# Fluid Overload and Risk of Mortality in Critically Ill Patients

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*Background: Fluid overload (FO) is a condition present in critical care units, and it is associated with clinical complications and worse outcomes for severe patients.*
*Objective: The aim of this study was to verify if FO is a risk factor for mortality in critically ill patients.*
*Methods: Retrospective study performed in a Brazilian intensive care unit, from January to March 2016, with patients older than 18 years and hospitalized for more than 24 hours. Demographic and clinical data, as well as fluid balance and overload, were analyzed to verify the risk factors for mortality. A logistic regression model was elaborated, and significance was set at P < .05.*
*Results: There were 158 patients included, of which only 13 (8.2%) presented FO. Mortality was verified in individuals 30 (18.9%), of whom only 7 (23.3%) developed FO, which was lower in survivors 6 (4.9%), P = .001. In the simple regression model, the FO was significant (odds ratio [OR], 6.23; 95% confidence interval [CI], 2.04–19.53), P = .001. However, in the multiple regression model, there were significant findings only for mechanical ventilation (OR, 5.86; 95% CI, 2. 10–18.12, P = .001), acute kidney injury (OR, 4.05; 95% CI, 1.53–11; P = .001), and noradrenaline (OR, 3.85; 95% CI, 1.01–9.51; P = .041); FO was not significant (OR, 3.68; 95% CI, 0.91–15.55; P = .069).*
*Conclusion: Fluid overload is higher in patients who died. Therefore, it was not considered a risk factor for mortality.*
*Keywords: fluid balance, fluid overload, intensive care units, risk factors*
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Assessment of the amount of fluids administered and eliminated in a given period is essential to monitoring fluid balance (FB). Fluid balance is defined as the difference between the amount of fluid entering and leaving a patient, and in the context of severe patient, FB becomes all the more important because clinical decision making will be determined by the value obtained.[1] Fluid overload (FO) is frequently found in critical units and has worried health care teams because of its impact on patients' morbidity and mortality.[2]

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First, fluid accumulation can be defined as a positive FB irrespective of FO,[3] whereas FO can be defined as a pathological increase of fluid and dilution of electrolytes as this excess accumulates in the interstitial spaces resulting in edema and organic changes.[3,4] In short, FO is associated with altered cognition, altered gas exchange, diastolic dysfunction, cholestasis, intestinal malabsorption, reduced glomerular filtration rate, and difficulty in wound healing.[4]

Both accumulation and FO are problems experienced in the intensive care unit (ICU), which may be related to fluid administration. In the last decade, administration of fluids has become a cause of debate because of its adverse effects especially regarding excessive administration of volume. Hence, when analyzing the FB of patients with septic shock, an accumulation of fluid of up to 11 L was found within 4 days after admission as the individuals who presented this accumulation developed an FO and displayed worse clinical outcomes.[5]

Postoperative patients in the ICU with FB greater than 2 L in the intraoperative period were found to need prolonged stay in intensive care. They also showed an increased incidence of infections and neurological, cardiovascular and respiratory complications, as well as higher hospital mortality.[6] When analyzing individuals who developed acute renal injury (AKI) and their fluid status, the results showed that FB is greater in these patients. Nevertheless, FO is considered to be a risk factor for AKI as well as to worsen the severity of its condition.[7] In the latter study, FO was considered an important factor for 28-day mortality in the presence of AKI.[7]

On the other hand, negative or neutral FB showed better results in clinical outcome of patients with acute pulmonary edema, acute respiratory distress syndrome, intra-abdominal hypertension, and even mechanical ventilation (MV)[8] besides functioning as a strategy in conservative treatments, such as management of pulmonary injury secondary to septic shock.[9]

Therefore, daily analysis of FB is extremely important in the treatment and safety of critical patients. Nursing is essential in this process as it is responsible for providing/guaranteeing FB, which is one of the parameters comprising the Nursing Activities Score,[10] an instrument for measuring the workload of the nursing team in the ICU. The score for performing FB carries a certain value that will impact the activities of the nursing team.[10] For this reason, it is essential that nurses train their staff to perform and register FB as clinical decisions will be made according to FB registry.[11]

Given the importance of FB analysis as a consequence of a possible FO and its complications, a further investigation of this variable in critically ill patients may be necessary in order to improve their quality of care. Because of the importance of nursing to analyze FB and try to prevent the FO and their complication in organ systems, the aim of this study was to verify if the FO can be considered as a risk factor for mortality in critically ill patients.

