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

Authors: Ewa Trejnowska, Szymon Skoczyński, Paul Armatowicz Małgorzata Knapik, Paulina Kurdyś, Krystian Ślusarz, Magda Tarczyńska-Słomian, Piotr Knapik

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

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

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 Anaesthesia and Intensive Care, Medical University of Silesia, Katowice, Poland.

5 Third Department of Cardiology, Silesian Centre for Heart Diseases in Zabrze, Poland.

Brief title “Fluid balance in critically ill patients”

Corresponding author:

Ewa Trejnowska MD, PhD

ewatrejnowska@gmail.com

+48 322732731

1Department of Anaesthesiology, Intensive Therapy and Emergency Medicine, Silesian Centre for Heart Diseases, Medical University of Silesia, Zabrze, Poland.

Conflict of interest: none declared.
What’s new?

Appropriate fluid management in critically ill patients is one of the most challenging and difficult aspects of care. Sufficient fluid resuscitation is important for stabilizing 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 of not only the fluid balance but also the fluid administered during the first three days of therapy. This has a double meaning; on one hand, it points out that a positive fluid balance in the first 72 hours of treatment is associated with an increased risk of mortality. On the other hand, it indicates a group of patients who need more fluids to achieve stabilization. This group of patients are at an increased risk of death and should be treated with particular caution.

Acknowledgements:

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

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

Aim: The purpose of this study was to investigate whether a cumulative fluid balance had an influence on mortality in critically ill ICU patients.

Methods: Data was obtained from the ICU medical records at the Silesian Centre for Heart Diseases. All patients admitted to the ICU between 2012 and 2016 were analysed. Patients who died or were discharged from the ICU within 48 hours after admission, were excluded. Fluid balance (FB) and the type of fluids infused during the first seven days were analysed. 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 ICU admission and the cumulative FB after 7 days were significantly lower in survivors. FB exceeding 1000 mls and the use of colloid solutions in the first 72 hours were independently associated with ICU mortality, along with the diagnosis of stroke and shock at ICU admission.

Conclusion: A positive fluid balance exceeding 1000 mls in the first 72 hours after ICU admission 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 fluid balance.

Key words: critically ill patients, fluid balance, intensive care unit.
**Introduction:**

Fluid resuscitation in the setting of impaired organ perfusion is recognized to be 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 and difficult aspects of care.

Fluid resuscitation is of particular importance 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 of particular importance for the stabilization of haemodynamic status and improvement of 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, very little evidence is available to define 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.

The purpose of this study was to investigate whether a cumulative FB has an influence on mortality in critically ill ICU patients.

**Methods:**

Data was obtained from the ICU medical records at the Silesian Centre for Heart Diseases. The Centre includes five departments of cardiology, department of cardiac surgery and transplantation, department of vascular surgery - supported by a postoperative intensive care department, and general ICU - dedicated mainly for acutely ill cardiovascular patients from the
Silesian Centre and those transferred for more specialized cardiovascular treatment from the surrounding local hospitals.

Retrospective data was obtained from the general ICU medical records. Patients older than 18 years and admitted to the ICU between 01/01/2012 and 31/12/2016 were included and screened. 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, parameters describing medical status on ICU admission (mechanical ventilation, catecholamines, etc.), basic demographic variables and major preadmission comorbidities such as: arterial hypertension, coronary arteries disease, a history of myocardial infarction (MI), presence of heart failure (HF) before the admission, previous cardiac arrest, a history of stroke, presence of diabetes, extracardiac vascular disease (EVD) and chronic kidney disease.

Heart failure was defined as a set of typical symptoms (ie. dyspnea, oedema of the lower limbs, decreased exercise tolerance), which may be accompanied by variations in physical examination (such as scares over the lungs, peripheral oedema), caused by disturbances in the structure and/or cardiac activities that cause decreased cardiac output and/or increased intracardiac pressure at rest or during exercise [3].

