



Original Article

Health related quality of life and predictive factors six months after intensive care unit discharge



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ABSTRACT

Background: Advances in critical care medicine have improved patients' survival rate. However, physical and cognitive sequels after Intensive Care Unit (ICU) discharge remain substantial. Our objectives were to evaluate the Health-related Quality of Life (HRQL) at 6-month after ICU discharge and identify the risk factors of this outcomes.

Methods: We performed a single-centre prospective observational study. The components of Short Form 36 (SF-36) were analysed for assessing HRQL on preadmission and at 3- and 6-month after ICU discharge. **Results:** During the study period, 438 patients were eligible for recruitment and 220 of them were included in the trial. During the follow-up period, bodily pain and role limitations relating to emotion were both improved in comparison to the preadmission status while physical role component was lower at 3- and 6-month after ICU discharge. There was no other significant change in the SF-36 domains. Mental as well as physical aggregates remained also unchanged. Most of preadmission SF-36 scores were lower in patients who died within the first 6 months of follow-up compared to those who are still alive. Factors independently associated with the 6-month HRQL were age, preadmission HRQL score, SAPS II, prolonged mechanical ventilation (> 3 days) and the occurrence of acute respiratory distress syndrome. **Conclusion:** In our Cohort, ICU stay does not seem to alter globally neither the mental nor the physical component of the HRQL at 6-month after the discharge. However, some domains of the SF-36 are subject to significant changes.

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1. Introduction

Despite considerable medical progress, admission to Intensive Care Unit (ICU) of patients is associated with a significant high rate of morbidity [1–4]. A growing body of evidence clearly demonstrates that intensive care survivors have severe physical, cognitive and mental health impairments such as neuromuscular dysfunction and weakness, respiratory impairment, posttraumatic stress disorder, anxiety and depression after discharge from ICU [5–13]. These adverse consequences of critical care have recently been described as the post-intensive care syndrome,

defined as a new or worsened deficiencies in physical, cognitive and mental health after discharge from ICU [14,15]. Although an increasing number of trials evaluate survivors' Health-Related Quality of Life (HRQL) after ICU discharge to determine the magnitude of the post-intensive care syndrome [14,16,17], this outcome receives less attention than mortality in assessing critically ill patients' outcomes. However, in order to obtain a better overview and a thorough knowledge of patient outcome discharged from ICU, it is quintessential to encompass HRQL in order to improve patient care. In fact, it has been suggested that HRQL measurements should be included in interventional clinical studies design including critically ill patients [18]. Therefore, the primary objective of the present trial was to determine patients' HRQL score 6-month after ICU discharge and to identify the independent prognostic factors.

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2. Materials and methods

2.1. Setting and participants

This prospective single-centre observational study was conducted between May 2015 and March 2016 in a 22-beds mixed medical and surgical ICU of the approximately 2700-bed University Hospital Centre of Bordeaux. In 2014, a total of 1370 patients were admitted in our unit. The reason for ICU admission was surgical in 60% of patients and medical in 40% of patients. The all-cause ICU mortality rate was 6.0%. During the study period, the staff in charge of patients included five physicians working daily, 6 to 8 residents and nurses with a 2.5:1 patients/nurse ratio. All patients were aged ≥ 18 years with an ICU length of stay expected to be > 48 hours were screened for eligibility. Exclusion criteria were death in ICU, patients unable to communicate adequately, patients not fluent in French, patients with psychiatric disorder or cognitive impairment and those who refused to participate to the study. The current trial was approved by the research ethics board of the University Hospital of Bordeaux (Comité de Protection des Personnes Sud-Ouest et Outre Mer III/Number DC 2015/177). Agreement from the Commission Nationale de l'Informatique et des Libertés was also obtained (Registration number 1921102v0). In this purely observational trial, patients were treated according to standard of care of the institution. Thus, authorisation was granted to waive written informed consent for the present study.

2.2. Procedure

All patients admitted in ICU during the study period were screened. Patients were enrolled once eligible. Demographic and clinical data, such as age, sex, reason for admission (surgical or medical), severity of illness measured by Simplified Acute Physiology Score II (SAPS II) [19] and highest Sequential Organ Failure Assessment (SOFA) score during the ICU stay [20], ICU length of stay, duration of invasive ventilation, need for renal replacement therapy, blood transfusion, infusion of vasoactive drugs and occurrence of acute respiratory distress syndrome (ARDS) according to the Berlin definition, were collected.

