Long-stay medical-surgical intensive care unit patients in South Africa: Quality of life and mortality 1 year after discharge

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Background. Although mortality is the primary measure of critical care outcome, the health-related quality of life (HRQOL) of survivors is often diminished. There is a paucity of South African research on HRQOL in intensive care unit (ICU) survivors.

Objectives. To evaluate the 1-year post-discharge data of long-stay ICU patients, a group known to consume 20 - 40% of ICU resources.

Methods. A 1-year prospective observational study was conducted in a multidisciplinary medical-surgical ICU. Adult patients who were mechanically ventilated beyond 6 days were included. Clinical and mortality data were collected. Pre-admission and 6- and 12-month HRQOL were measured with the Short Form-36 questionnaire. Physical and mental component summary scores (PCS and MCS) were calculated. Associations between 12-month mortality and poor HRQOL scores were determined.

Results. Of 119 patients enrolled, 40.3% had sustained trauma, 19.3% were post-surgical and 40.3% had medical conditions; 29.2% were HIV-positive (HIV status was known for 74.8% of the cohort). The hospital and 12-month mortality rates were 42.9% and 57.4% (n=66/115), respectively. Age, longer ICU stay, higher disease severity scores and vasopressor use were associated with 12-month mortality. The survivors’ median PCS and MCS at 6 and 12 months were significantly lower compared with pre-admission scores (both p<0.001). At 12 months, 53.1% of survivors demonstrated a poor PCS and 42.9% a poor MCS. Associations with poor 12-month PCS included longer ICU stay, male gender and trauma, while trauma and sepsis were associated with a poor 12-month MCS. Among the 19 trauma survivors, 78.9% had a poor MCS and/or PCS. Of previously employed patients, 54.8% were unemployed at 12 months.

Conclusions. Patients ventilated beyond 6 days in a multidisciplinary ICU had a high mortality. Poor HRQOL at 12 months post discharge was frequently observed among survivors. Trauma was associated with poor 12-month outcomes. These findings highlight the need to further explore the outcomes of long-stay ICU patients in Africa.
preponderance of surgical emergency and trauma admissions\[17,19]\). These variations and the large proportion of the ICU budget that is spent on long-stay ICU survivors necessitate that we ascertain survival and the HRQOL in the SA setting.

**Objectives**

To determine mortality and HRQOL at 6 and 12 months after discharge of long-stay survivors in a tertiary ICU.

**Methods**

This prospective observational study was conducted in a closed multidisciplinary medical-surgical 16-bed tertiary ICU in Eastern Cape Province, SA. The ICU offers full-time on-site medical practitioner cover as well as specialist physician cover. There is a registered nurse-to-patient ratio of 3:4. Physiotherapy services are offered daily except on Sundays. The tertiary hospital serves ~1.6 million people residing in an area of 60 000 km\(^2\). From 3 May 2017 to 2 May 2018, all patients aged ≥18 years admitted to the ICU for the first time and who required mechanical ventilation for ≥7 days were eligible for study inclusion. Patients for whom a pre-admission (i.e. the acute illness leading to admission) HRQOL questionnaire could not be completed, prisoners, and patients who were not fluent in isiXhosa, English or Afrikaans were excluded. Ethical clearance was obtained from the Walter Sisulu University Human Research Ethics Committee (ref. no. 120/2018). Written informed consent was obtained from patients or their surrogate decision-maker. In the situation of assent from a surrogate, the patient's consent was obtained when the patient was able to give it.

Data captured included demographics, comorbidities, employment status, clinical condition and treatment, as well as the occurrence of complications, sepsis or organ dysfunction during the course of the ICU stay. The Simplified Acute Physiology Score 3 (SAPS) and the maximum Sequential Organ Failure Assessment (SOFA) score were also noted on admission. Acute kidney injury was diagnosed according to the Kidney Diseases Improving Global Outcomes definition\[20\] and acute respiratory distress syndrome according to the Berlin classification\[21\]. Sepsis and septic shock were defined according to the Sepsis-3 criteria\[22\].

