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THE PRE-HOSPITAL EMERGENCY HEALTH SERVICES ADHERENCE FOR ACUTE CARDIOGENIC PULMONARY EDEMA TREATMENT PROTOCOLS

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ABSTRACT

INTRODUCTION: Acute Cardiogenic Pulmonary Edema (ACPE) has been the subject of Prehospital Emergency Health Services (PHEMS) for many years and is included in treatment protocols. Although these protocols were created from current literature information with proven accuracy, the rapid developments in the medical literature can sometimes take time to reflect on protocols and some differences may occur between the literature discussions and protocols. This study aimed to examine the differences between PHEMS protocols and current literature discussions in ACPE and the effects of these differences on PHEMS personnel.

MATERIAL AND METHODS: The present study, which was planned in descriptive type, consisted of two stages. In the first stage, the PHEMS protocols were examined worldwide, and seven protocols, which included the ACPE treatment protocols, were evaluated. In the second stage, questions were asked to the participants, including current information about the treatment of ACPE, and whether they followed up-to-date literature information. Participants were asked to answer the questions with their up-to-date knowledge regardless of the PHEMS protocols they were responsible for. The sample consisted of 600 participants and the data were collected between February and April 2022.

RESULTS: It was observed that Continuous Positive Airway Pressure (CPAP) application was included in all the protocols evaluated, that there were differences in nitrate usage dose and furosemide application, and that aggressive nitrate application was not included in any of the protocols. In this study, 67.2% of the participants stated that they followed up-to-date information about their profession; 32.7% would prefer the use of aggressive nitrate in SPD, 33.8% would apply furosemide if the patient did not feel relief after nitrate use, 29.7% would apply morphine sulfate, and 70.5% would apply CPAP if there were an indication.

CONCLUSIONS: The differences between the PHEMS protocols and the current literature on the treatment of ACPE may cause confusion among PHEMS personnel. Further studies are needed to clarify protocols for the aggressive use of nitrates and furosemide. In the case of morphine sulfate use, limitations and side effects should be stated more clearly.

KEYWORDS: acute cardiogenic pulmonary edema; prehospital emergency health services; paramedic; aggressive nitrate use

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INTRODUCTION

Acute Cardiogenic Pulmonary Edema (ACPE) may occur with acute myocardial infarction or ischemia, congestive heart failure, cardiomyopathy, heart valve diseases, arrhythmias, and hypertensive emergencies [1, 2]. ACPE is a life-threatening emergency with a prevalence of 75% to 83% in patients with heart failure and low ejection fraction [3]. In their study, Sert et al. [4] reported the mortality rate for ACPE was 13.8%. Severe hypoxia may develop due to respiratory failure for ACPE, and as a result, organ damage or multiple organ failure may occur [3, 5]. Whatever causes the occurrence of ACPE, it should be recognized and treated quickly [6]. Pre-hospital Emergency Health Services (PHEMS) provided for ACPE are considered a life-saving intervention. In this process, the correct organization and rapid intervention are of crucial importance [7, 8]. It is stated that the survival of patients who receive PHEMS is twice as long as those who start their treatment in the emergency room [1].

ACPE has been the subject of PHEMS for many years and is included in PHEMS treatment protocols. PHEMS treatment protocols are off-line medical control tools that set the standards that PHEMS personnel should follow in service delivery. It is expected that PHEMS treatment protocols will be created from current literature information with proven accuracy [9]. However, the rapid developments in the medical literature can sometimes take time to reflect on the PHEMS treatment protocols. In this case, some differences may occur between the current literature discussions and PHEMS treatment protocols. There may be some differences in the PHEMS protocols on issues with no full agreement in the literature. It is possible that the differences between current literature discussions and PHEMS protocols may create some dilemmas for PHEMS personnel, who consider an important professional responsibility to follow up-to-date scientific knowledge [7, 10]. When evaluated from these perspectives, ACPE, in which the debate on the use of aggressive nitrate and furosemide continues in the literature, is a vital issue in treating PHEMS and is seen as a subject worthy of study.