2.3. Measurement of health-related Quality of Life

The preadmission ICU HRQL was assessed through the French version of Short-Form (SF)-36. This questionnaire has been validated in primary care for members of the general population but has also been demonstrated to have acceptability, reliability and validity within the ICU population [21–23]. The preadmission ICU HRQL was assessed by asking to the patient to complete the questionnaire as soon as possible once the inclusion criteria were met. Patient ability to complete the SF-36 was assessed daily. The ability to complete it was defined as their capacity to accurately recall factual data about their preadmission status. In ICU, patients were invited to fill out the SF-36 questionnaire either by doctors, nurses or medical students. Patients were allowed to complete the questionnaire alone when they mentioned that they were not comfortable with a face-to-face interview. However, relatives were not allowed to fill the SF-36 for the patients. After ICU discharge, two physicians (N.F or K.F) evaluated the post ICU HRQL through a phone interview at 6-month. To assess the variation of HRQL over time, an additional follow-up was also done 3 months after ICU discharge. Patients were considered as lost to follow-up when they could not be contacted after ten phone calls. At 3- and 6-month follow-ups, death was confirmed either by patients' relatives, general practitioners or consulting the national registry of deaths.

The SF-36 questionnaire contains 36 items measuring eight domains: physical functioning (PF, 10 items), role limitations

relating to physical health (RP, four items), bodily pain (BP, two items), general health perceptions (GH five items), vitality (VT, four items), social functioning (SF, two items), role limitations relating to emotion (RE, 3 items), mental health (MH, 5 items), each with values ranging from 0 to 100. Each item is weighted with an additive scaling to calculate the final domain score. A high score indicates a low impairment and a low score designates an important impairment. Furthermore, specific scores could be aggregated to form two other domains: the Physical Component Score (PCS) and the Mental Component Score (MCS). The former offers a global appreciation of patients' physical functioning, physical role, pain and general health whereas the latter offers a comprehensive indication of patients' vitality, social functioning, emotional role and mental health [21,24,25]. The SF-36 PCS and MCS scoring algorithms have been extensively described in detail elsewhere [23,25].

2.4. Statistical analysis

As continuous variables were non-normally distributed (Shapiro–Wilks test was used to test the distribution), they were expressed as medians [interquartile range = IQR]. Categorical data were expressed as frequency (proportion). Comparisons between patients were performed using a Chi² test or Fisher exact test for categorical variables and by Mann–Whitney U test for continuous variables. Each SF-36 domain scores across time was compared using an analysis of variance for repeated measures. Factors with a *P*-value < 0.2 in the univariate analysis associated with HRQL score at 6-month were included in a linear regression model for multivariate analysis. All *P*-values were two-tailed and a threshold < 0.05 was required to reject the null hypothesis.

3. Results

The flow chart of the study is displayed in Fig. 1. During the study period, 793 patients admitted to the ICU were screened. More than half of them (51.7%) were admitted following major thoraco-abdominal surgical procedures. The main remaining causes for admission were septic shock (18.5%) and gastrointestinal bleeding (16.9%). Among these screened patients, 295 (37.2%) of them stayed less than 48 hours in ICU and were consequently excluded from the analysis. Among the patients with an ICU length of stay longer than 48 hours, the ICU mortality rate was 12.0% ($n = 60$). Consequently, four hundred and thirty-eight patients were assessed for eligibility. Of those 438 patients remaining for inclusion 170 patients were not recruited because they did not fill out the QOL questionnaire before being discharged from ICU, 32 did not meet the inclusion criteria and 16 declined to answer the SF-36, leaving 220 patients for the final analysis. Over 6 months, 22 (10%) patients were lost to follow-up. Thirty-eight patients (19.2%, 95% CI: 13.7–24.7) died within six months following the ICU discharge. The majority of them (35 out of 38) died within the first three months after the ICU discharge. Patients' demographic and clinical characteristics are shown in Table 1.

