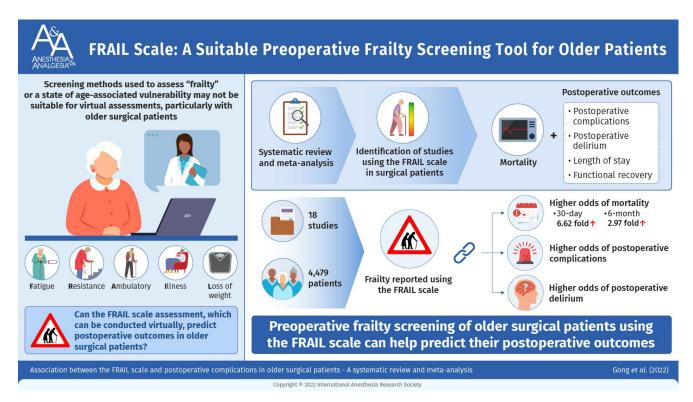


DPEN Association Between the FRAIL Scale and **Postoperative Complications in Older Surgical Patients: A Systematic Review and Meta-Analysis**

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BACKGROUND: Several frailty screening tools have been shown to predict mortality and complications after surgery. However, these tools were developed for in-person evaluation and cannot be used during virtual assessments before surgery. The FRAIL (fatigue, resistance, ambulation, illness, and loss of weight) scale is a brief assessment that can potentially be conducted virtually or self-administered, but its association with postoperative outcomes in older surgical patients is unknown. The objective of this systematic review and meta-analysis (SRMA) was to determine whether the FRAIL scale is associated with mortality and postoperative outcomes in older surgical patients.

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METHODS: Systematic searches were conducted of multiple literature databases from January 1, 2008, to December 17, 2022, to identify English language studies using the FRAIL scale in surgical patients and reporting mortality and postoperative outcomes, including postoperative complications, postoperative delirium, length of stay, and functional recovery. These databases included Medline, Medline ePubs/In-process citations, Embase, APA (American Psychological Association) PsycInfo, Ovid Emcare Nursing, (all via the Ovid platform), Cumulative Index to Nursing and Allied Health Literature (CINAHL) EbscoHost, the Web of Science (Clarivate Analytics), and Scopus (Elsevier). The risk of bias was assessed using the quality in prognosis studies tool.

RESULTS: A total of 18 studies with 4479 patients were included. Eleven studies reported mortality at varying time points. Eight studies were included in the meta-analysis of mortality. The pooled odds ratio (OR) of 30-day, 6-month, and 1-year mortality for frail patients was 6.62 (95% confidence interval [CI], 2.80–15.61; P < .01), 2.97 (95% CI, 1.54–5.72; P < .01), and 1.54 (95% CI, 0.91–2.58; P = .11), respectively. Frailty was associated with postoperative complications and postoperative delirium, with an OR of 3.11 (95% CI, 2.06–4.68; P < .01) and 2.65 (95% CI, 1.85–3.80; P < .01), respectively. The risk of bias was low in 16 of 18 studies.

CONCLUSIONS: As measured by the FRAIL scale, frailty was associated with 30-day mortality, 6-month mortality, postoperative complications, and postoperative delirium. (Anesth Analg 2023;136:251–61)

KEY POINTS

- **Question:** Is frailty as assessed by the FRAIL (fatigue, resistance, ambulation, illness, and loss of weight) scale associated with mortality and postoperative outcomes in older surgical patients?
- **Findings:** Frailty as measured by the FRAIL scale was associated with 30-day mortality, 6-month mortality, postoperative complications, and postoperative delirium.
- Meaning: The FRAIL scale is a useful tool for preoperative screening for frailty of older adults before surgery.

GLOSSARY

ADLs = activities of daily living; **CAM** = confusion assessment method; **CFS** = Clinical Frailty Scale; **CGA** = comprehensive geriatric assessment; **CI** = confidence interval; **CINAHL** = Cumulative Index to Nursing and Allied Health Literature; **FRAIL** = fatigue, resistance, ambulation, illness, and loss of weight; **GRADE** = Grading of Recommendations Assessment, Development and Evaluation; **IADL** = instrumental activities of daily living; **LOS** = length of stay; **OR** = odds ratio; **PRISMA** = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **QUIPS** = quality in prognosis studies; **SD** = standard deviation; **SRMA** = systematic review and meta-analysis; **TRST** = Triage Risk Screening Tool

Frailty is a clinical state of increased vulnerability due to age-associated decline in physiological reserve, resulting in compromised ability to cope with external everyday or acute stressors. Frailty before surgery is associated with increased risk of mortality and postoperative complications and various longterm negative outcomes, including falls, lower quality of life, and disability.^{1,2} Although there are many screening tools for frailty that predict adverse outcomes in older surgical patients,³ most were developed for inperson evaluation. The pandemic has accelerated the adoption of virtual (online and telephonic) care for preoperative assessments, precluding the use of screening tools that require in-person evaluation.