HRQOL was adjudged with the use of the Short Form-36 (SF-36) questionnaire, which was developed by the RAND Corporation as part of the Medical Outcomes Study\[23\]. The SF-36 questionnaire comprises eight domains, namely physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. The physical and mental component summary scores (PCS and MCS, respectively) are calculated from these eight domains. Oblique rather than orthogonal scores were formed for the PCS and MCS. The oblique method as opposed to orthogonal scoring reduces the correlation between the components due to the inherent correlation between the items which are used to form the components\[24\]. No population norms for the PCS and MCS are available for SA or any African countries. The original US norms for the mean (standard deviation (SD)) PCS and MCS were 50 (10),\[25\] and a minimally important difference (MID) of at least 3 points is suggested for the SF-36\[26\]. For the purposes of the present study, a poor HRQOL was defined as a combination of a decrease in the 12-month PCS or MCS of ≥3 compared with the pre-admission score, as well as a score of <47 (a decrease of more than the MID below 50). These criteria were to ensure that the poor-outcome group was accurately characterised by excluding patients who despite a decrease still had a reasonable HRQOL, and also to take into account the effect of a pre-existing poor HRQOL. The retrospective pre-admission HRQOL was worked out with the patient and/or a family member. The SF-36 was repeated telephonically or in person at 6 and 12 months after hospital discharge, and employment status was also documented. The hospital, ICU, and 6- and 12-month mortality was recorded.

Data were captured in Excel 2016 (Microsoft Corp., USA) and analysed with RStudio, version 3.6.1, 2019 (RStudio, USA, http://www.r-project.org) and Statistica version 13 (TIBCO Software Inc., USA). Continuous data were tested for normality using Pearson's \(\chi^2\) test.Normally distributed data are reported as means (SD) and skewed data as medians (interquartile range (IQR)). Discrete data are presented as numbers (percentages). Group comparisons were done in relation to survival at 12 months. Patients with a poor HRQOL (PCS and MCS) at 12 months were compared with patients who had a good HRQOL outcome at 12 months. Student's \(t\)-test and the Mann-Whitney \(U\)-test were used to compare continuous data and the \(\chi^2\) and Fisher's exact tests were used for discrete data, as appropriate. Variables with a bivariate analysis demonstrating a 10% level of significance (alpha level ≤0.1) between groups were considered in the logistic regression models. A \(p\)-value <0.05 was set as the threshold of statistical significance.

**Results**

During the study period, 934 admissions were screened for potential inclusion, of whom 133 were mechanically ventilated for ≥7 days. There were 14 exclusions, as there were 2 prisoners and 2 cases in which informed consent could not be obtained, and 10 patients were <18 years old. Of 119 patients enrolled, 49 were ultimately reviewed at the 12-month visit (Fig. 1). Four patients were lost to follow-up between 6 and 12 months.

The characteristics of the cohort are presented in Table 1. The main admission diagnoses were trauma (n=48; 40.3%), community-acquired pneumonia (n=16; 13.4%), complicated intra-abdominal sepsis (n=8; 6.7%), pancreatitis (n=6; 5%), self-harm (n=4; 3.4%), complicated soft-tissue infections (n=4; 3.4%) and neuro-muscular weakness (n=5; 4.2%). The diagnoses of the 5 patients with neuromuscular weakness on admission were Guillain-Barré syndrome (3 cases), and a myasthenic crisis and severe hypokalaemia (1 case each). Among the trauma patients, 28 (23.5% of the total of 119 patients) had been involved in motor vehicle accidents, 16 (13.4%) were assault cases, 2 (1.68%) had burn wounds and 1 presented following a fall. Eighty-nine patients (74.8%) had known HIV status, of whom 29.2% were HIV-positive.

