DEPARTMENT OF ANESTHESIOLOGY

JOURNAL CLUB

Monday June 19, 2017
1800 HOURS

LOCATION:
The River Mill Restaurant
2 Cataraqui Street

PRESENTING ARTICLES:
Dr's Imelda Galvin & Danika Vautour

SPONSORED BY:
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SUGGESTED GUIDELINES FOR CRITICAL APPRAISAL OF PAPERS
ANESTHESIOLOGY JOURNAL CLUB
QUEEN'S UNIVERSITY

Two presenters will be assigned to choose and present summaries of their papers. Ideally the two papers will represent similar topics but contrasting research methodologies. The focus remains on critical appraisal of the research and manuscript, more than on the actual contents of the article. Each presenter will then lead an open discussion about the article, based around the guidelines below. The object is to open up the appraisal to wide discussion involving all participants.

GENERAL

1. Title of paper: Does it seem like an important problem? Does it reflect the purpose/results?
2. Authors, institution and country of origin

INTRODUCTION

1. What is the problem being addressed?
2. What is the current state of knowledge of the problem studied?
3. What is the hypothesis being tested?
4. How does testing the hypothesis help solve the stated problem?

METHODOLOGY

1. Study design:
    a) Clinical trial vs. systematic review/meta-analysis
    b) Prospective vs. retrospective
    c) Observational vs. Experimental
    d) Randomized or not
    e) Blinded or not

2. Population studied:
    a) Human, animal, other
    b) Justification
    c) Control groups: experimental vs. historical
    d) Is the sample size/power calculated, and how?
    e) Is the population similar to your own practice?
    f) Single vs. multi-centre

3. Is the study ethically sound?
    a) Clinical equipoise
    b) Does treatment meet standard of care (esp controls)?
    c) Appropriate consent and institutional ethics approval

4. Exclusions: what groups are excluded and why?

5. Experimental protocol
    a) Is it designed to test the hypothesis?

b) Is it detailed enough to be reproducible?
c) Is the methodology validated?
d) Are the drugs/equipment used detailed?
e) How does the randomization take place?

6. What are the primary endpoints?
7. Is power sufficient to justify secondary endpoints?
8. Is the protocol clinically relevant?
9. Data collection and analysis
10. Statistical analysis: Is it appropriate? Are results

RESULTS

1. Are the groups comparable?
2. Were any subjects/data eliminated?
3. Analyzed by intent to treat?
4. Are adequate details of results provided? - data, graphs, tables

DISCUSSION

1. What is the main conclusion of the study?
2. Do the results support this conclusion?
3. Do the results address the stated purpose/hypothesis of the study?
4. How do the authors explain the results obtained?
5. Are there any alternative interpretations to the data?
6. Are the results clinically as well statistically relevant?
7. How do the results compare with those of previous studies?
8. What do the results add to the existing literature?
9. What are the limitations of the methods or analysis used?
10. What are the unanswered questions for future work?

APPLICABILITY OF THE PAPER

1. Have you learned something important from reading this paper?
2. Will the results of this study alter your clinical practice?

Lin et al. BMC Geriatrics (2016) 16:157
DOI 10.1186/s12877-016-0329-8

BMC Geriatrics

RESEARCH ARTICLE Open Access

Frailty and post-operative outcomes in older surgical patients: a systematic review

Hui-Shan Lin*, J. N. Watts, N. M. Peel and R. E. Hubbard

Abstract

Background: As the population ages, increasing numbers of older adults are undergoing surgery. Frailty is prevalent in older adults and may be a better predictor of post-operative morbidity and mortality than chronological age. The aim of this review was to examine the impact of frailty on adverse outcomes in the 'older old' and 'oldest old' surgical patients.

Methods: A systematic review was undertaken. Electronic databases from 2010 to 2015 were searched to identify articles which evaluated the relationship between frailty and post-operative outcomes in surgical populations with a mean age of 75 and older. Articles were excluded if they were in non-English languages or if frailty was measured using a single marker only. Demographic data, type of surgery performed, frailty measure and impact of frailty on adverse outcomes were extracted from the selected studies. Quality of the studies and risk of bias was assessed by the Epidemiological Appraisal Instrument.

Results: Twenty-three studies were selected for the review and they were assessed as medium to high quality. The mean age ranged from 75 to 87 years, and included patients undergoing cardiac, oncological, general, vascular and hip fracture surgeries. There were 21 different instruments used to measure frailty. Regardless of how frailty was measured, the strongest evidence in terms of numbers of studies, consistency of results and study quality was for associations between frailty and increased mortality at 30 days, 90 days and one year follow-up, post-operative complications and length of stay. A small number of studies reported on discharge to institutional care, functional decline and lower quality of life after surgery, and also found a significant association with frailty.

Conclusion: There was strong evidence that frailty in older-old and oldest-old surgical patients predicts post-operative mortality, complications, and prolonged length of stay. Frailty assessment may be a valuable tool in peri-operative assessment. It is possible that different frailty tools are best suited for different acuity and type of surgical patients. The association between frailty and return to pre-morbid function, discharge destination, and quality of life after surgery warrants further research.

Keywords: Post-operative complications, Mortality, Geriatric, Oldest old, Frailty

Abbreviations: FI, Frailty index; CSHA, Canadian Study of Health and Aging; EAI, Epidemiological appraisal instrument; CGA, Comprehensive geriatric assessment; MACCE, Major cardiac and cerebral adverse events

* Correspondence: huishan.lin@uq.net.au
Centre for Research in Geriatric Medicine, Princess Alexandra Hospital, The University of Queensland, Level 2, Building 33, Ipswich Road, Woolloongabba, QLD 4102, Australia

Background

As the population ages, the rate of surgical procedures in the older population is rising. In England, 2.5 million people over the age of 75 years underwent surgery between years 2014 and 2015, as opposed to just under 1.5 million between 2006 and 2007 [1, 2]. Nearly 30 % of these 2.5 million were over 85 years old [1]. Similarly, women aged 85 years and over now represent the largest proportion in emergency surgical admissions in Australia compared with all other age and sex groups [3].

It has long been recognised that advanced age can carry increased risk of mortality and morbidity after surgery. However, new knowledge is emerging that frailty, an age-related cumulative decline in multiple physiological systems, is a better predictor of mortality and morbidity than chronological age [4, 5]. Patients of the same age do not all have the same risk. The identification and assessment of frailty may facilitate identification of vulnerable surgical patients so that appropriate surgical and anaesthetic management can be implemented.

Experienced clinicians may feel that they can identify frailty by end-of-bed 'gestalt' assessments. However, 'eyeballing' is subjective and tends to be inconsistent between different observers [6]. Currently there is no standardised method of measuring frailty, with more than 20 different frailty instruments identified in a systematic review [7]. These different scales are based on the two main models which characterise how frailty develops and manifests. In the 'phenotype' model described by Fried et al. [8], frailty manifests as decline in lean body mass, strength, endurance, balance, walking performance and low activity. Patients who have three or more of the five features of slowness, weakness, exhaustion, weight loss and low physical activity are deemed frail, while those who have none of the features are non-frail. Patients who display one or two of the five features are "pre-frail" [8].

The second model by Rockwood et al. is the Frailty Index (FI), or the cumulative deficit model, developed in the Canadian Study of Health and Aging (CSHA) [9]. This model conceptualises aging as the accumulation of deficits and views frailty as a multidimensional risk state quantified by the number of deficits rather than by the nature of the health problems. An FI can be based on comprehensive geriatric assessment and is calculated by counting the number of deficits present in an individual, divided by the total number of deficits measured [10]. The deficits encompass co-morbidities, physical and cognitive impairments, psychosocial risk factors and common geriatric syndromes [10]. The FI score ranges between 0 and 1, with higher scores indicating greater degree of frailty. FI represents a continuum; however, it can also be trichotomised to indicate low, intermediate and high level of frailty (FI ≤ 0.25, FI >0.25-0.4, FI >0.4) [11].

There has been a significant increase in literature over the last five years on the subject of frailty in surgical patients. A search for articles on Pubmed published between the years 2011 and 2015 using search terms 'frailty' AND 'surgical outcome' identified 173 titles, whereas the same search for publications between 2006 and 2010 yielded only 34 titles. The majority of the current literature investigating frailty and surgery has defined 'geriatric' as those above 60 or 65 years old. However, there has been a change in who is thought of as 'old'. Basing studies on someone 65 years old may not provide insight into appropriate treatment for the 'new' geriatric patient [12]. Despite frailty being more prevalent with increasing age, and the large proportion of those over 75 years old undergoing surgery, frailty in the 'old old' and the 'oldest old' (aged 75–85 and over 85 years) surgical patients has been less comprehensively explored.

The aim of this systematic review, therefore, was to examine the association between frailty and adverse post-surgical outcomes in patients aged 75 years and over.

Methods

Search strategy

PUBMED, MEDLINE, EMBASE and Cochrane online databases were searched using search terms of 'frail*' AND 'surg*' in combination with ('outcome' OR 'morbidity' OR 'complication'). An asterisk was used to indicate the term was truncated or had a variation in spelling. The search was conducted between October and December 2015 with filters applied to limit results to the English language, human research, and publications from year 2010 and onwards.

Publication selection

The inclusion criteria for the search were: 1) the mean participant age was over 75 years; 2) the patient population had a surgical procedure; 3) frailty was assessed as a composite measure of more than one domain of health deficit, which accords with the current conceptualisation of frailty [13, 14] and was the main factor of interest in the study; and 4) the relationship between frailty and adverse outcomes was evaluated. Exclusion criteria were review articles, conference abstracts, and studies which measured frailty as a single item, such as a scan finding, a blood marker, or a physical performance test such as gait speed.

Data extraction

Two reviewers (HL, JW) conducted the searches independently and compared results after assessing all identified abstracts for their compliance with the review criteria. Where agreement could not be reached a third

independent reviewer (NP) was consulted. Reasons for exclusion were documented.

