

Scientific Review

UDC 616.98: 578.828.6]-092: 612.017.1]-008.64-036.88-07

DOI: 10.17816/pmj42455-63

ANALYSIS OF THE CAUSES OF LETHAL OUTCOME IN PATIENTS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS

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АНАЛИЗ ПРИЧИН ЛЕТАЛЬНОСТИ ПАЦИЕНТОВ, ИНФИЦИРОВАННЫХ ВИРУСОМ ИММУНОДЕФИЦИТА ЧЕЛОВЕКА

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Over 37 million HIV-infected people live in the world and many of them die due to the progression and decompensation of somatic diseases. The aim of the study is to determine the rating of fatal outcomes causes of HIV-infected patients according to the data of the authors from different countries of the world.

Data from 287 full-text articles were analyzed, from which 32 sources most relevant to the purpose of the study were selected. The leading causes of death in HIV-infected patients were infectious complications and opportunistic infections characteristic of the AIDS stage, along with concomitant tuberculosis infection (55.1 %). Cardiovascular diseases ranked second (20.6 %), followed by cancer (14.6 %), liver diseases, including alcoholic and viral hepatitis and cirrhosis (8.5 %), and only 1.1% are accounted for by all other diseases. Mortality from infective endocarditis, myocardial infarction, sudden cardiac death, acute cerebrovascular event,

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pulmonary embolism and acute decompensation of chronic heart failure together account for 82.5 % of all cardiovascular causes of mortality.

Monitoring of patients with HIV infection should be comprehensive, involving infectious disease specialists, therapeutic and cardiology services, with increased cancer vigilance. The challenges of HIV infection concerning early development of cardiovascular pathology and elevated mortality from cardiovascular diseases should not be ignored.

Keywords. HIV, mortality, cause of death, sudden cardiac death, myocardial infarction, infective endocarditis, chronic heart failure.

Более 37 млн ВИЧ-инфицированных проживает в мире, и многие из них заканчивают свою жизнь вследствие развития и декомпенсации соматических заболеваний. Проанализированы данные 287 полнотекстовых статей, из которых выбраны 32 источника, наиболее соответствующих цели исследования: определить рейтинг причин летальных исходов ВИЧ-инфицированных больных по данным авторов разных стран мира. Среди причин летального исхода ВИЧ-инфицированных лидируют инфекционные осложнения и оппортунистические инфекции, присущие для стадии СПИД, а также присоединившаяся туберкулезная инфекция (55,1 %). На втором месте оказались сердечно-сосудистые заболевания (20,6 %), на третьем – онкологические заболевания (14,6 %), далее следуют заболевания печени, в том числе алкогольные и вирусные гепатиты и циррозы (8,5 %), и только 1,1 % занимают все другие заболевания. Смерть от инфекционного эндокардита, инфаркта миокарда, внезапной сердечной смерти, острого нарушения мозгового кровообращения, тромбоэмболии легочной артерии и острой декомпенсации хронической сердечной недостаточности в совокупности составляют 82,5 % всех сердечно-сосудистых причин летальности.

Наблюдение больных с ВИЧ-инфекцией должно проводиться комплексно с привлечением инфекционистов, терапевтической и кардиологической службы, с проявлением повышенной онконастороженности. Нельзя игнорировать вызовы ВИЧ-инфекции в аспекте раннего развития сердечно-сосудистой патологии и высокого риска смерти от сердечно-сосудистых заболеваний.

Ключевые слова. ВИЧ, смертность, причина смерти, внезапная сердечная смерть, инфаркт миокарда, инфекционный эндокардит, хроническая сердечная недостаточность.

INTRODUCTION

More than 37 million people worldwide are living with HIV, and many of them die as a result of the development and decompensation of somatic diseases [1]. The prevalence of somatic diseases among HIV-infected individuals contributes significantly to disability and mortality both globally [2] and in the Russian Federation [3]. The availability of modern electronic libraries allows us to analyze the causes of death in patients with HIV infection.

The aim of the study is to determine the main causes of death among HIV-infected patients based on data from various studies.

MATERIALS AND METHODS

A group of researchers analyzed full-text articles in the electronic search engines PubMed, Google Scholar, and Elibrary using the keywords: HIV, mortality, cause of death. A total of 287 sources were identified. Subsequently, 28 studies that best corresponded to the research objective were selected. Studies conducted on animals or in pediatrics were not included in the study. The following aspects of the problem were analyzed: ranking of the most common causes of death and ranking of possible diseases within the cause of death from cardiovascular pathology. The average frequency of fatalities

was determined using Microsoft Excel tables, and the significance of the differences between the average values was calculated using the Review Manager program.