Chronic kidney disease was defined as kidney structural and/or functional abnormalities present for more than three months with health implications. A rise of more than 1.5 times the serum creatinine baseline was considered an AKI according to the creatinine-based Kidney Disease Improving Global Outcome criteria [9]. Heart failure and chronic kidney disease were diagnosed on admission or based on patient's previous medical documentation.

Septic shock was defined as a subset of sepsis in which 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) and total fluid output were recorded on a daily basis in the first 7 consecutive days.

Types of fluids infused were also analysed. Total fluid input was broadly divided into colloids and crystalloids and analysed separately.

Patients were admitted to the ICU at various times of the day, therefore to obtain precise information on a daily FB, we constantly calculated fluid input and fluid output during 24 hours. The time when the patient was admitted to the ICU was the first hour of the 24-hour period of time. 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 the type of fluid transfused based on haemodynamic parameters and symptoms of hypoperfusion.

Statistics:

Data of patients who survived and who died in the ICU were compared with the use of t-Student, Mann-Whitney or Fischer exact test. T-Student test was used for comparison of normally distributed numeric variables and Mann-Whitney test was used when the distribution of numeric variables was not normal. Fischer exact test was used for comparison of binary variables. The effect of independent variables on the outcome variable of interest was calculated by means of univariate logistic regression. Variables with $p$ value $< 0.05$ were then included in multivariate logistic regression analysis. The multivariate model was fitted using the stepwise method, where $p < 0.05$ was set as inclusion and exclusion criteria. Statistical significance was assumed for the $p$ value $< 0.05$.

Results
560 patients were treated in the ICU during the analysed period. Overall, 65 patients were excluded from the analysis – 60 patients died within 48 hours of 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 analysed – 303 (61.2%) survived and 192 (38.8%) died in the ICU.

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

Volume of infused crystalloid and colloid solutions was significantly higher in non-survivors in the first days and overall during the first week of ICU stay (Table 3). As a result, non-survivors were found to have a higher mean FB in the first three days of ICU stay (Figure 1).

Data from Table 1, Table 2 and Figure 1, with significant differences between the groups, in the univariate analysis were included in a multivariate model. Colloid use and FB > 1000 mls during each day in the first 72 hours were identified as independent predictors of ICU mortality in our cohort, along with the diagnosis of stroke and shock at ICU admission (Table 4).

**Discussion:**

Our results suggest that patients admitted to the ICU in life-threatening conditions caused mostly by acute cardiac disorders or cardiologic co-morbid diseases, who presented with negative FB in the initial three days of ICU treatment, were more likely to survive. To the best of our knowledge, this is the first study investigating daily FB, where a total fluid input and output were analysed in 24-hour intervals, starting from the hour of admission.
Although it is a monocentric retrospective study, we suggest that a positive balance in the first 72 hours after admission to the ICU, is associated with an increased risk of hospital mortality. Indication of which factors affect mortality in this group of patients is extremely important because mortality is very high. Ostręga et al., [11] in their analysis of 112 patients from the COMMIT-AHF registry 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 stabilization of the patient's condition and proper tissue perfusion may indicate the severity of the patient's condition. In addition, the need for even small positive balances may also be evidence of persistent disturbances of homeostasis in spite of apparent stabilization.

The conclusion from our study is that among patients admitted to the ICU with a cardiovascular and cardiosurgical profile, as in other groups of patients [12, 13, 14], not only the amount of fluids but also the time where fluids are administered, is important.

There is still no awareness among intensivists, that liberal fluid policy can be detrimental to the patient. Cecconi et al. [15] showed fluid challenges practices in intensive care units in Europe. They concluded that the current practice and evaluation of fluid challenges in critically ill patients are highly variable. Prediction of fluid responsiveness is not used routinely, safety limits are rarely used and information from previous failed fluid challenges is not always taken into account [15].