The following data were extracted from the eligible studies: sample size, mean age, country of origin of the study population, study design, type of surgery performed, frailty measure, and impact of frailty on adverse outcome.

Assessment of study quality and risk of bias

Two reviewers (HL, JW) independently assessed the quality of the included studies using a modified version of the Epidemiological Appraisal Instrument (EAI), a valid and reliable tool for rating the quality of observational studies [15]. The EAI checklist addressed the following five domains of risk of bias: reporting, subject selection, measurement quality, data analysis, and generalisation of results. Each of the 23 questions in the EAI applicable to the selected studies was scored as yes (=2), partial (=1), no or unable to determine (=0) with the highest possible score being 46.

An a priori decision was made to divide the total possible score into quartiles. Quartile 1 (Q1) was 35–46 (the highest quality), quartile 2 (Q2) was 23–34, quartile 3 (Q3) was 12–23 and quartile 4 (Q4) was 0–11 (the lowest quality). Any disagreement regarding the assessment of the quality of a study was resolved by consulting a third reviewer (NP).

Grading the overall strength of the evidence

The overall strength of the evidence was evaluated using principles outlined by the Agency for Healthcare Research and Quality [16]. The key elements of evaluation were quality (based on study design according to the hierarchy of evidence and study execution), quantity (based on the number of studies) and consistency.

Results

The literature search identified 686 articles (187 from Pubmed, 169 from Medline, 300 from Embase and 28 from the Cochrane database). From these, 270 duplicate articles were removed. The titles, abstracts and the full texts of the articles were reviewed. Articles were selected based on inclusion and exclusion criteria. The references of selected articles were hand searched for further eligible articles. There were 23 articles included in the final analysis. The study selection process as well as the reasons for exclusion are shown in Fig. 1.

In the 23 articles selected for this review, there were 16 cohorts of patients with a mean or median age ranging from 75 to 87 years. Twenty studies were of prospective design with sample sizes ranging from 30 to 450 [17–36], and three were of retrospective design [37–39], one of which contained a large sample size of nearly 13,000 participants [37]. Publications came from different countries, including USA [17, 18, 35, 37–39], UK

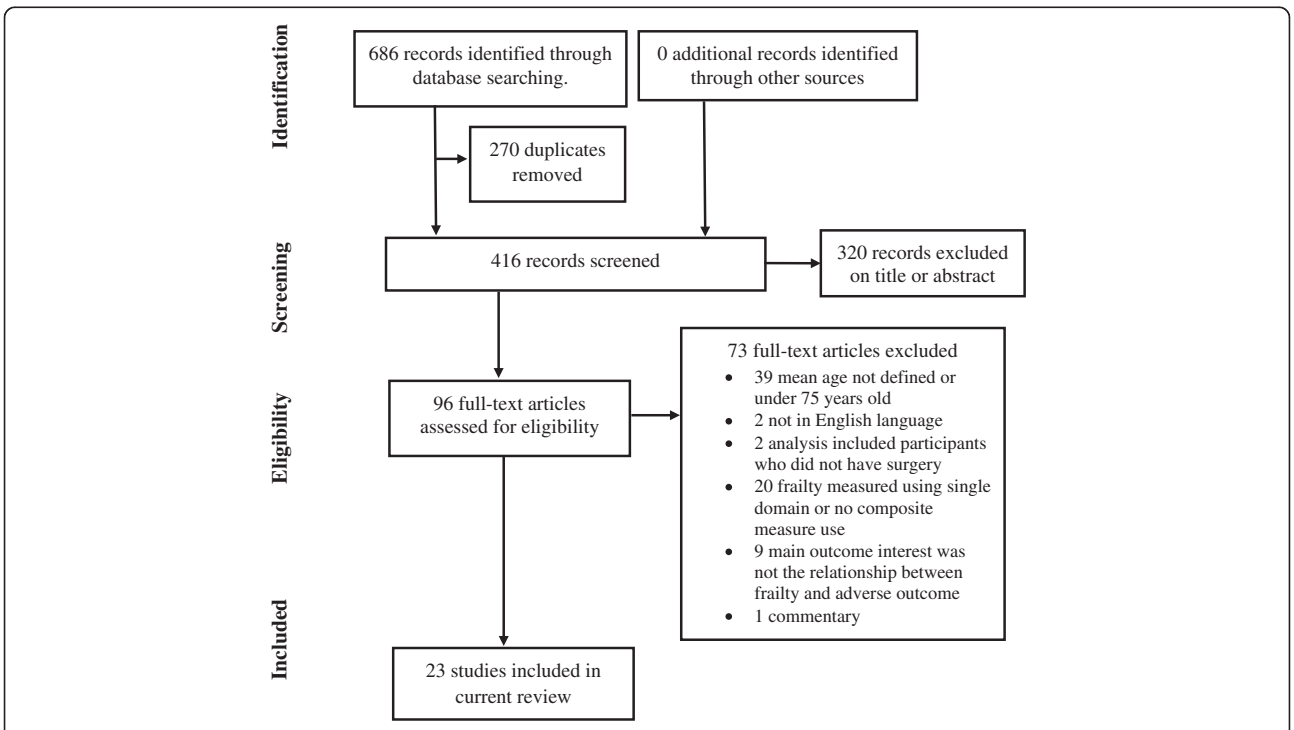

Fig. 1 PRISMA flow diagram for study selection

[30, 32, 34, 36], Europe [19–28, 31], and Asia [29, 33]. The proportion of females ranged from 31 % [34] to 83 % [35]. Five studies did not report the gender distribution of the cohorts [22, 23, 29, 32, 38]. A meta-analysis was not conducted due to a lack of homogeneity of frailty measures and the diversity of surgical procedures.

Nine studies measured frailty in cardiac surgery [17–24, 39], six in oncological surgery (predominantly focusing on colorectal cancer) [25–29, 37], three in general surgery [30, 31, 33], three in hip fracture surgery [35, 36, 38] and two in vascular surgery [32, 34]. Sixteen articles involved participants undergoing elective surgery [17–29, 33, 37, 39], five involved those undergoing acute surgery [30, 31, 35, 36, 38], while two included those undergoing both elective and acute surgery [32, 34]. Table 1, grouped by the type of surgery, describes the demographics, measurement of frailty and adverse outcome predicted by frailty for the selected studies.

Study quality and risk of bias

The EAI scores of the 23 studies ranged from 31 to 45, indicating they were in the upper two quartiles of study methodological quality. The EAI scores were in the in the second quartile for eight studies [18, 19, 22–24, 28, 29, 32] while the remainder 15 studies were in the first quartile [17, 20, 21, 25–27, 30, 31, 33–39]. There was a high level of agreement of quality assessment between the two independent reviewers. The most poorly reported items across all studies were: sample size calculation, adjustment for covariates and the report of losses to follow up. Study quality scores are incorporated into Table 2.

Frailty instruments

Of the 23 included studies, 21 different instruments were used to measure frailty. Variations of the Fried Criteria or instruments based on Comprehensive Geriatric Assessment (CGA), including the Frailty Index, were used in the majority of studies. Scales based on CGA are obtainable from patient interview as well as clinical notes without physical performance based measures, and were used in both acute and elective surgical cohorts. In contrast, the Fried frailty measure required physical performance-based tests, and was used exclusively in elective surgical cohorts. Four instruments, such as Multidimensional Frailty Score [33] and Comprehensive Assessment of Frailty [22–24], combined aspects of CGA with performance based tests (e.g. balance assessments, chair rise, stair climb) and medical investigations (e.g. blood test and respiratory function test). Details of measurement of frailty are presented in Table 1.

Adverse outcomes predicted by frailty

Table 2 shows the adverse outcomes associated with frailty, grouped by the quality of the studies. Short, intermediate and long term mortality were assessed by 16 papers. Of ten studies evaluating the relationship between frailty and 12 month mortality, all found a significant relationship with frailty [18, 19, 21, 23, 24, 32, 33, 37–39]. Odds Ratios ranged between 1.1 and 4.97 for the frail patients compared with those who were non-frail [18, 21, 23, 24, 38, 39]. This association was found regardless of the instruments used to measure frailty and irrespective of the type of surgery performed.

In the two papers that assessed long term mortality, frailty was associated with increased two year mortality with an Odds Ratio of 4.01 [38] and increased five year mortality with an Odds Ratio of 3.6 [27]. The association between frailty and 90 day mortality was evaluated in two studies [30, 37]. One found a significant association with an Odds Ratio of 10.4 [37] while the other did not find a significant association [30]. Thirty day mortality was evaluated in six studies [21, 22, 26, 30, 31, 36]; all but one [30] found a significant association, with Odds Ratios ranging between 1.4 and 8.33 [21, 26, 31]. This latter study included only a small proportion (31 %, n = 105) of patients who underwent surgery [30].

Post-operative complications, as graded by the Clavian-Dindo severity classification [40] or predefined by the authors, were evaluated in nine papers [17, 18, 25, 29, 31, 33–35, 39]. Frailty was associated with increased post-operative complications in four studies with Odds Ratios ranging from 1.5 to 4.8 [18, 25, 29, 31]. The remaining five studies reported no significant association [17, 33–35, 39]. The definitions used for post-operative complications in these 10 studies were heterogeneous. Conditions pre-specified in the studies which counted as a post-operative complication included cardiac complications (namely myocardial infarction, heart failure, arrhythmia), pulmonary embolism, pneumonia, wound infection, major bleeding, renal failure, delirium, unplanned return to theatre and unplanned intensive care unit admission.

Specific items of post-operative complications were also examined by several studies. An association between frailty and major cardiac and cerebral adverse events (MACCE) was reported by one of the three studies evaluating this outcome [19, 21, 23]. One study explored the association between frailty and delirium and did not find a significant association [35]. Of two studies evaluating frailty and readmission rate, one study found a significant association [32] while the other did not [30]. One study showed a significant association between frailty and the need for resuscitation [23].