In 2008, the FRAIL (fatigue, resistance, ambulation, illness, and loss of weight) scale was conceptualized by the International Association of Nutrition and Aging task force.⁴ The FRAIL scale is based on the Fried frailty phenotype, which includes 5 components:

loss of weight, self-reported exhaustion, grip strength, slow walking speed, and low physical activity.⁵ The Fried frailty phenotype assessment is conducted inperson by a clinician and takes approximately 10 minutes. The FRAIL scale is a 5-item, self-reported questionnaire using yes/no questions that allows for rapid identification of frail and prefrail individuals.^{6,7} The FRAIL scale (Appendix 1) assesses frailty based on 5 components: fatigue, resistance (ability to climb stairs), ambulation (ability to walk a certain distance), illness, and loss of weight.7 Each of the components is scored with 1 point for presence or 0 for absence, for a total score ranging from 0 to 5. A score of 0 indicates nonfrail, 1 to 2 indicates that the individual is prefrail, and a score of 3 to 5 indicates frailty. The FRAIL scale can be administered in a few minutes, either over the telephone by clinicians or self-administered, and does not require specialized tools or equipment⁵ or in-person clinician assessments.8 In 2012, the FRAIL scale was validated to correlate with Instrumental Activities of Daily Living (IADLs) and mortality in a study of 998 Black adults between 49 and 65 years of age, of whom 7.5% participants were classified as frail.⁷ A longitudinal study of 10,412 women found frailty, as measured with the FRAIL scale, to increase with age, from 5.8% at 50 years of age to 11.3% at 66 years of age.⁹ Given the evidence of greater risk of adverse outcomes for frail older adults undergoing surgery, there is a need for accurate, easy-to-administer frailty screening tools.

While increased frailty as assessed by the FRAIL scale has been significantly associated with higher mortality risk in community-dwelling adults,⁹⁻¹¹ the association between the FRAIL scale and mortality and postoperative outcomes in older surgical patients is not known. The objective of this systematic review and meta-analysis (SRMA) was to determine the association of frailty as assessed by the FRAIL scale with postoperative outcomes, including mortality, postoperative complications, delirium, length of stay (LOS), and functional and cognitive recovery of older surgical patients.

METHODS

This SRMA was conducted according to the Cochrane Handbook and in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.^{12,13} The protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO; registration No. CRD42021261745) on July 18, 2021.

Study Selection

We included randomized controlled trials, quasi-experimental studies (nonrandomized controlled trials), and observational studies (prospective and retrospective). Studies were included if participants underwent any surgical procedures, elective or emergency, and if they reported one or more of the outcomes of interest (mortality, LOS, functional recovery, delirium, or postoperative complications). Postoperative complications included cardiovascular, respiratory, infectious, renal failure, and neurological. Studies were excluded if they were case reports, reviews, qualitative studies, abstracts, or protocols, or if they were not published in English.

Information Sources

With the assistance of an information specialist (M.E.), systematic searches were performed in multiple literature databases, including Medline, Medline ePubs/In-process citations, Embase, APA (American Psychological Association) PsycInfo, Ovid Emcare Nursing (all via the Ovid platform), Cumulative Index to Nursing and Allied Health Literature (CINAHL) EbscoHost, the Web of Science (Clarivate Analytics), and Scopus (Elsevier). If more data were required or if information was unclear, study authors were contacted for clarification.

Search Strategy

All databases were initially searched from January 1, 2012, to May 4, 2021, as the validation study was published in 2012.⁷ This was the first incidence in which the FRAIL scale was used in a sample of participants. A secondary search was performed on July 7, 2021, from January 1, 2008, to December 31, 2011, after we realized the conceptualization of the 5-item FRAIL scale was published in 2008.⁶ An updated search was performed on December 17, 2021. Citation searching of the validation study⁷ was conducted on the Web of Science and Scopus. The searches used both controlled vocabulary and text word searching (Supplemental Digital Content 1, Supplemental File 1, http://links.lww.com/AA/E93). The searches comprised concept blocks of terms: perioperative/surgery, elderly, and Frail scale.

Data Extraction

All studies identified via the search strategy were uploaded into Covidence and deduplicated. Two blinded reviewers (S.G. and D.Q.) independently screened the studies for titles and abstracts using Covidence (Covidence.org). Studies that could not be included based on title and abstract were moved for full-text review. Full-text screening, data extraction, and quality assessment were performed by 2 reviewers (S.G. and D.Q.), and a third reviewer (J.W.) resolved any discrepancies. Studies during the full-text review that did not meet all inclusion criteria were excluded, and a reason for exclusion was identified, such as reasons including but not limited to wrong study population, wrong intervention, or wrong outcome.

A standardized form was used for data extraction of the included studies. Extracted information included: study identification (author, setting, and country), study methods and design, and study population (inclusion and exclusion criteria, the total number of study participants, mean age of participants, type and urgency of surgery, and percentage of male participants). The prevalence of frailty was based on the percentage of participants identified as frail (3–5 points of 5 on the FRAIL scale), prefrail (1–2 points), and nonfrail (0 points) via the FRAIL scale.⁷

Primary and secondary outcomes were also extracted via standardized forms. The primary outcome was mortality, with no restrictions placed on the time frame. The secondary outcomes included postoperative complications, postoperative delirium, LOS, and functional recovery. Postoperative complications included cardiovascular, respiratory, infectious, and renal failure after surgery. Delirium was described by validated assessment tools such as the confusion assessment method (CAM) after surgery. Functional recovery was defined as any improvement in condition after surgery via improvement in physical function or returning to preoperative levels of activities of daily living (ADLs). LOS included any time measurement from surgery to discharge.

Risk of Bias Assessment

Two authors (S.G. and D.Q.) independently used the quality in prognosis studies (QUIPS) tool recommended by the Cochrane prognosis methods group to assess risk of bias.¹⁴ Disagreements were resolved by a third author (J.W.). A standardized form was used to rate each study, with various items clustered to 6 domains. Each domain scored bias as high, moderate, or low. The following domains were scored: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting.

