The impact of frailty on perioperative outcomes in patients receiving short-level posterior lumbar interbody fusion: a stepwise propensity score matching analysis

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Abstract

Background There were many literatures reporting the impact of frailty on postoperative complications, however, studies according to stepwise propensity score matching (PSM) to offset the influence of age were limited.

Methods We gathered data for all patients undergoing short-level posterior lumbar interbody fusion from January to December 2021. Accroding to Fried frailty phenotype, we segragated patients into three groups (not-frailty, pre-frailty, and frailty), then, stepwise propensity score matching for age, sex, American Society of Anesthesiologists (ASA) and fusion levels were performed to keep comparable clinical data between groups. Uni- and multivariate logistic regression were used to identify the impact of clinical demographics on postoperative complications.

Results A total consecutive 559 patients with complete medical records were enrolled (237 males and 322 females; mean age 72.55 ± 5.86 years). After PS matching, we found pre-frail patients were more vulnerable to develop urinary retention ($p = 0.031$) and surgical site infection ($p = 0.021$) than non-frail patients. Meanwhile, longer length of stay (LOS), ambulation time and removal of urinary catheter time were observed in pre-frail patients. However, there was significant difference only in LOS between pre-frail and frail patients. Binary logistic regression revealed that C-reaction protein (CRP) and frailty status were independently associated with postoperative complications between non-frail and pre-frail patients, while only CRP was independently correlated with that of between pre-frail and frail patients.

Conclusions In this study, after PS matching, we found higher rate of urinary retention and surgical site infection in pre-frail patients than that of non-frail patients. CRP was independently related to postoperative complications, while frailty status was only independently associated with postoperative complications between pre-frail and non-frail patients. And pre-frail/frail patients tended to have severer stress response than that of non-frail patients.

Introduction

Kehlet proposed enhanced recovery after surgery (ERAS) in 1997[1]. It provides a multimodal, multidisciplinary management strategy[2, 3]. The primary purpose of ERAS is to reduce postoperative adverse events and accelerate recovery by decreasing stress responses, shortening the length of stay (LOS) and hospitalization costs[4, 5]. Established and maturely implemented in 2019[6], numerous patients benefited from ERAS in our department, although there was a reduction in LOS and lower complication rates, specific patients cannot be discharged as quickly as expected despite ERAS, demonstrating that some other preoperative evaluations should be emphasized.

In previous studies, there were many factors associated with prolonged LOS and postoperative complications have been discussed. According to a retrospective study of 217 patients, Strickland et al[7] reported that the old were more prone to develop postoperative urinary retention and have longer LOS. Kong et al[8] demonstrated smaller body mass index (BMI□24.32kg/m2) was related to minor

complications. In a retrospective study of 630 patients undergoing elective lumbar disc arthroplasty, Ansari et al[9] illustrated longer operation length was correlated with prolonged LOS and patients with prolonged LOS were more vulnerable to venous thromboembolisms, pneumonia, surgical site infections, and reoperations.

Frailty is a syndrome of decreased physiological reserve, daily activities as well as strength[10, 11]. Accurate risk stratification and predicting postoperative complication in time are imperative in older patients undergoing lumbar fusion surgery[12]. In recent years, there were many studies reporting convincing results that frailty is a stronger predictor than age for postoperative morbidity[13, 14]. However, old people are a heterogeneous group of patients and frailty is abviously related to age, so when discussing the effect of frailty on postoperative outcomes, it is necessary to eliminate the effect of age on frailty status. The purpose of this study is to discuss the effect of frailty on postoperative outcomes in patients undergoing short-level lumbar fusion surgery after eliminating the influence of age as a confounding factor according to propensity score matching.

Patients And Methods

Study design

This was a retrospective, monocentric, and consecutive cohort study. All patients with completed clinical demographic data and undergoing short-level posterior lumbar interbody fusion (PLIF) between 1 January 2021 and 31 December 2021 were enrolled. Frailty, as distinguished by Fried frailty phenotype and modified frailty index, both were evaluated by trained nurses after admission to ward. And in this study, Fried frailty phenotype was utilized to describe frailty status. Then, segregating patients into 3 groups according to the frailty status and stepwise PS matching was performed to ensure groups with comparable clinical data. The institutional review board in Xuanwu Hospital Capital Medical University approved the study (No. 2018008), which followed the Declaration of Helsinki principles. A written informed consent was obtained from all participates of this study.