Of the six studies that included prolonged length of stay as an outcome, an association with frailty was found

Table 1 Study demographics grouped by type of surgery

Author	Sample size Country of origin Mean or median age % female Study design	Type of surgery	Frailty measure	Adverse outcome predicted by frailty	Association between frailty and adverse outcomes
Cardiac					
Afilalo, J et al. [17][a]	152 USA, Canada Mean age 75.9 34 % female Prospective cohort study	Cardiac surgery (Elective)	Fried criteria (or Cardiovascular Health Study frailty scale) Modified CHS frailty scale *Fried + cognitive impairment + depressed mood* 4-item MSSA frailty scale *gait speed, handgrip strength, inactivity, cognitive impairment* Gait speed	Composite end point of post-operative mortality or major morbidity	Fried criteria, non-sig Modified CHS frailty scale, non-sig 4 item MSSA frailty scale, non-sig Gait speed, OR 2.63 ($p < 0.05$)
Green, P et al. [39][a]	244 USA Median age, %female - frail 87.1,53 % - non-frail 85.4,45 % Post-hoc analysis of PARTNER trial	Transcatheter Aortic Valve Replacement (TAVR) (Elective)	Fried criteria condensed into 4 domains *gait speed, grip strength, serum albumin, Katz index of ADL* Frail ≥6/12	1) Adverse clinical events at 30 days 2) 1 year mortality 3) Poor outcome (composite mortality & QoL assessed by KCCQ-OS) a) 6 months b) 1 year	Adjusted for covariates 1) non-sig 2) OR 2.5 ($p = 0.0002$) 3) a) OR 2.21 ($p = 0.03$) b) OR 2.4 ($p = 0.02$)
Green, P. et al. [18][b]	159 USA Mean age 86 50 % female Prospective cohort study	Transcatheter aortic valve replacement, (TAVR) (Elective)	Fried criteria condensed into 4 domains *gait speed, grip strength, serum albumin, Katz index of ADL* Frail >5/12	1) 1 year mortality 2) LOS 3) Procedural outcomes (any of major bleeding event, major vascular complications, stroke, acute kidney injury, 30 day mortality)	Adjusted for covariates 1) OR 3.5 ($p = 0.006$) 2) 9 vs 6 days ($p = 0.004$) 3) OR 2.2 ($p = 0.04$) for major bleeding but not other adverse outcomes
Kamga, M et al. [19][b]	30 Belgium Mean age 86 47 % female Prospective cohort study	TAVI (Elective)	Score Hospitalier d'Evaluation du Risque de Perte d'Autonomie (SHERPA-risk of functional decline) score *MMSE, age, perceived poor health, fall in the last year, number of iADL independently performed before admission* Identification of Seniors at Risk (ISAR) score *>3 medications, self reported memory problems, sensory problems, hospital admission within the last 6 months, increased need for help at home*	1) 1 year mortality 2) Major cardiac and cerebral adverse events (MACCE)	Adjusted for covariates 1) SHERPA HR2.74 for every 1 point increase in score ($p = 0.004$) ISAR non-sig 2) SHERPA non-sig ISAR non-sig
Schoenenberger, A.W. et al. [20][a]	119 Switzerland Mean age 83.4 55.5 % female Prospective cohort study	TAVI (Elective)	Mini Mental State Exam, Mini Nutritional Assessment, TUG, BADL, IADL, pre-clinical mobility disability Frail ≥3	1) Functional decline (BADL ↓ ≥1 point) 2) Functional decline or death among all participants at 6 months	Univariate 1) OR 3.31 ($p = 0.02$) 2) OR 4.46 ($p = 0.001$)

Table 1 Study demographics grouped by type of surgery *(Continued)*

Stortecky, S. et al. [21][a]	100 Switzerland Mean age 83.7 60 % female Prospective cohort study	TAVI (Elective)	Mini Mental State Exam, Mini Nutritional Assessment, TUG, BADL, IADL, pre-clinical mobility disability Frail ≥3	1) 30 day MACCE 2) 30 day mortality 3) 1 year MACCE 4) 1-year mortality	Univariate analysis 1) OR 4.78 ($p = 0.05$) 2) OR 8.33 ($p = 0.03$) 3) OR 4.89 ($p = 0.003$) 4) OR 3.68 ($p = 0.02$)
Sundermann S, et al. [22][b]	400 Germany Mean age 80.3 % female not reported Prospective cohort study	Cardiac surgery (Elective)	Comprehensive Assessment of Frailty *Fried minus unintentional weight loss, plus balance assessment, albumin, creatinine, brain natriuretic peptide, FEV1 and Clinical Frailty Scale* moderately frail = 11–25 points severely frail = 26–35 points	30 day mortality	Severely frail vs non frail 21.7 % vs 3.6 % AUC = 0.71 on logistic regression
Sundermann S, et al. [23][b]	213 Germany Mean age 80.1 % female not reported Prospective cohort study	Cardiac surgery (Elective)	CAF FORECAST (Frailty predicts death One year after Elective Cardiac Surgery Tests)	1) 1 year mortality 2) Requirement for resuscitation 3) ICU stay 4) MACCE 1) 1 year mortality	Adjusted for EuroSCORE 1) OR 1.097 ($p = 0.001$) AUC 0.70 Frail vs non frail 2) 16 % vs 2 % ($p < 0.05$) 3) non-sig 4) non-sig 1) FORECAST AUC 0.76
Sundermann S, et al. [24][b]	450 Germany Mean age 79 50 % female Prospective cohort study	Cardiac surgery (Elective)	CAF FORECAST *chair rise test, subjective weakness on questionnaire, stair climbing, Clinical Frail Scale and serum creatinine.*	1 year mortality	Adjusted for age CAF OR 1.091 ($p < 0.001$) FORECAST OR 1.265 ($p < 0.001$)
Oncologic					
Kristjansson S.R. et al. [25][a]	178 Norway Mean age 79.63 57 % female Prospective cohort study	Colorectal cancer surgery (Elective)	Balducci Frailty Criteria from CGA *Cumulative Illness Rating Scale (CIRS), pADL, iADL, polypharmacy, MNA, MMSE, and GDS*	30 day post-operative complications (Clavian-Dindo grading)	Adjusted for covariates OR 3.13 (95 % CI 1.65–5.92)
Kristjansson S.R. et al. [26][a]	176 Norway Mean age 80 57 % female Prospective longitudinal study	Cancer surgery (Elective)	Balducci Frailty Criteria from CGA Modified Fried criteria	30 day mortality	Adjusted for cancer stage and age Balducci OR 3.39 ($p < 0.001$) Modified Fried OR 2.67 ($p = 0.029$)
Neuman, H.B. et al. [37][a]	12,979 USA Mean age 84.4 61.4 % female Retrospective analysis of Surveillance, Epidemiology and End Results(SEER)-Medicare database	Colectomy for stage I to III colon cancer (Elective)	11 item frailty measure defined by the John Hopkins Adjusted Clinical Group case-mix system *Difficulty walking, weight loss, frequent falls, malnutrition, impaired vision, decubitus ulcer, incontinence (plus 4 additional unnamed conditions)* Frail ≥1/11	1) 90 day survival 2) 1-year survival	Adjusted for covariates 1) OR 10.4 ($p < 0.001$) 2) OR 8.4 ($p < 0.001$)

Table 1 Study demographics grouped by type of surgery *(Continued)*

Ommundsen, N. et al. [27][a]	178 Norway Mean age 80 57 % female Prospective cohort study	Colorectal cancer surgery (Elective)	Balducci Frailty Criteria from CGA	5 year mortality	Multivariate adjusted for TNM stage and sex OR 3.6 ($p < 0.001$)
Ronning, B. et al. [28][b]	84 Norway Median age 82 59 % female Prospective cohort study	Colorectal cancer surgery (Elective)	Balducci Frailty Criteria from CGA	Post-operative functional status 1) Barthel Index ↓ 2) NEADL ↓ 3) TUG ↑ 4) Grip strength ↓	Logistic regression (95 % CI) 1) non-sig 2) non-sig 3) non-sig 4) non-sig
Tan, K-Y et al. [29][b]	83 Singapore and Japan Mean age 81.5 % female not reported Prospective cohort study	Colorectal cancer (Elective)	Fried criteria	Postop complications (Clavien-Dindo ≥ II)	Bivariate analysis OR 4.08 ($p = 0.006$)
General/abdominal					
Hewitt, J. et al. [30][a]	325 UK Mean age 77.6 57 % female Prospective cohort study	General surgical patients (Acute) - only 31 % underwent surgery	Clinical Frailty Scale *7 frailty levels based on visual observation combined with an abbreviated review of medical records* Frail is ≥5	1) 30 day mortality 2) 90 day mortality 3) LOS 4) 30 day hospital readmission	Adjusted for age and polypharmacy, frail vs non frail 1) non-sig 2) non-sig 3) 19 vs 7 days ($p = 0.02$) 4) non-sig
Kenig, J et al. [31][a]	184 Poland Mean age 76.9 53 % female Prospective cohort study	Abdominal surgery (Acute)	Vulnerable Elder Survey (VES) *age, self-rated health, limitation in physical function and functional disabilities* Triage Risk Screening Tool (TRST) *cognitive impairment, difficulty walking/transferring/recent falls, ≥5 medications, ED use in previous 30 days or hospitalization in previous 90 days, lives alone and/or no available caregiver, geriatric syndrome* G8 *7 items from the Mini Nutritional Assessment (MNA) questionnaire and age* Groningen Frailty Indicator (GFI) ADLs, sensory impairment, nutrition, polypharmacy, cognitive impairment, psychosocial wellbeing and subjective physical fitness Rockwood's brief clinical instrument to classify frailty (4 frailty levels) Balducci Frailty Criteria	1) 30 day post-operative complications (Clavian-Dindo grading) 2) 30 day mortality	Adjusted for covariates 1) VES: OR 2.4 ($p < 0.05$) TRST: non-sig G8: OR 1.5 ($p < 0.05$) GFI: OR 1.5 ($p < 0.05$) Rockwood: non-sig Balducci: OR 1.7 ($p < 0.05$) 2) VES: OR 2.4 ($p < 0.05$) TRST: non-sig G8: OR 1.8 ($p < 0.05$) GFI: OR 1.4 ($p < 0.05$) Rockwood: non-sig Balducci: OR 1.4 ($p < 0.05$)
Kim, S et al. [33][a]	275 Korea Mean age,% female	Intermediate or high risk general surgery (Elective)	Multidimensional Frailty Score (MFS) *Malignant disease, Charleston comorbidity Index, Albumin, ADLs,*	1) 1 year mortality 2) Discharge to residential care 3) Postoperative complications	Adjusted for covariates, for every 1 point increase in MFS 1) OR 2.05 ($p < 0.001$)

