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Predictive value of frailty and nutritional risk screening for in-hospital complications in elderly patients with hip fractures

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ABSTRACT

Background and Objectives: To investigate the underlying inflammatory markers of frailty and evaluate the predictive power of frailty and nutritional risk screening for in-hospital complications in elderly patients with hip fractures. **Methods and Study Design:** A total of 233 elderly patients with hip fractures participated in the study between August and October 2021. Frailty and nutritional risk screening was performed on all participants, who were then divided into frail ('frail only' and 'frail and malnourished') and non-frail ('robust' and 'malnourished only') cohorts. The clinical data were collected for all participants, and in-hospital complications were followed up. **Results:** Among the patients, 39.9% were frail, 26.2% were malnourished and 15.5% were both frail and malnourished. The frail group were older and had higher Charlson comorbidity index (CCI) scores, systemic immune-inflammation index (SII) levels and fibrinogen levels than patients in the other cohorts. After adjusting for age, CCI and nutritional status, the SII was an independent predictor of frailty, indicating its role as an inflammatory marker of frailty. Frail patients had significantly higher rates of total complications, lower limb deep vein thrombosis (DVT), infections and cardiac complications than the non-frail group. Patients who were both frail and malnourished had a 1.98 times higher risk of nosocomial infection than those who were only frail. **Conclusions:** The SII is a significant predictor of frailty, and it may be used as an inflammatory marker of frailty. The fatigue, resistance, ambulation, illnesses and loss of weight scale can effectively predict the in-hospital complications of elderly patients with hip fractures. Combined with nutritional risk screening, it can improve the prediction ability of nosocomial infection complications in frail elderly patients with hip fractures.

Key Words: hip fracture, frailty, inflammatory marker, nutritional status, complications

INTRODUCTION

Geriatric hip fractures, defined as intertrochanteric fractures or femoral neck fractures caused by low-energy injuries in individuals aged 65 and older, represent a major public health issue.¹ The rising number of hip fractures is attributed to the ageing population and the associated increase in osteoporosis and falls.² Patients with hip fractures are often characterised by advanced age, frailty and the presence of multiple comorbidities, such as cardiovascular diseases, diabetes and chronic respiratory conditions.³ These factors contribute to a complex clinical presentation and pose significant challenges in the management of these

patients. Furthermore, these individuals frequently present with poor nutritional status upon admission. This condition can worsen during hospitalization as a result of traumatic stress, pain, immobility and anorexia, leading to further frailty and an increased risk of complications.⁴ Complications associated with hip fractures in the elderly are numerous and can include lung infections, urinary tract infections, pressure ulcers and DVT in the lower extremities.⁵ These complications not only increase the mortality rate but also lead to prolonged hospital stays and increased healthcare costs. Additionally, hip fractures often result in a significant decline in functional status, reducing the patient's quality of life and increasing their dependency on caregivers and social services.

Preoperative frailty and malnutrition are critical factors influencing the prognosis of elderly patients with hip fractures. Frailty is a state of increased vulnerability resulting from a decline in physiological reserves and function across multiple systems. Malnutrition, characterised by deficiencies in energy, protein and other nutrients, exacerbates frailty and impairs the body's ability to recover from injury and illness. Both frailty and malnutrition have been independently associated with poor outcomes, including higher rates of complications, prolonged recovery times and increased mortality.⁶⁻⁹ Comprehensive screening tools that integrate both frailty and nutritional risk could provide valuable insights into the overall health status of elderly patients with hip fractures. Such assessments could facilitate the early identification of high-risk individuals, enabling targeted interventions to mitigate the risk of complications and improve clinical outcomes. The fatigue, resistance, ambulation, illnesses and loss of weight (FRAIL) scale is a hybrid measure comprising components from the Fried frailty phenotype of the Cardiovascular Health Study and the Frailty Index. It is simple, valid and feasible for routine use. There is no gold standard for screening nutritional risk. The Mini Nutritional Assessment Short-Form (MNA-SF) and Nutritional Risk Screening 2002 (NRS-2002) are the two most commonly used malnutrition screening tools in elderly patients with hip fractures. The NRS-2002 includes an assessment of the patient's nutritional status and disease severity. It has prognostic implications and is a nutritional screening tool recommended by the European Society for Clinical Nutrition and Metabolism guidelines. The MNA-SF is known as the gold standard test for malnutrition screening and assessment in the elderly. It can also predict re-admissions and mortality.^{10,11} Despite the recognised importance of these factors, the combined assessment of frailty and nutritional status is rarely utilised in clinical practice.