## METHODS

A retrospective research based on quantitative analysis was used in this study, performed in an adult ICU in a large private hospital, located in the southern area of São Paulo (Brazil). The unit provides care in all specialties, both clinical and surgical. It consists of 42 beds, divided into 9 units, and receives approximately 243 patients per month, of which the majority are clinical patients.

The sample consisted of patients hospitalized in the ICU from January to March 2016, characterized by nonprobabilistic calculation, using a previous database used by the ICU. Inclusion criteria were patients older than 18 years, of both genders, and length of hospitalization longer than 24 hours for more accurate analysis of FB.

First, a data collection instrument was prepared by the authors and structured in 2 parts: the first by demographic and clinical profile of patients and the second with FB records followed up to the fifth day of hospitalization.

With this project being of retrospective nature with no identification of patients, no type of experiment with humans, and therefore no individual risk involved, a request for use of the informed consent form (CAAE:79769317.0.0000.0071) was sent to and approved by the Research Ethics Committee of the Israelita Albert Einstein Hospital. Researchers are committed to maintaining confidentiality of all the information obtained in the medical records for analysis.

The criterion of Kidney Disease Improving Global Outcomes was used to determine the occurrence of AKI. In order to do this, 2 values of creatinine were analyzed, always guided by baseline: at admission and the first after hospitalization.[12] This criterion is characterized by an increase in serum creatinine in values greater than or equal to 0.3 mg/dL in 48 hours or a 1- to 5-fold increase in serum creatinine over baseline (known or preestablished) in 7 days or urine flow lower than 0.5 mL/kg per hour for 6 hours.[12]

Fluid overload is calculated by adding FB from the first day of ICU until the fifth day of hospitalization stay, divided by its admission weight and multiplied by 100. Results greater than 0.1 indicate a positive FO.[2]

If the patient's hospitalization length of stay is less than 5 days, FB will be added to the days of hospitalization, provided hospitalization length of stay is longer than 24 hours as previously mentioned in the inclusion criteria.

The descriptive analysis was performed for all variables of the study aiming at the characterization of the sample. The qualitative variables were described by absolute and relative frequencies (%). For the quantitative variables, the mean and SD were calculated.

Inferential analysis was performed using the $\chi^2$ test and Fisher exact test to compare qualitative characteristics of group survivors and nonsurvivors. For measuring the quantitative variable, the Student *t* test and the Mann-Whitney *U* test were used to analyze the means of group survivors and nonsurvivors. The distributions of the numerical variables were studied by means of histograms, boxplots, and Shapiro-Wilk normality tests.

Regarding the risk factors for mortality, a simple logistic regression model was structured, in which the variables of interest were selected according to their *P* value ($P \leq .05$) in the inferential analysis. The variables presenting statistical significance in simple logistic regression model ($P \leq .05$) were adjusted together in the multiple model, and the final model was defined using the stepwise backward variable selection method.

Statistical significance was considered for the values of $P \leq .05$. The data obtained were entered in Excel 2007 spreadsheet, Microsoft Windows (Microsoft, Redmond, Washington), and statistical R package (R Foundation, Vienna, Austria) was used for the analyses.

## RESULTS

One hundred seventy-one patients were analyzed from January to March 2016. However, only 158 patients were included after the exclusion criteria were verified. All the 13 patients excluded had ICU length of stay shorter than 24 hours.

Table 1 shows the distribution of patients according to death. The mortality outcome is reported in 18.9% of the patients. It is observed that the majority of males (63.3%) died, *P* = .277, and the mean age of the patients presenting the same outcome was 79.23 ± 13.06 years, *P* = .283. The main hospitalization diagnoses were related to respiratory changes (24.1%) followed by surgical (22.2%), neurological (18.4%), and sepsis (12.0%).