Patients selection

We retrospectively reviewed patients receiving short-level PLIF between 1 January 2021 and 31 December 2021. Inclusion criteria were as follows: 1) lumbar disk herniation, lumbar spinal stenosis, and lumbar spondylolisthesis according to radiographic examination and magnetic resonance imaging by two experienced surgeons; 2) no history of surgery; 3) age greater than 65 years; and 4) short-level lumbar fusion surgery defined as the number of fusion levels no more than 2. The exclusion criteria were 1) emergency operation; 2) lack of clinical data; 3) combined surgery; and 4) other severe surgical contraindications. Finally, there were 559 patients with completed clinical data enrolled, the detailed flowchart was showed in Figure 1.

Data collection

All information relating to the patient was obtained from medical records. The collected preoperative clinical data included age, sex, body mass index (BMI), concomitant diseases (hypertension, diabetes, osteoporosis, gastrointestinal, heart diseases, and hyperlipidemia), operation time, estimated blood loss (EBL), fusion levels, 30-day readmission rates, postoperative ICU and American Society of Anesthesiologists (ASA) classification. As a routine postoperative laboratory examination item, CRP was extracted according to the result of the first laboratory test within two days after surgery. Length of stay (LOS) was defined as a period from postoperative day 1 to discharge. Besides, urinary catheter extraction time, and postoperative mobilization time were also extracted. Postoperative complications included nausea and vomiting, surgical site infection, cerebrospinal fluid leakage, urinary retention, urinary tract infection, deep venous thrombosis, and myocardial ischemia.

Fried frailty phenotype

Fried frailty phenotype we used in this study was described by Fried and colleagues[15], which was comprised of five variables including unintentional weight loss, self-reported exhaustion, low physical activity, slowness and weakness. The score assigns 1 point for any above factors and the Fried frailty score was calculated for each subject by adding each variable. According to the Fried criteria, we categorized patients as not frail (a score of 0), pre-frail (a score of 2 - 3), and frail (a score of 3 - 5).

Statistical analysis

Continuous variables were expressed as mean value ± standard deviation (mean ± SD) when the normal distribution was met, if not, median with interquartile range (IQR) was used. Continuous variables were analyzed using the T-test or analysis of variance (ANOVA), and the Bonferroni test was used for post hoc analysis, while statistical analysis for categorical variables was performed using the Chi-square test or the Fisher exact test. According to previous studies,[16-18] we found that frailty was significantly related to age. Hence, 1:1 nearest-neighbor propensity score matching for age, sex, fusion levels, and ASA was implemented between not frailty group and pre-frailty group to keep preoperative comparable clinical data as much as possible. Analogously, the same procedure was performed between pre-frailty group and frailty group. Match tolerance was set at 0.02. Uni- and multivariate logistic regression were used to identify the impact of clinical demographics on postoperative complications. All statistical analyses were performed using SPSS software version 25.0 (SPSS, Inc., Armonk, NY, USA), and P-values < 0.05 were considered statistically significant.

Results

Baseline demographics

There were 559 consecutive patients who met the criteria enrolled (237 males and 322 females; mean age 72.55 ± 5.86 years). According to Fried frailty phenotype, 279 were not frailty with 57.3% being female, 185 pre-frailty with 60% being female, and 95 were frailty with 53.7% being female. The mean age were 70.48 ± 4.87, 73.38 ± 5.70, and 77.01 ± 5.96 years, respectively. The clinical characteristics were displayed in Table 1. After PS matching, there were 147 well-balanced pairs of patients between not frailty and pre-frailty, 84 well-balanced pairs of patients between pre-frailty and frailty. The detailed demographic data after PS matching are revealed in Table 2.