This study aims to explore the predictive value of combining frailty assessment with nutritional risk screening for in-hospital complications in elderly patients with hip fractures.

By examining frailty and nutritional status between the frail and non-frail groups, this research seeks to enhance our understanding of how these factors contribute to patient outcomes and to develop more effective strategies for managing this vulnerable population. Ultimately, the goal is to improve clinical care, reduce healthcare costs and enhance the quality of life for elderly patients with hip fractures.

MATERIALS AND METHODS

Patients

Between August and October 2021, 260 consecutive patients aged ≥ 65 years with acute hip fractures presenting to the emergency department of Beijing Jishuitan Hospital were included in the study. The exclusion criteria were as follows: (1) conservatively treated patients; (2) patients with a pathological fracture; (3) patients unable to cooperate with simple questions and answers; (4) patients with severe oedema.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Beijing Jishuitan Hospital, Capital Medical University (202201-10). Written informed consent was obtained from all participants.

Data collection

The patients' demographic and comorbid data were then collected. This included gender, age, body mass index (BMI), calf circumference and CCI. Frailty was assessed using the 5-item FRAIL scale.^{12,13} The score ranges from 0 to 5 points, with one point given for each affirmative response. Individuals are classified as non-frail (0 to 2 points) or frail (≥ 3 points). The NRS-2002 (age < 90 years) and MNA-SF (age ≥ 90 years) were used for nutritional risk screening; NRS-2002 ≥ 3 points or MNA-SF < 12 points were judged as 'at risk' and 'malnourished', respectively. We combined the two categories into one category called 'malnourished'. This study classified patients into four groups based on their frailty and nutritional status: 'robust', 'malnourished only', 'frail only' and 'frail and malnourished'. The classification was made using the FRAIL scale for frailty assessment, where a score ≥ 3 points indicated frailty, and the NRS-2002 or MNA-SF for nutritional risk, with NRS-2002 ≥ 3 points or MNA-SF < 12 points indicating malnourishment. Initial complete blood count on admission was used to calculate the SII: (platelet count) \times (neutrophil-to-lymphocyte ratio).

Routine biochemical and coagulation analytes, thyroid hormone, parathyroid hormone, 25-OH-vitaminD3 (25(OH)D3) and some blood bone turnover markers were tested. The main in-hospital complications (infections [respiratory, urinary, cutaneous, wound] cardiovascular [ischaemic, arrhythmic, congestive], neurologic [cerebrovascular] and venous thromboembolic) were recorded. All patients with hip fractures without contraindications to anticoagulation were administered low molecular weight heparin (LMWH) sodium subcutaneously by injection (5,000 IU once daily, discontinued the night before surgery).

Statistical analysis

The SPSS 26 (IBM Corporation, Armonk, NY, USA) and R 3.6.1 software were used for statistical analysis. Continuous data were expressed as mean \pm standard deviation (normal distribution) or median and interquartile ranges (non-normal distribution), and the comparison between groups was performed using the Student's t-test or Kruskal–Wallis test. Categorical variables were presented as number and percentage and compared using Fisher's exact or Chi-square tests. To identify a subset of independent variables that were associated with frailty, a univariate logistic regression was performed based on age, malnutrition, CCI, SII and plasma fibrinogen level. As for complications, a subgroup analysis and multivariate analysis was performed. All tests were two-tailed, and p -values <0.05 were considered significant.

RESULTS

Prevalence of frailty, malnourishment and in-hospital complications

In total, 260 patients with hip fractures aged ≥ 65 were admitted to the hospital during the study period. Of these, 27 were excluded because of severe dementia (12 cases) or being non-operable (15 cases), with 233 patients (mean age 78.64 ± 8.47 years, 64.4% women) eventually included. In terms of types of fracture, 123 (52.8%) were femoral neck fractures, 107 (45.9%) were femoral intertrochanteric fractures and 3 (1.3%) were femoral subtrochanteric fractures. In addition, 59.7% of the patients were comorbid with two or more diseases, 93 (39.9%) were frail, 61 (26.2%) were malnourished and 34 (15.5%) were frail and malnourished.

