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#### Protocol paper

# Prediction of one-year mortality by five different frailty instruments: A comparative study in hospitalized geriatric patients



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#### ABSTRACT

*Background*: Data comparing the ability of different major frailty instruments for predicting mortality in hospitalized geriatric patients are scare.

Material and methods: 307 patients ≥65 years who were hospitalized on geriatric wards were included in this prospective analysis. A fifty-item frailty index (FI), a ten-domain+co-morbidity frailty index based on a standardized comprehensive geriatric assessment (FI-CGA), the nine category Clinical Frailty Scale (CFS-9), the CSHA rules-based frailty definition (CSHA-RBFD), and the frailty phenotype (FP) were assessed during the patients' hospital stays. Patients were followed up over a one-year period.

Results: Follow-up data after one year could be obtained from 305 out of the 307 participants. Sixty two participants (20.3%) had died after that time. The FI, FI-CGA, CFS-9, CSHA-RBFD, and FP could all discriminate between patients who died and those who survived during follow-up (areas under the ROC curves: 0.805, 0.808, 0.852, 0.703 and 0.757, all P < 0.001, respectively). The CFS-9 showed a better discriminative ability for one-year mortality compared to the FI, FI-CGA, CSHA-RBFD, and FP (all P < 0.05, respectively). The FI and the FI-CGA did not differ in their discriminative ability for one-year mortality (P = 0.440). The CSHA-RBFD and the FP demonstrated a comparable discriminative ability (P = 0.241) and, when compared to the CFS-9, FI, and FI-CGA, an inferior discriminative ability for one-year mortality (all P < 0.05, respectively).

Conclusion: Among those frailty instruments that were evaluated, the CFS-9 emerged as the most powerful for prediction of one-year mortality.

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#### 1. Introduction

Frailty denotes a condition of increased vulnerability to stressors due to a reduction in physiological reserves of multiple organ systems (Morley et al., 2013). Frail old people show an increased incidence of negative health outcomes, including mortality, compared to non-frail ones (Morley et al., 2013). Several approaches for measuring frailty have been developed and evaluated, which are mainly based on the work of Rockwood and colleagues, as well as Fried and colleagues (Bouillon et al., 2013; Morley et al., 2013). Rockwood and colleagues utilized the classic frailty index based on multiple, individual health deficits (Mitnitski, Mogilner, & Rockwood, 2001; Rockwood & Mitnitski,

2012; Rockwood, Rockwood, & Mitnitski, 2010; Searle, Mitnitski, Gahbauer, Gill, & Rockwood, 2008), the frailty index based on severity of impairment of different functional domains of a standardized comprehensive geriatric assessment, and co-morbidity burden (Jones, Song, & Rockwood, 2004; Jones, Song, Mitnitski, & Rockwood, 2005), the Clinical Frailty Scale (Rockwood et al., 2005), and the Canadian Study of Health and Aging (CSHA) rules-based frailty definition (Rockwood et al., 1999). Fried and colleagues developed and evaluated the frailty phenotype (Fried et al., 2001).

These frailty instruments reflect different concepts. Rockwood and colleagues' classical frailty index is based on multiple (30 or more) individual potential health deficits, i.e., items (Searle et al., 2008). It represents an arithmetical approach which is independent of pre-set items (Searle et al., 2008) and can be constructed from different data sets, for example, from data of a CGA (Rockwood & Mitnitski, 2012; Searle et al., 2008). Another approach, developed and evaluated by Rockwood and colleagues,

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is to assess, in a standardized fashion, the level of impairment in the functional domains of a standardized, comprehensive geriatric assessment, together with the co-morbidity burden of the patients (Jones et al., 2004, 2005). The Clinical Frailty Scale (Rockwood et al., 2005) takes physical activity, functional impairment, comorbidity (including dementia severity), and the patient's remaining life expectancy into account. The CSHA rules-based frailty definition (Rockwood et al., 1999) is a measure based on functional criteria and the cognitive status of the patients. In contrast, the frailty phenotype (Fried et al., 2001) is based on five physical phenotypic criteria.

In geriatric medicine, estimation of the patient's remaining life expectancy is of relevance to clinical decision making. Patients on geriatric wards often show multiple co-morbidities and functional impairment. In these patients decisions with respect to diagnosis, treatment and intervention are frequently undertaken in absence of strong evidence base (American Geriatrics Society, 2012; Tinetti, Bogardus, & Agostini, 2004). This might result in inappropriate management in some old patients (American Geriatrics Society, 2012). Some patients might be subject to overtreatment or adverse effects of interventions that causes distress at the end of their lives. Other patients, who would potentially benefit from intervention, might, however, not undergo such interventions solely on the ground of their advanced chronological age alone. Thus, in older patients, analysis with respect to frailty and frailty degree, which is an indicator of biological age (Mitnitski et al., 2001), is, amongst other aspects, of interest in terms of estimation of the individual patient's remaining life expectancy.

