

# The role of frailty in acute care assessment during the COVID-19 pandemic and beyond: A rapid review

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## Abstract

Healthcare strain due to the novel coronavirus (COVID-19) pandemic has left clinicians struggling to manage patient care and identify those most at risk of COVID-19 mortality. Although chronological age-based triage strategies have been adopted, these practices have been criticized for being ageist. Improved care for each unique patient with COVID-19 may be achieved through the addition of frailty assessment in acute care. While current data demonstrates that hospitalized patients with frailty and COVID-19 are at increased risk for adverse outcomes, most data thus far has not considered patient treatment nor illness severity analyses. Therefore, frailty assessment is recommended as an adjunct tool for directing patient care in addition to factors such as acute illness severity and the presence of comorbidities. Moving forward, incorporating frailty status into patient decision-making and the analyses of COVID-19 therapies are warranted to ensure that approaches are efficacious in the most vulnerable patients. Clinicians in acute care should familiarize themselves with frailty and its assessment to improve care during the COVID-19 pandemic and beyond.

*Keywords: frailty; COVID-19; ageing; prognosis; risk stratification*

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## Introduction

The spread of severe acute respiratory syndrome coronavirus (SARS-CoV-2) has led to over 80 million cases of coronavirus disease (COVID-19) and over 1.7 million deaths worldwide.<sup>1</sup> With over 313.3 cumulative hospitalizations due to COVID-19 per 100 000 people in the United States,<sup>2</sup> this pandemic has taxed medical resources across the globe. Current data demonstrates an increased risk for adverse outcomes due to COVID-19 as age increases.<sup>3–5</sup> This trend was identified globally early in the pandemic, with data from a systematic review demonstrating increasing case fatality rates and disease severity with age.<sup>6</sup> In addition, patients with comorbidities such as hypertension and respiratory disease also demonstrate increased risk for adverse COVID-19 prognosis.<sup>5</sup> As cases increased and healthcare systems were inundated with patients requiring hospitalization, healthcare bodies such as the Italian College of Anesthesia, Analgesia, Resuscitation, and Intensive Care (SIAARTI), discussed the need to adopt triaging strategies that incorporate chronological age in the acute care setting.<sup>7</sup> This decision may have been based on the finding that older age and comorbidities were associated with adverse outcomes given that

likely benefits from treatment have been recommended as an important consideration when allocating scarce healthcare resources.<sup>8–11</sup> However, some geriatricians and geriatric groups argue that resource triaging using age is “ageist” and fails to identify those at greatest risk for adverse outcomes associated with COVID-19 at the individual level due to the heterogeneity of aging.<sup>8,9,11,12</sup>

## Frailty

Frailty is characterized by a reduced reserve to respond to health stressors induced by multisystem physiological declines.<sup>13</sup> While frailty is correlated with chronological aging,<sup>14</sup> these are not synonymous concepts.<sup>15</sup> Importantly, frailty is a more valuable indicator of risk for adverse health outcomes than age.<sup>15–17</sup> Frailty predicts a wide range of adverse health outcomes including falls,<sup>18</sup> hospitalization,<sup>18</sup> morbidity<sup>16,18–21</sup> and mortality.<sup>16,20,22</sup> Over 50 frailty assessment tools have been developed for a variety of clinical contexts, each with inherent strengths and limitations.<sup>23,24</sup> As such, prevalence estimates for frailty in countries worldwide range from 7–24% in those 50 years of age or older de-

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pending on the assessment tool utilized.<sup>25</sup> Generally, frailty assessments can be categorized as those that are phenotypic-based or those based on a more holistic accumulation of deficits.<sup>23,24</sup> Two approaches to frailty include the Fried phenotype<sup>18</sup> and the Frailty Index (FI).<sup>26</sup> The Fried phenotype<sup>18</sup> approach to frailty examines the following criteria: grip strength, walking speed, unintentional weight loss, self-reported exhaustion and low physical activity levels. Comparatively, the FI<sup>26</sup> accumulation of deficits approach looks at a wide range of health deficits on a continuum and can include variables such as cognition and lab-based biomarkers.