Data Synthesis

For the meta-analyses, studies were pooled according to the outcome assessed if ≥ 3 studies identified the same health outcome. All outcomes were binary, and study populations were stratified as either frail (score of 3-5) or nonfrail. Scores of 0 (nonfrail) and 1 to 2 (prefrail) were considered nonfrail. Odds ratios (ORs) for frail versus nonfrail patients were calculated if not reported in the primary studies. The estimated results were graphically represented as forest plots. When ORs were not available, raw data were used to calculate the OR and the 95% confidence interval (CI). ORs were calculated using a specific calculator for studies with 0 events in the exposed or unexposed group, for which a constant of 0.5 was added to all cells.¹⁵ Random-effects estimates with compound symmetry covariance structures were produced due to the likelihood of high heterogeneity across the studies. The included studies were not stratified via surgery type and setting (emergency versus elective). Heterogeneity due to variation across the studies was assessed using the I² statistic, for which high heterogeneity was noted when the I² statistic was >75%. The meta-analysis evaluated the ORs for outcomes of interest. Statistical significance was considered when the *P* value was <.05. Data analysis was performed with R software using the packages meta and metafor.¹⁶⁻¹⁸

Confidence in Cumulative Evidence

The final results were summarized into a Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence profile.^{19,20} The quality of evidence was assessed across the domains of risk of bias, consistency, directness, precision, and publication bias. The overall quality was rated as 1 of the 4 following levels of evidence: high (additional research

is very unlikely to change our confidence in the estimated effect), moderate (additional research is likely to have an important impact on our confidence in the estimated effect and may change the estimate), low (additional research is very likely to have an important impact on our confidence in the estimated effect and is likely to change the estimate), or very low (very uncertain about the estimated effect).

RESULTS

A total of 18 studies with 4479 participants^{21–38} were included after screening 7800 citations and 85 fulltext articles (Figure 1). An additional 4 studies were found to match our inclusion and exclusion criteria³⁹⁻⁴²; however, they were missing necessary data for our analysis (ie, percent frail)³⁹⁻⁴¹ or used the same population as a previously published study.42 Authors were contacted for additional data, and studies were excluded if authors did not respond or provide the additional data. All were observational studies with 16 prospective²³⁻³⁸ and 2 retrospective cohort studies (Table 1).^{21,22} The sample size varied from 58 to 672. The mean age was 74.8 years (6.54), and 49.48% were male. Five studies were from Spain,^{23–25,35,38} 8 were from the United States,^{21,26–31,36} and other studies were from China,^{32,37} Canada,³⁴ Poland,³³ and Italy.²² The common types of surgery were abdominal,^{23,24,26,32} cardiac,^{25,33,35} and spinal.^{28,29} Fifteen studies were elective, and 4 were emergency surgeries.^{21,23,24,30} The total prevalence of frailty as measured by the FRAIL score (>2) across the 18 studies was 30% (95% CI, 0.29–0.32).

Mortality

Mortality was assessed in 11 studies (n= 3001), with 5 reporting 30-day mortality,^{21–23,32,35} 2 reporting 90-day mortality,^{32,36} 3 reporting 6-month mortality,^{25,35,38} and 3 reporting 1-year mortality (Table 2).^{27,30,35} Five studies (n = 2084) were pooled for 30-day mortality, and greater frailty was significantly associated with mortality outcomes (OR, 6.62 [95% CI, 2.80–15.61]; *P* < .01; I² = 39.5%; Figure 2A).^{21–23,32,35} Greater frailty at 6 months in 3 studies (n = 437) was also significantly associated with mortality, 3 studies (n = 486) were pooled, and frailty based on the FRAIL scale was nonsignificantly associated with an OR of 1.54 (95% CI, 0.91–2.58; *P* = .11; I² = 0%; Figure 2C).^{27,30,35}

Postoperative Complications

Postoperative complications were reported in 6 studies (n = 1403), with all studies indicating greater risk of postoperative complications for patients who were assessed to be frail.^{21–23,25,35,37} We reported postoperative complications as defined by the primary study. Primary studies defined postoperative complications

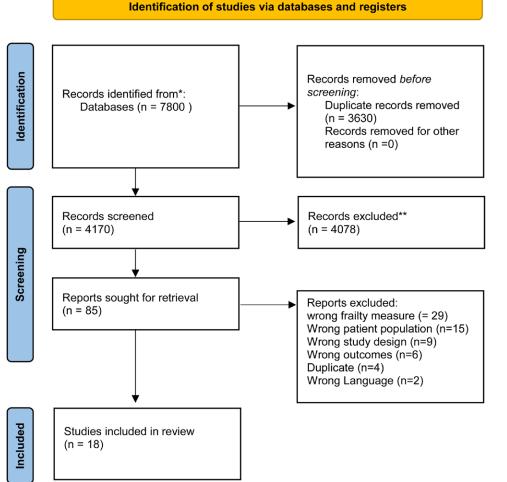


Figure 1. PRISMA flowchart of included studies. PRISMA indicates Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

differently. Studies used the Clavien-Dindo classification, or they defined complications as one morbidity or a collection of morbidities relating to respiratory, renal, vascular, or neurological complications. Metaanalysis of 6 studies (n = 1403) showed an OR of 3.110 (95% CI, 2.06–4.68; P < .01; $I^2 = 26.8\%$) for frail participants compared to nonfrail participants (Figure 3A).^{21–23,25,35,37}

Length of Stay

LOS was reported in 2 studies (n = 281).^{31,33} One study found that frail patients were more likely to experience longer LOS.³¹ The proportion of patients who remained hospitalized after elective abdominal surgery at 90-day follow-up was higher in frail versus nonfrail patients (23.1% vs 1.0%; P < .001).³¹ Another study found that the FRAIL scale was not significantly associated with hospital LOS in patients undergoing elective joint replacement.³³

Functional Outcomes

Two studies (n = 328) assessed functional outcomes through composite functional status scores using ADLs and IADLs.^{27,29} One study found that 66.7% of

frail patients had recovered to their functional baseline at 3 months after surgery compared to 76.9% of robust patients.²⁹ Two studies (n = 616) assessed the risk of falls.^{25,29} One study found the FRAIL scale to have the highest specificity (90%), but the lowest sensitivity (29.2%) in predicting falls compared to the Clinical Frailty Scale (CFS) and trauma-specific frailty index. Higher frailty rating was associated with increased odds of a fall.³⁰ Another study found both frail (25.9%) and prefrail (26.9%) participants to have higher odds of a fall compared to nonfrail participants (13.4%).²⁶ Results for functional outcomes were not pooled due to the heterogeneity of the outcomes.