The ICU, hospital, and 6- and 12-month mortality rates for the cohort were 31.1%, 42.9%, 52.9% and 57.4% (n=66/115), respectively. The presence or development of sepsis was associated with a significant increase in hospital mortality (14.6% v. 45.1%; \(p=0.03\)). Patient characteristics, complications and therapy in relation to 12-month mortality are shown in Table 1. Where numbers permitted, multiple logistic regression analysis was performed, and this confirmed these associations with comparable odds ratios. Age, longer ICU stay, higher SAPS and maximum SOFA scores as well as vasopressor use were found to be significantly associated with 12-month mortality. There were trends for male sex and sepsis (on admission or ICU acquired) to be associated with increased mortality.

Seventy-five percent of the pre-admission SF-36 questionnaires were completed by the patients themselves and the rest by a surrogate. On follow-up, they were completed by the patients. The median (IQR) pre-admission PCS was 58.5 (50.6 - 60.9). At 6 months it was significantly lower at 40.5 (28.9 - 52.5) (\(p<0.001\), and this lower median score persisted at 12 months at 42.6 (31.2 - 51.3) (\(p=0.84\), 6 v. 12 months) (Fig. 2). The median pre-admission MCS was 55.5 (47.4 -
60.7). At 6 months it was significantly lower at 44.0 (32.9 - 54.4) (p<0.001), and this lower score also persisted at 12 months at 45.4 (35.8 - 54.8) (p=0.64, 6 v. 12 months) (Fig. 3). Similar to the 6-month scores, the median 12-month PCS and MCS were significantly lower compared with the pre-admission scores (p<0.001 for both).

At 12 months, 26 (33.1%) of the survivors were observed to have a poor mean PCS, while 21 (47.2%) demonstrated a poor mean MCS. The pre-admission PCS and MCS of patients with poor outcomes were comparable to the good-outcome group (Table 2). There was considerable overlap between patients with a poor PCS and MCS: 19 patients (38.8% of the survivors) had low scores for both. While there was a significant decline in the poor-outcome group's score from pre-admission to 12 months, the good-outcome group's 6- and 12-month scores were comparable to the pre-admission scores (Table 2).

A longer ICU stay (median (IQR) 23.5 (15 - 36) days v. 15 (11 - 22) days; p=0.035), male sex (69.2% v. 47.8%; p=0.016) and trauma (57.7% v. 17.4%; p=0.007) were associated with a poor 12-month outcome. The median 12-month PCS and MCS were significantly lower compared with the pre-admission scores (p<0.001 for both).

| Table 1. Patient characteristics, therapy and complications in relation to 12-month survival |
|---------------------------------------------------------------|
| **Cohort (N=119)**                                             | **12-month survivors (N=49)** | **12-month non-survivors (N=66)** | **OR (CI) (per unit change for continuous variables)** |
| Age (years), median (IQR)                                     | 37 (27 - 53)                  | 32 (24 - 47)                      | 41 (31 - 55)                      | 0.01 | 1.04 (1.01 - 1.07) |
| Male gender, n (%)                                            | 82 (68.9)                     | 29 (59.2)                        | 50 (75.8)                        | 0.069 | 2.15 (0.97 - 4.80) |
| ICU days, median (IQR)                                        | 16 (10 - 23)                  | 17 (13 - 28)                     | 13 (9 - 21)                      | 0.015 | 0.96 (0.93 - 0.99) |
| SAPS, median (IQR)                                            | 55 (49 - 62)                  | 51 (44 - 58)                     | 57 (51 - 64)                     | 0.025 | 1.04 (1.01 - 1.07) |
| Maximum SOFA score, median (IQR)                             | 8.0 (5.0 - 11.0)              | 7.0 (4 - 9)                      | 8.0 (6 - 13)                     | 0.002 | 1.18 (1.07 - 1.32) |
| Days ventilated, median (IQR)                                | 12 (8 - 19)                   | 14.0 (9 - 20)                    | 10.0 (8 - 19)                    | 0.167 | 0.98 (0.95 - 1.01) |
| ARDS, n (%)                                                   | 25 (21.0)                     | 13 (26.5)                        | 12 (18.2)                        | 0.361 | 0.62 (0.25 - 1.50) |
| Vasopressor, n (%)                                            | 61 (51.3)                     | 18 (36.7)                        | 41 (62.1)                        | 0.009 | 2.82 (1.32 - 6.07) |
| AKI, n (%)                                                    | 91 (76.4)                     | 34 (69.4)                        | 53 (80.3)                        | 0.194 | 1.80 (0.76 - 4.24) |
| Dialysed, n (%)                                               | 29 (24.4)                     | 10 (20.4)                        | 18 (27.3)                        | 0.51  | 1.46 (0.61 - 3.53) |
| Sepsis (community acquired or nosocomial), n (%)              | 81 (68.1)                     | 29 (59.2)                        | 50 (75.8)                        | 0.069 | 2.16 (0.97 - 4.80) |
| Comorbidity present, n (%)                                    | 49 (41.2)                     | 19 (38.8)                        | 30 (45.5)                        | 0.568 | -                 |
| Referring discipline, n (%)                                   | -                             | -                               | -                               | -     | -                 |

