Original Article



# Predictive value of frailty in the mortality of hospitalized patients with COVID-19: a systematic review and meta-analysis

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**Background:** The present study aimed to analyze the impact of frailty on mortality risk among hospitalized patients with coronavirus disease 2019 (COVID-19).

**Methods:** Literature searches were conducted using the MEDLINE, Embase, and Cochrane databases for articles reporting the association between frailty and mortality in hospitalized patients with COVID-19. The quality of the included studies was assessed using the Newcastle-Ottawa scale (NOS). A random-effects meta-analysis was performed to calculate the pooled effects.

**Results:** A total of 21 studies with 26,652 hospitalized patients were included. Sixteen studies used the Clinical Frailty Score (CFS), and five used other frailty assessment tools. The pooled estimates of frailty in hospitalized patients with COVID-19 were 51.4% [95% confidence interval (CI): 39.9–62.9%]. In the CFS group, frail patients experienced a higher rate of short-term mortality than non-frail patients [odds ratio (OR) =3.0; 95% CI: 2.3–3.9; $I^2$=72.7%; P<0.001]. In the other tools group, frail patients had a significantly increased short-term mortality risk compared with non-frail patients (OR =2.4; 95% CI: 1.4–4.1; P=0.001). Overall, a higher short-term mortality risk was observed for frail patients than non-frail patients (OR =2.8; 95% CI: 2.3–3.5; P<0.001). In older adults, frail patients had a higher rate of short-term mortality than non-frail patients (OR =2.3; 95% CI: 1.8–2.9; P<0.001).

**Conclusions:** Compared to non-frail hospitalized patients with COVID-19, frail patients suffered a higher risk of all-cause mortality, and this result was also found in the older adult group.

**Keywords:** Meta-analysis; frailty; mortality; coronavirus disease 2019 (COVID-19)

Submitted Nov 22, 2021. Accepted for publication Feb 14, 2022.
doi: 10.21037/atm-22-274
**View this article at:** https://dx.doi.org/10.21037/atm-22-274

## Introduction

Since the first reported case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China at the end of 2019, coronavirus disease 2019 (COVID-19) has rapidly become a pandemic causing unprecedented health and economic challenges (1). The majority of COVID-19 patients are asymptomatic or have mild symptoms. However, some individuals develop severe complications leading to death. According to the World Health Organization (WHO) (2), there have been more than four million deaths from COVID-19 across 223 countries as of September 1, 2021. Studies have shown that COVID-19 patients who are elderly and have pre-

existing comorbidities, such as obesity, hypertension, diabetes, chronic renal insufficiency, or coronary heart disease, have worse clinical outcomes (3).

Frailty is a multidimensional geriatric syndrome characterized by impaired stress tolerance due to a decline in physiological reserves and functioning of different organs and is associated with poor health outcomes, including mortality, admissions to nursing homes, and falls. Frailty is a common syndrome in older individuals (4), with a prevalence rate of 41.3% in those aged over 65 and 65.2% in those aged over 80 (5). Nevertheless, aging and frailty are not synonymous (6). Compared with aging, a diagnosis of frailty arises from a comprehensive geriatric assessment that reflects the overall health status of individuals. Several recent studies have explored the association between frailty and the clinical outcomes of patients infected by SARS-CoV-2, but the results remain inconclusive (7-10). Frailty was associated with being female and having comorbidities in patients with COVID-19, and the level of white blood cell count, D-dimer, and C-reactive protein were higher in frail patients (11,12). Most studies have demonstrated that frailty in hospitalized COVID-19 patients is a risk factor for short-term outcomes, such as in-hospital death and intensive care unit (ICU) admission (7,8). However, some studies have found that frailty is not correlated with mortality (9,10). Therefore, it is necessary to synthesize all available evidence to understand whether frailty is a predictor of mortality so as to inform evidence-based decisions in clinical practice. This study provides a systematic review and meta-analysis to compare the mortality risk of frail *vs.* non-frail hospitalized patients with COVID-19. We present the following article in accordance with the MOOSE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-274/rc).

## Methods

### *Search strategy*

MEDLINE, Embase, and the Cochrane Library databases were comprehensively searched for relevant studies up to September 11, 2021. The search algorithms consisted of Medical Subject Headings (MeSH) and keywords as follows: "frail" or "frailty" (MeSH) and ("COVID-19" OR "Coronavirus Infection Disease 2019" OR "SARS-CoV-2" OR "Coronavirus Infection") and ("mortality" or "deceased" or "death"). Additionally, we reviewed the reference lists of eligible articles to identify potential gray literature. The complete search strategy is available in Tables S1,S2.

### *Eligibility criteria*

Two reviewers (PZ and MH) blindly and independently selected the eligible studies if they met the following inclusion criteria: (I) studies that reported the associations between frailty and mortality in hospitalized patients with COVID-19; (II) studies that reported short-term mortality outcomes, i.e., in-hospital mortality, 30-day mortality, or 60-day mortality. Studies were excluded if they met the following criteria: (I) review articles or letters; (II) studies with less than 20 participants; (III) studies with insufficient data; (IV) non-English language studies. Any differences of opinion between the reviewers regarding an article's qualification for inclusion were resolved by discussion.

