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National Trends and Variation of Functional Status Deterioration in the Medically Critically Ill

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Abstract

Objectives: Physical and psychological deficits after an intensive care unit (ICU) admission are associated with lower quality of life, higher mortality, and resource utilization. This study aimed to examine the prevalence and secular changes of functional status deterioration (FS $\downarrow$) during hospitalization among non-surgical critical illness survivors over the past decade.

Design: We performed a retrospective longitudinal cohort analysis

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NEI- Study design, data analysis, data interpretation, writing, and critical revision; VV- Study design, data analysis, data interpretation, writing, and critical revision; KP - Study design, data interpretation, writing, and critical revision; AJR - Study design, data interpretation, writing, and critical revision; RLF - Study design, data analysis, data interpretation, writing, and critical revision; EFN - Study design, data analysis, data interpretation, writing, and critical revision; MB - Study design, data interpretation, writing, and critical revision; AC - Study design, data collection, data interpretation, writing, and critical revision; JGC - Study design, data interpretation, writing, and critical revision; CJT - Study design, data collection/analysis/interpretation, writing, and critical revision

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Setting: Analysis performed using the Cerner APACHE outcomes database which included manually abstracted data from 236 U.S. hospitals from 2008 to 2016.

Patients: We included non-surgical adult ICU patients who survived their hospitalization and had a functional status documented at ICU admission and hospital discharge. Physical functional status was categorized as fully independent, partially dependent, or fully dependent.

Measurements and Main Results: FS↓ occurred in 38,116 (29.3%) patients. During the past decade, FS↓ increased in each disease category, as well as overall (IRR 1.15, 95% CI 1.13–1.17, $P<0.001$). Magnitude of FS↓ also increased over time (OR 1.03, 95% CI 1.03–1.03, $P<0.001$) with hematological, sepsis, neurological, and pulmonary disease categories having the highest odds of severe FS↓.

Conclusions: Following non-surgical critical illness, the incidence of FS↓ and magnitude increased in a nationally representative cohort, despite efforts to reduce ICU dysfunction over the past decade. Identifying the incidence of FS↓ and primary etiologies associated with FS↓ will elucidate vital areas for further research and targeted interventions. Reducing ICU debilitation for key disease processes may improve ICU survivor mortality, enhance quality of life, and decrease healthcare utilization.

Keywords

Survivorship; Rehabilitation; Activities of Daily Living; Physical Functional Performance; Physical Performance; Intensive Care Units; Outcome Assessment; Health Care

INTRODUCTION

Intensive care unit (ICU) mortality has been decreasing over the past two decades. (1–3) In contrast with other countries, the rate of increase in intensive care beds in the U.S outpaces general hospital beds.(4) Increasing capacity and decreasing mortality have created an evolving and diverse population of ICU survivors. Today’s survivors of critical illness are increasingly burdened by extensive physical and psychological comorbidities, often resulting in reduced quality of life.(5, 6)

Functional status deterioration (FS↓) occurs to some degree in at least 50% of critically ill survivors.(7–10) In those greater than 80 years of age, functional status limitations can be as high as 97%.(11) Alarming, deficits in physical and cognitive functioning have been shown to persist for months following recovery from critical illness.(12) The term post-intensive care syndrome (PICS) has been used to encompass the physical, emotional, and neuropsychological sequelae from critical illness. In response to increasing recognition of PICS, international critical care societies have developed and endorsed guidelines and bundles targeted at improving the delivery of care, particularly as it relates to sedation management, delirium recognition and mitigation, and early mobility practices. Societies have also recognized the need for longitudinal care of the ICU survivor population with post-ICU clinics being established at a growing number of institutions.(13, 14).

The purpose of this study was to evaluate the change in FS↓ after critical illness over the past decade. We hypothesized that functional status decline among ICU admissions has changed

over time, both overall and within specific disease processes. Using a national prospective cohort, we also sought to quantify the amount of FS $\downarrow$ in different diseases. In our secondary outcome, we sought to characterize the magnitude of decline and temporally model this change to further stratify these temporal changes. Characterization of these trends could help determine high yield targets for future research, intervention, and resource allocation. Some of the results of this study have been previously reported in the form of an abstract.(15)

MATERIALS AND METHODS

Study Design

We used data from the Cerner APACHE outcomes database (Cerner Corporation, Kansas City, MO) and included all patients requiring ICU admission at 236 participating hospitals in the United States.(16) Of these hospitals, 90 reported functional status during this time period. This data was manually collected by trained clinical abstractors at all hospitals participating in this national quality improvement and benchmarking program.(16–18) Abstractors underwent rigorous training and recurrent audits to ensure data accuracy and reliability. Information regarding data collection, data auditing, and validity are described in further detail elsewhere.(17, 18) Our study was approved by the Institutional Review Board at our institution (UMN STUDY00001489).