Postoperative Delirium and Cognitive Recovery

Four studies (n = 1390) showed that frail patients had a greater likelihood to develop postoperative delirium,^{24,28,31,36} and one study found cognitive recovery to be inversely correlated with frailty²⁸ (Supplemental Digital Content 2, Table 1, http://links.lww.com/ AA/E94). All included studies used the CAM or variations of the CAM to assess delirium. Cognitive recovery was measured as part of the postoperative quality of recovery scale and was not included in the

Table 1. Summary Table of Included Studies	ed Studies							
Study, year, country	Study design	z	Age	% Male	Type of surgery	Urgency of surgery Comparators used	Comparators used	% Frail (FRAIL scale)
Arteaga et al, ²³ 2020, Spain	Prospective cohort	92	78.7 (6.3)	46.7	Abdominal	Emergency	CFS, TRST, SHARE-FI	14.1
Berastegui Garcia et al, ³⁷ 2020, Spain	Prospective cohort	200	78.2 (4.6)	56	Aortic valve	Elective	N/A	18.5
Chen, ³⁷ 2021, China	Prospective cohort	229	71.2 (4.8)	61.7	Pulmonary resections	Elective	N/A	28.2
Duchnowski et al, ³³ 2020, Poland	Prospective cohort	672	64 (12)	57	Cardiac valve	Elective	N/A	3.27
Gleason et al, ²¹ 2017, United States	Retrospective cohort	175	82.3 (7.4)	25.1	Orthopedic trauma	Emergency	N/A	41.7
Hosler et al, ²⁷ 2019, United States SAVR	Prospective cohort	91	77.8 (5.3)	56	SAVR	Elective	CFS	40.1
Hosler et al, ²⁷ 2019, United States TAVR	Prospective cohort	137	84.5 (5.8)	48.2	TAVR	Elective	CFS	42.3
Mahanna-Gabrielli et al, ³¹ 2020, United States	Prospective cohort	167	70ª	44.9	Major noncardiac	Elective	N/A	18.6
Miguelena-Hycka et al, ²⁵ 2019, Spain	Prospective cohort	120	76.6 (4.2)	75.8	Cardiac	Elective	Fried frailty scale, CFS	12.4
Pedemonte et al, 36 2021, United States	Prospective cohort	558	80.16 (7.49)	29.6	Orthopedic	Elective	N/A	22.6
Rothrock et al, ²⁹ 2019, United States	Prospective cohort	100	71 (4.0)	63	Spinal	Elective	N/A	18
Sanchez, 2020, Spain	Prospective cohort	446	78ª	44.4	Abdominal	Emergency	N/A	13.2
Sokas et al, 26 2020, United States	Prospective cohort	230	70.1 (7.1)	47.6	Abdominal	Elective	N/A	22.2
Susano et al, ²⁸ 2020, United States	Prospective cohort	219	75ª	57	Spinal	Elective	N/A	24
Tejiram et al, ³⁰ 2021, United States	Prospective cohort	58	74ª	48.2	Trauma	Emergency	CFS, FI	18.5
Torrez-Perez, ³⁸ 2021, Spain	Prospective cohort	117	58.9 (13.9)	50.4	Brain tumor	Elective	Tillburg frailty scale	18.8
Valdatta et al, ²² 2019, Italy	Retrospective cohort	587	80.3ª	58.4	nonmelanoma skin cancer	Elective	N/A	63.7
Wang et al, ³⁴ 2018, Canada	Prospective cohort	87	72.0 (9.0)ª	34.5	Total joint replacement	Elective	CFS,	22.9
Yin, ³² 2020, China	Prospective cohort	194	79 (14) ^a	46.4	Abdominal	Elective	CFS, FI	43.8
Abbreviations: CFS, Clinical Frailty Scale; FI, frailty index; FRAIL, fatigue, resistance, ambulation, illness, and loss of weight; IQR, interquartile range; SAVR, surgical aortic valve replacement; SD, standard deviation; SHARE-FI, Survey of Health, Ageing and Retirement in Europe frailty instrument; TAVR, transcatheter aortic valve replacement; TRST, Triage Risk Screening Tool.	Ity index; FRAIL, fatigue, ri ent in Europe frailty instru	esistance, aı ment; TAVR,	nbulation, illness transcatheter ao	s, and los: rtic valve i	s of weight; IQR, interquartile r replacement; TRST, Triage Risk	ange; SAVR, surgical a Screening Tool.	aortic valve replacement; \$	SD, standard deviation;

pooled results for delirium. Meta-analysis of 4 studies found that the FRAIL scale was associated with post-operative delirium (OR, 2.65 [95% CI, 1.85–3.80; P < .01; $I^2 = 0\%$]; Figure 3B).^{24,28,31,36}

Nonhome Discharge

Two studies (n = 317) reporting nonhome discharge had conflicting correlations with frailty.^{26,34} One study measured discharge to a tertiary care facility (ie, rehabilitation facility and long-term acute care facility), and found frail patients significantly more likely to have a nonhome discharge after abdominal surgery.²⁶ On the contrary, another study found nonhome discharge was not correlated with frailty after joint replacement surgery.³⁴