The most prevalent clinical history in the group whose condition gradually deteriorated into death was systemic arterial hypertension (50.0%, *P* = 1.000), diabetes (43.3%, *P* = .016), and heart failure (36.7%, *P* = .196).

The patients who died had a longer ICU length of stay of 34.60 ± 58.51 versus 21.92 ± 24.71 days (*P* = .274), a lower ICU readmission requirement of 6.7% versus 31.2% (*P* = .201), and a higher severity index by Simplified Acute Physiology Score 3 with 60.80 ± 13.33 versus 48.84 ± 13.82 (*P* = .717).

Concerning the need for intensive support, use of vasopressor therapy is greater among patients who died (73.3% vs 63.3%, *P* = .158), with noradrenaline being the most frequently used drug (70.0% vs 43.7%, *P* = .041). The use of MV is also higher for these individuals who died (76.7% vs 32.0%, *P* < .001), as well as their days of MV use (6.71 ± 11.24 vs 1.41 ± 2.96 days, *P* < .001). Renal replacement therapy (RRT) was observed in 56.7% of the same group of patients (*P* < .001), and the most widely used modality for these patients was the continuous method, with 50.0% (*P* < .001).

Regarding renal function, AKI was demonstrated in 63.3% of the individuals who died (*P* < .001). For this same group of patients, accumulative FB was higher (928.70 ± 896.20 vs 573.50 ± 900.52, *P* = .938), as well as FO (13.3% vs 7.0%, *P* = .035). There was no significant difference in the weight of patients in either group.

When hydroelectrolytic condition was observed, a similarity between potassium values (4.12 ± 0.45 vs 4.09 ± 0.67, with *P* = .002) was noted and with no difference between the values of sodium (139.81 ± 22.30 vs 138.81 ± 4.91, with *P* = .826).

The Figure shows the division of patients according to death and FO. It is evident that the individuals who died had a higher amount of FO than those who survived (7 [23.2%] vs 6 [4.6%], *P* = .001).

Table 2 shows the simple logistic regression model with death as a result. The variables with the highest odds of death are MV with 6.97 (95% confidence interval [CI], 2.89–18.80; *P* < .001), FO with 6.23 (95% CI, 2.04–19.53; *P* = .001), AKI with 6.17 (95% CI, 2.67–14.90; *P* < .001), RRT with 5.97 (95% CI, 2.57–14.27; *P* < .001), and noradrenaline with 1.86 (95% CI, 0.75–5.31; *P* = .030).

Table 3 presents the multivariate model with death as an outcome. From the multiple model, it is estimated that the main risk factor is MV with 5.86 (95% CI, 2.10–18.12; *P* = .001), followed by AKI with 4.05 (95% CI, 1.53–11.20; *P* = .005) and noradrenaline with 3.85 (95% CI, 1.01–9.51; *P* = .041). The FO was not significant and was 3.68 (95% CI, 0.91–15.55; *P* = .069).

## DISCUSSION

The present study shows a considerable FO in the patients who died than in those who survived. Although this condition is significant in simple regression, when transposed to multivariate regression it was not considered a risk factor for mortality. However, the FO is a factor that must be analyzed by nursing and multidisciplinary team in the critical patient, principally due to its impact on the functioning of the organ systems.

A study in an emergency department showed 71.5% of patients had FO.[13] In emergency units, fluid administration is related to volume replacement in sepsis and stabilization hemodynamics in shock, among others.[13] When analyzing the patients who died, it was verified that all of them had FO, *P* < .001, showing the danger of aggressive volume replacement.[13] Fluid overload impacts clinical parameters such as arterial gasometry, such as reduction in

