ORIGINAL ARTICLE

The importance of fluid balance in critically ill patients: a retrospective observational study

Ewa Trejnowska[1], Szymon Skoczyński[2], Paul Armatowicz[3], Małgorzata Knapik[1], Paulina Kurdyś[4], Krystian Ślusarz[4], Magda Tarczyńska-Słomian[5], Piotr Knapik[1]

1 Department of Cardiac Anesthesia and Intensive Therapy, Silesian Centre for Heart Diseases, Zabrze, Medical University of Silesia, Zabrze, Poland
2 Department of Pneumonology, School of Medicine in Katowice, Medical University of Silesia, Katowice, Poland
3 Department of General, Endocrine and Vascular Surgery, Medical University of Warsaw, Warsaw, Poland
4 Students' Scientific Circle, Department of Cardiac Anesthesia and Intensive Care, Medical University of Silesia, Katowice, Poland
5 3rd Department of Cardiology, Silesian Centre for Heart Diseases in Zabrze, Zabrze, Poland

KEY WORDS
critically ill patients, fluid balance, intensive care unit

EDITORIAL
by Bichovsky, Klein, and Brotfain, see p. 1121

ABSTRACT

BACKGROUND Fluid therapy in critically ill patients remains one of the most demanding and difficult aspects of care. This is particularly important in patients admitted to the intensive care unit (ICU) due to cardiovascular disorders.

AIMS The aim of this study was to investigate whether a cumulative fluid balance (FB) affects mortality in critically ill patients hospitalized at the ICU.

METHODS Data were obtained from the medical records of the ICU at the Silesian Centre for Heart Diseases. All patients admitted to the ICU between 2012 and 2016 were evaluated. Patients who died or were discharged from the ICU within 48 hours from admission were excluded. Fluid balance and the type of fluids infused during the first 7 days were assessed. The primary outcome was ICU mortality.

RESULTS Overall, 495 patients were included in the study and 303 (61.2%) survived the ICU stay. Daily FB in the first 24, 48, and 72 hours after admission and the cumulative FB after 7 days were significantly lower in survivors. Fluid balance exceeding 1000 ml and the use of colloid solutions in the first 72 hours were independently associated with mortality, along with the diagnosis of stroke and shock on admission.

CONCLUSIONS A positive FB exceeding 1000 ml in the first 72 hours from admission to the ICU is independently associated with an increased risk of mortality in critically ill patients with cardiovascular disorders. The use of colloid solutions is associated with a higher positive FB.

Correspondence to:
Ewa Trejnowska, MD, PhD, Department of Anaesthesiology, Intensive Therapy and Emergency Medicine, Silesian Centre for Heart Diseases, Medical University of Silesia, ul. Marii Skłodowskiej-Curie 9, 41-800 Zabrze, Poland, phone: +48 32 273 27 31, email: ewatrejnowska@gmail.com
Received: May 8, 2019.
Revision accepted: September 25, 2019.
Published online: September 26, 2019.
Kardiol Pol. 2019; 77 (12): 1147-1154
doi:10.33963/KP.14991

INTRODUCTION Fluid resuscitation in the setting of impaired organ perfusion is recognized as the mainstay of management in critically ill patients. Despite the fact that fluid administration is a common therapeutic intervention in the ICU, appropriate fluid management in critically ill patients is still one of the most challenging tasks in intensive care.

Fluid resuscitation is particularly important in patients admitted to the ICU with hypotension caused by severe cardiac dysfunction. The purpose of fluid resuscitation is to increase venous return and stroke volume, as this is crucial for achieving hemodynamic stability and improving tissue oxygenation.[1,2] Cardiogenic shock with clinical signs of hypoperfusion and / or elevated serum lactate levels of more than 2 mmol/l, despite adequate fluid resuscitation, poses a direct threat to patients admitted to the ICU with disorders that result from cardiac and multiorgan failure.[3] Several studies have indicated that a positive cumulative fluid balance (FB) is a strong predictor of mortality in sepsis and septic shock.[4-8] Nonetheless, there is scarce evidence on a correlation between FB and mortality in critically ill patients with cardiovascular disorders. It has not been confirmed whether the benefit of restricted fluid management also applies to this population. Therefore, the aim of this

WHAT'S NEW?