This study aimed to evaluate the effects of the differences between current literature discussions and the PHEMS protocols on PHEMS personnel in the treatment of ACPE. The decisive role of PHEMS personnel for ACPE, where PHEMS saves lives with early and correct organization, makes this study significant.

MATERIAL AND METHODS

This descriptive study consisted of two phases. In the first stage, ACPE protocols were evaluated in PHEMS treatment protocols. In this context, protocols worldwide were examined, and seven protocols, which included ACPE treatment protocols, were evaluated. These protocols were Türkiye Prehospital Protocols 2009 (Protocol 1) [11], USA Massachusetts Prehospital Protocols 2022 (Protocol 2) [12], USA Connecticut Prehospital Protocols 2022 (Protocol 3) [13], Canada BCEHS Clinical Practice Guidelines 2021 (Protocol 4) [14], Australian Clinical Practice Guidelines 2019 (Protocol 5) [15], Irish Clinical Practice Guidelines 2021 (Protocol 6) [16] and Israel Prehospital Protocols 2016 (Protocol 7) [17]. Protocol 1 was included in the present study because this study was conducted in Türkiye. For other protocols included in the study, all EMS protocols that serve according to the Anglo-Saxon system and whose web pages can be accessed were systematically examined. Among these protocols, those with cardiogenic pulmonary edema protocol were included. Only one of the protocols that were exactly similar to each other was included in this study. In this direction, the PHEMS protocols of 50 states in the USA were examined, and among these protocols, those with ACPE care protocols were selected. Among them, two up-to-date protocols (Protocol 2 and Protocol 3) were included in this study. Other protocols were not included because they were similar to each other. The other four protocols were selected from the current protocols including the treatment protocols of ACPE among the 30 protocols presented in PHEMS according to the Anglo-Saxon system worldwide (Fig. 1).

The data from the field study, which constituted the second stage of this research, were collected between February and April 2022. The study population consisted of paramedics who were members of the Paramedic and Prehospital Emergency Medicine Association (PARHAD), the largest professional association of paramedics in Türkiye and actively worked in the PHEMS system (n = 1500). The OpenEpi program was used while calculating the sample size of this study. The sample size was determined as 306 people from the population of 1500 people with a 50% prevalence, 5% margin of error, and 95% confidence interval with the help of the OpenEpi program. In this study, an invitation to participate in the present study was sent to the entire universe, and 600 participants agreed to participate.

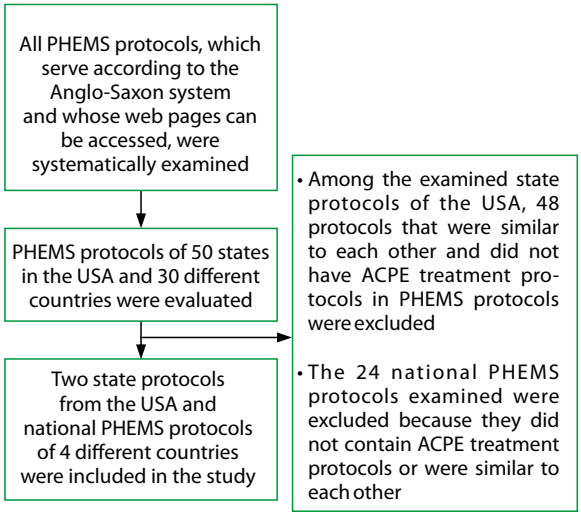

FIGURE 1. Flow chart showing the protocol identification

Research data were collected with a questionnaire form created in light of current literature information. In the questionnaire, together with the questions defining the participants, five questions were asked, including the status of the PHEMS personnel to follow up-to-date information about their professional fields and the treatment of ACPE. Participants were asked to answer the questions with their up-to-date knowledge regardless of the PHEMS protocols they were responsible for. The created questionnaire was sent to 10 experts in the field, and the form was finalized in line with the expert opinions. Data were collected online.

Data analysis

The data analysis obtained from this research results was performed with the Statistical Package for Social Science (IBM SPSS Statistics 24) program. Frequency distribution and chi-square test were used to determine the relationship between independent variables and dependent variables. The results were evaluated within the 95% confidence interval, and $p < 0.05$ was considered statistically significant.

