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SYSTEMATIC REVIEW

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Unraveling the impact of frailty on postoperative delirium in elderly surgical patients: a systematic review and meta-analysis

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Abstract

Background Frailty has been consistently implicated as a pivotal factor in the onset of delirium following anesthesia and surgery. Nonetheless, a comprehensive understanding of the relationship between frailty and delirium remains to be elucidated. This study addresses that knowledge gap.

Methods A comprehensive search of literature databases identified 43 relevant studies involving 14,441 participants. The studies were subjected to a rigorous quality assessment using the Newcastle-Ottawa Scale. Statistical analysis was conducted using Review Manager (*v*5.4.1), including subgroup and sensitivity analyses.

Results Meta-analysis revealed a significant association between preoperative physical frailty and postoperative delirium (pooled odds ratio: 2.47; 95% confidence interval: 2.04–2.99; $I^2 = 46.7\%$). The baseline frailty rate was 34.0% (4,910/14,441), while the overall incidence of postoperative delirium was 20% (2,783/14,441). Subgroup analyses based on characteristics such as race, frailty-assessment tools, and surgical types were conducted to explore potential sources of heterogeneity. This meta-analysis provided compelling evidence supporting a notable link between preoperative physical frailty and an increased risk of postoperative delirium in older surgical patients. Early identification through frailty screening can enable targeted interventions, potentially enhancing overall management and individualized treatment. Integrating frailty assessment into preoperative evaluation may improve predictive accuracy in surgical planning and anesthesia management.

Conclusions Future research could focus on optimizing the integration of frailty assessment into preoperative protocols for timely intervention and improved patient outcomes.

Trial registration The review protocol was registered with PROSPERO (CRD42023390486), date of registration: Aug 11, 2023.

Keywords Frailty, Delirium, Aged, Elderly, Meta-analysis

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Background

Postoperative delirium (POD) is a critical neurological complication of anesthesia and surgery that can significantly impact patient outcomes [1]. The clinical importance of POD is highlighted by its correlation with major morbidity, encompassing prolonged hospital stays, functional and cognitive decline, nursing home admission, and mortality [2]. With the aging of the population, understanding the factors contributing to POD in vulnerable elderly patients is becoming increasingly vital for effective clinical management.

It is important to differentiate POD from early postoperative cognitive decline (POCD), which represents a closely related diagnosis. POD is most often seen within the first 3 postoperative days [3]. POCD occurs at the end of the first postoperative week, has no effect on consciousness, and may last up to 3 months after surgery [3, 4]. POD is considered a risk factor and strong predictor of POCD development [3].

Our previous research [5], along with other studies [6, 7], has pointed towards frailty as a potential factor influencing the occurrence of POD. Frailty, which is characterized by increased vulnerability and reduced physiological reserve, may play a pivotal role in the development of POD in elderly surgical patients [6, 8]. However, existing studies exhibit inconsistencies in terms of sample sizes, population characteristics, and study designs, which hinder a comprehensive understanding of the frailty-delirium relationship [9–13].

Our study provides a timely and comprehensive analysis of the effect of frailty on delirium in older surgical patients, filling a gap in the literature and offering valuable insights into this critical topic. The importance of this research is underscored by the increasing number of older surgical patients due to population aging and by the high risk of severe outcomes, including death and disease progression, due to the co-occurrence of frailty and delirium in this special population [10, 12, 14, 15]. Our meta-analysis addresses research gaps by focusing on the impact of frailty on POD in elderly surgical patients, and aims to offer evidence-based insights to inform clinical practice and improve care for this vulnerable group.

Methods

The current systematic review and meta-analysis was conducted and reported following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 guidelines [16]. The review protocol was registered with PROSPERO (CRD42023390486).

Search strategy

A systematic literature search was performed in PubMed, EMBASE, Web of Science, and the Cochrane Library from the inception of the databases until June 29, 2024. To ensure the comprehensiveness of the literature retrieval, we manually searched references, citations, and other relevant articles from the authors of the studies that were initially retrieved. Free terms and subject terms were used as search terms, combined with Boolean conjunctions (OR/AND). No language restrictions were imposed. The details of the search strategy are as follows:

Frailty (MeSH) OR Frail OR Frailty syndrome OR Frail elderly OR Frailties OR Frailness OR Debility OR Debilities OR Sarcopenia OR Muscle wasting

AND

Delirium (MeSH) OR Perioperative neurocognitive disorder OR Postoperative delirium OR Postoperative cognitive dysfunction OR Delayed cognitive recovery OR Postoperative neurocognitive dysfunction OR Mild cognitive impairment OR Pre-existing cognitive impairment OR Preoperative cognitive impairment OR Neurocognitive impairment OR Cerebral dysfunction OR Cognitive decline OR Neurological complications OR Delirious OR POD OR Deliri* OR Acute confusional syndrome OR Acute confusional AND Aged (MeSH) OR Elderly OR Elder OR Older adults OR Functionally-impaired elderly OR Functionally-impaired.

Eligibility criteria

Full-text articles published in peer-reviewed journals were eligible. If multiple studies used the same cohort, the study with the longest follow-up period or the largest sample size was included in the meta-analysis. The inclusion criteria were based on the PICO process, as outlined below.

(1) **Population**: Patients over 60 years who were undergoing surgery and did not have neurocognitive disorder at the baseline.
(2) **Intervention**: Assessment of frailty before surgery using common, validated, and recognized criteria. Frailty is characterized by a state of vulnerability and poor homeostatic capacity to respond to stressors due to cumulative physiological decline, resulting in poorer health outcomes [17]. Various frailty-assessment tools, including the frailty phenotype [18], deficit-accumulation frailty index (FI) [19] Clinical Frailty Scale (CFS) [20], and Edmonton Frail Scale (EFS) [21], have been used in acute settings.
(3) **Comparison**: Preoperative non-frailty.
(4) **Outcomes**: The incidence of POD, diagnosed based on established criteria, such as the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) or the Confusion Assessment Method (CAM) [22, 23].
(5) **Study design**: Prospective or retrospective cohort study.

Exclusion criteria

(1) Randomized controlled trials, observational case-control studies, systematic reviews, review articles, and case series.
(2) Non-English language articles.
(3) Animal studies, editorials, commentary, letters, book chapters, and conference proceedings.
(4) Studies with data on outcome indicators that could not be extracted.

Study selection

Efforts were made to comprehensively include all studies published to date on the association between frailty and POD. To identify eligible studies, we first searched several electronic databases since their inception for articles exploring frailty and delirium, by utilizing various combinations of Medical Subject Headings (MeSH) and non-MeSH terms. The search process was then complemented by: (i) reviewing the reference sections of all relevant studies, (ii) manually searching key journals and abstracts from major annual meetings in the field of delirium, and (iii) reaching out to experts.

The initial database search was independently conducted by 2 researchers (HW, SY), and any discrepancies were resolved through consultation with an investigator not involved in the initial search (HZ). The 2 researchers then independently screened the retrieved literature and extracted and cross-checked data according to predetermined criteria. In the event of disagreements, resolutions were achieved through discussion or consultation with a third researcher. Literature screening involved the removal of duplicates and a review of the titles and abstracts of the remaining studies. Following the exclusion of evidently irrelevant literature, a thorough examination of the full text determined whether a given study was included. The following data were extracted from the retrieved studies: author, year of publication, region, population source, number of men/women, mean age, and screening tools for cognitive frailty. If there was a deficiency in the data, attempts were made to communicate with the original study authors to acquire supplementary information.

Data extraction

For document management, EndNote 21 software was utilized, and Excel tables were employed for data extraction.

Statistical analysis

Odds ratios (ORs) with their corresponding 95% confidence intervals (CIs) were used as the general indicator to assess the associations between preoperative physical frailty and POD in older surgical patients. Preoperative physical frailty was considered as a categorical variable, and ORs were calculated by comparing groups with preoperative physical frailty to those without preoperative physical frailty. We performed random-effects models to pool the ORs for the incidence of POD in individual studies in order to compare patients with and without preoperative physical frailty. Heterogeneity among the included studies was assessed using Cochrane's Q test and the I^2 statistic. $I^2 > 50\%$ and $P \leq 0.10$ reflected the presence of significant heterogeneity, in which case, the random-effects model was utilized. Otherwise, a fixed-effects model was used.

