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Survival after ICU discharge is shaped more by chronic disease than admission severity

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ABSTRACT

Background: Mortality is high both during intensive care unit (ICU) stay and in the year following discharge, yet factors influencing long-term survival remain poorly defined. We hypothesized that pre-existing chronic conditions may be more strongly associated with post-ICU survival than acute illness severity or admission diagnosis. **Methods:** This is a *post-hoc* analysis of the prospective, observational, multicenter FROG-ICU cohort, which included all consecutive patients admitted to 21 French ICUs and followed for one year after discharge. ICU survivors with complete data on admission severity scores (Sequential Organ Failure Assessment [SOFA], Simplified Acute Physiology Score II [SAPS-II]), comorbidities (Charlson Comorbidity Index [CCI]), and cardiovascular/renal biomarkers at discharge ($n = 1400$) were included. Associations with one-year mortality were assessed using Cox models. Discriminatory performance was evaluated with time-dependent area under the receiver operating characteristic curve (AUC).

Results: Among 1548 ICU survivors, 1400 were analyzed (median age 61 years, 63 % male). Admission diagnoses included acute respiratory failure (19 %), septic shock (24 %), and neurologic conditions (16 %). The CCI was the strongest predictor of mortality at day 7 (AUC 0.70 [95 % Confidence Interval [CI], 0.64–0.77]), at 3 weeks (AUC

Abbreviations: AUC, Area Under the Curve; bio-ADM, Bioactive Adrenomedullin; CCI, Charlson Comorbidity Index; eGFR, Estimated Glomerular Filtration Rate; hs-cTnT, High-Sensitivity Cardiac Troponin T; ICU, Intensive Care Unit; IQR, Interquartile Range; NT-proBNP, N-Terminal pro-Brain Natriuretic Peptide; penKid, Proenkephalin A 119–159; PICS, Post-Intensive Care Syndrome; pNGAL, Plasma Neutrophil Gelatinase-Associated Lipocalin; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; uNGAL, Urine Neutrophil Gelatinase-Associated Lipocalin.

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0.75 [0.69–0.78]), and remained high over one year, outperforming SAPS-II (0.63 [0.54–0.72]) and SOFA (0.61 [0.53–0.68]). Although cardiovascular (NT-proBNP, bio-ADM) and kidney (pNGAL) biomarkers had comparable short-term discriminatory value, CCI performed better for long-term outcomes across different admission diagnoses.

Conclusion: In this analysis, pre-existing chronic conditions were primary drivers of short- and long-term survival after ICU discharge, exceeding prognostic value of acute illness severity at admission.

Clinical trial registration: French and European Outcome Registry in Intensive Care Units (FROG-ICU) study: [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01367093) NCT01367093. Registered 3 June 2011.

1. Introduction

Intensive Care Unit (ICU) stay is associated with a high mortality, both during the ICU stay and after discharge. It is increasingly recognized that patients discharged alive from the ICU often face a challenging post-ICU trajectory. While the literature on ICU survivors has largely focused on post-intensive care syndrome (PICS)—which affects approximately one in two patients at three months [1,2]—its relationship with long-term post-ICU mortality remains poorly understood [3].

The FROG-ICU (French and European Outcome Registry in Intensive Care Units) study, a large multicenter European cohort, reported an ICU mortality of 22 %, and a post-discharge one-year mortality of 21 % [4]. Other studies have shown even higher post-ICU mortality rates, with 27 % at four weeks and up to 46 % at one year among patients with cardiogenic shock [5] and 27 % in those with septic shock [6]. Despite these concerning figures, the prognostic determinants of long-term post-ICU survival remain insufficiently defined.

Severity scores at ICU admission, such as Sequential Organ Failure Assessment (SOFA) and the Simplified Acute Physiology Score II (SAPS-II), have traditionally been used to estimate prognosis. However, these tools have shown limited accuracy in predicting long-term outcomes, as they often fail to account for key clinical variables at discharge. Recent evidence suggests that biomarkers may provide additional prognostic value [7–9]. Moreover, we previously identified other potential predictors of one-year post-ICU mortality, including age, comorbidities, red blood cell transfusion, ICU length of stay, and other abnormalities in routine clinical parameters (e.g., low systolic blood pressure, hypothermia, low total protein, thrombocytopenia, and leukopenia) [4].