Clearly, all aforementioned, major frailty instruments have been found to predict mortality (Fried et al., 2001; Jones et al., 2005; Mitnitski et al., 2001; Rockwood et al., 1999, 2005, 2010; Wallis, Wall, Biram, & Romero-Ortuno, 2015). However, the predictive power of these frailty instruments may differ. Of note, data comparing the ability of different frailty instruments to predict mortality in hospitalized geriatric patients are scarce (Pilotto et al., 2011; Ritt, Radi et al., 2015; Ritt, Schwarz et al., 2015). In particular, no study, up until now, has compared the ability of all the aforementioned different major frailty instruments, which are based on the work of Rockwood and colleagues, as well as Fried and colleagues, together and in parallel to predict mortality in a cohort of hospitalized geriatric patients. Against this background, our study aim was to analyze and compare the ability of five different major frailty instruments (i.e., a fifty-item frailty index, tendomain + co-morbidity frailty index based on a comprehensive geriatric assessment (FI-CGA), the Clinical Frailty Scale, the CSHA rules based frailty definition and the frailty phenotype), which reflect aforementioned different concepts, together and in parallel, to predict one-year mortality in old patients who were hospitalized on geriatric wards.

#### 2. Methods

#### 2.1. Study design and study population

This study was a prospective cohort study of hospitalized patients who were admitted to the geriatric wards of the Geriatrics Centre, Erlangen, of the Hospital of the Congregation of St. Francis Sisters of Vierzehnheiligen, Erlangen, Germany. The inclusion criterion was being aged 65 years or older. Exclusion criteria were the inability to give written informed consent or non-availability of a legal guardian to give written informed consent for the study participant. The objective of the study was to compare the ability of different frailty instruments, i.e., a fifty-item frailty index, a tendomain + co-morbidity FI-CGA, the Clinical Frailty Scale, the CSHA rules-based frailty definition and the frailty phenotype to predict one-year mortality. The data for the baseline analysis were

collected during the study participants' hospital stays following initial treatment of the acute disease or the exacerbation of chronic disease leading to hospital admission. Follow-up data were obtained for a further 12 months after the baseline examination. These data included, amongst other, information about the death of the study participants during follow-up. Follow-up data were collected by using telephone interviews with patients, their physicians, specialists, relatives or legal guardians. The study followed the principles of the Declaration of Helsinki and Good Clinical Practice. The study protocol was approved by the local ethics committee. Written informed consent was obtained from each study participant or from his or her legal guardian.

#### 2.2. The frailty instruments

#### 2.2.1. The classical fifty-item frailty index

The fifty-item frailty index was adapted from the fifty-two-item frailty index of Rockwood et al. (2010). In contrast to Rockwood et al. (2010), we did not assess the items "orthostatic hypotension" and "functional reach", so that the frailty index in the current study was based solely on fifty items. In brief, the fifty-items were as follows: (1) requiring help bathing, (2) requiring help dressing, (3) requiring help getting in/out of a chair, (4) requiring help walking around the house, (5) requiring help with mobility outside house, (6) requiring help eating, (7) requiring help grooming, (8) requiring help using the toilet, (9) requiring help up/down the stairs, (10) requiring help lifting 10 lbs, (11) requiring help shopping, (12) requiring help with housework, (13) requiring help with meal preparation, (14) requiring help taking medication, (15) requiring help with finances. (16) urinary incontinence. (17) bowel incontinence, (18) lost more than 10 lbs in the last year, (19) self-rating of health, (20) history of falls, (21) impaired vision, (22) impaired hearing, (23) difficulty speaking, (24) sleep disturbance, (25) high blood pressure, (26) hearth rhythm disorder, (27) heart attack, (28) congestive heart failure, (29) peripheral vascular disease, (30) stroke, (31) cancer, (32) diabetes mellitus, (33) arthritis, (34) chronic lung disease, (35) kidney disease, (36) constipation, (37-38) other medical problems, (39) depression, (40) anxiety, (41) alcohol use, (42) other psychiatric problems, (43) slowness on Timed Up and Go test (TUG), (44) low Mini-Mental State Examination score, (45) measured systolic hypertension, (46) measured diastolic hypertension, (47–50) number of medications. The individual items were scored according to their severity with a maximum score of 1 per item according to the criteria previously described in detail by Rockwood et al. (2010). The inability to perform the TUG resulted in a score of 1 in item 43. The fifty-item frailty index was finally calculated according to the sum of the score of each item divided by the total number of items considered, resulting in a score ranging from 0 to 1.

### 2.2.2. The ten-domain+co-morbidity frailty index based on a standardized comprehensive geriatric assessment (FI-CGA)

The ten-domain+comorbidity FI-CGA was adopted from work by Jones et al. (Jones et al., 2005). It is based on severity of impairment in the ten functional domains of a standardized comprehensive geriatric assessment (Rockwood, Silvius, & Fox, 1998) and co-morbidity burden, as assessed by the Cumulative Illness Rating Scale (Cornwell, Forbes, Cox, & Caine, 1993). The ten domains of a standardized comprehensive geriatric assessment include: (1) cognition, (2) emotion, (3) communication, (4) mobility, (5) balance, (6) bladder function, (7) bowel function, (8) nutrition, (9) instrumental activities of daily living/activities of daily living, and (10) social situation. The health deficit in each domain was scored as no (0 points), minor (0.5 points) or major deficit (1 point) and co-morbidity burden was scored up to 4 additional points according to the criteria previously described by

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