Risk of Bias

Using the QUIPS tool, risk of bias was assessed to be low in 16 studies and moderate in 2 studies (Supplemental Digital Content 3, Table 2, http://links. lww.com/AA/E95).^{22,34} No studies had a high risk of bias. All studies except 318,19,31 had adequate adjustments for study confounding. The domain study attrition was found to have high/moderate risk of bias compared to other categories. Reasons for high risk of study attrition bias were due to the lack of information for outcomes, prognostic factor information, and potential impact of subjects for those lost to followup. The quality of the evidence as assessed by the GRADE tool (Supplemental Digital Content 4, Table 3, http://links.lww.com/AA/E96) was very low to moderate, with 5 articles being very low,^{22,24,29,34,36} 10 being low,^{21,25,27,29–35,37} and 3 being moderate.^{23,26,28}

DISCUSSION

^aMean age (SD) unavailable; median age (IQR) presented if possible

In this SRMA of 18 studies with 4479 patients utilizing the FRAIL scale, we found that frailty assessed with the FRAIL scale was associated with a 6.62-fold and 2.97-fold increased odds of mortality at 30 days and 6 months after surgery, respectively, compared to nonfrail patients. Frailty as assessed by the FRAIL scale was also associated with increased risk for postoperative complications and delirium in older surgical patients. Our findings suggest that the FRAIL scale is useful to identify surgical patients who are at higher risk for postoperative mortality at 30 days and 6 months, as well as complications and delirium.

Many screening tools have been developed to assess risk and level of frailty in the general population.⁴³ The FRAIL scale has been used in community settings since 2012. However, the first study using the FRAIL scale in surgical patients was identified in 2017.²¹ Our findings regarding frailty and its association with greater risk for negative surgical outcomes are consistent with studies using the FRAIL scale in the community. In middle-aged women, frailty as identified with the FRAIL scale was correlated with increased

Table 2. Mortality Outco	Table 2. Mortality Outcomes of Studies That Reported Mortality											
Study, year	% Frail	% Prefrail	30-d Mortality	90-d Mortality	6-mo Mortality	1-y Mortality						
Arteaga et al, ²³ 2020	14.1	NR	OR, 16.07 (3.65-70.85)	NR	NR	NR						
Berastegui Garcia et al,37 2020	18.5	67.5	NR	NR	OR, 2.44	OR, 1.34						
					(1.18-5.04)	(0.64-2.81)						
Duchnowski et al, ³³ 2020	3.27	9	OR, 2.802 (1.28-6.16)	NR	NR	NR						
Gleason et al, ²¹ 20172017	41.7	41.7	OR, 5.90 (0.65–53.50)	NR	NR	NR						
Hosler et al, ²⁷ SAVR 2019	40.1	NR	NR	NR	NR	OR, 1.42						
						(0.13-17.07)						
Hosler et al, ²⁷ TAVR 2019	42.3	NR	NR	NR	NR	OR, 1.79						
						(0.77-4.13)						
Miguelena-Hycka et al, ²⁵ 2019	12.4	64	NR	NR	OR, 1.47	NR						
					(0.29–7.35)							
Pedemonte et al, ³⁶ 2021	22.6	38.9	OR, 8.59 (2.24–32.89)	OR, 7.26 (2.89–18.25)	NR	NR						
Tejiram et al, ³⁰ 2021	18.5	NR	NR	NR	NR	OR, 1.75						
						(0.20 - 10.58)						
Torrez-Perez, ³⁸ 2021,	18.8	NR	NR	NR	5.76	NR						
					(2.05-16.22)							
Valdatta et al, ²² 2019	63.7	29	OR, 19.70 (1.18-329.28)	NR	OR, 19.70	NR						
					(1.18-329.28)							
Yin, ³² 2020	43.8	34	NR	OR, 2.01 (1.28-3.17)	NR	NR						
Abbreviations: NR, not reported; (replacement.	OR, odds	ratio (with 9	5% confidence interval); SAV	R, surgical aortic valve rep	placement; TAVR, transca	theter aortic valve						

likelihood of disability, death, and depression.⁹ When the FRAIL scale was used as a diagnostic screening tool for frailty in community-dwelling adults, frailty was significantly associated with mortality.¹⁰ Our results are also consistent with a recent systematic review showing that various frailty screening tools were associated with postoperative mortality, complications, and postoperative delirium.³ In our SRMA, the studies reported mortality at different time points ranging from 30 days to 1 year after surgery. The lack of association of frailty with mortality at 1 year may be due to the relatively small numbers of patients in the studies reporting mortality at 1 year.^{27,30,35} Frail patients had a 2.5-fold increased risk of postoperative complications such as cardiovascular, respiratory, infectious, and renal failure, and a 2.4-fold higher risk of postoperative delirium than nonfrail patients. This increased risk of experiencing postoperative delirium for participants classified as frail by the FRAIL scale is consistent with the increased risk for participants classified as frail by the Edmonton Frailty scale or Fried Phenotype.44

In our SRMA, the prevalence of frailty in the surgical population was 30%, which is higher than in community-dwelling populations.^{7,9} The higher prevalence may be due to the higher age or more comorbidities in the surgical population. Four studies reported a greater percentage of frail participants, 40.1% to 63.7%, likely due to the high mean age (80.8 years; SD 1.84) of participants in these studies.^{21,22,27,32} These studies included different types of surgery, with 3 elective surgeries^{22,27,32} and 1 emergency surgery.²¹