Appropriate fluid management in critically ill patients is one of the most challenging tasks in intensive care. Sufficient fluid resuscitation is important for stabilizing the hemodynamic status and improving tissue oxygenation. However, there is a proven correlation between fluid overload and adverse outcomes in critically ill patients. In our study, we emphasized the importance not only of the fluid balance but also of the fluid administered during the first 3 days of therapy. This observation has 2 implications. On one hand, it shows that a positive fluid balance in the first 72 hours of treatment is associated with an increased risk of death. On the other hand, it indicates a group of patients who require a larger fluid volume to achieve stabilization. These patients are at increased risk of death and should be managed with particular caution.

study was to investigate whether a cumulative FB has an influence on mortality in critically ill patients hospitalized at the ICU.

METHODS Data were obtained from the medical records of the ICU at Silesian Centre for Heart Diseases, Katowice, Poland. The center includes 5 departments of cardiology, department of cardiac surgery and transplantation, department of vascular surgery (supported by a postoperative intensive care unit), and a general ICU providing care mainly to acutely ill cardiovascular patients from the center itself and those transferred for more specialized treatment from nearby local hospitals.

Retrospective data were obtained from the medical records of the general ICU. Patients older than 18 years and admitted to the ICU between January 1, 2012 and December 31, 2016 were included in the study. Patients who died or were discharged from the ICU within 48 hours from admission or those with incomplete data were excluded.

Parameters selected for analysis included: main diagnosis on admission, medical status on admission to the ICU (mechanical ventilation, catecholamines, etc), basic demographic data, and major comorbidities such as arterial hypertension, coronary artery disease, history of myocardial infarction, stroke, or cardiac arrest, heart failure before admission, diabetes, extracardiac vascular disease, and chronic kidney disease.

Heart failure was defined as a set of typical symptoms (ie, dyspnea, edema of the lower limbs, reduced exercise tolerance), which may be accompanied by abnormalities on physical examination (such as lung scarring, peripheral edema), caused by disturbances in cardiac structure and/or function that lead to reduced cardiac output and/or increased intracardiac pressure at rest or during exercise.[3]

Chronic kidney disease was defined as structural or functional abnormalities of the kidney present for more than 3 months, with health implications. An increase in the serum creatinine level more than 1.5 fold from baseline was considered as acute kidney injury according to Kidney Disease Improving Global Outcome criteria.[9] Heart failure and chronic kidney disease were diagnosed on admission or based on a patient's medical records.

Septic shock was defined as a subset of sepsis in which the underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality.[10]

Total fluid input (including colloids, crystalloids, blood products, total parenteral and enteral nutrition, enteral feeding, and fluid intake associated with various medications) as well as total fluid output were recorded on a daily basis during the first 7 days. The types of fluids infused were also evaluated. Total fluid input was broadly divided into colloids and crystalloids and assessed separately.

Patients were admitted to the ICU at various times of the day. Therefore, to obtain precise information on daily FB, we constantly calculated fluid input and output during 24 hours. The time when the patient was admitted to the ICU was considered as the first hour of the 24-hour period. After that, days were counted according to 24-hour intervals. Patients were treated according to the standard policies and procedures adopted in the ICU. The attending physician determined the amount and type of fluid based on hemodynamic parameters and symptoms of hypoperfusion.

Statistical analysis Data of patients who survived and who died in the ICU were compared using the *t* test, Mann–Whitney test, or Fischer exact test. The *t* test was used for comparison of normally distributed numeric variables, and the Mann–Whitney test was applied when the distribution of numeric variables was not normal. The Fischer exact test was used for comparison of binary variables. The effect of independent variables on the outcome variable of interest was calculated using univariate logistic regression. Variables with a P value of less than 0.05 were then included in a multivariate logistic regression analysis. The multivariate model was fitted using the stepwise method, where a P value of less than 0.05 was set as an inclusion and exclusion criterion. Statistical significance was assumed for the P value of less than 0.05.

RESULTS A total of 560 patients were treated in the ICU during the study period. Overall, 65 patients were excluded from the analysis: 60 patients died within 48 hours from admission, while 5 patients had incomplete data, not allowing for the full interpretation of the results. No patients were discharged alive from the ICU within 48 hours from admission. Finally, 495 patients were analyzed, of whom 303 (61.2%) survived and 192 (38.8%) died in the ICU.

