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Causes of Death in Patients Asking for Polyclinic Care for Coronary Heart Disease

Aim	Retrospective analysis of the underlying causes for death of patients who did and did not seek outpatient medical care (OPMC) for ischemic heart disease (IHD), and discussion of a possibility for using administrative anonymized but individualized databases for analysis.
Material and methods	The electronic database of the Central Administration of the Civil Registry Office of the Moscow Region (Unified State Register of the Civil Registry Office of the Moscow Region), including medical death certificates (MDC) for 2021, was used to select all cases of fatal outcomes with the disease codes of the International Classification of Diseases, Tenth Revision (ICD-10) (codes of external causes, injuries, poisonings excluded) that were indicated as the primary cause of death (PCD). Personalized data of the deceased were combined with data from electronic medical records of patients who sought OPMC at institutions of the Moscow Region within up to 2 years before death. In addition to IHD, the following PCD codes were taken into account: malignant tumors, COVID-19, diabetes mellitus, cerebrovascular diseases, hypertension, chronic obstructive pulmonary disease, alcohol-associated diseases, and, as examples of unspecified PCD, old age and unspecified encephalopathy.
Results	In total, among those who died from diseases, the proportion of those who died from IHD was 18.9%; for another 8.4%, IHD was indicated as a comorbid disease in Part II of the MDC. Among those who sought OPMC for IHD, the IHD proportion indicated as PCD was 27.5%, and among those who did not seek OPMC 17.4% (p <0.0001). Those who died from IHD and who had sought OPMC were older (mean age, 75.59±10.94 years) than those who died from IHD and had not sought OMPM (mean age, 73.96±10.94 years; p<0.0001). The frequency of myocardial infarction as PCD among those who had and had not sought OPMC was the same (12%), chronic forms of IHD were 83.9% and 79.7%, the frequencies of "unspecified" acute forms of IHD (codes I24.8-9) were 4.1% and 8.3%, respectively. The proportion of deaths from COVID-19 was the highest (21.7% and 24.3%, respectively), from malignant neoplasms 11.6% and 12.7%, respectively, and from unspecified encephalopathy 10.6% and 10.7%, respectively.
Conclusion	Only 25% of patients who had sought OPMC for IHD died from IHD, otherwise the causes of death were the same as for patients who had not sought OPMC for IHD. Analysis of administrative databases allows identifying disparities in the PCD structure and to direct the efforts of specialists to reconciling the criteria for death from various forms of IHD.
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Introduction

Despite the fact that ischemic heart diseases (IHD) are a leading cause of death worldwide, there is still no uniform definition of certain concepts, terms, and diagnostic criteria for individual forms of IHD among different medical communities and scientific schools [1]. The World Health Organization (WHO) and the International Society of Cardiology defined IHD in 1979 [2] as myocardial damage caused by an imbalance between coronary blood flow and myocardial demand. This imbalance can be caused by functional changes or organic lesions of the coronary arteries. The term «coronary artery disease» is frequently employed in lieu of the term «IHD». The Russian Society of Cardiology also defines IHD as myocardial damage caused by coronary blood flow disturbance, which results from organic (irreversible) and functional (transient) changes [3]. The Russian Society of Pathologists defines IHD as a group of diseases that result in acute or chronic

cardiac dysfunction due to a relative or absolute decrease in myocardial arterial blood supply [4, 5]. The morphologic basis of IHD is typically the narrowing or obstruction of the coronary arteries by atherosclerotic plaques. However, coronary microvascular dysfunction and coronary artery spasm also contribute to the development of IHD [3, 6]. The term «acute coronary syndrome» is employed as a provisional diagnostic category (until a definitive diagnosis is established) and in 2019 the European Society of Cardiology introduced the concept of chronic coronary syndrome [7, 8].