TABLE 1 **Distribution of Patients Admitted to the ICU According to Death (São Paulo, 2018)**

| Variables | Survivors (n = 128) | Nonsurvivors (n = 30) | Total (n = 158) | P |
|---|---|---|---|---|
| Male sex, n (%) | 68 (53.1) | 19 (6.3) | 87 (55.1) | .277[a] |
| Age, y | 67.14 ± 16.85 | 79.23 ± 13.06 | 69.44 ± 16.85 | .283[b] |
| Hypertension, n (%) | 64 (50.0) | 15 (50.0) | 79 (50.0) | 1.000[a] |
| Diabetes, n (%) | 17 (13.2) | 13 (43.3) | 27 (17.0) | 0.016[a] |
| Heart failure, n (%) | 34 (26.6) | 11 (36.7) | 45 (28.5) | .196[a] |
| Hepatopathy, n (%) | 7 (5.5) | 2 (6.7) | 9 (5.7) | 1.000[c] |
| CKD | 17 (13.3) | 9 (30.0) | 26 (16.4) | .051[c] |
| COPD | 13 (10.1) | 6 (20.0) | 19 (12.0) | .207[c] |
| Stroke | 11 (8.5) | 8 (26.7) | 19 (12.0) | .032[c] |
| Readmission in ICU, n (%) | 40 (31.2) | 2 (6.7) | 42 (26.5) | .201[a] |
| ICU length of stay, d | 21.92 ± 24.71 | 34.60 ± 58.51 | 6.06 ± 5.75 | .274[d] |
| Vasopressor therapy, n (%) | 81 (63.3) | 22 (73.3) | 103 (65.2) | .158[a] |
| Noradrenaline | 56 (43.7) | 21 (70.0) | 77 (48.7) | .041[a] |
| Dobutamine | 16 (12.5) | 6 (20.0) | 22 (13.9) | .389[c] |
| Adrenaline | 5 (4.0) | 2 (6.7) | 7 (4.4) | .618[c] |
| Nitroglycerin | 11 (8.5) | 2 (6.7) | 13 (8.2) | 1.000[c] |
| Sodium nitroprusside | 14 (11.0) | 4 (13.3) | 18 (11.4) | .750[c] |
| MV, n (%) | 41 (32.0) | 23 (76.7) | 64 (40.5) | <.001[a] |
| MV, d | 1.41 ± 2.96 | 6.71 ± 11.24 | 5.97 ± 8.08 | <.001[d] |
| RRT, n (%) | 23 (18.0) | 17 (56.7) | 40 (25.3) | <.001[a] |
| Continuous method | 18 (14.0) | 15 (50.0) | 30 (18.9) | <.001[a] |
| Intermittent method | 5 (4.0) | 2 (6.7) | 7 (4.4) | .648[c] |
| AKI, n (%) | 28 (21.9) | 19 (63.3) | 47 (29.7) | <.001[a] |
| Accumulative FB, mL | 573.50 ± 900.52 | 928.70 ± 896.20 | 640.94 ± 904.80 | .938[b] |
| Weight, kg | 73.25 ± 17.50 | 70.50 ± 16.00 | 72.96 ± 17.89 | .575[b] |
| UO, mL | 5636.06 ± 3855.90 | 4614.60 ± 3490.17 | 1569.85 ± 858.82 | .328[b] |
| Potassium | 4.12 ± 0.45 | 4.09 ± 0.67 | 4.11 ± 0.50 | .002[b] |
| Sodium | 139.81 ± 22.30 | 138.81 ± 4.91 | 139.62 ± 20.10 | .826[b] |
| SAPS 3 | 48.84 ± 13.82 | 60.80 ± 13.33 | 51.11 ± 14.48 | .717[b] |

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; FB, fluid balance; ICU, intensive care unit; MV, mechanical ventilation; RRT, Renal Replacement Therapy; SAPS, Simplified Acute Physiology Score; UO, urinary output.

[a] $\chi^2$ Test.

[b] Student *t* test.

[c] Fisher exact test.