RESULTS AND DISCUSSION

According to data from a Swiss cohort study, only 9.0 % of deaths among HIV-infected individuals are associated with acquired immunodeficiency syndrome (AIDS) against a background of opportunistic infections, 22.9 % are due to causes unrelated to AIDS and cancer, 10.2 % of deaths are associated with the development of liver failure, and 9.7 % of deaths occur due to decompensation of cardiovascular diseases [4]. At the same time, according to data from a joint American and European registry, AIDS, cancer, and cardiovascular disease are the leading causes of death among HIV-infected individuals [5]. The incidence of sudden cardiac death among HIV-infected individuals is significantly higher than among people without HIV [6].

According to M. Farahani et al., cardiovascular disease is the most common cause of death in HIV-infected patients, apart from death from AIDS [7]. The study by J. Chelli et al. (2016) indicates that in 44.4 % of cases, the cause of death in HIV-infected patients is opportunistic infections as a manifestation of the AIDS stage, mainly pneumonia [8]. Among HIV-infected patients undergoing inpatient treatment for various reasons, sudden cardiac death and decompensation of cardiovascular diseases as the cause of death occurred in 43.51 % of cases [9]. According to V.A. Narla et al. (2021), the incidence of sudden cardiac death among patients with HIV infection and chronic heart failure (CHF) is 21 % [10]. In 21.8 % of cases, fatal outcomes are observed in HIV-infected patients diagnosed with tuberculosis coinfection [11]. The study by M.S. Freiberg et al. (2021) showed that among patients with HIV in-

fection, there were fewer cases of illness and death from chronic diseases of the tracheobronchial tree and diabetes mellitus than among patients without HIV infection [12].

Based on the results of various studies from different countries around the world and calculations of average mortality rates, it was possible to obtain an overall picture of the spectrum of causes of mortality in patients with

HIV infection (Table 1). While infectious complications and opportunistic infections characteristic of the AIDS stage, as well as associated tuberculosis infection, traditionally rank first (55.1 %), cardiovascular diseases rank second, accounting for a total of about 20.6 %. Slightly less common causes of death are cancer (14.6 %), liver disease, including alcoholic and viral hepatitis and cirrhosis (8.5 %), and only 1.1 % are all other diseases.

While a specialized system of AIDS centers is actively involved in the diagnosis and treatment of infectious diseases and complications associated with HIV infection in Russia, the diagnosis and treatment of cardiovascular disease, liver disease, and cancer are primarily the responsibility of primary health care organizations. The latter requires the development of additional clinical algorithms for diagnosis, treatment, identification of risk factors, and target organs of the disease.

The main diseases of the cardiovascular system – causes of death in patients with HIV infection – are analyzed separately in this study, as this pathology requires a clinical approach that differs from that of an infectious disease specialist. Cardiovascular diseases are the cause of death in 20.6 % of HIV-infected patients. An analysis of the spectrum of cardiovascular diseases – causes of death in HIV patients – was conducted based on data from the current literature.

Table 2 presents a sample of cardiovascular causes of death in HIV-infected patients.

Table 1

**The main causes of death in patients with HIV infection
according to clinical studies by authors from different countries**

Cause of death	Author	Country	Prevalence, %	Number of patients / deaths
AIDS and opportunistic infections	Weber, 2024	Switzerland	9.0	1630/47
	Trickey, 2024	United States	25.0	16897/4222
	Chelli, 2016	Tunisia	44.4	54/24
Oncology	Weber, 2024	Switzerland	22.9	1630/166
	Trickey, 2024	United States	13.7	16897/2314
	Chelli, 2016	Tunisia	9.2	54/ 5
	Yakovlev, 2015	Russia	13.5	52/7
Hepatic insufficiency	Weber, 2024	Switzerland	10.2	1630/166
	Trickey, 2024	United States	6.9	16897/ 1167
Decompensation of CVD and sudden cardiac death	Weber, 2024	Switzerland	9.7	1630 / 158
	Trickey, 2024	The USA	8.3	16897/1406
	Tseng, 2021	The USA	43.5	610 / 265
	Narla, 2021	The USA	21.0	344 / 72
Tuberculosis of various locations	Lelisho, 2023	Spain	21.8	363/79
	Yakovlev, 2015	Russia	36.5	52/19

Note: AIDS – acquired immunodeficiency syndrome, CVD – cardiovascular disease.