Daily FB in the first 24, 48, and 72 hours after admission was lower in survivors than in nonsurvivors. The analysis of the population profile (represented by diagnostic categories on admission to the ICU), medical status on admission, as well as demographic parameters revealed that there were more patients with cerebral stroke and with signs of shock on admission among nonsurvivors (TABLE 1). Demographic parameters as well as comorbidities were generally found to be similar in both groups (TABLE 2).

The volume of infused crystalloid and colloid solutions was significantly higher in nonsurvivors in the first days and overall during the first

TABLE 1 Medical diagnosis and status on admission to the intensive care unit

Diagnosis and medical status	Survivors (n = 303)	Nonsurvivors (n = 192)	*P* value
Acute coronary syndrome	69 (22.8)	44 (22.9)	0.94
Exacerbation of chronic HF	42 (13.9)	24 (12.5)	0.77
Complications of cardiac surgery	81 (26.7)	66 (34.4)	0.09
Complications of vascular surgery	0 (0.0)	4 (2.1)	0.04
Exacerbation of COPD	25 (8.3)	6 (3.1)	0.04
Pneumonia	12 (4.0)	3 (1.6)	0.21
Cerebral stroke or other neurologic disorders	16 (5.3)	29 (15.1)	<0.01
Other reasons	58 (19.1)	16 (8.3)	<0.01
Shock	48 (15.8)	58 (30.2)	<0.01
Mechanical ventilation	208 (68.7)	123 (64.1)	0.34

Data are presented as number (percentage).

Abbreviations: COPD, chronic obstructive pulmonary disease; HF, heart failure; ICU, intensive care unit

TABLE 2 Demographic data, major comorbidities, and fluid balance in the first 72 hours after admission to the intensive care unit

Parameter	Survivors (n = 303)	Nonsurvivors (n = 192)	*P* values
Age, y, mean (SD)	63.4 (14.7)	65.0 (13.8)	0.56
Female sex	131 (43.2)	67 (34.9)	0.08
Body weight, kg, mean (SD)	80.9 (17.8)	80.5 (21.8)	0.84
BMI, kg/m^2	27.9 (5.9)	27.6 (7.3)	0.41
Arterial hypertension	156 (51.5)	90 (46.9)	0.36
Coronary artery disease	157 (51.8)	93 (48.4)	0.52
Previous MI	95 (31.4)	61 (31.8)	1,00
HF before admission	97 (32.0)	52 (27.1)	0.29
Previous cardiac arrest	34 (11.2)	21 (10.9)	0.96
Previous cerebral stroke or other neurologic disorders	82 (27.1)	51 (26.6)	0.99
Diabetes	26 (8.6)	17 (8.9)	0.95
Extracardiac vascular disease	55 (18.2)	48 (25.0)	0.09
Chronic kidney disease	156 (51.5)	90 (46.9)	0.36
FB >1000 ml in the first 72 hours[a]	225 (74.3)	160 (83.3)	0.02
Colloid use in the first 72 hours[a]	203 (67.0)	160 (83.3)	<0.01

Data are presented as number (percentage) unless otherwise indicated.

a During each day in the first 72 hours

Abbreviations: BMI, body mass index, MI, myocardial infarction, FB, fluid balance; others, see TABLE 1 week of the ICU stay (TABLE 3). As a result, nonsurvivors were found to have a higher mean FB in the first 3 days of the ICU stay (FIGURE 1).

Data with significant differences between groups in the univariate analysis (as presented in TABLE 1, TABLE 2, and FIGURE 1) were included in the multivariate model. Colloid use and an FB exceeding 1000 ml during each day in the first 72 hours of the ICU stay were identified as independent predictors of ICU mortality in our cohort, along with the diagnosis of stroke and shock on admission (TABLE 4).