The incidence of total in-hospital complications was 57.1%. Of these, 91 (39.1%) patients had lower limb DVT, 46 (19.7%) had an infection, 10 (4.3%) had cardiac complications, 3 (1.3%) had cerebrovascular complications and 8 (3.4%) had delirium. Only one person died during hospitalisation. Because most patients were routinely treated with proton pump inhibitors, the occurrence of stress ulcer was not included in the study.

Characteristics of elderly patients with hip fractures considered frail

The clinical characteristics of the sample are described in Tables 1–3. There was no significant difference in gender or serum creatinine and glycosylated haemoglobin levels between the frail and the non-frail groups ($p > 0.05$). The average age and CCI score of the frail group were lower than those of the non-frail group ($p < 0.01$), and malnourishment was more prevalent in the frail group (19.3% vs 36.6%; $p < 0.01$). The BMI, calf circumference and levels of serum hemoglobin, albumin, prealbumin, blood calcium, 25(OH)D3 and β -glucuronidation products (β -CTX) in the frail group were higher than those in the non-frail group (Table 2). The SII, hs-CTNI and fibrinogen levels were higher in the frail group than in the non-frail group. Free Triiodothyronine (FT3) and Total Triiodothyronine (T3) levels were lower in the frail group than in the non-frail group (Table 3). Multivariate logistic regression analysis revealed that age, CCI and SII were closely related to frailty, and the SII could be used as an inflammatory marker of frailty. Although malnourishment was more prevalent in the frail population, malnourishment and frailty were weakly correlated (Figure1).

Comparison of complications between the groups

The main complications of elderly patients with hip fractures were categorised into three major types: infections, cardiovascular diseases and neurological diseases (Table 4).

Infections

The frail group had a significantly higher rate of infections than the non-frail group (32.3% vs 11.4%, $p < 0.01$). In the subgroup analysis, patients who were both frail and malnourished had a 1.98 times higher risk of nosocomial infection than those who were only frail. This suggests a possible synergistic effect between frailty and nutritional risk, which may contribute to the increased incidence of infections in the frail and malnourished subgroup (Table 5).

Cardiovascular diseases

The incidence of cardiovascular complications, including ischaemic and arrhythmic events, was significantly higher in the frail group than in the non-frail group (8.6% vs 1.4%, $p = 0.011$).

Neurological diseases

Neurological complications such as cerebrovascular events were rare but present in 2.1% of frail patients, with no cases reported in the non-frail group.

To clarify the effects of malnutrition and frailty on infections, multivariate analysis was performed using R software. A correlation was identified between frailty and malnourishment ($p < 0.01$). Patients who were frail and malnourished were 1.33 times more likely to develop infections than those who were robust ($p < 0.05$), indicating a synergistic effect between frailty and malnourishment in infections (Figure 2).

DISCUSSION

Geriatric patients with hip fractures often experience an overlap in problems such as frailty, undernutrition and sarcopenia. This study used the FRAIL scale, NRS-2002 and MNA-SF to assess frailty and malnutrition risk. We determined that 39.9% of elderly inpatients with hip fractures were frail, which is consistent with previous studies.^{12,13} Malnutrition is common in elderly patients with hip fractures. The prevalence of 'at malnutrition risk' varies depending on the screening methods used, ranging from approximately 26.5 % to 60 %.^{6,11,14} In this study, the incidence of malnourishment (nutritional risk and malnutrition) was only 26.2%. This may be related to the fact that our study did not include patients with severe dementia or non-operable patients, as these individuals tend to be in poorer clinical condition and are more often at nutritional risk. In the present study, patients with frailty had a higher incidence of malnourishment than non-frail patients, with lower levels of nutritional indicators such as BMI, calf circumference and levels of albumin, prealbumin, calcium and 25(OH)D3 as well as higher levels of β -CTx. Beta-CTx is a fragment released into the blood after the degradation of medium collagen in the process of bone reconstruction, reflecting the degree of bone resorption and increased bone loss. This suggests that frail patients are more likely to have nutritional problems such as muscle and bone loss. Lower haemoglobin levels were also observed in participants with frailty. This is probably due to the higher incidence of intertrochanteric fractures (increased blood loss) and the poorer underlying nutritional status of the patients in this group.