Table 1 Study demographics grouped by type of surgery *(Continued)*

	- survivors 75.2, 46 % - deceased 77.6, 32 % Prospective cohort study		*IADLs, dementia, risk of delirium, malnutrition, mid-arm circumference* Low risk ≤5 High risk >5	4) LOS (median)	2) OR 1.42 ($p = 0.01$) 3) non-sig 4) 14 vs 9 days for high vs low risk group ($p < 0.001$)
Vascular					
Ambler, G.K. et al. [32][b]	410 UK Median age 77 % female not reported Prospective cohort study	Vascular surgery (Elective and Acute)	Addenbrooke's Vascular Frailty Score (AVFS; 6 items, score 0–6) *Not independently mobile on admission, depression, polypharmacy on admission (>8 medications), anaemia, Waterlow score >13 on admission, emergency admission*	1) 1 year mortality 2) Readmission-free survival 3) Discharge to residential care 3) Prolonged LOS	Univariate; most vs least frail 1) 58 % vs 0 %, AUC 0.83 2) 0 % vs 68 % ($p < 0{\cdot}001$), AUC 0.71 3) AUC 0.78 4) AUC 0.74
Partridge, J.S.L. et al. [34][a]	125 UK Mean age 76.3 31 % female Prospective observational study	Vascular surgery (Elective and Acute)	Edmonton Frail Scale (EFS) *cognitive impairment, dependence in iADL, recent burden of illnesses, self-perceived health, depression, weight loss, medication issues, incontinence, inadequate social support and mobility difficulties.* Frail is >7/18	1) Composite measure post-operative complications 2) Composite measure adverse functional outcomes 3) LOS ≥12 days	Multivariate, adjusted for significant baseline associations and age 1) non-sig 2) non-sig 3) non-sig
Hip fracture					
Kistler, E et al. [35][a]	35 USA Mean age 86 83 % female Prospective cohort study	Hip fracture surgery (Acute)	Modified Fried Criteria	1) Post-operative complications 2) Delirium 3) LOS 4) Time to surgery	Frail vs Non-frail 1) non-sig 2) non-sig 3) 7.3 vs 4.1 ($p = 0.038$) 4) non-sig
Krishnan, M et al. [36][a]	178 UK Mean age 81 73.5 % female Prospective cohort study	Hip fracture surgery (Acute)	FI (51 items)	1) 30-day mortality 2) Inpatient mortality 3) LOS-failure to return home by 30 days	Frail vs Non-frail 1) 17.2 % vs 0 % ($p < 0.001$) 2) 28.1 % vs 0 % ($p < 0.001$) 3) AUC 0.82
Patel K.V. et al. [38][a]	218 USA Mean age 81.2 % female not reported Retrospective chart review	Hip fracture (Acute)	Modified FI (19 items)	1 year mortality 2-year mortality	OR 4.97 ($p < 0.001$) OR 4.01 ($p < 0.001$)

[a]indicates quartile 1 in the quality assessment
[b]indicates quartile 2 in the quality assessment
LOS length of stay, *MACCE* major cardiac & cerebral adverse events, *non-sig* no statistically significant association, *AUC* area under the ROC curve for prediction of adverse outcomes

Table 2 Adverse outcome associated with frailty, grouped by the quality of studies

Outcome	Number of studies									
		1	2	3	4	5	6	7	8	9	10
Mortality											
1 year Mortality	Quality [ref]	**Q1** [21]	**Q1** [33]	**Q1** [39]	**Q1** [37]	**Q1** [38]	**Q2** [18]	**Q2** [19]	**Q2** [23]	**Q2** [24]	**Q2** [32]
n = 10	N sample	**100**	**275**	**244**	**12979**	**218**	**159**	**30**	**213**	**450**	**410**
2 Year Mortality	Quality [ref]	**Q1** [38]									
n = 1	N sample	**218**									
5 year Mortality	Quality [ref]	**Q1** [27]									
n = 1	N sample	**178**									
30 Day Mortality	Quality [ref]	**Q1** [21]	**Q1** [26]	**Q1** [31]	**Q1** [36]	**Q2** [22]	Q1 [30]				
n = 6	N sample	**100**	**176**	**184**	**178**	**400**	325				
90 Day Mortality	Quality [ref]	**Q1** [37]	Q1 [30]								
n = 2	N sample	**12979**	325								
Post-Operative Complications											
Non-routine recovery	Quality [ref]	**Q1** [25]	**Q1** [31]	**Q2** [18]	**Q2** [29]	Q1 [17]	Q1 [33]	Q1 [34]	Q1 [35]	Q1 [39]	
n = 10	N sample	**178**	**184**	**159**	**83**	152	275	125	35	244	
Need for resuscitation	Quality [ref]	**Q2** [23]									
n = 1	N sample	**213**									
Delirium	Quality [ref]	Q1 [35]									
n = 1	N sample	35									
MACCE	Quality [ref]	**Q1** [21]	Q2 [23]	Q2 [19]							
n = 3	N sample	**100**	213	30							
Discharge											
Length of stay	Quality [ref]	**Q1** [36]	**Q1** [35]	**Q1** [30]	**Q2** [32]	**Q2** [18]	Q1 [34]				
n = 6	N sample	**178**	**35**	**325**	**410**	**159**	125				
Discharge to Institution	Quality [ref]	**Q1** [33]	**Q2** [32]								
n = 3	N sample	**275**	**410**								
Functional Decline	Quality [ref]	Q1 [34]									
n = 1	N sample	125									
Post-Discharge											
Readmission rate: 1 year	Quality [ref]	**Q2** [32]	Q1 [30]								
n = 2	N sample	**410**	325								
Functional Decline	Quality [ref]	**Q1** [20]	Q2 [28]								
n = 2	N sample	**119 *at 6 months***	84 *16–28 months*								
Quality of Life: 6 months, 1 year	Quality [ref]	**Q1** [39]									
n = 1	N sample	**244**									

Bold: studies which found statistically significant association

Q1 quartile one quality assessment, *Q2* quartile two quality assessment, *MACCE* major cardiac & cerebral adverse events

in five [18, 30, 32, 35, 36]. Three studies evaluated functional decline as an outcome, of which only one found a significant association [20]. Discharge to a residential care facility was found to be associated with frailty by both studies in which this outcome was evaluated [32, 33]. Quality of life was evaluated in one study and frailty was associated with the composite poor outcome of mortality or poorer quality of life [39].

Based on quality, quantity and consistency of the included studies, there is evidence for an association between frailty and adverse postoperative outcomes. Although cohort studies are lower on the hierarchy of evidence than randomised controlled trials, it is acknowledged that the cohort study design is entirely appropriate for investigating this particular research question. The literature search identified 23 studies that met the inclusion criteria and 15 of those were in the upper quartile of quality assessment, indicating the majority were methodologically sound. The consistency was evidenced by the finding that 20 of the included studies found evidence of an association between frailty and at least one adverse outcome.

Discussion

The reviewed studies consistently found that in patients aged over 75 years, frailty was associated with increased mortality, post-operative complications, prolonged length of stay and discharge to residential care facility. The strongest evidence of association was between frailty and 30 day mortality. The association was consistent across different frailty instruments and regardless of the type of surgery performed.

Our findings are congruent with other reviews of frailty in surgical patients. Beggs et al. found eight out of 19 articles demonstrating frailty to be significantly associated with mortality and post-operative complications [41]. Other systematic reviews have concentrated on specific surgical subspecialties, namely oncologic surgery [42], cardiac surgery [43] and thoracic surgery [44]. They also found frailty to impact negatively on post-operative outcomes. Two other reviews written on cardiac surgery also identified frailty as a risk factor that provided important prognostic information in older adults needing surgical or transcatheter aortic valve replacement [45] and found that frailty increased the predictive power of conventional risk scores [46].

The strength of this review is that it is inclusive of all types of surgery, both elective and acute, and focuses on those over 75 years old. This review provided insight into how frailty is measured and how it correlates with adverse outcomes in the 'old-old' and the 'oldest old' surgical population. Our search was limited to English publications, so may have excluded relevant publications in other languages. Another limitation was that studies using single markers to determine frailty, such as measurement of muscle mass or gait speed, were excluded based on the consensus view of frailty being a multidimensional state of increased vulnerability. Finally, due to the differences in frailty instruments used and heterogeneity of the surgical patient population, meta-analysis could not be conducted, and the magnitude of the adverse impact of frailty on outcome could not be estimated.

There is evidence that frailty is associated with increased mortality and morbidity in the older surgical patients. As patients over 75 years old are presenting more commonly for surgery, frailty assessment may have considerable value as a tool for peri-operative assessment. However, for the value of frailty assessment to be realised, it must not only predict outcomes but also be easily incorporated into routine assessment or created from existing information, without placing further resource burden on clinical staff and the patient. Once established, such a tool may offer a valuable addition to the risk assessment of older persons undergoing surgery, alongside the standard surgical and anaesthetic assessment tools. With the increasing focus on patient centred care, the ongoing development of frailty assessment has the potential to improve how well patients can be informed by their surgeons and anaesthetists prior to their procedures, thus enhancing informed consent. The clinical utility, time taken to make frailty assessments and the ease of use of most of the tools in the 23 included studies were not reported, which would be useful in assisting clinicians to decide which tool to adopt into clinical practice.

