

One-year outcome of patients admitted after cardiac arrest compared to other causes of ICU admission. An ancillary analysis of the observational prospective and multicentric FROG-ICU study

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- 1 One-year outcome of patients admitted after cardiac arrest compared to other causes of
- 2 ICU admission. An ancillary analysis of the observational prospective and multicentric
- 3 FROG-ICU study.

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Abstract

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1 2 **Objective.** While cardiac arrest (CA) patients discharged alive from intensive care unit (ICU) 3 are considered to have good one-year survival but potential neurological impairment, 4 comparisons with other ICU sub-populations non-admitted for CA purpose are still lacking. 5 This study aimed to compare long-term outcome and health-related quality of life (HRQOL) 6 between CA patients and patients admitted to ICU for all other causes. 7 **Methods.** In 1635 patients discharged alive from 21 European ICUs in an ancillary analysis of 8 a prospective multicentric cohort, we compared CA causes of ICU admission to all other causes 9 of ICU admissions (named non-CAs). The primary endpoint was one-year survival rate after 10 ICU discharge. Secondary endpoints included HRQOL at 3, 6 and 12 months after ICU 11 discharge using the outcome survey short form-36 (SF36). Propensity score matching was used 12 to consider the probability of having CA. 13 **Results.** Of the 1635 patients, 1561 were included in this study comprised of 1447 non-CAs 14 and 114 CAs. At one-year in the non-matched population, survival rate was greater in the CA 15 group 89% versus the non-CA group 78% (log rank p=0.0056). In the matched population, this 16 difference persisted between CAs and non-CAs (log rank p=0.049). The physical component 17 summary of the SF36 scale was higher in the CA group than in the non-CA group at all time 18 points in both non-matched and matched populations. 19 **Conclusions.** CA patients discharged alive from ICU have a better one-year survival and a 20 better HRQOL specifically on physical functions than patients admitted to ICU for other causes.

Trial registration: ClinicalTrials.gov NCT01367093; registered on June 6, 2011.

Introduction

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2 The average survival rate of out-of-hospital cardiac arrest (OHCA) globally remains low, i.e. under 10%, while in-hospital CA (IHCA) survival rate reaches roughly 20% ¹⁻³. In both 3 instances, when discharged alive from intensive care unit (ICU), evidence suggests that one-4 year mortality remains in the vicinity of 15% ⁴⁻⁷. Previous comparisons with other populations 5 6 have often been performed using healthcare system registries or populations which did not experience the burden of ICU stay 4, 8. Major issues also remain on long-term functional 7 8 outcomes in CA patients in whom literature is debatable. Furthermore, comparison of long-9 term outcome has only been performed between ICU CA patients and ward non-CA patients while the burden of ICU stay has never been considered 9. As a result, no study to date has 10 11 compared CA patients to non-CA patients hospitalized in the same ICUs with regard to long-12 term outcome. 13 Update of the Utstein resuscitation registry template for CA now emphasizes that assessment of outcomes at one year should consistently include health-related quality of life (HRQOL) 14 parameters ¹⁰. Indeed, while a majority of CA patients discharged alive from ICU have a good 15 16 neurological outcome assessed on common scales (such as cerebral performance categories or 17 modified Rankin scale), assessment of HRQOL, for which there is no specific scales for CA, is 18 less well characterized. Depending on the HRQOL questionnaire used, certain studies have 19 reported a return to pre-CA levels of functioning one year after CA ^{5, 6, 8}. By contrast, other 20 studies underline that many patients also experience altered neurological functioning such as attention deficits and more anxiety and depression symptoms over a period of several years ¹¹, 21 ¹². In view of these confusing results, many physicians seemingly believe that CA patients 22 23 discharged alive from ICU are likely or very likely to suffer severe cognitive or neurological impairments, which is far from evidence ¹³. 24

1 A means to reconcile physician perceptions and evidence regarding CA outcomes would be to

2 perform a comparison at ICU discharge of long-term survival rate and HRQOL between

patients admitted to the same ICUs for CA and those admitted for all other causes including

septic shock or respiratory failure. We hypothesized that one-year survival and HRQOL of

patients hospitalized in ICU for a CA is likely to be at least similar to outcome of patients

6 admitted for non-CA purposes.

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Methods

- 2 Study design
- 3 This study is an ancillary analysis from the French and euRopean Outcome reGistry in Intensive
- 4 Care Units (FROG-ICU) cohort. The original study was a prospective, observational,
- 5 multicenter cohort study of 2087 patients and was designed to assess the long-term survival
- 6 rates of patients admitted to ICU. The study was approved by the local ethics committees
- 7 (Comité de Protection des Personnes, Ile de France IV, IRB n°00003835 and Commission
- 8 d'éthique biomédicale de l'hôpital de Louvain, IRB n° B403201213352) and registered on
- 9 <u>https://clinicaltrials.gov/ct2/show/NCT01367093</u>. The methodology and results of the original
- study have previously been published ^{14, 15}.
- 11 Participants and inclusion criteria in the original study
- 12 The FROG-ICU study involved 21 medical, surgical or mixed ICUs. All consecutive patients
- admitted to ICU were screened for eligibility. Inclusion criteria were mechanical ventilation
- and/or administration of at least one vasoactive agent (except dopamine) for more than 24
- hours. Exclusion criteria were at admission age <18 years old, severe head injury, obvious brain
- death, pregnancy or breastfeeding, an organ transplantation occurring in the past 12 months,
- 17 and lack of social security coverage ¹⁵.
- 18 Definition of the CA and non-CA population
- 19 CA patients correspond to patients for whom CA was the cause of ICU admission whether CA
- was out-of hospital or in-hospital. Non-CA patients correspond to all other causes of ICU
- 21 admission.
- 22 Inclusion Criteria
- All patients admitted to ICU with a diagnosis and subsequently discharged alive from ICU.
- 24 Non-Inclusion Criteria
- 25 Patients with no diagnosis at admission and lost of follow up were not included.