Table 2

**Major cardiovascular diseases – causes of death in patients
with HIV infection according to clinical studies by authors from different countries**

Cause of death	Author	Country	Prevalence, %	Number of patients / deaths
Sudden cardiac death	Narla, 2021	The USA	21	2578/540
	Tseng, 2021	The USA	0.05	100000/53,3
	Freiberg, 2021	The USA	1.75	44407/777
	Basel, 2021	The USA	1	2860/30
Myocardial infarction	Hsue, 2019	The USA	5	189/9
	Protasov, 2024	Russia	34	2464/842
ACHF and AHF	Bredy, 2016	The USA	2.6	685/18
	Abeya, 2018	The USA	43	216/ 93
PTE	Alvaro-Meca, 2018	Spain	12.2	1356/1120
ACIS	Alvaro-Meca, 2018	Spain	2.3	1356/32
	Silva-Pinto, 2018	England	13	23/3
Infectious endocarditis	Belyakov, 2016	Russia	17.2	1500/360
	Muñoz-Moreno, 2019	Spain	51.4	1439/290

Note: ACHF – acute decompensation of chronic heart failure, AHF – acute heart failure, ACIS – acute cerebrovascular accident, PTE – pulmonary thromboembolism

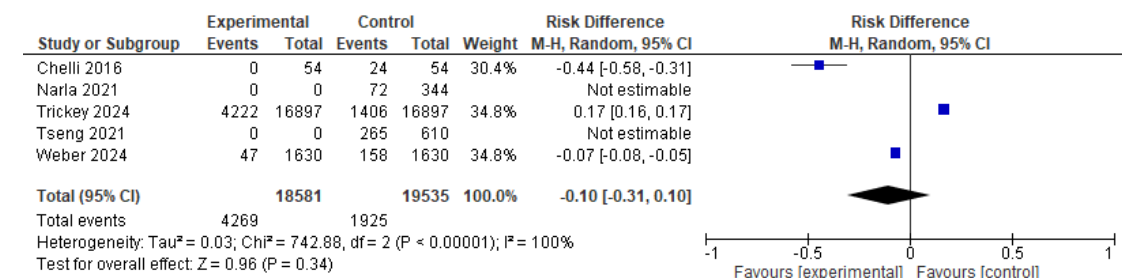
It has been found that infectious endocarditis is the leading cardiovascular cause of death among HIV-infected individuals [13; 14]. The second leading cause of death is acute decompensation of CHF or acute heart failure [15; 16]. Myocardial infarction ranks third among causes of death in HIV-infected individuals [17; 18]. Less common causes of death include pulmonary embolism [19], stroke [19; 20], and sudden cardiac death [9; 10; 12; 21].

According to the data obtained, death from infectious endocarditis, myocardial infarction, sudden cardiac death, acute cerebrovascular accident, pulmonary embolism, and acute decompensation of chronic heart failure to-

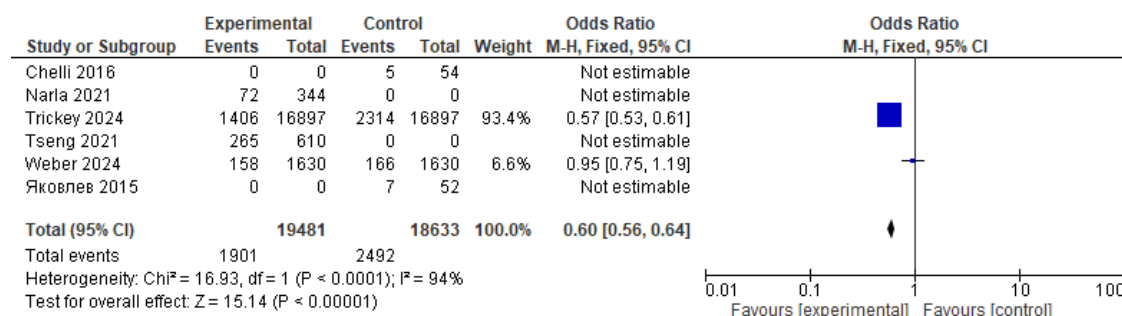
gether account for 82.5 % of all cardiovascular causes of mortality. Other causes account for no more than 17.5 %.