There was no statistical difference between the two groups in terms of whether a certain disease was comorbid, but CCI was significantly higher in frail patients than in non-frail patients. After adjusting for age and nutritional risk factors, CCI was closely related to frailty, and CCI was conducive to the identification of frailty.

The inflammatory response is one of the molecular mechanisms of frailty and ageing, and the current assessment of inflammatory ageing and frailty is mainly based on levels of C-reactive protein, interleukin 6, tumour necrosis factor α and fibrinogen.^{15,16} The search for more new inflammatory biomarkers of frailty remains challenging. In recent years, a few

studies^{17,18} have reported on the relationship between the neutrophil-to-lymphocyte ratio and red blood cell distribution width and frailty. Blood cells are closely associated with inflammatory response and frailty. The SII is a comprehensive index of integrated platelets that may reflect cumulative changes in blood cells in response to inflammation and thrombosis. It has been shown to be a prognostic predictor of malignancy, cardiovascular disease and hip fracture.¹⁹⁻²¹ Luo et al.²² found that the SII increases with age in the general population and may be associated with ageing, but few studies on the relationship between SII and frailty have been reported. The median SII of patients in the frail group in this study was $2,218 \times 10^9 /L$, which was significantly higher than that of the non-frail group. After adjusting for age, CCI and nutritional factors, the SII was an independent predictor of frailty; thus, the SII may be used as an inflammatory marker of frailty. Fibrinogen is a key factor in the coagulation process and is also a sensitive indicator of low levels of inflammation. In this study, fibrinogen levels were significantly higher in the frail group than in the non-frail group, but its correlation with frailty was not significant after adjusting for age, nutritional risk and comorbidities ($p > 0.05$). Inflammatory response and immune system imbalance may be a potential cause of infections. There are intricate links and interactions between the inflammatory response, oxidative stress and vascular endothelial function, the immune system and coagulation pathways, all of which can increase DVT formation in the lower limbs, myocardial injury and cardiovascular disease.

Frailty is also closely related to thyroid function. The study by Bertoli et al.²³ identified FT3 as a possible marker of frailty in the elderly. A study by Cai Meng et al. also found that low T3 levels in elderly patients with hip fractures were associated with increased all-cause mortality in patients 30 days postoperatively.²⁴ The results of our study demonstrated that serum T3 and FT3 levels were significantly lower in frail patients than in non-frail patients, whereas there were no significant differences in thyroxine, free thyroxine or thyroid-stimulating hormone, which is consistent with the findings of Bertoli et al.²³

Both frailty and malnourishment in elderly patients with hip fractures represent states of physiological impairment that can overlap. Therefore, screening for both frailty and nutritional risk is essential. There are few studies on the prognostic value of combined frailty and nutritional risk screening in elderly patients with hip fractures. Wilson's study²⁵ found that postoperative complications were significantly higher in patients with hip fractures than in those with frailty or hypoproteinaemia in isolation. In the retrospective observational cohort study, malnutrition was defined by an albumin level of < 3.5 mol/dL. However, hypoproteinaemia does not provide a comprehensive picture of the nutritional risk of patients,

which is the risk of adverse clinical outcomes associated with disease or surgery due to nutritional or metabolic status. In our study, malnourishment included two categories, 'at risk' and 'malnutrition', screened using NRS-2002 or MNA-SF. Frailty combined with malnourishment was identified in 15.5 % of patients. The frailty assessment had a high predictive value for major in-hospital complications, and the combined nutritional risk screening further improved the prediction of infection in frail patients. However, it was not able to further improve the predictive ability for total complications and lower limb DVT. There was synergy between frailty and nutritional risk in the prediction of infection.