Participants

All adult patients (age ≥ 18 years) admitted to the ICU at participating centers between January 1, 2008 and December 31, 2016 with a documented functional status on admission and hospital discharge were included in the study.

We excluded patients who had a primary surgical admission as the majority of patients may have a higher propensity for recovery due to the nature of the procedure, while other procedures' normal post-operative trajectory may include an expected functional status decline prior to discharge. Furthermore, surgical patients tend to experience less morbidity and mortality compared to non-surgical critical care patients in other large ICU studies.(2, 3) Resultantly, we were concerned the differing phenotypes may create an inaccurate depiction of critical illness associated functional status decline and proceeded to focus on the non-surgical patients for our study. We also excluded those who died during their hospitalization and focused on survivors from critical illness. As hospitals were not required to participate each year, we sought to minimize selection bias by excluding patients who had an admission diagnosis with less than 100 occurrences, were admitted to a hospital with less than three years of data or admitted to a hospital with less than 100 total cases during the study time period (Figure 1). Patient (Table E1) and hospital (Table 1) characteristics are presented in table form.

Definitions and Outcomes

Functional status was documented on ICU admission and hospital discharge based on data manually abstracted by trained individuals who would categorize the patient's functional status as fully independent, partially dependent, or fully dependent. Functional status was obtained from the patient or surrogate to determine functional status prior to ICU admission

(termed admission functional status). Functional status was also recorded just prior to discharge based on information provided by the healthcare team (i.e. provider, nursing, physical therapy, occupational therapy documentation). Categories were determined by an assessment of basic activities of daily living (ADLs). Definitions for each category included: fully independent – the patient was able to perform all activities of daily living without assistance, partially dependent – the patient needed assistance to perform ADLs, fully dependent – the patient cannot perform ADLs and must be cared for by another person. We categorized the primary admission diagnoses into organ system-disease based groups to facilitate data modeling. (See Table E2 for classification details)

Our primary outcome was the secular changes of FS↓ among ICU survivors. In our primary outcome, we categorized FS↓ as a dichotomous variable – decline or no decline. A decline was defined as a decline from the admission functional status category (status before critical illness) to the hospital discharge functional status category.

We hypothesized FS↓ may be increasing over time; however, FS↓ is a spectrum. In our secondary outcome, we sought to characterize the magnitude of the decline and temporally model this change to further stratify these temporal changes. The outcome was ordered as, no change, fully independent to partially dependent, partially dependent to fully dependent, and fully independent to fully dependent, in order of progressing severity. We modeled our outcome in this fashion to address concerns that classification at the margins favors partial dependence whereas being completely independent or dependent in ADLs are very specific definitions. Given this issue, we separated independent to partially dependent and partially dependent to fully dependent into their own categories with the latter category as more severe than the former.

Data Collection

We collected patient-level variables including: patient demographics (age, sex, race, and insurance status), illness severity (APACHE III score, based on worst parameters in the first 24 hours), shock index (heart rate/systolic blood pressure), and admission characteristics (vital signs, organ system-disease based category, year of admission, code status, and length of stay).

Statistical Analysis

For descriptive purposes, parametric continuous variables are expressed as mean and standard deviation (SD) and non-parametric continuous variables are expressed as the median and interquartile range (IQR). Categorical variables are expressed as N and percent. Imputation was not performed as missingness of data was less than 5% (N=1,179 [0.5%]).

We fit quasi-Poisson models to assess the incidence of FS↓ from admission to hospital discharge. Data were aggregated to the hospital-level and covariates, including age and APACHE III score, were averaged by hospital and year. All variables were scaled and centered prior to model fitting. For the overall model, we used an offset of the log number of admissions in each hospital and year. In contrast, we used the log number of patients in each hospital, year, and disease-system category as offsets to model our outcomes within each

disease-system category. The estimate for the exponentiated centered year term is reported with a 95% confidence interval (CI) to determine if the incidence rate ratio (IRR) per year of FS↓ is changing over time.

We used proportional odds logistic regression (a form of ordinal logistic regression) to evaluate the change in the magnitude of FS↓ over time. The outcome was ordered as, no change, fully independent to partially dependent, partially dependent to fully dependent, and fully independent to fully dependent, in order of progressing severity. The effect of year was modeled overall and within each epidemiological group (disease-system category) at the patient level via an interaction term adjusting for age and APACHE III score. To evaluate the odds of FS↓, within each disease process, we used proportional odds logistic regression, adjusted for age, APACHE III, and year. Sum-to-zero parameterization was implemented to compare the odds for each disease group against the overall odds of FS↓. All analyses were performed using R version 3.6.1,(20) Stata MP, version 15 (StataCorp, College Station, TX), or Microsoft Excel.