Subgroup analyses were used to identify potential sources of heterogeneity as well as characteristics that might strengthen the association between preoperative physical frailty and POD. We conducted subgroup analyses according to frailty-assessment methods (FI vs. Fried vs. Fatigue, Resistance, Ambulation, Illness, and Loss of weight [FRAIL] vs. EFS vs. CFS vs. others), racial groups (Asian vs. non-Asian), and types of surgery (cardiovascular surgery vs. orthopedic surgery vs. abdominal surgery vs. elective surgery). Furthermore, Cochrane's Q test and the I^2 statistic were utilized to test for subgroup differences. The Newcastle-Ottawa Scale (NOS) was used to assess the methodological quality of the included studies. This scale is based on selection, comparability, and outcome or exposure criteria, and has a maximum score of 9. Studies with NOS scores of 7 or more were considered to be of high quality and have a low risk of bias. Two researchers (HW, SY) independently conducted NOS scoring, and any discrepancies were resolved through consultation with an investigator not involved in the initial assessment (HZ). Sensitivity analysis involved systematically excluding one study at a time to assess result stability. Funnel plots were generated to visualize potential publication bias, and the Egger test was used to assess the asymmetry of the funnel plot.

Meta-analysis was conducted using Review Manager (RevMan; version 5.4.1) software and R (version 4.3.3) software. $P < 0.05$ was considered statistically significant for a two-tailed test throughout the analyses.

Results

Study selection

Through a comprehensive search of the 4 electronic databases, we identified 6176 studies. After removing duplicates automatically and manually, we excluded 1181 studies. The titles and abstracts of 4995 studies were screened, after which 122 studies that met the eligibility criteria were retained for a full-text review. Of these 122 studies, 79 studies were excluded due to various reasons: insufficient effect-size information (6 studies), no preoperative frailty assessment (11 studies), no POD assessment (12 studies), no international frailty-assessment tool used (9 studies), no reported international delirium assessment (10 studies), non-full study designs (e.g., letters, comments, reviews, or conference abstracts; 13 studies), and outcomes other than delirium (18 studies). Ultimately, 43 cohort studies (involving 14,441 patients) with adequate methodological quality were identified and included in our review (Fig. 1). The baseline frailty rate was 34.0% (4910 patients), and the overall incidence of POD was 20% (2783 patients). None of the studies had a low NOS score. The NOS results for cohort studies are presented in Supplementary Table 1. According to the NOS scores, the included studies had a high overall quality, with a median NOS score of 7.8 (range: 6–9). The characteristics of the studies included in the meta-analysis are detailed in Table 1 [22–62].

Meta-analysis of the association between preoperative frailty and POS

Of the 14,441 elderly participants included in the selected studies in this systematic review, a total of 4,910 participants (34.0%) were determined to have preoperative frailty. Meta-analyses of the 43 included studies showed evidence of a significant association between preoperative frailty and POS (OR: 2.47; 95% CI: 2.04–2.99; I^2 = 46.7%; Fig. 2).

Subgroup analyses

(1) Frailty-assessment methods

The associations between preoperative frailty and POD in different groups based on frailty-assessment methods are presented in Fig. 3. The most prevalent method was the FI and its related modifications (9 studies [24.4%]), followed by the Fried frailty phenotype and its related modifications (10 studies [19.4%]), FRAIL (5 studies [12.3%]),

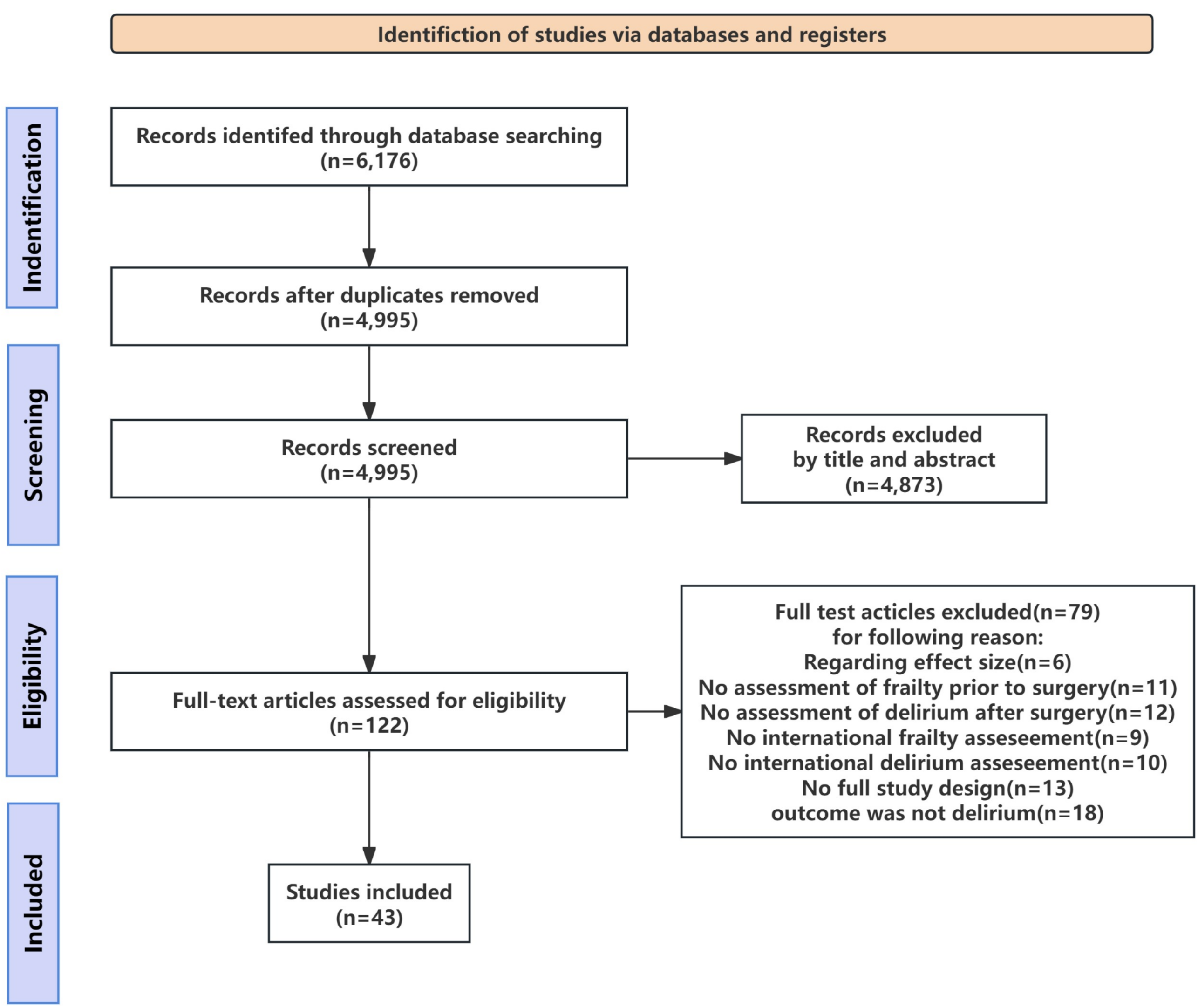

Fig. 1 PRISMA flowchart of included studies. PRISMA, preferred reporting items for systematic reviews and meta-analyses

Table 1 Characteristics of the studies included in the meta-analysis ($n=43$)