[d] Mann-Whitney *U* test.

the pressure of oxygen rates, and higher lactate levels, $P < .001$, which is probably associated with tissue hypoperfusion, which takes mortality up to 30 days.[13]

Regarding postoperative surgical patients in the ICU, 22.3% of individuals who accumulated fluid in the intraoperative period were observed.[6] Similarly, positive FB was found in 49.3% of patients.[6,14] The intraoperative period requires careful attention to bleeding and shock, and the administration of fluids is an alternative for hemodynamic control. However, occurrence of neurological, respiratory, and cardiac dysfunctions, as well as increased infections, is found to occur in patients who accumulated fluid in this period.[6] Thus, intraoperative fluid accumulation is considered an independent factor for hospital mortality (odds ratio [OR], 1.024; CI, 1.00–1.04; $P = .006$),[6] MV (OR, 20.03; CI, 2.74–146.6.82; $P = .003$) and age (OR, 2.23; CI, 1.26–3.96; $P < .001$), because these 2 last corroborate with the findings of this study.[14]

These findings reflect the importance of the nurses' performance in ICU, in what concerns first the identification

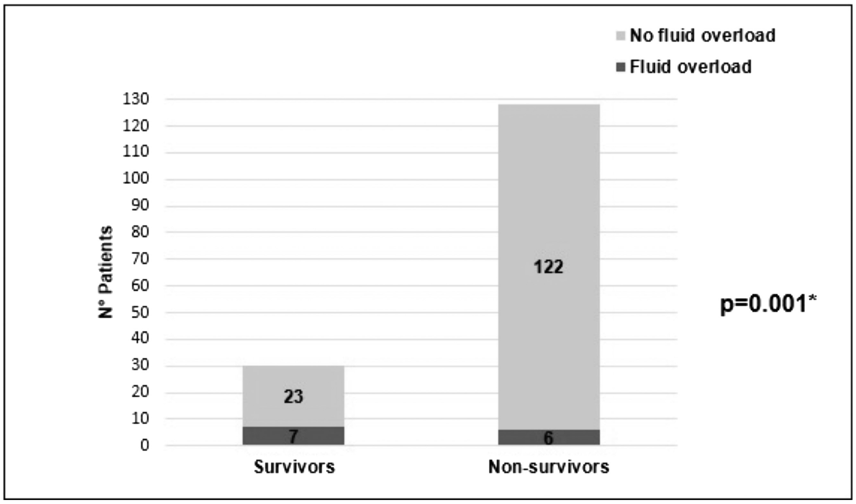


**Figure.** Division of patients according to death and fluid overload, São Paulo, Brazil, 2018. *$x^2$ Test.

of risks related to accumulative FB and the elaboration of interventions aimed at reducing and avoiding the complications of FO in vital organs such as lung and kidney.

In what concerns the impact of FO on the respiratory system, there is a change in the hydrostatic and oncotic forces of the pulmonary capillaries, which causes imbalance in hematose through the formation or worsening of pulmonary edema.[4] This mechanism can result in the formation of an acute lung injury and to the need for MV.[15] Fluid accumulation has already been described in the literature as one of the risk factors for acute lung injury in postoperative thoracotomy (OR, 20.48; CI, 2.31–180.90; $P$ = .007).[16]

The high need for MV by nonsurviving patients in this study reflects the need for intensive support and severity according to Simplified Acute Physiology Score 3. Accumulation of fluid is related to greater risks of complications concerning MV management (OR, 8.39; CI, 2.99–23.50; $P$ < .001). Additionally, patients whose condition deteriorates as a result of these complications require more days of MV, ICU stay, and mortality.[17] Furthermore, fluid accumulation is also associated with extubation failure in critically ill patients.[18] Thus, FO is directly related to higher mortality in 30 days in patients submitted to MV, probably associated with aggression to lung tissue (OR, 1.08; CI, 1.00–1.17; $P$ = .03).[19]

Besides the pulmonary impact, the renal system also suffers from the impact of FO. In the present study, the prevalence of renal impairment, whether acute or chronic, as well as RRT during the hospitalization period, showed a larger proportion among nonsurvivors. The prevalence of AKI found in this study is lower when compared with data in the literature.[7,20] However, when the patients who died were analyzed, the prevalence of AKI is twice that of the survivors, which is corroborated by the literature.[7,20]