RESULTS

A total of 129,917 patients were included in the final analysis with FS↓ occurring in 38,116 (29.3%) patients. The overall patient population had a median age of 63 years old (IQR 50–75). They were more likely to be male (54.0%) and white (80.9%). Table 1 shows characteristics for patients who had functional status decline versus those who did not. Patients with FS↓ after admission were older (68 vs. 60 years old) and had a higher proportion of patients that were white (83.6% vs. 79.2%). Other variables associated with FS↓ included: higher APACHE III score (54.4 vs. 43.6), increased ICU length of stay (LOS) (2.9 vs. 1.7), and increased hospital LOS (9.1 vs. 4.7).

Incidence of FS↓

The incidence of FS↓ increased overall throughout the period of observation (IRR 1.15, 95% CI 1.13–1.17, $P<0.001$). (Figure 2) This trend was present across all disease categories: Neurologic (IRR 1.09, 95% CI 1.05–1.13, $P<0.001$), Cardiac (IRR 1.12, 95% CI 1.07–1.17, $P<0.001$), Pulmonary (IRR 1.11, 95% CI 1.07–1.16, $P<0.001$), Gastrointestinal (IRR 1.15, 95% CI 1.10–1.20, $P<0.001$), Renal (IRR 1.08, 95% CI 1.03–1.13, $P=0.003$), Non-surgical trauma (IRR 1.13, 95% CI 1.09–1.17, $P<0.001$), Toxicology (IRR 1.15, 95% CI 1.09–1.21, $P<0.001$), Vascular (IRR 1.12, 95% CI 1.06–1.18, $P<0.001$), Septic Infection (IRR 1.10, 95% CI 1.06–1.15, $P<0.001$), Endocrine/Metabolic (IRR 1.08, 95% CI 1.02–1.14, $P=0.008$), and Hematologic/Oncologic (IRR 1.10, 95% CI 1.04–1.17, $P=0.003$).

Magnitude of FS↓

The magnitude of FS↓ increased overall (Odds Ratio [OR] 1.04, 95% CI 1.04–1.04, $P<0.001$) and in most categories. The only category showing a decrease in the magnitude of FS↓ overtime was non-surgical trauma (OR 0.97, 95% CI 0.97–0.97, $P<0.001$) (Figure 3). However, despite the decreasing magnitude of FS↓ in non-surgical trauma, many admission diagnoses in this category remain in the top quartile of higher risk for FS.

Diagnosis variation of FS↓ and Magnitude

Using the average hospital admission as the reference group, FS↓ was highest in patients admitted with head & polytrauma (OR 4.47, 95% CI 4.46–4.48, $P<0.001$), non-surgical intracranial hemorrhage (OR 3.39, 95% CI 3.37– 3.40, $P<0.001$), chest & spine trauma (OR 3.38, 95% CI 3.38–3.39, $P<0.001$), and spine trauma (OR 3.19, 95% CI 3.18–3.19, $P<0.001$). Lowest odds of FS↓ was seen in diabetic ketoacidosis (OR 0.27 95% CI 0.27–0.27, $P<0.001$) and asthma (OR 0.35, 95% CI 0.35–0.36, $P<0.001$). (Figure 4) The top quartile of diseases with the highest odds for FS↓ included non-surgical trauma, neurological, pulmonary, and gastrointestinal diseases.

DISCUSSION

We sought to identify temporal changes and disease variation in FS↓ during hospitalization among critical illness survivors. We found that, after controlling for age and severity of illness, the incidence of FS↓ was increasing, both overall and throughout all system-disease groups for the duration of the study. Additionally, we found that in addition to incidence the magnitude of FS↓ was also increasing overall and in each category (aside from non-surgical trauma) over time. The magnitude of FS↓ varied in relation to the admission diagnosis. The top quartile of admission diagnoses with the highest odds of FS↓ included the following system-disease categories: non-surgical trauma, neurological, pulmonary, and gastrointestinal. All these high-risk system-disease groups have an increasing incidence of FS↓ and apart from non-surgical trauma, also have an increasing magnitude of FS↓.