A comparative meta-analysis of deaths from AIDS and opportunistic infections was conducted in comparison with deaths from cardiovascular causes based on the results of a survey of 19,535 patients, whose observation data are described in five clinical studies (Figure, a).

The study found that deaths from AIDS and opportunistic infections were the leading cause of death among HIV-infected patients, compared to deaths from cardiovascular disease ($p = 0.034$).



a



b

Яковлев - Yakovlev

Fig. Comparative meta-analysis of causes of death among HIV-infected individuals:
 a – from AIDS and opportunistic infections and death from cardiovascular disease;
 b – from cardiovascular disease and cancer

According to the data obtained, when comparing cardiovascular and oncological causes of death in HIV-infected patients, cardiovascular causes prevail over oncological pathology ($p < 0.001$) (Figure, *b*).

Thus, we analyzed the causes of death among HIV-infected patients by combining data from 20 studies involving 177,668 HIV-positive patients, among whom 7,804 deaths (4.39 %) were recorded during a follow-up period ranging from 10 days to 6 months. Our analysis showed that HIV-infected individuals die more often from AIDS (26.1 %), HIV + tuberculosis coinfection (29.1 %), and cardiovascular events (20.6 %) than from other causes. People living with HIV are among the most vulnerable patient groups and require increased attention from healthcare professionals. The results obtained emphasize the importance of involving cardiology and therapeutic specialists in the dispensary observation of HIV-infected patients in order to prevent the premature development of adverse endpoints – death from cardiovascular causes.

According to contemporary authors, the incidence of sudden cardiac death is significantly higher among people with HIV infection and concomitant CHF, while effective antiretroviral therapy and timely diagnosis can protect people living with HIV from sudden cardiac death and decompensation of cardiovascular diseases [22].

High mortality rates are observed in cases of HIV + tuberculosis co-infection. Much evidence indicates that HIV-positive patients have socio-demographic factors that contribute to the development of tuberculosis infection, and immunosuppression only exacerbates the situation [23; 24]. Low CD4 T-lymphocyte counts and unsuppressed viral

load correlate more strongly with death from all causes in HIV-infected individuals, as well as from cardiovascular disease. It is known that HIV replication is an iron-dependent process, and an increase in non-transferrin-bound iron levels is associated with the risk of opportunistic infections, while the severity of anemia correlates with a high risk of death in HIV-infected individuals from all causes, regardless of whether they are related to CHF or not [25; 26]. Among the factors indicating imminent death in HIV-infected individuals are the development of severe thrombocytopenia [27; 28], alcoholic cardiomyopathy [29; 30], a decrease in glomerular filtration rate below 60 ml/min/1.73 m² [31], and a low body mass index [32]. Given the significance of cardiovascular disease among the leading causes of mortality in HIV-infected patients, early preventive cardiological examination and monitoring of symptoms and signs of cardiovascular disease are recommended.

CONCLUSIONS

AIDS, opportunistic infections, and tuberculosis are the leading causes of death among HIV-infected patients, according to scientists from various countries around the world. Cardiovascular diseases are the second leading cause of death. Cancer closes out the top three causes of death. The monitoring of HIV-infected patients should be carried out comprehensively, involving infectious disease specialists, therapeutic and cardiological services, with increased cancer awareness. The challenges of HIV infection in terms of the early development of cardiovascular pathology and the high number of deaths from cardiovascular diseases cannot be ignored.

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Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest.

Author contributions:

Tukhasheva F.Y. – searching for literary sources, analyzing information, writing a fragment of the article.

Markova A.V. – searching for literary sources, analyzing information, writing a fragment of the article.

Zhelobov V.G. – idea and design of the final version of the article.

Goryacheva O.G. – idea, concept of the work, meta-analysis;

Malelin E.G. – searching for literary sources, analyzing information, writing a fragment of the article.

Mekhonoshin K.D. – searching for literary sources, analyzing information, writing a fragment of the article.

All authors approved the final version of the article.

Received: 02/18/2025

Revised version received: 07/25/2025

Accepted: 07/30/2025

Please cite this article in English as: Tukhasheva F.Ya., Markova A.V., Zhelobov V.G., Goryacheva O.G., Malelin E.G., Mekhonoshin K.D. Analysis of the causes of lethal outcome in patients infected with human immunodeficiency virus. *Perm Medical Journal*, 2025, vol. 42, no. 4, pp. 55-63. DOI: 10.17816/pmj42455-63