TABLE 3 Amount of infused crystalloid and colloid solutions

Fluid intake		Survivors (n = 303)	Nonsurvivors (n = 192)	*P* value
Crystalloids, ml/kg/d	Day 1	54.61 (28.37)	61.18 (29.35)	0.01
	Day 2	37.34 (13.21)	40.96 (18.49)	0.03
	Day 3	35.33 (13.48)	39.06 (16.64)	0.02
	Day 4	34.35 (14.08)	37.96 (17.30)	0.02
	Day 5	33.81 (14.63)	38.47 (16.25)	<0.01
	Day 6	33.33 (15.03)	36.15 (15.96)	0.12
	Day 7	35.73 (13.66)	38.22 (15.00)	0.19
	Total	250.17 (94.76)	273.23 (112.47)	0.06
Colloids, ml/kg/d	Day 1	5.45 (8.37)	9.85 (13.56)	<0.01
	Day 2	2.21 (3.98)	5.25 (6.71)	<0.01
	Day 3	1.48 (3.16)	3.87 (4.96)	<0.01
	Day 4	1.39 (2.84)	3.41 (4.33)	<0.01
	Day 5	1.51 (3.27)	3.54 (5.30)	<0.01
	Day 6	1.53 (3.67)	3.93 (5.80)	<0.01
	Day 7	1.65 (4.31)	4.35 (6.77)	<0.01
	Total	14.56 (20.43)	32.22 (31.01)	<0.01
FB >1000 ml,[a] n (%)		225 (74.3)	160 (83.3)	0.02
Colloid use,[a] n (%)		203 (67.0)	160 (83.3)	<0.01

Data are presented as mean (SD) unless otherwise indicated.

a During each day in the first 72 hours

Abbreviations: see TABLE 2

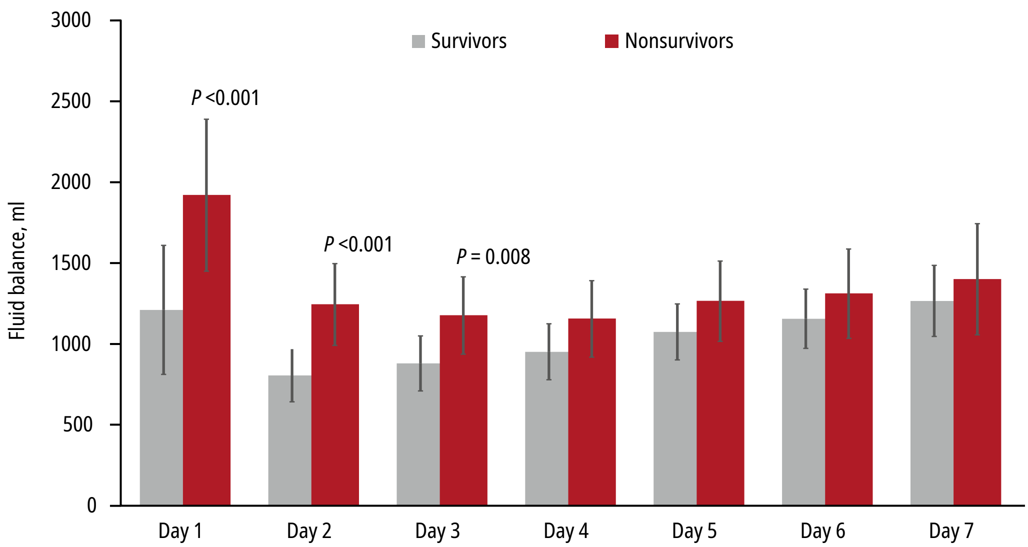

FIGURE 1 Amount of fluid balance during each day in the first 72 hours of the intensive care unit stay. Whiskers denote ranges..

TABLE 4 **Independent predictors of intensive care unit mortality**

Variable	OR	95% CI	*P* value
Cerebral stroke or other neurologic disorders	3.1	1.6–5.9	<0.01
Colloid use[a]	2.2	1.4–3.4	<0.01
Shock on ICU admission	2.1	1.3–3.3	<0.01
FB >1000 ml[a]	1.8	1.1–2.8	<0.02

a During each day in the first 72 hours

Abbreviations: OR, odds ratio; others, see TABLES 1 and 2

DISCUSSION Our results suggest that patients admitted to the ICU with life-threatening conditions caused mostly by acute or chronic cardiovascular disorders, who present with negative FB in the first 3 days since admission, are more likely to survive the ICU stay. To the best of our knowledge, this is the first study investigating daily FB, where total fluid input and output were analyzed in 24-hour intervals, starting from the hour of admission.