Ethical disclosures

This study was conducted in accordance with the Declaration of Helsinki and was approved by the decision of the Medical Research Ethics Committee of the Deanship of the Faculty of Medicine of Ege University, dated 22.11.2021 and numbered 21-11.1T/29. Written permission was obtained from PARHAD to conduct this study with its members.

RESULTS

Among the PHEMS treatment protocols evaluated within the scope of this study, in Protocols 1, 2, 5, 6, and 7 the use of nitrate, furosemide, and CPAP application was included in the treatment of ACPE, while morphine sulfate was not included [11, 12, 15–17]. In Protocol 3, nitrate use and CPAP application were included in the treatment of ACPE, furosemide and morphine use were not included [13]. Protocol 4 included using nitrate, furosemide, morphine sulfate, and CPAP application [14] (Tab. 1).

When the nitrate application method and dose recommendations in the treatment of ACPE were examined:

— in Protocols 1, 3, and 4, if systolic blood pressure (SBP) is > 100 mmHg, nitrate is applied and can be repeated up to three times if blood pressure is appropriate and symptoms persist [11, 13, 14];
— in Protocol 2, if systolic blood pressure (SBP) is > 120 mmHg, nitrate is administered and can be repeated up to three doses [12];
— in Protocol 5, if systolic blood pressure (SBP) is > 110 mmHg, nitrate is administered and can be repeated up to three doses [15];
— in Protocol 6, if systolic blood pressure (SBP) is > 100 mmHg, nitrate is administered and can be repeated only once [16];

Table 1. Application recommendations for acute cardiac pulmonary edema treatment of examined protocols

Protocols Application	Protocol 1	Protocol 2	Protocol 3	Protocol 4	Protocol 5	Protocol 6	Protocol 7
Nitrate use	+*	+	+	+*	+	+	+
CPAP application	+	+	+	+	+	+	+
Morphine use	–	–	–	+*	–	–	–
Furosemide use	+*	+*	–	+	+	+	+

*Online medical controller approval is required

Table 2. The distribution of the participants' knowledge of following up-to-date information and the treatment of ACPE

Variables	N	[%]
Do you follow up-to-date information about your profession?		
Yes	403	67.2
No	7	1.1
Sometimes	190	31.7
What is your opinion about the use of furosemide in the treatment of ACPE?		
If the patient does not feel relief after nitrate use, I apply furosemide	314	52.4
I apply furosemide before using nitrate	203	33.8
I do not prefer to apply furosemide	83	13.8
Total	600	100
Do you apply morphine sulfate in the treatment of ACPE?		
Yes	178	29.7
No	422	70.3
Total	600	100
Would you apply PHEMS CPAP if there is an indication in the treatment of ACPE?		
Yes	423	70.5
No, I prefer to leave the intervention to the hospital	177	29.5
Total	600	100

— in Protocol 7, SL spray is applied when systolic blood pressure (SBP) is > 100 mmHg; if a sufficient effect is not achieved, IV nitrate is administered [17];
— aggressive nitrate use was not included in any of the protocols.

In the field research conducted within the scope of this study, 67.2% of the participants stated that they followed up-to-date information about their profession and 33.8% they would apply furosemide if the patient did not feel relief after nitrate use in treating ACPE. 29.7% of the participants stated that they could apply morphine sulfate in treating ACPE and 70.5 indicated this (Tab. 2).

In this study, 32.7% of the participants stated that they would prefer the use of aggressive nitrates in treating ACPE, and 30% would administer a single dose of nitrate, repeated every 3–5 minutes, in patients with respiratory distress as long as systolic blood pressure (SBP) was above 100 mmHg. Also, 9.13% of the participants stated that they would apply a single dose of nitrate and would not repeat it. On the other hand, 28% of the participants stated that they would not use nitrate for ACPE (Tab. 3).

No statistically significant relationship was found between independent variables and dependent variables (p greater than 0.05).