The Charlson Comorbidity Index (CCI) is a simple, rapid, and widely used tool for assessing major comorbidities. It has been employed to predict mortality in various settings [10–13], but its potential correlation with standard ICU severity scores and its prognostic value for long-term outcomes are not well-established [14]. Further research is needed to fill this gap and improve the accuracy of post-ICU outcome prediction.

This study assessed whether chronic disease burden (CCI) or acute illness severity at ICU admission (SOFA, SAPS-II) better predicts mid- and long-term mortality among patients discharged alive from the ICU. We also examined whether select biological biomarkers improve post-ICU risk stratification beyond these clinical measures.

2. Methods

2.1. Study design and patients

Our study is based on data from the FROG-ICU (French and European Outcome Registry in Intensive Care Units) study (NCT01367093) [4]. FROG-ICU was a prospective, observational, multicenter (21 French centers and 1 Belgian center) cohort study, designed to assess one-year mortality following ICU discharge and to identify associated risk factors. The study design and primary results have been previously published [15].

This study was conducted across the 21 French ICUs, including medical, surgical, and mixed ICUs. A total of 2087 consecutive eligible patients were enrolled between August 2011 and June 2013. Patient recruitment per center reflected differences in ICU size. Eligible patients

met at least one of the following inclusion criteria: invasive mechanical ventilation for ≥ 24 h and/or administration of vasoactive agents for ≥ 24 h. Exclusion criteria included: less than 18 years old, severe head injury (initial Glasgow Coma Scale < 8), brain death or a persistent vegetative state, pregnancy or breastfeeding, organ transplantation within the previous 12 months, a prognosis of imminent death or hospital non-discharge, and lack of social security coverage [4]. The study was conducted in accordance with Good Clinical Practice (GCP), the Declaration of Helsinki, and approved by the ethical committee or Institutional Review Board (IRB) [16]. Informed consent was obtained from all patients or their relatives.

Among the 2087 enrolled patients, 1548 were discharged alive from the ICU. Of these, 1400 had complete data on comorbidity scores and biomarker measurements and were therefore included in the present secondary analysis.

2.2. Data collection and biological samples

In the FROG-ICU study, for each patient included, an electronic case report form was completed that documented relevant data throughout the ICU stay. The following patient data were collected: demographics, past medical history, ICU admission diagnosis, hemodynamic and respiratory parameters, and severity of disease classification scores. Blood samples were collected in ethylenediaminetetraacetic acid [EDTA] at patient inclusion and discharge. The following biomarkers were measured in plasma: hemoglobin, lactate, creatinine (with estimated glomerular filtration rate [eGFR] calculated), high-sensitivity troponin T (hs-cTnT), N-Terminal pro-Brain Natriuretic Peptide (NT-proBNP), bioactive adrenomedullin (bio-ADM), proenkephalin A 119–159 (penKid), plasma Neutrophil Gelatinase Associated Lipocalin (pNGAL), and urine NGAL (uNGAL).

2.3. Endpoints

The primary objective was to determine whether pre-existing comorbidities (CCI) and selected biologic biomarkers measured at ICU discharge improve prediction of short- and long-term post-ICU mortality among ICU survivors, compared with admission severity scores (SOFA, SAPS-II). Secondary objectives included: (1) subgroup analyses among patients admitted with acute respiratory failure (ARF), cardiogenic shock (CS), septic shock (SS), or neurologic conditions; (2) comparison of discharge plasma biomarkers—cardiovascular (NT-proBNP, bio-ADM) and renal (plasma NGAL [pNGAL], estimated GFR [eGFR])—in the overall survivor cohort and within these subgroups; and (3) additional analyses in the overall survivor cohort including high-sensitivity cardiac troponin T (hs-cTnT), proenkephalin (penKid), and urinary NGAL (uNGAL). An exploratory objective assessed the predictive value of the same comorbidity scores and biomarkers in the full ICU population at study inclusion.