Participants	Exposures/interventions		Comparison	Outcome (frailty)		Outcome (non-frailty)	
Author, year Country No. of patients/No. of male patients Age/Age criterion Mean ± SD or median (IQR) age Type of surgery	**Frailty measure category**	**Delirium measure category**	**Comparator**	**Delirium**	**Total**	**Delirium**	**Total**
Tsai 2023[40] China, Taiwan 345/206 ≥ 65 years 73 years (65–99 years) Elective abdominal surgery	CGA	CAM	Fit group: $n=159$ (46.1%) Frail group: $n=186$ (53.9%)	15	186	4	159
Tian 2023[26] China 1372 /781 > 65 years Not mentioned Elective lung cancer surgery	mFI	DSM-V	Frail group: $n=388$ (mFI-5, 2–5), Pre-frail group: $n=503$ (mFI-5, 1) Robust group: $n=481$ (mFI-5, 0)	121	388	15	984
Tomoyuki Sugi, 2023[27] Japan 158 /111 ≥ 75 years 79 years (75–91 years) Gastroenterological surgery	Fried	CAM	Postoperative delirium (+): $n=53$ Postoperative delirium (–): $n=105$	27	48	26	110
J. Steenblock 2023[28] Germany 701/367 ≥ 70 years 77.1 ± 4.7 years Elective surgery	FI	A combination of I-CAM and chart review	Non-frail group: $n=173$ Frail group: $n=528$	134	528	31	173
Hunter 2023[29] Australia 300/89 > 50 years 81.1 ± 9.8 years Hip fracture surgery	CFS	3D-CAM	CFS ≥ 5: $n=160$ CFS < 5: $n=121$	66	164	16	135
Gandossi 2023[30] Italy 984/241 > 65 years 84 years (79–89 years) Urgent surgery	FI	4AT	FI < 0.25: $n=504$ FI ≥ 0.25: $n=480$	228	480	83	504
Abdelfatah 2023[31] USA 411/203 > 65 years 75.1 ± 6.60 years Colorectal resection	RAI-A	ICD-9 ICD-10	Not frail: 42/288 (14.6%) Frail: 37/123 (30.1%)	6	123	2	288
Zhao 2022[66] China 381/98 ≥ 65 years High CFI group: 83 ± 5 years Low CFI group: 78 ± 7 years Hip fracture repair surgery	CFI	CAM	High CFI group: $n=102$ Low CFI group: $n=279$	17	102	8	279

Table 1 (continued)

Participants	Exposures/interventions		Comparison	Outcome (frailty)		Outcome (non-frailty)	
Author, year Country No. of patients/No. of male patients Age/Age criterion Mean ± SD or median (IQR) age Type of surgery	**Frailty measure category**	**Delirium measure category**	**Comparator**	**Delirium**	**Total**	**Delirium**	**Total**
Xiang 2022[33] China 226/Not mentioned 65–85 years No POD: 70.4 ± 2.7 years POD: 71.7 ± 3.0 years Laparoscopic surgery for gynecologic cancers	mFI	DSM-V	POD No: $n = 187$ Yes: $n = 39$	10	31	29	195
Sieber 2022[67] USA 324/196 ≥ 65 years 4AT < 4: 73.1 ± 6.2 years 4AT ≥ 4: 77.5 ± 6.3 years Elective surgery	EFS	4AT	4AT < 4: $n = 309$ 4AT ≥ 4: $n = 15$	10	83	5	241
Musacchio 2022[35] Italy 244/39 ≥ 65 years 85 ± 6.9 years Hip fracture surgery	MPI	4AT	Delirium: $n = 104$ No delirium: $n = 140$	76	143	28	101
Esmaeeli 2021[36] USA 557/169 ≥ 65 years POD: 85 ± 7 years No POD: 80 ± 8 years Orthopedic trauma patients	FRAIL	CAM	POD: $n = 80$ No POD: $n = 477$	4	18	76	539
Thillainadesan 2021[70] USA 150/102 ≥ 65 years 79.5 years (7.7 years) Vascular surgery	CFS FI	CAM	Frail: $n = 34$ Fit: $n = 116$ CFS ≥ 5: $n = 45$ CFS < 5: $n = 105$	10	45	5	105
Pedemonte 2021[38] USA 558/165 ≥ 65 years 80.16 years (8.57 years) Orthopedic trauma patients	FRAIL	CAM	Robust: $n = 166$ Pre-frail: $n = 217$ Frail: $n = 126$	25	126	24	217
Mauri 2021[39] Germany 661/322 Not mentioned 82.3 ± 6.6 years TAVR	EFT	CAM-ICU	Delirium: $n = 66$ No delirium: $n = 595$	46	199	20	462
Gandossi 2021[30] Italy 988/250 ≥ 65 years 84.9 years (80.6–89.2 years) Hip fracture surgery	FI	4AT DSM-5	FI < 0.25: $n = 628$ FI ≥ 0.25: $n = 360$	183	360	228	628

Table 1 (continued)

Participants	Exposures/interventions		Comparison	Outcome (frailty)		Outcome (non-frailty)	
Author, year **Country** **No. of patients/No. of male patients** **Age/Age criterion** **Mean ± SD or median (IQR) age** **Type of surgery**	**Frailty measure category**	**Delirium measure category**	**Comparator**	**Delirium**	**Total**	**Delirium**	**Total**
Cheng 2021[41] China, Taiwan 152/104 ≥ 20 years 63.07 years (11.17 years) Cardiac surgery	Fried	CAM	Non-delirium: $n=5142$ Delirium: $n=510$	2	21	8	131
Chen 2021[24] China 383/132 65–85 years 73.2 ± 3.3 years Elective total joint arthroplasty	mFI	DSM-V	High mFI (> 0.18): $n=207$ Low mFI (< 0.18): $n=176$	44	207	22	176
Banning 2021[42] The Netherlands 639/497 Not mentioned 69.4 ± 10.0 Elective vascular surgery	GFI	Not mentioned	Frail: $n=183$ (28.6%) Non-frail: $n=456$ (71.4%)	17	183	27	456
Ishihara 2020[43] Japan 295/216 ≥ 65 years 74 years (65–89 years) Hepatic resection	KCL	ICDSC	Delirium group: $n=22$ Non-delirium group: $n=273$	10	15	12	295
Susano 2020[44] Portugal 219/124 ≥ 70 years 75 years (73–79 years) Elective spine surgery	FRAIL	CAM	No POD: $n=164$ (75%) POD: $n=55$ (25%)	24	53	31	166
Saljuqi 2020[25] USA 163/85 ≥ 65 years 71 ± 7 years Emergency general surgery	ESFI	CAM	Delirium: $n=38$ No delirium: $n=107$	15	30	23	80
Sanchez 2020[45] Spain 446/198 ≥ 65 years 78 years (65–103 years) Urgent abdominal surgery	FRAIL	CAM	No delirium: $n=385$ Delirium: $n=61$	18	59	43	387
Nakano 2020[46] Japan 133/97 ≥ 55 years Non-frail: 71.3 ± 7.1 years Frail: 73.5 ± 8.1 years Cardiac surgery	Fried	CAM	Non-frail: $n=89$ Frail: $n=44$	19	44	37	89

Table 1 (continued)

Participants	Exposures/interventions		Comparison	Outcome (frailty)		Outcome (non-frailty)	
Author, year Country No. of patients/No. of male patients Age/Age criterion Mean ± SD or median (IQR) age Type of surgery	**Frailty measure category**	**Delirium measure category**	**Comparator**	**Delirium**	**Total**	**Delirium**	**Total**
Mahanna-Gabrielli 2020[47] USA 178/75 ≥ 65 years Robust: 70 years (67–74.5 years) Prefrail: 70.5 years (67–75 years) Frail: 71 years (66–74 years) Non-cardiac surgery	FRAIL	CAM-ICU	Robust: *n* = 64 Pre-frail: *n* = 72 Frail: *n* = 31	11	31	27	106
Goudzwaard 2020[48] The Netherlands 543/297 Not mentioned 79.1 ± 8.0 years TAVI	EFS	DSM-IV	Delirium: *n* = 75 No delirium: *n* = 468	24	97	51	446
Atsunori Itagaki 2020[49] Japan 114/73 ≥ 65 years 74.9 ± 5.5 years Cardiac surgery	J-CHS	ICDSC	Non-frailty, non-MCI: *n* = 23 Non-frailty, MCI: *n* = 32 Frailty, non-MCI: *n* = 11 Frailty, MCI: *n* = 23	21	72	4	17
Chan 2019[64] Canada 423/267 ≥ 65 years 82.5 ± 8.4 years Total arthroplasty, hemiarthroplasty, dynamic hip or cannulated screws, intramedullary nail	CFS	A validated chart-abstraction instrument	Not frail (CFS 1–3): *n* = 71 Vulnerable (CFS 4): *n* = 72 Mildly frail (CFS 5): *n* = 92 Frail (CFS 6–9): *n* = 187	211	279	50	143
Saravana-Bawan 2019[50] Canada 322/176 ≥ 65 years 76.1 ± 7.66 years Intestinal, appendix, gallbladder, or hernia repair surgery	CFS	Inouye chart review method	No delirium: *n* = 249 Delirium: *n* = 73	33	78	40	244
Goudzwaard 2019[48] The Netherlands 213/46.5% Not mentioned 82.03 years (78.2–85.6 years) TAVI	EFS	DSM-IV	Non-frail: *n* = 153 Frail (EFS ≥ 3): *n* = 60	27	61	15	152
Nomura 2019[51] USA 133/97 ≥ 65 years 69.33 ± 7.90 years CABG, valve procedures, or other surgery	Fried	CAM	Non-frail: *n* = 15 Pre-frail: *n* = 74 Frail: *n* = 44	19	40	37	88