### *Data collection*

The data were extracted by two reviewers (PZ and MH) independently, and any differences of opinion were resolved by discussion. Data extracted from the articles included the following: name of the first author, study year, institution(s), number of participating centers, study design, enrollment period, the number of patients, age, gender, frailty assessment tools, and prevalence of frailty. The primary outcome was short-term mortality, defined as a composite outcome of in-hospital mortality, 30-day mortality, or 60-day mortality. The secondary outcome was ICU admission.

### *Quality assessment*

The methodological quality of the included studies was assessed using the Newcastle-Ottawa scale (NOS) (13). Two reviewers (PZ and MH) independently assessed the methodological quality of the included studies. The results of the quality assessment are reported in Table S3.

### *Statistical analysis*

The effect size (ES) (the exact number of frail patients and mortality) was used to assess the association between frailty and mortality risk in patients with COVID-19. The pooled odds ratio (OR) with 95% confidence intervals (CIs) were calculated using a random-effects model to compare mortality and ICU admission rates between frail and non-frail patients from the data of the included

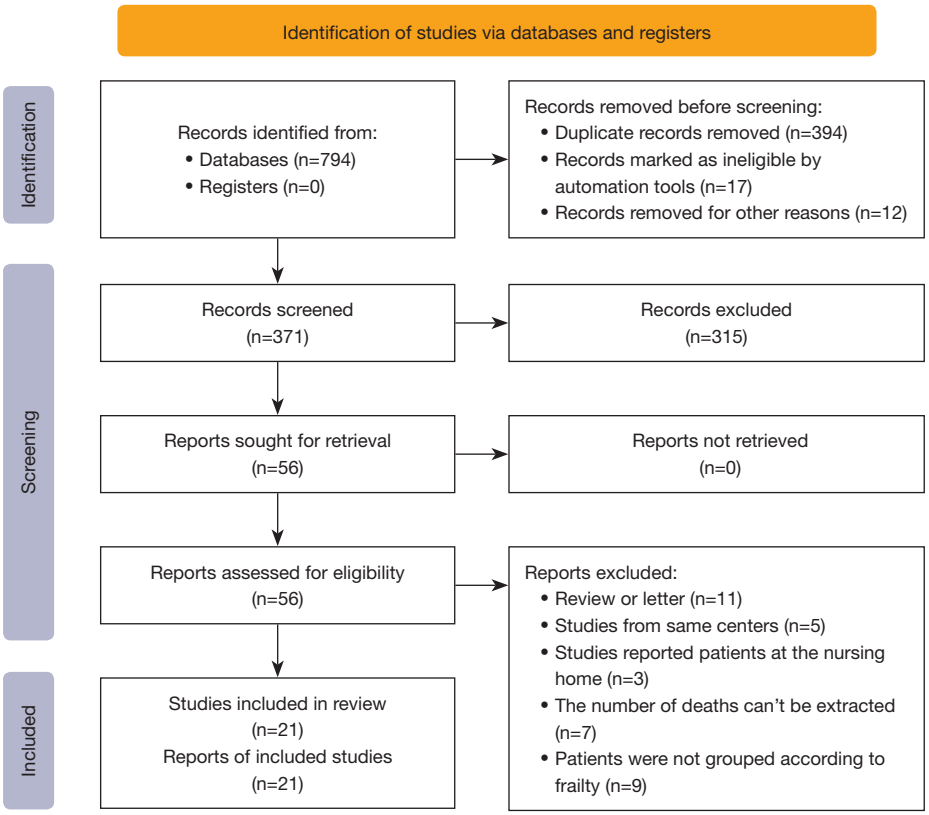


**Figure 1** PRISMA flowchart of the study selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

studies. Heterogeneity between studies was tested using the $I^2$ statistic. The potential publication bias was evaluated quantitatively with Egger's test and assessed qualitatively with funnel plots. Sensitivity analysis was carried out to assess the heterogeneity and robustness of pooled outcomes. We performed subgroup analyses based on the frailty assessment tools. We also demonstrated the outcome estimates for older patients (age ≥65 years). All statistical analyses were carried out using STATA statistical software, version 15.1 (StataCorp., TX, USA). In all analyses, a P value less than 0.05 was considered statistically significant.

## Results

### *Study selection*

After removing duplicate publications, a total of 371 articles were identified from the electronic database searches. After screening the titles and abstracts, 315 irrelevant articles were removed. Full-text articles were carefully reviewed, and an additional 35 studies were excluded. Eventually, 21 studies meeting the inclusion and exclusion criteria were included in this meta-analysis (7-10,14-29). A PRISMA flow chart of the article selection is shown in *Figure 1*.

