Universiteit Leiden

Psychologie
Faculteit der Sociale Wetenschappen

The association between frailty and cognition in elderly with psychiatric disorders

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(August, 2017)
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Abstract

Objective: Frailty is a syndrome of reduced resistance to respond to stressors, causing increased vulnerability to adverse outcomes. Associations between frailty and cognitive impairment in non-psychiatric elderly have been found, however this association is unclear for psychiatric elderly patients. The aim of this study was to examine the prevalence of frailty, gender and Diagnostic and Statistical Manual of Mental Disorders (DSM-5) differences in this prevalence, and the relationship between cognitive impairment and frailty in elderly with psychiatric disorders.

Methods: We conducted a cross-sectional study with 50 patients of 65 years and older, hospitalized at a Dutch psychiatric institution. If three of the Fried criteria were present (weight loss, weakness, exhaustion, slowness, and low physical activity), a patient was considered frail. Cognitive functioning was assessed by the Mini Mental State Examination and the clock drawing test. Multiple logistic regressions, adjusted for age and gender, were performed to examine the association between cognitive impairment and frailty.

Results: The frailty prevalence was 36.0%, we found no gender differences or differences in DSM-5 diagnosis concerning this prevalence. The prevalence of the co-occurrence of frailty and cognitive impairment was 16.7%. Cognitive impairment predicted frailty (OR=5.45 p= .019), as well as two components of frailty: weakness (OR = 8.89 p = .012) and slowness (OR=6.81 p= .020). The regression analyses were significant before and after correction for age and gender.

Conclusion: Both frailty and the co-occurrence of frailty and cognitive impairment are highly prevalent in psychiatric elderly patients. There is a strong association between the two syndromes, therefore therapists should be aware of the higher chance of a cognitively impaired patient to also be frail. Future research is needed to examine the interrelationship, underlying mechanisms, cognitive domains, and interventions in this population.

Introduction

According to the World Health Organization (WHO; 2015) the elderly population of the world is expected to increase from 900 million in 2015 to two billion in 2050. This rapid increase is, among other things, due to the extension of life expectancy (WHO, 2015). As a result of this ageing of the world's population, the number of people with disabilities and chronic health conditions is increasing. Caring for dependent elderly is a costly challenge for modern healthcare (Robertson, Savva, & Kenny, 2013). This is one of many reasons to further examine this group, as better understanding of elderly could lead to new evidence-based interventions and consequently to the reduction in healthcare costs. However, not every elderly of the same chronological age has the same risk to experience health problems and becoming dependent upon help from others. One 70-year-old can be completely healthy, while the other 70-year-old can experience various health problems. The concept of frailty tries to explain this difference of adverse health outcomes among elderly of the same chronological age (Theou et al., 2015).

Frailty is a common, heterogeneous biologic syndrome of reduced physiologic reserve and resistance to respond to external stressors, causing increased vulnerability to adverse outcomes (e.g., disability, falls, hospitalization, institutionalization, and mortality; Fried et al., 2001; Langlois et al., 2012). Frailty is recognized to be a distinct clinical syndrome that is separated from, although associated with, ageing, comorbidity, disability, and chronic diseases (Houles et al., 2012). The most widely used operationalization of frailty is the physical frailty phenotype of Fried et al. (2001). This phenotype of frailty is classified if three or more of the following criteria are present: unintentional weight loss, weakness, exhaustion, slowed gait, and low physical activity level (Fried et al., 2001). The prevalence of frailty increases with age, as shown in the Canadian Study of Health and Aging where a frailty prevalence of 7.0% was found for elderly aged 65-74, 17.5% for elderly aged 75-84, and 36.6% for elderly aged 85+ (Rockwood et al., 2004). A higher prevalence has been found in women, they have almost twice as much chance to be frail compared to men. (Fried et al., 2001; Rockwood et al., 2004). Alongside the physical complaints, cognitive impairment has been suggested as an additional factor present in frail elderly (Langlois et al., 2012).

Frailty and cognitive impairment are two common syndromes in elderly people (Morley, 2015). The association between these two syndromes in elderly received considerable attention, and has been found in both cross-sectional (Ávila-Funes et al., 2009; Jurschik et al., 2012; Macuco et al., 2012) and longitudinal studies (Ávila-Funes et al., 2012; Samper-Ternent, Al Snih, Raji, Markides, & Ottenbacher, 2008; Solfrizzi et al., 2013). The cross-sectional studies have shown a strong correlation between cognitive impairment and frailty. Compared to non-frail elderly, frail elderly have significant higher rates of cognitive impairment (Robertson et al., 2013). This correlation was not explained by demographic variables or the number of chronic diseases (Buchman et al., 2014). In the relation between cognitive impairment and frailty, age is an effect modifier, meaning that the oldest elderly showed a stronger correlation than younger elderly (Assis Faria, Lourenco, Ribeiro, & Lopes, 2013). Of the different components of frailty, the highest correlations with cognitive impairment have been found with weakness and slowed gait speed (Robertson, Savva, Coen, & Kenny, 2014). Alongside the correlational research, other studies have analyzed the predictive values of cognition and frailty (Jacobs, Cohen, Ein-mor, Maaravi, & Stessman, 2011; Han, Lee, & Kim, 2014; Ottenbacher et al., 2005). It is assumed that cognitive impairment precedes frailty and vice versa (Auyeung, Lee, Kwok, & Woo, 2011). For instance, impairment in executive functioning, a cognitive domain, can lead to slowed gait speed, a frailty component (Robertson et al., 2013). Han et al. (2014) conducted a cross-sectional study with cognitive impairment, measured by the Mini Mental State Examination (MMSE), as a predictor of physical frailty, measured by the Fried et al. (2001) criteria. They found that cognitively impaired participants were almost twice as likely to be frail than cognitively intact participants.

