

BMJ Open Protocol for a prospective observational study to develop a frailty index for use in perioperative and critical care

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ABSTRACT

Introduction Frailty is of increasing importance to perioperative and critical care medicine, as the proportion of older patients increases globally. Evidence continues to emerge of the considerable impact frailty has on adverse outcomes from both surgery and critical care, which has led to a proliferation of different frailty measurement tools in recent years. Despite this, there remains a lack of easily implemented, comprehensive frailty assessment tools specific to these complex populations. Development of a frailty index using routinely collected hospital data, able to leverage the automated aspects of an electronic medical record, would aid risk stratification and benefit clinicians and patients alike.

Methods and analysis This is a prospective observational study. 150 intensive care unit (ICU) patients aged ≥ 50 years and 200 surgical patients aged ≥ 65 years will be enrolled. The primary objective is to develop a frailty index. Secondary objectives include assessing its ability to predict in-hospital mortality and/or discharge to a new non-home location; the performance of the frailty index in predicting postoperative and ICU complications, as well as health-related quality of life at 6 months; to compare the performance of the frailty index against existing frailty measurement and risk stratification tools; and to assess its modification by patients' health assets.

Ethics and dissemination This study has been approved by the Melbourne Health Human Research Ethics Committee (20 January 2017, HREC/16/MH/321). Dissemination will be via international and national anaesthetic and critical care conferences, and publication in the peer-reviewed literature.

INTRODUCTION

Frailty is increasingly recognised as a clinical entity of importance to clinicians, patients and the health system at large. In particular, the relevance of patient frailty to perioperative and critical care is growing, as older adults comprise an increasing proportion of patients presenting for surgery and to intensive care units (ICUs) worldwide. Over the next decade, adults aged >65 years will account for more than one-quarter of all ICU admissions in many countries, and up to half of all surgical patients.^{1–5} In the largest

Strengths and limitations of this study

- This is a prospective, large-scale study in a tertiary metropolitan setting.
- There are limited prospective studies using well-constructed comprehensive frailty indices in the surgical and critical care fields.
- It is not known how frailty indices compare with traditional risk stratification tools in these areas.
- A limitation is that routinely collected hospital data varies slightly between health services, although sensitivity analyses will help to determine the impact of individual variables on results.

ICU study to date,⁶ frailty was associated with almost twice the odds of mortality and new functional dependence, and in the largest meta-analysis of postsurgical complications (encompassing over 12 000 surgical patients across 44 studies) frailty was perhaps the most important predictor of adverse outcome, with more than doubled odds of postoperative complications.⁷ In the almost-decade since the 2010 UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD) examined older adults undergoing surgery, the recommendation that 'An agreed means of assessing frailty in the perioperative period should be developed and included in risk assessment' remains unfulfilled.⁸

Frailty can be described as either a phenotypic construct (criteria such as exhaustion, weakness, low activity or weight loss are present) or as a deficit model (risk accumulates due to impairments in health-related domains such as medical comorbidities, cognition, mood and behaviour, communication, sensorium, continence, nutrition and medications).^{9 10} Although various frailty measurement tools have been devised, these can be of limited use in the ICU or surgical setting. Performance-based measures, for example, such as 'timed-up-and-go' tests or grip strength assessment are impossible for



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mechanically ventilated or acutely unwell patients to perform.¹¹ Similarly, assessments including subjective questions requiring patient input may not be possible in this cohort, with potential for error when information is derived from surrogates.¹² Conversely, the perioperative and ICU environments are incredibly data-rich, with much information collected routinely for all admitted patients. Particularly in the era of electronic medical records, this has the potential to allow automated data integration and rapid derivation of relevant risk stratification scores.

In addition to potential automated calculation, a frailty index based on accumulated deficits has other advantages. As described by Searle *et al*, frailty indices demonstrate reproducibility across different populations, despite differences in composition related to which individual health deficits are present in a particular index.¹³ As such, as long as certain prerequisites regarding candidate deficits are met (at least 30 deficits should be included, they should be associated with health status, increase in prevalence with age, not saturate too early, cover a range of systems and remain constant if intended for repeated use in the same population), subtle variation in terminology or specific data collected between health services for use in a frailty index do not matter.