Table 1 (continued)

Participants	Exposures/interventions		Comparison	Outcome (frailty)		Outcome (non-frailty)	
Author, year Country No. of patients/No. of male patients Age/Age criterion Mean ± SD or median (IQR) age Type of surgery	**Frailty measure category**	**Delirium measure category**	**Comparator**	**Delirium**	**Total**	**Delirium**	**Total**
Haugen 2018[52] USA 893/545 Not mentioned 50.3 ± 13.7 years KT	Fried	A validated instrument for chart review	No delirium: n = 851 Delirium: n = 42	13	146	29	747
Tanaka 2018[53] Japan 217/149 ≥ 65 years Non-frail: 75 years (65–88 years); Frail: 72 years (65–88 years) Hepatic resection	KCL	ICDSC	Frail group: n = 63 Non-frail group: n = 154	8	63	3	154
Bagienski 2017[54] Poland 141/52 ≥ 75 years 82.0 years (77.5–85.0 years) TAVI	FI	CHART DEL	No delirium: n = 112 Delirium: n = 29	15	47	14	94
Brown 2016[55] USA 55/41 ≥ 55 years Non-frail: 64.7 ± 5.6 years; Frail: 67.7 ± 8.4 years CABG	Fried	CAM	Non-frail: n = 38 Frail: n = 17	8	17	1	38
Assmann 2016[56] The Netherlands 89/47 ≥ 75 years 80.4 years (6.3 years) MT, SAVR, TAVI	FI	DSM-IV	No delirium: n = 64 Delirium: n = 25	15	47	10	42
Khan 2016[74] Singapore 25/17 ≥ 65 years 79 years (74–83 years) Femur fracture fixation surgery, abdominal laparotomy; total knee replacement	Fried	CAM-ICU	Nonfrail: n = 11 Frail: n = 14	1	14	1	11
Eide 2015[58] Norway 143/62 ≥ 80 years 83.5 ± 2.7 years TAVI, SAVR	FI	CAM DSM-IV	No delirium: n = 60 Delirium: n = 76	32	56	44	87
Jung 2015[59] Canada 133/98 ≥ 18 years Non-frail: 68.7 ± 7.4 years; Frail: 73.0 ± 8.2 years CABG, valve procedures	Fried	CAM-ICU, CAM	Non-frail: n = 61 Frail: n = 72	20	72	5	61

Table 1 (continued)

Participants	Exposures/interventions		Comparison	Outcome (frailty)		Outcome (non-frailty)	
Author, year **Country** **No. of patients/No. of male patients** **Age/Age criterion** **Mean ± SD or median (IQR) age** **Type of surgery**	**Frailty measure category**	**Delirium measure category**	**Comparator**	**Delirium**	**Total**	**Delirium**	**Total**
Kistler 2015[60] USA 35/6 ≥ 65 years 86 ± 4 years Hip fracture surgery	Fried	CAM	Frail: *n* = 18 Non-frail: *n* = 17	10	18	4	17
Partridge 2015[61] UK 125/86 ≥ 60 years 76.3 ± 7.27 years Arterial vascular surgery	EFS	CAM	EFS < 6.5: *n* = 60 (48.0%) EFS > 6.5: *n* = 65 (52.0%)	15	65	9	60
Leung 2011[62] USA 63/29 ≥ 65 years Delirium: 74.2 ± 6.0 years; No delirium: 71.9 ± 6.3 years General, arthroplasty, spine, or thoracic surgery	EFS	CAM	Delirium: *n* = 16 No delirium: *n* = 47	9	21	7	32
Pol 2011[63] The Netherlands 142/100 21–87 years 68 ± 11 years Vascular surgery	GFI	DSM-IV-TR	GFI > 4: *n* = 50 GFI ≤ 4: *n* = 92	6		50 4	92

ASA, American Society of Anesthesiologists; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CAM, Confusion Assessment Method; CHART-DEL, chart-based delirium identification instrument; DOS, Delirium Observation Score; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; ICDSC, Intensive Care Delirium Screening Checklist; KT, kidney transplant; NR, not reported; POD, postoperative delirium; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

the EFS (5 studies [11.4%]), CFS (4 studies [7.56%]), and other instruments (11 studies [4.32%]). Among all the frailty-assessment method groups, the association between preoperative frailty and POD was strongest in the CFS group (OR: 7.56, 95% CI: 3.42–16.73) and weakest in the Fried group (OR: 2.33, 95% CI: 1.51–3.59). However, no statistically significant differences were detected within the 6 frailty-assessment method groups ($P = 0.08$).

(2) Racial group

The associations between preoperative frailty and POD in different racial groups are illustrated in Fig. 4. In all, 12 (27.9%) studies included Asian patients, and 31 (72.1%) studies included non-Asian patients. The association was stronger in Asian patients (OR: 4.01, 95% CI: 1.83, 8.78) than in non-Asian patients (OR: 2.96, 95% CI: 2.39, 3.65). However, no statistically significant difference was found within the 2 racial groups ($P = 0.46$).

(3) Type of surgery

The associations between preoperative frailty and POD in different groups based on the type of surgery are shown in Fig. 5. Cardiovascular surgery was the most commonly performed surgery in the studied population (16 studies [36.7%]), followed by orthopedic surgery (13 studies [31.9%]), abdominal surgery (10 studies [22.9%]), and other elective surgery (4 studies [9.8%]). The association between preoperative frailty and POD was strongest in the abdominal surgery group (OR: 6.04, 95% CI: 3.08–11.82) and weakest in the elective surgery group (OR: 2.20, 95% CI: 1.28–3.81). However, no statistically significant differences were detected within the 4 surgical groups ($P = 0.10$).

Publication Bias and sensitivity analysis

Publication bias in the included studies was assessed using a funnel plot. The plot exhibited a symmetrical pattern, suggesting no publication bias (Supplementary Fig. 1). Sensitivity analysis, performed by excluding one

