

SUPPLEMENTARY

Table 1. Characterization of patients regarding the variables sex, age range, age, nutritional status, clinical background, oncohematological, sepsis and PIM3 of patients in total, in the retrospective phase, and in the prospective phase of the study

| Variable | Total | Retrospective | Prospective | P-value |
|----------------------------|--------------------|----------------------|--------------------|----------------|
| | <i>N</i> = 122 (%) | <i>n</i> = 71 (%) | <i>n</i> = 51 (%) | |
| Sex | | | | |
| Male | 65 (53.3) | 36 (50.7) | 29 (56.9) | 0.501 |
| Female | 57 (46.7) | 35 (49.3) | 22 (43.1) | |
| Age group | | | | |
| Less than 1 year | 25 (20.5) | 16 (22.5) | 9 (17.6) | 0.754 |
| From 1 to 2 years | 21 (17.2) | 10 (14.1) | 11 (21.6) | |
| From 3 to 5 years | 15 (12.3) | 9 (12.7) | 6 (11.8) | |
| From 6 to 10 years | 22 (18.0) | 12 (16.9) | 10 (19.6) | |
| From 11 to 14 years | 22 (18.0) | 12 (16.9) | 10 (19.6) | |
| More than 14 years | 17 (14.0) | 12 (16.9) | 5 (9.8) | |
| Age (years) | | | | |
| Mean ± SD | 6.7 ± 5.7 | 6.9 ± 6.0 | 6.5 ± 5.4 | 0.913 |
| Median (Q1–Q3) | 6.7 (1.0–5.5) | 6.00 (1.0–12.9) | 5.00 (1.50–12.00) | |
| Min–Max | 0.1–17.8 | 0.1–17.8 | 0.1–17.0 | |
| Underweight | | | | |
| Yes | 29 (23.8) | 18 (25.4) | 11 (21.6) | 0.628 |
| No | 93 (76.2) | 53 (74.6) | 40 (78.4) | |
| Clinical background | | | | |

TABLE 1. Cont.

| | | | | |
|-------------------|---------------|---------------|---------------|--------------|
| Surgical | 74 (60.6) | 41 (57.7) | 33 (64.7) | 0.579 |
| Medical | 48 (39.4) | 30 (42.3) | 18 (35.3) | |
| Oncohematological | | | | |
| Yes | 41 (33.6) | 23 (32.4) | 18 (35.3) | 0.738 |
| No | 81 (66.4) | 48 (67.6) | 33 (64.7) | |
| Sepsis | | | | |
| Yes | 51 (41.8) | 31 (43.7) | 20 (39.2) | 0.623 |
| No | 71 (58.2) | 40 (56.3) | 31 (60.8) | |
| PIM 3 | | | | |
| Mean \pm SD | 3.9 \pm 6.5 | 4.1 \pm 7.3 | 3.6 \pm 5.3 | 0.674 |
| Median (Q1–Q3) | 1.4 (0.8–4.2) | 1.4 (0.8–3.8) | 1.4 (0.8–4.6) | |
| Min–Max | 0.2–38.2 | 0.2–38.2 | 0.2–31.8 | |

The *P*-values for sex, age group, nutritional status, clinical background, oncohematological, and sepsis refer to Pearson's χ^2 test, the *P*-value for age comparison refers to the non-parametric Mann-Whitney test, and the *P*-value for PIM3 refers to Student's *t*-test.

SD – standard deviation, Q1 – first quartile, Q3 – third quartile, Min – minimum, Max – maximum

Table 2. Clinical outcomes and cumulative fluid balance trajectory according to patient groups: total, retrospective, and prospective analyses