2.4. Statistical methods

Results are presented as count and percentage for categorical variable or median and first to third quartile range for continuous variables. The one-year survival after ICU discharge was defined as the delay

between ICU discharge and death from any cause. Survival was censored either at one year or at the last follow-up if below one-year. Survival was estimated using the Kaplan-Meier method. The impact of studied risk factors was assessed using Cox proportional hazard models. The discriminatory ability of each risk factor was evaluated using time-dependent area under the receiver operating characteristic curve (AUC) with their 95 % confidence intervals (CI) [17,18]. Estimations of cumulative/dynamic time-dependent ROC curve were plotted against time. In this framework, the definition of cases and controls varies with time. At each time T , a case is defined as a subject with a time to death below or equal to T and a control is defined as a subject with a follow-up above T . Subgroup analyses were performed similarly as well as the analyses based on biomarkers. All analyses were performed with R 4.0.1 [19]. The main packages used were 'survival' and 'timeROC'.

3. Results

3.1. Patient characteristics

Among the 1548 patients discharged alive from the ICU, 1400 had complete data on clinical scores and biomarkers measures at admission and were included in our analysis (Tables 1 and B). The consort diagram is presented in **suppl. Fig. 1**. The remaining 148 patients with missing data were excluded and are described in **suppl. Table 1**. The final analytical cohort had a median age of 61 years [IQR 48; 72] and were predominantly male ($n = 885$, 63 %). Main causes for ICU admission were ARF (19 %), SS (24 %), CS (7 %), and neurologic conditions (16 %) (Table 1A). At the time of ICU discharge, most clinical parameters including vital signs and laboratory values had normalized (Table 1B).

3.2. Predictive factors of post-ICU outcome

Of the 1400 studied ICU survivors, 267 (19 %) died within one year following ICU discharge, including 92 patients (7 %) who died during the hospital stay (Table 1A). Fig. 1 illustrates the time-dependent AUC curves for predicting one-year mortality using the CCI, SAPS-II, and SOFA scores. CCI was the best predictor of mortality very early following ICU discharge, with a better performance compared to the ICU severity scores throughout the follow-up period (Graphical abstract). As detailed in **suppl. Table 2**, CCI had an AUC of 0.70 (CI 95 %: 0.64; 0.77) at day 7, outperforming SAPS-II (AUC: 0.63 [0.54; 0.72]) and SOFA (0.61 [0.53; 0.68]). The AUC of CCI increased steadily until the third week (0.74 [0.69; 0.78]) and remained higher than that of either SAPS-II or SOFA throughout the one-year period, with no overlap in confidence interval.

Suppl. Fig. 2A shows that CCI, within the first few weeks after ICU discharge, demonstrated greater predictive value for post-ICU mortality than severity scores across each of the four main admission categories: ARF, SS, CS and neurologic conditions.

When exploring the predictive value of both routinely available and novel biomarkers on post-ICU mortality, plasma cardiovascular biomarkers measured at discharge, such as NT-proBNP or bio-ADM, as well as plasma kidney biomarkers like pNGAL, showed predictive performance comparable to the CCI during the first six months after ICU discharge, as illustrated in Fig. 2 and detailed in **Supplementary Fig. 3**. Beyond six months, however, CCI remained the most accurate predictor of mortality. In contrast, eGFR, PenKid, hs-cTnT, and uNGAL consistently demonstrated poor prognostic value throughout the one-year follow-up period.

Predictive values of biomarkers for post-ICU mortality differed with the causes of ICU admission (Suppl. Fig. 2B). In ARF, pNGAL, bio-ADM and NT-proBNP showed predictive performance comparable to that of CCI during the first six months after ICU discharge, but not thereafter, when CCI continued to show higher AUC values, reflecting its superior prognostic value. In SS, bio-ADM was the best predictive biomarker, with a performance similar to CCI in the first six months but declining

Table 1

Characteristics of ICU survivors at discharge.

