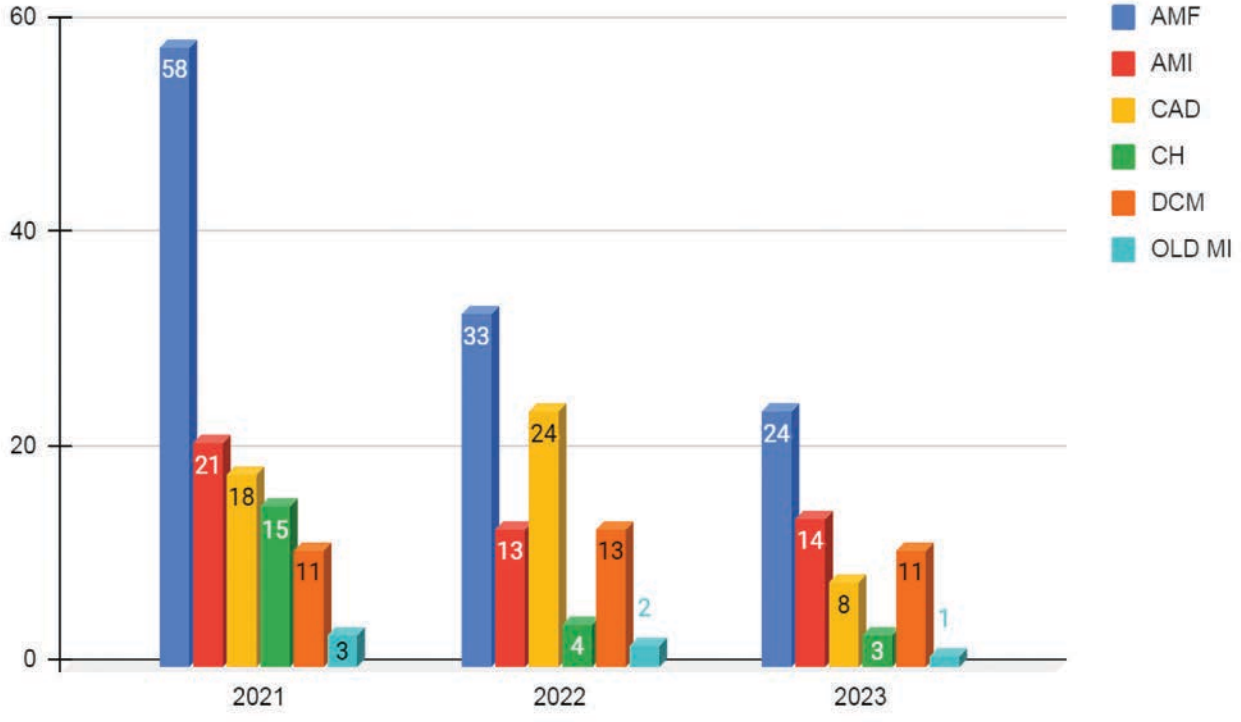

FIGURE 2. A bar chart showing the frequencies of different SCD causes per each year