### *Study characteristics*

Twenty-one included studies, composed of 26,652 hospitalized patients with COVID-19, reported the association between frailty and mortality risk. The principal characteristics of the included studies are reported in *Table 1*. Over half of the studies included older adults (age ≥65 years), and 50.1% (13,187/26,303) of patients were female. Six frailty assessment tools were used, including the Clinical Frailty Score (CFS) (n=16) (7-9,11,16-25), the Hospital Frailty Risk Score (HFRS) (n=1) (26), the Geriatric Nutritional Risk Index (GRNI) (n=1) (27), the modified Frailty Index (mFI) (n=1) (28), the Multidimensional Prognostic Index (MPI) (n=1) (29), and the Frail Non-Disabled Survey (FIND) (n=1) (10). The prevalence of

**Table 1** Characteristics of the studies included in the meta-analysis

| Study | Design | Region | Sample | Consecutive | Female | Age, year[a] | Age limitation, year-old | Prevalence of frailty | Frailty criteria | Outcome measures |
|---|---|---|---|---|---|---|---|---|---|---|
| Poco 2021 | RCS | Brazil | 711 | 1 | 306 | 66±11 | ≥50 | 25.5% (181/711) | CFS | In-hospital mortality |
| Owen 2021 | RCS | UK | 206 | NM | NM | NM | ≥65 | 53.9% (110/206) | CFS | 30-day mortality |
| Mendes 2020 | RCS | Switzerland | 235 | NM | 133 | 67 [61–74] | ≥65 | 78.7% (185/235) | CFS | In-hospital mortality |
| Chinnadurai 2020 | RCS | UK | 215 | 1 | 85 | [36–88] | NM | 51.2% (110/215) | CFS | In-hospital mortality |
| Aw 2020 | RCS | UK | 664 | 1 | 305 | NM | ≥65 | 70.8% (470/664) | CFS | In-hospital mortality |
| Labenz 2020 | RCS | Germany | 42 | NM | 13 | 63 [55–71] | NM | 14.2% (6/42) | CFS | In-hospital mortality |
| Hewitt 2020 | RCS | UK and Italy | 1,559 | NM | 661 | 69 [35–85] | NM | 51.3% (799/1,559) | CFS | In-hospital mortality |
| De Smet 2020 | RCS | Belgium | 81 | 1 | 48 | NM | ≥65 | 79.0% (64/81) | CFS | In-hospital mortality |
| Aliberti 2021 | RCS | Brazil | 1,830 | 1 | 769 | 68.7±10.1 | ≥50 | 27.0% (494/1,830) | CFS | 30-day mortality |
| Andrés-Esteban 2021 | RCS | Spain | 254 | NM | 96 | 62±7.2 | ≥65 | 17.3% (44/254) | CFS | In-hospital mortality |
| Dres 2021 | PCS | France, Switzerland, and Belgium | 1,085 | NM | 326 | 68.9±10.9 | ≥70 | 9.1% (99/1,085) | CFS | 30-day mortality |
| Maniero 2021 | RCS | UK | 124 | 1 | 61 | 73 [48–88] | ≥65 | 77.8% (89/124) | CFS | In-hospital mortality |
| Lozano-Montoya 2021 | RCS | Spain | 300 | 1 | 188 | 70.3±9.2 | ≥75 | 72.0% (216/300) | CFS | In-hospital mortality |
| Ramos-Rincon 2021 | RCS | Spain | 290 | NM | 119 | 66±13 | ≥18 | 60.1% (54/90) | CFS | In-hospital mortality |
| Burns 2020 | RCS | UK | 28 | NM | 13 | 63.5±10.4 | NM | 60.7% (17/28) | CFS | In-hospital mortality |
| Tehrani 2021 | RCS | Sweden | 143 | 0 | NM | 68.2±11.4 | NM | 49.7% (71/143) | CFS | 60-day mortality |
| Kundi 2020 | RCS | Turkey | 18,234 | NM | 9736 | 74.1±7.4 | ≥65 | 68.1% (12420/18,234) | HFRS | In-hospital mortality |
| Recinella 2020 | RCS | Bologna | 109 | 1 | 55 | NM | ≥65 | 72.5% (79/109) | GRNI | In-hospital mortality |
| Fumagalli 2021 | RCS | Italy | 221 | 1 | 87 | 82 [78–86] | ≥75 | 72.5% (79/221) | mFI | In-hospital mortality |
| Pilotto 2021 | PCS | Italy | 227 | 1 | 134 | 80.5 [65–99] | ≥65 | 73.6% (167/227) | MPI | In-hospital mortality |
| Steinmeyer 2020 | RCS | France | 94 | NM | 52 | 85.5±7.5 | ≥65 | 87.2% (82/94) | FIND | In-hospital mortality |

[a], data are expressed as mean ± standard deviation or median [range] or mean or [range]. RCS, retrospective cohort study; PCS, prospective cohort study; CFS, Clinical Frailty Score; NM, not mentioned; HFRS, Hospital Frailty Risk Score; GNRI, Geriatric Nutritional Risk Index; MFI, modified Frailty Index; MPI, Multidimensional Prognostic Index; FIND, Frail Non-Disabled Survey.