A Characteristics of ICU survivors at discharge		
Variable	n	Statistics
Age	1400	61 [48;72]
Male	885	63 %
Scores		
Charlson Comorbidity Index	1400	3 [1;4]
SAPS-II	1400	46 [34;59]
SOFA	1400	6 [4;9]
Comorbidities		
Chronic heart failure	98	7 %
Hypertension	559	40 %
Diabetes mellitus	231	16 %
Obesity	139	10 %
Chronic Kidney Disease	135	10 %
Cause of ICU admission		
Cardiogenic shock	102	7 %
Septic shock	337	24 %
Acute Respiratory Failure	264	19 %
Neurologic	229	16 %
Other	468	34 %
Organ support		
Inotropes/ vasopressors	961	69 %
RRT	260	19 %
LOS and death		
LOS in ICU	1400	12 [7;21]
Death during hospitalization	92	7 %
Death at 1-year	267	19 %

B Clinical and biological characteristics of ICU survivors at inclusion and at discharge

Variable	At inclusion		At discharge	
	n	Statistics	n	Statistics
Clinical parameters				
SOFA	1400	6 [4;9]	1278	0 [0;2]
Glasgow Coma Scale	983	13 [3;15]	1171	15 [15;15]
Systolic Blood Pressure (mmHg)	1380	123 [109;139]	1218	124 [111;139]
Diastolic Blood Pressure (mmHg)	1322	62 [55;72]	1159	68 [59;77]
Mean Blood Pressure (mmHg)	1322	82.7 [73.7;93]	1159	87.3 [77.7;96.3]
Heart Rate (bpm)	1358	90 [77;104]	1211	89 [78;100]
Biology				
Hemoglobin (g/dL)	1341	10 [9;11.5]	1217	10 [9;11.2]
Lactate (mmol/L)	1088	1.2 [0.9;1.7]	569	1 [0.7;1.3]
Troponin (pg/mL)	1400	36.3 [14.3;111.1]	1115	30 [13.8;72.8]
NT-proBNP (pg/mL)	1400	859 [223.4;3287]	1115	543.1 [146.4;2086]
Bio-ADM (pg/mL)	1400	54.6 [29.3;107.9]	1114	32.9 [19.9;59.1]
Creatinine (μmol/L)	1389	77 [57;131]	1270	66 [51;95]
eGFR	1400	86 [46.1;125]	1348	104.5 [67.6;141.3]
penKid (pmol/mL)	1400	53.3 [34.2;96.1]	1114	58.9 [42.1;94.6]
Plasma NGAL (ng/mL)	1377	169 [85;398]	1102	123 [74;218]
Urinary NGAL (ng/mL)	1328	97.5 [31.9;486.3]	973	52.8 [23.8;170.1]

Data are presented as percentages or as median with interquartile range (IQR), as appropriate.

Abbreviations: ICU Intensive Care Unit; LOS Length of stay; RRT Renal Replacement Therapy; SAPS-II Simplified Acute Physiology Score II; SOFA Sequential Organ Failure Assessment.

Data are presented as percentages or as median with interquartile range (IQR), as appropriate.

Abbreviations: bio-ADM bioactive adrenomedullin; eGFR estimated Glomerular Filtration Rate; NGAL Neutrophil Gelatinase Associated Lipocalin; NT-proBNP N-Terminal pro-Brain Natriuretic Peptide; penKid Proenkephalin A 119–159.