**TABLE 2 Simple Logistic Regression Model With Outcomes as Death (São Paulo, 2018)**

| Variables | OR (95% CI) | *P* |
|---|---|---|
| MV | 6.97 (2.89–18.80) | <.001 |
| FO | 6.23 (2.04–19.53) | .001 |
| AKI | 6.17 (2.67–14.90) | <.001 |
| RRT | 5.97 (2.57–14.27) | <.001 |
| Noradrenaline | 1.86 (0.75–5.31) | .030 |
| Diabetes | 0.77 (0.15–2.02) | .378 |
| Stroke | 0.69 (0.02–1.57) | .208 |
| Potassium | 0.52 (0.71–1.17) | .453 |

Abbreviations: AKI, acute kidney injure; CI, confidence interval; FO, fluid overload; MV, mechanical ventilation; OR, odds ratio; RRT, renal replacement therapy.

**TABLE 3 Multiple Logistic Regression Model With Outcomes as Death (São Paulo, 2018)**

| Variables | OR (95% CI) | *P* |
|---|---|---|
| MV | 5.86 (2.10–18.12) | .001 |
| AKI | 4.05 (1.53–11.20) | .005 |
| Noradrenaline | 3.85 (1.01–9.51) | .041 |
| FO | 3.68 (0.91–15.55) | .069 |
| RRT | 1.51 (0.88–1.41) | .154 |

Abbreviations: AKI, acute kidney injure; CI, confidence interval; FO, fluid overload; MV, mechanical ventilation; OR, odds ratio; RRT, renal replacement therapy.

In this sense, FO can alter renal function and lead to the development of AKI.[4] It is already found in the literature that fluid accumulation is a predictor for the development of AKI (OR, 1.00; CI, 1.00–1.01; $P = .02$).[20] In correlation with nursing practice, for patients who develop AKI, a greater nursing workload is observed by the Nursing Activities Score due to the impact of the care performed. Nevertheless, there is still no evidence of the nursing workload in patients with FO.[21]

Regarding risk, individuals with AKI who develop FO tend to have a higher risk of mortality.[7,22] A systematic review and meta-analysis shows that FO is associated with increased risk of mortality in patients with AKI. The same result is also found in a clinical study (OR, 1.04; CI, 1.01–1.07; $P = .006$).[7,22]

Among the patients who develop AKI and require RRT, FO is present and impacts on the outcome of the critical patient. It is observed in the literature that patients with continuous RRT have an incidence of 26.9% of FO, and more than half of them died.[2] And it is found that FO in these individuals is also considered a risk factor for mortality for 30 and 90 days.[2,23]

In summary, the impact of FO on critical patient morbidity and mortality is extremely significant. Fluid administration, FB values, and their association with the condition of the patient should be carefully evaluated, because according to the evaluation of fluids it is possible to create therapeutic goals that lead to the enhancement of vital organs.

Nursing has the role of ensuring best practice and avoiding unnecessary FO for patient safety. This can be through the pulmonary evaluation diary with auscultating the lungs, x-ray, and gasometric and oxygenation parameters. For renal evaluation, it is necessary for the nurse to observe the drug dilution volumes, reliable measurement of UO, daily serum creatinine value analysis and RRT parameters settings.

Teamwork is an essential contribution to this goal of avoiding complications of FO. In the case of invasive ventilatory support, the evaluation of the team in weaning of MV and extubation is a context that requires joint work of the nursing, physicians, and physiotherapy team. The elaboration of a restriction of fluid administration is necessary interaction between physicians, nursing, and nutritionist. In this way, other evaluations must be done together with the multiprofessional team, with the purpose of performing a safe and quality care for the patients.

This study has limitations, such as being retrospective and single-center and having a small sample because a previous database of the ICU studied was used. Therefore, more in-depth multicenter studies with larger samples concerning FO and its correlation with the nursing workload are needed.

## CONCLUSION

It was observed that patients with death as an outcome accumulated an FO. Although FO was considered significant in the simple regression analysis, there was no statistical difference in the multiple regression analysis. However, the impact of FO is considerable, and nursing plays a fundamental role in the multidisciplinary team regarding the prevention, identification, and control of FO, mainly due to its impact on organ systems and critical patient mortality.

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