Although all patients received subcutaneous injections of LMWH for thromboprophylaxis, the incidence of DVT in the frail group remained significantly higher than in the non-frail group. This may be attributed to several factors beyond the efficacy of LMWH. Frailty is associated with a decline in physiological reserves, including reduced mobility, impaired venous return and inflammation, which may contribute to a hypercoagulable state that LMWH alone may not fully address. Additionally, frail patients in our study had lower nutritional status, as evidenced by lower albumin, prealbumin and BMI levels, which have been associated with an increased risk of thromboembolism. Malnutrition may impair vascular integrity and haemostasis, compounding the risk of DVT despite anticoagulation. Thus, the combination of frailty and malnutrition might explain why frail patients experienced a higher rate of DVT, even with prophylactic LMWH. Future studies could investigate whether higher doses or longer durations of LMWH, or adjunct therapies, may be necessary for frail, malnourished patients.

This study only looked at the incidence of short-term perioperative complications and death in elderly patients with hip fractures, and the sample size was too limited for further analysis of rare complications such as cerebrovascular events and unplanned intubation or in-hospital death. In the future, a multicentre and long-term cohort study with interventions on frailty and malnutrition could be conducted to find ways to improve the postoperative prognosis of frail elderly patients with hip fractures.

Conclusion

The SII is an important predictor of frailty and can be used as an inflammatory marker of frailty. The overlap between undernutrition and frailty is a characteristic of frail patients with hip fractures. The FRAIL scale, combined with nutritional risk screening, may improve the prediction of in-hospital complications, including infection, in frail patients. This combined

assessment approach provides a more comprehensive prediction model for overall complications, contributing to improved patient management and outcomes.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Demographic characteristics and comorbidities

Clinical features	Non-frail group (n=140)	Frail group (n=93)	t/ χ^2 /Z value	p value
Intercrural fracture	56 (40%)	51 (54.8%)	4.955 [‡]	0.026
Female	85 (60.7%)	65 (69.9%)	2.053 [‡]	0.152
Age	75.48 \pm 7.68	83.40 \pm 7.34	-7.847 [†]	0.000
CCI	1 (2)	1 (1)	-3.501	0.000
Hypertension	82 (58.6%)	60 (64.5%)	0.83	0.362
Diabetes	31 (22.1%)	25 (26.9%)	0.687	0.407
Coronary heart disease	28 (20%)	23 (24.7%)	0.732	0.392
Cerebrovascular disease	30 (21.4%)	29 (31.2%)	2.812	0.094
Underlying lung disease	6 (4.3%)	8 (8.6%)	1.844	0.175

CCI: Charlson comorbidity Index

[†] t-values; [‡] χ^2 -values; the rest are Z values.**Table 2.** Nutrition-related indicators and bone metabolism-related indicators

Clinical features	Non-frail group (n=140)	Frail group (n=93)	t/ χ^2 /Z value	p value
Nutritional risks	27 (19.3%)	34 (36.6%)	8.627 [‡]	0.003
Hemoglobin	126.39 \pm 16.26	115.01 \pm 20.15	4.549 [†]	0.000
Albumin	39.94 \pm 3.55	37.75 \pm 3.92	4.421 [†]	0.000
Prealbumin	194.59 \pm 48.74	163.34 \pm 54.68	4.562 [†]	0.000
BMI	23.64 (4.2)	22.6 (5.24)	-2.576	0.010
Calf circumference	33 (2)	32 (2.5)	-4.892	0.000
Total cholesterol	4.45 (1.15)	4.23 (1.23)	-1.612	0.107
Triglycerides	1.09 (0.58)	1(0.73)	-0.288	0.774
Blood Calcium	2.2 (0.18)	2.17 (0.15)	-2.474	0.013
Blood phosphorus	0.92 (0.24)	0.92 (0.27)	-0.381	0.703
PTH	45.8 (25.2)	49.9 (28.3)	-1.108	0.268
25(OH)D3	19.9 (13.94)	13.03 (9.59)	-5.210	0.000
β -CTX	0.36 (0.27)	0.45 (0.3)	-3.464	0.001
tP1NP	42.15 (22.41)	45.09 (32.71)	-1.876	0.061
OC	12.33 (6.85)	12.18 (10.53)	-0.443	0.658

BMI: the body mass index; PTH: Parathyroid hormone; β -CTX: β - Glued degradation products; tP1NP: total type I collagen amino terminal lengthening peptide; OC: osteocalcin[†] t-values; [‡] χ^2 -values; the rest are Z values.

