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# Tipping the balance: early post-resuscitation fluid accumulation and outcome after cardiac arrest

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## Abstract

In a cohort of 109 adults resuscitated from out-of-hospital cardiac arrest and admitted to a tertiary intensive care unit (ICU), non-survivors showed higher mean fluid intake, reduced urine output, and greater cumulative positive fluid balance during the first 96 h after resuscitation. Daily increases in mean fluid balance were independently associated with ICU mortality after adjustment for confounding factors. These observations suggest that sustained positive fluid balance is linked to adverse outcomes, underscoring the potential value of more individualized or restrictive fluid management following cardiac arrest.

Recently, a multicentre prospective cohort of out-of-hospital cardiac arrest (OHCA) patients admitted to the intensive care unit (ICU) has provided compelling evidence in an area where guidance remains poor, namely fluid strategies during the post-resuscitation period [1]. Indeed, a positive cumulative fluid balance by day-7 was independently associated with higher 90-day mortality and worse neurological outcome [1]. Following return of spontaneous circulation (ROSC), circulatory shock is common, affecting approximately 50–70% of patients [2]. While in the early post-ROSC phase, cardiogenic shock is frequent, over the ensuing hours to days, however, the inflammatory response, typically triggered by reperfusion, may progress to distributive shock, often

associated with increased endothelial permeability and relative hypovolemia [3]. In this context, fluid requirements can vary significantly, yet evidence to guide optimal management remains limited [2]. Therefore, we wish to contribute to this discussion by reporting data from our own retrospective single-centre cohort, which offers insights into the timing, amount, and prognostic implications of fluid balance after OHCA. Hundred-nine consecutive adult non-traumatic OHCA patients admitted to our tertiary ICU, from January 2016 to December 2024, were included in the analysis [4]. Post-ROSC care was delivered according to current guidelines [2], without a standardized fluid management protocol. Available data included demographic and cardiac arrest-related variables, Sepsis-related Organ Failure Assessment (SOFA) score at ICU admission, vasoactive-inotropic score (VIS), hemodynamic parameters, arterial lactate levels and pH, PaO<sub>2</sub>/FiO<sub>2</sub> ratios, and serum creatinine. Daily fluid intake (i.v. crystalloids, medications, nutrition; excluding blood products) and output (urine and ultrafiltration, if initiated) were recorded for up to 96 h after ICU admission. Fluid balance was calculated as intake minus output and

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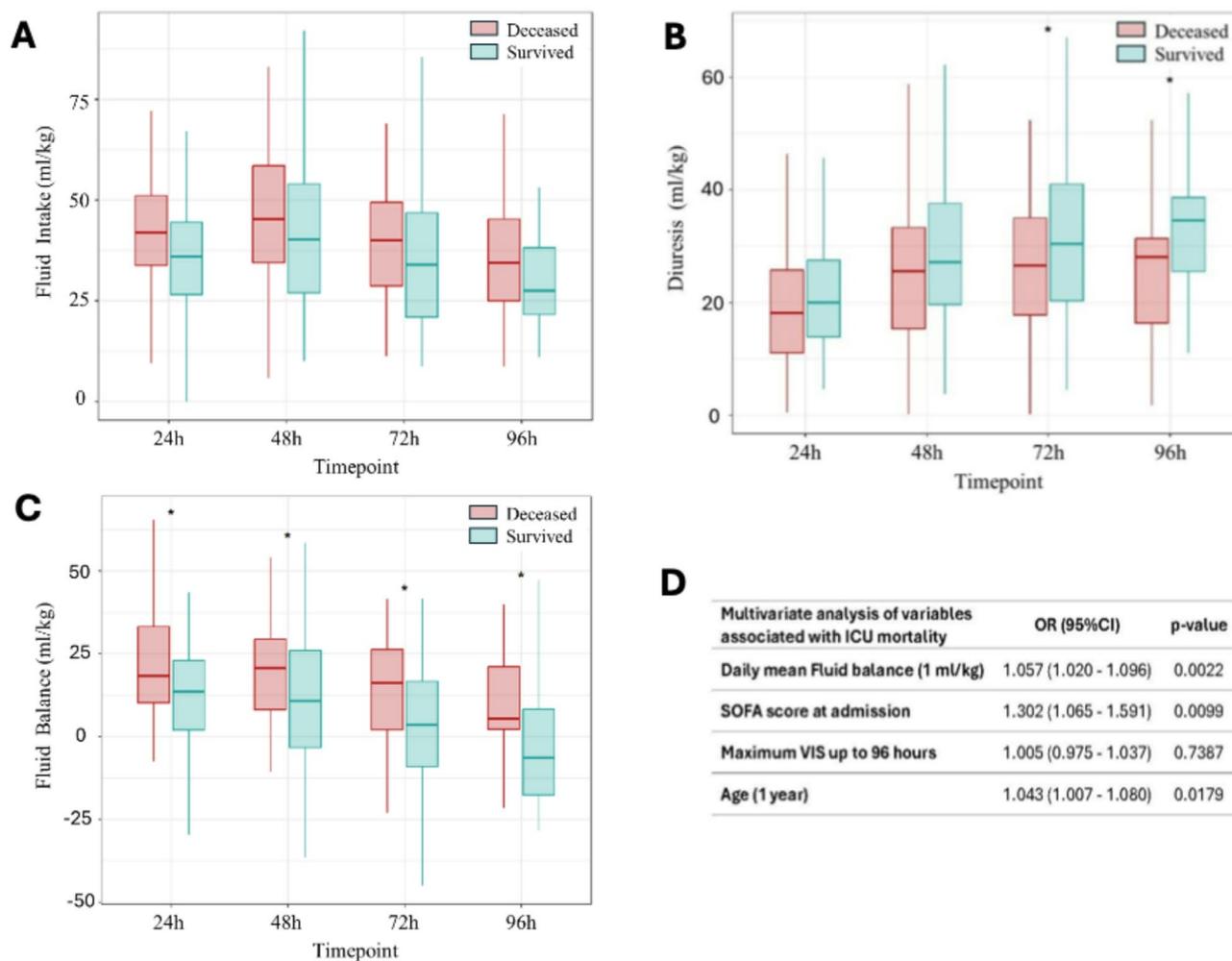
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**Fig. 1** Box plots showing **A**) fluid intake, **B**) diuresis output, **C**) fluid balance indexed to body weight over the 96 hr of ICU stay, and **D**) Table showing multivariate analysis with adjusted odds ratio (OR) and 95% confidence interval (CI) for ICU mortality.\* $p < 0.05$  vs. non-survivors, after adjustment for SOFA score at admission