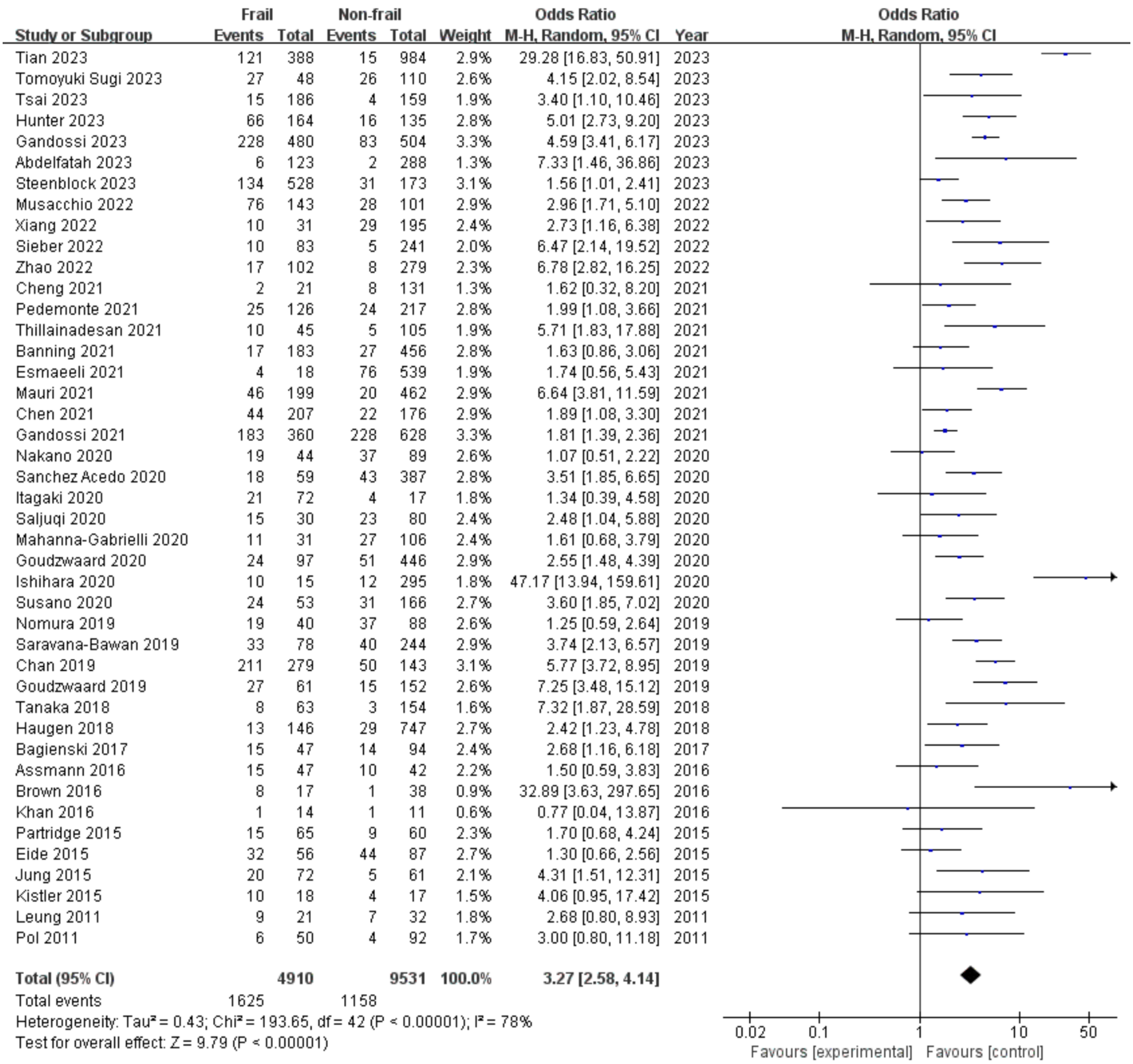

Fig. 2 Forest plot for crude association between preoperative frailty and postoperative delirium

study at a time, showed that the combined prevalence rate remained stable, indicating the robustness of the meta-analysis results (Supplementary Table 2).

Discussion

This meta-analysis synthesized data from 43 studies involving a total of 14,441 patients to investigate the link between preoperative frailty and POD. The baseline frailty rate was 34.0%, and the incidence of POD was 20%. These results highlight the global prevalence of frailty in older adults and its significant impact on surgical outcomes, underscoring the importance of medical vigilance. Frailty is identified as a key prognostic factor associated with surgical complications and patient prognosis, reinforcing the value of preoperative frailty assessment.

Frailty and delirium share an intrinsic connection, with the inflammatory cytokine cascade postulated to initiate neuroinflammation and disruption of extensive neuronal networks in the brain, leading to acute declines in cognitive and functional capacities [24, 25, 38]. Studies have revealed that frailty is correlated with compromised DNA-repair mechanisms, mitochondrial dysfunction, elevated free-radical production, reduced telomere integrity, inflammation, impairments in innate immune function [26], and dysregulation of the hypothalamic-pituitary-adrenal axis [27, 63]. Additionally, frailty has been linked to hormonal imbalances [29, 30] and insulin

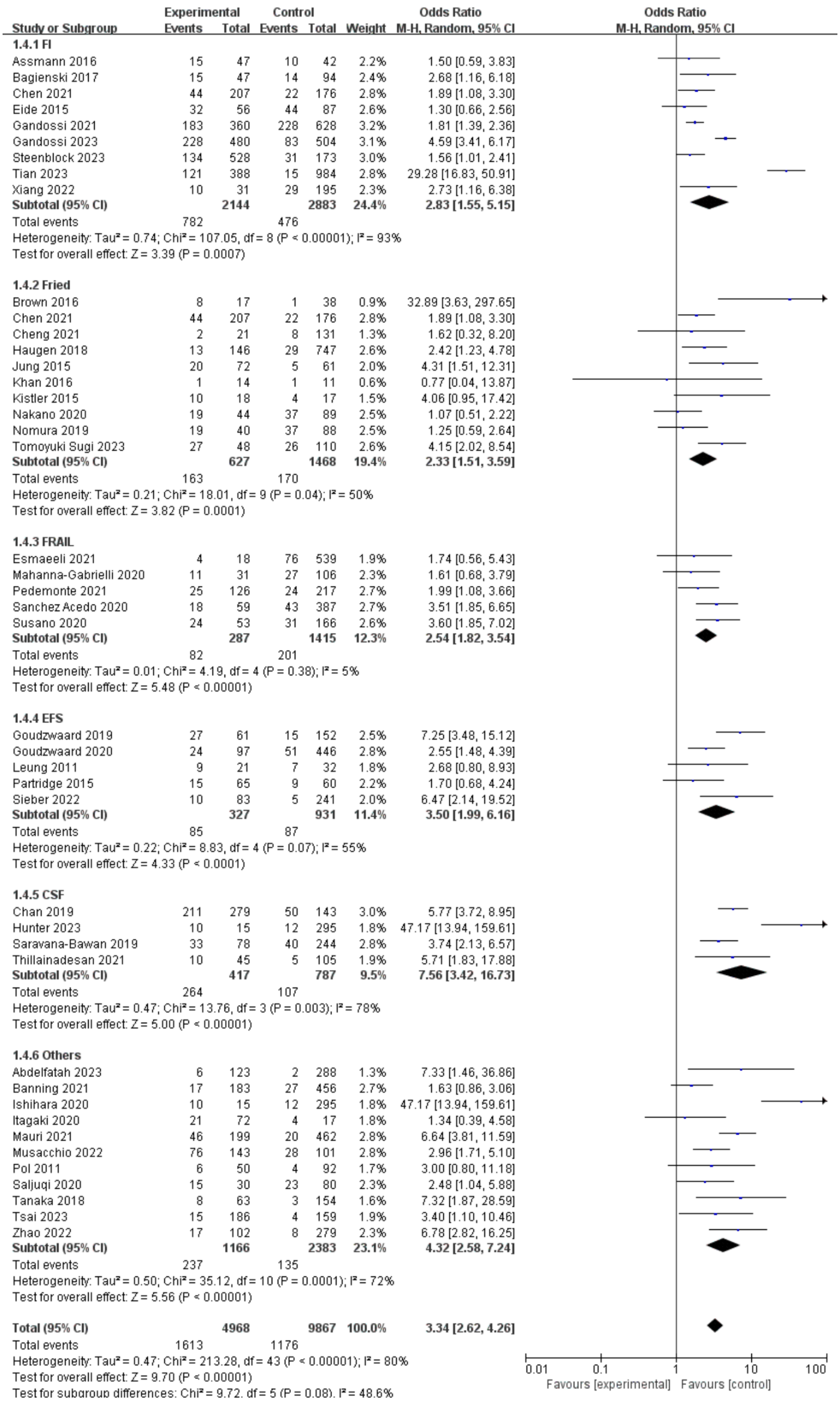

Fig. 3 Forest plots displaying pooled effect estimates for frailty-assessment methods