| Variable | Total | Retrospective | Prospective | <i>P</i> -value |
|-----------------------------|-----------------|----------------|-----------------|-----------------|
| | <i>N</i> = 122 | <i>n</i> = 71 | <i>n</i> = 51 | |
| Number of vasoactive amines | | | | |
| Mean ± SD | 1.8 ± 1.0 | 1.9 ± 1.0 | 1.6 ± 0.9 | 0.162 |
| Median (Q1–Q3) | 1.5 (1.0–2.0) | 2.0 (1.0–2.0) | 1.0 (1.0–2.0) | |
| Min–Max | 1.0–5.0 | 1.0–5.0 | 1.0–5.0 | |
| Duration of IMV (days) | | | | |
| Mean ± SD | 5.5 ± 4.2 | 5.4 ± 3.6 | 5.5 ± 4.7 | 0.429 |
| Median (Q1–Q3) | 4.0 (2.0–8.5) | 4.0 (3.0–7.5) | 3.5 (2.0–9.0) | |
| Min–Max | 1.0–18.0 | 1.0–15.0 | 1.0–18.0 | |
| PICU stay (days) | | | | |
| Mean ± SD | 10.6 ± 5.4 | 9.6 ± 4.5 | 11.7 ± 6.1 | 0.091 |
| Median (Q1–Q3) | 10.0 (6.0–15.0) | 9.0 (6.0–13.0) | 11.0 (6.0–18.0) | |
| Min–Max | 3.0–20.0 | 3.0–19.0 | 3.0–20.0 | |
| RRT | | | | |
| Yes | 15 (12.3%) | 7 (10.0%) | 8 (15.7%) | 0.349 |
| No | 107 (87.7) | 64 (90.0) | 43 (84.3) | |
| Death | | | | |
| Yes | 20 (16.4) | 18 (25.4) | 2 (3.9) | 0.002 |
| No | 102 (83.6) | 53 (74.6) | 49 (96.1) | |
| CFB trajectory | | | | |
| Fluid accumulation | 42 (41.2) | 25 (47.2) | 17 (34.7) | 0.201 |
| Fluid evacuation | 60 (58.8) | 28 (52.8) | 32(65.3) | |

The *P*-values for number of vasoactive amines, duration of IMV (days), and PICU stay (days) were calculated using the non-parametric Mann-Whitney test, while the *P*-values for RRT comparison, death, and CFB trajectory (survivors) were calculated using Pearson's χ^2 test.

Supplementary Table 3. Characterization of patients regarding the clinical background of patients in total, in the retrospective phase and in the prospective phase of the study

| Variable | Total | Retrospective | Prospective |
|--------------------------|----------------|---------------|---------------|
| | <i>N</i> = 122 | <i>n</i> = 71 | <i>n</i> = 51 |
| Surgical | 74 (60.6) | 41 (57.7) | 33 (62.8) |
| Pediatric surgery | 41 (33.6) | 24 (33.8) | 17 (33.3) |
| Neurosurgery | 12 (9.8) | 5 (7.0) | 7 (13.7) |
| Digestive system surgery | 8 (6.5) | 3 (4.2) | 5 (9.8) |
| Cardiovascular surgery | 7 (5.7) | 6 (8.4) | 1 (1.9) |
| Orthopedics | 3 (2.4) | 3 (4.2) | 0 (0.0) |
| Vascular surgery | 3 (2.4) | 0 (0.0) | 3 (5.8) |
| Medical | 48 (39.4) | 30 (42.3) | 18 (37.2) |
| Cardiovascular | 27 (22.1) | 16 (22.5) | 11(21.5) |
| Respiratory | 12 (9.8) | 9 (12.6) | 3 (5.8) |
| Neurological | 9 (7.3) | 5 (7.0) | 4 (7.8) |

Supplementary Table 4. Analysis of the variation in percentage fluid accumulation (FA%), across the Resuscitation, Optimization, Stabilization, and Evacuation phases in the retrospective and prospective cohorts

| FA% | Retrospective | Prospective | <i>P</i> -value |
|--|----------------|----------------|-----------------|
| | <i>N</i> = 71 | <i>n</i> = 51 | |
| Resuscitation | | | |
| Mean ± SD | 4.4 ± 3.3 | 4.9 ± 2.9 | 0.244 |
| Median (Q ₁ –Q ₃) | 3.5 (2.0–6.0) | 4.7 (2.4–6.9) | |
| Min-Max | 0.8–16.0 | 0.3–13.0 | |
| Optimization | | | |
| Mean ± SD | 5.4 ± 9.5 | 5.1 ± 5.3 | 0.261 |
| Median (Q ₁ –Q ₃) | 3.0 (0.1–6.7) | 4.2 (1.0–7.9) | |
| Min-Max | –7.0–60.0 | –2.9–22.7 | |
| Stabilization | | | |
| Mean ± SD | 3.6 ± 5.3 | 5.0 ± 4.6 | 0.043 |
| Median (Q ₁ –Q ₃) | 2.5 (0.0–6.9) | 4.2 (2.0–8.9) | |
| Min-Max | –8.7–24.0 | –7.1–17.5 | |
| Evacuation | | | |
| Mean ± DP | 2.3 ± 7.5 | 3.4 ± 5.7 | 0.256 |
| Median (Q ₁ –Q ₃) | 2.5 (–2.6–5.3) | 2.4 (–0.0–7.4) | |
| Min-Max | –11.7–32.0 | –7.1–26.0 | |

P – probability of significance of the Mann-Whitney test.