This review found several important gaps in the current literature. Frailty in acute surgical patients is under-studied. Only 7 out of 23 studies assessed acute surgical patients and all of them used scales based on comprehensive geriatric assessment to measure frailty. Reliance on performance based tests may be impractical in the acute surgical patients. More research into how frailty impacts on surgical patients in the acute setting and how best to measure frailty in acute surgical patients is needed. An instrument which is robust and valid for measuring frailty in elective patients in a surgical preadmission clinic may not be applicable to the acute patients. Despite the need to find a unified tool for measuring frailty, it is possible that different frailty tools are best suited for different acuity and type of surgical patients. Furthermore, these instruments need to be time-efficient and suitable for application at the bedside by staff who are not geriatricians.

Mortality and post-operative complications are the most commonly studied and reported outcomes in the 23 articles reviewed. Quality of life post-surgery was assessed in only one out of the 23 studies; similarly,

functional decline and discharge to a care facility were only evaluated in three and two studies respectively. The association between frailty and functional outcome, discharge destination, and quality of life after surgery warrants further research. Factors and outcomes important to the individual elderly patient undergoing surgery must also be considered when performing pre-operative assessment, such as the consideration of premorbid status and return to the premorbid level of function.

Conclusion

Frailty is consistently found is to be associated with adverse outcomes after surgery. In the 23 articles reviewed, the strongest evidence lies in the association with increased 30 day, 90 day and 1 year mortality, post-operative complications and length of stay. This highlights the importance of detecting frailty in peri-operative assessment. The possibility that different frailty tools may be best suited for different acuity and type of surgical patients is worth exploring. The association between frailty and return to pre-morbid function, discharge destination, and quality of life after surgery warrants further research.

Acknowledgements
Nil.

Funding
This research was partially funded by the Princess Alexandra Research Support Scheme to support a Fellowship in Clinical Research for first author.

Availability of data and materials
This paper is a systematic review. Articles selected for this review were referenced in bibliography. All data extracted from the selected studies were presented in the tables. There is no raw data to be made available.

Authors' contributions
HL and JW were responsible for the literature search, selection of articles for review, quality assessment of the articles and data extraction from the articles. HL was additionally responsible for writing the first draft of the paper and the synthesis of the results. NP and RH were responsible for the conception of the study design and aims and resolving any disagreement in the article assessment by HL and JW. All authors participated in the editing of the manuscript and have approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Ethics approval and consent to participate
Not applicable.

Received: 21 April 2016 Accepted: 15 August 2016
Published online: 31 August 2016

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BJA

British Journal of Anaesthesia, 118 (1): 123–31 (2017)

doi: 10.1093/bja/aew396
Critical Care

Intensive care utilization and outcomes after high-risk surgery in Scotland: a population-based cohort study

M. A. Gillies[1]*, E. M. Harrison[2], R. M. Pearse[3], S. Garrioch[1], C. Haddow[4], L. Smyth[4], R. Parks[2], T. S. Walsh[1] and N. I. Lone[1,5]

[1]Department of Anaesthesia, Critical Care and Pain Medicine, [2]Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh, UK, [3]Faculty of Medicine and Dentistry, Queen Mary University London, London, UK, [4]NHS Services Scotland, Information Services Division, South Gyle, Edinburgh, UK and [5]Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK

*Corresponding author. E-mail: michael.gillies@ed.ac.uk

Abstract

Background. The optimal perioperative use of intensive care unit (ICU) resources is not yet defined. We sought to determine the effect of ICU admission on perioperative (30 day) and long-term mortality.
Methods. This was an observational study of all surgical patients in Scotland during 2005–7 followed up until 2012. Patient, operative, and care process factors were extracted. The primary outcome was perioperative mortality; secondary outcomes were 1 and 4 yr mortality. Multivariable regression was used to construct a risk prediction model to allow standard-risk and high-risk groups to be defined based on deciles of predicted perioperative mortality risk, and to determine the effect of ICU admission (direct from theatre; indirect after initial care on ward; no ICU admission) on outcome adjusted for confounders.
Results. There were 572 598 patients included. The risk model performed well (c-index 0.92). Perioperative mortality occurred in 1125 (0.2%) in the standard-risk group (n=510 979) and in 3636 (6.4%) in the high-risk group (n=56 785). Patients with no ICU admission within 7 days of surgery had the lowest perioperative mortality (whole cohort 0.7%; high-risk cohort 5.3%). Indirect ICU admission was associated with a higher risk of perioperative mortality when compared with direct admission for the whole cohort (20.9 *vs* 12.1%; adjusted odds ratio 2.39, 95% confidence interval 2.01–2.84; $P<0.01$) and for high-risk patients (26.2 *vs* 17.8%; adjusted odds ratio 1.64, 95% confidence interval 1.37–1.96; $P<0.01$). Compared with direct ICU admission, indirectly admitted patients had higher severity of illness on admission, required more organ support, and had an increased duration of ICU stay.
Conclusions. Indirect ICU admission was associated with increased mortality and increased requirement for organ support.
Trial registration. UKCRN registry no. 15761.

Key words: epidemiology; intensive care; surgery

Latest estimates suggest that more than 310 million people undergo surgery worldwide each year,[1] and there is evidence that improvements in surgical care have led to a reduction in mortality after surgery in recent decades.[2–4] Estimates of hospital mortality after surgery range from 1 to 4%, but postoperative complication rates of up to 10 times this figure have been reported, and these influence long-term survival.[5] Variation in outcome remains, particularly in high-risk surgery. This phenomenon has been reported between and within nations[6 7] and between hospitals.[8 9] Incidence and outcome after postoperative complications have also been shown to differ

Editorial decision: October 10, 2016; **accepted:** November 5, 2016

Editor's key points

- High-dependency and intensive care beds are limited in many parts of the world.
- Unplanned admission to intensive care is a well-validated clinical indicator of quality and safety.
- This study found a strong association between unplanned admission to intensive care with both short- and long-term mortality.
- Routine preoperative identification of those most at risk of serious postoperative complications should lead to a direct admission to intensive care.

between hospitals, suggesting that institutional factors may be implicated.[8–10] Historically, reduced access to intensive care resources has been cited as a reason for variation in outcome after surgery.[11]

Identifying the patients at highest risk of dying or developing major complications in the postoperative period remains a major challenge. There is evidence that the proportion of patients who die from postoperative complications varies between hospitals; the so-called 'failure-to-rescue' group.[8] Thus, routine postoperative admission to critical care after many types of high-risk surgery has long been regarded as an important standard of care;[11] however, little evidence to support this exists and that which does is conflicting.[7 9 12] There is great interest in identifying which groups of patients are likely to benefit from use of perioperative critical care and whether it offers advantages over standard care after major surgery. The effect of intensive care unit (ICU) admission on postoperative outcome is not something that can easily be tested in a clinical trial, hence the reliance on observational studies.[13]

High-quality, linked data are available for all patients treated in National Health Service hospitals in Scotland. We sought to use these data to describe the patient characteristics and short- and long-term outcomes of all patients in Scotland undergoing non-cardiac surgery, to explore factors associated with greater risk of death, and to describe current use of intensive care services in Scotland for surgical patients. In particular, we wished to determine the association between mortality and direct admission to the ICU compared with patients admitted to the ICU after a period of care on the ward.

Methods

Ethics, sponsorship, and indemnity

The Chairs of South East Scotland Research Ethics Committees 01 and 02 reviewed the study protocol and waived the need for a full ethics submission. The study underwent review by Information Services Division's (ISD) Privacy Advisory Committee, which undertakes the role of Caldicott guardianship (Reference PAC 58/11).

Study population and data sources

We used a cohort study design with data held by ISD Scotland. These data are complete, linked, comprise all hospital and ICU admissions in Scotland, and have a low incidence of missing data.[14 15] Further details of the linkage process are available in the online supplementary material. We extracted a complete record of surgical inpatients managed in Scotland between January 1, 2005 and December 31, 2007 from the ISD Scottish Morbidity Record (SMR01) database. All adult patients undergoing inpatient general surgery were eligible for inclusion in this study. The Operating Procedure Coding System-4.2 (OPCS)[16] was used to identify general surgical procedures. We excluded cardiac and neurosurgical procedures because these patients all have established patient pathways or are managed in specialist centres. In addition, we excluded admissions involving endoscopy, organ transplantation, obstetrics, or the surgical management of burns. For patients with more than one included surgical procedure during the 3 yr study period, we used only the first surgical procedure.

Variables

For each patient, a full data extract was requested, including: age; gender; socio-economic status; surgical OPCS code; diagnosis on admission to hospital [using International Classification of Diseases, 10th Edition (ICD-10) code]; surgical status (elective *vs* emergency classification); and number of hospital admissions in the 5 yr before the index hospital admission. The OPCS codes and ICD-10 codes were grouped based on frequency. In addition, we reported a measure of co-morbidity using a count of co-morbidities that constitute the Charlson co-morbidity index, a measure of co-morbidity derived from 17 chronic conditions.[17] This approach has been used in other investigations.[18] Socio-economic status was assigned using quintiles of the Scottish Index of Multiple Deprivation (SIMD), which is based on area of residence and comprises multiple domains of differentially weighted measures of deprivation, including income, employment, education, crime, and housing.[19] Operative severity was assigned to each procedure using the 'BUPA Schedule of Procedures'.[20] BUPA operative severity and emergency surgical status are used in 'Physiological and Operative Severity for the Enumeration of Morbidity and Mortality' (POSSUM), a widely used risk prediction tool for comparative surgical audit.[21] We ascertained admission to an ICU by linkage to the Scottish Intensive Care Society Audit Group (SICSAG) database and obtained ICU-specific variables for those admitted to the ICU, as follows: severity of illness score on ICU admission [measured by Simplified Acute Physiology Score II (SAPS II)]; SAPS II-predicted mortality; requirement and duration of organ support (mechanical ventilation, renal replacement therapy, and cardiovascular support); ICU length of stay; and ICU mortality. Patients were classified by the main exposure variable as follows: those not admitted to ICU during the first 7 days after surgery ('no ICU admission'); those whose ICU admission occurred immediately after surgery (i.e. transferred directly from theatre or recovery room to ICU, 'direct ICU admission'); and those who were admitted to the ICU after $\leq$7 days in a non-ICU environment after surgery ('indirect ICU admission').

