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Review Article

Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis

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ABSTRACT

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Introduction: Frailty is one of the most important concerns regarding our aging population. Evidence grows that the syndrome is linked to several important health outcomes. A general overview of frailty concepts and a comprehensive meta-analysis of their relation with negative health outcomes still lacks in literature, making it difficult for health care professionals and researchers to recognize frailty and the related health risks on the one hand and on the other hand to appropriately follow up the frailty process and take substantiated action. Therefore, this study aims to give an overview of the predictive value of the main frailty concepts for negative health outcomes in community-dwelling older adults.

Methods: This review and meta-analysis assembles prospective studies regarding the relation between frailty and any potential health outcome. Frailty instruments were subdivided into frailty concepts, so as to make comprehensive comparisons. Odds ratios (ORs), hazard ratios (HRs), and relative risk (RR) scores were extracted from the studies, and meta-analyses were conducted in OpenMeta Analyst software.

Results: In total, 31 articles retrieved from PubMed, Web of Knowledge, and PsycInfo provided sufficient information for the systematic review and meta-analysis. Overall, (pre)frailty increased the likelihood for developing negative health outcomes; for example, premature mortality (OR 2.34 [1.77—3.09]; HR/RR 1.83 [1.68—1.98]), hospitalization (OR 1.82 [1.53—2.15]; HR/RR 1.18 [1.10—1.28]), or the development of disabilities in basic activities of daily living (OR 2.05 [1.73—2.44]); HR/RR 1.62 [1.50—1.76]).

Conclusion: Overall, frailty increases the risk for developing any discussed negative health outcome, with a 1.8- to 2.3-fold risk for mortality; a 1.6- to 2.0-fold risk for loss of activities of daily living; 1.2- to 1.8-fold risk for hospitalization; 1.5- to 2.6-fold risk for physical limitation; and a 1.2- to 2.8-fold risk for falls and fractures. The analyses presented in this study can be used as a guideline for the prediction of negative outcomes according to the frailty concept used, as well as to estimate the time frame within which these events can be expected to occur.

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Conceptually, frailty can be defined as "a condition or syndrome that results from a multisystem reduction in reserve capacity, to the extent that a number of physiological systems are close to, or pass, the threshold of symptomatic clinical failure. As a consequence, the frail person is at increased risk of disability and death from minor external stresses."[1] However, this frailty concept is operationalized in various ways, complicating the identification of frail older persons in clinical practice. In fact, the prevalence of frailty in community-dwelling older persons ranges between 4% and 59%, and for nursing home patients between 19% and 76%, depending on the frailty definition used.[2,3] Moreover, some frailty instruments distinguish besides a frail and robust (= nonfrail) also a prefrail state, reflecting a transition phase between robustness and frailty.[4] More importantly, because frailty status provides prospective information for negative health outcomes, it can be expected that the predictive value can be different according to the operationalization of the frailty concept.

Several researchers have studied negative health outcomes possibly linked to frailty, with death, hospitalization, and institutionalization as the most described end points.[5,6] However, many other outcomes have been put forward as possible repercussions of frailty, including fractures, falls, disability in activities of daily living (ADLs), mobility limitation, and cognitive decline.[7,8] Yamada et al[9] found that their newly developed frailty screening index predicts healthy life expectancy in community-dwelling older people. They reported that prefrail (hazard ratio [HR] 8.4 [5.0–14.2]) and frail (HR 22.7 [13.3–38.8]) older adults had a significantly higher risk for making use of the "long-term care insurance" services compared with robust older adults.[9] This was supported by the findings of Chang and Lin[10] in the Cardiovascular Health Study[4] for both a frail and prefrail status. According to Luo et al,[11] the FRAIL NH-scale showed strong predictive power for several negative health outcomes, such as incident falls (HR 2.00 [1.41–2.83]), ADL-decline (HR 3.73 [2.69–5.16]), hospitalization (HR 2.35 [1.57–3.54]), and death (HR 2.00 [1.41–2.83]) in nursing home residents. Almeida et al[12] demonstrated that community-dwelling men aged 75 years and older show a strong relationship in the presence of frailty on the one hand, and an increased mortality associated with past depression on the other hand (HR 1.79 [1.21–2.62] after adjustment for frailty). Most studies found in the literature focus on the relation between a certain frailty concept and 1 or 2 negative health outcomes, providing relevant information on the possible health risks induced by frailty. However, because of the various operationalizations of frailty concepts, results may vary significantly. A general overview of frailty concepts and a comprehensive meta-analysis of their relation with negative health outcomes still lacks in literature, which makes it difficult for health care professionals and researchers to recognize frailty and the related health risks on the one hand and on the other hand to appropriately follow up the frailty process and take substantiated action. Therefore, this study aims to give an overview of the prospective predictive value of the main frailty concepts for negative health outcomes in community-dwelling older adults. As prospective evidence will systematically be quantified in this meta-analysis, we expect to provide important information for clinical practice so as to develop adequate interventions and to counter the development and outcomes of frailty.