Study or Subgroup	Frail Events	Frail Total	Non-frail Events	Non-frail Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.2.1 Asian							
Khan 2016	1	14	1	11	0.6%	0.77 [0.04, 13.87]	2016
Tanaka 2018	8	63	3	154	1.6%	7.32 [1.87, 28.59]	2018
Ishihara 2020	10	15	12	295	1.8%	47.17 [13.94, 159.61]	2020
Itagaki 2020	2	44	5	89	1.3%	0.80 [0.15, 4.30]	2020
Nakano 2020	19	44	37	89	2.6%	1.07 [0.51, 2.22]	2020
Cheng 2021	2	21	8	131	1.3%	1.62 [0.32, 8.20]	2021
Chen 2021	44	207	22	176	2.9%	1.89 [1.08, 3.30]	2021
Zhao 2022	17	102	8	279	2.4%	6.78 [2.82, 16.25]	2022
Xiang 2022	10	31	29	195	2.4%	2.73 [1.16, 6.38]	2022
Tian 2023	121	388	15	984	2.9%	29.28 [16.83, 50.91]	2023
Tomoyuki Sugi 2023	27	48	26	110	2.6%	4.15 [2.02, 8.54]	2023
Tsai 2023	15	186	4	159	2.0%	3.40 [1.10, 10.46]	2023
Subtotal (95% CI)		**1163**		**2672**	**24.3%**	**4.01 [1.83, 8.78]**	
Total events	276		170				
Heterogeneity: Tau² = 1.55; Chi² = 92.69, df = 11 (P < 0.00001); I² = 88%							
Test for overall effect: Z = 3.47 (P = 0.0005)							
1.2.2 Non-Asian							
Leung 2011	9	21	7	32	1.8%	2.68 [0.80, 8.93]	2011
Pol 2011	6	50	4	92	1.7%	3.00 [0.80, 11.18]	2011
Partridge 2015	15	65	9	60	2.3%	1.70 [0.68, 4.24]	2015
Eide 2015	32	56	44	87	2.7%	1.30 [0.66, 2.56]	2015
Jung 2015	20	72	5	61	2.1%	4.31 [1.51, 12.31]	2015
Kistler 2015	10	18	4	17	1.5%	4.06 [0.95, 17.42]	2015
Assmann 2016	15	47	10	42	2.2%	1.50 [0.59, 3.83]	2016
Brown 2016	8	17	1	38	0.9%	32.89 [3.63, 297.65]	2016
Bagienski 2017	15	47	14	94	2.4%	2.68 [1.16, 6.18]	2017
Haugen 2018	13	146	29	747	2.7%	2.42 [1.23, 4.78]	2018
Nomura 2019	19	40	37	88	2.6%	1.25 [0.59, 2.64]	2019
Saravana-Bawan 2019	33	78	40	244	2.9%	3.74 [2.13, 6.57]	2019
Chan 2019	211	279	50	143	3.1%	5.77 [3.72, 8.95]	2019
Goudzwaard 2019	27	61	15	152	2.6%	7.25 [3.48, 15.12]	2019
Susano 2020	24	53	31	166	2.7%	3.60 [1.85, 7.02]	2020
Sanchez Acedo 2020	18	59	43	387	2.8%	3.51 [1.85, 6.65]	2020
Saljuqi 2020	15	30	23	80	2.4%	2.48 [1.04, 5.88]	2020
Mahanna-Gabrielli 2020	11	31	27	106	2.4%	1.61 [0.68, 3.79]	2020
Goudzwaard 2020	24	97	51	446	2.9%	2.55 [1.48, 4.39]	2020
Pedemonte 2021	25	126	24	217	2.8%	1.99 [1.08, 3.66]	2021
Thillainadesan 2021	10	45	5	105	1.9%	5.71 [1.83, 17.88]	2021
Banning 2021	17	183	27	456	2.8%	1.63 [0.86, 3.06]	2021
Esmaeeli 2021	4	18	76	539	1.9%	1.74 [0.56, 5.43]	2021
Mauri 2021	46	199	20	462	2.9%	6.64 [3.81, 11.59]	2021
Gandossi 2021	183	360	228	628	3.3%	1.81 [1.39, 2.36]	2021
Musacchio 2022	76	143	28	101	2.9%	2.96 [1.71, 5.10]	2022
Sieber 2022	10	83	5	241	2.0%	6.47 [2.14, 19.52]	2022
Steenblock 2023	134	528	31	173	3.1%	1.56 [1.01, 2.41]	2023
Hunter 2023	66	164	16	135	2.8%	5.01 [2.73, 9.20]	2023
Gandossi 2023	228	480	83	504	3.3%	4.59 [3.41, 6.17]	2023
Abdelfatah 2023	6	123	2	288	1.3%	7.33 [1.46, 36.86]	2023
Subtotal (95% CI)		**3719**		**6931**	**75.7%**	**2.96 [2.39, 3.65]**	
Total events	1330		989				
Heterogeneity: Tau² = 0.20; Chi² = 89.35, df = 30 (P < 0.00001); I² = 66%							
Test for overall effect: Z = 10.03 (P < 0.00001)							
Total (95% CI)		**4882**		**9603**	**100.0%**	**3.26 [2.57, 4.14]**	
Total events	1606		1159				
Heterogeneity: Tau² = 0.43; Chi² = 194.34, df = 42 (P < 0.00001); I² = 78%							
Test for overall effect: Z = 9.72 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.54, df = 1 (P = 0.46), I² = 0%							

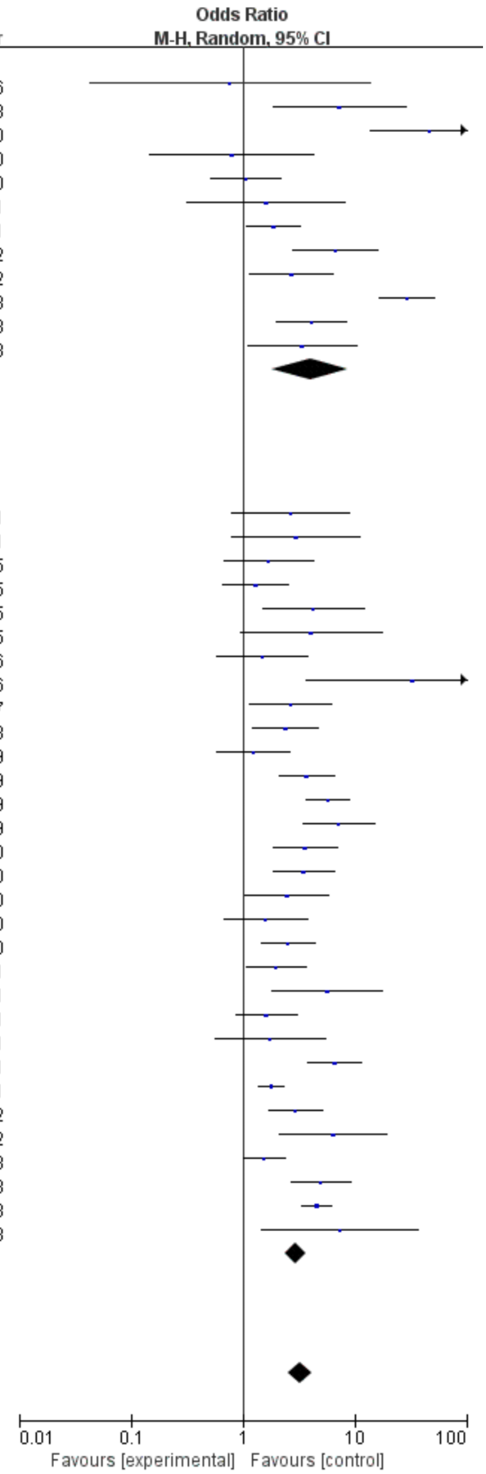

Fig. 4 Forest plots displaying pooled effect estimates for racial groups

resistance, along with deregulation of glucose metabolism [31, 32].