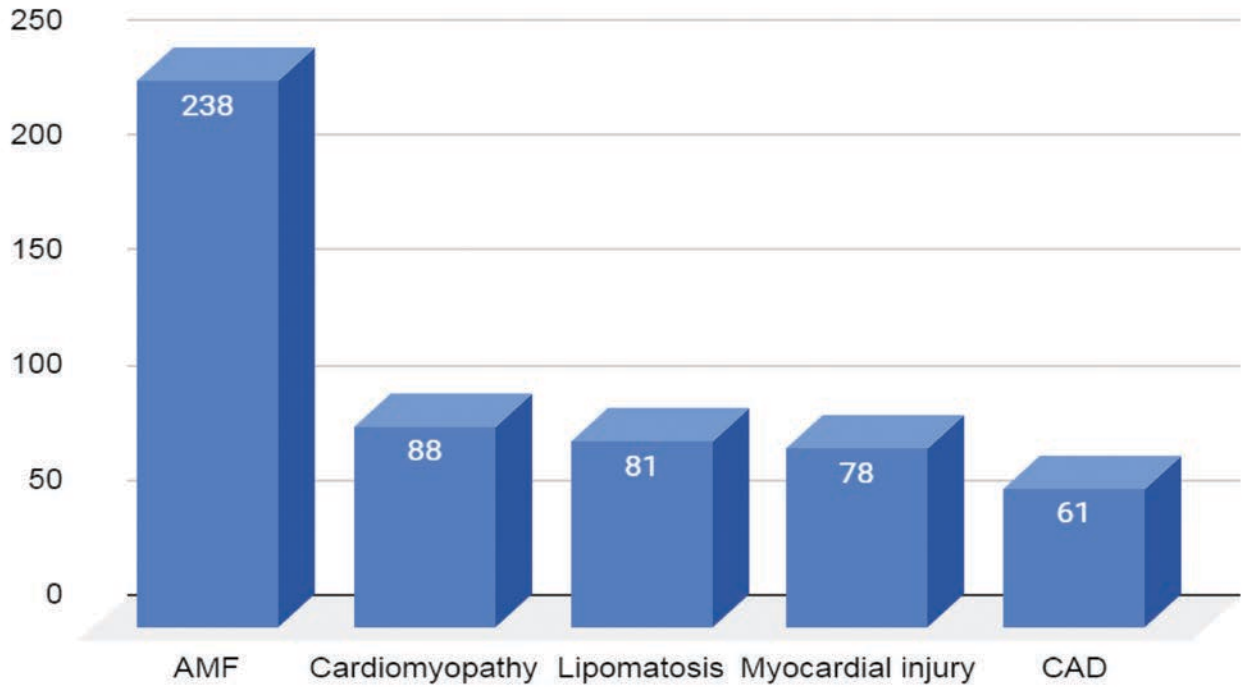

FIGURE 3. A bar chart showing the frequencies of the 5 identified histopathological features

nary artery disease was found in 22% of cases, while cardiomyopathy (hypertrophic and dilated) and lipomatosis were observed in 32% and 29% of cases, respectively. The cardiomyopathy group comprised both hypertrophic and dilated cardiomyopathy since it is not possible to distinguish between these types based solely on microscopic examination (Figure 3).

Table 2 shows gender distribution for each diagnosis. The analysis reveals that males experience a higher frequency of acute myocardial infarction (AMI) compared to females, with a significant difference noted (20.19% in males vs. 8.82% in females, p = 0.045). Other causes of SCD (CH, DCM, and Old MI) showed higher numerical differences in males compared to females but with no statistical significance. In contrast, females show a higher frequency of coronary artery disease (CAD) (25.00%) compared to males (15.87%), and higher frequency of advanced myocardial fibrosis (51.47%) compared to males (38.46%), though this difference is not yet statistically significant (p = 0.09 and 0.13, respectively). The average age at which each condition occurs varies, with no significant differences found in mean age across the groups (p = 0.4), obtained by one way ANOVA test.

TABLE 2. Comparative analysis of sudden cardiac death causes by gender and age

Age ranges	Values	Males	Females	Total	P-value
AMF	Frequency (%)	38.46%	51.47%	41.67%	0.13
	Age (M±SD)	58.4±10.4	64±11	60±10.9	0.4*
AMI	Frequency (%)	20.19%	8.82%	17.39%	0.045**
	Age (M±SD)	56±10	59.8±10.8	56.6±10	
CAD	Frequency (%)	15.87%	25.00%	18.12%	0.09
	Age (M±SD)	57.2±9.6	62.2±11	58.9±11.3	
CH	Frequency (%)	9.62%	2.94%	7.97%	0.12
	Age (M±SD)	58.75±11.7	67±18.4	59.5±12	
DCM	Frequency (%)	13.46%	10.29%	12.68%	0.53
	Age (M±SD)	55.35±8.9	63±14.3	56.9±10.5	
OLD MI	Frequency (%)	2.40%	1.47%	2.17%	0.39
	Age (M±SD)	55.6±13.6	72	58.3±13.9	

** P value from one way ANOVA showing no significant differences in the mean ages across the six groups (AMF, AMI, CAD, CH, DCM, and OLD MI)*