The SF-36 assessment of HRQL before ICU admission, at 3- and 6-month after ICU discharge is displayed on Fig. 2. In comparison to preadmission value (50 [0–100]), we observed that RP was significantly lower at 3-month 0 [0–81] and 6-month 0 [0–81] after the ICU discharge. Conversely, the preadmission BP was lower than the values found at 3- and 6-month after ICU discharge, 62 [32–100] versus 74 [49–100] and 100 [51–100], respectively. The RE domain was higher at 6-month (100 [0–100] versus 100 [59–100], $P < 0.05$). Concerning the SF-36 mental (MCS) and physical (PCS) aggregates, they remained unchanged during the follow-up at 3- and 6-month.

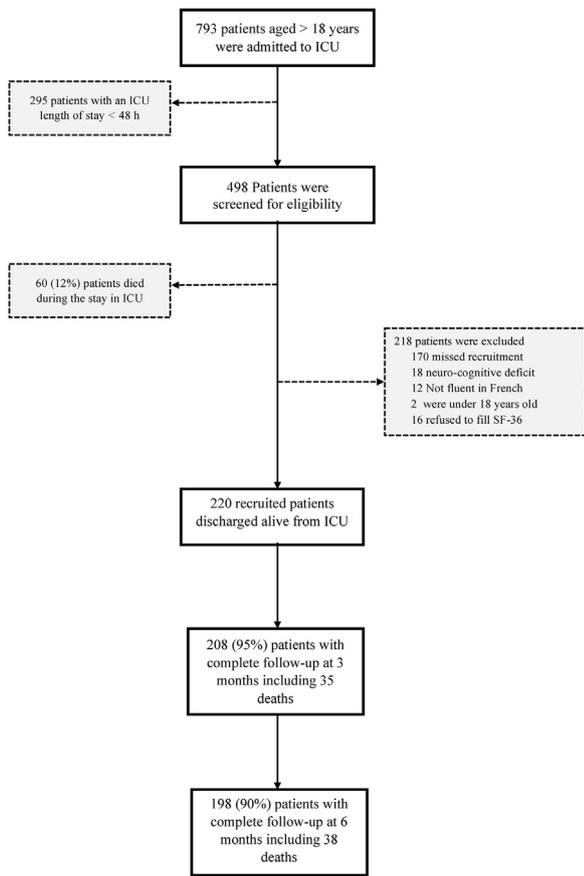


Fig. 1. Flow chart of the study.

Table 1
Baseline characteristics of patients enrolled in the study (n = 220).

Variables	
Age, year	63 [54–71]
Male, n (%)	156 (71)
SAPS II	39 [30–48]
SOFA ^a	4 [3–7]
ICU length of stay, (days)	6 [4–10]
Duration of mechanical ventilation, (days)	1 [0–2]
ARDS, n (%)	20 (9)
Inotropic drugs, n (%)	105 (48)
Renal replacement therapy, n (%)	16 (8)
Blood transfusion, n (%)	101 (46)
Type of ICU Admission, n (%)	
Medical	79 (36)
Elective surgery	102 (46)
Emergency surgery	39 (18)

Data are expressed as median [interquartile range] or n (%). SAPS II: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; ICU: intensive care unit and ARDS: Acute Respiratory Distress Syndrome.

^a The highest SOFA score during ICU stay was considered.

Most of preadmission SF-36 domain scores were lower in patients who died within the first 6 months of follow-up than those still alive (Fig. 3). Similarly, the SF-36 mental aggregate score MCS was significantly lower in patients who died within the first 6 months from ICU discharge (34 [25–43] versus 43 [31–53], $P = 0.02$) while their physical aggregate score PCS that was also lower did not reach the level of significance (38 [32–48] versus 44 [34–54], $P = 0.06$).