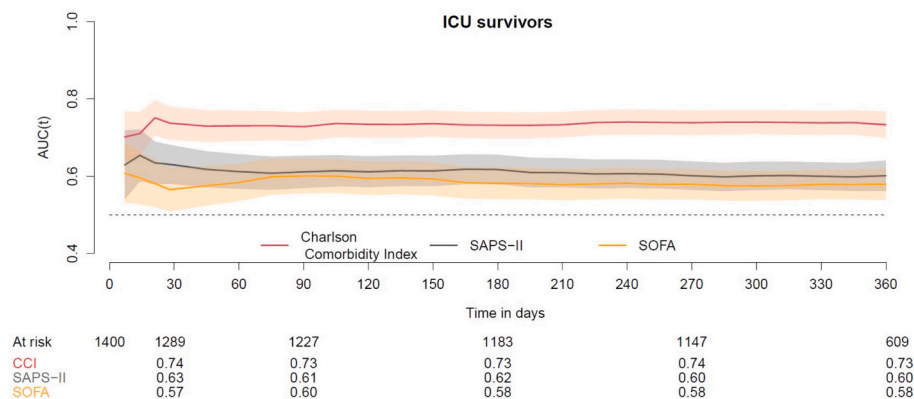


Fig. 1. Charlson Comorbidity Index (CCI) better predicts one-year post-ICU survival at discharge. Time-dependent AUC curves for one-year mortality in ICU survivors at discharge ($N = 1400$), comparing the Charlson Comorbidity Index (CCI) with standard severity scores assessed at ICU admission: SAPS-II (Simplified Acute Physiology Score II) and SOFA (Sequential Organ Failure Assessment). Number of patients at risk are listed below as well as AUC for each specific score.

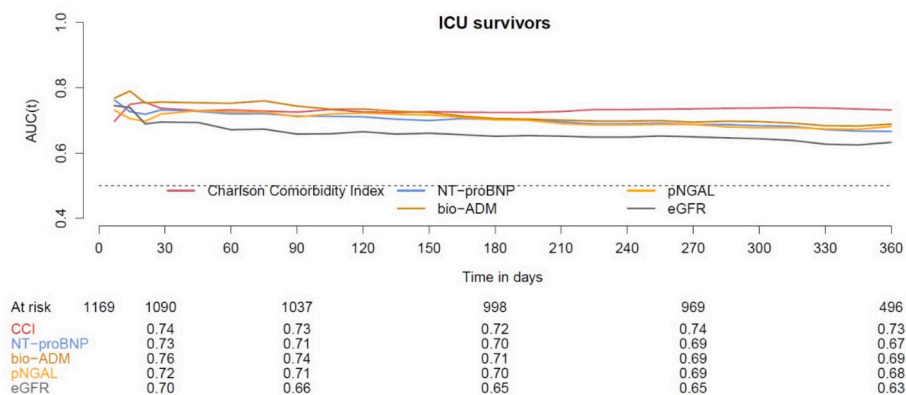


Fig. 2. Biomarkers at discharge predict mid-term post-ICU survival. Time-dependent AUC curves for one-year mortality in ICU survivors at discharge ($n = 1169$), comparing the Charlson Comorbidity Index (CCI) with cardiovascular and renal biomarkers: NT-proBNP (N-Terminal Pro-brain natriuretic peptide), bio-ADM (bio-adrenomedullin), pNGAL (plasma Neutrophil Gelatinase-Associated Lipocalin) and eGFR (estimated Glomerular Filtration Rate). Number of patients at risk are listed below the curves, as well as AUC for each specific score.

thereafter when CCI became the dominant predictor. In CS, both cardiovascular and renal plasma biomarkers demonstrated predictive values that were comparable to—and in some instances exceeded, like for NT-proBNP—those of CCI throughout the entire one-year follow-up. In the group with neurologic conditions, bio-ADM had predictive value similar to CCI over the whole post-ICU year.

Fig. 3 displays the association between one-year survival and three categories of CCI, stratified by SAPS-II (Fig. 3A) or SOFA (Fig. 3B) scores. It shows that the prognostic impact of CCI appeared to be more pronounced among patients with lower severity at ICU admission.

3.3. Predictive factors of one-year outcome starting at ICU admission

Baseline characteristics of all ICU patients with available SOFA scores at admission ($n = 1778$) are described in suppl Table 3. As shown in Suppl. figs. 4 A & B, SAPS-II, SOFA, NT-proBNP, bio-ADM or pNGAL—measured at ICU admission—were strong predictors of early mortality. However, later and starting around three months after ICU admission, the CCI progressively emerged as the most prominent predictor of mortality throughout the remainder of the one-year follow-up.