- 1 Goals
- 2 The primary endpoint was to assess in patients discharged alive from ICU the survival rate at
- 3 one-year after ICU discharge while secondary endpoints included the HRQOL, the hospital
- 4 anxiety and depression scale (HADS) and the revised impact of event scale (IES-R) assessed at
- 5 3, 6 and 12 months after ICU discharge.
- 6 Data collection
- 7 Data regarding CA patients at ICU discharge were retrospectively collected from medical
- 8 reports according to Utstein-style guidelines ¹⁰. Briefly, these recommendations provide to
- 9 researchers a structured framework to uniformly report CA.
- 10 Details regarding general data collection at ICU discharge have been reported in the original
- study ¹⁵. Causes of ICU admission were also recorded and classified in 19 categories. Beside
- 12 CA, most prevalent causes of ICU admission were individualized: respiratory failure, septic
- shock, neurological causes, cardiogenic shock, immediate post-operative room (urgent or
- scheduled surgery). The remaining 13 causes were coded as "other causes of ICU admission".
- 15 The time point of baseline characteristics was defined at ICU discharge.
- 16 Health-related quality of life parameters.
- Briefly, from ICU discharge, patients were contacted by phone-calls at 3, 6 and 12 months in
- order to collect, among other things, the vital status, potential re-admission for any cause and
- cardiovascular treatments prescribed. Quality-of-life questionnaires were sent 15 days before
- 20 each phone-call. Interviewer ensured that questionnaires were received by the patient itself. As
- 21 they were self-reported questionnaires, patients had to send back the completed questionnaires
- 22 in dedicated pre-addressed envelopes. Relative were not allowed to complete these
- 23 questionnaires.
- 24 The French version of the medical outcome survey short form-36 (SF-36). Briefly, SF-36 is a
- 25 measurement of mental and physical health status independently of the underlying disease. The

score is constructed with 36 items divided into 8 scales. The mental health component summary (MCS) score includes the following items: mental health, vitality, role limitations related to emotional distress and social function. The physical health component summary (PCS) score includes the following items: physical function, bodily pain, general health, and role limitations due to impaired physical function ¹⁶. High scores are indicative of a good mental and physical health status. The French version of revised impact of event scale (IES-R). The IES-R is a symptomatic scale encompassing three main symptom clusters: intrusion, avoidance and hyperarousability. These clusters assess the symptoms of post-traumatic stress disorder (PTSD) induced by the ICU stay. Based on literature findings, a threshold at 33 was chosen for the probability of having PTSD 17, 18 The French version of hospital anxiety and depression scale (HADS). HADS is a validated scale for screening emotional distress. It assesses anxiety and depression. This score includes seven questions for anxiety and seven questions for depression. Based on literature findings, a threshold of 8 points for each dimension was chosen in this study to indicate probable anxiety and depression ¹⁸⁻²⁰. Statistical analyses Data are expressed as median [interquartile range, IQR] or number (%) as appropriate. After visual assumption of normality and variance homogeneity by the F-test, Student's, Welch or Wilcoxon rank tests were applied for univariate analysis as appropriate. In order to balance CA with non-CA populations at ICU discharge, an analysis derived from the propensity score was performed. Propensity score is used in observational studies to estimate the effect of an intervention by creating a pseudo-randomization in order to reduce selection bias. With the matching propensity score method chosen, we expected a very good matching at the cost of a strong reduction in final populations. In the propensity score model herein, exposure was,

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in a population of patients discharged alive from ICU, CA as cause of initial admission. Model variables included in the propensity score were variables associated with one-year outcome at 0.05 level and with less than 20% of missing data 15. These variables, included according to both the biological plausibility and the statistical analysis, were already validated and published in the original study¹⁵: age, Charlson score, prior severe valvular disease, prior severe artery disease, chronic renal disease, recent active malignant tumor, prior physical or mental disabilities, red blood pack transfusion during ICU stay and length of stay. The following variables at ICU discharge were also included: systolic arterial pressure, temperature, platelets, white blood count, and total protein. CA and non-CA patients were matched using a 1:1 nearest neighbor matching algorithm with no replacement, along with a caliper of 0.1 of the standard deviation of the propensity score. Imbalance between the two groups before and after propensity score matching was assessed using a standardized difference, with a value < 10% considered as acceptable for defining the study patients' characteristics as being balanced with respect to the previously described features. Thereafter, one-year survival and HRQOL parameters were assessed in the matched dataset. A Holm post-hoc test was applied for multiple comparisons. Kaplan-Meier curves were drawn and overall one-year survival was estimated by using the log-rank test in non-matched and matched CA and non-CA populations. Secondary, a multivariate analysis using a logistic regression model including the variables described above was also performed to assess if CA was independently associated with one-year mortality. For each continuous variable in the multivariate analysis, the linearity assumption was tested. If there was no linear relationship a log and square transformation was tested. If the linearity assumption was still not suitable, the variable was broken considering the biological plausibility. Hazard ratios (HR) and odds ratios (OR) with their respective 95% confidence intervals (CI) were also calculated.

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Lastly, analyses were performed to assess i) the association between CA and one-year mortality according to the aforementioned variables plus two cardiac biomarkers (hs troponin I and N-terminal pro-type B natriuretic peptide) and ii) the association between CA and one-year mortality according to other most prevalent causes. For secondary analyses, the above-mentioned continuous variables were divided on their medians. OR and their 95% CIs were also calculated. No imputation analysis has been performed on missing data. All tests were two-sided and a p value < 0.05 was considered statistically significant. All analyses were performed

using R 3.51 statistical software (The R Foundation for Statistical Computing, Vienna, Austria).