Several medical societies recommend that frailty be assessed routinely before surgery in older adults.^{45,46} However, screening for frailty is currently not performed as part of routine preoperative assessments.⁴⁶ Screening for frailty may not be performed due to barriers such as a lack of time to administer and score lengthy assessments in preoperative clinics, and reliance on an administrator for assessments. The longer assessments, such as the Fried Phenotype,⁵ frailty index,⁸ or comprehensive geriatric assessment (CGA),⁴⁶ are useful for long-term health management of older patients but are not feasible in busy preoperative clinics. As well, most screening tools for frailty, including brief tools such as the CFS, require in-person administration.⁴⁷⁻⁴⁹ Of the studies included in the review, 2 studies used self-reported questionnaires to report frailty.^{26,31} These 2 studies did not report any patients to be unable to complete the questionnaire on their own. All other studies had clinicians, researchers, or other health care professionals administering the questions to the patients and did not report specific dropout due to difficulty completing the frailty assessment. Most of the studies did not report the time needed to complete the FRAIL scale. One study reported the administration of the survey to take <2 minutes.24 An online version of the FRAIL scale was found to be valid for identifying frailty in older adults in community settings.⁵⁰ The practicality of the 5-item FRAIL scale, especially as a telehealth or self-administered frailty assessment, is a huge asset, especially when standard in-person frailty assessments are not possible. The items assessed by the FRAIL scale are simple to answer, but they are subjective, being based on the participants' judgment of their ability. Other objective components of frailty instruments, such as grip strength⁵ or ability to rise from a chair,⁵¹ are less likely to incur response bias, but do require equipment, face-to-face administration, or video to assess.

Α

Author(s) and Year	N	% frail	% non-frail					OR [95% CI]
Arteaga 2020	92	14.1	85.9		1.0			16.07 [3.65, 70.84]
Duchnowski 2020	672	3.27	96.73			•		2.80 [1.28, 6.16]
Gleason 2017	175	41.7	58.3		-i			5.90 [0.65, 53.50]
Valdatta 2019	587	63.7	36.3				•	19.70 [1.18, 329.28]
Pedemonte 2021	558	22.6	77.4					8.59 [2.24, 32.89]
Random effects mode (Q=6.00,p< .01,I ² =39		0.36)						6.62 [2.80, 15.61]
							1	
				0.14	1	7.39	54.6	403.43
					Ob	served Outo	ome	

В

Author(s) and Year	Ν	% frail	% non-frail							OR [95% CI]
Berastegui Garcia 2020	200	18.5	81.5			-		-		2.44 [1.18, 5.04]
Miguelena-Hycka 2019	120	12.4	87.6		,					1.47 [0.29, 7.35]
Torrez-Perez 2021	117	18.8	81.2					•	-	5.76 [2.05, 16.22]
Random effects model (Q=2.59,p< .01,I ² =20.0%,ti	au²=0.07)							_		2.97 [1.54, 5.72]
					-		1	1	_	
				0.14	0.37	1	2.72	7.39	20.09	
					Ot	serve	d Outcor	me		

С

Author(s) and Year	N	% frail	% non-frail								OR [95% CI]
Berastegui Garcia 2020	200	18.5	81.5				4	<u> </u>			1.34 [0.64, 2.81]
Hosler 2019	91	40.1	59.9								1.42 [0.12, 17.07]
Hosler 2019	137	42.3	57.7					-			1.79 [0.78, 4.13]
Tejiram 2021	58	18.5	81.5				-	•			1.75 [0.29, 10.58]
Random effects model (Q=0.28,p= 0.11,I ² =0.0%	,tau ^z =0.0	00)						_			1.54 [0.91, 2.58]
8 D 1/80 0 1					-	1	t	-	1		
				0.05	0.14	0.37	1	2.72	7.39	20.09	
						Obsen	ved O	utcome			

Figure 2. Forest plots of association of frailty with mortality outcomes at 30 d, 6 mo, and 1 y after surgery. A, Association of frailty with 30-d mortality. B, Association of frailty with 6-mo mortality. C, Association of frailty with 1-y mortality. Cl indicates confidence interval; OR, odds ratio.

Similar to other frailty assessments that evaluate physical ability, the FRAIL scale has limitations for assessing patients with physical disabilities or trouble with walking.

LIMITATIONS

This SRMA has some limitations. There was significant heterogeneity in the clinical outcomes reported, preventing us from pooling all of the studies to perform meta-analyses on all outcomes. For example, mortality was reported at different time points ranging from 30 days to 1 year. Therefore, we were only able to conduct a meta-analysis for the studies reporting similar time points. As well, various tools and measures were used to assess functional recovery, LOS, and postoperative complications. We reported postoperative complications as defined by the primary study. Primary studies defined postoperative

A Author(s) and Year	Ν	% frail	% non-frail							OR [95% C]
Arteaga 2020	92	14.1	85.9			·	•	•		5.92 [1.71,	20.50]
Berastegui Garcia 2020	200	18.5	81.5		-					2.02 [0.98,	4.17]
Gleason 2017	175	41.7	58.3		÷					2.03 [1.07,	3.86]
Miguelena-Hycka 2019	120	12.4	87.6		÷					3.11 [1.36,	7.13]
Valdatta 2019	587	63.7	36.3		÷				<u> </u>	9.70 [1.18, 3	329.28]
Chen 2021	229	28.2	71.8				H			4.65 [2.44,	8.87]
Random effects model (Q=7.20,p< .01,I ² =26.8%	6.tau²=0).07)				-				3.11 [2.06,	4.68]
(-,	,			— i						
				0.14	1		7.39	54.6	403.43	;	
					(Observ	ed Outco	ome			

Author(s) and Year	Ν	% frail	% non-frail		OR [95% CI]
Mahanna-Gabrielli 2020	167	18.6	81.4		2.28 [0.96, 5.44]
Sanchez 2020	446	13.2	86.8	· · · · · · · · ·	1.30 [0.52, 3.30]
Susano 2020	219	24	76	·	3.72 [1.90, 7.28]
Pedemonte 2021	558	22.6	77.4	-	2.91 [1.63, 5.18]
Random effects model (Q=3.44,p< .01,I ² =0.0%,tau	u²=0.00)			_	2.65 [1.85, 3.80]
	,				
				0.37 1 2.72 7.39	

Observed Outcome

Figure 3. Forest plots of association of frailty with other postoperative outcomes. A, Association of frailty with postoperative complications (all causes). B, Association of frailty with postoperative delirium. Cl indicates confidence interval; OR, odds ratio.

complications differently, and this is a limitation of the study. While the cumulative quality of evidence as assessed by the GRADE tool was low, this may be due to the types of studies included. There were no randomized, controlled trials, and all studies were observational, which is considered low quality of evidence.