The objective of this study, then, is to develop a frailty index, based on accumulated health deficits, that is able to be incorporated into routine hospital management of ICU and surgical patients.

AIMS

The primary aim of this study is to develop a frailty index based on accumulated health deficits, using routinely collected hospital data, enabling rapid and easily scalable assessment of surgical and ICU patients' frailty. Secondary aims are to assess the performance of the frailty index in predicting in-hospital mortality and/or discharge to a new non-home location, postoperative and ICU complications, as well as health-related quality of life at 6 months; to compare the performance of the frailty index against existing frailty measurement and risk stratification tools; and to assess its modification by patients' health assets (protective factors that support health and well-being).

METHODS

Study design

This study is designed as a prospective, single-centre cohort study, with follow-up period 6 months postdischarge.

Study setting

This study will be conducted at the Royal Melbourne Hospital (RMH), Melbourne, Australia, a tertiary metropolitan hospital that admits over 2000 ICU patients and with a surgical volume of over 25 000 operations annually. Enrolment and follow-up are expected between February 2017 and December 2018.

Inclusion and exclusion criteria

Patients are eligible if they are:

- ▶ Aged ≥ 65 years on admission for any surgery (emergency or elective).
- ▶ Aged ≥ 50 years on admission to the ICU for any indication.
- ▶ Provide written informed consent (or the person responsible in the event of incapacitation).

Patients are ineligible if they are:

- ▶ Non-English speaking (or the person responsible is non-English speaking).
- ▶ Admitted to the ICU or operating theatre for reasons of organ retrieval.

Data collection (routine for all patients)

Baseline demographics: preoperatively (surgical patients) or on admission to the ICU (ICU patients): age, gender, height and weight will be collected.

Surgical data: operative type (surgical specialty)/severity (defined according to the P-POSSUM scoring system), blood loss and American Society of Anesthesiology score will be recorded.

ICU data: routine ICU data collected (relating to the entire ICU admission episode) will include mechanical ventilation, renal replacement therapy, cardiac arrest, inotropes/vasoactive infusions, Acute Physiology and Chronic Health Evaluation (APACHE) III illness severity score and presence of any limitations to medical treatment.

Other hospital data: routine data recorded on admission for RMH patients (and common to most health services) will be used to generate a frailty index, consisting of 36 health deficits (table 1). Data will be derived from the falls risk assessment and management plan (RMH form designation: form IP8L), malnutrition risk assessment and management plan (IP63C), pressure injury prevention plan (IP8G), daily nursing care plan (IP8F), and nursing admission and assessment (IP8). Chosen deficits increase in prevalence with age and encompass a range of systems associated with health status.

Data collection (additional, by study investigators)

Additional admission data: the Katz Index of independence in activities of daily living and Charlson comorbidity score will be collected, with information added to the frailty index (table 1) below. Data related to surgical risk stratification will be collected, including the P-POSSUM Score,¹⁴ albumin and lactate (where available), and will be compared with the frailty index for prediction of secondary outcomes listed.

Other frailty measurements: the Clinical Frailty Score¹⁰ and the Edmonton Frailty Score¹⁵ will both be collected. For patients who are unable to perform the 'Timed Up and Go Test' component of the latter scale (eg, emergency surgical or mechanically ventilated ICU patients), a Reported Edmonton score will be derived.¹⁶ Data collected represent the health status of the patient prior to the onset of acute illness.

Table 1 Frailty Index (from routine data collection)