Result

- 2 Patients
- 3 Of the 2087 patients included in the FROG-ICU study, 1635 patients were discharged alive
- 4 from ICU. Of the latter, 1561 were included in the present study population comprised of 114
- 5 (7%) CA patients and 1447 (93%) non-CA patients discharged alive from ICU (Figure 1).
- 6 Details about the 74 patients excluded due to lack of data are provided in **eTable 1**.
- 7 *Characteristics* of the *non-matched* and matched cohort at ICU discharge.
- 8 The general characteristics at ICU discharge according to CA diagnosis prior to propensity-
- 9 score matching are presented in **Table 1**. Briefly, in the non-matched population, the CA group,
- 10 compared to the non-CA group, had a lower Charlson score (0.0 [0.0 1.0] vs. 1 [0.0-2.0],
- p<0.0001) and less recent active malignant tumors (1% vs. 13%, p=0.0001). Less transfusion
- of blood products was observed in the CA group compared to the non-CA group: red blood
- concentrate, 27% vs. 44% respectively (p=0.0004) and platelet concentrate, 5% vs. 16%
- respectively (p=0.003). At ICU discharge, hemoglobin, sodium, protein and creatinine levels
- were higher in the CA group compared to the non-CA group (hemoglobin: 10.5 [9.7 11.5]
- 16 g/dL vs. 10.0 [8.9 11.1] g/dL, p=0.002; sodium: 141 [138 143] mmol/L vs. 139 [136 142]
- 17 mmol/L, p=0.003; protein: 64 [58 69] g/L vs. 62 [56 69] g/L p=0.018; creatinine: 74 [60 -
- 18 94] mmol/L vs. 66 [50 96] mmol/L p=0.011). eTable 2 described in detail characteristics and
- management of CA patients. Briefly, 73% of patients in the CA group experienced OHCA,
- 20 78% of whom were cerebral performance category (CPC) 1 or 2, while 20% were CPC 3 and
- 21 2% were CPC 4, all at ICU discharge.
- 22 Comparison of one-year survival between CA and non-CA patients.
- Among the 1561 included patients, 1237 (79%) were alive at one year. In the non-matched
- population, one-year survival was 89% in the CA group and 78% in the non-CA group (log
- 25 rank p=0.0056) (**Figure 2, panel A**). Propensity score-matching allowed creating 68 pairs of

- 1 ICU patients. Standardized differences in percent, before and after matching, on the predefined
- 2 characteristics are presented in **Table 2** and in **eFigure 1**. In the matched population,
- 3 differences in one-year survival between CA and non-CA observed in the non-matched
- 4 population also persisted after matching (log rank p=0.049) (**Figure 2, panel B**). In the
- 5 multivariate analysis, CA discharged alive from ICU was also found as being an independent
- 6 factor associated with one-year survival (**eFigure 2**)
- 7 Health-related quality of life parameters.
- 8 In the non-matched population but not in the matched population, MCS aggregate score was
- 9 higher at 3 months in the CA group compared to the non-CA group (p=0.0006 and p=0.06
- respectively) (**Figure 3A** and **3B**). In the non-matched population, PCS aggregate scores of the
- 11 SF-36 questionnaire was greater at all studied time points in the CA group compared to the
- 12 non-CA group (p=0.0009, 0.002 and 0.002 at 3, 6 and 12 months respectively) (**Figure 3C**) All
- of these differences also persisted in the matched population (p=0.033, 0.033 and 0.048 at 3, 6
- and 12 months respectively) (**Figure 3D**). IES-R and HADS scores are described in **eTable 3**
- 15 for non-matched and matched populations. At one-year post-ICU discharge, in the non-matched
- population, proportions of anxiety and depression symptoms (HADS \geq 8 for both parameters)
- were respectively 38% and 34% in the non-CA group compared to 28% and 28% in the CA
- group (p=0.184 and 0.60 respectively). Proportion of patients with PTSD (IES-R scale \geq 33) at
- one year was 20% in the non-CA group compared to 6% in the CA group, (p=0.036). In the
- 20 matched population, no difference between groups was observed for these two scales at any
- 21 time points.
- 22 Subgroup analysis.
- 23 Cardiac arrest was a protective factor with regard to one-year mortality compared to the most
- frequent causes of ICU admission except for neurological causes of admission (**Figure 4**).
- 25 Association between CA and one-year mortality after ICU discharge according to comorbidities

- as well as clinical and biological parameters are depicted in **eFigure 3 and eFigure 4** showing
- 2 a persistent protective effect of CA versus non-CA for the majority of the analyzed subgroups.

1 **Discussion**

2 In this ancillary study of FROG-ICU which enrolled a large population of ICU patients alive at 3 discharge from ICU, a better long-term survival and physical health status in CA patients 4 compared with those admitted for any other cause were observed in patients with similar 5 severity. Conversely, mental health status remained similar between CA and non-CA groups. 6 Our study shows that, in the FROG-ICU cohort, survival within the year following ICU 7 discharge was consistently greater in CA than non-CA patients. Long-term post-ICU mortality 8 rate in CA or non-CA patients were previously studied in separate cohorts and showed a greater mortality rate in non-CA than in CA patients ^{5-7, 21-24}. However, one major bias in interpreting 9 10 differences in post-ICU outcome between non-CA and CA patients may be related to 11 differences in baseline characteristics among studied cohorts. In one study which included only 12 myocardial infarction patients, post-discharge mortality of the few patients with CA was similar to that of non-CA myocardial infarction patients 9. To the best of our knowledge, there is no 13 14 published study comparing long-term mortality between CA and non-CA patients hospitalized 15 in the same ICUs. In the present study, survival benefit in the CA group might be explained at 16 first glance by fewer co-morbidities and lower occurrence of ICU complications. However, 17 adjustments on the many confounding factors maintained the observed survival benefit in CA 18 patients. Explanations for this benefit are not straightforward. It can only be assumed that, in 19 survivors, CA is a rapid and fully reversible hemodynamic condition, with little long-term 20 consequences on organ functions, except for brain function. Conversely, non-CA causes of ICU 21 admission, including septic shock, most often occurs on a background of severe pre-existing 22 comorbidities and are associated with persistent long-term organ dysfunction at ICU discharge 23 ^{25, 26}. For instance, our team previously demonstrated the persistence of long-lasting immune illness disorders one year after ICU discharge in patients admitted with septic shock ²⁷. 24