A considerable number of studies that assess the incidence of the disease and causes of death in patients included in registries refer to different forms of IHD. These studies employ different criteria for the diagnosis of IHD, as well as different inclusion and exclusion criteria. Furthermore, in such works, causes of death are typically recorded as «cardiovascular event-related death» and

«all-cause death», rather than based on the International Statistical Classification of Diseases and Related Health Problems (ICD). Consequently, regardless of the size of the registry studies, they are unable to provide an accurate representation of the population as a whole. In addition to the registries, so-called administrative databases also play an important role in the organization of medical care. In contrast to clinical trials and registries, administrative databases collect and analyze information using the ICD, clinical modifications of the ICD and clinical statistical groups. It is currently not possible to utilize administrative databases to estimate the risk of death from IHD among patients who have been diagnosed with IHD during their lifetime. However, these databases do permit the clarification of other equally important clinical and organizational issues.

Given the retrospective nature of the data and the fact that they were administrative databases rather than

Central illustration. Causes of Death in Patients Asking for Polyclinic Care for Coronary Heart Disease
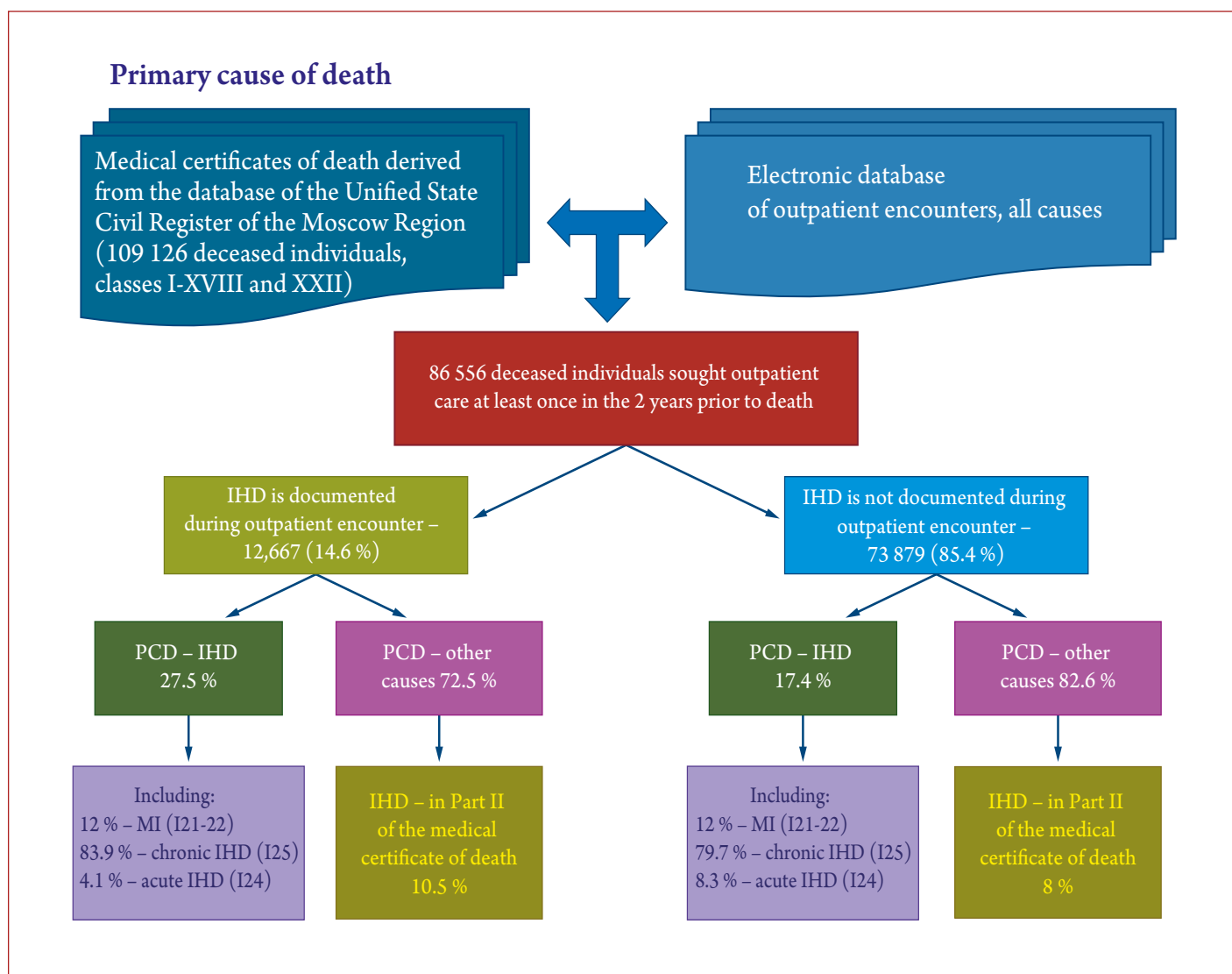
IHD, ischemic heart disease; MI, myocardial infarction; PCD, primary cause of death.