More recently, frailty assessment has been suggested as a means to identify best care practices for older adults in the acute care setting.<sup>8,26–28</sup> Current triage tools in acute care often incorporate chronological age, which does not take the heterogeneity of aging into account. It may also underestimate risk, thereby leading to interventions that are unlikely to benefit a higher risk patient with frailty.<sup>29,30</sup> Patients with frailty are more likely to experience adverse outcomes in acute care settings including increased length of hospital stay, admission to nursing home, and mortality.<sup>31,32</sup> These adverse outcomes can be attributed to not only the presenting illness, but also to iatrogenic stress introduced. However, the use of the Fried approach or the FI can be cumbersome in acute care settings.<sup>33</sup> The subsequent Clinical Frailty Scale (CFS) was developed to address this issue.

The CFS is a simple, rapid assessment tool used in acute care settings for those 65 years of age and older. It is based on clinical judgement and functional status.<sup>34–36</sup> This tool assesses frailty on a 9-item scale ranging from more robust or fit (1–3), mild or moderate frailty (4–6), more severe frailty (7–8), to terminally ill (9). Placement on this scale is based on patient status of mobility, function, and cognition from two weeks prior. In the case of an intubated or obtunded patient, information can also be collected from collateral sources such as caregivers. Determination of frailty status with the CFS has shown to be highly correlated with the FI ( $r = 0.80$ ).<sup>35</sup>

## Frailty-aware care and COVID-19

In the community setting, two separate analyses of data from the United Kingdom Biobank database have reported on associations between frailty and COVID-19.<sup>37,38</sup> One analysis found that frailty status assessed with the Fried approach was not associated with COVID-19 diagnosis ( $N = 502\,640$ ).<sup>37</sup> However, the second analysis found that frailty status assessed by both the modified Fried and FI were associated with a higher risk of severe infection, hospital admission, and subsequent mortality independent of multimorbidity in those who tested positive for COVID-19 ( $N = 383\,845$ ).<sup>38</sup> Additionally, a large retrospective cohort study of Medicare beneficiaries in the United States ( $N = 24\,367\,476$ ) found that advanced frailty as

assessed by a FI was associated with increased COVID-related hospitalization and mortality.<sup>39</sup>

Interest in adopting tools to direct resource allocation has been driven by necessity during the pandemic. Age-based approaches can miscategorise older adults as they do not all have concomitant comorbidity and/or frailty.<sup>8</sup> Since older adults are disproportionately affected by COVID-19,<sup>5</sup> it is essential to develop care and triage systems with older adults in mind. Assessing frailty in critical care can elucidate the heterogeneity present in aging<sup>15</sup> and has garnered increased attention as a method of triaging and identifying best care practices in COVID-19 patients.<sup>8,9,34,40</sup> Furthermore, older adults, and specifically those with frailty, may present with COVID-19 atypically<sup>41</sup> (for example, with delirium).<sup>42</sup> This lends importance to frailty assessment when considering care management. The National Institute for Health and Care Excellence adopted the use of frailty assessment as part of their “COVID-19 Rapid Guidelines: Critical Care” and proposed assessing patients using the CFS upon hospital admission.<sup>43</sup> A mobile application was developed by the National Health Services to support the use of the CFS in their clinical context,<sup>44</sup> and additional online training resources were developed to teach clinicians how to use the tool.<sup>45</sup>

The CFS has previously demonstrated predictive validity for hospitalization, ICU admission, and mortality.<sup>36,46,47</sup> However, the predictive validity of this frailty assessment, or others, for adverse outcomes or treatment efficacy is unknown in patients with novel COVID-19. Frailty assessment should not be used alone in acute care settings, but in conjunction with assessment of illness acuity and likelihood of treatment benefit given the role of other mediators in health recovery.<sup>48</sup> Data is needed to support the use of frailty assessment as an important holistic assessment in acute care settings in patients with COVID-19.<sup>40</sup>