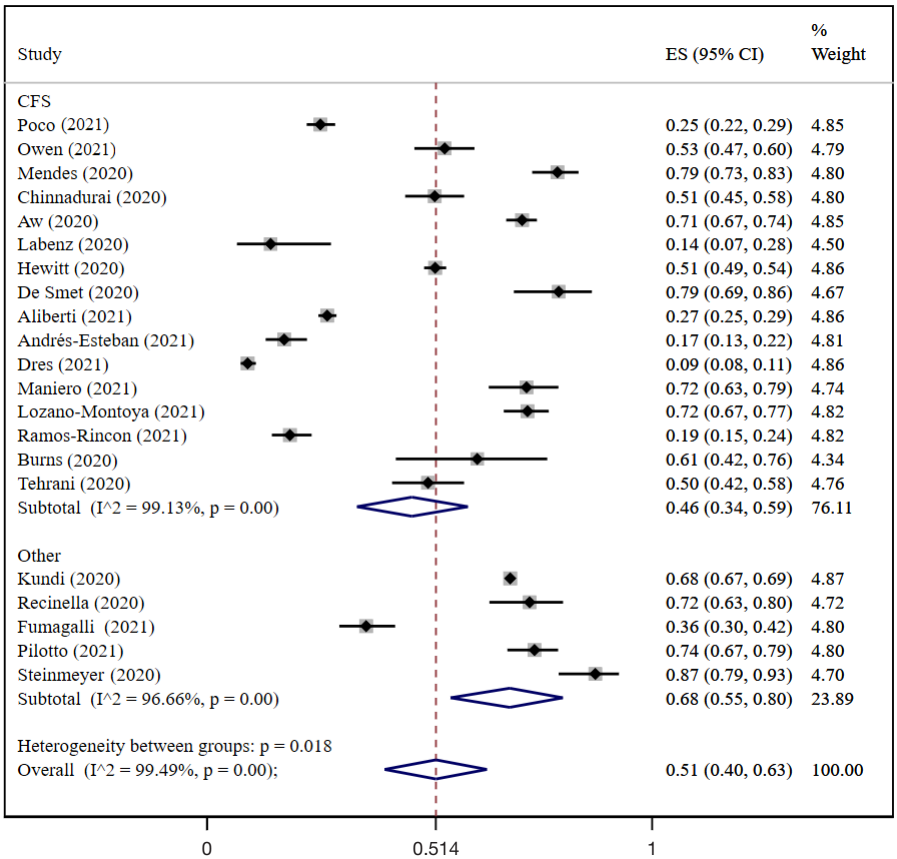


**Figure 2** Pooled proportion of frailty in hospitalized patients with COVID-19. COVID-19, coronavirus disease 2019; ES, effect size; CI, confidence interval; CFS, Clinical Frailty Score.

frailty ranged from 9.1–87.2%, with a summary estimate rate of 51.4% (95% CI: 39.9–62.9%; $I^2$=99.49%; *Figure 2*). The result of Egger's test indicated no apparent publication bias (t=1.89; P=0.07; Figure S1). The sensitive analysis showed that there was no substantial change on the overall pooled OR (Figure S2).

### *Association between frailty and short-term mortality*

The short-term mortality outcome measures were in-hospital mortality in 17 studies, 30-day mortality in three studies, and 60-day mortality in one study. We performed a subgroup analysis based on the frailty assessment tools used. In the CFS group, frail patients experienced a higher rate of short-term mortality than non-frail patients (OR =3.0; 95% CI: 2.3–3.9; $I^2$=72.7%; P<0.001; *Figure 3*). In the other tools group (HFRS, GRNI, mFI, MPI, and FIND), frail patients had a significantly higher short-term mortality risk than non-frail patients (OR =2.4; 95% CI: 1.4–4.1; $I^2$=63.8%; P=0.001). Overall, a higher rate of short-term mortality was observed for frail patients compared with non-frail patients (OR =2.8; 95% CI: 2.3–3.5; $I^2$=78.0%; P<0.001).

The subgroup analysis of older adults (age ≥65 years) revealed that frail patients with COVID-19 in the CFS group had a 2.34-fold higher risk of short-term mortality compared with non-frail patients (OR =2.3; 95% CI: 1.7–3.3; $I^2$=62.5%; P<0.001; *Figure 4*). In the other tools group, frail COVID-19 patients experienced a higher rate of short-term mortality than non-frail patients (OR =2.4; 95% CI: 1.4–4.1; $I^2$=63.8%; P=0.001). The overall results revealed that frail patients over 65 years old had significantly increased short-term mortality compared with non-frail patients (OR =2.3; 95% CI: 1.8–2.9; $I^2$=60.9%; P<0.001).

