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The impact of frailty on depressive disorder in later life: Findings from the Netherlands Study of depression in older persons

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ABSTRACT

Background: Physical frailty and depressive symptoms are reciprocally related in community-based studies, but its prognostic impact on depressive disorder remains unknown.

Methods: A cohort of 378 older persons (≥ 60 years) suffering from a depressive disorder (DSM-IV criteria) was reassessed at two-year follow-up. Depressive symptom severity was assessed every six months with the Inventory of Depressive Symptomatology, including a mood, motivational, and somatic subscale. Frailty was assessed according to the physical frailty phenotype at the baseline examination.

Results: For each additional frailty component, the odds of non-remission was 1.24 [95% CI = 1.01–1.52] ($P = .040$). Linear mixed models showed that only improvement of the motivational ($P < .001$) subscale and the somatic subscale ($P = .003$) of the IDS over time were dependent on the frailty severity.

Conclusions: Physical frailty negatively impacts the course of late-life depression. Since only improvement of mood symptoms was independent of frailty severity, one may hypothesize that frailty and residual depression are easily mixed-up in psychiatric treatment.

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1. Introduction

Depressive disorder is a highly prevalent condition among older persons, with pooled prevalence rates of 1.8% for independently living persons aged 55 years and over [1], and 7.2% for persons aged over 75 years irrespective of their living arrangement [2]. Depression in later life constitutes an important worldwide health issue due to its chronic course with high recurrence and relapse rates [3,4]. In the Netherlands Study of Depression in Older Persons (NESDO), it was previously found that after two years, 48% suffered from a depressive disorder and that 61% had a chronic course of depression [5]. Diagnosis of depression is often complicated by the presence of somatic comorbidity, pain and frailty [6–8]. To optimize treatment of late-life depression, understanding the processes involved in the course of this mental

illness is essential. In an overview of evidence-based practices, the most extensive research support was found for the effectiveness of pharmacological and psychosocial interventions for the treatment of late-life depression [9]. Aspects such as comorbid somatic diseases and (potentially modifiable) frailty have not been incorporated in evidence-based antidepressant treatment strategies. An important step would be to identify risk factors that predict an unfavorable course of depression. To date, only a few studies investigated risk factors of an adverse course of late-life depression. Known risk factors are higher severity of depressive symptoms, higher number of previous episodes, later age of onset, cognitive decline and medical comorbidity [10,11]. Frailty may be an additional risk factor [12,13].

Frailty is a condition of increased risk of adverse health outcomes [14]. In a recent consensus meeting, it has been concluded that physical frailty is an important medical syndrome with multiple causes and contributors [15]. The physical frailty phenotype is defined as the presence of three or more of the following five characteristics: weight loss, weakness, slowness, exhaustion and low activity level [14]. The dimensional nature of

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frailty is acknowledged by including a prodromal frailty state in this definition; prefrailty, which is defined as the presence of only one or two of the characteristics. When no frailty characteristics are present, an older person is classified as robust [14]. Meta-analytic research has shown that approximately one out of ten persons over 65 years can be classified as physically frail [16]. Remarkably, the hallmark study of Fried et al. [14], developing the physical frailty phenotype, excluded patients with depression and/or on antidepressant treatment. The authors wanted to preclude that persons were classified physically frail on the presence of one disorder only. Recently, we showed that more than a quarter of clinically depressed older persons fulfil criteria for physical frailty [17]. As this proportion is comparable to chronic somatic diseases, it simply implies that frailty deserves a similar level of attention in geriatric psychiatry as in chronic somatic diseases.

The association between physical frailty and depressive symptoms in the population is assumed to be bidirectional [6,17]. This leads to the question whether frailty and late-life depression are causal factors for each other, or whether they share the same underlying mechanisms that may also influence the presentation of one another. Suggestions for the latter hypothesis involve both psychosocial factors and stress-related pathophysiological dysregulations [12]. On the other hand, three longitudinal studies in the general population have identified physical frailty as an independent predictor of the increase and protracted course of depressive symptoms [12,13,18], while one study showed that depression is a predictor of incident frailty [19]. Because these studies focused on depressive symptoms instead of a depressive disorder according to DSM criteria, results may be confounded by overlap between self-report depressive symptoms and signs of frailty. Moreover, these community-based findings cannot be extrapolated to a psychiatric population. Latent class analyses on the individual components of physical frailty and DSM-IV criteria for major depressive disorder also showed that physical frailty and major depressive disorder identify the same set of persons, especially among those suffering from severe depression [20]. Nonetheless, these analyses also pointed to a cluster of patients suffering from either physical frailty or depression alone. This has led to the conclusion that the most appropriate model for understanding the depression-frailty association is one of comorbidity [12,13,18,20]. The next step would be to assess frailty and the course of depression in a clinically depressed sample.