## Rapid review of frailty as a predictor of adverse outcomes in hospitalized COVID-19 patients

The growing publications of data and expert opinion regarding the use of frailty assessments in hospitalized older adults with COVID-19 was summarized in a systematic scoping review in July 2020.<sup>40</sup> This review found mainly editorials and recommendations supporting the clinical role of frailty assessments in COVID-19 patients with supporting data from only four observational studies.<sup>49–52</sup> Of these observational studies, two found that more advanced frailty status was associated with increased hospital mortality.<sup>49,50</sup> Another found that advanced frailty was associated with a longer disease course.<sup>51</sup> In contrast, Miles et al. found high rates of mortality in more robust patients. This was attributed to potentially be a result of immunosenescence in frailty preventing COVID-19 mortality associated with immune hyperactivation.<sup>52</sup> The review importantly identified that many recommendations were

given with a paucity of evidence to support them.<sup>40</sup> Additionally, the search did not identify any trials examining the use of interventions specifically for patients with more advanced frailty and COVID-19, nor the impact of frailty status on the effectiveness of currently studied COVID-19 therapeutic interventions. These considerations are important if patients with more advanced frailty are at increased risk for adverse outcomes from COVID-19.

Published at almost the same time as the aforementioned review, Hewitt et al. reported that frailty assessment using the CFS in patients with COVID-19 showed better in-hospital and 7-day mortality prediction compared to either age or comorbidity. This study used data from the COVID-19 in Older People (COPE) study ( $N = 1564$ ).<sup>53</sup> Letters to the editor responding to their research identified important limitations when examining frailty in this context. Specifically, the CFS was used by investigators on adults younger than its validated use<sup>54</sup> and the lack of information on patient treatment or illness severity make it difficult to use their data to support the findings presented.<sup>55,56</sup>

Since the Hewitt et al. paper, several studies examining the relationship between CFS score and mortality in COVID-19 patients have been published and summarized in a systematic review and meta-analysis by Pranata et al.<sup>57</sup> Their review included seven studies<sup>41,42,53,58-61</sup> in the final analysis and described a total of 3817 patients with a mean age of 80.3 years ( $SD = 8.2$ ). The Hewitt et al. paper was also included in this analysis, and was the only study to include adults under 65 years of age.<sup>53</sup> Frailty prevalence (95% CI) in the pooled cohort was CFS 1-3 at 34% (32-36%), CFS 4-6 at 42% (40-45%) and CFS 7-9 at 23% (21-25%). Pranata et al. found that CFS score and COVID-19 mortality had a linear dose-response relationship where each increasing point on the CFS was associated with a 12% increased odds of patient mortality (OR 1.12; 95% CI 1.04-1.20).<sup>57</sup> Of the included manuscripts, two were prospective cohort studies<sup>53,60</sup> and five were retrospective cohort studies.<sup>41,42,58,59,61</sup> Funnel-plot analysis indicated possible publication bias. Further potential bias was introduced as most studies were retrospective. Two of the included papers found that CFS score was not associated with COVID-19 mortality.<sup>60,61</sup> The remaining five studies described odds ratios for mortality per one-point increase in CFS score ranging from 1.12 (95% CI 1.04-1.20)<sup>58</sup> to 1.75 (95% CI 1.10-3.43).<sup>59</sup> As identified in the Maltese et al. scoping review,<sup>40</sup> lack of information on patient treatment and acute illness severity in the meta-analysis make these results harder to interpret. Exceptions to this were Aw et al. and Owen et al., who both performed analyses controlling for acute illness severity.<sup>58,61</sup> Illness severity seemed to attenuate the observed relationship in both of these studies.<sup>58,61</sup>