Analyses by main cause of ICU admission showed distinct prognostic patterns (suppl. Fig. 5 A): in ARF and neurologic conditions, CCI outperformed SAPS-II and SOFA throughout the post-ICU year in predicting mortality and showed superior prognostic value compared with admission biomarkers from three months onward. In SS, SAPS-II, SOFA and

CCI had similar good predictive value, while CCI maintained an advantage over biomarkers after three months. In CS, both CCI and SOFA performed better than SAPS-II; however, in contrast to other conditions, several biomarkers demonstrated predictive performance comparable to CCI, with NT-proBNP exhibiting a slight but consistent superiority. The only exception was eGFR, which demonstrated lower prognostic value (suppl. Fig. 5B).

4. Discussion

In this *post-hoc* analysis of ICU survivors from the FROG-ICU cohort, we found that the burden of chronic comorbidities—captured by the CCI—was a stronger predictor of post-ICU mortality than acute illness severity scores assessed at admission, such as SOFA and SAPS-II. This relationship held true across a range of conditions, including ARF, SS, CS, and neurologic disease. While several cardiovascular and kidney biomarkers showed comparable short-term prognostic value, their predictive accuracy declined over time, whereas the CCI maintained its superiority throughout the one-year follow-up. Notably, the prognostic impact of chronic disease burden was particularly pronounced among patients with lower severity of acute illness at ICU admission, suggesting that—even when acute derangement appear limited—long-term outcomes can still be substantially affected by preexisting comorbidities. These findings suggest that long-term outcomes in ICU survivors may be driven more by underlying comorbidity profile than by the acuity of the

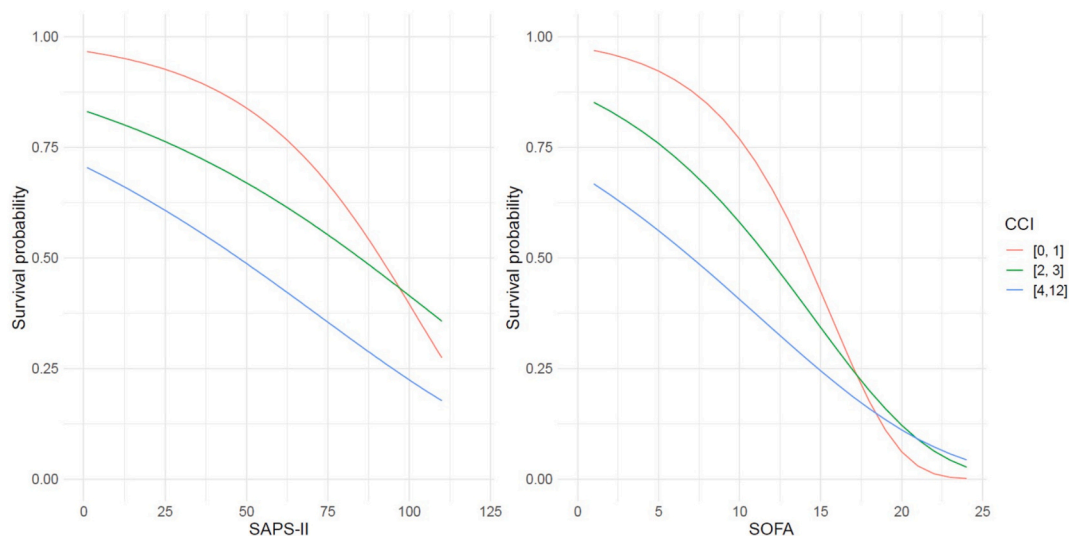


Fig. 3. Probability of one-year survival according to SOFA and SAPS-II in the different Charlson Comorbidity Index (CCI) categories.

A. Survival probability at one year according to SAPS-II at ICU admission in all-comer ICU patients ($n = 1988$), stratified by CCI category.