It is already known that a higher fluid balance is associated with worse survival in septic patients and this has been published in numerous studies. Endothelium plays the main role in maintaining appropriate hydration in critically ill patients. The inflammatory cascade of sepsis
is thought to disrupt the endothelial surface, alter the microvascular system and cause capillary
leakage [16, 17]. Fluid therapy may enhance filling pressures and improve microcirculation in
early sepsis but not in late sepsis, therefore, the time when fluid is administered is very
important [16, 18]. Hemodilution-induced hemodynamic effects can cause a redistribution of
oxygen delivery away from weak microcirculatory units within organs, as well as between
organs. The observed correlation between fluid overload and outcome may in part be caused
by the development of interstitial oedema leading to disrupted organ architecture, increased
diffusion distances for oxygen and metabolites, and increased interstitial pressure [17, 19].

The detrimental consequences of fluid accumulation in critically ill patients, including
mortality, have previously been reported in acute lung injury [12], in sepsis [20, 21, 22], and in
patients with AKI with or without requirements for dialysis [23, 24].

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

Fluid management is of paramount importance in the treatment of patients with heart failure.
The guidelines from the European Society of Cardiology for the diagnosis and treatment of
heart failure in 2016 recommend similar treatment for patients in cardiogenic shock and acute
decompensation of chronic HF. Urgent administration of intravenous fluids (physiological
saline or Ringer's 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.

Clinicians often believe, that a positive fluid balance is not similarly harmful for a patient with a fluid retention and for a hypovolemic one. Inappropriate dehydration or relative reduction of circulating blood volume, in turn, may result in distant organ damage caused by inadequate perfusion [25]. In fact, it has been proved that even in a severely hypovolaemic septic patients, a positive cumulative fluid balance on discharge from ICU (FBD) was found to be an independent predictor of ICU mortality [18].

Persistent net positive fluid balance is generally not advised, however it has been confirmed that early, within the first 3 hours, aggressive fluid and vasopressor support have resulted in significant improvement in patient outcomes [10, 20]. We have already learned that a longer excessive fluid administration leads to the development of serious complications, such as worse lung function, prolonged duration of mechanical ventilation, the need for renal replacement therapy and many others [26-28]. All these complications are known to be associated with increased mortality.

According to the Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016 recommendation, early aggressive fluid and vasopressor support have resulted in significant improvement in patient outcomes. In resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hours. Following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status. Reassessment should include a thorough clinical examination and evaluation of available physiologic variables (heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urine output, and others, as available) as well as other non-invasive or invasive monitoring, as available [10]. We have adopted similar assumptions in our study.
The impact of FB on survival of ICU patients has been investigated in various groups of patients. In our study, we analysed patients admitted to the ICU in life-threatening conditions caused mostly by acute cardiac disorders or decompensated cardiologic co-morbid diseases. Fluid administration usually increases cardiac output and improves tissue perfusion, but in some cardiac patients fluid therapy will not change the cardiac output, causing only unfavourable results such as tissue oedema and hypoxia [29]. Patients admitted to the ICU do not always show visible clinical signs of their 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 three days of ICU stay was associated with a higher risk of death among septic patients. In addition, non-survivors 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].

Another study in this field was performed by Shum et al. [32]. The authors investigated 639 mixed 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 influence on ICU mortality [32]. In this study, “the day” was defined as a 24-hour period from midnight. In our study, the total fluid input and output was analysed in 24-hour intervals, starting from the hour of admission. This makes it possible to compare the results of treatment of patients admitted to the ICU at different times during the day.

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

In our population, we found that the percentage of patients with renal insufficiency was the same in survivors and in non-survivors (51.5 % vs 46.9 %, p 0.36) (Table 2). It had already been confirmed, that a positive FB is associated with an increased incidence of acute kidney failure [34]. In a large multicentre European observational study, Payen et al. [23] proved that a positive FB was an important factor associated with 60-day mortality in patients with AKI. Therefore, the conclusion from these two findings is that maintaining a restrictive FB might be particularly important in patients with renal failure.

The largest study in this field to date was performed by Lee et al. [35], who studied an impressive number of 15,395 patients with heart or kidney failure. Similar to our study, the authors studied a mixed population of medical, surgical, cardiac and cardiothoracic intensive care patients in whom daily balances were accurately calculated. Positive FB at the time of ICU discharge was associated with an increased risk of death, after adjusting for markers of illness 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 already been well described [36]. Krzych et al. [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, balanced 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 in our ICU. Fluid therapy is based on the knowledge and experience of the clinician, but the ability to achieve a negative FB may be an important initial sign of recovery of cardiac and renal function.