Although it was a single-center retrospective study, our results suggest that a positive FB in the first 72 hours after admission to the ICU was associated with an increased risk of hospital mortality.

Identification of factors affecting mortality in this patient population is extremely important because of high mortality rates. In their analysis of 112 patients from the COMMIT-AHF registry, Ostręga et al[11] demonstrated that, independently of the cause of myocardial injury and despite the use of a broad spectrum of invasive and noninvasive treatments, the mortality of patients with acute severe heart failure remains high, and 1 in 4 patients dies during hospitalization. The need to transfer more fluids to achieve hemodynamic stability and proper tissue perfusion may indicate the severity of the patient's condition. In addition, the need for even small positive FB may also be a sign of persistent hemostatic disturbances despite apparent stabilization.

The major conclusion from our study is that not only the amount of fluids but also the time when they are administered is important among cardiovascular and cardiosurgical patients admitted to the ICU, just as in other patient populations.[12-14]

There is still little awareness among intensivists that a liberal FB policy can be detrimental to the patient's health. Cecconi et al[15] described the practices used for fluid challenge in European ICUs. They concluded that the current practice and evaluation of fluid challenge in critically ill patients are highly variable. Prediction of fluid responsiveness is not routinely used, safety limits are rarely observed, and information from previous failed fluid challenges is not always considered.[15]

Numerous studies have shown that a higher FB is associated with worse survival in patients with sepsis. The endothelium plays the main role in maintaining appropriate hydration in critically ill patients. The inflammatory cascade of sepsis is thought to damage endothelial cells, alter the microvascular system, and cause capillary leakage.[16,17] Fluid therapy may enhance filling pressures and improve microcirculation in early but not in late sepsis; therefore, the time when fluid is administered is extremely important.[16,18] Hemodilution-induced hemodynamic effects can cause a redistribution of oxygen delivery away from weak microcirculatory units within and between the organs. The observed correlation between fluid overload and outcome may in part be caused by the development of interstitial edema leading to disrupted organ architecture, increased diffusion distances for oxygen and metabolites, and increased interstitial pressure.[17,19]

The adverse effects of fluid accumulation in critically ill patients, including mortality, have previously been reported in acute lung injury,[12] sepsis,[20-22] and in patients with acute kidney injury with or without indications for dialysis.[23,24]

Patients who are in severe condition tend to have a higher endothelial permeability and therefore require a larger fluid volume to correct hypovolemia. However, this is associated with adverse effects and exacerbation of multiorgan failure. According to the 2016 Surviving Sepsis Campaign guidelines, the initial management of sepsis includes goal-directed therapy measures. Early aggressive fluid and vasopressor support have resulted in a significant improvement in patient outcomes. Additionally, according to the current sepsis guidelines, fluid challenge should be performed within the first 3 hours when the blood pressure is low.[10]

Fluid management is of paramount importance in the treatment of patients with heart failure. The 2016 European Society of Cardiology guidelines for the diagnosis and treatment of heart failure recommend similar treatment for patients with cardiogenic shock and acute decompensation of chronic heart failure at the reference. Urgent administration of intravenous fluids (physiological saline or Ringer solution) is recommended as part of the first-line treatment in the absence of symptoms of acute decompensation.[3]

There is a very narrow window of optimal hydration for patients with heart failure. Overhydration can result in myocardial stretching and potential decompensation.

It is a common belief among clinicians that a positive FB is not equally harmful to patients with fluid retention and those with hypovolemic one. In turn, it is believed that inappropriate dehydration or a relative reduction in circulating blood volume may result in distant organ damage caused by inadequate perfusion.[25] In fact, it has been proved that even in patients with sepsis and severe hypovolemia, a positive cumulative FB on discharge from the ICU was an independent predictor of 90-day mortality in critically ill patients.[18]

Persistent net positive FB is generally not recommended; however, it has been proven that early (within the first 3 hours) aggressive fluid and vasopressor support results in a significant improvement of patient outcomes.[10,20] It is well known that a longer excessive fluid administration leads to the development of many serious complications, such as worse lung function, prolonged duration of mechanical ventilation, and need for renal replacement therapy.[26-28] All these complications were shown to be associated with increased mortality.