### *Association between frailty and ICU admission*

Five studies investigated the association between frailty and ICU admission. Three studies used the CFS, one used the

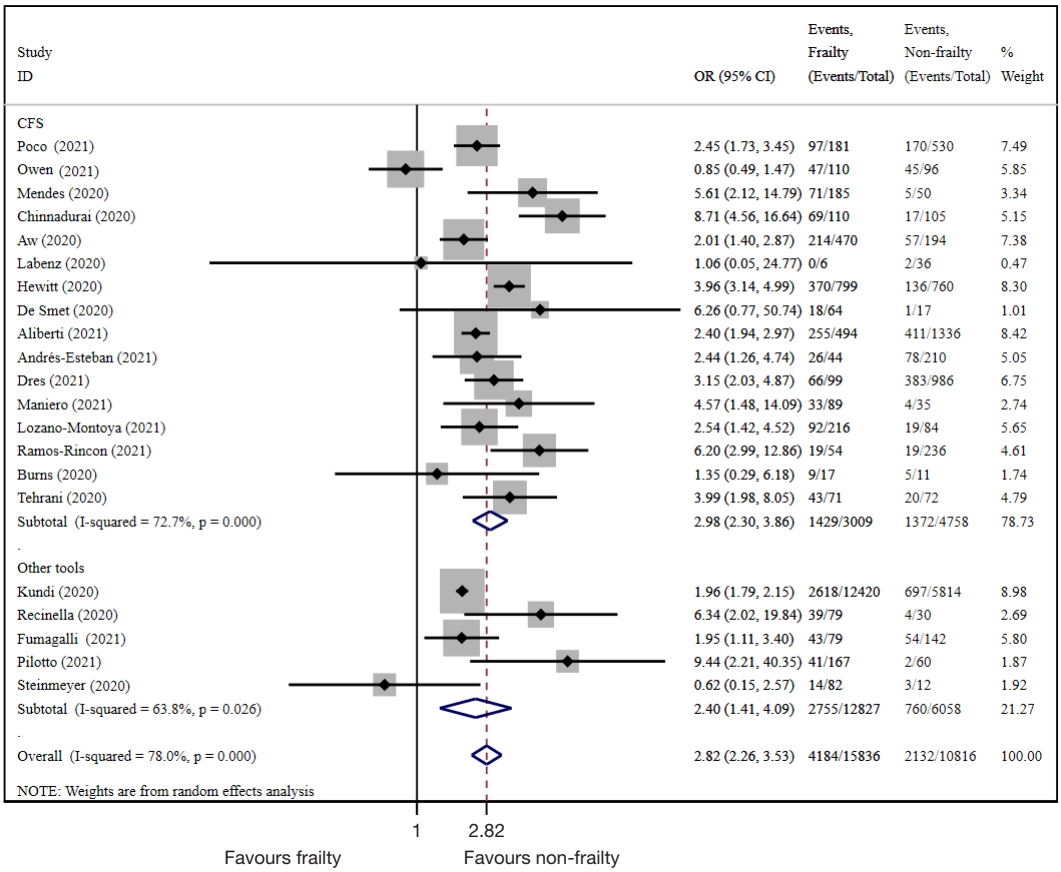


**Figure 3** Forest plots of outcomes for short-term mortality in frail *vs.* non-frail COVID-19 patients. COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; CFS, Clinical Frailty Score.

HFRS, and one used the MPI. In the studies using the CFS, the results showed that frail patients had a lower risk of ICU admission than non-frail patients (OR =0.2; 95% CI: 0.1–0.5; $I^2$=0.0%; P<0.001; Figure S3). In contrast, in the other tools group, frail COVID-19 patients demonstrated a higher risk of ICU admission than non-frail patients (OR =2.0; 95% CI: 1.8–2.1; $I^2$=0.0%; P<0.001). The overall results revealed no significant difference in ICU admission rates between frail and non-frail patients (OR =0.5; 95% CI: 0.1–2.1; $I^2$=89.4%; P=0.37).

## Discussion

This systematic review and meta-analysis included 21 studies with 26,652 hospitalized COVID-19 patients and aimed to assess the influence of frailty on clinical outcomes. We pooled the prevalence of frailty and found that over half of COVID-19 patients were frail. CFS was the most commonly used frailty assessment in the studies of hospitalized COVID-19 patients. Frail patients had a higher rate of short-term mortality than non-frail patients, which was also evident in older adults. However, the results from studies investigating ICU admissions that used CFS and other frailty assessment tools were conflicting.

Frailty is a complex age-related clinical state or syndrome characterized by increasing susceptibility to stress, with a functional decline across multiple physiological systems (30,31). COVID-19 caused by SARS-CoV-2 has created a global pandemic and challenged healthcare systems worldwide (1,32). COVID-19 is a systemic disease that can rapidly cause hypoxemic respiratory symptoms and even acute respiratory distress syndrome (ARDS) (33). It is worth mentioning that, compared with computed tomography, lung ultrasound is a non-invasive bedside and low cost technique with high diagnostic accuracy. Lung ultrasound might play an important role in early diagnosis, monitoring of COVID-19 pneumonia, especially in the COVID-19 patients with frailty, which might reduce the pressure