1	Falls in last 12 months	0=no, 1=yes
2	Dementia diagnosis	0=no, 1=yes
3	Altered cognition	0=no, 1=yes
4	On four or more medications, at least one affecting CNS/ CVS	0=no, 1=yes
5	Vision impairment	0=no, 1=yes
6	Hearing impairment	0=no, 1=yes
7	Assistance with transferring	0=no, 1=yes
8	Assistance with mobilising	0=no, 1=yes
9	Assistance with toileting	0=no, 1=yes
10	Assistance with bathing	0=no, 1=yes
11	Assistance with dressing	0=no, 1=yes
12	Postural hypotension/dizziness	0=no, 1=yes
13	Bowel incontinence	0=no, 1=yes
14	Urinary incontinence	0=no, 1=yes
15	Eating poorly?	0=no, 1=yes
16	Lost weight without trying?	0=no, 0.5=1–10kg, 1 =>10kg
17	Pressure injury- current or past	0=no, 1=yes
18	Neuropathic foot disease	0=no, 1=yes
19	Problems managing at home prior to admission	0=no, 1=yes
20	Often feels sad or depressed? (Edmonton)*	0=no, 1=yes
21	Requires assistance with eating? (Katz)†	0=no, 1=yes
<i>Charlson Comorbidity Data‡</i>		
22	Ischaemic heart disease	0=no, 1=yes
23	Congestive heart failure	0=no, 1=yes
24	Peripheral vascular disease	0=no, 1=yes
25	Cerebrovascular disease	0=no, 1=yes
26	Hemiplegia	0=no, 1=yes
27	Chronic lung disease	0=no, 1=yes
28	Connective tissue disease	0=no, 1=yes
29	Peptic ulcer disease	0=no, 1=yes
30	Chronic liver disease	0=no, 1=yes
31	Diabetes	0=no, 1=yes
32	Leukaemia/lymphoma	0=no, 1=yes
33	Malignant tumour	0=no, 1=yes
34	Metastatic cancer	0=no, 1=yes
35	Moderate/severe kidney disease	0=no, 1=yes
36	Moderate/severe liver disease	0=no, 1=yes
		Total=

*Derived from the Edmonton Frail Scale.

†Derived from the Katz Index of independence in activities of daily living.

‡Derived from the Charlson Comorbidity Index.

CNS, central nervous system; CVS, cardiovascular system.

Health asset data: the health assets index developed by Gregorevic *et al*¹⁷ will be used, with data collected including educational level, family proximity, financial means, social engagement and psychosocial well-being

(representing patients' baseline state prior to hospital admission).

Outcomes: endpoints collected will include in-hospital mortality (primary outcome); length of stay (time in days between either admission to the intensive care unit and discharge from hospital, or surgical operation and discharge from hospital); discharge destination (including new non-home discharge, including assisted living facility, rehabilitation or other acute hospital location); and postoperative/ICU complications (acute myocardial infarction, cardiac arrest, sepsis, acute pulmonary oedema, deep venous thrombosis, pulmonary embolism, stroke/transient ischaemic attack, wound infection, unplanned return to operating theatre, unplanned ICU/HDU admission) (all secondary outcomes). The outcome assessors will have access to frailty information collected.

6-month follow-up: health-related quality of life (EQ-5D scale), place of residence (home, residential care facility and hospital) and Clinical Frailty Scale will be recorded. A scripted telephone text will be used, proven feasible and valid in both geriatric populations and ICU survivors.^{18 19} In addition, we believe that this study will be the first to administer the Clinical Frailty Scale by telephone, thus will provide an assessment of its feasibility through this modality.

Statistical analyses

We will calculate a frailty index score for each patient with $\geq 80\%$ non-missing health deficit scores.²⁰ A frailty index score will be derived for each patient as the sum of the deficit scores divided by the total number of non-missing deficit scores thus ranging from 0 (no deficits) to 1 (all deficits). Patients with a frailty index score of ≥ 0.25 will be considered frail.²¹ A histogram and descriptive statistics of the frailty index scores will be provided for the entire patient sample and by surgical/ICU patients, gender and age. Mean frailty index scores will be plotted versus age for all patients and by surgical/ICU status. A linear regression analysis of the frailty index on age will be performed and by surgical/ICU status to obtain the rate of accumulation of health deficits over age, in case of positive skewness, the frailty index scores may be log transformed before analysis. A random sampling procedure using 80% of frailty index items without replacement will be used and repeated several times to investigate the impact of an individual item on the rate. This approach has been successfully used in similar studies of frailty indices.²²