DISCUSSION

For ACPE, which has a high mortality rate and the clinical course can change in seconds, the interventions of PHEMS personnel at the scene are life-saving [1, 10]. There seems to be confusion in the literature and PHEMS protocols, especially regarding the recognition and treatment of ACPE [20]. Although the adherence of PHEMS personnel to treatment protocols in PHEMS is crucial, nowadays, besides the ease of access to information, personnel can be fed from different sources of information as a requirement for their professional development [9]. In this study, two-thirds of the participants stated that they regularly followed the current literature. ACPE is a special issue where there are many disagreements in both the literature and the PHEMS protocols. The high mortality rate for ACPE cases makes the discussions even more significant.

Table 3. Nitrate use of participants on the treatment of ACPE

How do you manage aggressive Nitrate (Isordil 5 mg, SL spray 0.4 mg) therapy in acute pulmonary edema of cardiac origin?		
Variables	N	[%]
I apply aggressive nitrate*	196	32.7
As long as the systolic blood pressure is above 100 mmHg, I administer a single dose of nitrate, repeated every 3–5 minutes, in patients with respiratory distress.	180	30
I apply a single dose of Nitrate; I do not repeat the dose	56	9.3
I don't use nitrate	168	28
Total	600	100

*Aggressive nitrate use was asked as three doses if the systolic blood pressure is above 180 mmHg, two doses if it is between 140 and 180 mmHg, and a single dose of nitrate if it is between 100 and 140 mmHg [18, 19]

Respiratory distress is the most important reason for calling an ambulance for ACPE cases [21]. It has been observed that CPAP application to patients with respiratory distress in PHEMS has become quite common in recent years, and the application has positive effects on improving the clinical condition of the patients and mortality. Austin et al. [22] study showed that CPAP application for ACPE cases in PHEMS caused a 76% decrease in mortality rate compared to treatment with a typical mask and mask with reservoir. The duration of hospitalization was significantly reduced. Many studies show that CPAP application for ACPE reduces the mortality rate and the need for endotracheal intubation of patients [23, 24]. In all of the PHEMS treatment protocols reviewed in this study, CPAP is recommended for patients with severe respiratory distress. Most of the paramedics participating in this study state that they may prefer CPAP application in severe respiratory distress. This finding suggests that there is a significant compromise in applying CPAP in the treatment of severe respiratory distress for ACPE.

Studies showed that patients who had received nitrate in PHEMS for ACPE cases had an improvement in blood pressure and oxygen saturation when they were brought to the hospital emergency department compared to those who did not [25, 26]. Thanks to nitrate application, the need for mechanical ventilation and endotracheal intubation of patients is reduced. In addition, the length of hospitalization and the hospitalization rate in intensive care units decrease. After nitrate is used, it turns into nitric oxide, a strong vasodilator in the body; low doses of nitrates provide venodilation, while higher doses provide arteriodilation. In arteriodilation, blood pressure decreases, and both the preload and afterload of the heart are reduced. This provides a significant improvement in mortality for ACPE [18, 19]. In all of the PHEMS protocols examined, for ACPE cases, if the patient's systolic blood pressure is appropriate, the first recommended drug is nitrate. However, none of them includes aggressive nitrate administration. In other words, high-dose nitrate administration in patients with appropriate blood pressure for ACPE has not yet taken its place in PHEMS protocols. Although it is not included in the protocols, it is understood that a significant part of PHEMS personnel considers aggressive nitrate application as an important application. Another crucial datum was that about one-third of the participants stated that they might not use nitrate for ACPE. There appears to be severe confusion among PHEMS personnel regarding using nitrate for ACPE.

There are studies showing that the use of furosemide in the treatment of ACPE increases the risk of kidney damage, the rate of intubation, and the hospitalization rate of patients in intensive care, compared to nitrate administration [27]. However, it has an effect on morbidity and mortality by causing chronic kidney damage and the progression of cardiovascular diseases [28]. Although there is a lack of controlled studies on the benefit of using furosemide in the treatment of ACPE, its use in patients with fluid overload is recommended in some studies [8]. However, the current approach in the treatment of ACPE has focused on reducing preload with aggressive nitrate administration and non-invasive ventilation instead of diuresis with furosemide [29]. For ACPE cases, the correct treatment and the use of the correct drugs in the PHEMS process are significant for the patient to return to his daily life. Thus, the benefits of the drugs to be administered

should always outweigh the risks [30]. Furosemide application is still in place in all protocols examined in this study, except for Protocol 3. Despite this, only 14% of the participants in this study avoided the application for ACPE cases, although furosemide was recommended in the PHEMS Protocol. Although there is some confusion among PHEMS personnel in the application of furosemide in the treatment of ACPE, further studies on using furosemide are needed to develop protocols.