- 1 Altogether, in this FROG-ICU cohort, CA demonstrated a post-ICU survival benefit compared
- 2 to non-CA patients.
- 3 Interestingly, this survival gain in CA patients was accompanied by HRQOL benefits. Our
- 4 population of non-CA patients presented HRQOL scores in the year following ICU discharge
- 5 in the range of what has already been published ²⁸. With regard to CA survivors, a recent review
- 6 highlighted the absence of a specific measure of HRQOL and that SF-36 represented a reliable
- 7 scale ²⁹. However, using the SF-36, our CA population had a similar HRQOL to those
- 8 previously reported in CA patients ^{6, 11, 30, 31}. No comparison of HRQOL has been published to
- 9 date between CA and non-CA patients discharged from ICU. Furthermore, our study shows
- 10 that physical capacities are consistently better in CA compared to non-CA patients for all
- studied time points. Conversely, the burden of ICU stay on mental health status at one-year post
- 12 ICU discharge was found to be similarly altered in both CA and non-CA patients. Lastly, one
- 13 lingering issue could be the effectiveness of specific follow-up after ICU discharge in
- 14 improving HRQOL. Preliminary data have demonstrated that in CA survivors, long-term
- 15 HRQOL may be improved by managing emotional and psychological distress induced by CA
- 16 ³².
- 17 Limitations
- 18 Several limitations of this study should be acknowledged. First, the design of our study prevents
- any firm conclusion with regard to causality between CA and non-CA on outcomes, even
- 20 though this association persisted after adjustment by using propensity score-matching. While
- 21 propensity score-matching appears to be a powerful solution to balance both fundamentally
- 22 different populations, this score is not primarily intended to be used for this purpose. Indeed,
- 23 the variable of exposure was CA at admission but, as we aimed to assess the survival rate at
- one-year, only in patient discharged alive from ICU, the variables used in matching were post-
- exposure, *i.e.* at discharge. It is also likely that propensity score-matching might have missed

1 some important parameters. However, parameters included in the propensity score were factors 2 associated to one-year survival, validated in the multivariate analysis of the original study ¹⁵. 3 Third, regarding the considerable differences in population sizes and in baseline characteristics 4 between CA and non-CA populations, propensity score deeply reduced the sample size in the 5 matched population confirming its matching capacities. Thus, for the survival analysis, a 6 significant difference was observed on the log rank test although the HR confidence interval 7 slightly crossed 1. To strengthen survival analysis results obtained from the propensity score-8 matching, a multivariate analysis including the whole population was also undertaken and 9 found a similar result, i.e. CA is an independent factor associated with one-year survival. 10 Fourth, this study only looked at the long-term outcome of patients discharged alive from ICU 11 and our results could not be generalized to the pre-discharge period. Fifth, roughly only 1/3 of 12 non-CAs and only 2/3 of CAs provided quality-of-life data. Even considering the number of 13 deaths during the one-year follow-up, these missing data could be an important source of bias. 14 Finally, we included both IHCA and OHCA. IHCA usually has a better prognosis, and thus the 15 inclusion of IHCA would have biased the analysis towards a "healthier" CA group ³³.

Conclusions

This study shows that, in patients discharged alive from ICU, CA patients had better one-year survival and better quality of life compared to non-CA patients. This work highlights that despite the burden of ICU stay, in patients discharged alive from ICU, the long-term outcome after a CA remains the most favorable among all main causes of ICU admission.

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- 5 EG: Statistical analysis. EG, AM: Administrative, technical, or material support. EG, AM:
- 6 Study supervision. All authors read and approved the final manuscript.
- 7 Availability of supporting data. EG and AM had full access to all data in the study and take
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- Nicolas Deye. ND received lecture and travel fees for Zoll and Bard outside the present work.
- 19 All remaining authors have declared no conflicts of interest.

1 Figure Legends

- 2 Figure 1: Flow chart. * Proportion of non-CA excluded patients was similar to CA excluded
- 3 patients (p=1).
- 4 ICU: Intensive care unit.
- 5 Figure 2: Survival curve from intensive care unit discharge to 1-year post-discharge in non-
- 6 cardiac arrest and cardiac arrest patients in the non-matched (Panel A) and matched (Panel B)
- 7 population.
- 8 Figure 3: SF-36 (MCS and PCS) in the non-matched and matched populations at 3, 6 and 12
- 9 months in cardiac arrest and non-cardiac arrest patients. Panel A: MCS non-matched; Panel
- 10 B: MCS matched; Panel C: MCS non-matched; Panel D: MCS matched. *: p≤0.05
- 11 MCS: Mental component summary, PCS: Physical component summary.

1 References

- 2 [1] Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac
- 3 arrest and survival rates: Systematic review of 67 prospective studies. Resuscitation.
- 4 2010;81:1479-87.
- 5 [2] Reynolds JC, Grunau BE, Rittenberger JC, Sawyer KN, Kurz MC, Callaway CW.
- 6 Association Between Duration of Resuscitation and Favorable Outcome After Out-of-Hospital
- 7 Cardiac Arrest: Implications for Prolonging or Terminating Resuscitation. Circulation.
- 8 2016;134:2084-94.
- 9 [3] Kleinman ME, Perkins GD, Bhanji F, Billi JE, Bray JE, Callaway CW, et al. ILCOR
- 10 Scientific Knowledge Gaps and Clinical Research Priorities for Cardiopulmonary Resuscitation
- and Emergency Cardiovascular Care: A Consensus Statement. Resuscitation. 2018;127:132-
- 12 46.
- 13 [4] Siudak Z, Birkemeyer R, Dziewierz A, Rakowski T, Zmudka K, Dubiel JS, et al. Out-of-
- 14 hospital cardiac arrest in patients treated with primary PCI for STEMI. Long-term follow up
- data from EUROTRANSFER registry. Resuscitation. 2012;83:303-6.
- 16 [5] Smith K, Andrew E, Lijovic M, Nehme Z, Bernard S. Quality of life and functional
- outcomes 12 months after out-of-hospital cardiac arrest. Circulation. 2015;131:174-81.
- 18 [6] Geri G, Dumas F, Bonnetain F, Bougouin W, Champigneulle B, Arnaout M, et al. Predictors
- of long-term functional outcome and health-related quality of life after out-of-hospital cardiac
- 20 arrest. Resuscitation. 2017;113:77-82.
- 21 [7] Shuvy M, Morrison LJ, Koh M, Qiu F, Buick JE, Dorian P, et al. Long-term clinical
- 22 outcomes and predictors for survivors of out-of-hospital cardiac arrest. Resuscitation.
- 23 2017;112:59-64.