Functional status before, during, and after admission is critical to patient outcomes. Baseline functional status has been associated with short and long-term mortality for many subsets of hospitalized patients which include critically ill, immunocompromised, severe pneumonia, and lung transplant patients.(21–27) Functional status is comparable, if not superior to common variables (i.e. age and illness severity) used to predict patient outcomes.(28–30) In fact, pre-morbid FS was shown to be superior to antibiotic timing for predicting mortality in patients with pneumonia.(31) These associations have led to growing interest in assessing frailty, which Fried et al. have advocated not be used synonymously with functional status.(32) Both are risk factors for poor outcomes and will be key to improving risk-stratification in research and clinical care.(23, 33) Beyond predicting absolute end-points (i.e. mortality) after admission, preoperative FS has been shown to affect not only long-term FS, but also the trajectory of functional status change.(34) Other important outcomes linked to baseline functional status include: quality of life, readmission, rate of admission to the ICU, and decisions to withhold or withdraw care. (35, 36)

As ICU admissions are generally not elective, baseline functional status serves mainly in risk assessment without targets for intervention; however, in-hospital functional status can be used for both. A 2016 study of ICU survivors by Rydingsward et. al found decreased functional status on discharge, irrespective of admission functional status, was associated with mortality. Additionally, they found patients with improving functional status prior to discharge, versus no improvement, had a 64% lower 90-day mortality.(37) While our current study is limited to functional status decline during hospitalization, the duration this decline is rarely short and may persist without return to baseline.(9, 38) A 2015 study showed only

10% of patients had improvement in their functional status at 3 months.(9) Furthermore, in relation to other health-related quality of life measures, functional status is the least likely to return to population norms after critical illness at 1 year.(38) The increasing incidence of FS↓ may be in part to increasing survivorship as mortality in the ICU has decreased over prior decades.(2) New interventions, such as prone positioning(39) and neuromuscular blockade(40) for acute respiratory distress syndrome have shown survival benefit; however, the increasing incidence of FS↓ may be the cost exchanged for these advances.

Increasing survivorship from critical illness has led to new challenges for both patients and providers.(41, 42) ICU patients that survive to discharge have higher mortality after critical illness, especially in the first 3 months, when matched to comparable general hospital patients.(43) When compared to the general population, ICU survivors have decreased quality of life, due in part, to FS↓ which can persist up 12 years later.(5) In contrast, patients undergoing planned surgery and requiring ICU admission may be an exception, as one study found a majority of patients can return to their baseline functional status and quality of life after ICU admission.(44) The ICU involves caring for a remarkably large variety of illness and severity. Identifying the patients with the highest risk and magnitude for FS↓ can assist in resource allocation and quality improvement projects. We identified admission diagnoses associated with the highest odds of FS↓ (Figure 4) while also showing that most epidemiological categories have increasing rates of FS↓ (Figure 3). Models were attempted to identify each diagnosis however given the large number of admission diagnoses we could only fit models to attempt temporal change within the larger epidemiological categories.

Patient-centered decision-making hinges on being able to prognosticate outcomes, including level of function. Unfortunately, our ability to predict functional status outcomes is worse than our ability to predict mortality.(45) This highlights the need to identify high-risk patient groups. Currently, several tools exist and recommendations have been laid out to accurately assess a patient's risk for functional status deterioration.(7) This includes using patient and surrogate information to identify a patient's ability to perform activities of daily living and independent mobility.(46) In the modern age with large amounts of data, we need to utilize these databases to help determine critical care needs and services.(47) Future studies using validated functional scales are needed to further refine risk factors and tailor interventions to prevent deterioration.

Interventions for prevention of FS↓ are limited, and future research is essential.(42, 48) Currently, efforts aimed at improving early mobility and delirium prevention have shown the most promise in mitigating deterioration in functional status. A study in 2009 showed early physical therapy and interruption of sedation were associated with regaining function after critical illness (OR 2.7).(49) Implementation of ABCDE bundles has led to improvements in mobilizing patients sooner in ICUs but this has not translated to improved rates of discharge to independent functional status or return home. (50) More recently, implementation specifically of early mobility, added to an abbreviated bundle of awakening, breathing, and delirium was associated with reduced mechanical ventilation, LOS, and cost.(51) Delirium is known to be associated with long term cognitive decline and long term disability in activities of daily living in ICU survivors.(12) Multifaceted interventions to reduce delirium have been found to increase the rate of patients being able to return home.(52) Daily cognitive

screening and delirium prevention are key in improving patient outcomes. Taken in composite, these studies suggest that continued efforts targeted at the prevention of ICU delirium may be integral to preventing further FS↓. Efforts aimed at improving the identification of patients at high risk for functional status deterioration will be an important area of further study.