A logistic regression model will be fitted to the outcomes of in-hospital mortality (primary outcome), discharge to a new non-home location, in-hospital mortality or discharge to a new non-home location, postoperative and ICU complications, including in the model the frailty index, surgical/ICU status, gender and age. Receiver operating characteristic (ROC) curves and the area under the ROC curves will be obtained to assess the ability of the model to discriminate between two classes of these outcomes. Health-related quality of life at 6 months, whereby death will be coded as 0, will be analysed with

a linear regression model using the explained variation to evaluate overall model performance. Anticipating about 5% missing quality of life data, we will use multiple imputations to explore the sensitivity of the results to underlying missing data assumptions. We will obtain Spearman's rank correlation between the frailty measurement tools (the frailty index, Edmonton and Clinical Frailty Scales) on admission and between the frailty index and risk stratification tools (APACHE for ICU and P-POSSUM for surgery). Each patient's score will be categorised into frail, vulnerable and non-frail (reference); for the frailty index (frail ≥ 0.25 , vulnerable $0.2 < 0.25$, non-frail $0 < 0.2$), Edmonton (frail ≥ 8 , vulnerable 6–7, non-frail 0–5) and Clinical Frailty Scale (frail ≥ 5 , vulnerable 4, non-frail 1–3). We will examine the difference in the strength in an association between each categorised frailty scale and the outcomes using the models described earlier. Furthermore, we will obtain the measures listed above to compare the ability of the models to predict these outcomes between the three categorised frailty tools and to predict in-hospital mortality between the frailty index and risk stratification tools. Modification of the effect in frail versus non-frail patients by health assets for outcomes (death, new non-home discharge location, and postoperative and ICU complications) will be examined for the frailty index using interaction tests.

Sample size

A convenience sample of 200 surgical and 150 ICU patients from a single hospital is planned. Based on comparative literature (including a systematic review and meta-analysis of over 8000 surgical patients, and the largest multicentre study of ICU frailty), we assume that 20% of surgical patients and 30% of ICU patients, combined about 24%, will be frail.^{6 23} We will be able to obtain a 95% CI of $\pm 4.4\%$ around the prevalence of frailty of 24% with a sample size of 350. In addition, we anticipate an in-hospital mortality of 5% in surgical patients (based on the pooled mortality rate in the meta-analysis above) and 21% in ICU patients, overall about 10%. Assuming the odds of in-hospital mortality of frail patients is 3.5 times than that of non-frail patients (based on pooled ORs from previous systematic reviews^{23 24}) and in-hospital mortality is 6.8% in those who are not frail, the power to detect this effect with a sample size of 350 patients is 87% (two-sided 5% alpha).

Patient and public involvement

The development of the study design was informed by patient-centred endpoints—rather than just assessing mortality, new residential care admission, postoperative and post-ICU complications are outcome measures of importance to patients. Similarly, assessment of the quality of life (and potential decrement in quality of life) is also patient-centred. During the consent process, patients or their person responsible are given verbal and written information that study results are available to be disseminated to them. A written summary of the study

findings will be provided in this instance. Specific patients were not however formally involved in the study design.

DISCUSSION

The importance of routine frailty assessment in the perioperative and ICU setting has been emphasised by various organisations, including the American College of Surgeons, the American Geriatrics Society and the Association of Anaesthetists of Great Britain and Ireland.^{25 26} Given this pressing need for an easily implementable and valid frailty assessment tool, various scales have been developed. One such frailty measure, the 'modified frailty index' (mFI), has the advantage of using automatically collected variables from the US National Surgical Quality Improvement Program (NSQIP) database. Unfortunately, only 11 items are contained in this index, with the majority (9) representing medical comorbidities, thus it can perhaps be more accurately described as predominantly a 'comorbidity' scale.²⁷ The Groningen frailty scale, although encompassing a wider range of health deficits, numbers only 15 deficits in total.²⁸ A third proposed scale, the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses indicator, only comprises 12 items and includes criteria such as 'poverty' and 'barriers to access to care' which may more accurately be described as absent health assets, rather than deficits contributing to frailty per se.²⁹ More recently, frailty indices in non-surgical/ICU specific populations have been developed using other health databases such as Medicare claims-based data,³⁰ or the inter-RAI assessment system, which aids the comprehensive geriatric assessment of older hospitalised inpatients.²²

This study will thus provide a comprehensive and timely assessment measure of frailty, and its importance in an increasingly elderly surgical and critically ill population. Although routinely collected data do vary slightly between health services, potentially limiting generalisability, conducting sensitivity analyses will allow for an individual variable effect to be assessed. As this group poses new challenges for anaesthetists, intensivists, surgeons, perioperative physicians and health services alike, derivation of an automated frailty index using routine hospital data has the potential to revolutionise risk stratification and improve outcomes, as the prevalence of frailty increases dramatically in coming years.

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