Morphine sulfate, together with its anxiolytic effect, reduces the sensitivity of the brain to oxygen, making the patient less aware of the respiratory distress experienced [1]. Morphine sulfate has severe side effects, such as respiratory depression, hypotension, and reduction in cardiac output, which are reflected in the literature [8]. In current studies, it is seen that the use of morphine sulfate for ACPE cases can cause severe harm to patients [31, 32]. Morphine sulfate application for ACPE increases the need for tracheal intubation, the hospitalization rate in intensive care units, the length of hospital stay, and the mortality rate [1, 8, 33–35]. Among the protocols examined in this study, only Protocol 4 includes a recommendation for morphine sulfate. In addition, although the use of morphine sulfate is not recommended in Protocol 1, almost one-third of the participants state that they use morphine sulfate in ACPE. The inadequacy of prehospital workers' compliance with the ACPE protocol is because there are studies in the literature suggesting Morphine as a standard treatment in the treatment of ACPE [20]. In addition, the low awareness of the pre-hospital staff about the negative effects of morphine sulfate may be effective in this situation. Due to time pressure and stressful patient management, pre-hospital staff may use morphine sulfate to quickly control existing dyspnea and anxiety, rather than wait for respiratory distress to improve with treatment [31]. Although it has almost no place in the prehospital treatment of APCE, it is noteworthy that there is still confusion in the literature regarding the use of morphine sulfate, which can cause severe side effects.

CONCLUSIONS

Regardless of the protocols they are responsible for when PHEMS personnel are asked about their knowledge of treatment approaches, there may be differences between the treatment practices they want to apply and the protocols. There appears to be a significant compromise in the application of CPAP in the PHEMS treatment of ACPE cases. More studies are needed to clarify protocols for the aggressive use of nitrate and furosemide. Using morphine sulfate, usage limitations, and side effects should be explained more clearly.

Limitations

One of the limitations of this study is the inability to reach the participants face-to-face due to the COVID-19 process. Data collection only online has negatively affected the number of accessible participants in the universe. We should note that 50% prevalence, 5% margin of error, and 95% confidence interval from the population of 1500 people were met, but it was predicted that the number of accessible participants would be much higher if the data were collected together with online and face-to-face. In addition, among the countries where the evaluated protocols are applied, only PHEMS personnel working in Türkiye were determined as the study population. Personnel in other countries were not included in this study under the protocols in force in their own countries. In further studies, it would be beneficial to conduct studies with emergency healthcare personnel working in different countries to compare protocol applications.

Article information and declarations

Data availability statement

None.

Ethics statement

This study was conducted in accordance with the Declaration of Helsinki and was approved by the decision of the Medical Research Ethics Committee of the Deanship of the Faculty of Medicine of Ege University, dated 22.11.2021 and numbered 21-11.1T/29. Written permission was obtained from PARHAD to conduct this study with its members.

Author contributions

Durmuş and Ekşi conceived the study; Durmuş and Ekşi researched the data; Durmuş and Ekşi made a survey and statistical analysis; Durmuş and Ekşi wrote, reviewed and edited manuscript.

