VENTRICULAR EXTRASYSTOLES OF VARIOUS ORIGINS, THE FREQUENCY OF THEIR DETECTION AND THE RELATIONSHIP WITH VARIOUS FACTORS

Rashida R. Mutigullina - independent researcher
Gulnora A. Nagayeva - D.M.Sc., associate professor
Military Medical Institute of the Military Security and Defense University of the Republic of Uzbekistan
rashidochka1985@mail.ru

Abstract. *Ventricular extrasystole (VE) is one of the most common cardiac rhythm disorders detected both in healthy individuals and in patients with cardiovascular diseases. This article reviews data from population-based and clinical studies on the prevalence of ventricular extrasystole and analyzes factors associated with its occurrence. The review demonstrates that the frequency of VE increases with age and is strongly influenced by the duration of electrocardiographic monitoring. Major predictors of ventricular extrasystole include hypertension, smoking, reduced left ventricular ejection fraction, myocardial infarction, thyroid dysfunction, anemia, and occupational stress. Particular attention is paid to the impact of environmental and occupational factors, including air pollution, heat stress, and intensive physical and psycho-emotional workloads. The findings emphasize the importance of early detection and continuous monitoring of ventricular extrasystole, especially among individuals exposed to increased cardiovascular risk factors. A comprehensive assessment of clinical, occupational, and environmental determinants may improve preventive strategies and contribute to reducing the burden of cardiovascular complications associated with ventricular arrhythmias.*

Keywords: *ventricular extrasystole, premature ventricular contractions, ventricular arrhythmias, cardiovascular risk factors, Holter monitoring, thyroid dysfunction, anemia syndrome, occupational stress, air pollution, cardiovascular diseases.*

Prevalence of ventricular extrasystole: analysis of data from population and clinical studies. Many studies describing the prevalence of ventricular extrasystole (VE) originate from ECG databases or Holter monitoring ECG (HMECG)studies among those seeking clinical care, where the prevalence is expected to be elevated. In one of the first major population assessments conducted back in 1962, a survey of 12,2043 U.S. Air Force personnel showed that 7.8 out of 1,000 experienced VE during a 48-second ECG recording, with the prevalence increasing with age. [3]. In a more modern cohort of a multiethnic community-based study of men and women aged 45 to 64 years (ARIC (Atherosclerosis Riskin Communities) study - Risk of atherosclerosis in communities), at least 1 VE occurred in 252 (1.8%) of 14,000 routine 10-second ECGs in participants without heart failure (HF) [2]. In the Cardiovascular Health study, in a cohort of individuals aged at least 65 years at the community level, 243 of 4,710 (5.2%) patients had an ECG during their baseline 10-second ECG after excluding individuals with advanced HF [20]. Unsurprisingly, the prevalence of EE increases as the duration of monitoring increases. In the same ARIC study, a 2-minute ECG revealed FE in 5.5% of the population. [39]. In the Framingham Heart Study, evidence of HE or other more complex ventricular arrhythmias was observed in 12% of people without coronary heart disease (CHD) who were observed for 1 hour [17]. In one population-based study of healthy individuals aged 25-41 years, 24-hour HMECG revealed at least a single VE in 69% of particip D.M.Sc., associate professorants [4].

In another study conducted on a random sample of 1,139 Americans using 24-hour ECG, it was found that extrasystoles account for a median of 0.011% of the total number of heartbeats (interquartile range 0.002%-0.123%) [22]. It was also found that among participants who had repeated 24-hour HMECG in the same population 5 years after the first examination, the median number of extrasystoles per hour increased to 5 (interquartile range 0.1–4.7), and it was 1.2

(interquartile range 0.1–13.8) [37]. These data can be compared with the results obtained using HMECG monitors. For example, Heckbert and colleagues [6] presented the results of a study conducted with 1,122 participants from the MESA (Multi-Ethnic Study of Atherosclerosis) study who used a ZIO patch (manufactured by Rhythm Technologies). In the study, 99.5% of the elderly participants (average age 75 years) showed at least one manifestation of JE. The median number of extrasystoles was 1.9/hour (interquartile range 0.3–12).