a registry, the objective of the study was formulated as follows: to retrospectively analyze the primary causes of death (PCD) of patients who did and did not seek outpatient medical care for IHD and to discuss the possibility of using administrative anonymized but personalized databases for the analysis.

Material and Methods

The study design is a retrospective study based on the data of the electronic database of the archive of the Head Civil Registry Office of the Moscow Region (the Unified State Civil Register of the Moscow Region). Laboratory tests, clinical investigations, and medical interventions were not conducted or analyzed in this study.

The data utilized in this study were obtained from the electronic database of the Unified State Civil Register of the Moscow Region based on medical certificates of death for 2021. In the initial stage of the study, all fatal cases (109,126 deaths) with ICD-10 disease codes provided as PCD were selected (all codes for external causes, trauma, and poisoning were excluded).

In the second stage of the study, anonymized but personalized data from deceased individuals were merged with the electronic database of outpatient encounters in medical care facilities in the Moscow region within a maximum of two years preceding the lethal outcome. A total of 86,556 people of those who died in 2021 sought medical care for any reasons. The total number of reasons for outpatient encounters in medical facilities in the Moscow region between 2020 and 2021 was determined based on four-digit ICD-10 codes. Of these, 12,667 were for IHD.

At the third stage, groups of ICD-10 codes for PCD were identified: IHD, malignant neoplasms, COVID-19 as the most common causes of death; diabetes mellitus (DM), cerebrovascular diseases, hypertensive heart disease (HHD), chronic obstructive pulmonary disease (COPD), disorders due to use of alcohol as the most common multimorbidity in patients with IHD, and old age and unspecified encephalopathy as examples of unspecified PCD codes. The numerical values and the corresponding percentages were established:

- Deaths from IHD (all nosologies included in IHD) among those who sought and did not seek outpatient care for IHD;
- Deaths from other causes among those who sought and did not seek outpatient care for IHD;
- Deaths from other causes among those who sought and did not seek outpatient care for IHD, with IHD registered in the second part of medical certificates of death;

Furthermore, the percentage of male and female deaths and the mean age at death were calculated for each group.

The statistical analysis was conducted using the SPSS 26.0 software suite and Microsoft Excel. The individual ICD-10 codes were grouped, and the frequency of code use by group was then assessed. The groups were compared by nominal indicators (frequency of registration of individual codes) using a chi-squared test. The quantitative data (mean±standard deviation) were compared using a nonparametric Mann-Whitney test.

Results

In total, IHD accounted for 18.9% (16,339) of disease-related deaths, with a further 8.4% having IHD listed in Part II of the medical certificate of death (other significant conditions contributing to death).

In the 2020–2021 period, 12,667 individuals (14.6% of the total number of deaths from diseases in 2021, which was 86,556) sought outpatient care for IHD. There were no statistically significant differences in the rate of encounters between males and females (p = 0.12): 14.9% (5,763) and 14.5%, respectively. The mean age of women was 78.74±10.49 years, while that of men was 69.42±12.46 years (p<0.0001).