CONCLUSIONS

We found frailty as measured by the FRAIL scale to be associated with greater mortality at 30 days and 6 months, as well as increased postoperative complications and postoperative delirium. The FRAIL scale may be a useful tool to screen older surgical patients for frailty. Future studies investigating whether the FRAIL scale is a feasible screening tool for assessing frailty in older surgical patients with telehealth or virtual assessments should be considered.

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DISCLOSURES

Name: Selena Gong, BhSc.

Contribution: This author helped with study conceptualization, investigation, data synthesis, writing the original draft, and reviewing and editing the manuscript. **Conflicts of Interest:** None. Name: Dorothy Qian, BhSc.

Contribution: This author helped with investigation, data synthesis, and writing the original draft of the manuscript.

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Name: Sheila Riazi, MD, FRCPC.

Contribution: This author helped with reviewing and editing the manuscript.

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Name: Frances Chung, MD, FRCPC.

Contribution: This author helped with data interpretation, and writing, reviewing, and editing the manuscript.

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Name: Marina Englesakis, MLIS.

Contribution: This author helped with the literature search and reviewing and editing the manuscript.

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Name: Qixuan Li, MSc.

Contribution: This author helped with analysis and reviewing and editing the manuscript.

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Name: Ella Huszti, PhD.

Contribution: This author helped with analysis and reviewing and editing the manuscript.

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Name: Jean Wong, MD, FRCPC.

Contribution: This author helped with study conceptualization, data interpretation, supervision, writing the original draft, and reviewing and editing the manuscript.

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REFERENCES

- 1. Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med.* 2011;27:1–15.
- Lin HS, Watts JN, Peel NM, Hubbard RE. Frailty and postoperative outcomes in older surgical patients: a systematic review. *BMC Geriatr.* 2016;16:157.
- 3. Aucoin SD, Hao M, Sohi R, et al. Accuracy and feasibility of clinically applied frailty instruments before surgery: a systematic review and meta-analysis. *Anesthesiology*. 2020;133:78–95.
- Abellan VG, Rolland Y, Bergman H, Morley JE, Kritchevsky SB, Vellas B. The I.A.N.A task force on frailty assessment of older people in clinical practice. *J Nutr Health Aging*. 2008;12:29–37.
- 5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146–M156.
- 6. Abellan VG, Rolland YM, Morley JE, Vellas B. Frailty: toward a clinical definition. *J Am Med Dir Assoc.* 2008;9:71–72.
- Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging. 2012;16:601–608.
- 8. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007;627:722–727.
- 9. Susanto M, Hubbard RE, Gardiner PA. Validity and responsiveness of the FRAIL scale in middle-aged women. *J Am Med Dir Assoc.* 2018;19:65–69.
- Thompson MQ, Theou O, Tucker GR, Adams RJ, Visvanathan R. FRAIL scale: predictive validity and diagnostic test accuracy. *Australas J Ageing*. 2020;39:e529–e536.
- Lopez D, Flicker L, Dobson A. Validation of the FRAIL scale in a cohort of older Australian women. J Am Geriatr Soc. 2012;60:171–173.
- Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. The Cochrane Collaboration; 2011. Accessed March 1, 2021. http://handbook-5-1.cochrane.org
- 13. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.
- Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med.* 2013;158:280–286.
- 15. MedCalc Software Ltd. Odds ratio calculator. Version 20.110. Accessed June 29, 2022. https://www.medcalc.org/calc/odds_ratio.php.
- R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing; 2020. Accessed January 11, 2022. https://www.R-project.org/.
- 17. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health*. 2019;22:153–160.
- 18. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Software*. 2010;36:1–48.
- Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines:
 Introduction–GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64:383–394.
- Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64:401–406.