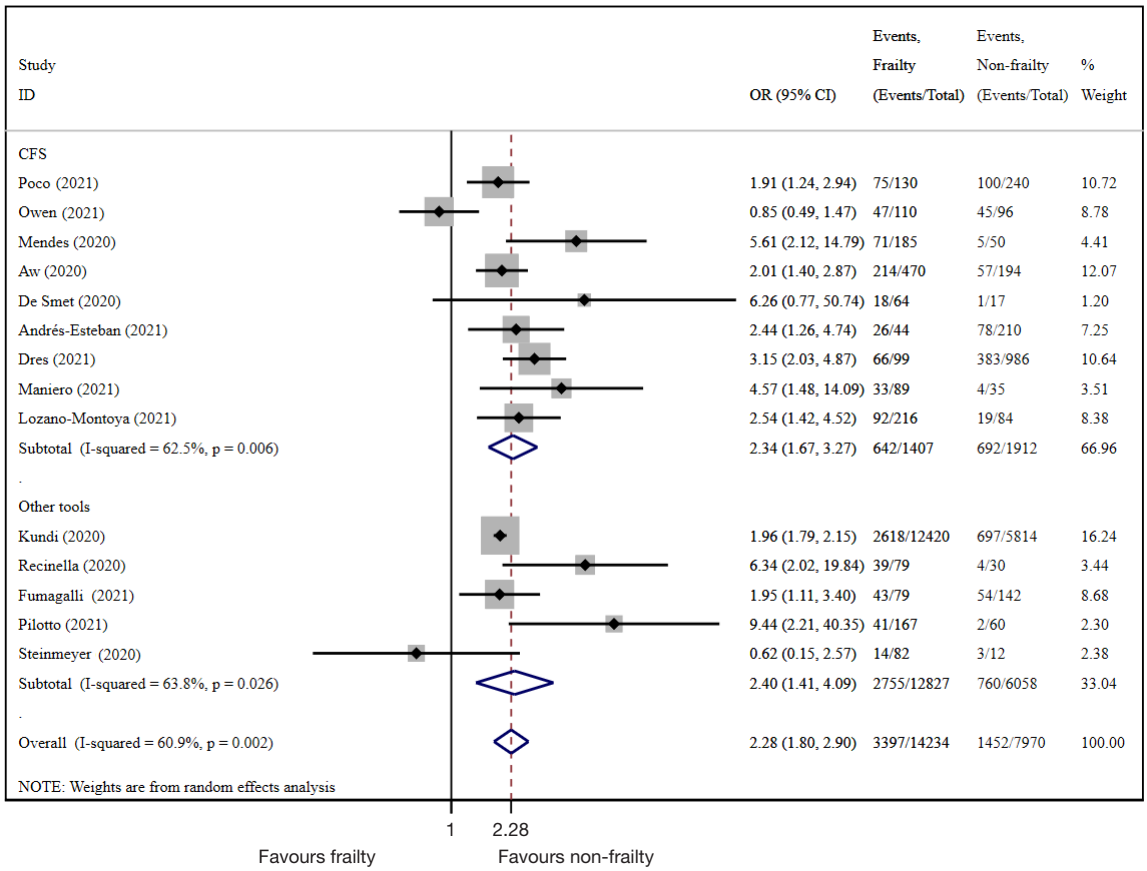


**Figure 4** Forest plots of outcomes for short-term mortality in frail *vs.* non-frail COVID-19 patients ≥65 years old. COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; CFS, Clinical Frailty Score.

on the patients' body and handling time, and decrease the risk of SARS-CoV-2 transmission (34,35). Besides, based on the blood dissemination of hemophagocytic lymphohistiocytosis, COVID-19 can have secondary effects on extrapulmonary organs, including the nervous system, heart, intestine, kidney, and liver, resulting in multiple organ system dysfunction syndrome (36-38). As a consequence, patients infected with COVID-19 have an increased vulnerability to frailty. Therefore, to improve the prognosis of patients with COVID-19, identifying whether they are frail and need more intensive care is of utmost importance.

There are several well-validated frailty assessment tools used for screening and quantifying frailty status. Many studies across different diseases have revealed that frailty is associated with a variety of poor health outcomes, such as falls, dementia, mortality, hospitalization, and poor quality of life (39-41). As such, it is important to evaluate frailty status comprehensively to optimize outcomes. In this study, we found that frailty was a predictor of all-cause mortality in hospitalized COVID-19 patients, similar to the results of previous systematic reviews. There may be several reasons for this result. First, compared with non-frail patients, patients in a frail condition are characterized by reduced physiological reserves, chronic malnutrition, and a loss of resistance to stressors due to accumulated deficits, all of which increase the risk of a poor outcome for patients infected by SARS-CoV-2 (42,43). Second, frail patients tend to develop a pro-inflammatory status with an elevated level of inflammatory markers in cells and tissues. A leading cause of severe COVID-19 is the cytokine storm syndrome, associated with various cytokines such as IFNα, IL-6, and IL-1, which are elevated in frail patients (36,37). This can lead to immunologic derangement and increase the risk of extrapulmonary organ dysfunction. Third, most frail patients are older adults, and high COVID-19-associated mortality occurs among the older population. This may be due to the high prevalence of comorbidities, such as

hypertension, diabetes mellitus, chronic heart disease, and dementia in the geriatric population, which have been identified as risk factors for mortality in patients ≥65 years old with COVID-19 (44).