The mean age of individuals who died of IHD and sought outpatient care for IHD was 75.59±10.94 years, which was higher than the mean age of those who died of IHD and did not seek outpatient care for IHD (73.96±10.94 years; p<0.0001). Over the two-year period preceding death, the mean number of causes for outpatient encounters among those seeking outpatient care for IHD was 7.6±5.5, as determined by four-digit ICD-10 codes. This number was almost twofold higher than in those who did not seek treatment for IHD (4.42±3.8 causes; p<0.0001). The observed difference was recorded for both women (7.4±5.6 and 4.5±3.9 causes; p<0.0001) and men (7.8±5.4 and 4.3±3.7 causes; p<0.0001). Less pronounced but statistically significant differences (p<0.0001) were observed among those who sought outpatient care for IHD and died of IHD (6.8±5.1 causes) and those who sought outpatient care for IHD and died of other causes (7.9±5.7 causes), as well as among those who did not seek outpatient care for IHD but died of IHD (3.9±3.4 causes) and those who did not seek outpatient care for IHD and died of other causes (4.6±4.0 causes).

It is shown in Table 1, the structure of the causes of death among those who died from diseases differs depending on whether or not they sought outpatient care for IHD in 2020–2021. Among those who died from IHD, there were statistically significantly more individuals who sought outpatient care or received follow-up care for IHD. The proportion of deaths from myocardial infarction (MI) (three-character codes I21-I22) accounted for 12% (12.0% and 11.96%, respectively) of deaths from IHD, among both those who sought and did not seek outpatient care (421 and 1538, respectively). The proportion of nosologies

Table 1. Main groups of primary causes of death for those who died in 2021 from diseases based on whether or not they sought outpatient care for IHD in 2020-2021

Causes of death by groups of primary cause of death	Outpatient encounters for IHD, n (%)		
	No	Yes	Total
IHD (three-character codes I20–I25),	12 850 (17.4)	3 489 (27.5)	16 339 (18.9)
COVID-19 (three-character codes U07)	17 989 (24.3)	2 753 (21.7)	20 742 (24)
Malignant neoplasms (class C codes)	9 417 (12.7)	1467 (11.6)	10 884 (12.6)
Cerebrovascular diseases (three-character codes I60–I67, I69)	5 110 (6.9)	803 (6.3)	5 913 (6.8)
Hypertension (three-character codes I10–I13)	320 (0.4)	51 (0.4)	371 (0.4)
DM (three-character codes E10–E14)	1519 (2.1)	294 (2.3)	1813 (2.1)
COPD, chronic bronchitis (three-character codes J40–J44)	767 (1.0)	150 (1.2)	917 (1.1)
Old age (R54)	780 (1.1)	207 (1.6)	987 (1.1)
Encephalopathy, unspecified (G93.4)	7 937 (10.7)	1344 (10.6)	9 281 (10.7)
Disorders due to use of alcohol (F10.2,4,5, 8 G31.2 G62.1 I42.6 K70.0,1,2,3 K86.0)	1657 (2.2)	65 (0.5)	1722 (2)
Other causes	15 535 (21)	2 054 (16.2)	17 589 (20.3)
Total	73 879 (100.0)	12 677 (100.0)	86 556 (100.0)

IHD, ischemic heart disease; PCD, primary cause of death; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease.

from the group of chronic forms of IHD (three-character code I25) was 83.9% (2,927) of the number of deaths from IHD among those who sought outpatient care and 79.7% (10,242) among those who did not seek outpatient care.

The remaining 4.1% and 8.3% were acute forms of IHD without MI (99% for I24.8 Other forms of acute ischemic heart disease and single cases of I24.9 Acute ischemic heart disease, unspecified). Consequently, if the frequency of registration of MI among those who sought and those who did not seek outpatient care was comparable, the frequency of registration of other acute forms of IHD among those who did not seek outpatient care for IHD was approximately twice as high.

Table 2 indicates that the majority of those who died did not seek outpatient care for IHD during the 2020–2021 period. However, among those who died from IHD, the proportion of those who sought outpatient care for IHD was approximately twofold higher (p<0.0001) than among those who died from other causes.