Postoperative outcomes

The detailed clinical demographics were displayed in Table 3, after PS matching, we found pre-frail patients were more vulnerable to develop urinary retention ($p = 0.031$), and surgical site infection ($p = 0.021$) than that of non-frail patients. However, there were no significant difference in nause and vomiting, urinary tract infection, deep venous thrombosis, myocardial ischemia, postoperative ICU, 30-day readmission, and cerebrospinal fluid leakage between non-frail and pre-frail groups. Besides, comparing with pre-frail patients, the length of stay was reduced from 7.21 ± 2.99 to 6.35 ± 2.66 days ($p = 0.010$), the ambulation time was reduced from 2.46 ± 1.29 to 2.06 ± 1.18 days ($p = 0.006$), and removal of urinary catheter time was reduced from 2.14 ±1.30 to 1.79 ± 1.12 days ($p = 0.015$), respectively. And frail patients were more prone to have prolonged LOS (7.06 ± 2.95 versus 8.23 ± 3.40, $p = 0.019$) than pre-frail patients. However, there were no significant difference in other metrics. Binary logistic regression revealed that CRP and frailty status were independently associated with postoperative complications between non-frail and pre-frail patients, while only CRP was independently correlated with that of between pre-frail and frail patients.The detailed outcomes were showed in Table 4.

CRP

As an indicator to evaluate the stress response associated with surgery, CRP has been confirmed to be correlated with postoperative complications in previous studies[19-21], Consistent with previous studies, in our study, after PS matching for age, sex, ASA, and fusion levels, we found that pre-frail patients may be likely to have severe stress response than non-frail patients (12.26 ± 11.68 versus 17.25 ± 25.37 mg/L, $p = 0.033$), analogous suitation was observed between pre-frail and frail patients (16.84 ± 26.43 versus 26.49 ± 32.73 mg/L, $p = 0.038$). The characteristics of these groups are detailed in Figure 2.

Discussion

While it is widely accepted that increased age serving as an indactor to predict postoperative complications, however, because the heterogeneity of different population, some younger people can be frail, and some older people can be robust[16]. In recent years, frailty, as distinguished by 5-item Fried frailty phenotype was one of the most commonly uesd to evaluate postoperative outcomes[22]. Nevertheless, on one hand, in previous literatures, comparing frailty and age the superiority to predict

postoperative complications was the focus. In a retrospective analysis of 199 patients, Leung et al[23] demonstrated that age was a significant moderator of the relationship between pre-frailty and body measures. Analogously, in a retrospective analysis of 8174 patients, performed by Moguilner et al[17], the results of receiver operating characteristic curve indicated that the addition of age to an frailty index could improve its mortality prediction. However, it cannot be ingored that frailty is significantly related to increasing age, which has been verified in previous studies[16–18]. On the other hand, in previous literatures, patients were dichotomized as non-frailty and pre-frality/frailty groups, without considering pre-frailty as an independent group[16, 24]. Hence, in our study, PS matching for age, sex, ASA, fusion levels was used to guarantee comparable clinical characteristics between groups and pairwise comparisions was performed to compare the effects of frailty on complications. After PS matching, we found that the LOS, the rate of urinary retention and surgical site infection of pre-frailty patients were greater than that of non-frailty patients, meanwhile, the pre-frail patients were more vulnerable to greater stress response associated with surgery than that of non-frail patients. Binary logistic regression indicated that CRP and pre-frailty were independently correlated with postoperative complications between non-frailty patients and pre-frailty patients. While there were statistically difference just in LOS and CRP between pre-frail and frail patients, which reflected the reasonability of grouping dichotomously in some extent.

As frailty is being increasingly studied as a common characteristic impacting postoperative outcomes in spine surgery. In a prospective cohort analysis of 668 patients following spine surgery, frailty, as distinguished by risk assessment index, Agarwal et al[16] found that pre-frail and frail patients suffered longer LOS (3.9 d ± 3.6 vs 3.1 d ± 2.8, $p < 0.001$). Likewise, in a retrospective cohort study of geriatric patients receiving single-level lumbar fusion, after propensity score matching, Shahrestani et al[24] showed significantly greater LOS (9.9 ± 10.1 versus 4.0 ± 3.9, $p < 0.0001$) in frail patients than non-frail patients. In line with previous studies, we found that after propensity score matching, pre-frail patients had longer LOS (7.21 ± 2.99 versus 6.35 ± 2.66, $p = 0.010$) than non-frail patients and similar result was found between frail patients and pre-frail patients (8.23 ± 3.40 versus 7.06 ± 2.95, $p = 0.019$). With the aging population as well as the prevalence of frality among spine surgery patients, evaluating the impact of frailty on postoperative complications has been a hot topic. In a retrospective review of 426 patients undergoing elective posterior thoracolumbar fusion surgery, frailty, as distinguished by modified frailty index, Sun et al[25] showed that frailty was independently associated with adverse events. Shahrestani et al[24] reported that frail patients encountered higher rate of UTI (OR: 3.97, 95%CI: 3.21–4.95, $p < 0.0001$), infection (OR: 6.87, 95%CI: 4.55–10.86, $p < 0.0001$), and 30-day readmission (OR: 1.24, 95%CI: 1.02–1.51, $p = 0.035$). Nevertheless, in a retrospective review of 5296 patients, Elsamadicy et al[18] reported that modified frailty index cannot independently predict complications. In our study, while higher rate of urinary retention ($p = 0.031$), and surgical site infection ($p = 0.021$) were observed in pre-frail patients than that of non-frail patients, there were no significant difference in other complications, binary logistic regression indicated that pre-frailty was independently related to postoperative complications. However, similar results were not observed between pre-frail patients and frail patients. Whereas the current findings were inconsistent with previously publicated in some extent by our department. The possible