Table 3. Inflammatory factors, coagulation function, thyroid function and other indicators

Clinical features	Non-frail group (n=140)	Frail group (n=93)	Z value	p value
SII	1545 (1152)	2190 (1780)	-4.771	0.000
Fibrinogen	332.8(145)	371.8(176)	-2.258	0.024
D-dimer	12.11 (30.58)	14.94 (28.3)	-0.298	0.766
hs-CTNI	4.4 (4.5)	7.4 (10.7)	-4.070	0.000
Blood creatinine	56 (18.75)	61(24.5)	-1.962	0.050
HbA1c	5.9(1)	5.9(1.2)	-0.433	0.665
FT3	4(0.9)	3.7(1.1)	-4.423	0.000
T3	1.4 (0.4)	1.2 (0.6)	-4.325	0.000
T4	98.3 (23.8)	95.2 (28.1)	-1.032	0.302
TSH	1.44 (1.65)	1.51 (1.52)	-0.533	0.594
FT4	17(3.47)	17.2 (3.55)	-1.068	0.286

SII: systemic immune-inflammation index; hs-CTNI: high-sensitivity troponin I; T3: total triiodothyronine; FT3: free triiodothyronine; T4: total thyroxine; FT4: free thyroxine; TSH: thyroid-stimulating hormone; HbA1c: glycosylated hemoglobin

Table 4. Comparison of complications between the two groups

Complications	Non-frail group (n=140)	Frail group (n=93)	RR (95% CI)	p-value
Total complications	51 (36.4%)	82 (88.2%)	2.42 (1.92-3.05)	0.000
DVT	35 (25%)	56 (60.2%)	2.37 (1.7 - 3.23)	0.000
Infectious complications	16 (11.4%)	30 (32.3%)	2.82 (1.63-4.88)	0.000
Cardiac complications	2 (1.4%)	8 (8.6%)	6.02 (1.31 - 27.73)	0.011
Cerebrovascular complications	0	3 (3.2%)		
Delirium	3 (2.1%)	5 (5.4%)		
Death	0	1 (1.1%)		

DVT: deep vein thrombosis; RR: relative risk; CI: confidence interval

Table 5. Analysis of subgroup complications

Complications	Non "malnourished" (n=113)	"Malnourished" (n=27)	χ^2	p value
Non-frail group (n=140)				
Total complications	42 (37.2%)	9 (33.3%)	0.138	0.71
DVT	31 (27.4%)	4 (14.8%)	1.851	0.174
Infectious complications	14 (12.4%)	2 (7.4%)	0.534	0.465
Frail group (n=93)				
Non "malnourished" (n=59)				
Total complications	50 (84.7%)	32 (94.1%)	1.817	0.178
DVT	36 (61%)	20 (58.8%)	0.043	0.835
Infectious complications	14 (23.7%)	16 (47.1%)	5.373	0.002