The multiple linear regression analyses found that preadmission PCS, age and the presence of ARDS were associated with PCS at 6-month after ICU discharge (Table 2). The multiple linear

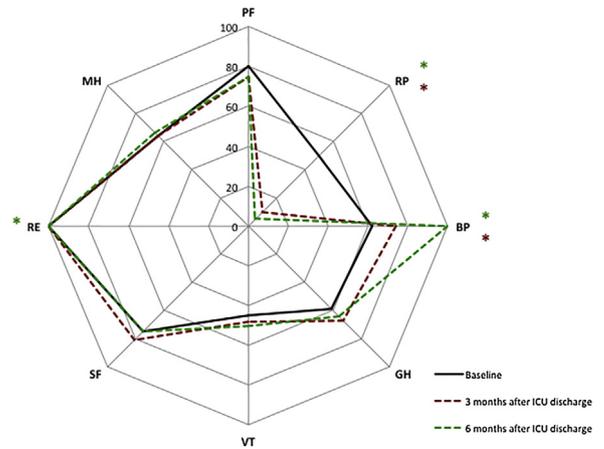


Fig. 2. Median Short-Form 36 (SF-36) domain scores at baseline (preadmission), 3 months and 6 months in patients being still alive at 6 months after ICU discharge (n = 160). Higher scores mean better health-related quality of life. PF: physical functioning; RP: role limited by physical problem; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role limited by emotional problems; MH: mental health. * $P < 0.05$ versus baseline value (preadmission) for each domain score.

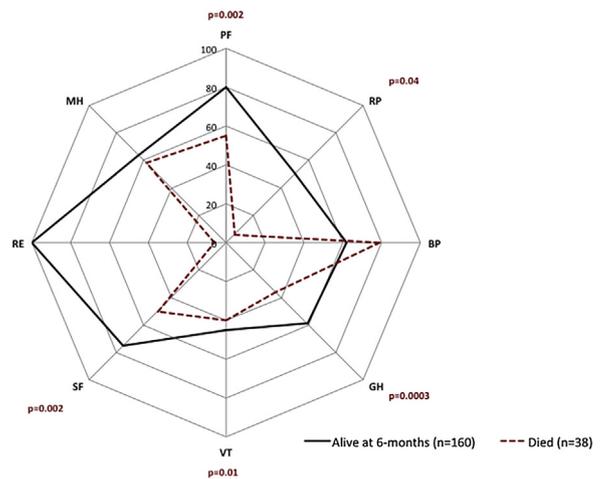


Fig. 3. Preadmission median Short-Form 36 (SF-36) domain scores between patients still alive (n = 160) and those who died (n = 38) at 6 months after ICU discharge. Higher scores mean better health-related quality of life. PF: physical functioning; RP: role limited by physical problem; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role limited by emotional problems; MH: mental health. * $P < 0.05$ versus baseline value (preadmission) for each domain score.

Table 2
Factor significantly associated with the 6 month PCS (multiple linear regression).

Variables	Beta	95% CI	P-value
Age	-0.16	-0.26 to -0.01	0.01
ARDS	-7.45	-12.59 to -2.29	0.004
PCS at preadmission	0.25	0.08 to 0.42	0.003

ARDS: Acute Respiratory Distress Syndrome. PCS: Physical Component Score.

regression analyses also found that preadmission MCS, age, length of mechanical ventilation > 3 days and SAPS II at inclusion were associated with MCS score at 6-month after discharge (Table 3).

4. Discussion

The main findings of the present study were that:

Table 3
Factor significantly associated with the 6-month MCS (multiple linear regression).

Variables	Beta	95% IC	P-value
Age	-0.17	-0.32 to -0.01	0.03
SAPS II at inclusion	-0.18	-0.04 to 0.33	0.02
Mechanical ventilation > 3 days	-7.2	-13.46 to -0.94	0.02
MCS at preadmission	0.22	0.08 to 0.35	0.002

SAPS II: Simplified Acute Physiology Score; MCS: Mental Component Score.

- the stay in ICU did not alter neither the mental nor the physical component of the HRQL at 6-month after the discharge;
- the risk factors associated with impairment of HRQL at 6-month are age, respiratory outcomes, high SAPS II and prolonged ICU stay;
- the overall mortality rate at 6-month after discharge from ICU remains significantly high and seems to occur mainly within the first 3 months after the ICU discharge.