OR = odds ratio; CI = confidence interval; IQR = interquartile range; ICU = intensive care unit; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment; ARDS = acute respiratory distress syndrome; AKI = acute kidney injury.
Table 2. Comparison between the poor-outcome and good-outcome groups’ Short Form-36 PCS and MCS scores

| Variable     | Time frame | Poor-outcome group | Good-outcome group | p-value |
|--------------|------------|--------------------|--------------------|---------|
| PCS, median (IQR) | n          | 26                 | 23                 |         |
| Pre-admission | 59.9 (54.3 - 60.9) | 55.5 (42.3 - 59.8) | 0.063              |
| 6 months     | 30.3 (24.6 - 42.0)  | 51.8 (36.6 - 59.7)  | <0.001             |
| 12 months    | 32 (25.5 - 37.9)    | 51.7 (47.7 - 59.6)   | <0.001             |
| p-value (pre-admission v. 12 months) | <0.001 | 0.677             |
| MCS, median (IQR) | n          | 21                 | 28                 |         |
| Pre-admission | 58.6 (53.5 - 61.6) | 52.3 (43.9 - 59.5) | 0.0738            |
| 6 months     | 34.6 (28.0 - 45.3)  | 45.1 (42.2 - 58.6)  | 0.003              |
| 12 months    | 35.8 (23.3 - 39.8)  | 53.9 (48.4 - 57.1)  | <0.001             |
| p-value (pre-admission v. 12 months) | <0.001 | 0.850             |

MCS = mental component summary score; PCS = physical component summary score; IQR = interquartile range.

While the 1-year mortality rate of 57.4% is comparable to studies from high-income countries, it is nonetheless high taking into account the median age of this study population and that the oldest patient was 55 years old.[9,26,27] In the past 15 years, reports from HICs have consistently shown that chronic critical illness with or without prolonged mechanical ventilation is associated with a high 1-year mortality that varies from 48% to 68%. The ICU and hospital mortality of 31.1% and 42.9%, respectively, in our long-stay cohort are also high taking into account that the overall 2017 ICU and hospital mortality in the same unit and hospital for all ICU admissions were 13.3% and 21.4%, respectively.[17] It is worth noting that 21.2% of the deaths occurred while in hospital post ICU discharge, and a further 18.2% occurred within 6 months after hospital discharge. This finding points towards the fact that long-stay patients warrant some form of monitoring after discharge from the ICU for setbacks, both in the hospital and on an outpatient basis.