From the general health system, it was found that among the 16.8 million California residents who visited emergency departments, hospitals, or outpatient surgical centers between 2005 and 2009, 35,817 (0.2%) had a VE code in their medical records. [20].

The relevance of the study of the prevalence of VE among these patients is due to the unique physical and psychological stresses they are exposed to. In conditions of prolonged training, intense physical exertion and stress typical of this service, the likelihood of cardiac arrhythmias increases significantly. Considering that arrhythmias may not appear at early stages and are often detected only with prolonged monitoring, the use of modern diagnostic methods, in particular HMECG, is necessary for the timely diagnosis and prevention of heart diseases. Thus, in order to ensure the health of these patients and optimize preventive measures aimed at reducing the risk of cardiovascular diseases (CVD), further research is required aimed at early detection, timely and adequate monitoring of VE in this population. This will not only improve the quality of medical care, but also increase the effectiveness of measures to preserve health in the long term.

Predictors of ventricular extrasystole: risk factors and their relation to clinical characteristics. Although the term "predictors" may imply a causal relationship, it is important to emphasize that most studies on this topic simply report characteristics that are statistically significantly associated with the presence of VE or a higher frequency of VE. Most of these studies are cross-sectional, since the presence of VE is almost always determined during the basic visit.

An analysis of the ARIC study showed that older age, male gender, black race, a history of hypertension, the presence of other heart diseases (CHD, digitalis or other antiarrhythmic drugs), higher heart rate (HR), lower level of education and hypomagnesemia were associated with the presence of at least one VE during the 2ndone-minute ECG recording [36]. Other factors, particularly smoking, were not included in this analysis. Among the 1,412 examined, it was found that an increase in age, taller height, and a lower left ventricular ejection fraction (LVEF) were associated with an increase in the frequency of VE after multifactorial adjustment [37] (Fig. 1)

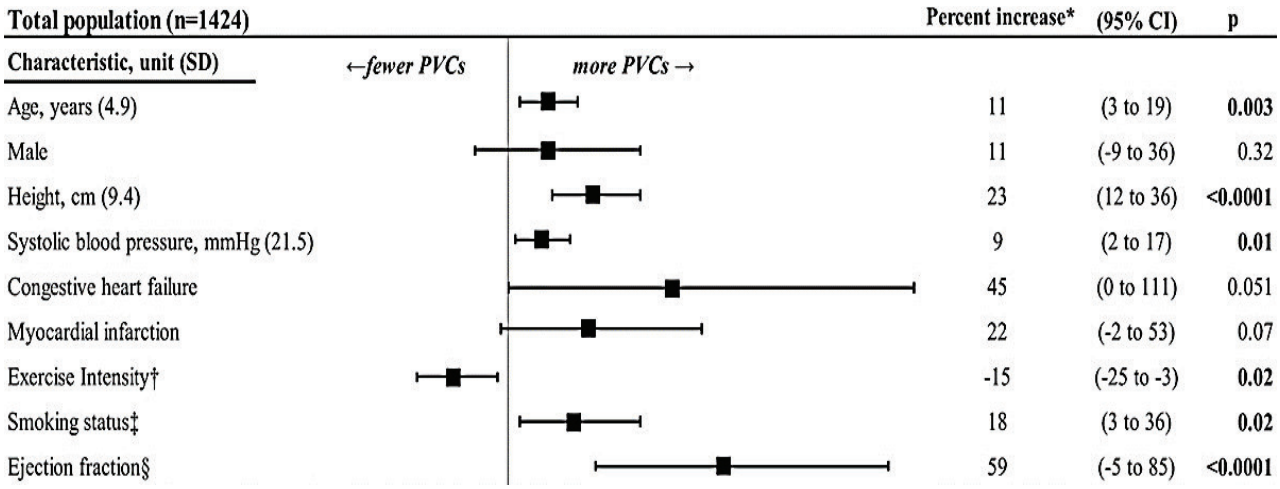


Fig. 1. Multidimensional adjusted predictors of VE frequency.

Notes: *The model includes all the listed covariates.*

** Percentage increase in VE per hour per SD of continuous covariates or the presence (versus absence) of each categorical variable.*

† Dichotomous division into high- and medium-intensity physical exercises versus low-intensity physical exercises and non-physical exercises. The dichotomous division into smokers versus never smokers.