Our findings align with those of previous meta-analyses, which also found a significant link between frailty and delirium in elderly surgical patients. One recent meta-analysis of 11 studies, with a total of 794 patients, reported an adjusted OR of 2.45 (95% CI: 1.58–3.81) for POD in frail patients undergoing elective surgery [33], while another meta-analysis of 9 studies yielded an adjusted OR of 2.14 (95% CI: 1.43–3.19) [6]. Both

Study or Subgroup	Frail Events	Frail Total	Non-frail Events	Non-frail Total	Weight	Odds Ratio M-H, Random, 95% CI
1.3.1 cardiovascular surgery						
Assmann 2016	15	47	10	42	2.2%	1.50 [0.59, 3.83]
Bagienski 2017	15	47	14	94	2.4%	2.68 [1.16, 6.18]
Banning 2021	17	183	27	456	2.8%	1.63 [0.86, 3.06]
Brown 2016	8	17	1	38	0.9%	32.89 [3.63, 297.65]
Cheng 2021	2	21	8	131	1.3%	1.62 [0.32, 8.20]
Eide 2015	32	56	44	87	2.7%	1.30 [0.66, 2.56]
Goudzwaard 2019	27	61	15	152	2.6%	7.25 [3.48, 15.12]
Goudzwaard 2020	24	97	51	446	2.9%	2.55 [1.48, 4.39]
Itagaki 2020	21	72	4	17	1.8%	1.34 [0.39, 4.58]
Jung 2015	20	72	5	61	2.1%	4.31 [1.51, 12.31]
Mauri 2021	46	199	20	462	2.9%	6.64 [3.81, 11.59]
Nakano 2020	19	44	37	89	2.6%	1.07 [0.51, 2.22]
Nomura 2019	19	40	37	88	2.6%	1.25 [0.59, 2.64]
Partridge 2015	15	65	9	60	2.3%	1.70 [0.68, 4.24]
Pol 2011	6	50	4	92	1.7%	3.00 [0.80, 11.18]
Thillainadesan 2021	10	45	5	105	1.9%	5.71 [1.83, 17.88]
Subtotal (95% CI)		**1116**		**2420**	**35.5%**	**2.52 [1.73, 3.67]**
Total events	296		291			
Heterogeneity: Tau² = 0.36; Chi² = 45.29, df = 15 (P < 0.0001); I² = 67%						
Test for overall effect: Z = 4.82 (P < 0.00001)						
1.3.2 orthopedic surgery						
Chan 2019	211	279	50	143	3.1%	5.77 [3.72, 8.95]
Chen 2021	44	207	22	176	2.9%	1.89 [1.08, 3.30]
Esmaeeli 2021	4	18	76	539	1.9%	1.74 [0.56, 5.43]
Gandossi 2021	183	360	228	628	3.3%	1.81 [1.39, 2.36]
Gandossi 2023	228	480	83	504	3.3%	4.59 [3.41, 6.17]
Hunter 2023	66	164	16	135	2.8%	5.01 [2.73, 9.20]
Khan 2016	1	14	1	11	0.6%	0.77 [0.04, 13.87]
Kistler 2015	10	18	4	17	1.5%	4.06 [0.95, 17.42]
Leung 2011	9	21	7	32	1.8%	2.68 [0.80, 8.93]
Musacchio 2022	76	143	28	101	2.9%	2.96 [1.71, 5.10]
Pedemonte 2021	25	126	24	217	2.8%	1.99 [1.08, 3.66]
Susano 2020	24	53	31	166	2.7%	3.60 [1.85, 7.02]
Zhao 2022	17	102	8	279	2.3%	6.78 [2.82, 16.25]
Subtotal (95% CI)		**1985**		**2948**	**31.9%**	**3.17 [2.31, 4.36]**
Total events	898		578			
Heterogeneity: Tau² = 0.20; Chi² = 43.16, df = 12 (P < 0.0001); I² = 72%						
Test for overall effect: Z = 7.09 (P < 0.00001)						
1.3.4 abdominal surgery						
Abdelfatah 2023	6	123	2	288	1.3%	7.33 [1.46, 36.86]
Haugen 2018	13	146	29	747	2.7%	2.42 [1.23, 4.78]
Ishihara 2020	10	15	12	295	1.8%	47.17 [13.94, 159.61]
Sanchez Acedo 2020	18	59	43	387	2.8%	3.51 [1.85, 6.65]
Saravana-Bawan 2019	33	78	40	244	2.9%	3.74 [2.13, 6.57]
Tanaka 2018	8	63	3	154	1.6%	7.32 [1.87, 28.59]
Tian 2023	121	388	15	984	2.9%	29.28 [16.83, 50.91]
Tomoyuki Sugi 2023	27	48	26	110	2.6%	4.15 [2.02, 8.54]
Tsai 2023	15	186	4	159	1.9%	3.40 [1.10, 10.46]
Xiang 2022	10	31	29	195	2.4%	2.73 [1.16, 6.38]
Subtotal (95% CI)		**1137**		**3563**	**22.9%**	**6.04 [3.08, 11.82]**
Total events	261		203			
Heterogeneity: Tau² = 0.94; Chi² = 61.30, df = 9 (P < 0.00001); I² = 85%						
Test for overall effect: Z = 5.25 (P < 0.00001)						
1.3.5 elective surgery						
Mahanna-Gabrielli 2020	11	31	27	106	2.4%	1.61 [0.68, 3.79]
Saljuqi 2020	15	30	23	80	2.4%	2.48 [1.04, 5.88]
Sieber 2022	10	83	5	241	2.0%	6.47 [2.14, 19.52]
Steenblock 2023	134	528	31	173	3.1%	1.56 [1.01, 2.41]
Subtotal (95% CI)		**672**		**600**	**9.8%**	**2.20 [1.28, 3.81]**
Total events	170		86			
Heterogeneity: Tau² = 0.15; Chi² = 6.03, df = 3 (P = 0.11); I² = 50%						
Test for overall effect: Z = 2.83 (P = 0.005)						
Total (95% CI)		**4910**		**9531**	**100.0%**	**3.27 [2.58, 4.14]**
Total events	1625		1158			
Heterogeneity: Tau² = 0.43; Chi² = 193.65, df = 42 (P < 0.00001); I² = 78%						
Test for overall effect: Z = 9.79 (P < 0.00001)						
Test for subgroup differences: Chi² = 6.33, df = 3 (P = 0.10), I² = 52.6%						

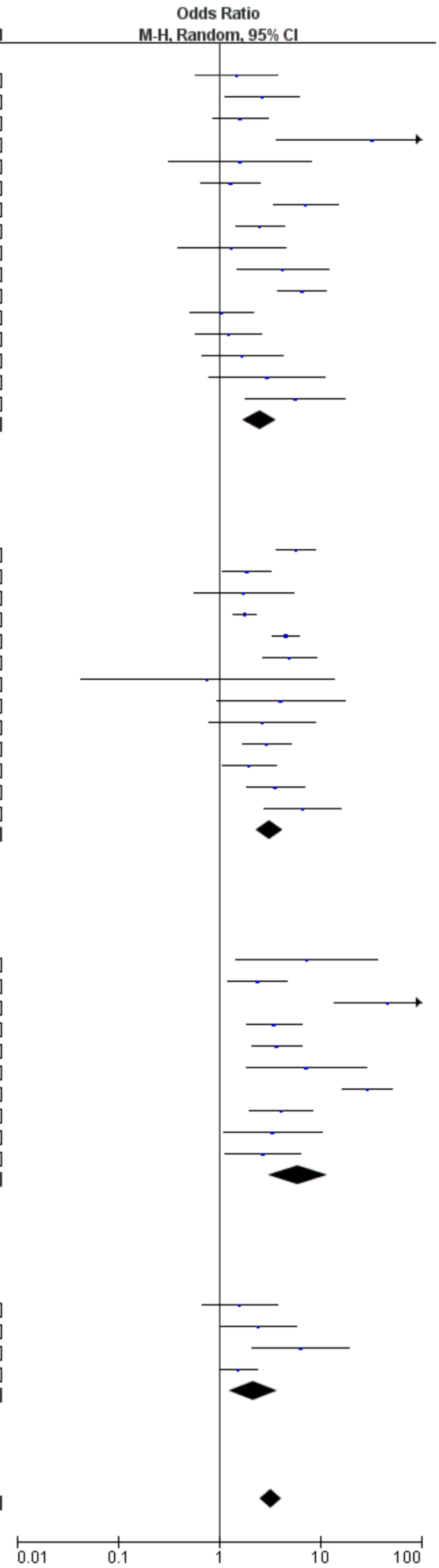

Fig. 5 Forest plots displaying pooled effect estimates for types of surgery

highlighted the challenge of study heterogeneity and the need for further research to better understand the mechanisms by which frailty contributes to delirium and to evaluate the impact of different frailty assessments in various settings. Therefore, we aimed to provide a clearer understanding of the frailty-delirium relationship. Our literature review updated these previous meta-analyses as it identified more studies and included more recent publications [6, 33]. This ensured an accurate representation of older frail adults undergoing surgery that did not have neurocognitive disorders at baseline, and provided a robust sample size on which to base our conclusions. Our included studies were of high methodological quality, in contrast to the previous meta-analyses, which included studies with moderate to critical risk of bias [6].