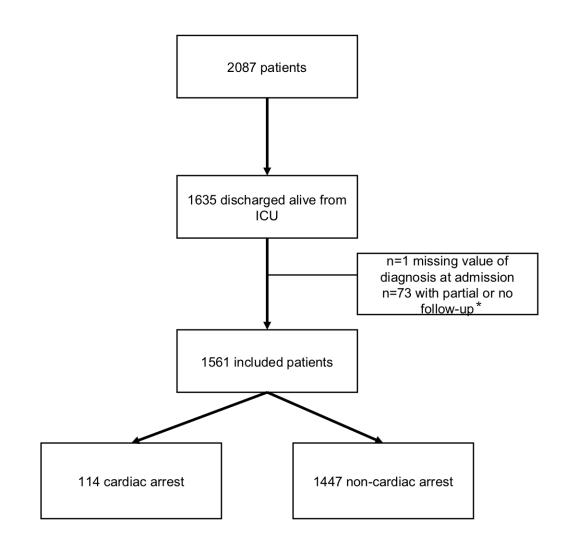
- 1 [8] Bunch TJ, White RD, Gersh BJ, Meverden RA, Hodge DO, Ballman KV, et al. Long-term
- 2 outcomes of out-of-hospital cardiac arrest after successful early defibrillation. N Engl J Med.
- 3 2003;348:2626-33.
- 4 [9] Lettieri C, Savonitto S, De Servi S, Guagliumi G, Belli G, Repetto A, et al. Emergency
- 5 percutaneous coronary intervention in patients with ST-elevation myocardial infarction
- 6 complicated by out-of-hospital cardiac arrest: early and medium-term outcome. Am Heart J.
- 7 2009;157:569-75.e1.
- 8 [10] Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. Cardiac Arrest
- 9 and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation
- 10 Registry Templates for Out-of-Hospital Cardiac Arrest: A Statement for Healthcare
- 11 Professionals From a Task Force of the International Liaison Committee on Resuscitation
- 12 (American Heart Association, European Resuscitation Council, Australian and New Zealand
- 13 Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart
- 14 Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the
- 15 American Heart Association Emergency Cardiovascular Care Committee and the Council on
- 16 Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Resuscitation. 2015;96:328-
- 17 40.
- 18 [11] Cronberg T, Lilja G, Horn J, Kjaergaard J, Wise MP, Pellis T, et al. Neurologic Function
- 19 and Health-Related Quality of Life in Patients Following Targeted Temperature Management
- 20 at 33 degrees C vs 36 degrees C After Out-of-Hospital Cardiac Arrest: A Randomized Clinical
- 21 Trial. JAMA Neurol. 2015;72:634-41.
- 22 [12] Green CR, Botha JA, Tiruvoipati R. Cognitive function, quality of life and mental health
- 23 in survivors of our-of-hospital cardiac arrest: a review. Anaesth Intensive Care. 2015;43:568-
- 24 76.

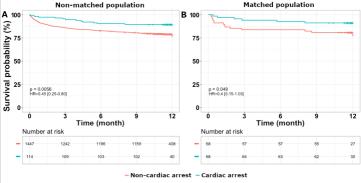
- 1 [13] Jones K, Garg M, Bali D, Yang R, Compton S. The knowledge and perceptions of medical
- 2 personnel relating to outcome after cardiac arrest. Resuscitation. 2006;69:235-9.
- 3 [14] Mebazaa A, Casadio MC, Azoulay E, Guidet B, Jaber S, Levy B, et al. Post-ICU discharge
- 4 and outcome: rationale and methods of the The French and euRopean Outcome reGistry in
- 5 Intensive Care Units (FROG-ICU) observational study. BMC Anesthesiol. 2015;15:143.
- 6 [15] Gayat E, Cariou A, Deye N, Vieillard-Baron A, Jaber S, Damoisel C, et al. Determinants
- 7 of long-term outcome in ICU survivors: results from the FROG-ICU study. Crit Care.
- 8 2018;22:8.
- 9 [16] Leplege A, Ecosse E, Verdier A, Perneger TV. The French SF-36 Health Survey:
- translation, cultural adaptation and preliminary psychometric evaluation. J Clin Epidemiol.
- 11 1998;51:1013-23.
- 12 [17] Creamer M, Bell R, Failla S. Psychometric properties of the Impact of Event Scale -
- 13 Revised. Behav Res Ther. 2003;41:1489-96.
- 14 [18] Contou D, Canoui-Poitrine F, Coudroy R, Preau S, Cour M, Barbier F, et al. Long-term
- quality of life in adult patients surviving purpura fulminans: an exposed-unexposed multicenter
- 16 cohort study. Clin Infect Dis. 2018;69:332-40.
- 17 [19] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand.
- 18 1983;67:361-70.
- 19 [20] Vodermaier A, Millman RD. Accuracy of the Hospital Anxiety and Depression Scale as a
- screening tool in cancer patients: a systematic review and meta-analysis. Support Care Cancer.
- 21 2011;19:1899-908.
- 22 [21] Rockwood K, Noseworthy TW, Gibney RT, Konopad E, Shustack A, Stollery D, et al.
- One-year outcome of elderly and young patients admitted to intensive care units. Crit Care
- 24 Med. 1993;21:687-91.