*** Indicates significant difference between males and females regarding the frequency of AMI in favor of males.*

DISCUSSION

Sudden cardiac death (SCD) is defined as death supposed to be of a cardiac origin that occurs within 1 hour of the onset of cardiac symptoms or 24 hours of last being seen in a person without any prior condition that would appear fatal [16]. The WHO (according to the International classification of diseases, version 10 (ICD-10)) defines SCD as non-violent, unexpected death occurring less than 24 hours from the onset of symptoms [17]. Because of a lack of international agreement concerning the precise definition of sudden cardiac death, the true incidence cannot be determined. Hence, putting unified definitions would guide towards conducting further longitudinal studies. Warming et al. have conducted a study validating

different definitions of SCD for optimal adjudication in research settings. SCD cases were categorized into three classifications: "definite", "probable", and "possible". "Definite SCD" includes cases where an autopsy confirms a cardiac cause, or where a ventricular arrhythmia is documented before death. "Probable SCD" refers to sudden deaths in generally healthy individuals with a presumed cardiac origin based on available information, with an established time frame from the onset of symptoms to death, but without an autopsy. "Possible SCD" is used for cases where the time frame is not clearly established, and no autopsy has been conducted [18].

The aim of this study was to investigate and statistically analyze the pathological backgrounds of patients who died from definite sudden cardiac death (SCD) in Maramures County, Romania, between 2021 and 2023. By identifying trends and defining the occurrence of various cardiac diseases, the study sought to enhance clinical diagnosis and understanding of the factors leading to SCD. As the first study of its kind in the region, it included 276 confirmed SCD cases, excluding those with traumatic injuries, toxicological findings, or non-cardiac causes. Detailed histopathological examinations were performed on cardiac tissues, with diagnoses categorized into five groups: myocardial injury, advanced myocardial fibrosis, lipomatosis, atherosclerosis and coronary issues, and cardiomyopathy.

As we observed in the study, sudden cardiac deaths (SCD) account for approximately 23% of all forensic legal-medical autopsies conducted in the region between 2021 and 2023, with a predominant occurrence in males (75%). Advanced myocardial fibrosis (AMF) emerged as the most common cause of SCD, particularly among older age groups, constituting 41.6% of cases. Acute myocardial infarction (AMI) and coronary artery disease (CAD) followed as significant causes, with AMI notably more frequent in males (20.19%) compared to females (8.82%), a difference that reached statistical significance ($p = 0.045$).

Age group 51-60 showed the highest prevalence of all causes of SCD. This is consistent with other studies that have reported similar findings [4,19,20]. This means that people of this age group are more susceptible to the condition than others. It can be attributed to various factors such as the overall health status, increased mental stressors, close to retirement age, lack of exercise and other physical activities, significant changes in the lifestyle and surrounding environment and many other associated factors. The second age group with the most number of patients is the group of 61-70 years of age. This means that old age is a high-risk factor for sudden cardiac death in the population, maybe from developing CAD [21]. The patients of these age groups must be evaluated for their lifestyle modifications, changes in daily routines and other factors that can be changed to decrease susceptibility to diseases that can lead to sudden cardiac death. It is interesting to note that there were very few cases of sudden cardiac deaths in patients aged more than 70 years. It can be due to a higher incidence of other mortal diseases, complicated comorbidity, or other unknown factors. This decline in SCD in elderly was also reported by Khan et al.: that the proportion of deaths that were sudden (SCD/All cause mortality (ACD) ratio) decreased significantly with age, from 0.51 before age 50 to 0.26 after age 80 ($P = 0.002$). Finally, in our study there was not a single case of sudden cardiac death under the age of 30 years in our sample of study [22].

AMF was the most prevalent diagnosis in all age groups except for the age group between 31 and 40 years, AMI scored the highest prevalence (44.4%). The analysis also highlighted age-specific trends, with different cardiac pathologies becoming more prevalent in older age groups. These findings highlight the importance of considering both gender and age in understanding and preventing SCD, particularly in targeting AMF and AMI in high-risk populations.

The male predominance in SCD can be attributed to various factors such as unhealthy lifestyles, high-stress levels, increased workloads, poor dietary habits, genetic predisposition, and the protective effects of estrogen well-known in the female population [23, 24]. The population under study closely mirrors the global trend of a higher male predisposition to develop sudden cardiac death (SCD) [19, 25].