Mortality in Intensive Care Units in Poland, in comparison with other European countries, is high [38, 39]. This depends on many factors, mainly related to organizational and cultural conditions in which the ICU staff have no influence. On the basis of data from the Silesian ICU Registry, 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 of the patient to ICU is particularly important and may have an impact on mortality.

The results of this study need to be confirmed in a randomized controlled trial. Clinicians should not strive to achieve a negative FB for the balance itself. However, if the results of our study would be confirmed in larger prospective studies, it can be proved that FB in the first three days of treatment is of particular importance for the critically ill patients.

The study has several limitations. The sample size is relatively small. The FB prior to ICU admission was not known. In addition, patients who underwent cardiac surgery or renal replacement therapy were not excluded from the study. However, several valid hypotheses have been formulated and our study may provide evidence for further research in this field.

In conclusion, a positive fluid balance exceeding 1000 mls during each day in the first 72 hours after ICU admission was independently associated with an increased risk of mortality in
critically ill patients with cardiovascular disorders. The use of colloid solutions was associated with a higher positive FB.

References:


Table 1. Medical diagnosis at Intensive Care Unit admission.

<table>
<thead>
<tr>
<th>Diagnosis and medical status at admission</th>
<th>Survivors (n = 303)</th>
<th>Non-survivors (n = 192)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute coronary syndrome</td>
<td>69 (22.8%)</td>
<td>44 (22.9%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Exacerbation of chronic heart failure</td>
<td>42 (13.9%)</td>
<td>24 (12.5%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Complications following cardiac surgery</td>
<td>81 (26.7%)</td>
<td>66 (34.4%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Complications following vascular surgery</td>
<td>0 (0.0%)</td>
<td>4 (2.1%)</td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>Exacerbation of Chronic Obstructive Pulmonary Disease</td>
<td>25 (8.3%)</td>
<td>6 (3.1%)</td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>12 (4.0%)</td>
<td>3 (1.6%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Cerebral stroke or other neurological disorders</td>
<td>16 (5.3%)</td>
<td>29 (15.1%)</td>
<td>&lt; <strong>0.01</strong></td>
</tr>
<tr>
<td>Other reasons</td>
<td>58 (19.1%)</td>
<td>16 (8.3%)</td>
<td>&lt; <strong>0.01</strong></td>
</tr>
<tr>
<td>Shock at ICU admission</td>
<td>48 (15.8%)</td>
<td>58 (30.2%)</td>
<td>&lt; <strong>0.01</strong></td>
</tr>
<tr>
<td>Mechanical ventilation on ICU admission</td>
<td>208 (68.7%)</td>
<td>123 (64.1%)</td>
<td>0.34</td>
</tr>
</tbody>
</table>
Table 2. Demographic data, major comorbidities and fluid balance in the first 72 hours.

<table>
<thead>
<tr>
<th></th>
<th>Survivors (n = 303)</th>
<th>Non-survivors (n = 192)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.4 ±14.7</td>
<td>65.0 ±13.8</td>
<td>0.56</td>
</tr>
<tr>
<td>Female sex</td>
<td>131 (43.2%)</td>
<td>67 (34.9%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>80.9 ±17.8</td>
<td>80.5 ±21.8</td>
<td>0.84</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.9 ±5.9</td>
<td>27.6 ±7.3</td>
<td>0.41</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>156 (51.5%)</td>
<td>90 (46.9%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>157 (51.8%)</td>
<td>93 (48.4%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Previous MI</td>
<td>95 (31.4%)</td>
<td>61 (31.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>HF before admission</td>
<td>97 (32.0%)</td>
<td>52 (27.1%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Previous cardiac arrest</td>
<td>34 (11.2%)</td>
<td>21 (10.9%)</td>
<td>0.96</td>
</tr>
<tr>
<td>History of Cerebral stroke or other neurological disorders</td>
<td>82 (27.1%)</td>
<td>51 (26.6%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Diabetes</td>
<td>26 (8.6%)</td>
<td>17 (8.9%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Extracardiac vascular disease</td>
<td>55 (18.2%)</td>
<td>48 (25.0%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>156 (51.5%)</td>
<td>90 (46.9%)</td>
<td>0.36</td>
</tr>
<tr>
<td>FB &gt; 1000 ml in the first 72 hours*</td>
<td>225 (74.3%)</td>
<td>160 (83.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Colloid use in the first 72 hours*</td>
<td>203 (67.0%)</td>
<td>160 (83.3%)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Abbreviations: BMI – Body Mass Index, HF- Heart Failure, MI- Myocardial Infarction, FB- Fluid balance *during each day
Table 3. Amount of infused crystalloid and colloid solutions (expressed as ml/kg per day).