B. Survival probability at one year according to SOFA at ICU admission in all-comer ICU patients ($n = 1778$), stratified by CCI category.

CCI was divided into three groups: 0–1 (patients without comorbidity), 2–3 (low-intermediate comorbidities), and > 3 (high comorbidities; above the cohort median).

initial critical illness.

PICS was originally described in survivors of acute respiratory distress syndrome (ARDS) and SS and is now widely recognized as a common consequence of critical illness, affecting almost all ICU survivors to varying degrees [20–23]. It encompasses cognitive, psychological, physical, and functional impairments that often persist beyond ICU discharge and often does not resolve after one year [24,25]. In addition to these disabilities, one fifth of ICU survivors die within the year following discharge [4,5,26–28]. Recent trials targeting early physical and psychological rehabilitation have shown no increase in adverse events or mortality, but have not consistently improved benefit on long-term survival, suggesting that mechanisms underlying post-ICU mortality extend beyond functional recovery alone [29,30].

In this context, our findings suggest that chronic health status may exert a greater influence on long-term prognosis than the initial severity of acute illness — in terms of mortality, as shown in our study, and of quality of life, as previously reported [31]. This observation is in line with the study by Iwashyna et al., which showed that physiologic derangements (e.g., ICU scores) strongly predicted early mortality but lost predictive value within two weeks, after which patient characteristics such as age and comorbidities became more relevant [32]. However, their study only analyzed 28-day (i.e. short-term) mortality, while our analysis extends the observation to one-year following ICU discharge in a large, unselected cohort. Notably, the prognostic impact of chronic disease burden was independent of the cause of ICU admission, and particularly prominent in patients with high CCI scores.

In addition, we found that specific biomarkers measured at ICU discharge—particularly NT-proBNP, bio-ADM, and pNGAL—had predictive performances comparable to CCI, especially during the first six months post-discharge. These biomarkers reflect underlying cardiovascular, endothelial, and renal dysfunction, which may not be clinically evident but nonetheless portend poor outcomes. Their prognostic relevance was observed across all major categories of ICU admission, suggesting a broad applicability. In patients with CS, NT-proBNP showed particularly strong predictive value, while bio-ADM was most informative in septic shock.

Accordingly, our data suggest that, despite meeting criteria for ICU discharge, many ICU survivors may carry unrecognized organ damage or subclinical dysfunction that increases their vulnerability, as observed in recent publications [33,34]. The elevated levels of biomarkers at

discharge may reflect both pre-existing disease burden and ICU-acquired organ injury, though the precise mechanisms remain unclear. What emerges, however, is the likely limitation of standard ICU scores to capture these chronic or cumulative insults.

The comparison between acute severity scores and chronic disease burden was designed to explore how these distinct but interrelated domains contribute to the prognosis. Although SOFA and SAPS II are primarily calibrated for short-term mortality, they capture the extent of organ dysfunction and the physiologic reserve at ICU admission, factors that could plausibly influence outcomes well beyond the acute phase. Our results indicate that chronic comorbidity, as assessed by the CCI, exerts a more sustained prognostic effect after ICU discharge, suggesting that baseline vulnerability, probably aggravated, continues to influence post-discharge phase despite apparent resolution of the acute episode.

For the assessment of the comorbidity burden, we selected the CCI for its simplicity, broad recognition, and integration into many clinical workflows, as it is automatically calculated in some electronic health record systems. Despite its limitations and its inability to capture the full complexity of ICU patients, the CCI remains a valid and reliable index in this population, with proven incremental value for mortality prediction beyond standard clinical assessment [35].

Our results suggest that simple tools such as CCI may help identify ICU survivors at increased long-term risk and could complement more refined approaches to post-discharge risk stratification. In addition, integrating CCI with biomarker data could help clinicians identify high-risk patients and implement more tailored post-ICU care strategies, both during hospitalization and in outpatient follow-up. Future studies should test whether interventions guided by comorbidity burden and biomarker profiles can improve long-term post-discharge outcomes. Moreover, it will be important to test the prognostic value of newer and more precise comorbidity scores, potentially supported by artificial intelligence, which could facilitate their registration and computation.