explanations were as follows. Firstly, comparing with results of Sun et al, “ the severity of frailty was an independent predictor of minor complication in the short spinal fusion (SSF) group ” whose frailty was evaluted by 11-item modified frailty index, in current research, however, 5-item Fried frailty phenotype was used to describe frailty status. Secondly, propensity score matching was performed in current study to offset the effects of confounding factors, which elevating the reliablility of current study. The contradictory results revealed that high-quality studies are needed for a more precise evaluation of the impact of frail status on postoperative complications.

In previous studies[26, 27], early ambulation could significantly reduce the rate of postoperative complications and early mobilization within 24 hours after short-level lumbar fusion surgery was feasible. In our department, all patients receiving short-level fusion surgery were advocated to ambulate within 24 hours if there were no patient-reported discomfort. In this matching cohorts, not-frail patients were more likely to ambulate (2.06 ± 1.18 versus 2.46 ± 1.29, $p = 0.006$) and remove urinary catheter (1.79 ± 1.12 versus 2.14 ± 1.30 $p = 0.015$) earlier than pre-frail patients. However, there were no statistically difference between pre-frail patients and frail patients.

CRP is usually used to serve as an indicator to evaluate the stress response associated with surgery and in previous studies, which was confirmed to be correlated with postoperative complications[21, 28]. In current study, after PS matching, severer stress response was observed in pre-frail patients than non-frail patients (Fig. 2A) and even frail patients suffered more stress response than pre-frail patients (Fig. 2B), which means pre-frail and frail patients have higher risk of postoperative complications than non-frail patients. Therefore, in the perioperative management, in order to reduce postoperative complications, more attention should be paid to patients idnetified with pre-frailty or frailty.

There were several limitations in resent study. Firstly, this was a monocentric, retrospective cohort study, which may have introduced selection bias. Secondly, as only patients receiving short-level lumbar fusion surgery were included, there were 559 patients enrolled in this study, after propensity score matching, there were only 84 well-balanced patients between pre-frailty and frailty, the small sample sizes may lead to the current results. Despite above limitation, segragating patients into 3 groups according to Fried frailty phenotype and comparing stepwise is a noval attempt to evaluate the impact of frailty on postoperative complications.

Conclusion

In this study, after propensity score matching, we found higher rate of urinary retention and surgical site infection in pre-frail patients than that of non-frail patients. CRP was independently related to postoperative complications, while frailty status was only independently associated with postoperative complications between pre-frail and non-frail patients.

Abbreviations

PLIF: posterior lumbar interbody fusion; PSM: propensity score matching; ASA: American Society of Anesthesiologists; LOS: length of stay; CRP: C-reaction protein; EBL: estimated blood loss; BMI: body mass index.

Declarations

Enthics approval and consent to participate

The institutional review board in Xuanwu Hospital Capital Medical University approved the study (No. 2018008), which followed the Declaration of Helsinki principles.

Consent for publication

A written informed consent was obtained from all participates in this study.

Availability of data and meterials

The data used to support the findings of this study were included within the article.

Competing interests

The authors declare that there are no conflicts of interest in this work.