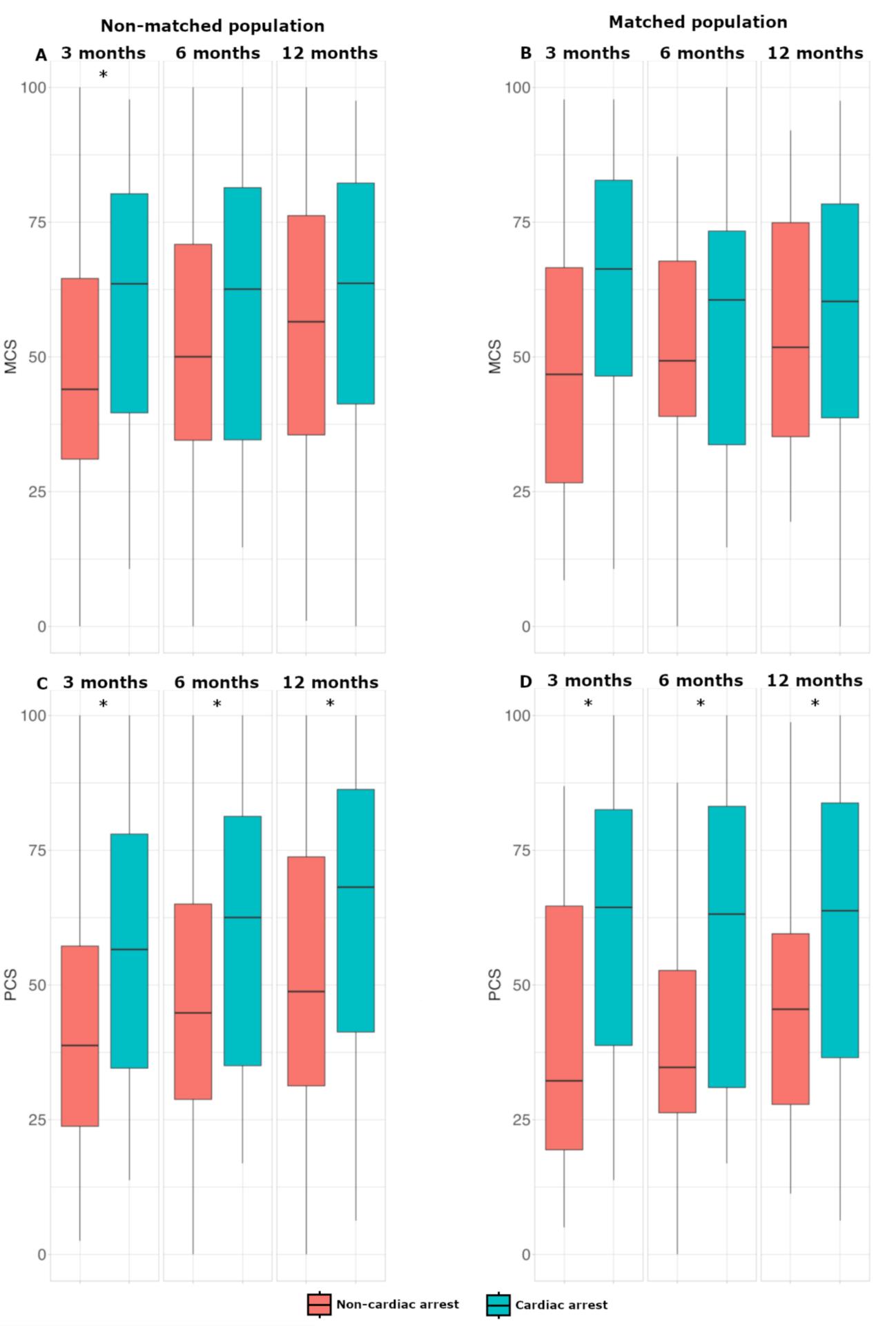
- 1 [22] Niskanen M, Kari A, Halonen P. Five-year survival after intensive care--comparison of
- 2 12,180 patients with the general population. Finnish ICU Study Group. Crit Care Med.
- 3 1996;24:1962-7.
- 4 [23] Bagshaw SM, Mortis G, Doig CJ, Godinez-Luna T, Fick GH, Laupland KB. One-year
- 5 mortality in critically ill patients by severity of kidney dysfunction: a population-based
- 6 assessment. Am J Kidney Dis. 2006;48:402-9.
- 7 [24] Orwelius L, Nordlund A, Nordlund P, Simonsson E, Backman C, Samuelsson A, et al.
- 8 Pre-existing disease: the most important factor for health related quality of life long-term after
- 9 critical illness: a prospective, longitudinal, multicentre trial. Crit Care. 2010;14:R67.
- 10 [25] Azoulay E, Adrie C, De Lassence A, Pochard F, Moreau D, Thiery G, et al. Determinants
- of postintensive care unit mortality: a prospective multicenter study. Crit Care Med.
- 12 2003;31:428-32.
- 13 [26] Brinkman S, Bakhshi-Raiez F, Abu-Hanna A, de Jonge E, de Keizer NF. Determinants of
- mortality after hospital discharge in ICU patients: literature review and Dutch cohort study. Crit
- 15 Care Med. 2013;41:1237-51.
- 16 [27] Riche F, Chousterman BG, Valleur P, Mebazaa A, Launay JM, Gayat E. Protracted
- immune disorders at one year after ICU discharge in patients with septic shock. Crit Care.
- 18 2018;22:42.
- 19 [28] Gerth AMJ, Hatch RA, Young JD, Watkinson PJ. Changes in health-related quality of life
- after discharge from an intensive care unit: a systematic review. Anaesthesia. 2019;74:100-8.
- 21 [29] Haywood KL, Pearson N, Morrison LJ, Castren M, Lilja G, Perkins GD. Assessing health-
- 22 related quality of life (HRQoL) in survivors of out-of-hospital cardiac arrest: A systematic
- 23 review of patient-reported outcome measures. Resuscitation. 2018;123:22-37.

- 1 [30] Lilja G, Nielsen N, Bro-Jeppesen J, Dunford H, Friberg H, Hofgren C, et al. Return to
- Work and Participation in Society After Out-of-Hospital Cardiac Arrest. Circ Cardiovasc Qual
- 3 Outcomes. 2018;11:e003566.
- 4 [31] Bohm M, Lilja G, Finnbogadottir H, Cronberg T, Unden J, Friberg H, et al. Detailed
- 5 analysis of health-related quality of life after out-of-hospital cardiac arrest. Resuscitation.
- 6 2019;135:197-204.

- 7 [32] Moulaert VR, van Heugten CM, Winkens B, Bakx WG, de Krom MC, Gorgels TP, et al.
- 8 Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year:
- 9 A randomised controlled trial. Int J Cardiol. 2015;193:8-16.
- 10 [33] Sandroni C, Nolan J, Cavallaro F, Antonelli M. In-hospital cardiac arrest: incidence,
- prognosis and possible measures to improve survival. Intensive Care Med. 2007;33:237-45.