Among those who died of IHD, the following ICD-10 codes listed as primary cause of death (in Part I of the medical certificate of death) accounted for 96.1% of cases: 45.3% (7428) – I25.1 Atherosclerotic heart disease, 22.7% (3718) – I25.8 Other forms of chronic ischemic heart

disease, 8.9% (1460) – I25.5 Ischemic cardiomyopathy, 7.2% (1184) – I24.8 Other forms of acute ischemic heart disease, 10% (1633) – I21 Acute myocardial infarction, 2% (326) – I22 Subsequent myocardial infarction. The mean age of those who died from chronic forms of IHD (three-character code I25) was 75.8±11.3 years, while the mean age of those who died from MI was 73±11.5 years (p<0.0001).

Among those seeking outpatient care for IHD and when IHD was mentioned in Part II of the medical certificate of death, the following conditions were cited as a primary cause of death: COVID-19 in 39% (2823) of cases, unspecified encephalopathy (G83.4) in 21% (1510) of cases, malignant neoplasms in 9% (635) of cases, and other causes in 33% of cases. Furthermore, the causes of seeking patient care included HHD (43%), malignant neoplasms (19%), and DM (15.4%). Among those with disorders due to use of alcohol established as the primary cause of death, the causes for seeking outpatient care were IHD (3.8%), HHD (30.3%), malignant neoplasms (2.1%), and DM (4.4%).

Discussion

The fact that the majority of individuals who died from IHD in 2020–2021 did not seek outpatient care for IHD suggests that death from IHD (including eventual

Table 2. Indication of nosologies from the group of IHD in parts I and II of the medical certificate of death for those who died in 2021 among those who sought and did not seek outpatient care for IHD in 2020-2021, n (%)

Outpatient encounters for IHD	IHD is the primary cause of death (part I of the medical certificate of death)	IHD is not indicated the medical certificate of death	IHD is a comorbidity (part II of the medical certificate of death)
Yes	3 489 (21.4)	7 862 (12.5)	1 326 (18.3)
No	12 850 (78.6)	55 116 (87.5)	5 913 (81.7)
Total	16 339 (100.0)	62 978 (100.0)	7 239 (100.0)

IHD, ischemic heart disease.

hospitalization and death from MI) was the initial manifestation of the disease for many of them. It is also important to note that many patients may have sought treatment prior to 2020, before the onset of the COVID-19 pandemic, during which they did not seek outpatient care, as evidenced by other studies [9, 10]. At the same time, there is no consensus or recommendation at the global level regarding the classification of COVID-19 as a risk factor for death or as a cause of death, particularly in cases of significant deterioration of organ and system functions after COVID-19 or in cases of so-called long COVID [11].

In this study, we observed a nearly twofold increase in the number of causes for outpatient encounters, as determined by four-digit ICD-10 codes, among those who sought outpatient care for IHD (7.6±5.5 cases) compared with those who did not seek care for IHD (4.42±3.8 cases). This discrepancy may be attributed to the fact that the IHD group encompasses 35 four-digit ICD codes, and the same patient presenting with one disease (IHD) had different ICD codes registered at the outpatient clinic at different times.

At present, there are no clear criteria for establishing nosologies units from the IHD group as PCD in deceased persons without a lifetime diagnosis of IHD (in those cases without signs of MI). Furthermore, we were unable to find explanations or recommendations for establishing PCD in cases of a lifetime diagnosis (or suspicion) of coronary microvascular dysfunction, coronary artery spasm or deaths that do not meet the universal definition of MI [12]. The universal MI criteria have been designed with the intention of improving diagnostic and treatment algorithms for suspected MI. However, they do not contain any rules for establishing the diagnosis of MI or filling out the medical certificate of death in the event of a patient's death, particularly in cases where the patient has died outside of a hospital setting and the necessary diagnostic «set» (electrocardiogram, biomarkers) is not available. Significant variability in mortality rates and the proportion of deaths from IHD is likely attributable to the differing approaches to defining PCD [13–15]. As observed by Timonin et al. [16], experts who fill in medical certificates of death in different countries have different interpretations of the criteria for determining the cause of death from MI. This may explain that in Russia MI accounted for only 12% of all fatal outcomes with IHD as PCD, while, for example, in Norway this figure is 63%. The higher number of deaths from chronic forms of IHD compared to acute forms observed in our study may be attributed to both miscoding and underdiagnosis of acute forms of IHD. In the multicenter Russian study RESONANCE, conducted more than a decade ago, it was demonstrated that the frequency of deaths from acute forms of IHD, verified on the basis of a specific algorithm in both men and women, was masked by the chronic forms of IHD [17].