Supplementary Table 5. Analysis of the variation in time (hours), across the Resuscitation, Optimization, Stabilization, and Evacuation phases in the retrospective and prospective cohorts

| Time (hours) | Retrospective | Prospective | <i>P</i> -value |
|--|--------------------|--------------------|-----------------|
| | <i>n</i> = 71 | <i>n</i> = 51 | |
| Resuscitation | | | |
| Mean ± SD | 2.2 ± 0.7 | 2.6 ± 1.0 | 0.073 |
| Median (Q ₁ –Q ₃) | 2.0 (2.0–3.0) | 3.0 (2.0–3.0) | |
| Min-Max | 1.0–4.0 | 1.0–6.0 | |
| Optimization | | | |
| Mean ± SD | 24.2 ± 22.2 | 21.2 ± 19.3 | 0.270 |
| Median (Q ₁ –Q ₃) | 18.0 (10.0–24.0) | 15.0 (9.0–24.0) | |
| Min-Max | 6.0–120.0 | 3.0–96.0 | |
| Stabilization | | | |
| Mean ± SD | 84.3 ± 54.2 | 97.5 ± 75.5 | 0.722 |
| Median (Q ₁ –Q ₃) | 72.0 (48.0–120.0) | 72.0 (48.0–144.0) | |
| Min-Max | 18.0–240.0 | 24.0–336.0 | |
| Evacuation | | | |
| Mean ± SD | 114.7 ± 58.4 | 169.1 ± 110.6 | 0.020 |
| Median (Q ₁ –Q ₃) | 120.0 (72.0–144.0) | 144.0 (83.5–219.0) | |
| Min-Max | 24.0–264.0 | 3.0–456.0 | |

P – probability of significance of the Mann-Whitney test.

Supplementary Table 6. Analysis of the variation in time lactate (mmol/l), across the Resuscitation, Optimization, Stabilization, and Evacuation phases in the retrospective and prospective cohorts

| Lactate (mmol L ⁻¹) | Retrospective | Prospective | <i>P</i> -value |
|--|------------------|------------------|-----------------|
| | <i>n</i> = 71 | <i>n</i> = 51 | |
| Resuscitation | | | |
| Mean ± SD | 4.34 ± 2.88 | 3.61 ± 2.29 | 0.108 |
| Median (Q ₁ –Q ₃) | 3.50 (2.51–5.49) | 2.79 (2.10–4.38) | |
| Min-Max | 1.11–16.00 | 1.02–12.00 | |
| Optimization | | | |
| Mean ± SD | 4.13 ± 3.14 | 2.77 ± 1.85 | 0.001 |
| Median (Q ₁ –Q ₃) | 3.50 (2.40–4.27) | 2.35 (1.64–3.61) | |
| Min-Max | 0.79–15.00 | 0.75–12.00 | |
| Stabilization | | | |
| Mean ± DP | 1.71 ± 0.65 | 1.64 ± 0.86 | 0.212 |
| Median (Q ₁ –Q ₃) | 1.50 (1.27–1.87) | 1.42 (1.10–1.86) | |
| Min-Max | 0.73–4.23 | 0.45–4.90 | |
| Evacuation | | | |
| Mean ± DP | 1.31 ± 0.47 | 1.42 ± 0.48 | 0.194 |
| Median (Q ₁ –Q ₃) | 1.29 (0.97–1.50) | 1.35 (1.11–1.60) | |
| Min-Max | 0.63–3.20 | 0.89–3.60 | |

P – probability of significance of the Mann-Whitney test.