One-year mortality

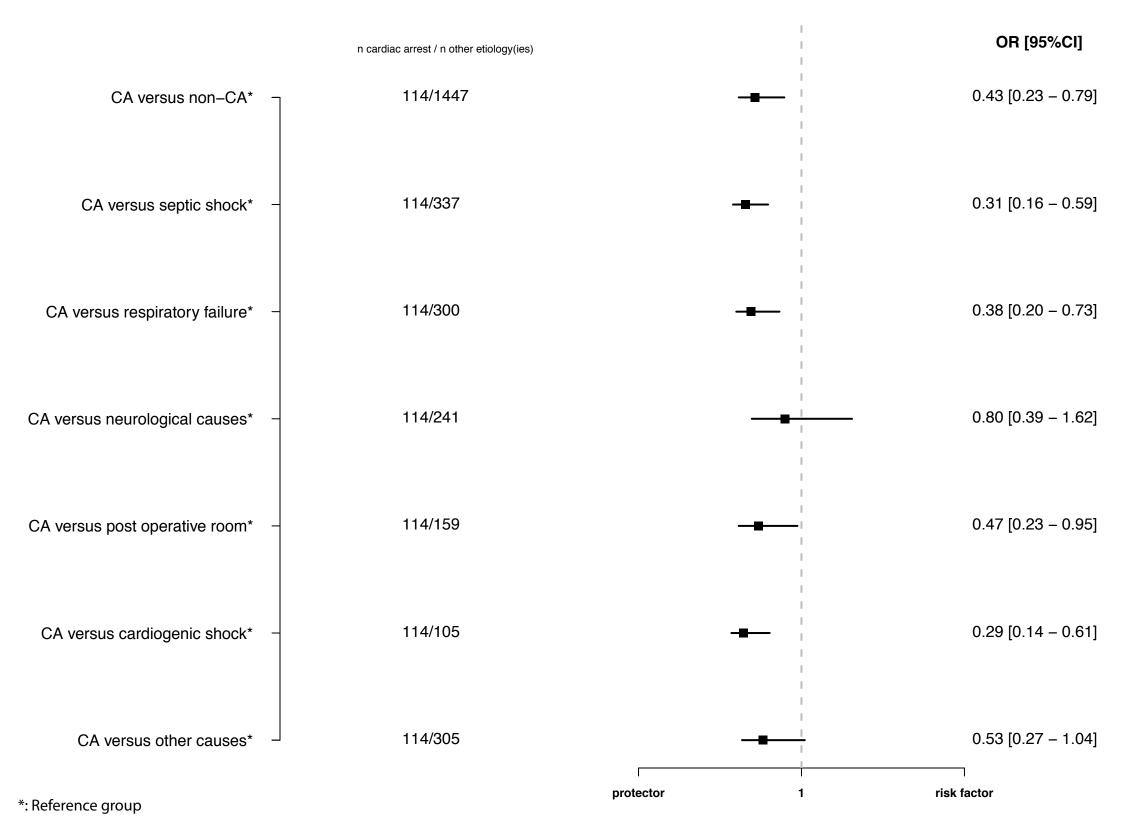


Table 1: Characteristics of the non-matched populations at ICU discharge.