<table>
<thead>
<tr>
<th>Fluid intake</th>
<th>Survivors (n = 303)</th>
<th>Non-survivors (n = 192)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystalloids day 1</td>
<td>54.61 ±28.37</td>
<td>61.18 ±29.35</td>
<td>0.01</td>
</tr>
<tr>
<td>Crystalloids day 2</td>
<td>37.34 ±13.21</td>
<td>40.96 ±18.49</td>
<td>0.03</td>
</tr>
<tr>
<td>Crystalloids day 3</td>
<td>35.33 ±13.48</td>
<td>39.06 ±16.64</td>
<td>0.02</td>
</tr>
<tr>
<td>Crystalloids day 4</td>
<td>34.35 ±14.08</td>
<td>37.96 ±17.30</td>
<td>0.02</td>
</tr>
<tr>
<td>Crystalloids day 5</td>
<td>33.81 ±14.63</td>
<td>38.47 ±16.25</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Crystalloids day 6</td>
<td>33.33 ±15.03</td>
<td>36.15 ±15.96</td>
<td>0.12</td>
</tr>
<tr>
<td>Crystalloids day 7</td>
<td>35.73 ±13.66</td>
<td>38.22 ±15.00</td>
<td>0.19</td>
</tr>
<tr>
<td>Crystalloids total (7 days)</td>
<td>250.17 ±94.76</td>
<td>273.23 ±112.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Colloids day 1</td>
<td>5.45 ±8.37</td>
<td>9.85 ±13.56</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids day 2</td>
<td>2.21 ±3.98</td>
<td>5.25 ±6.71</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids day 3</td>
<td>1.48 ±3.16</td>
<td>3.87 ±4.96</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids day 4</td>
<td>1.39 ±2.84</td>
<td>3.41 ±4.33</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids day 5</td>
<td>1.51 ±3.27</td>
<td>3.54 ±5.30</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids day 6</td>
<td>1.53 ±3.67</td>
<td>3.93 ±5.80</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids day 7</td>
<td>1.65 ±4.31</td>
<td>4.35 ±6.77</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloids total (7 days)</td>
<td>14.56 ±20.43</td>
<td>32.22 ±31.01</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>FB &gt; 1000 ml*</td>
<td>225 (74.3%)</td>
<td>160 (83.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Colloid use*</td>
<td>203 (67.0%)</td>
<td>160 (83.3%)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

*during each day in the first 72 hours

Abbreviations — see Table 2
Table 4. Independent predictors of Intensive Care Unit mortality.

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral stroke or other neurological disorders</td>
<td>3.1</td>
<td>1.6</td>
<td>5.9</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Colloid use in the first 72 hours*</td>
<td>2.2</td>
<td>1.4</td>
<td>3.4</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Shock at ICU admission</td>
<td>2.1</td>
<td>1.3</td>
<td>3.3</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>FB &gt; 1000 ml in the first 72 hours*</td>
<td>1.8</td>
<td>1.1</td>
<td>2.8</td>
<td>&lt; 0.02</td>
</tr>
</tbody>
</table>

* during each day in the first 72 hours

Abbreviations: OR – odds ratio, CI – confidence interval, FB - Fluid balance

Figure 1. Amount of fluid balance during each day in the first 72 hours