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Authors' contributions

Peng Cui, Peng Wang, Chao Kong and Shibao Lu discussed and designed this experiment. Peng Cui and Peng Wang performed this experiment. Jialin Wang and Xu Liu reviewed and analyzed the data. Peng Cui and Peng Wang were equal contributors in writing the paper. Chao Kong and Shibao Lu revised the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1

Patient demographics

Variable	Non-frailty (n=279)	Pre-frailty (n=185)	Frailty (n=95)	p
Age,mean (SD)	70.48 ± 4.87	73.38 ± 5.70	77.01 ± 5.96	< 0.001
Sex				0.595
Male	119	74	44	
Female	160	111	51	
ASA				0.774
I	2	1	1	
II	153	101	52	
III	119	81	42	
IV	5	2	0	
Fusion level				0.572
1 level	129	83	38	
2 levels	150	102	57	
Comorbidities				0.878
Hypertension	160	114	58	
Diabetes	83	48	33	
Osteoporosis	33	25	11	
Gastrointestinal	6	5	4	
Heart diseases	54	43	23	
Hyperlipidemia	24	21	6	
EBL, mean (SD)	239.46 ± 217.39	274.00 ± 205.18	270.21 ± 199.57	0.177
BMI, mean (SD)	25.83 ± 3.73	25.37 ± 3.45	25.04 ± 3.62	0.137
Operation time, mean (SD)				
	180.53 ± 48.19	189.64 ± 58.27	200.15 ± 54.20	0.005

ASA: American Society of Anesthesiologists; EBL: estimated blood loss; BMI body mass index

Table 2

Results of propensity score matching patient groups

Variable	Matched patients(N=294)		
	Not frailty (n=147)	Pre-frailty (n=147)	p
Age, mean (SD)	71.63 ± 5.02	72.07 ± 5.25	0.468
Sex			0.814
Male	64	62	
Female	83	85	
ASA			0.670
I	0	1	
II	86	82	
III	60	63	
IV	1	1	
Fusion levels			0.906
1	65	64	
2	82	83	
Comorbidities			0.702
Hypertension	80	89	
Diabetes	45	38	
Osteoporosis	15	21	
Gastrointestinal	4	2	
Heart diseases	32	30	
Hyperlipidemia	13	16	
EBL, mean (SD)	255.86 ± 251.79	283.33 ± 201.79	0.303
BMI, mean (SD)	25.24 ± 3.42	25.52 ± 3.53	0.497
Operation time, mean (SD)	181.57 ± 48.99	190.08 ± 56.55	0.169
Variable	Matched patients(N=168)		
	Pre-frailty (n=84)	Frailty (n=84)	p
Age, mean (SD)	76.14 ± 5.76	76.15 ± 5.67	0.989
Sex			0.537

Male	43	39	
Female	41	45	
ASA			0.523
II	41	45	
III	42	39	
IV	1	0	
Fusion levels			0.876
1	36	37	
2	48	47	
Comorbidities			0.784
Hypertension	52	48	
Diabetes	22	28	
Osteoporosis	9	7	
Gastrointestinal	2	3	
Heart diseases	24	22	
Hyperlipidemia	9	5	
EBL, mean (SD)	280.24 ± 198.64	257.83 ± 178.94	0.445
BMI, mean (SD)	25.21 ± 3.39	24.85 ± 3.30	0.477
Operation time, mean (SD)			
	189.49 ± 53.60	197.82 ± 53.97	0.318

ASA: American Society of Anesthesiologists; EBL: estimated blood loss; BMI: body mass index

Table 3

Postoperative outcomes between matching patient groups

Variable	Matched patients(N=294)		
	Not frailty (n=147)	Pre-frailty (n=147)	p
Nausea and vomiting	9	5	0.273
Urinary retention	2	9	**0.031**
Urinary tract infection	1	4	0.176
Surgical site infection	5	15	**0.021**
Deep venous thrombosis	1	5	0.090
Myocardial ischemia	7	12	0.236
Cerebrospinal fluid leakage	1	2	0.562
LOS, mean (SD)	6.35 ± 2.66	7.21 ± 2.99	**0.010**
Postoperative ICU	2	5	0.251
30-day readmission	5	6	0.759
Ambulation time, mean (SD)	2.06 ± 1.18	2.46 ± 1.29	**0.006**
Removal urinary catheter time, mean (SD)	1.79 ± 1.12	2.14 ±1.30	**0.015**
Variable	Matched patients(N=168)		
	Pre-frailty (n=84)	Frailty (n=84)	p
Nausea and vomiting	6	4	0.514
Urinary retention	6	5	0.755
Urinary tract infection	3	5	0.469
Surgical site infection	8	13	0.243
Deep venous thrombosis	4	6	0.514
Myocardial ischemia	5	8	0.386
Cerebrospinal fluid leakage	1	0	0.316
LOS, mean (SD)	7.06 ± 2.95	8.23 ± 3.40	**0.019**
Postoperative ICU	5	4	0.732
30-day readmission	3	9	0.072
Ambulation time, mean (SD)	2.59 ± 1.43	2.89 ± 1.25	0.148