The primary outcome measure was death within 30 days of the procedure (perioperative mortality). Secondary outcomes were 1 and 4 yr mortality and duration of hospital admission. The 4 yr follow-up was assumed to be complete for all patients. Scottish national statistics indicate that the population has low levels of emigration; $\sim$1.3% in total and 0.7% in those aged $>$35 yr.[22]

Statistical analysis

Univariable analyses were done to test the association of patient and operative factors with mortality at 30 days and 1 and

4 yr. Independent predictors of mortality at these three time points were identified using multivariable logistic regression models. Using 30 day mortality as the dependent variable, we grouped patients into deciles by predicted mortality using variables in the multivariable model with the addition of first-order interactions that improved model fit based on the area under the receiver operating curve and Bayesian Information Criterion (interaction terms comprised: BUPA surgical status*OPCS procedure chapter; emergency surgical status*OPCS procedure chapter). We undertook model checks and assessed discrimination, overall performance, and calibration, reporting the area under the receiver operator curve, Brier score, and Hosmer–Lemeshow goodness of fit. Patients in the highest risk decile were deemed 'high risk'; all other patients were deemed 'standard risk'.

All analyses were undertaken using Stata 13 (StataCorp, College Station, TX, USA) and R (R Foundation, Vienna, Austria). We report descriptive and outcome data for standard- and high-risk groups and for patients with no ICU admission, direct ICU admission, and indirect ICU admission, with statistical testing where appropriate. We evaluated the association between ICU admission status and survival in high-risk patients using direct admission to the ICU as the reference category, adjusting for potential confounders using multivariable logistic regression. We present these associations on both relative and absolute scales of risk. Risk on a relative scale remains constant across risk deciles but gives less clear indication of its impact at a population level. We therefore calculated adjusted absolute risk differences across deciles of predicted risk using the 'margins' command in Stata. Survival analysis was undertaken for 4 yr mortality and groups were compared using the log-rank test. Statistical significance was set at $P<0.05$.

Subgroup and sensitivity analyses

To examine patterns of ICU use more fully and potentially to reduce confounding, the following subgroups were analysed: all high-risk patents and patients having elective, major colorectal surgery, and emergency vascular surgery. We chose the last two groups because the procedures are commonly performed major procedures with a high rate of ICU admission. Given that a potential immortal time bias exists (those in the indirect ICU group were required to survive long enough to be admitted to the ICU to a maximum of 7 days after surgery, which was not the situation in the other two groups), we undertook a sensitivity analysis restricted to those alive on successive postoperative days up to postoperative day 8 to ascertain the potential magnitude of this bias.

Results

Study cohort characteristics

A full description of the study cohort, including outcome data, is provided in Table 1. There were 1 014 796 patient records with included codes identified. After exclusion of records relating to re-admissions, patients aged <16 yr, non-surgical or diagnostic procedural codes, and discordant operative or death dates, 572 598 patients remained. A flowchart outlining the selection of the study cohort is presented in Supplementary Fig. 1. A total of 5294 (0.9%) patients died before discharge from hospital and 59 799 (10.4%) died by the end of the 4 yr follow-up period. The commonest five 'complex major' surgical procedures for the whole cohort and important subgroups are outlined in Table 2.

Predictors of 30 day mortality and creation of risk groups

In univariable and multivariable analyses of the whole cohort, statistically significant associations were seen between mortality at each of the three time points and all variables (Supplementary Tables 1 and 2). A multivariable model constructed to predict perioperative mortality with additional interaction terms demonstrated excellent discrimination (area under the receiver operating curve=0.922; Supplementary Fig. 2) and reasonable calibration and overall performance, with slight underprediction of mortality in risk decile 8 (Supplementary Fig. 3; Hosmer–Lemeshow test statistic $\chi^2=34.7$, $P=<0.001$; Brier Score 0.008). Baseline descriptive and outcome data for standard- and high-risk groups derived from this model are provided in Table 1.

Postoperative ICU admission

The rate of direct admission to the ICU in standard- and high-risk cohorts was 0.4 and 4.8% and the rate of indirect admission to the ICU 0.1 and 1.6%, respectively (Table 1). Patients admitted directly to the ICU from the operating theatre or recovery room were more likely to be older and having emergency or BUPA category 4 or 5 ('major+ or complex major') surgery when compared with those admitted indirectly. When restricted to the high-risk group, increased representation of major+ and complex major surgery was the only significant difference between groups. The total duration of hospital admission was longer in patients admitted to the ICU after surgery; this was greatest in the group with indirect admission. When compared with direct ICU admission, patients admitted indirectly to the ICU had greater severity of illness on ICU admission, higher predicted and observed risk of mortality, longer duration of ICU stay, and increased requirement for ventilation and other forms of organ support (Table 3).

Compared with direct admission to the ICU, the unadjusted risk of death at 30 days was lowest in patients who were not admitted to the ICU during the 7 days after surgery [odds ratio (OR) 0.46; 95% confidence interval (CI) 0.43–0.52; $P<0.01$] and increased in those with indirect ICU admission (OR 1.91, 95% CI 1.65–2.22; $P<0.01$). After adjustment for case-mix and risk factors, these associations persisted; no postoperative ICU admission was associated with reduction in the risk of death at 30 days (OR 0.26, 95% CI 0.23–0.29; $P<0.01$), and indirect ICU admission was associated with further increased risk of 30 day mortality (OR 2.39; 95% CI 2.01–2.84; $P<0.01$) when compared with direct ICU admission. Figure 1 illustrates the increased risk in indirect compared with direct ICU admission adjusted for confounding across deciles of predicted risk on an absolute scale of risk. The magnitude of increased risk of perioperative mortality in the indirect *vs* direct ICU admission groups was <1% for risk deciles 1–6, increasing to 1.9% (95% CI 1.4–2.4%) in decile 8, 4.2% (95% CI 3.2–5.2%) in decile 9, and 13.5% (95% CI 10.6–16.4%) in the highest risk decile. Increased long-term mortality was observed in the indirect ICU admission group relative to other groups for 1 and 4 yr mortality (Table 4) and in survival analysis throughout the full follow-up period of 4 yr (Fig. 2).

Subgroup and sensitivity analyses

In subgroup analyses, similar associations were seen in analyses restricted to the high-risk group (Table 4); after adjustment for case-mix and risk factors, no postoperative ICU admission was associated with a reduction in the risk of death at 30 days

Table 1 Patient characteristics and outcomes in the whole cohort and by risk groups. Missing data were as follows: gender *n*=2, socio-economic status *n*=3868, BUPA (British United Provident Association) operative category *n*=965, and ICU admission status (operation during ICU stay or unknown) *n*=930. Low- and high-risk groups were derived from a complete patient regression analysis of the data set; missing *n*=4834 (0.84%). ICU, intensive care unit; IQR, interquartile range

	Whole cohort	Standard risk	High risk
N	572 598	510 979	56 785
Age [yr; mean (SD)]	53.2 (16–106; 19.5)	50.7 (16–104; 18.7)	75.9 (16–104; 10.1)
Gender [*n* (%)]			
Male	258 249 (45.1)	228 798 (44.8)	26 852 (47.3)
Female	314 347 (54.9)	282 181 (55.2)	29 933 (52.7)
Surgical status [*n* (%)]			
Elective	468 176 (81.8)	44 2080 (86.5)	23 900 (42.1)
Emergency	104 422 (18.2)	68 899 (13.5)	32 885 (57.9)
Socio-economic status quintile [*n* (%)]			
1 (least deprived)	95 605 (16.8)	86 880 (17.0)	8592 (15.1)
2	107 644 (18.9)	97 516 (19.1)	9984 (17.6)
3	117 680 (20.7)	105 947 (20.7)	11 484 (20.2)
4	123 642 (21.7)	110 068 (21.5)	13 340 (23.5)
5 (most deprived)	124 159 (21.8)	110 568 (21.6)	13 385 (23.6)
Count of Charlson co-morbidities [*n* (%)]			
0	515 241 (90.0)	472 213 (92.4)	38 347 (67.5)
1	51 734 (9.0)	35 804 (7.0)	15 793 (27.8)
2	4976 (0.9)	2654 (0.5)	2308 (4.1)
3+	647 (0.1)	308 (0.1)	337 (0.6)
BUPA operative severity category [*n* (%)]			
Minor	97 391 (17.0)	92 050 (18.0)	4779 (8.4)
Intermediate	201 089 (35.2)	189 568 (37.1)	10 328 (18.2)
Major	184 511 (32.3)	161 176 (31.5)	21 917 (38.6)
Major+	30 393 (5.3)	21 368 (4.2)	8595 (15.1)
Complex major	58 249 (10.2)	46 817 (9.2)	11 166 (19.7)
Total number of previous hospital admissions [*n* (%)]			
0	267 929 (46.8)	249 982 (48.9)	14 269 (25.1)
1	123 676 (21.6)	113 659 (22.2)	9515 (16.8)
2	64 238 (11.2)	56 243 (11.0)	7758 (13.7)
3	36 380 (6.4)	30 701 (6.0)	5557 (9.8)
4	22 438 (3.9)	18 220 (3.6)	4144 (7.3)
5+	57 937 (10.1)	42 174 (8.3)	15 542 (27.4)
Hospital length of stay [days; median (IQR)]	1 (0, 3)	0 (0, 2)	9 (3, 22)
ICU admission status [*n* (%)]			
No ICU admission within 7 days of surgery	565 493 (98.9)	507 863 (99.5)	52 866 (93.6)
Direct admission to ICU from theatre	4593 (0.8)	1837 (0.4)	2696 (4.8)
Indirect admission to ICU within 7 days	1582 (0.3)	680 (0.1)	893 (1.6)
Mortality [*n* (%)]			
Hospital	5294 (0.9)	1011 (0.2)	4239 (7.5)
30 day	4806 (0.8)	1125 (0.2)	3636 (6.4)
1 yr	21 412 (3.7)	9054 (1.8)	12 261 (21.6)
4 yr	59 799 (10.4)	34 339 (6.7)	25 276 (44.5)

(OR 0.32, 95% CI 0.28–0.36; $P<0.01$), and indirect ICU admission was associated with further increased risk of 30 day mortality (OR 1.71; 95% CI 1.41–2.08; $P<0.01$), when compared with direct ICU admission. The subgroups of major elective colorectal and emergency vascular surgery demonstrated a similar magnitude of increased risk of perioperative mortality in the indirect ICU admission group relative to the direct group (Table 4).