Several studies assessed the post-ICU HRQL [26–30]. However, these studies are heterogeneous because of the difference in the type of population admitted in ICU, the method used to evaluation HRQL and the duration of follow-up. The majority of these studies found an initial post-ICU decrease in the HRQL followed by a slow improvement during the follow-up, sometimes reaching the ICU preadmission HRQL status [31,32]. Conversely, other authors reported a persistent decrease of post-ICU HRQL without significant improvement over time [27,33]. In our study, neither MCS nor PCS were globally affected after ICU discharge. One plausible reason for this discrepant result is that we have enrolled a significant proportion of patient undergoing elective surgeries that were not as frail as the population enrolled in previous published trials [27,32,33]. Furthermore, PCS was unchanged at 6-month after ICU discharge because two components of this score evolved inversely during the follow-up. Indeed, RP component was significantly decreased while a significant improvement in BP component could be observed.

We found that independent factors associated with 6-month decrease in HRQL were age, the presence of ARDS during the stay in ICU, length of mechanical ventilation > 3 days and SAPS II. It should be point out that other factors have been previously reported to be associated with poor post-ICU QOL as trauma patients, severe sepsis, emergency surgery [17], shock, 1-year weakness [34], decrease sleep quality at 6-month, depression, anxiety and stress [35].

In the present study, preadmission HRQL score was positively associated with the 6-month HRQL score. These results confirm results from previous trials suggesting that preadmission HRQL could be useful to predict post-ICU HRQL outcomes [17,31]. Other previous works also reported that preadmission HRQL was significantly correlated with in-hospital as well as 6-month mortality [30,36–39]. In the present study, such association has not been investigated. However, we must point out that most of preadmission SF-36 domain scores (5 of the eight domains) were lower in patients who died within the first 6 months of follow-up.

In our study, patients' age could be identified as an independent risk factor for decreased PCS and MCS 6-month after ICU discharge. Some authors have already reported that elderly patients suffer from physical and cognitive impairments with functional decline and increase dependency after ICU [37–39]. Nevertheless, they generally adapted well to these limitations and perceived their HRQL as good [17].

Our observational and single-centre study has several limitations. The observed mortality rate in our study was lower than the one usually reported. This could be explained by the fact that a large proportion of patient included in the present study were

admitted after elective surgery. Second, we have excluded patients with neuro-cognitive deficit, whom were predominantly elderly patients. However, this elderly and frail population might have been the one more prone to present low QOL score with better post-ICU discharge QOL improvement. Similarly, a large number of eligible patients were screened but not included because they did not fill out the preadmission HRQL questionnaire during their ICU stay. This may have induced a bias in the results, which may not reflect the HRQL of the whole eligible population. Third, the validity of the preadmission HRQL remains questionable. Self-reported data may be subject to recall bias through the retrospective nature of QOL assessment that reflects the patient's status upon ICU admission. Fourth, we did not study the post-intensive care syndrome which, includes weakness, anxiety, stress and depression, known to be largely associated with low QOL score after ICU discharge [35]. Finally, our study does not include sample size calculation and it could be suspected that our study is underpowered.

5. Conclusion

The ICU stay does not seem to alter neither the mental nor the physical component of the HRQL assessed via the SF-36 questionnaire at 6-month after ICU discharge. However, after discharge from ICU it seems that some domains of the SF-36 such as the bodily pain and the role limitations relating to emotion could be improved. Finally, low preadmission HRQL seems to be a risk factor of decreased HRQL at 6-month after ICU discharge. Therefore, physician should bare this information in mind during patients' ICU stay.

Ethical statements

This single-center and observational was approved by the Institutional Review Board (Comité de Protection des Personnes Sud-Ouest et Outre-Mer III, Bordeaux, France, Number DC 2015/177). Agreement was obtained also from the Commission Nationale de l'Informatique et des Libertés was also obtained (registration number 1921102v0).

Author's contributions

NF, BC, AD, AO helped to conceive, design and conduct the study. NF and KF helped supervise data collection. NF, BC, AD and AO supervised the conduct of the trial. NF, AD and AO helped analyse and review the data, to provide statistical advice and to performed statistical analyses. NF, AD, CZ and AO review the manuscript gave final approval of the version. All authors read and approved the final manuscript.

Disclosure of interest

The authors declare that they have no competing interest. Only departmental funds were used for this study. No external funds were obtained.

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