Many risk factors have been identified in the context of SCD including all risk factors for atherosclerotic cardiovascular diseases (ASCVD), left ventricular hypertrophy, and cardiac conduction abnormalities. SCD risk was reported to be relatively low in populations with lower incidences of ASCVD and structural heart disease [26, 27]. In literature, coronary artery disease (CAD) is responsible for most cases of SCD overall. However, it depends on age [28]. This does not go in line with our findings that CAD represented only 18% of SCD cases in this study. Waldmann et al. have reported that Up to half of SCD cases in the 4th decade of life arise from acute coronary syndrome (ACS) which goes in parallel with our findings in this age group [29]. Murai et al. have reported that of about 10, 000 unusual deaths examined per year in Tokyo, two thirds were determined to have died of natural causes (SCD). The most common cause of sudden natural death was ischemic heart disease, especially acute myocardial infarction. However, pathological examination proved acute myocardial ischemia in only one third of autopsies [30]. This clinical-histopathology controversy can be explained by several factors. Rapid onset of death after the onset of ischemia does not allow the typical pathological

changes, such as necrosis, to develop. Additionally, subtle or microinfarctions might be missed during routine autopsy, especially if overshadowed by other cardiac conditions like advanced myocardial fibrosis or hypertrophy. SCD can also result from non-ischemic triggers, such as arrhythmias or sudden plaque rupture without complete artery blockage, which may not leave clear signs of infarction. Furthermore, limitations in autopsy techniques might prevent the detection of early or subtle ischemic changes, making it challenging to definitively diagnose AMI as the cause of death in these cases.

As reported in our study, the most common cause of death and microscopic diagnosis observed in autopsies in sudden cardiac death was advanced myocardial fibrosis (AMF). Cardiac fibrosis is a process of pathological extracellular matrix remodeling, impairing the heart muscle function. Fibrosis of the cardiac muscle most commonly occur after myocardial infarction; however, there are various other conditions having the potential to promote cardiac fibrosis such as hypertensive heart disease, myocarditis, aortic stenosis, pulmonary hypertension, atrial fibrillation, diabetic hypertrophic cardiomyopathy and idiopathic dilated cardiomyopathy [31,32]. Ischemic heart disease involves reduced blood supply due to coronary artery disease leading to fibrosis; chronic high blood pressure that can strain the heart muscle and lead to structural changes; cardiomyopathies are various heart muscle diseases impairing function and lead to fibrosis; myocarditis is inflammation from infections or autoimmune conditions, resulting in fibrosis as tissue heals; diabetic hypertrophic cardiomyopathy; aortic stenosis; pulmonary hypertension; atrial fibrillation; exposure to cardiotoxic agents; aging naturally leads to fibrous tissue accumulation; genetic disorders predispose individuals to fibrosis due to mutations affecting heart muscle proteins [33].

This diagnosis of advanced myocardial fibrosis (myocardial sclerosis) is used frequently in cases of sudden cardiac deaths not only in this region but also in other regions of Romania [34, 35]. It is well established that coronary artery disease (CAD) is the leading cause of death in cardiovascular diseases and that myocardial infarction is a critical event and complication associated with coronary artery disease [36]. However, our statistical analysis revealed that the most common cause of death in sudden cardiac and microscopic diagnostics is advanced diffuse myocardial fibrosis. It is important to emphasize that this diagnosis is one of exclusion, used only when no other cardiac pathology can explain the cause of death. Diffuse myocardial fibrosis is present in nearly all chronic cardiac diseases. Advanced myocardial fibrosis can lead to death by arrhythmia, often leaving no other visible signs during autopsy [37].

In essence, advanced myocardial fibrosis (AMF) has a broader diagnostic range. In some autopsy cases of SCD, you can find advanced myocardial fibrosis without the presence of coronary atherosclerosis (CAD). Even coronary artery disease is a more general term and can be a diagnosis of exclusion if no other more specific cardiac pathology can be identified. The frequent use of advanced myocardial fibrosis (AMF) diagnostics in forensic legal-medicine has a straightforward explanation: some diagnoses of acute myocardial infarction can be missed during microscopic examinations. It is widely accepted that routine light microscopy typically does not detect any observable changes within the first 4-6 hours following the onset of acute myocardial infarction (AMI) [38]. Immunohistostaining should be utilized more frequently to establish a more accurate diagnosis in cases where ischemia is present, but changes in routine light microscopy are not visible. It is highly recommended in cases with significant legal implications to utilize immunohistochemistry to determine the presence and extent of ischemia in the myocardium. Some immunohistochemical markers are well-known and widely used for forensic purposes in cases of early myocardial infarction, while others are recently studied and emerging [39]. The legal-medicine departments, through their histopathological analyses performed on various groups of people, can help in better understanding the causes that lead to SCD and its distribution more objectively. The evidence collected through the results of the study can help in the progression of further research, which can ultimately lead to defining the heart pathology that is responsible for sudden cardiac death.