Supplementary Table 7. Distribution of Therapeutic Interventions and Mortality across the ROSE Phases (Resuscitation, Optimization, Stabilization, Evacuation) in the retrospective cohort ($n = 71$)

| Variable | Resuscitation | Optimization | Stabilization | Evacuation |
|-----------------------|---------------|--------------|---------------|------------|
| IMV | 71 (100%) | 71 (100%) | 53 (100%) | 6 (11.3%) |
| Vasoactive amines | 71 (100%) | 71 (100%) | 53 (100%) | 0 (0.0%) |
| Epinephrine | 49 (69.0%) | 46 (64.7%) | 27 (50.9%) | 0 (0.0%) |
| Norepinephrine | 27 (38.0%) | 37 (52.1%) | 25 (47.1%) | 0 (0.0%) |
| Dobutamine | 4 (5.6%) | 14 (19.7%) | 6 (11.3%) | 0 (0.0%) |
| Milrinone | 5 (7.0%) | 8 (11.2%) | 7 (13.2%) | 0 (0.0%) |
| Vasopressin | 1 (1.4%) | 1 (1.4%) | 0 (0.0%) | 0 (0.0%) |
| Crystalloid | 63 (88.7%) | 40 (56.3%) | 8 (15.0%) | 0 (0.0%) |
| NaCl 0.9% | 48 (67.6%) | 18 (25.3%) | 6 (11.3%) | 0 (0.0%) |
| Ringer's lactate | 31 (43.6%) | 23 (32.3%) | 5 (9.4%) | 0 (0.0%) |
| Plasma-Lyte | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Blood product | 27 (38.0%) | 38 (53.5%) | 21 (39.6%) | 0 (0.0%) |
| Albumin | 3 (4.2%) | 21 (29.5%) | 14 (26.4%) | 0 (0.0%) |
| Albumin 5% | 3 (4.2%) | 8 (11.2%) | 3 (5.6%) | 0 (0.0%) |
| Albumin 10% | 0 (0.0%) | 11 (15.4%) | 7 (13.2%) | 0 (0.0%) |
| Albumin 20% | 0 (0.0%) | 2 (2.8%) | 4 (7.5%) | 0 (0.0%) |
| Furosemide | 0 (0.0%) | 28 (39.4%) | 34 (64.1%) | 33 (62.2%) |
| Continuous furosemide | 0 (0.0%) | 7 (9.8%) | 5 (9.4%) | 0 (0.0%) |
| RRT | 0 (0.0%) | 3 (4.2%) | 4 (7.5%) | 2 (3.7%) |

IMV – invasive mechanical ventilation, NaCl – sodium chloride, RRT – renal replacement therapy

Supplementary Table 8. Distribution of therapeutic interventions and mortality across the ROSE phases (Resuscitation, Optimization, Stabilization, Evacuation) in the prospective cohort ($n = 51$)

| Variable | Resuscitation | Optimization | Stabilization | Evacuation |
|-----------------------|---------------|--------------|---------------|------------|
| IMV | 51 (100%) | 51 (100%) | 49 (100%) | 5 (10.2%) |
| Vasoactive amines | 51 (100%) | 51 (100%) | 49 (100%) | 0 (0.0%) |
| Epinephrine | 27 (52.9%) | 29 (56.8%) | 19 (38.7%) | 0 (0.0%) |
| Norepinephrine | 23 (45.0%) | 26 (50.9%) | 24 (48.9%) | 0 (0.0%) |
| Dobutamine | 3 (5.8%) | 5 (9.8%) | 4 (8.1%) | 0 (0.0%) |
| Milrinone | 0 (0.0%) | 5 (9.8%) | 5 (10.2%) | 0 (0.0%) |
| Vasopressin | 4 (7.8%) | 2 (3.9%) | 2 (4.0%) | 0 (0.0%) |
| Crystalloid | 46 (90.1%) | 22 (43.1%) | 11 (22.40%) | 0 (0.0%) |
| NaCl 0.9% | 39 (76.4%) | 14 (27.4%) | 6 (12.2%) | 0 (0.0%) |
| Ringer's lactate | 27 (52.9%) | 11 (21.5%) | 5 (10.2%) | 0 (0.0%) |
| Plasma-Lyte | 1 (1.9%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Blood product | 30 (58.8%) | 20 (39.2%) | 15 (30.6%) | 4 (8.1%) |
| Albumin | 7 (13.7%) | 15 (29.4%) | 11 (22.4%) | 3 (6.10%) |
| Albumin 5% | 6 (11.7%) | 5 (9.8%) | 0 (0.0%) | 0 (0.0%) |
| Albumin 10% | 1 (1.9%) | 10 (19.6%) | 5 (10.2%) | 0 (0.0%) |
| Albumin 20% | 0 (0.0%) | 0 (0.0%) | 6 (12.2%) | 3 (6.1%) |
| Furosemide bolus | 2 (3.9%) | 20 (39.2%) | 23 (46.9%) | 25 (51.0%) |
| Continuous furosemide | 0 (0.0%) | 5 (9.8%) | 4 (8.1%) | 0 (0.0%) |
| RRT | 2 (3.9%) | 4 (7.8%) | 7 (14.2%) | 5 (10.2%) |