- Gleason LJ, Benton EA, Alvarez-Nebreda ML, Weaver MJ, Harris MB, Javedan H. FRAIL questionnaire screening tool and short-term outcomes in geriatric fracture patients. *J Am Med Dir Assoc.* 2017;18:1082–1086.
- Valdatta L, Perletti G, Maggiulli F, Tamborini F, Pellegatta I, Cherubino M. FRAIL scale as a predictor of complications and mortality in older patients undergoing reconstructive surgery for non-melanoma skin cancer. *Oncol Lett.* 2019;17:263–269.
- 23. Arteaga AS, Aguilar LT, González JT, et al. Impact of frailty in surgical emergencies. A comparison of four frailty scales. *Eur J Trauma Emerg Surg*. 2020;47:1613–1619.
- Acedo PS, Córdoba IE, Ripa CZ, Cabezón JH, Castilla AT. Prospective study of factors associated with postoperative delirium after urgent abdominal surgery. *Cir Esp (Engl Ed)*. 2020;98:450–455.
- Miguelena-Hycka J, Lopez-Menendez J, Prada PC, et al. Influence of preoperative frailty on health-related quality of life after cardiac surgery. *Ann Thorac Surg.* 2019;108:23–29.
- Sokas CM, Cowan J, Dalton MK, et al. Association between patient-reported frailty and non-home discharge among older adults undergoing surgery. J Am Geriatr Soc. 2020;68:2909–2913.
- Hosler QP, Maltagliati AJ, Shi SM, et al. A Practical twostage frailty assessment for older adults undergoing aortic valve replacement. J Am Geriatr Soc. 2019;67:2031–2037.
- Susano MJ, Grasfield RH, Friese M, et al. Brief preoperative screening for frailty and cognitive impairment predicts delirium after spine surgery. *Anesthesiology*. 2020;133:1184–1191.
- 29. Rothrock RJ, Steinberger JM, Badgery H, et al. Frailty status as a predictor of 3-month cognitive and functional recovery following spinal surgery: a prospective pilot study. *Spine J*. 2019;19:104–112.
- 30. Tejiram S, Cartwright J, Taylor SL, et al. A prospective comparison of frailty scores and fall prediction in acutely injured older adults. *J Surg Res.* 2021;257:326–332.
- Mahanna-Gabrielli E, Zhang K, Sieber FE, et al. Frailty is associated with postoperative delirium but not with postoperative cognitive decline in older noncardiac surgery patients. *Anesth Analg.* 2020;130:1516–1523.
- 32. Yin Y, Jiang L, Xue L. Comparison of three frailty measures for 90-day outcomes of elderly patients undergoing elective abdominal surgery. *ANZ J Surg.* 2021;91:335–340.
- Duchnowski P, Szymański P, Kuśmierczyk M, Hryniewiecki T. Usefulness of FRAIL scale in heart valve diseases. *Clin Interv Aging*. 2020;15:1071–1075.
- 34. Wang HT, Fafard J, Ahern S, Vendittoli PA, Hebert P. Frailty as a predictor of hospital length of stay after elective total joint replacements in elderly patients. *BMC Musculoskelet Disord*. 2018;19:14.
- 35. Berastegui Garcia E, Camara Rosell ML, Moret Ruiz E, et al. The impact of frailty in aortic valve surgery. *BMC Geriatr*. 2020;20:426.
- 36. Pedemonte JC, Sun H, Franco-Garcia E, et al. Postoperative delirium mediates 180-day mortality in orthopaedic trauma patients. *Br J Anaesth*. 2021;127:102–109.
- 37. Berastegui Garcia E, Camara Rosell ML, Moret Ruiz E, et al. The impact of frailty in aortic valve surgery. *BMC Geriatr*. 2020;20:426.
- Torres-Perez P, Álvarez-Satta M, Arrazola M, et al. Frailty is associated with mortality in brain tumor patients. *Am J Cancer Res.* 2021;11:3294–3303.
- Kim DU, Park HK, Lee GH, et al. Central sarcopenia, frailty and comorbidity as predictor of surgical outcome in elderly patients with degenerative spine disease. J Korean Neurosurg Soc. 2021;64:995–1003.

- 40. Yoon SH, Kim BR, Lee SY, et al. Influence of comorbidities on functional outcomes in patients with surgically treated fragility hip fractures: a retrospective cohort study. *BMC Geriatr.* 2021;21:283.
- 41. Sánchez Arteaga A, Tinoco González J, Tallón Aguilar L, et al. Long-term influence of frailty in elderly patients after surgical emergencies. *Eur J Trauma Emerg Surg.* 2021;48:3855–3862.
- 42. Esmaeeli S, Franco-Garcia E, Akeju O, et al. Association of preoperative frailty with postoperative delirium in elderly orthopedic trauma patients. *Aging Clin Exp Res.* 2021;21:625–631.
- 43. Aguayo GA, Donneau AF, Vaillant MT, et al. Agreement between 35 published frailty scores in the general population. *Am J Epidemiol*. 2017;186:420–434.
- Gracie TJ, Caufield-Noll C, Wang NY, Sieber FE. The association of preoperative frailty and postoperative delirium: a meta-analysis. *Anesth Analg.* 2021;133:314–323.
- 45. Alvarez-Nebreda ML, Bentov N, Urman RD, et al. Recommendations for preoperative management of frailty from the society for perioperative assessment and quality improvement (SPAQI). J Clin Anesth. 2018;47:33–42.

- 46. Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg.* 2012;215:453–466.
- 47. Eamer G, Gibson JA, Gillis C, et al. Surgical frailty assessment: a missed opportunity. *BMC Anesthesiol*. 2017;17:99.
- Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. J Am Geriatr Soc. 2004;52:1929–1933.
- Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173:489–495.
- 50. Yu R, Tong C, Leung G, Woo J. Assessment of the validity and acceptability of the online FRAIL scale in identifying frailty among older people in community settings. *Maturitas*. 2021;145:18–23.
- 51. Kiely DK, Cupples LA, Lipsitz LA. Validation and comparison of two frailty indexes: the mobilize Boston study. *J Am Geriatr Soc.* 2009;57:1532–1539.

All/most of the time -1

APPENDIX 1. FRAIL SCALE

Fatigue	Are you fatigued?	Some/a little/none of the = time = 0
Resistance	Do you have difficulty walking up one flight of stairs without assistance?	Yes = $1/No = 0$
Ambulatory	Do you have difficulty walking 1 block without assistance?	Yes = 1/No = 0
/Ilness	Do you have more than 5 illnesses (confirm with doctor or medical records)?	Yes = 1/No = 0
Loss of Weight	Have you lost more than 5% of your weight in the past year?	Yes = 1/No = 0

Scoring: robust (score = 0), prefrail (score = 1-2), and frail (score = 3-5).

Adapted with permission from Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle-aged African Americans. J Nutr Health Aging. 2012;16:601–608.