According to the 2016 Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock,[10] early aggressive fluid and vasopressor support results in a significant improvement of patient outcomes. In resuscitation from sepsis-induced hypoperfusion, at least 30 ml/kg of intravenous crystalloid fluid should be given within the first 3 hours. After initial fluid resuscitation, administration of additional fluids should be guided by frequent reassessment of the hemodynamic status, which should include a thorough clinical examination and evaluation of available physiologic parameters (heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urine output, and others) as well as noninvasive or invasive monitoring, as available. We followed these guidelines in our study.

The impact of FB on survival of ICU patients has been investigated in various populations. In our study, we analyzed patients admitted to the ICU with life-threatening conditions caused mostly by acute or decompensated cardiovascular diseases. Fluid administration usually increases cardiac output and improves tissue perfusion; however, in some cardiac patients, the therapy will not change the cardiac output but will only exert some unfavorable effects such as tissue edema and hypoxia.[29] Patients admitted to the ICU do not always present with overt clinical signs of cardiac disease. In light of current research findings in critically ill patients with multiple organ failure, intravenous fluids have an equal chance of bringing significant benefit and harm.[30,31]

The impact of negative FB on clinical outcomes has already been described in several studies in specific groups of ICU patients. In a large international study, Sakr et al[21] demonstrated that the cumulative FB in the first 3 days of ICU stay was associated with a higher risk of death among patients with sepsis. In addition, nonsurvivors had a positive FB every day during the first week of their ICU stay, while survivors had a positive FB only on the first and second day. The sample size of this study was large (n = 1808), but only septic patients were included.[21]

Shum et al[32] investigated 639 various ICU patients treated for at least 3 days and confirmed that the FB on the second and third day and overall FB had a significant effect on ICU mortality.[32] In this study, "day" was defined as a 24-hour period from midnight. In our study, the total fluid input and output were analyzed in 24-hour intervals, starting from the hour of admission. This makes it possible to compare treatment outcomes of patients admitted to the ICU at different times during the day.

Acheampong and Vincent[33] reported that maintaining a positive FB is significantly correlated with a higher risk of death in patients with sepsis. In their study, the FB was similar in survivors and nonsurvivors only in the first hours after admission. From the beginning of the second day, nonsurvivors had a significantly higher daily FB. An increasing difference between the mean FB in both groups was also observed on the subsequent days. In addition, the mean FB in the survivor group became negative between the fourth and fifth day and remained negative for the rest of the ICU stay. However, the study had a relatively small sample size (n = 173) compared with our study (n = 492) and included only patients with sepsis.

In our population, we found that the percentage of patients with renal insufficiency was similar between survivors and nonsurvivors. It has been confirmed that a positive FB is associated with an increased incidence of acute kidney failure.[34] In a large European multicenter observational study, Payen et al[23] proved that a positive FB was an important factor associated with 60-day mortality in patients with acute kidney failure. Therefore, it may be concluded that it is particularly important to maintain a restrictive FB in patients with renal failure.

The largest study in this field to date was performed by Lee et al,[35] who investigated 15 395 patients with heart or kidney failure. Similar to our study, the authors included a mixed population of patients treated at general, surgical, cardiac, and cardiothoracic ICUs, in whom daily FB was accurately calculated. Positive FB at the time of ICU discharge was associated with an increased risk of death, after adjusting for markers of disease severity and chronic medical conditions. On the basis of these findings, the authors concluded that restoration of euvolemia prior to discharge may improve survival after acute illness.[35]

Adverse effects of crystalloid and colloid solutions have been well documented.[36] Krzych and Czempik,[37] in their experimental ex vivo study, confirmed that commonly used balanced fluids had little impact on electrolyte composition of human plasma. However, in metabolic acidosis, succinylated gelatin should be used with caution due the presence of lactate as a buffering agent.

In our study, FB during the first 72 hours and often for the first 7 days, was positive in the majority of patients treated at the ICU. The outcome of fluid therapy depends on a clinician's knowledge and experience, but it can be difficult to achieve a negative FB, which is most often the first sign of the restoration of heart and kidney function.