Finally, our findings have implications for the design of future ICU trials. First, comorbidity assessment should be integrated in post-ICU prognostic models. Second, most interventional studies in critical care still rely on short-term endpoints such as 28-day mortality. As both our study and prior evidence suggest [32], acute-phase interventions may influence early outcomes, while long-term survival, namely longer than 2–4 weeks after the acute event, may depend more heavily on chronic disease trajectories and recovery from ICU-acquired organ damage.

Distinguishing between these mechanisms could help refine endpoints and optimize treatment strategies across the continuum of critical illness and recovery.

4.1. Limitations

This study has several limitations. First, as a *post-hoc* analysis, it is subject to inherent biases related to hypothesis generation and model overfitting, despite the large, well-characterized cohort and near-complete follow-up. Moreover, AUROC's represent only one of several approaches to evaluate predictive performance of individual variables and were chosen here as an initial step for this analysis. Incorporating calibration metrics in future multivariate models, together with decision curve analysis, would provide a more comprehensive assessment of model performance and clinical utility. Second, we focused solely on all-cause mortality and did not assess other important outcomes such as functional status, quality of life, or rehospitalization. Third, while several biomarkers showed prognostic value, their interpretation remains complex due to overlapping pathophysiology and unclear thresholds for clinical significance. The variability in biomarker performance across subgroups underscores the need for better phenotyping tools, potentially through machine learning or AI-based approaches. Finally, as an observational study, residual confounding cannot be excluded, and causal inferences should be made with caution. Future interventional studies are needed to test whether biomarker-guided or comorbidity-informed strategies can improve outcomes in ICU survivors.

CRedit authorship contribution statement

Alice Blet: Writing – original draft, Methodology, Formal analysis, Conceptualization. **Anouk Walter-Petrich:** Formal analysis. **Ménysssa Chérifa:** Writing – review & editing, Formal analysis. **Jolie Bruno:** Writing – review & editing. **Alexy Tran Dinh:** Writing – review & editing. **Elie Azoulay:** Writing – review & editing. **Benjamin Chousterman:** Writing – review & editing. **Gad Cotter:** Writing – review & editing. **Beth Davison:** Writing – review & editing. **Benjamin Deniau:** Writing – review & editing. **Etienne Gayat:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Bertrand Guidet:** Writing – review & editing. **Anatole Harrois:** Writing – review & editing. **Antoine Kimmoun:** Writing – review & editing. **Marc Leone:** Writing – review & editing. **Xavier Wittebole:** Writing – review & editing. **Andrew P. Ambrosy:** Writing – review & editing. **Alexandre Mebazaa:** Writing – original draft, Supervision, Resources, Methodology, Formal analysis, Data curation. **Matthieu Resche-Rigon:** Writing – review & editing, Formal analysis, Data curation.

Consent for publication

All participants (or their legal representatives) consented to the use of their data for research purposes, including scientific publication, as part of the original informed consent process.

Ethical approval and consent to participate

This study is a secondary analysis of previously collected data, conducted in France and in Belgium in accordance with Good Clinical Practice and Declaration of Helsinki 2002. The study was approved by the Comité de Protection des Personnes - Ile de France IV (IRB n°00003835) and the Commission d'éthique biomédicale hospitalo-facultaire de l'hôpital de Louvain (IRB n°B403201213352). Informed consent was obtained from all patients or their legal representatives.

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Declaration of competing interest

Benjamin G Chousterman served as a member of an advisory board for Roche Diagnostic. Antoine Kimmoun had lecture fees for Aspen et Aguetant. Marc Leone lecturers for MSD, Aspen and Consultants for Gilead, Amomed. The others authors do not have any conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcrc.2025.155401>.

Data availability

All data supporting the findings of this study are available within the article and its Supplementary Information files. No third-party material requiring permission has been used.

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