In the sensitivity analysis to assess the potential effect of immortal time bias, the adjusted risk of death for those admitted indirectly to the ICU compared with those admitted directly to the ICU was highest for those alive on the third postoperative day (OR 2.65, 95% CI 2.20–3.20, compared with OR 2.39 in the primary analysis). This indicated that the likely magnitude of the immortal time bias was small (Supplementary Fig. 4).

Discussion

The principal finding of this study was that after adjustment for case-mix and risk factors, indirect postoperative admission to an ICU was associated with increased perioperative and long-term mortality. A 4 yr follow-up was available for all patients in this study; however, 30 day to 1 yr mortality is likely to be the time period most affected by postoperative ICU admission. These findings were observed in the whole cohort and when restricted to a high-risk cohort and specific groups of high-risk

Table 2 Commonest five complex major procedures undertaken in high-risk group by ICU admission status. Three-digit code refers to Operating Procedure Coding System-4.2 code. ICU, intensive care unit

Whole cohort (n=13 935)	n (%)	No ICU admission within 7 days (n=12 475)	n (%)	Direct admission to ICU from theatre (n=1116)	n (%)	Indirect admission to ICU within 7 days (n=344)	n (%)
H33 excision of rectum	2253 (20.2)	H33 excision of rectum	1770 (19.1)	H33 excision of rectum	326 (23.0)	H33 excision of rectum	143 (34.9)
T30 opening of abdomen	948 (8.5)	L59 other bypass of femoral artery	869 (9.4)	L18 emergency replacement of aneurysmal segment aorta	222 (15.6)	T30 opening of abdomen	76 (18.5)
L59 other bypass of femoral artery	895 (8.0)	W37 total prosthetic replacement of hip	841 (9.1)	L19 other replacement of aneurysmal segment	153 (10.8)	H10 excision of sigmoid colon	35 (8.5)
W37 total prosthetic replacement of hip	877 (7.9)	L29 reconstruction of carotid artery	765 (8.3)	T30 opening of abdomen	153 (10.8)	L19 other replacement of aneurysmal segment aorta	24 (5.9)
L29 reconstruction of carotid artery	788 (7.06)	T30 opening of abdomen	695 (7.5)	G01 excision of oesophagus and stomach	130 (9.2)	L18 emergency replacement of aneurysmal segment	22 (5.4)

surgical procedures. In absolute terms, the magnitude of increased risk is most marked for patients in the top two deciles of postoperative risk, suggesting a number needed to treat of 7 to prevent one postoperative death in the highest risk decile. Compared with direct ICU admission, no ICU admission was associated with lower risk of death even in the high-risk cohort. This is likely to represent residual confounding.

Surgical patients make up a sizeable proportion of ICU admissions. Of particular concern to clinicians are 'failure-to-rescue' patients (i.e. those who die from early postoperative complications).[8] Other studies have suggested increased mortality associated with delayed ICU admission as a result of lack of bed availability in mixed medical–surgical populations[23 24] or in patients held in postanaesthesia care units.[25] Our work focuses on the decision to admit patients directly to the ICU after surgery, for logic dictates that if patients are identified as being at high risk of developing postoperative complications, elective admission to an ICU will enable early recognition and prompt treatment should they occur, resulting in improved survival.

Our findings are consistent with other recent estimates of 30 day and 1 yr mortality after high-risk surgery[26] and another recent epidemiological study of ICU use in Medicare beneficiaries undergoing major surgical procedures in the USA.[12] The latter study suggested little consensus on admission criteria and no evidence of improved outcome associated with routine ICU admission. After certain procedures, the study demonstrated an association between ICU admission, increased length of hospital admission, and costs.

We believe that the present study has the following strengths. Firstly, to our knowledge, this is the first direct-linkage cohort study to report complete short- and long-term outcomes after surgery at a national level. Other studies have used data from large administrative databases that do not have full national coverage (e.g. Medicare,[12] Veterans Affair beneficiaries[5 27] in the USA) or data sets with no linkage to ICU or registry data, thereby necessitating an ecological approach, with potential for bias.[7 9] Secondly, previous studies have defined the high-risk surgical group by surgical procedure only.[13] The methodology used in our study has the advantage of considering both patient-level and operative-level factors to predict outcome, with excellent discrimination and overall model performance, although the risk prediction model requires validation in an external data set. This study demonstrates a group of patients at particularly high risk of perioperative mortality and the variable use of critical care facilities, which has not been reported previously at a population level.

Despite access to high-quality data, these findings may be subject to bias and residual confounding. Only first admissions in the 3 yr period were included to allow long-term follow-up. As re-admitted patients are often sicker and have more comorbidities, this may have introduced selection bias. We were unable reliably to identify patients admitted to high-dependency units in our data extract. Finally, the decision to admit a patient to the ICU after surgery is often multifactorial and includes reasons not easily captured in administrative data, such as unexpected perioperative events, concerns by the clinical team, and the availability of ICU beds. Even with exhaustive attempts to adjust for differences in case-mix, we were not able to account fully for these factors.

This study highlights important issues around how ICU resources are used after surgery. Firstly, absolute increases in mortality between indirect and direct admission to the ICU are greatest in higher risk deciles, as expected. If it were possible to

Table 3 Patient characteristics and outcome by ICU admission status for the whole cohort and the high-risk group. *P*-values are presented for hypothesis tests comparing the direct ICU admission group with the indirect ICU admission group. Missing data for ICU-specific variables were as follows (whole cohort/high-risk cohort): SAPS II score and mortality prediction *n*=211/*n*=57, ICU length of stay *n*=85/*n*=52, all organ support variables *n*=291/*n*=142, and ICU mortality *n*=21/*n*=12. CVS, cardiovascular support; ICU, intensive care unit; RRT, renal replacement therapy; SAPS II, Simplified Acute Physiology Score II

	Whole cohort				High-risk cohort			
n	No ICU admission 565 489	Direct ICU admission 4593	Indirect ICU admission 1582	*P*-value	No ICU admission 52 866	Direct ICU admission 2696	Indirect ICU admission 893	*P*-value
Age [yr; mean (SD)]	53.0 (16–106; 19.5)	64.4 (16–104; 16.5)	63.3 (16–100; 17.0)	0.03	76.2 (23–106; 10.1)	71.9 (20–102; 10.4)	72.5 (23–100; 10.2)	0.11
Gender [*n* (%)]				0.44				0.40
Male	254 381 (45.0)	2487 (54.1)	839 (53.0)		24 662 (46.7)	1511 (56.0)	487 (54.5)	
Female	311 106 (55.0)	2106 (45.9)	743 (47.0)		28 204 (53.3)	1185 (44.0)	406 (45.5)	
Surgical status [*n* (%)]				<0.01				0.07
Elective	464 192 (82.1)	2602 (56.7)	821 (51.9)		22 124 (41.8)	1228 (45.5)	376 (42.1)	
Emergency	101 297 (17.9)	1991 (43.3)	761 (48.1)		30 742 (58.2)	1468 (54.5)	517 (57.9)	
Count of Charlson co-morbidities [*n* (%)]				0.22				0.35
0	509 909 (90.2)	3367 (73.3)	1188 (75.1%)		35 766 (67.7)	1744 (64.7)	598 (67.0)	
1	50 175 (8.9)	1083 (23.6)	335 (21.2%)		14 636 (27.7)	832 (30.9)	244 (27.3)	
2+	4782 (0.8)	126 (2.7)	53 (3.4%)		2146 (4.1)	107 (4.0)	45 (5.0)	
BUPA operative severity category [*n* (%)]				<0.01				<0.01
Minor	97 191 (17.2)	105 (2.3)	69 (4.4)		4744 (9.0)	12 (0.4)	17 (1.9)	
Intermediate	199 797 (35.4)	439 (9.6)	260 (16.4)		9947 (18.8)	142 (5.3)	96 (10.8)	
Major	182 805 (32.4)	1132 (24.6)	424 (26.8)		20 999 (39.7)	631 (23.4)	212 (23.7)	
Major+	29 329 (5.2)	757 (16.5)	247 (15.6)		7911 (15.0)	492 (18.2)	158 (17.7)	
Complex	55 403 (9.8)	2160 (47)	581 (36.7)		9265 (17.5)	1419 (52.6)	410 (45.9)	
ICU characteristics								
SAPS II [median (IQR)]	–	24.0 (15.0, 36.0)	28.0 (18.0, 41.0)	<0.01	–	29.0 (20.0, 40.0)	32.0 (23.0, 44.0)	<0.01
SAPS II mortality prediction [median (IQR)]	–	5.8 (2.0, 18.1)	8.8 (2.9, 26.6)	<0.01	–	9.7 (3.7, 24.7)	12.8 (5.2, 32.6)	<0.01
ICU length of stay [days; median (IQR)]	–	1.8 (0.9, 3.7)	2.2 (0.9, 5.0)	<0.01	–	2.0 (1.0, 4.1)	2.5 (1.1, 5.1)	<0.01
Ventilated at any time [*n* (%)]	–	2142 (49)	878 (58)	<0.01	–	1432 (55.3)	510 (55.9)	0.03
Ventilator days [mean (SD)]	–	1.9 (4.5)	3.3 (6.8)	<0.01	–	2.2 (4.8)	3.2 (6.6)	<0.01
RRT at any time [*n* (%)]	–	231 (5.3)	174 (11.5)	<0.01	–	170 (6.6)	104 (12.1)	<0.01
Days of RRT [mean (SD)]	–	0.3 (2.0)	0.7 (2.9)	<0.01	–	0.4 (2.1)	0.7 (2.6)	<0.01
CVS support at any time [*n* (%)]	–	1272 (29.1)	614 (40.5)	<0.01	–	974 (37.6)	384 (44.8)	<0.01
Days of CVS support [mean (SD)]	–	0.9 (2.0)	1.4 (3.1)	<0.01	–	1.1 (2.2)	1.5 (3.0)	<0.01
Hospital stay [days; median (IQR)]	1 (0, 3)	14 (8, 27)	16 (9, 31)	<0.01	9 (3, 21)	17 (10, 31)	17 (10, 33)	0.13
Mortality [*n* (%)]								
ICU	–	318 (6.9)	240 (15.2)	<0.01	–	271 (10.1)	158 (17.8)	<0.01
Hospital	4027 (0.7)	641 (14.0)	384 (24.3)	<0.01	3297 (6.2)	551 (20.4)	270 (30.2)	<0.01
30 day	3728 (0.7)	556 (12.1)	330 (20.9)	<0.01	2818 (5.3)	481 (17.8)	234 (26.2)	<0.01
1 yr	19 619 (3.5)	992 (21.6)	494 (31.2)	<0.01	10 921 (20.7)	827 (30.7)	355 (39.8)	<0.01
4 yr	56 997 (10.1)	1674 (36.4)	707 (44.7)	<0.01	23 213 (43.9)	1339 (49.7)	511 (57.2)	<0.01