Removal urinary catheter time, mean (SD)			
	2.38 ± 1.45	2.42 ± 1.34	0.868

LOS: length of stay; ICU: intensive care unit

Table 4

Binary logistic reegression for postoperative complications between matched groups

Variable	Matched patients(N=294)		
	Odds ratio	95% confidence interval	p
BMI	1.064	0.972-1.165	0.176
Operation time	1.002	0.996-1.009	0.419
CRP	1.063	1.040-1.087	**< 0.001**
Pre-frailty	2.080	1.108-3.907	**0.023**
EBL	1.000	0.998-1.001	0.559
Variable	Matched patients(N=168)		
	Odds ratio	95% confidence interval	p
BMI	1.072	0.945-1.215	0.279
Operation time	0.996	0.987-1.005	0.987
CRP	1.058	1.058-1.139	**< 0.001**
Frailty	0.951	0.418-2.164	0.905
EBL	1.001	0.998-1.003	0.636

BMI: body mass index; CRP :C-reaction protein; EBL:estimated blood loss

Figures

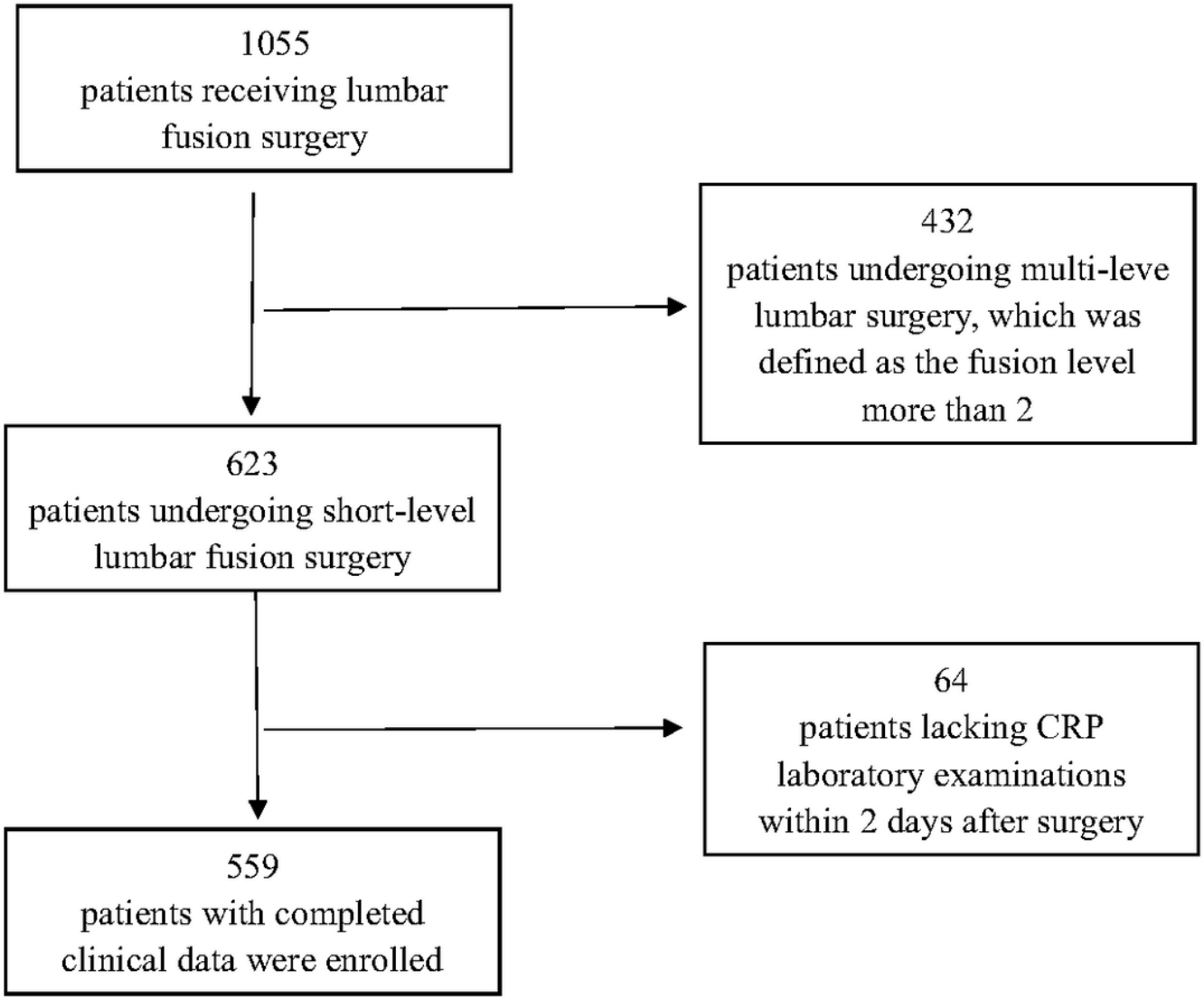

Figure 1

patient selection flowchart.

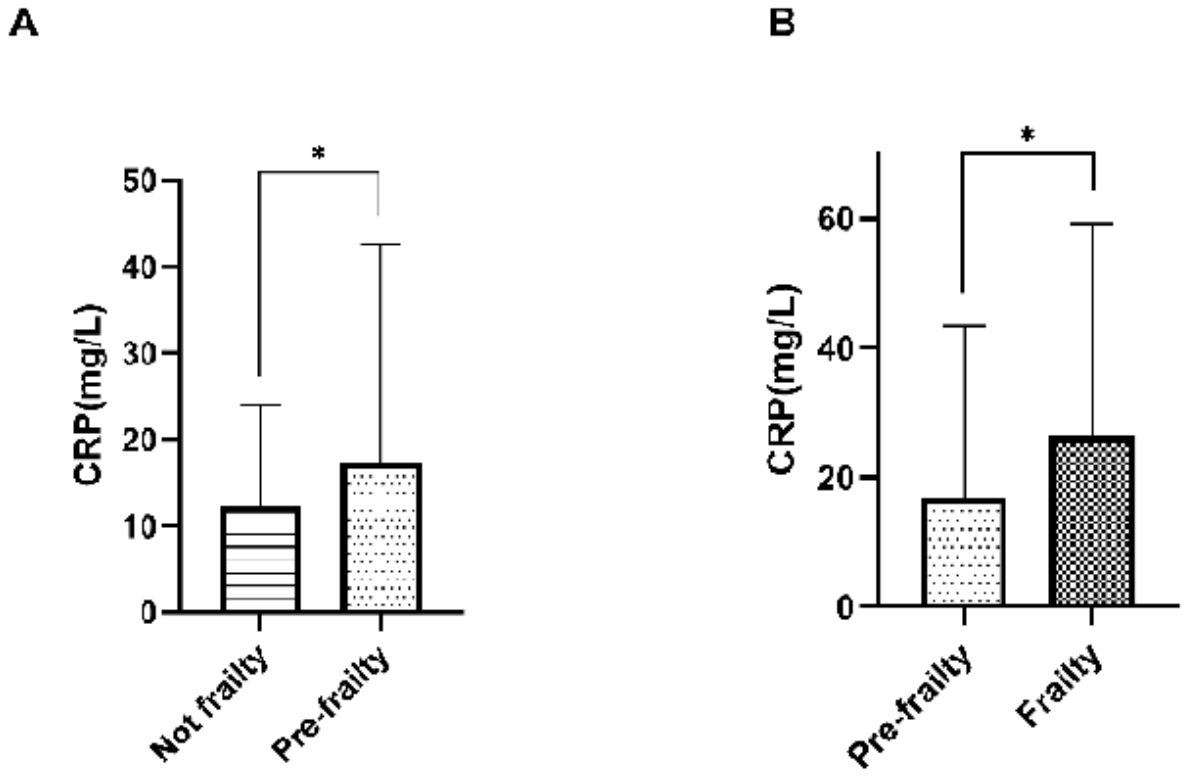

Figure 2

The outcomes of CRP between groups (Figure A demonstrates that CRP of pre-frail patients were severer than that of non-frail patients. Figure B reveals that CRP of frail patients were even severer than pre-frail patients) . * $p < 0.05$