It should also be noted that the proportion of erroneous code I22 (Subsequent myocardial infarction, this code is utilized exclusively when the patient is alive, and code I21 is selected in the event of death) constituted 16.7% of all cases of MI. Among those who did not seek outpatient care for IHD, the incidence of acute IHD without indicating MI as the PCD was 2 times higher (8.3% and 4.1%, respectively) than among those who did. Furthermore, 99% of the medical certificates of death indicated that the cause of death was I24.8 Other forms of acute ischemic heart disease. However, the ICD lacks criteria or recommendations regarding the appropriate use of I24.8 versus I24.9 (Acute ischemic heart disease, unspecified). In an article published on the website of the Russian Society of Cardiology [18], it was proposed that the code I24.8 be used as a synonym for sudden coronary death, rather than the code I24.9 [19]. Nevertheless, this article represents a scholarly discussion among experts rather than a regulatory document.

A similar argument can be made regarding the lifetime diagnosis and death from chronic forms of IHD. It is important to highlight that the proportion of unspecified codes I25.0, I25.1, and I25.9 accounted for 57.3% of all chronic forms of IHD. Code I25.1 is employed for the nosological unit «Atherosclerotic (diffuse small-focal) cardiosclerosis», which is not included in the classification of IHD [1, 17]. Concurrently, the proportion of deaths from I25.3 Aneurysm of heart and I25.5 Ischemic cardiomyopathy is relatively low at 12.3%. It is also important to note that according to the ICD-10 rules, postinfarction cardiosclerosis should be coded as I25.8 rather than I25.2 in the event of a fatal outcome. In our study, the proportion of erroneous code I25.2 was 2.3%. The existing accounting system is unable to ascertain the proportion of deaths attributable to chronic heart failure, fatal cases following surgical and endovascular treatment of IHD, or related to fatal arrhythmias in a compensated state without significant functional impairment. This information is crucial for optimizing health and social care and can help reduce mortality.

It is notable that the study identified a comparable proportion of deaths (among those seeking and those not seeking treatment for IHD) due to old age. In light of the aforementioned findings, it is pertinent to cite the WHO's explanations on this matter. The ICD does not categorize «old age» as a disease. The term is employed for coding purposes only, as physicians in different countries utilize it as a cause of death, necessitating guidance on its use [20]. The ICD-11 proposes the use of code MG2A and the term «old age» in the group «Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified» in lieu of code R54 and the term «senility» (as a synonym for «old age»). From our perspective, the term «old age» and the

majority of other terms within the group of chronic forms of IHD can be attributed to causes of death that are not precisely defined.

Limitations

A dearth of data regarding hospitalizations and the reasons for hospitalization in the period immediately preceding death. It is probable that a considerable proportion of deaths associated with MI in this study are accounted for in the group of individuals who did not seek outpatient care for IHD. This is because MI, as well as sudden coronary death, is often the first manifestation of IHD. Furthermore, the analysis of administrative databases based on ICD codes does not permit the consideration of clinical features or the use of nosological groupings employed in registries and clinical trials, which renders the comparison of data challenging.

Conclusion

A review of administrative databases revealed that only 25% of patients seeking outpatient care for ischemic heart disease ultimately die from ischemic heart disease. Nevertheless, the proportion of deaths from ischemic heart disease among those who did not seek outpatient care for ischemic heart disease is twice as high as among those who did seek such care. The observed discrepancies in the distribution of deaths from acute and chronic forms of ischemic heart disease are, in part, attributable to the fact that certain terms included in certain codes of the International Classification of Diseases, Tenth Revision (ICD-10) do not correspond to the terms and concepts used in clinical classifications, and there is no glossary to facilitate the harmonization of criteria for death from different forms of ischemic heart disease.

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