§ Dichotomous separation into abnormal and marginal ejection fraction versus normal ejection fraction. PVCs indicates a premature ventricular complex. [37].

In addition, after taking these factors into account, elevated systolic blood pressure, irregular physical training, and smoking were identified as potentially modifiable risk factors associated with an increase in the incidence of hypertension. Several hundred of these participants underwent a repeated 5-year HMECG study, which provided a rare opportunity to evaluate the predictors of an increase in the number of VE in the population. A history of myocardial infarction, lower LVEF, increased diastolic blood pressure, and smoking were associated with an increase in the frequency of VE over time after multifactorial adjustment [37].

Continuing to consider the predictors of EE, it is necessary to pay attention to several factors that can significantly affect the development and frequency of VE, especially among certain population groups. One of these factors is the state of thyroid hormones. An imbalance in the level of thyroid hormones, in particular hypothyroidism, can contribute to the development of arrhythmias, including VE [4]. The levels of T3 and T4 directly affect the electrical activity of the heart, changing the conduction and excitability of the myocardium. Hypothyroidism, for example, may be associated with an increased frequency of extrasystoles, and hyperthyroidism may be associated with cardiac arrhythmias. This factor should be taken into account when examining patients with suspected arrhythmias.

Basically, arrhythmias in patients with hyperthyroidism are atrial, ventricular arrhythmias are rare and occur in about the same way as in healthy people [28]. Ventricular tachycardia (VT) is one of the main causes of death in patients with cardiovascular diseases (CVD). Ventricular arrhythmia is observed in patients with thyrotoxicosis undergoing antithyroid therapy, although rarely [28, 8]. Ventricular tachycardia usually occurs in connection with background structural heart diseases or HF of various etiologies [1, 33].

In addition, anemia syndrome is another important predictor for the development of VE. Lack of hemoglobin and oxygen in the blood can contribute to myocardial hypoxia, which in turn increases the likelihood of premature ventricular contractions. In addition, anemia syndrome is another important predictor for the development of EE. Lack of hemoglobin and oxygen in the blood can contribute to myocardial hypoxia, which in turn increases the likelihood of premature ventricular contractionanemia, reducing oxygen delivery to tissues, causes hyperstimulation of the autonomic nervous system, which can lead to impaired conduction in the heart and the appearance of extrasystoles. From the point of view of pathological anatomy, the relationship of anemic syndrome with ventricular arrhythmia can be explained by diffuse myocardial fibrosis, which is a well-known substrate for the development of VE, especially in the context of arrhythmogenic triggers such as hypoxemia, acidosis, or cardiac electrical conduction disturbances, which are quite common in this population [32,29,38,16].

Special attention should be paid to specific professions where increased physical and psycho-emotional stress can affect the development of VE. For example, military personnel, pilots, firefighters, and other professionals whose professional activities involve constant stress and physical exertion are at increased risk of extrasystoles. Such people often have a combination of risk factors, such as intense exercise, physical fatigue, stressful situations, and effects on the heart. These loads can cause adaptive changes in cardiac conduction and increase the frequency of VE. Moreover,

professional activity under stress can contribute to an increase in catecholamine levels, which is also associated with the development of arrhythmias.

The sudden death of a young man is always a tragedy. Despite their physical fitness and health, cases of sudden death still occur among this population, although they are quite rare. Studies show that the rates of sudden deaths among recruits range from 2 to 13 per 100,000 recruits, and most of them are due to latent cardiac abnormalities that were not detected during medical examinations [7]. Another study found that in 86% of cases, physical activity was associated with death at the time of exercise [11]. The most common diseases leading to death are coronary artery abnormalities and hereditary cardiovascular disorders such as hypertrophic cardiomyopathy (HCM) and long QT syndrome (LQTS). However, regardless of the cause, most cases of sudden death occur due to ventricular tachyarrhythmia.

The modern rhythm of life, high level of urbanization and technological progress are widely associated with such concepts as air pollution. The latter is an important risk factor for CVD, and patients in this population are also susceptible to these risks, especially in conditions of constant exposure to polluted air at their workplace [27]

Solid particles (PM), which are solid and liquid microparticles suspended in the air, have an impact on health [19]. The particle size can range from hundreds of micrometers (microns) to units of nanometers (nm). The particles are divided by aerodynamic diameters into several fractions [25]:

• large (PM 10) — up to 10 microns,
• small (PM 2.5) — up to 2.5 microns
• Ultrafine particles (UDPS) — up to 100 nanometers.