The first objective is to examine whether physical frailty predicts non-remission of depressive disorder over a two-year follow-up. The second objective is to examine whether physical frailty is associated with an adverse course of depressive symptoms over time.

Hypothesizing a negative effect of physical frailty on depression outcome, we expect lower remission rates at follow-up and a worse course of depressive symptoms over time among those who are physically frail.

2. Method

Study participants came from the NESDO [21], an ongoing cohort study aimed at examining the long-term course and consequences of depressive and anxiety disorders in older persons (aged ≥ 60 years). Recruitment of depressed older persons took place in five regions in The Netherlands from both mental health institutes (in- and outpatients) and from primary care in order to include persons with late-life depression in various developmental and severity stages. The NESDO study has included a total of 378 depressed subjects (age range: 60 through 93 years) who suffered from a current DSM-IV diagnosis of major depressive

disorder (95%), dysthymia (26.5%), or minor depression (5.6%), of which 26.5% have two types of depressive disorders. Persons with a primary diagnosis of dementia, a Mini Mental State Examination-score (MMSE) under 18 or an organic or psychotic disorder were excluded, since the course of these persons will be largely determined by the primary disorder. Insufficient mastery of the Dutch language was another exclusion criterion. All participants were competent to consent to participation and all gave written informed consent. The ethical review boards of the participating institutes approved of this study. More detailed information about the NESDO is described elsewhere [5,21].

Data collection included an examination at one of the participating clinics or at the homes of the participants, including a structured diagnostic interview, physical tests (such as blood pressure and gait speed), and paper and pencil questionnaires. These assessments were conducted at baseline as well as after two years follow-up [5]. The course of late-life depression was followed up every six months by means of a postal assessment (five questionnaires were sent during the two years follow-up), including questionnaires on the severity of depressive symptoms and physical health in the past six months.

Because 93/378 (24.6%) dropped out before the two-year follow-up assessment, this study consisted of 285 eligible participants. Persons that were lost to follow-up had lower cognitive functioning (MMSE score 27.2 versus 27.9, $P=0.14$) and more frailty characteristics (2.2 versus 1.7, $P=0.02$) than the persons that did participate in the two-year follow-up. No baseline differences with regard to age, gender, educational level, severity of depression, number of diseases and use of antidepressants were found between persons that participated in follow-up and persons that did not participate in follow-up.

2.1. Measures

2.1.1. Depression

The Composite International Diagnostic Interview (CIDI), version 2.1 was used in order to determine the presence of depression at baseline, as well as at two years follow-up [22]. The CIDI is a structured interview that assesses psychiatric disorders in adults according to the criteria of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). To determine the research DSM-IV diagnosis of current minor depression, questions were added to the CIDI, as in the Netherlands Study of Depression and Anxiety (NESDA) [23]. Non-remission at two-year follow-up was defined as neither major depression or dysthymia in the past six months, nor minor depression in the past month.

Severity of depression was measured by the well-validated 30-item self-rating Inventory of Depressive Symptoms 30 item version (IDS) [24]. In the IDS, items are scored on a four-point scale, with each item equally weighted and summed up to a total score. IDS scores range from 0–84 points, with higher scores indicating more severe depression. In older persons, the IDS has three subscales, reflecting a mood-, motivation-, and somatic dimension of depression [25].

2.1.2. Frailty

Physical frailty was operationalized by the following five criteria of Fried et al. [14]:

- a six-meter walking test was used to assess slowness. For men ≤ 173 centimetres (cm) tall the cut off time was 9 s, for men > 173 cm the cut off time was 8 s. The cut off time for this criterion for women with a height of ≤ 159 cm was 9 s, for women > 159 cm the cut off time was 8 s (extrapolated from the data of Fried et al.) [14];

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