DVT: deep vein thrombosis

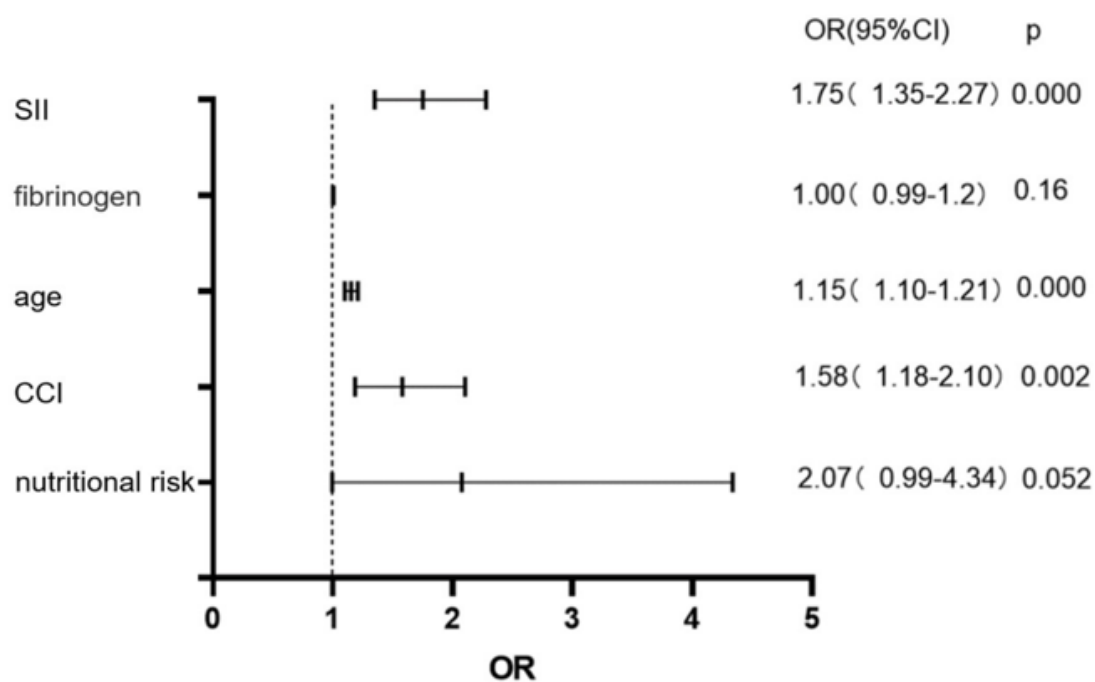


Figure 1. Logistic regression analysis of factors associated with frailty

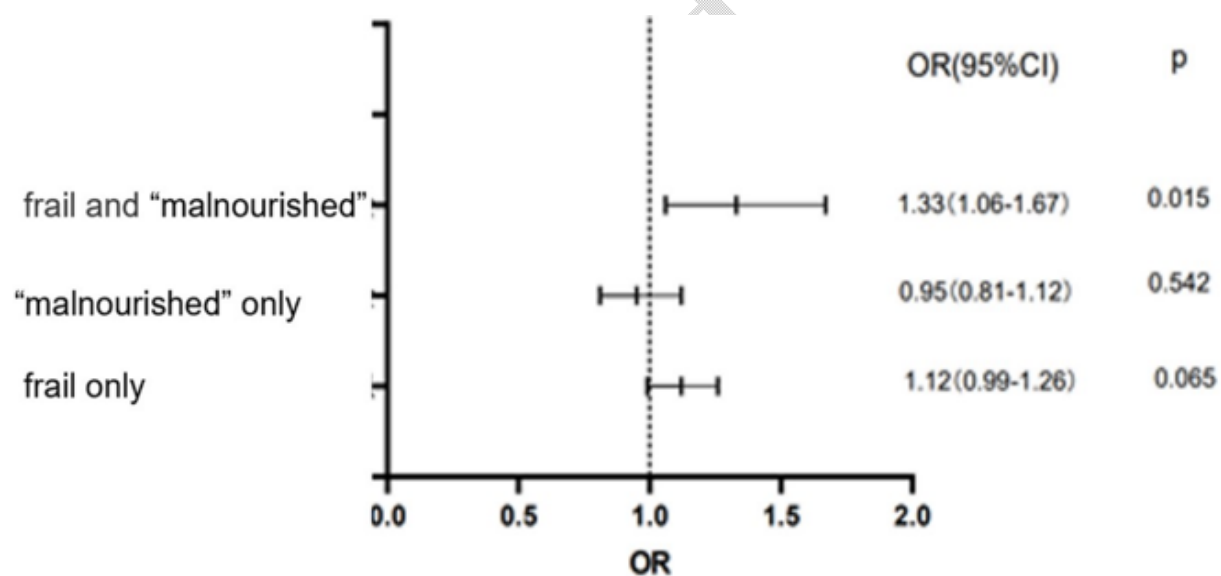


Figure 2. Simple effect analysis of frailty and "malnourished" on infection complications, OR values are for each group compared to the non-frailty and non "malnourished" group.