Frailty assessment may serve an adjunct role not only in community-dwelling and hospitalized patients, but also plays an important role after discharge from the hospital.<sup>62</sup> Vilches-Moraga et al. found that higher

frailty scores on the CFS pre-admission were associated with increased care requirements at discharge even after controlling for age and other comorbidities.<sup>62</sup> This finding supports the role of frailty assessment in care planning for the needs of individual patients even after discharge.<sup>62</sup> The importance of frailty assessment in assessing the efficacy of therapeutic interventions for COVID-19 is also true of vaccine response. To date, vaccine trials have largely excluded those with comorbidities and frailty,<sup>63</sup> who are the most vulnerable to COVID-19. As vaccines for COVID-19 are now being distributed globally, considerations should be made to ensure that favourable immune responses are also achieved in older adults with frailty who may have immunosenescence.<sup>63,64</sup>

This rapid review was completed as of January 4, 2021. New data on this topic area continues to rapidly develop, but the British Geriatrics Society has created a continually updating list of manuscripts describing frailty scores and COVID-19 outcomes in older adults to assist with keeping track of this evolving data.<sup>65</sup>

## Future directions

The current data and expert opinions support frailty assessment as an adjunct assessment in hospitalized older adults with COVID-19, not to be used alone for purposes of directing care plans or patient triage.<sup>11,34,57</sup> Most data thus far have not included illness severity nor patient treatments received in their analyses. This limits the ability to examine the effect of frailty alone on patient prognosis. It is essential to understand that frailty assessments have limitations in allocating health resources, and additional factors, such as comorbidity and illness acuity, play important roles in COVID-19 patient prognosis.<sup>48,57,66,67</sup> Experts have encouraged the use of frailty assessment on a continuum as opposed to simplifying it to a dichotomous variable in order to better describe the patient.<sup>48</sup> However, assessing patients on a continuum renders decisions for patient care pathways more challenging.<sup>57</sup> Instead of using the knowledge of frailty status as a means of shifting who receives care, Lee et al. describes using frailty in a “3F” approach: framing goals of care, working within the framework of frailty, and as a means of directing forward conversations.<sup>68</sup>

There is little research examining interventions specifically for patients with more advanced frailty status and COVID-19. The mediating role that frailty status may play in current therapeutic intervention response for older COVID-19 patients is also unknown. Older adults with frailty and comorbidity should be recruited or trials to ensure that those at the greatest risk are able to benefit from researched interventions. Future research should examine these important concepts to improve patient management in hospitalized older adults during the current pandemic and beyond. Additionally, the exact mechanisms that place frail older adults at increased risk for adverse outcomes in COVID-19 cases are not known, although increased vi-

ral shedding, atypical presentation, reduced cardiorespiratory reserve and immunosenescence have all been suggested.<sup>69</sup> Identifying these mechanisms could allow for targeted therapeutic interventions and improved management of COVID-19 patients with frailty.

## Conclusion

Preventing COVID-19 development in older adults with frailty is critical given the associated adverse outcomes, including hospitalization and mortality.<sup>39,57</sup> Specifically, those with advanced comorbidity and those residing in nursing homes are at increased risk.<sup>39</sup> The interest in tools for directing resource allocation and best care practices has been adopted out of necessity during the COVID-19 pandemic, but serves as an example of how best care practices for older adults can be aided through knowledge of frailty status.<sup>8,34</sup> Frailty-aware care plays an important role as an adjunct tool in all stages of the peri-hospitalization period for older adults with COVID-19.<sup>38,57,62</sup> These considerations will continue to be important throughout the pandemic and in the future in order to provide the best care for older adults by using global assessments of health status through frailty assessment.<sup>8</sup> The pandemic has brought ageist policies and discourse to the forefront.<sup>70</sup> Clinicians should focus on developing skills to improve care management for older adults through frailty assessment during the COVID-19 pandemic and beyond.

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