Variables	n available	Global population (n=1561) n (%) or median [IQR]	n available	Non-cardiac arrest (n=1447) n (%) or median [IQR]	n available	Cardiac arrest (n=114) n (%) or median [IQR]	р
Demographic data							
Age (year)	1561	61 [49 - 73]	1447	61 [48 – 73]	114	61 [50 – 72]	0.72
Women	1561	567 (36 %)	1447	530 (36.6 %)	114	37 (32.5 %)	0.37
Body mass index (kg/m ²)	975	26 [23 - 31]	906	26 [23 – 31]	69	26 [24 – 30]	0.99
Medical history		•					
Charlson score	1561	1.0 [0.0 - 2.0]	1447	1.0 [0.0 - 2.0]	114	0.0 [0.0 - 1.0]	<0.0001
Severe valvular disease	1559	53 (3 %)	1445	48 (3 %)	114	5 (4 %)	0.59
Peripheral vascular disease	1559	139 (9 %)	1445	125 (9 %)	114	14 (12 %)	0.19
Prior stroke	1559	64 (4 %)	1445	55 (4 %)	114	9 (8 %)	0.046
Hypertension	1559	638 (41 %)	1445	601 (42 %)	114	37 (32 %)	0.056
Coronary artery disease	1559	123 (8 %)	1445	109 (8 %)	114	14 (12 %)	0.071
Chronic heart failure	1559	107 (7 %)	1445	95 (7 %)	114	12 (11 %)	0.11
Diabetes mellitus	1559	273 (18 %)	1445	262 (18 %)	114	11 (10 %)	0.022
Chronic obstructive pulmonary disease	1559	172 (11 %)	1445	165 (11 %)	114	7 (6 %)	0.083
Chronic renal disease	1559	164 (11 %)	1445	158 (11 %)	114	6 (5 %)	0.057
Recent active malignant tumors	1559	187 (12 %)	1445	186 (13 %)	114	1 (1 %)	0.0001
Prior physical or mental disability	1559	52 (3 %)	1445	50 (3 %)	114	2 (2 %)	0.58
Causes of ICU admission		- ()		(/		(,	
Cardiac arrest	1561	114 (7 %)			114	114 (100%)	
Septic shock	1561	337 (22 %)	1447	337 (23 %)		11 (10070)	
Respiratory failure	1561	300 (19 %)	1447	300 (21 %)			
Neurological causes	1561	241 (15 %)	1447	241 (17 %)			
Post-operative	1561	159 (10 %)	1447	159 (11 %)			
Cardiogenic shock	1561	105 (7 %)	1447	105 (7 %)			
Others ^a	1561	305 (20 %)	1447	305 (21 %)			
ICU events	2502	333 (23 75)		000 (22 /0)			
Renal replacement therapy	1561	284 (18 %)	1447	268 (19 %)	114	16 (14 %)	0.23
Red blood concentrate administered	1561	670 (43 %)	1447	639 (44 %)	114	31 (27 %)	0.0004
Platelet concentrate administered	1561	234 (15 %)	1447	228 (16 %)	114	6 (5 %)	0.003
Tracheotomy	1561	240 (15 %)	1447	230 (16 %)	114	10 (9 %)	0.042
Inotrope and or vasopressors administered	1561	1146 (73 %)	1447	1052 (73 %)	114	94 (82 %)	0.023
Atrial fibrillation during ICU stay	1405	151 (11 %)	1299	142 (11 %)	106	9 (8 %)	0.44
Parameters at ICU discharge	2.00	101 (11 /0)	1233	-1-(70)	200	5 (5 75)	0
Temperature	1399	37.1 [36.8 - 37.5]	1299	37.1 [36.8 - 37.5]	100	37.2 [36.8 - 37.6]	0.17
Systolic blood pressure (mmHg)	1358	125 [111 - 139]	1259	125 [111 - 139]	99	121 [109 - 140]	0.51
Diastolic blood pressure (mmHg)	1299	68 [59 - 77]	1201	68 [59 - 77]	98	67 [60 - 75]	0.41
Heart rate (/min)	1342	90 [79 - 101]	1243	90 [79 - 101]	99	87 [78 - 100]	0.56
Lactate (mmol/L)	651	1.0 [0.7 - 1.3]	604	1.0 [0.7 - 1.3]	47	0.8 [0.7 - 1.1]	0.064
Sodium (mmol/L)	1446	139 [136 - 142]	1344	139 [136 - 142]	102	141 [138 - 143]	0.003
Potassium (mmol/l)	1431	3.9 [3.6 - 4.2]	1329	3.9 [3.6 - 4.2]	102	3.9 [3.6 - 4.2]	0.19
Protein (g/L)	1272	62 [56 - 69]	1179	62 [56 - 69]	93	64 [58 - 69]	0.018
Creatinemia (µmol/L)	1501	66 [51 - 95]	1392	66 [50 - 96]	109	74 [60 - 94]	0.011
Hemoglobin (g/L)	1358	10.0 [9.0 - 11.2]	1265	10.0 [8.9 - 11.1]	93	10.5 [9.7 - 11.5]	0.002
White blood count (G/L)	1348	9.6 [7.0 – 13.1]	1254	9.6 [7.0 – 13.2]	94	9.6 [7.7 – 12.1]	0.83
Platelet count (G/L)	1342	293 [184 - 436]	1254	297 [184 - 443]	91	250 [188- 374]	0.18
Glycemia (g/L)	1301	6.8 [5.7 - 8.3]	1203	6.8 [5.7 - 8.3]	98	6.7 [5.6 - 8.4]	0.89
Cardiac biomarkers	1301	0.0 [5.7 0.5]	1205	0.0 [5.7 0.5]	30	0.7 [5.0 0.4]	0.05
High sensitive troponin I (pg/mL)	1205	11.1 [4.1 - 38.4]	1113	10.0 [3.9 - 33.8]	92	42.0 [18.4 - 267.1]	<0.0001
N-terminal pro-B type natriuretic peptide	1203	11.1 [7.1 - 30.4]	1113	10.0 [3.3 - 33.0]	52	1421.0 [423.5 -	~0.000I
(pg/mL)	1203	543.1 [148.4 - 2073.0]	1112	518.1 [140.4 - 1968.0]	91	5719.0]	<0.0001
Outcome						3713.0]	
ICU length of stay (days)	1561	12 [7 - 21]	1447	13 [7 – 21]	114	9 [5 – 16]	0.0005
Survival one-year after ICU discharge	1561	12 [7 - 21]	1447	13 [7 – 21]	114	102 (89 %)	0.0005
a Others (n=305) included anaphylactic shock (n=2), acute p							

a Others (n=305) included anaphylactic shock (n=2), acute pancreatitis (n=10), hemorrhagic shock (n=84), hypovolemic shock (n=20), liver failure (n=18), metabolic causes (n=11), mixed (n=15), multiple organ failure (n=4), renal

failure (n=11), severe sepsis (n=38), trauma (n=86), thrombotic microangiopathies (n=6)

Table 2: Characteristics of non-cardiac arrest and cardiac arrest patients at ICU discharge before and after propensity score matching.

Variables	Non-matche	d population	Matched population				
	Non-cardiac arrest (n=1447) n (%) or median [IQR]	Cardiac arrest (n=114) n (%) or median [IQR]	SD	Non-cardiac arrest (n=68) n (%) or median [IQR]	Cardiac arrest (n=68) n (%) or median [IQR]	SD	
Age (years)	61 [48 – 73]	61 [50 – 72]	5.3	64 [54 – 76]	66 [52 – 74]	5.9	
Charlson score > 1	513 (35 %)	27 (24 %)	-25.9	18 (26 %)	19 (28 %)	3.3	
Severe vascular disease	125 (9 %)	14 (12 %)	11.8	8 (12 %)	6 (9 %)	-9.6	
Severe valvular disease	48 (3 %)	5 (4 %)	5.5	3 (4 %)	2 (3 %)	-7.8	
Chronic renal disease	158 (11 %)	6 (5 %)	-20.9	4 (6 %)	3 (4 %)	-6.6	
Recent active malignant tumor	186 (13 %)	1 (1 %)	-48.8	-	-	0	
Prior physical or mental disability	50 (3 %)	2 (2 %)	-10.7	1 (1 %)	1 (1 %)	-0	
Red blood pack administered	639 (44 %)	31 (27 %)	-35.9	16 (24 %)	18 (26 %)	6.7	
Temperature (°C)	37.1 [36.8 - 37.5]	37.2 [36.8 - 37.6]	14.7	37.0 [36.9 - 37.6]	37.1 [36.7 - 37.5]	-9.3	
Systolic blood pressure (mmHg)	125 [111 – 139]	121 [109 – 140]	-6.8	127 [116 – 138]	125 [108 – 142]	0.9	
Protein > 62 g/L	575 (49 %)	53 (57 %)	16.5	35 (51 %)	35 (51 %)	0	
White blood count > 9.6 G/L	626 (50 %)	45 (48 %)	-4.1	36 (53 %)	37 (54 %)	2.9	
Platelets > 290 G/L	642 (51 %)	38 (42 %)	-19.2	30 (44 %)	30 (44 %)	0	
Length of stay > 14 days	605 (42 %)	35 (31 %)	-23.2	17 (25 %)	20 (29 %)	9.9	

SD: standardized difference