Our study also aligns with the most recent European Society of Anaesthesiology and Intensive Care Medicine (ESAIC) guidelines, published in 2025 [64]. These guidelines recommend preoperative frailty screening with the CFS to predict postoperative outcomes, especially for assessing the risk of delirium. If a frailty phenotype is identified a multidisciplinary approach to patient care should be adopted, including an evaluation by a geriatrician. There is currently no consensus on the timing of frailty assessment in relation to surgery, identifying an evidence gap relevant to the implementation of frailty assessment in elderly surgical patients [65].

ESAIC guidelines recommend the CFS as a screening tool based on feasibility of use in the preoperative setting and its strong association with mortality and unfavorable discharge [64]. Alternative measures include the EFS, which correlates well with the development of postoperative complications, and the Fried Frailty Phenotype, which is best associated with the development of POD. The Frailty Phenotype is less feasible for use in the preoperative setting as it needs specific equipment and is a time burden (5 to 20 min vs. 44 s for the CFS) [64]. Our study highlighted the variety of tools currently in clinical use, including the Fried Frailty Phenotype, CFS, FI, and EFS, with our meta-analysis indicating a particular preference for the FI, Fried, and FRAIL tools.

High frailty prevalence was noted in a Singapore study of 234 older adults with surgical indications, with 68% of patients (95% CI: 62–74%) experiencing subsyndromal delirium [33]. A UK multicenter study of 1,507 patients also reported a high frailty rate of 66% (95% CI: 64–68%) [35]. In contrast, a study from Australia found a slightly lower frailty rate: 53% (95% CI: 48–59%) among 302 patients with atrial fibrillation [36]. In our previous study in China,[1] 48% of 148 elderly hip-fracture patients were found to be frail preoperatively. The incidence of POD was 24.3% by day 7, with frail patients being at a higher risk for this complication (42.3% vs. 7.8%, $P<0.001$). Moreover, preoperative frailty was found to be an independent risk factor for POD ($P=0.002$) [1]. Notably, our current study resolves the above inconsistencies in the prevalence of frailty among different populations, demonstrating comparable frailty prevalence between Asian and non-Asian populations (Asian: 61.9% [276/446] vs. non-Asian: 57.4% [1330/2319]) and reinforcing the global significance of frailty. Unfortunately, frailty research in China's large population remains limited, suggesting that assessments and screenings have not received adequate focus. This is lamentable, as it could lead to missed chances for early interventions and better health outcomes for the elderly.

Methods of anesthesia and anesthetics have been identified as risk factors for POD in the elderly [66]. Major surgery requires a constant state of unconsciousness, maintained using inhaled and intravenous anesthetics, benzodiazepines and opioids. Chest and abdominal surgeries may be performed using regional anesthetic methods, such as spinal and epidural anesthesia. The impact of general anesthesia compared to regional anesthesia on POD remains to be elucidated. The use of fewer drugs, the shorter duration of surgery and shallower depth of sedation with regional anesthesia may result in a lower incidence of POD compared to general anesthesia [66, 67]. However, several studies, including a recent systematic review and meta-analysis, revealed no benefits of regional anesthesia over general anesthesia for POD in the elderly, identifying the need for further studies that assess the associations between the type of anesthesia methods used in clinical practice and the incidence of POD [66, 68].

Delving into specific surgical types, our study reaffirms the heightened risk of delirium after cardiovascular procedures as compared to non-cardiovascular surgeries. However, frailty emerged as a crucial determinant of POD across various surgical domains, emphasizing the need for preoperative frailty assessment regardless of surgical type.

Evidence supporting pharmacological and non-pharmacological prophylaxis for POD is inconsistent, especially among homogeneous subpopulations of surgical patients such as frail older adults, identifying a critical clinical need for well-designed studies that rigorously evaluate the risks and benefits of potential interventions across a variety of patients [37]. Pharmacological options for prevention of POD include dexmedetomidine, olanzapine and risperidone [28]. Dexmedetomidine is a sedative, analgesic, neuroprotectant and anxiolytic. Randomized controlled trials and meta-analyses indicate that dexmedetomidine may reduce the incidence and duration of POD in cardiac and non-cardiac adult surgical populations. Mechanisms include altering the inflammatory and stress response to surgery. Dosing may be perioperative or postoperative in the ICU. Adverse events associated with dexmedetomidine administration include hemodynamic instability [39], such as bradycardia and hypotension. Olanzapine and risperidone are atypical antipsychotics that may also have a role in POD prevention. Randomized controlled trials show these atypical antipsychotics may reduce the incidence of POD in cardiac and non-cardiac adult surgical populations, but POD may be prolonged and more severe in patients who develop POD after receiving these drugs [40]. Non-pharmacological prophylaxis of POD includes avoiding the use of precipitating drugs such as benzodiazepines and atropine, maintaining patient mobility and the sleep-wake cycle, minimizing fasting, appropriately managing anesthesia, diagnosing and managing intraoperative complications in a timely manner, and providing guidance in the postoperative period [41, 42].

The limitations of this review include that studies were restricted to those published in the English language, populations and sample sizes varied across studies, and diverse methods were used for assessing frailty and delirium. First, the retrospective nature of our analysis limits the inference of causality, and despite adjustments for multiple factors, residual confounding may still influence the outcomes. Second, the use of various frailty- and delirium-assessment tools introduces clinical heterogeneity [43], potentially biasing the results, although our pseudo-risk-minimization method ensured the robustness of our models. Third, the inconsistency in delirium-screening tools and follow-up times among studies adds to the complexity [22]. Lastly, delirium was assessed inconsistently, potentially leading to underestimation, as it was not continuously monitored. The optimal timeframe for the diagnosis of POD remains undefined, with peaks typically occurring 1–3 days after surgery [44].

Conclusions

Our study underscores the global link between preoperative frailty and POD, emphasizing the need for clinical frailty assessment to guide interventions and improve outcomes. The meta-analysis shows that preoperative frailty is significantly tied to higher POD risk, with early screening aiding in targeted care. Further research should aim to streamline frailty evaluation in preoperative assessments, boosting timely identification and support for frail patients.

Abbreviations

CIs	Confidence intervals
CAM	Confusion Assessment Method
FRAIL	Fatigue, Resistance, Ambulation, Illness, and Loss of weight
CFS	Clinical Frailty Scale
EFS	Edmonton Frail Scale
MeSH	Medical Subject Headings
ORs	Odds ratios
POD	Postoperative delirium
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analyses
NOS	Newcastle-Ottawa Scale

Supplementary information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-02994-3 .

Supplementary Material 1

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Not applicable.

Author contributions
Haotian Wu: This author helped with data analysis, data interpretation, preparation of the first draft, and subsequent revisions. Siyi Yan: This author helped with data interpretation, preparation of the first draft, and review of the final draft. Chunyu Feng: This author helped with study design, data analysis, data interpretation, and manuscript revisions. Han Cao: This author helped with study design, manuscript review, data interpretation, and final revision. Huan Zhang: This author helped with study design, study execution, data analysis, data interpretation, and manuscript revisions.

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Data availability
The datasets generated and analyzed during the present study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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