It is known that the toxicity of particles increases with a decrease in their size, since such particles penetrate more easily into the deep parts of the lungs, creating additional risks for military personnel located in areas with high concentrations of pollutants [14,31,2]. Fine particles are usually formed as a result of combustion processes, which also poses a threat to the health of military personnel performing tasks in conditions of intense emissions and dust [15]. The particle size can serve as an indicator of the source of pollution, since larger particles are usually formed during mechanical processes, but various factors affecting the composition and size of particles, as well as secondary reactions in the atmosphere, make comparing such factors in different regions difficult and require additional analysis [12].

Rising global temperatures are one of the main challenges of the 21st century. According to the Intergovernmental Panel on Climate Change (IPCC), climate change has led to a significant increase in the average global temperature by 1.1°C since pre-industrial times. [26]. The facts show that the current trend of rising global average temperature and the occurrence of frequent, intense, and prolonged extreme heat events will continue in the future unless global action is taken. [35,30,21]. According to the International Labour Organization (ILO), assuming global temperatures rise by 1.5°C by the end of the twenty-first century, it is projected that by 2030 about 2.2% of total working hours and 880,000 years of working life will be lost due to occupational heat stress worldwide [24] .

Exposure to extreme temperature events can lead to many adverse health effects [10, 18]. Compared to the general population, the working population is more vulnerable to heat stress [23]. In some professions, workers are required to wear protective clothing that can prevent sweat evaporation and body heat dissipation, making workers more vulnerable to heat stress [13]. Workers in low- and middle-income countries in tropical and subtropical regions, where heat stress is a particular problem, may be more vulnerable to occupational diseases and heat-related deaths [5]

Conclusion.

Thus, when analyzing risk factors for VE, a wide range of factors should be taken into account, including hormonal changes, anemia, and specific occupational characteristics. This is necessary for more accurate diagnosis and effective prevention of arrhythmias in clinical practice.

REFERENCES

1. Agarwal SK, Simpson RJ, Rautaharju P, Alonso A, Shahar E, Massing M, Saba S, Heiss G. Relation of ventricular premature complexes to heart failure (from the Atherosclerosis Risk In Communities [ARIC] Study). *Am J Cardiol*. 2012;109:105–109. doi: 10.1016/j.amjcard.2011.08.009.

2. Agarwal V, Vittinghoff E, Whitman IR, Dewland TA, Dukes JW, Marcus GM. Relation between ventricular premature complexes and incident heart failure. *Am J Cardiol*. 2017;119:1238–1242. doi: 10.1016/j.amjcard.2016.12.029.

3. Ansah E.W., Ankomah-Appiah E., Amoadu M., Sarfo J.O. Climate change, health and safety of workers in developing economies: a scoping review. J Climate Change Health, 3 (2021), Article 100034, 10.1016/J.JOCLIM.2021.100034

4. BakeerN, James J, Roy S, et al. Sickle cell anemia mice develop a unique cardiomyopathy with restrictive physiology. Proc Natl AcadSci U S A, 113 (35) (2016), pp. E5182.

5. Bikkina M, Larson MG, Levy D. Prognostic implications of asymptomatic ventricular arrhythmias: the Framingham Heart Study. *Ann Intern Med*. 1992;117:990–996. doi: 10.7326/0003-4819-117-12-990.

6. Brunekreef B., Holgate S.T. Air pollution and health. Lancet. 2002;360(9341):1233–1242. doi: 10.1016/S0140-6736(02)11274-8.

7. de Lima C.Z., Buzan J.R., Moore F.C., Baldos U.L.C., Huber M., Hertel T.W. Heat stress on agricultural workers exacerbates crop impacts of climate change. Environ Res Lett, 16 (2021), 10.1088/1748-9326/abeb9f

8. Dukes JW, Dewland TA, Vittinghoff E, Mandyam MC, Heckbert SR, Siscovick DS, Stein PK, Psaty BM, Sotoodehnia N, Gottdiener JS, et al. Ventricular ectopy as a predictor of heart failure and death. *J Am CollCardiol*. 2015;66:101–109. doi: 10.1016/j.jacc.2015.04.062.