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Jaskółowska J, Gaszyński T. Prehospital management of the cardiogenic pulmonary edema. Journal of Public Health Nursing and Medical Rescue. 2019; 2: 43–48, doi: https://doi.org/10.48236/jphnmr.v2i.77.
2. Johnson JM. Management of acute cardiogenic pulmonary edema: a literature review. Adv Emerg Nurs J. 2009; 31(1): 36–43, doi: 10.1097/TME.0b013e3181946fd8, indexed in Pubmed: 20118852.
3. Iqbal, M. A.,Gupta, M. Cardiogenic pulmonary edema. In: StatPearls. StatPearls Publishing, Treasure Island (FL). 2019. https://europepmc.org/article/nbk/nbk544260#abstract (15.12.2022).
4. Sert ET, Kokulu K, Gul M, et al. Predictors of in-hospital mortality in patients admitted to the emergency department with cardiogenic pulmonary edema. , doi: 10.22541/au.164864518.86827807/v1.
5. Sureka B, Bansal K, Arora A. Pulmonary edema — cardiogenic or noncardiogenic? J Family Med Prim Care. 2015; 4(2): 290, doi: 10.4103/2249-4863.154684, indexed in Pubmed: 25949989.
6. Elsaka O. Cardiogenic pulmonary edema. Asian Journal of Research in Cardiovascular Diseases. 2021; 3(4): 1–9, doi: 10.5281/zenodo.5749770.
7. Howard I, Castle N, Shaikh LAl, et al. Safety and efficacy of a prehospital initiated protocol of nitrates plus non-invasive ventilation on prehospital and Emergency Department outcomes for acute cardiogenic pulmonary oedema. [preprint]. 2021, doi: 10.1101/2021.10.17.21265081.
8. Purvey M, Allen G. Managing acute pulmonary oedema. Aust Prescr. 2017; 40(2): 59–63, doi: 10.18773/austprescr.2017.012, indexed in Pubmed: 28507398.
9. Ekşi A. Prehospital emergency health services. EMA Medical Bookstore, Istanbul 2021.
10. Hodroge SS, Glenn M, Breyre A, et al. Adult patients with respiratory distress: current evidence-based recommendations for prehospital care. West J Emerg Med. 2020; 21(4): 849–857, doi: 10.5811/westjem.2020.2.43896, indexed in Pubmed: 32726255.
11. Turkey Prehospital Protocols, 2009. https://www.resmigazete.gov.tr/eskiler/2009/03/20090326-4-1.pdf (30.01.2023).
12. Canada BCEHS Clinical Practice Guidelines, 2021. https://handbook.bcehs.ca/Content/cpgmedia/BCEHS_ClinicalPracticeGuidelines.pdf (30.01.2023).
13. USA Connecticut Prehospital Protocols, 2022. https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/ems/pdf/statewide_protocols/2022/v20221_CTEMSStatewideProtocols_Apr2022-final.pdf (30.01.2023).
14. USA Massachusetts Prehospital Protocols, 2022. https://www.mass.gov/doc/emergency-medical-services-statewide-treatment-protocols-version-20221-effective-june-1-2022/download (30.01.2023).
15. Australian Clinical Practice Guidelines, 2019. https://www.ambulance.vic.gov.au/wp-content/uploads/2022/11/AVCPG-v6-18112022.pdf (30.01.2023).
16. Irish Clinical Practice Guidelines, 2021. https://www.phecit.ie/PHECC/Clinical_Resources/Clinical_Practice_Guidelines__CPGs_/2021_edition_CPGs.aspx (30.01.2023).
17. Israel Prehospital Protocols, 2016. https://www.mdais.org/media/1730/%D7%A4%D7%A8%D7%95%D7%98%D7%95%D7%A7%D7%95%D7%9C%D7%99%D7%9D-2016.pdf (30.01.2023).
18. Twiner MJ, Hennessy J, Wein R, et al. Nitroglycerin use in the emergency department: current perspectives. Open Access Emerg Med. 2022; 14: 327–333, doi: 10.2147/OAEM.S340513, indexed in Pubmed: 35847764.
19. Ekşi A. Prehospital emergency care in cardiovascular system emergencies. EMA Medical Bookstore, Istanbul 2022.
20. Ingbar DH. Cardiogenic pulmonary edema: mechanisms and treatment — an intensivist's view. Curr Opin Crit Care. 2019; 25(4): 371–378, doi: 10.1097/MCC.0000000000000626, indexed in Pubmed: 31116110.
21. Cekmen B, Bildik B, Bozan O, et al. Utility of non-invasive synchronized intermittent mandatory ventilation in acute cardiogenic pulmonary edema. Am J Emerg Med. 2022; 56: 71–76, doi: 10.1016/j.ajem.2022.03.044, indexed in Pubmed: 35367682.
22. Austin MA, Wills K, Kilpatrick D, et al. Continuous positive airway pressure plus low flow oxygen versus usual care of severe acute cardiogenic pulmonary edema in the pre-hospital setting: A randomised controlled trial. F1000Research. 2018; 7: 708, doi: 10.12688/f1000research.14577.1.
23. Killeen BM, Wolfson AB. Noninvasive positive pressure ventilation for cardiogenic pulmonary edema. Acad Emerg Med. 2020; 27(12): 1358–1359, doi: 10.1111/acem.13986, indexed in Pubmed: 32298495.
24. Bello G, De Santis P, Antonelli M. Non-invasive ventilation in cardiogenic pulmonary edema. Ann Transl Med. 2018; 6(18): 355, doi: 10.21037/atm.2018.04.39, indexed in Pubmed: 30370282.
25. Patrick C, Ward B, Anderson J, et al. Feasibility, effectiveness and safety of prehospital intravenous bolus dose nitroglycerin in patients with acute pulmonary edema. Prehosp Emerg Care. 2020; 24(6): 844–850, doi: 10.1080/10903127.2020.1711834, indexed in Pubmed: 31900011.
26. Perlmutter MC, Cohen MW, Stratton NS, et al. Prehospital treatment of acute pulmonary edema with intravenous bolus and infusion nitro-