This study demonstrated that 12-month mortality was associated with older age, higher SAPS and SOFA scores, and the need for vasopressor therapy. This is in keeping with previous findings of significant associations between mortality and increasing age, vasopressor use, thrombocytopenia, chronic kidney disease, acute kidney injury and renal replacement therapy in long-stay ICU patients.[11,30] Interestingly, severity of disease on admission has not been consistently linked to mortality among patients with long-stay chronic critical illness.[9] Findings from larger cohorts have shown that most severity scores and admission diagnoses lose their discrimination once ICU patients stay for longer than 7 - 10 days.[11,27,31] This is probably because patients undergo diverse intercurrent events that become the determinants of mortality, rather than the initial diagnosis or the severity of illness on admission.[11] As such, it is not surprising that the admission diagnoses in our cohort had no impact on 12-month survival. ICU-acquired sepsis contributes to self-perpetuating persistent inflammation, immunosuppression and catabolism syndrome in long-stay ICU patients.[11,30] This may well explain why patients who were either admitted with infections or subsequently developed ICU-acquired infections demonstrated a trend towards an increase in 1-year mortality. The longer ICU stay of 12-month survivors compared with non-survivors may be explained by the fact that 56.1% of deaths occurred during the ICU stay.

Among ICU survivors, the ability to live independently and return to work and a good HRQOL are important considerations. In the absence of population norms for the SF-36 in SA, the survivors’ pre-admission median (IQR) PCS of 58.5 (50.6 - 60.9) and MCS of 55.5 (47.4 - 60.7) were somewhat higher than the updated US population norms (mean (SD) PCS of 49.22 (15.13) and MCS of 53.78 (13.14)).[32]
and were comparable to the control group of a study of young, largely male, trauma survivors in Johannesburg with a mean (SD) PCS of 57.6 (5.1) and MCS of 50.3 (10.3). This last finding reflects the similar mean age and sex of the enrolled patients in these two studies. At 6 months our study cohort demonstrated a significantly lower median MCS and PCS compared with their pre-admission assessment, and this persisted even at 12 months. In alignment with previous findings, the PCS was more affected than the MCS. It has been suggested that this may signify an optimism obtained after seemingly ‘cheating death’. Another possible explanation may be that different aspects of quality of life recover at variable rates, although reports have not been consistent regarding the order and rate of recovery of the components. A large meta-analysis concluded that although physical aspects improved slowly over the years, mental and emotional aspects remained stagnant or declined further over time.

At 12 months, 53.1% of the cohort were found to have a poor PCS and 42.9% had a poor MCS. Furthermore, both of these poor-outcome subgroups’ median component summary scores were significantly lower than their pre-admission scores. The group with a good 12-month HRQOL (for PCS and MCS) had achieved recovery within 6 months. There are no studies in SA pertaining to the long-term HRQOL outcomes of long-stay patients. A 1-year follow-up study conducted in Cape Town of 46 critically ill trauma patients (intubated for a mean of 3 days) found low mean HRQOL domain scores (43 - 53%) at 12 months’ follow-up. In Johannesburg, a 6-month follow-up study among 42 patients admitted to an ICU with penetrating chest injury found that the 6-month PCS and MCS were significantly reduced for those ventilated for ≥5 days compared with their pre-admission HRQOL scores. Interestingly, the mean (SD) 6-month PCS (45 (8)) and MCS (53 (8)) in this study were somewhat higher than the corresponding 6-month values in our study. This may be explained by the differences in the case mix.

Previous studies have demonstrated that the ICU survivor’s pre-admission HRQOL has a significant effect on HRQOL after critical illness, so pre-ICU admission (both PCS and MCS) should also be measured in order to minimise bias. As expected, poor HRQOL pre-ICU also correlates with a poor outcome after ICU admission. In a large systematic review of the long-term HRQOL of ICU survivors, <20% of studies reported pre-admission HRQOL, and this was considered a limitation in terms of interpreting outcomes. Although most patients cannot complete questionnaires themselves at the time of ICU admission, this can be overcome by either completing the questionnaire retrospectively when the patient is capacitated or seeking the assistance of proxies. Although recall bias may influence the results, this is not considered a reason for not measuring the pre-admission HRQOL. Surrogates tend to underestimate the HRQOL, but the difference is small, and the assistance of proxies to reliably assess the HRQOL of critically ill patients on admission has been validated.