Based on the pooled analysis, we found contradictory results in the association between frailty and ICU admission. According to the results of studies using CFS, frail patients had a lower risk of ICU admission than non-frail patients (OR =0.2; 95% CI: 0.1–0.5). However, among the studies using other tools, frail patients experienced a higher risk of ICU admission than non-frail patients (OR =2.0; 95% CI: 1.8–2.1). Dumitrascu *et al.* (45) reported that eight studies showed an association between frailty as assessed by the CFS and ICU admission (OR =0.24; 95% CI: 0.08–0.71). This discrepancy in results might be caused by the sampling error between studies using the CFS *vs.* other assessment tools and the shortage of medical resources in the early stages of the COVID-19 pandemic. The National Institute for Health and Care Excellence (NICE) guidelines (46) suggest that the CFS should be used to assess whether COVID-19 patients need more intensive care. Based on previous research and the current meta-analysis, further studies are required to confirm this suggestion.

Several limitations of this meta-analysis need to be considered. Firstly, during the study selection, a number of studies reporting the association between frailty and mortality in COVID-19 hospitalized patients were excluded because of non-standard cut-off values for frailty groupings. Furthermore, the effect values of these studies were reported as either ORs or risk ratios. To maximize the pooling of the overall estimates and avoid inflated risk estimates by converting ORs into risk ratios, several studies were excluded where the data could not be extracted. Moreover, most studies were retrospective in design. Therefore, the pooled outcomes were inevitably affected by selection bias. Secondly, because most studies used the CFS as the frailty assessment tool, we conducted a pooled analysis combining the results from other tools used. The data were too limited to allow for further subgroup analysis, which may have decreased the reliability of the results in our meta-analysis.

## Conclusions

The results of this systematic review and meta-analysis indicated that frail patients suffered from a higher risk of all-cause mortality than non-frail hospitalized COVID-19 patients, and this result was also found in the older adult group. Therefore, an assessment of frailty could assist clinicians in identifying hospitalized COVID-19 patients who require more intensive treatment and care.

## Acknowledgments

*Funding:* This study was supported by the Science and Technology Department of Sichuan Province (Grant No. 2019JY0346) and the National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University (Grant No. Z2018A12).

## Footnote

*Reporting Checklist:* The authors have completed the MOOSE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-274/rc

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-274/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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(English Language Editor: D. Fitzgerald)

**Cite this article as:** Zou Y, Han M, Wang J, Zhao J, Gan H, Yang Y. Predictive value of frailty in the mortality of hospitalized patients with COVID-19: a systematic review and meta-analysis. Ann Transl Med 2022;10(4):166. doi: 10.21037/atm-22-274

 

## Supplementary

**Table S1** Search strategies of MEDLINE*

| Searches | Details | Results |
|---|---|---|
| 1 | frail.mp. or Frailty/ | 23,464 |
| 2 | Coronavirus Infections/or novel coronavirus.mp. | 51,954 |
| 3 | SARS-CoV-2/or COVID-19/or Coronavirus Infection Disease 2019.mp. | 113,435 |
| 4 | Mortality/or mortality.mp. | 1,262,840 |
| 5 | death.mp. or Death/ | 874,408 |
| 6 | deceased.mp. | 22,590 |
| 7 | 2 or 3 | 122,675 |
| 8 | 4 or 5 or 6 | 1,907,321 |
| 9 | 1 and 7 and 8 | 346 |

*, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions (R) 1946 to September 11, 2021.

**Table S2** Search strategies of Embase*

| Searches | Details | Results |
|---|---|---|
| 1 | frailty/or frail elderly/or frail.mp. | 38,414 |
| 2 | coronavirus disease 2019/or COVID-19/or Coronavirus Infection Disease 2019.mp. | 154,839 |
| 3 | SARS-CoV-2.mp. or Severe acute respiratory syndrome coronavirus 2/ | 77,470 |
| 4 | Coronavirus infection/or novel coronavirus.mp. | 21,630 |
| 5 | Mortality/or mortality.mp. | 1,642,475 |
| 6 | death.mp. or Death/ | 1,379,172 |
| 7 | deceased.mp. | 43,982 |
| 8 | 2 or 3 or 4 | 182,980 |
| 9 | 5 or 6 or 7 | 2,690,210 |
| 10 | 1 or 8 or 9 | 448 |

*, Embase 1974 to September 11, 2021.