indexed to body weight, with a positive balance defined as greater than zero. The mean daily balance over the observation period (i.e. 96 h or until discharge or death) was calculated for each patient. Associations with ICU mortality were analysed with multivariate logistic regression models, adjusted for age, SOFA score and VIS score. To assess potential bias from evolving clinical practices over time, a linear trend analysis of fluid intake and balance was conducted. Sixty-four patients (59%) were discharged alive from the ICU. Compared to survivors, non-survivors had significantly higher SOFA and VIS scores, arterial lactate levels, serum creatinine level, and lower mean arterial pressure ( $p < 0.01$ ). No other differences were observed. Over the first 96 h post-ROSC, non-survivors received higher daily mean fluid intake (42 mL/kg vs. 35 mL/kg,  $p = 0.012$ ), had lower daily mean urine output (1724 ml vs. 2067 ml,  $p = 0.03$ ), and accumulated a markedly higher positive daily mean fluid balance (18 mL/kg vs. 8 mL/kg,  $p < 0.01$ ). After adjustment for SOFA score, group differ-

ences in urine output and fluid balance remained significant beyond 72 h (Fig. 1). A negative linear trend in fluid intake ( $\beta = -1.53$ ,  $p = 0.004$ ) and fluid balance ( $\beta = -1.28$ ,  $p = 0.018$ ), expressed as mL/kg, was found over the years of enrollment. In the multivariate logistic regression model, 1 mL/kg increment in daily mean fluid balance was independently associated with ICU mortality (OR 1.06 [1.02–1.10],  $p = 0.002$ ; Fig. 1D). Previous studies in other critically ill populations, including sepsis, traumatic brain injury, and acute respiratory distress syndrome, have consistently shown that positive fluid balance is associated with worse outcomes [5]. In the post-ROSC phase, evidence of fluid management and its impact on outcomes remains limited. Our data indicate that post-resuscitation patients receive substantial fluid volumes, with a daily mean intake over the first 96 h exceeding 2.5 L (~38 mL/kg). This pattern likely reflects initial hemodynamic instability, early resuscitation requirements, and the evolving course of post-cardiac arrest syndrome, characterized by dynamic shifts

from cardiogenic to distributive shock [3, 4]. These results strengthen the association between sustained positive fluid balance and adverse outcome, as recently reported by Renaudier et al. [1]. In their study, 74% of patients had a positive fluid balance, compared with 81% in our cohort, possibly reflecting differences in illness severity or variations in clinical practice/intensity treatment, including vasopressor use which was more frequent in their population (maximum VIS 41 vs. 11 in ours). Additionally, their analysis extended to 7 days post-resuscitation, whereas ours focused on the first 96 h; a longer follow-up period may increase the likelihood of achieving a negative fluid balance. Despite these differences, our findings reinforce their conclusions and suggest that a more restrictive fluid management strategy, especially in the first 4 days post-ROSC, could improve outcomes. This study has several limitations. Our single-centre, retrospective design and modest sample size limit generalisability and precluded survival analyses. The extended recruitment period may have introduced variability in clinical practice. Although we observed a statistically significant downward trend in fluid intake over the years, the annual decrease was, however, minimal ( $\approx 1.5$  mL/kg) and unlikely to be clinically relevant. Nevertheless, these findings underscore the need for individualised fluid management strategies that carefully balance early resuscitation needs with the risk of fluid overload following ROSC Fig. 1.

#### Abbreviations

ICU	Intensive care unit
OHCA	Out-of-hospital cardiac arrest
ROSC	Return of spontaneous circulation
SOFA	Sepsis-related organ failure assessment
VIS	Vasoactive-inotropic score

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#### Author contributions

CC: Investigation, data curation, data validation, methodology, visualisation, writing – original draft; AM: Conceptualisation, data validation, writing – review & editing; GM: Investigation, data curation, data validation; FM: Formal analysis, software, data validation, methodology, visualisation, writing – review & editing; CD: Investigation, data curation, writing – original draft; MP: Supervision, writing – review & editing; GG: Funding acquisition, writing – review & editing; GR: Supervision, conceptualisation, methodology,

writing – review & editing. All authors read and approved the final version of the manuscript.

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#### Data availability

No datasets were generated or analysed during the current study.

#### Declarations

##### Ethics approval and consent to participate

The study complies with the Declaration of Helsinki and was approved by the Regional Ethics Committee “Lombardia 3” (approval no. OSMAMI-25/07/2024-0029769-U) and registered on ClinicalTrials.gov (NCT06608771). Written informed consent was waived in accordance with local regulations on retrospective study design.

##### Consent for publication

Not applicable.

##### Competing interests

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