A poor 12-month PCS was found to be more common in patients with a longer ICU stay, male sex or a traumatic injury, and a poor 12-month MCS was associated with sepsis (on admission or ICU acquired) or traumatic injury. Logistic regression analysis for markers of poor 12-month MCS and PCS was not feasible owing to the small final dataset, but it is likely that the association with male sex may be explained by the number of trauma cases, as 17 of the 19 trauma cases were male. A large systematic review has also reported that trauma is a risk factor for a poor long-term HRQOL in ICU patients. This, and the fact that the majority of the survivors who had both a poor 12-month MCS and PCS were trauma patients (12 of 19 patients), is in keeping with the previously recorded healthcare and social burden of trauma in SA.

Although most of the domain scores of the patients with poor MCS and PCS scores were low, the domains that were most affected in both groups comprised role limitations due to physical health and emotional problems. These two domains are indicative of problems with work or other daily activities as a result of physical health and emotional problems, respectively. A previous SA study among trauma ICU survivors has described similar findings.

The finding that 54.8% of previously employed ICU survivors were no longer employed at 12 months is a high figure and is in keeping with previous findings of post-ICU unemployment ranging from 32% to 48%, albeit in older patient cohorts. This finding may relate to physical, mental and neurocognitive problems among long-stay survivors and warrants further investigation. Extraneous economic forces may well contribute to employment status change; however, the SA unemployment rate has shown minimal changes during the study period of 2 years.

Study strengths and limitations

The strength of this study lies in the inclusion of a pre-admission HRQOL measurement as well as the small number of patients who were lost to long-term follow-up. The prospective enrolment, including the documentation of multiple contact numbers, as well as the fact that follow-up interviews were largely telephonic, may account for the low rate of attrition. This study also shows that despite challenges in SA such as informal housing and migrant labour, it is feasible to trace most patients telephonically 1 year after hospital discharge.

The small number of survivors at 12-month follow-up was a limiting factor, as it precluded logistic regression analysis.
for markers of a poor 12-month HRQOL outcome. An additional finding is the absence of population norms for HRQOL for SA patients, although this was partially overcome by comparing the patients’ scores with their own pre-admission scores. Both the use of proxies and recall bias may have influenced the retrospectively measured pre-admission HRQOL scores.

Conclusions

This study provides insights into the expected outcomes for medical-surgical patients who require ventilation beyond 6 days in a country where ICU resources are restricted and the practice of triaging referrals is a reality. Our findings demonstrate that long-stay patients have a high mortality risk, and that there is a high prevalence of poor quality of life at 12 months among the survivors. Considering that it has previously been observed that both physicians and surrogates over-estimate the chances of survival in patients who require 7 - 10 days of mechanical ventilation, these findings would provide an additional incentive to reassess the triaging process in a similar setting.

The findings are important in terms of adjusting the expectations of patients, surrogates and attending physicians, not only regarding the probability of survival but also the expected road to recovery, and in establishing whether these align with a particular patient’s goals and values. The finding that long-stay ICU survivors, and in particular the subset of trauma survivors, frequently had a poor long-term HRQOL makes a case for ensuring appropriate access to multidisciplinary rehabilitation and mental health services.

Furthermore, there is a definite need to evaluate long-term outcomes in particular the subset of trauma survivors, frequently had patient’s goals and values. The finding that long-stay ICU survivors, and in particular the subset of trauma survivors, frequently had a poor long-term HRQOL makes a case for ensuring appropriate access to multidisciplinary rehabilitation and mental health services.

Declarations

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Author contributions.

EvdM: study design, protocol, data collection, manuscript writing. DB: data collection, manuscript writing. GS: cleaned data, performed the statistical analysis and manuscript writing. MnV: data collection, manuscript writing. Fp: manuscript writing.

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Conflicts of interest.

None.

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