Methods

This systematic review was written according to the PRISMA guidelines for transparent reporting of systematic reviews and meta-analyses.[13]

Literature Search

A literature search was performed in PubMed, Web of Knowledge and PsycInfo (last search in January 2016). The following search terms were combined: frailty, frail elderly, aged, assessment, risk assessment, classification, diagnosis, prospective studies, longitudinal studies, cohort studies. Prospective longitudinal studies were eligible for this review if they investigated *frailty* in community-dwelling elderly persons (aged 65 years and older) and if the occurrence of health outcomes was reported. Studies were included if they were written in English, Dutch, French, or German. No limit was set on publication date.

The screening process was performed by 2 reviewers independently and blinded for each other's results. First, articles were screened based on title and abstract. Subsequently, full texts were screened. In case of disagreement on the inclusion of an article, a consensus was found by involving a third reviewer. In case insufficient information was available to include or exclude a study, the corresponding author was contacted.

The following data were extracted from the included studies: the number of participants tested, length of follow-up (categorized as 0–12 months, 12–24 months, 24–60 months, or >60 months), age, the frailty assessment tool and its concept (physical focus, multidomain, or deficit accumulation), the studied negative health outcomes and their assessment method, the (adjusted) predictive statistical measures: odds ratio (OR), HR, or relative risk (RR). Articles were initially ordered according to the outcome of the study. When no ratios were reported in the article, but frequencies were provided, the OR was calculated based on the frequencies of the group of robust subjects and the group of (pre)frail subjects. In case insufficient information was available in the article for calculating the ratio, the corresponding author was contacted to obtain the ratios or the frequencies necessary to calculate the ratios. In case of multiple ratios per frailty instrument (separate analysis per item), an overall predictive measure was calculated based on the total score of the instrument (as a whole).[14,15]

The systematic literature search yielded in January 2016 a total number of 1694 articles: 509 in PubMed, 464 in Web of Science, and 721 in PsycINFO. Fifty-nine doubles were removed and after screening the remaining articles based on title and abstract, 291 were left for further analysis. The full texts, independently read and assessed by at least 2 reviewers, were judged on content and methodological quality. In total, 255 articles were excluded. In 12 cases, the first 2 reviewers reported conflicting results; a third reviewer was asked to assess the article and a final decision was reached based on consensus. Finally, 31 articles were included for this systematic review and meta-analysis. In Figure 1, the flowchart of the literature selection is shown.

Risk of Bias: Assessment of Methodological Quality

Methodological quality was assessed by 2 reviewers by using methodology checklists of the National Institute for Health and Care Excellence.[16] An overview of the applied checklists and the results per study can be found in Appendix 2.

Meta-Analysis

Meta-analyses were performed separately for the OR and the HR/RR. The latter (HR and RR) were analyzed together, given their similarity.[17] Meta-analyses were conducted in OpenMeta[Analyst] software for advanced meta-analysis from the Brown University Evidence-Based Practice Center.[18] Subgroup-analyses were performed based on (1) the frailty assessment tool category (physical-oriented scales, multidomain scales, deficit accumulation methods), (2) length of follow-up (0–12, 12–24, 24–60, and >60 months) and (3) the level of frailty (prefrail or frail). I^2 (heterogeneity) values with significance level were reported as a measure of the degree of inconsistency in the studies' results. I^2 values may range from 0% (no observed heterogeneity) to 100% (complete heterogeneity) and values of 25%, 50%, and 75% can be considered as respectively low, moderate, and high.[19]