https://dx.doi.org/10.21037/atm-22-274

**Table S3** NOS quality assessment results of the cohort studies

| Author | Year | Representativeness of the exposed cohort | Selection of the nonexposed cohort | Ascertainment of exposure | Outcome of interest was not present at start of study | Comparability of cohorts on the basis of the design or analysis | Assessment of outcome | Was follow-up long enough for outcomes to occur | Adequacy of follow-up of cohorts | Total score |
|---|---|---|---|---|---|---|---|---|---|---|
| Poco | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Owen | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Mendes | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Chinnadurai | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Aw | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 7 |
| Labenz | 2020 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Hewitt | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| De Smet | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Aliberti | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Andrés-Esteban | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Dres | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Maniero | 2021 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Lozano-Montoya | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Ramos-Rincon | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Burns | 2020 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Tehrani | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Kundi | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Recinella | 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Fumagalli | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Pilotto | 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Steinmeyer | 2020 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |

NOS, Newcastle-Ottawa scale.


https://dx.doi.org/10.21037/atm-22-274

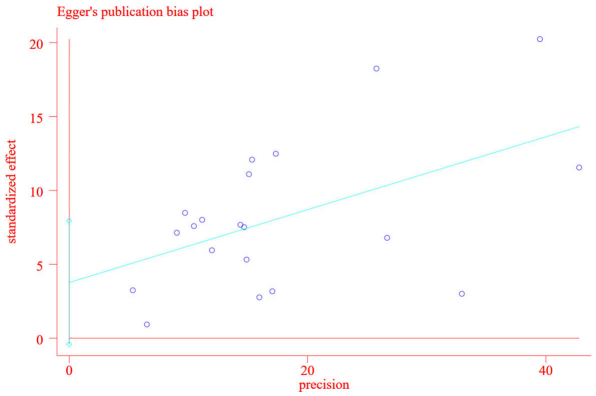


**Figure S1** Egger's test for publication bias.

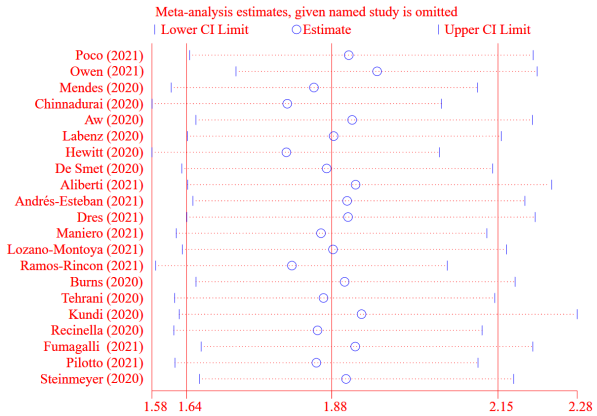


**Figure S2** Sensitivity analysis for the association between frailty and short-term mortality of hospitalized patients with COVID-19. COVID-19, coronavirus disease 2019; CI, confidence interval.

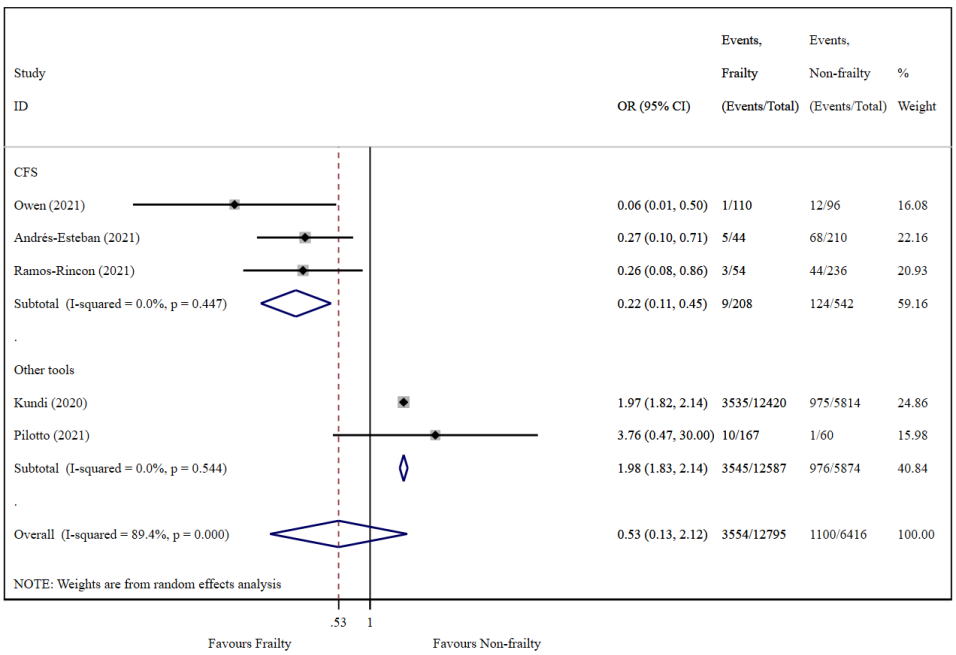


**Figure S3** Forest plots of outcomes for ICU admission in frail vs. non-frail COVID-19 patients. ICU, intensive care unit; COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; CFS, Clinical Frailty Score.


https://dx.doi.org/10.21037/atm-22-274