In Poland, the rates of ICU mortality are higher than in other European countries.[38,39] This results from numerous factors, mainly related to organizational and cultural rather than staff-related aspects. On the basis of data from the Silesian Registry of Intensive Care Units, it has been already confirmed that the observed mortality is lower than predicted, according to well-established systems of ICU scoring.[40] This means that patients are frequently transferred to ICUs in Poland only when they are dying or have no chance of survival. Thus, therapy in the first 72 hours after admission is particularly important and may affect mortality.

The results of our study suggest that FB in the first 3 days of treatment may be particularly important for critically ill patients with cardiovascular disease. However, larger prospective studies are needed to validate this hypothesis.

Our study has several limitations. First, the sample size was relatively small. Second, data on FB prior to ICU admission were lacking. Finally, patients who had undergone cardiac surgery or renal replacement therapy were not excluded.

In conclusion, a positive FB exceeding 1000 ml during each day in the first 72 hours after ICU admission was independently associated with increased mortality in critically ill patients with cardiovascular disorders. The use of colloid solutions was associated with a higher positive FB. Further research, including randomized clinical trials, is needed to confirm our findings.

ARTICLE INFORMATION

ACKNOWLEDGMENTS Special thanks to Ms. Jolanta Cieśla for editing the article.

CONFLICT OF INTEREST None declared.

HOW TO CITE Trejnowska E, Skoczyński S, Armatowicz P, et al. The importance of fluid balance in critically ill patients: a retrospective observational study. Kardiol Pol. 2019; 77: 1147-1154. doi:10.33963/KP.14991

REFERENCES

1 Malbrain ML, Marik PE, Witters I, et al. Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients. Anaesthesiol Intensive Ther. 2014; 46: 361-380.

2 Marik PE, Monnet X, Teboul JL. Haemodynamic parameters to guide fluid therapy. Ann Intensive Care. 2011; 1: 1.

3 Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Kardiol Pol. 2016; 74: 1037-1147.

4 Shen Y, Huang X, Zhang W. Association between fluid intake and mortality in critically ill patients with negative fluid balance: a retrospective cohort study. Crit Care. 2017; 21: 104.

5 Boldt J, Ince C. The impact of fluid therapy on microcirculation and tissue oxygenation in hypovolemic patients: a review. Intensive Care Med. 2010; 36: 1299-1308.

6 Brotfain E, Koyfman L, Toledano R, et al. Positive fluid balance as a major predictor of clinical outcome of patients with sepsis/septic shock after discharge from intensive care unit. Am J Emerg Med. 2016; 34: 2122-2126.

7 Boyd JH, Forbes J, Nakada T, et al. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med. 2011; 39: 259-265.

8 Vincent JL, Sakr Y, Sprung CL, et al. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med. 2006; 34: 344-353.

9 Kellum JA, Lameire N; KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013; 17: 204.

10 Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017; 43: 304-377.

11 Ostręga M, Gierlotka MJ, Słonka G, et al. Clinical characteristics, treatment, and prognosis of patients with ischemic and nonischemic acute severe heart failure. Analysis of data from the COMMITAHF registry. Pol Arch Intern Med. 2017; 127: 328-335.

12 Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med. 2006; 354: 2564-2575.

13 Fletcher JJ, Bergman K, Blostein PA, Kramer AH. Fluid balance, complications, and brain tissue oxygen tension monitoring following severe traumatic brain injury. Neurocrit Care. 2010; 13: 47-56.

14 Barmparas G, Liou D, Lee D, et al. Impact of positive fluid balance on critically ill surgical patients: a prospective observational study. J Crit Care. 2014; 29: 936-941.

15 Cecconi M, Hofer C, Teboul JL, et al. Fluid challenges in intensive care: the FENICE Study: Intensive Care Med. 2015; 41: 1529-1537.

16 Ince C. The microcirculation is the motor of sepsis. Crit Care. 2005; 9 (suppl 4): S13-S19.

17 Genga KR, Shimada T, Boyd JH, et al. The understanding and management of organism toxicity in septic shock. J Innate Immun. 2018; 10: 502-514.