9. Eckhart R, Scoville S, Campbell C, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. Ann Intern Med 2004;141:829–34. doi:10.7326/0003-4819-141-11-200412070-00005.

10. el Khayat M., Halwani D.A., Hneiny L., Alameddine I., Haidar M.A., Habib R.R. Impacts of climate change and heat stress on farmworkers' health: a scoping review. Front Public Health, 10 (2022)

11. Green H., Bailey J., Schwarz L., Vanos J., Ebi K., Benmarhnia T. Impact of heat on mortality and morbidity in low and middle income countries: a review of the epidemiological evidence and considerations for future research. Environ Res, 171 (2019), pp. 80-91, 10.1016/J.ENVRES.2019.01.010

12. Harrison R.M., Yin J. Particulate matter in the atmosphere: Which particle properties are important for its effects on health? Sci. TotalEnviron. 2000;249(1-3):85–101. doi: 10.1016/S0048-9697(99)00513-6.

13. Heckbert SR, Austin TR, Jensen PN, Floyd JS, Psaty BM, Soliman EZ, Kronmal RA. Yield and consistency of arrhythmia detection with patch electrocardiographic monitoring: the Multi-Ethnic Study of Atherosclerosis. *J Electrocardiol*. 2018;51:997–1002. doi: 10.1016/j.jelectrocard.2018.07.027.

14. Hiss RG, Lamb LE. Electrocardiographic findings in 122,043 individuals. *Circulation*. 1962;25:947–961. doi: 10.1161/01.cir.25.6.947.

15. International Labor Organization (ILO). Increase in heat stress predicted to bring productivity loss equivalent to 80 million jobs. https://www.ilo.org/global/about-the-ilo/newsroom/news/WCMS_711917/lang-en/index.htm

16. Intergovernmental Panel on Climate Change (IPCC). Global warming of 1.5 °C. Aromar Revi (2018). https://www.ipcc.ch/site/assets/uploads/sites/2/2019/05/SR15_SPM_version_report_LR.pdf

17. Intergovernmental Panel on Climate Change (IPCC) AR6 climate change 2021: the physical science basis (2021) AR6 Climate Change 2021: The Physical Science Basis https://www.ipcc.ch/report/ar6/wg1.

18. Ioannou L.G., Foster J., Morris N.B., Piil J.F., Havenith G., Mekjavic I.B., et al. Occupational heat strain in outdoor workers: a comprehensive review and meta-analysis. Temperature (2022), pp. 1-36, 10.1080/23328940.2022.2030634

19. Kazbanov IV, KHWJ ten Tusscher, Panfilov AV. Effects of heterogeneous diffuse fibrosis on arrhythmia dynamics and mechanism Sci Rep, 6 (1) (2016), Article 20835.

20. Kerola T, Dewland TA, Vittinghoff E, Heckbert SR, Stein PK, Marcus GM. Modifiable predictors of ventricular ectopy in the community. *J Am Heart Assoc*. 2018;7:e010078. doi: 10.1161/JAHA.118.010078.

21. Kerry Purtell, Torsten K. Roepke, Geoffrey W. Abbott. Cardiac arrhythmia and thyroid dysfunction: A novel genetic link. The International Journal of Biochemistry & Cell Biology, Volume 42, Issue 11, 2010:1767-1770. https://doi.org/10.1016/j.biocel.2010.07.013

22. Laden F., Neas L.M., Dockery D.W., Schwartz J. Association of fine particulate matter from different sources with daily mortality in six U.S. cities. Environ. Health Perspect. 2000;108(10):941–947. doi: 10.1289/ehp.00108941.

23. Lynch P, Ineson N, Jones A, et al. Sudden death in sport before and after introduction of the basic fitness test. J R Army Med Corps 1985;131:42–6. doi:10.1136/jramc-131-01-10.

24. MacNee W., Donaldson K. Mechanism of lung injury caused by PM10 and ultrafine particles with special reference to COPD. Eur. Respir. J. Suppl. 2003;40(Suppl. 40):47s–51s.