IMV – invasive mechanical ventilation, NaCl – sodium chloride, RRT – renal replacement therapy

Supplementary Table 9. Identification of risk factors associated with fluid accumulation – univariate binary logistic regression

| Variable | Fluid accumulation | | | | P-value | O.R. | IC _{95%} da O.R. |
|-----------------------------------|--------------------|------|-----------|------|---------|------|------------------------------|
| | Yes | | No | | | | |
| | n | % | n | % | | | |
| Age < 3 years | | | | | | | |
| Yes | 14 | 37.8 | 23 | 62.2 | 0.605 | 1 | 0.5–2.8 |
| No | 28 | 43.1 | 37 | 56.9 | | 1.2 | |
| Total | 42 | 41.2 | 60 | 58.8 | | | |
| Underweight | | | | | | | |
| Yes | 12 | 48.0 | 13 | 52.0 | 0.426 | 1.4 | 0.6–3.6 |
| No | 30 | 39.0 | 47 | 61.0 | | 1 | |
| Total | 42 | 41.2 | 60 | 58.8 | | | |
| Oncohematological | | | | | | | |
| Yes | 12 | 38.7 | 19 | 61.3 | 0.738 | 1 | 0.5–2.7 |
| No | 30 | 42.3 | 41 | 57.7 | | 1.2 | |
| Total | 42 | 41.2 | 60 | 58.8 | | | |
| Sepsis | | | | | | | |
| Yes | 16 | 44.4 | 20 | 55.6 | 0.621 | 1.2 | 0.5–2.8 |
| No | 26 | 39.4 | 40 | 60.6 | | 1 | |
| Total | 42 | 41.2 | 60 | 58.8 | | | |
| PIM3 (%) | | | | | | | |
| Mean ± SD | 4.5 ± 7.8 | | 3.4 ± 6.0 | | 0.412 | 1.0 | 0.97–1.1 |
| Median | 1.3 | | 1.4 | | | | |
| (Q ₁ –Q ₃) | (0.9–5.2) | | (0.8–3.7) | | | | |
| Min-Max | 0.2–38.8 | | 0.2–34.5 | | | | |

OR – odds ratio, IC_{95%} da O.R. – 95% confidence interval for the odds ratio, P – probability of significance of the Wald χ^2 test (logistic regression)

Supplementary Table 10. Multiple logistic regression analysis to identify risk factors associated with fluid accumulation

| Variable | β | Qui-quadrado (Wald) | P-value | O.R. | IC _{95%} P/OR |
|--------------------------|----------|------------------------|--------------|----------|------------------------|
| Intercepto (β_0) | 3.739 | 5.122 | 0.024 | – | – |
| Age < 3 years | | | | | |
| Yes | 0 | | | 1 | |
| No | 0.285 | 0.409 | 0.523 | 1.3 | (0.6; 3.2) |
| Underweight | | | | | |
| Yes | 0.326 | 0.444 | 0.505 | 1.4 | (0.5; 3.6) |
| No | 0 | | | 1 | |
| Oncohematological | | | | | |
| Yes | 0 | | | 1 | |
| No | 0.150 | 0.102 | 0.750 | 1.2 | (0.5; 2.9) |
| Sepsis | | | | | |
| Yes | 0.122 | 0.078 | 0.779 | 1.1 | (0.5; 2.7) |
| No | 0 | | | 1 | |
| PIM 3(%) | 0.018 | 0.325 | 0.569 | 1.0 | (0.96; 1.1) |

P – probability significance of the Wald test in logistic regression analysis. Pseudo R^2 (Cox & Snell) = 0.016.

Pseudo R^2 (Nagelkerke) = 0.022. Hosmer and Lemeshow Test – P = 0.482

Model variables: variable outcome fluid accumulation: 1 – Yes, 0 – No; dummy type independent variables: age < 3 years: 1 – No, 0 – Yes, underweight: 1 – Yes, 0 – No; oncohematological: 1 – No, 0 – Yes; sepsis: 1 – Yes, 0 – No; quantitative type variables: PIM 3(%)