18 Neyra JA, Li X, Canepa-Escaro F, et al. Cumulative Fluid balance and mortality in septic patients with or without acute kidney injury and chronic kidney disease. Crit Care Med. 2016; 44: 1891-1900.

19 Prowle JR, Echeverri JE, Ligabo EV, et al. Fluid balance and acute kidney injury. Nat Rev Nephrol. 2010; 6: 107-115.

20 Sirvent JM, Ferri C, Baró A, et al. Fluid balance in sepsis and septic shock as a determining factor of mortality. Am J Emerg Med. 2015; 33: 186-189.

21 Sakr Y, Rubatto Birri PN, Kotfis K, et al. Higher Fluid balance increases the risk of death from sepsis: results from a large international audit. Crit Care Med. 2017; 45: 386-394.

22 Alsous F, Khamiees M, DeGirolamo A, et al. Negative fluid balance predicts survival in patients with septic shock: a retrospective pilot study. Chest. 2000; 117: 1749-1754.

23 Payen D, de Pont AC, Sakr Y, et al. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. Crit Care. 2008; 12: R74.

24 Bouchard J, Soroko SB, Chertow GM, et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int. 2009; 76: 422-427.

25 Ronco C, Kaushik M, Valle R, et al. Diagnosis and management of fluid overload in heart failure and cardio-renal syndrome: the "5B" approach. Semin Nephrol. 2012; 32: 129-141.

26 Sakr Y, Vincent JL, Reinhart K, et al; Sepsis Occurrence in Acutely Ill Patients Investigators. High tidal volume and positive fluid balance are associated with worse outcome in acute lung injury. Chest 2005; 128: 3098-3108.

27 Ingelse S, Wiegers HM, Calis J, et al. Early fluid overload prolongs mechanical ventilation in children with viral-lower respiratory tract disease. Pediatr Crit Care Med. 2017; 18: e106-e111.

28 Zhang L, Chen Z, Diao Y, et al. Associations of fluid overload with mortality and kidney recovery in patients with acute kidney injury: a systematic review and meta-analysis. J Crit Care. 2015; 30: 860. e7-e13.

29 Koniari K, Parissis J, Paraskevaidis I, Anastasiou-Nana M. Treating volume overload in acutely decompensated heart failure: established and novel therapeutic approaches. Eur Heart J Acute Cardiovasc Care. 2012; 1: 256-268.

30 McMurray JJ, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur J Heart Fail. 2012; 14: 803-869.

31 Cotter G, Metra M, Milo-Cotter O, et al. Fluid overload in acute heart failure – re-distribution and other mechanisms beyond fluid accumulation. Eur J Heart Fail. 2008; 10: 165-169.

32 Shum HP, Lee FM, Chan KC, Yan WW. Interaction between fluid balance and disease severity on patient outcome in the critically ill. J Crit Care. 2011; 26: 613-619.

33 Acheampong A, Vincent JL. A positive fluid balance is an independent prognostic factor in patients with sepsis. Crit Care. 2015; 19: 251.

34 Kambhampati G, Ross EA, Alsabbagh MM, et al. Perioperative fluid balance and acute kidney injury. Clin Exp Nephrol. 2012; 16: 730-738.

35 Lee J, de Louw E, Niemi M, et al. Association between fluid balance and survival in critically ill patients. J Intern Med. 2015; 277: 468-477.

36 Hahn RG. Adverse effects of crystalloid and colloid fluids. Anaesthesiol Intensive Ther. 2017; 49: 303-308.

37 Krzych ŁJ, Czempik PF. Does fluid resuscitation with balanced solutions induce electrolyte and metabolic abnormalities? An in vitro assessment. Kardiol Pol. 2017; 75: 779-785.

38 Weigl W, Adamski J, Goryński P, et al. ICU mortality and variables associated with ICU survival in Poland: a nationwide database study. Eur J Anaesthesiol. 2018; 35: 949-954.

39 Weigl W, Adamski J, Goryński P, et al. Mortality rate is higher in Polish intensive care units than in other European countries. Intensive Care Med. 2017; 43: 1430-1432.

40 Knapik P, Krzych ŁJ, Weigl W, et al. Mortality rate in Polish intensive care units is lower than predicted according to the APACHE II scoring system. Intensive Care Med. 2017; 43: 1745-1746.