This study highlights the significant temporal and disease variation effect on FS↓ in the critically ill. Limited research has been able to capture functional status on a national level. There are several limitations to this study. First, the APACHE database was not prospectively built to answer this question. Second, there are limited hospitals that report consistently to the database, which may introduce selection bias. To mitigate this, we eliminated hospitals that had less than three years of data included during the study period. Moreover, we were only able to use hospitals that reported functional status. Table E3 compares hospitals that reported functional status to those that did not report functional status. Third, there were only three functional categories and a validated tool for functional status designation was not used, limiting the replicability of the study. Also, the source from which the ADL data was from is not included in the database (i.e. patient vs. surrogate). The categories also limited our ability to discern signals that existed within the partially dependent category. We hypothesized that a subset of patients within the partially dependent category may have had a small, but clinically significant, functional status decline that was not captured due to limitation in our categorization. In our ordinal categorization, we attempted to mitigate the dilutional effect (while maintaining clinically significant changes) by separating the stepwise decline to and from partial dependence (independent to partially dependent; partially dependent to fully dependent) into separate categories instead of labeling them as the same. Another important limitation includes the generalizability. Post-operative patients, which were excluded from this study, account for >20% of critical illness survivors. These findings cannot and should not be extrapolated to these patients. Analysis of the primary surgical patients from this cohort is currently under review and preliminary analysis supports our concern for large heterogeneity and thus separation of these patient populations. While we were able to determine that most system-disease cohorts had increasing FS↓ and magnitude of FS↓, we were not able to parse this out by specific admission diagnoses due to issues with model convergence. Furthermore, model convergence also limited our ability to include other covariates. Subsequent analyses to identify independent predictors of FS↓ are ongoing are not included in this manuscript. This study highlights the increasing prevalence of FS↓ in a large multi-center cohort while also identifying the variation that exists across different admission diagnosis categories.

CONCLUSION

FS↓ following non-surgical admission to the ICU occurred in almost 1/3 of patients in our study. Overall incidence and magnitude of FS↓ increased over the study period and there was significant variation among admission diagnoses associated with varying levels of decline. We believe our study provides important information that can be used in beginning to identify patients at high risk of functional status decline. Improving the identification of these patients and targeting appropriate interventions to mitigate this decline will be important directions for future studies in this area.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Impact:

Declining mortality increases the incidence of morbidity after critical illness, such as poor functional status. Identifying at-risk patients can inform prognostication and future interventions aimed to mitigate these sequelae while improving quality of life in critical illness survivors.

Figure 1:
 Inclusion and Exclusion Criteria
 Inclusion and Exclusion Criteria

Functional Status Decline

Estimates presented for the year estimate in separate quasipoisson models

Figure 2:

Incidence of Functional Status Deterioration by Admission Disease-System Category
Functional Status Decline by admission disease category. Functional status was categorized as no decline or decline. IRR is per year.

Figure 3:

Magnitude of Functional Status Deterioration by Admission Disease-System Category

Functional Status Decline by admission category with an ordinal model showing magnitude of functional status decline overtime. Functional status category was split into no change, independent to partially dependent, partially dependent to full dependent, and independent to fully dependent. Sum-to-zero parameterization was implemented to compare the odds for each disease group against the overall odds of FS↓. FS↓ = Functional status decline, CI = Confidence Interval

Figure 4:
 Magnitude of Functional Status Deterioration by Admission Diagnosis
 Decline in functional status magnitude by admission diagnosis. COPD = Chronic Obstructive Lung Disease; NOS = Not otherwise specified; GI = Gastrointestinal; MSK = Musculoskeletal; MI = Myocardial Infarction; DKA = Diabetic ketoacidosis
 Reference group is respiratory failure NOS.

Table 1.

ICU Characteristics during study period

Covariate	No Change N=91801	Functional Status decline N=38116
Admissions per ICU, per year	3983.3 ± 2838	3878.4 ± 2781
Hospital Bed Size	562 ± 335	600 ± 343
Region		
Midwest	43,575 (47.5%)	17,887 (46.9%)
Northeast	12,178 (13.3%)	5,466 (14.3%)
South	26,931 (29.3%)	11,609 (30.5%)
West	9117 (9.9%)	3154 (8.3%)
Teaching Status		
Large teaching hospital	40,545 (44.2%)	17,759 (46.6%)
Small teaching hospital	27,776 (30.3%)	10,551 (27.7%)
Non-teaching hospital	23,480 (25.6%)	9,806 (25.7%)

Descriptive statistics include N (Percent) or Mean ± Standard Deviation where indicated

ICU = Intensive Care Unit