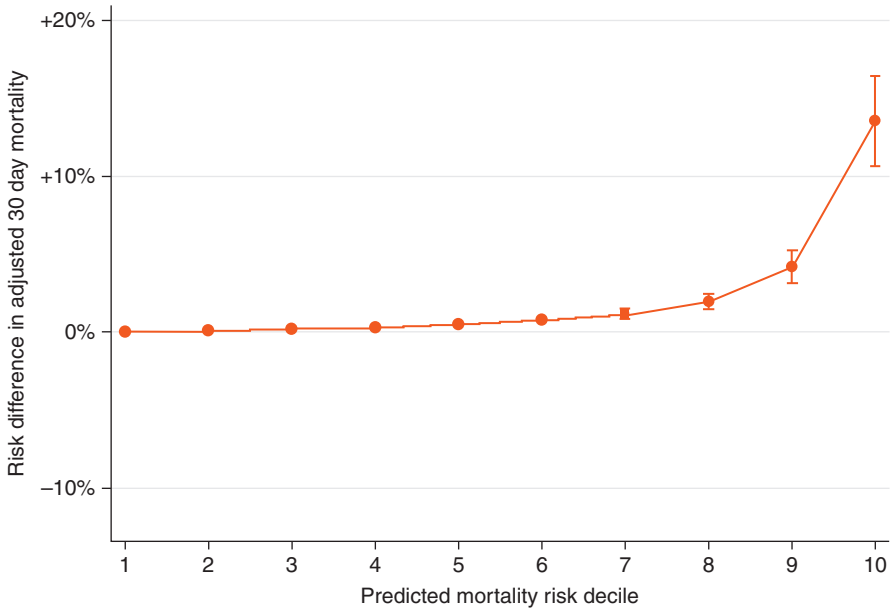

Fig 1 Absolute risk difference in adjusted 30 day mortality of indirect *vs* direct ICU admission across deciles of predicted mortality risk. ICU, intensive care unit.

Table 4 Adjusted risk of death according to ICU admission status in the whole cohort and subgoups. CI, confidence interval; ICU, intensive care unit; OR, odds ratio

	30 day mortality			1 yr mortality			4 yr mortality		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Whole cohort (*n*=566 835)									
Direct ICU admission	1			1			1		
No ICU admission	0.26	0.23, 0.29	<0.01	0.42	0.39, 0.46	<0.01	0.52	0.48, 0.56	<0.01
Indirect ICU admission	2.39	2.01, 2.84	<0.01	2.12	1.82, 2.47	<0.01	1.81	1.57, 2.10	<0.01
High-risk decile (*n*=56 455)									
Direct ICU admission	1			1			1		
No ICU admission	0.32	0.28, 0.36	<0.01	0.51	0.46, 0.56	<0.01	0.6	0.55, 0.66	<0.01
Indirect ICU admission	1.71	1.41,2.08	<0.01	1.56	1.31, 1.85	<0.01	1.39	1.17, 1.65	<0.01
Elective colorectal surgery (*n*=5902)									
Direct ICU admission	1								
No ICU admission	0.29	0.20, 0.41	<0.01	–	–	–	–	–	–
Indirect ICU admission	2.00	1.21, 3.30	<0.01	–	–	–	–	–	–
Emergency major vascular surgery (*n*=5528)									
Direct ICU admission	1								
No ICU admission	0.32	0.24, 0.42	<0.01	–	–	–	–	–	–
Indirect ICU admission	2.06	1.23, 3.44	<0.01	–	–	–	–	–	–

identify patients in advance who were admitted to the ward but who subsequently required ICU admission, admitting 24 of these patients in risk decile 9 electively to the ICU might prevent one perioperative death (number needed to treat=24); likewise, admitting seven of these patients in the highest risk decile might prevent one perioperative death (number needed to treat=7). This suggests that, at a population level, this group of patients would benefit most from direct ICU admission after surgery. Secondly our data suggest that the type of surgery rather than patient factors (e.g. co-morbidity) may drive the decision to admit patients to ICU after surgery. Finally, in common with other studies,[12] morality was higher in patients admitted directly to the ICU compared with no ICU admission either in the high-risk group or in predefined subgroups even after adjustment for potential confounders. This indicates residual confounding.

The indication for elective admission to the ICU after major surgery remains unclear. Many of the advantages of ICU care

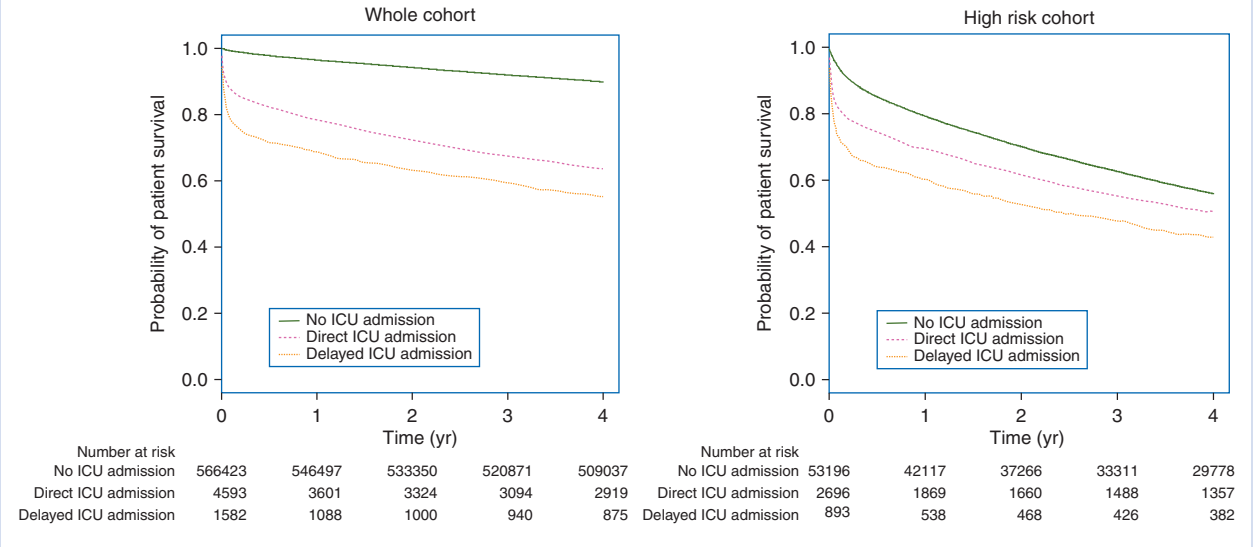

Fig 2 Survival analysis by ICU admission status: whole cohort and high-risk subgroup. ICU, intensive care unit.

can now be delivered in a specialist ward or high-dependency unit setting. Few surgical patients require invasive monitoring or organ support after surgery; instead, analgesia, early mobilization, fluid therapy, and early identification of complications can be delivered in other settings without some of the potential disadvantages associated with ICU admission, such as delayed mobilization or risk of hospital-acquired infection.[28] Thus, it may be the availability of ICU beds for those who require them[9 10] rather than routine admission for many types of low-risk major surgical procedures that is the more important factor.[12]

In conclusion, in a national linked cohort study and after adjustment for patient, surgical, and socio-economic factors, the highest mortality rates were observed in patients admitted to the ICU after a period of care on a standard ward, and the absolute increase in risk was most marked in the highest risk patients. Future studies are required to improve perioperative management pathways for this high-risk group, including optimal use of critical care resources.

Authors' contributions

Conceived the project and secured the funding: M.A.G., N.I.L., T.S.W., R.W.P., R.M.P.
Study design, interpretation of results and preparation of the manuscript: all authors.
M.A.G., N.I.L., C.H., L.S., S.G., E.M.H. designed and performed the data extraction, cleaned and recoded the data, and performed aspects of the analysis.
Overall responsibility for the integrity of the manuscript: M.A.G., N.I.L.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

Declaration of interest

M.A.G. is a Chief Scientist's Office (CSO) NHS Research Scheme Clinician. R.M.P. lectures and performed consultancy work for Nestle Health Sciences, Medtronic, Edwards Lifesciences, and Massimo Inc. All other authors report no conflict of interest.

Funding

Chief Scientist's Office Scotland (grant no. CHZ/821/4).

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Handling editor: P. S. Myles