25. Marrakchi, S., Kanoun, F., Idriss, S., Kammoun, I., and Kachboura, S. (2015). Arrhythmia and thyroid dysfunction. Herz 40(Suppl. 2), 101–109. doi: 10.1007/s00059-014-4123-0.

26. National Aeronautic and Space Administration (NASA). Global temperature. Global Climate Change (2021). https://climate.nasa.gov/vital-signs/global-temperature/ Intergovernmental Panel on Climate Change (IPCC). Special report on climate change and land (2019). https://www.ipcc.ch/site/assets/uploads/2019/11/SRCCL-Full-Report-Compiled-191128.pdf

27. Nguyen KT, Vittinghoff E, Dewland TA, Dukes JW, Soliman EZ, Stein PK, Gottdiener JS, Alonso A, Chen LY, Psaty BM, et al. Ectopy on a single 12-lead ECG, incident cardiac myopathy, and death in the community. *J Am Heart Assoc*. 2017;6:e006028

28. NissO, Fleck R, Makue F, et al. Association between diffuse myocardial fibrosis and diastolic dysfunction in sickle cell anemia. Blood, 130 (2) (2017), 205-213.

29. Osman, F., Gammage, M. D., Sheppard, M. C., and Franklyn, J. A. (2002). Clinical review 142: cardiac dysrhythmias and thyroid dysfunction: the hidden menace? *J. Clin. Endocrinol. Metab.* 87, 963–967. doi: 10.1210/jcem.87.3.8217.

30. Pallikadavath S, Vali Z, Patel R, Mavilakandy A, Peckham N, Clegg M, Sandilands AJ, Ng GA. The Influence of Environmental Air Pollution on Ventricular Arrhythmias: A Scoping Review. CurrCardiol Rev. 2022;18(6):e160422203685. doi: 10.2174/1573403X18666220416203716

31. Palupi A.A.R., Rizky Z.P., Puspita N., Atmajaya H., Ramdhan D.H. Physiological and Psychological Effects of Heat Stress on Automotive Manufacture Workers. KnE Life Sci, 4 (2018), pp. 148-155.

32. Perkins S.E. A review on the scientific understanding of heatwaves—Their measurement, driving mechanisms, and changes at the global scale Atmosph Res, 164–165 (2015), pp. 242-267.

33. Rajagopalan S., Al-Kindi S.G., Brook R.D. Air pollution and cardiovascular disease: JACC state-of-the-art review. J. Am. Coll. Cardiol. 2018;72(17):2054–2070. doi: 10.1016/j.jacc.2018.07.099.

34. Seaton A., MacNee W., Donaldson K., Godden D. Particulate air pollution and acute health effects. Lancet. 1995;345(8943):176–178.

35. Simpson RJ, Cascio WE, Schreiner PJ, Crow RS, Rautaharju PM, Heiss G. Распространенность преждевременных желудочковых сокращений в популяции афроамериканцев и белых мужчин и женщин: исследование риска атеросклероза в сообществах (ARIC). *AmHeart J.* 2002;143:535–540. doi: 10.1067/mhj.2002.12029

36. SunddP, Gladwin M, Novelli E. Pathophysiology of sickle cell disease. Annu Rev PatholMech Dis, 14 (1) (2019), pp. 263.

37. Thorpe A., Harrison R.M. Sources and properties of non-exhaust particulate matter from road traffic: A review. Sci. TotalEnviron. 2008;400(1-3):270–282. doi: 10.1016/j.scitotenv.2008.06.007.

38. von Olshausen, K., Bischoff, S., Kahaly, G., Mohr-Kahaly, S., Erbel, R., Beyer, J., et al. (1989). Cardiac arrhythmias and heart rate in hyperthyroidism. *Am. J. Cardiol.* 63, 930–933. doi: 10.1016/0002-9149(89)90142-2.

39. von Rotz M, Aeschbacher S, Bossard M, Schoen T, Blum S, Schneider S, Estis J, Todd J, Risch M, Risch L, et al. Risk factors for premature ventricular contractions in young and healthy adults. *Heart*. 2017;103:702–707. doi: 10.1136/heartjnl-2016-309632.