Accurate pathological findings are critical in the analyses of SCD to understand the underlying cardiac pathology better. Sudden cardiac death poses a threat to literally every person in this world due to its uncertainty. A multidisciplinary approach with evidence-based research is necessary to further enhance the diagnostic capabilities in cases of SCD. It is also widely accepted that genetic factors play an essential role in the incidence of SCD. Therefore, it becomes a necessity to evaluate the genetic basis of sudden cardiac deaths through recent technologies. Additionally, optimal understanding of risk factors help choose whom to apply a primary or secondary prophylaxis from SCD [40]. Sharing of data and better communication and collaboration with other researchers throughout the world via multiple means is also critical for future developments.

While this study provides valuable insights into the epidemiology and pathology of sudden cardiac death (SCD) in Maramureș County, Romania, several limitations should be acknowledged. First, the study is retrospective in nature, relying on the analysis of autopsy data, which may not capture all cases of SCD,

particularly those that did not undergo postmortem examination. This could lead to underreporting or bias in the data, particularly for cases where the cause of death was not definitively established. Additionally, the reliance on routine light microscopy for diagnosing conditions like acute myocardial infarction (AMI) may result in missed diagnoses, as early ischemic changes are often not detectable without more advanced techniques such as immunohistochemistry. The study also does not account for the presence of comorbidities or other potential contributing factors to SCD, which may influence the interpretation of the findings. Furthermore, the sample size, though significant, is limited to a specific geographical area and time frame, which may affect the generalizability of the results to other populations. Finally, this study lacks detailed analytical methods to explore statistical significant differences between different groups and to correlate provisional clinical diagnosis of SCD cause with the final diagnosis in forensic reports.

CONCLUSION

As observed in the statistical analysis conducted in the region, there is a consistent trend aligning with other studies indicating that the male population is more affected by sudden cardiac death, particularly within the 50s to 60s age range. This age and gender-specific distribution of SCD is crucial for guiding future research and public health initiatives. One key insight from our analysis is the frequent diagnosis of advanced myocardial fibrosis (AMF) as a cause of death, which may stem from the limitations of routine light microscopy in detecting acute myocardial infarction (AMI) in its early stages. This highlights the need for enhanced diagnostic protocols, including the incorporation of immunohistochemistry markers for ischemia, to improve the accuracy of postmortem examinations. Given the complex and multifaceted nature of SCD, it is vital to develop standardized protocols that involve advanced histopathological techniques, alongside biochemical and genetic analyses. Such an approach could offer more precise diagnostics and a better understanding of the underlying mechanisms of SCD. The ultimate aim of this research is not only to improve the accuracy of SCD diagnoses but also to pave the way for better prevention strategies. By integrating genomics, proteomics, and metabolomics with cutting-edge, non-invasive diagnostic technologies, we can potentially detect subtle changes in cardiac tissue and vessels at a micro-level, leading to earlier interventions and, ultimately, a reduction in SCD incidence. This research serves as a call to action for the medical and scientific communities to collaborate, share data, and advance the tools and techniques available for diagnosing and preventing sudden cardiac death, with the goal of saving more lives in the future.

Conflict of interest:
We do not have any financial or personal relationships that might bias the content of this work.

Authors' contributions:
Conceptualization - Radu Moldovan, Vlad Ichim; methodology - Radu Moldovan; software - Gabriel Aurelian Pufu; validation - Radu Moldovan, Vlad Ichim and Gabriel Aurelian Pufu; formal analysis - Radu Moldovan; investigation - Radu Moldovan; resources - Radu Moldovan; data curation - Radu Moldovan; writing—original draft preparation - Radu Moldovan; writing—review and editing - Radu Moldovan; supervision - Vladimir Belis.
All authors have read and agreed to the published version of the manuscript.

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