glycerin. Prehosp Disaster Med. 2020; 35(6): 663–668, doi: 10.1017/S1049023X20001193, indexed in Pubmed: 33023684.

27. López-Rivera F, Cintrón Martínez HR, Castillo LaTorre C, et al. Treatment of hypertensive cardiogenic edema with intravenous high-dose nitroglycerin in a patient presenting with signs of respiratory failure: a case report and review of the literature. Am J Case Rep. 2019; 20: 83–90, doi: 10.12659/AJCR.913250, indexed in Pubmed: 30662059.
28. McMahon BA, Chawla LS. The furosemide stress test: current use and future potential. Ren Fail. 2021; 43(1): 830–839, doi: 10.1080/0886022X.2021.1906701, indexed in Pubmed: 33971784.
29. Pescatore R. What to D.O. Shift Away from Loop Diuretics for Pulmonary Edema. Emergency Medicine News. 2021; 43(7): 5–5, doi: 10.1097/01.eem.0000758780.53311.a0.
30. Brown H. Furosemide: properties, alternatives, and the medication approval process.student writing, 33. 2017. https://commons.vccs.edu/student_writing/33 (26.12.2022).
31. Chioncel O, Metra M. Morphine in acute pulmonary oedema: a signal of harm but more questions than answers. Eur J Heart Fail. 2022; 24(10): 1963–1966, doi: 10.1002/ejhf.2698, indexed in Pubmed: 36161434.
32. Al-Ani M, Ismael M, Winchester D. Morphine in acute pulmonary oedema treatment. Current Emergency and Hospital Medicine Reports. 2017; 5(2): 88–93, doi: 10.1007/s40138-017-0131-8.
33. Witharana TN, Baral R, Vassiliou VS. Impact of morphine use in acute cardiogenic pulmonary oedema on mortality outcomes: a systematic review and meta-analysis. Ther Adv Cardiovasc Dis. 2022; 16: 17539447221087587, doi: 10.1177/17539447221087587, indexed in Pubmed: 35343809.
34. Gil V, Domínguez-Rodríguez A, Masip J, et al. Morphine use in the treatment of acute cardiogenic pulmonary edema and its effects on patient outcome: a systematic review. Curr Heart Fail Rep. 2019; 16(4): 81–88, doi: 10.1007/s11897-019-00427-0, indexed in Pubmed: 31183779.
35. Domínguez-Rodríguez A, Suero-Mendez C, Burillo-Putze G, et al. MIMO (MIdazolam versus MOrphine) Trial Investigators. Midazolam versus morphine in acute cardiogenic pulmonary oedema: results of a multicentre, open-label, randomized controlled trial. Eur J Heart Fail. 2022; 24(10): 1953–1962, doi: 10.1002/ejhf.2602, indexed in Pubmed: 35780488.