In contrast to the association between frailty and cognitive impairment, the prevalence of the co-occurrence of frailty and cognitive impairment has received less attention. To our knowledge, only Shimada et al. (2013) examined this, and found a prevalence of the co-occurrence of 2.7% in a Japanese sample. Examining the prevalence of the co-occurrence of frailty and cognitive impairment is important because elderly who are both frail and cognitively impaired, may be at higher risk of functional decline (Shimada et al., 2013). Replication in a Western sample will make conclusions and implications easier to generalize for Western patients.

Longitudinal studies have shown that the presence of frailty leads to higher risk of cognitive decline, mild cognitive impairment, vascular dementia, and Alzheimer's dementia (Ávila-Funes et al., 2012; Samper-Ternent et al., 2008; Solfrizzi et al., 2013). However, cognitive impairment also increased the risk of frailty, which suggests an interrelationship between cognition and frailty (Robertson et al., 2013). Multiple possible underlying mechanisms have been suggested to explain this relationship. The first mechanism is neuropathological. Buchman, Schneider, Leurgans, & Bennett (2008) found that Alzheimer's pathology, e.g., neurofibrillary tangles and amyloid plaques, was associated with increased levels of frailty. The second mechanism is a chronic inflammatory reaction. Stress reactions, chronic diseases, lifestyle factors, and other factors can generate an inflammatory response, e.g., increased pro-inflammatory cytokines, interleukin-1, and tumor necrosis factor (Robertson et al., 2013). With ageing, levels of interleukin-6 can increase. These inflammatory reactions can lead to reduced body mass, weakened muscles, and poorer physical performance; consequently leading to frailty (Kang et al., 2016). Additionally, these inflammatory reactions can lead to neurotoxicity; consequently causing cognitive impairment (Kang et al., 2016; Robertson et al., 2013). The third mechanism is hormonal. Testosterone has a protective effect on cognition. Consequently, reduced testosterone may lead to cognitive decline (Robertson et al., 2013). Additionally, reduced testosterone is also associated with weakened muscles, which is one of the frailty criteria (Robertson et al., 2013). Reduced insulin is associated with an increased risk for both cognitive impairment and frailty (Robertson et al., 2013). The fourth mechanism is cardiovascular risk. Cardiovascular disease has been found to be associated with frailty. Like inflammatory reactions, cardiovascular disease can lead to weakened muscles (Robertson et al., 2013). Additionally, vascular risk factors can lead to cognitive impairment and dementia (Robertson et al., 2013). The fifth mechanism is nutritional. Cognitively impaired elderly may not be able to adequately regulate their nutritional intake, which can lead to reduced body mass and weakened muscles; possibly leading to frailty (Kang et al., 2016). Additionally, elderly with sarcopenia (the loss of muscle mass and strength, associated to ageing) are at increased risk to develop cognitive impairment (Kang et al., 2016). The last mechanism is mental health. Mood disorders, as depression, have an amplifying influence on the relationship between frailty and

cognitive impairment. Depression can affect cognitive functions, but is also both a risk factor and outcome of frailty (Robertson et al., 2013).

Although a considerable amount of studies have examined frailty, the majority of the existing literature has focused on samples consisting of community dwelling elderly (e.g., Ávila-Funes et al., 2008; Clegg, Rogers, & Young, 2014; Theou et al., 2015). Frailty in elderly with Diagnostic and Statistical Manual of Mental Disorders (DSM-5) disorders has received relatively little attention. However, frailty is an important concept in old age psychiatry, because of the overlap between frailty and psychiatric disorders (e.g., cognitive impairment, depression). Furthermore, early detecting of frailty in elderly psychiatric patients could help to adjust the psychiatric treatment and may lead to effective interventions that could prevent or delay the adverse health outcomes of frailty. In research with non-psychiatric elderly this has already led to evidence-based interventions, like following an adequate diet and physiotherapy, which target two frailty components (Collard & Oude Voshaar, 2012). Frailty is strongly associated with healthcare costs, and interventions improving frailty could lead to a reduction in these costs (Butler et al., 2016). A better understanding of the association between frailty and cognitive impairment in elderly with psychiatric disorders may also lead to effective interventions and possible costs reductions.

The first aim of this study was to describe the prevalence of frailty in our sample of psychiatric elderly patients, and its association with gender and DSM-5 diagnosis, using the following research questions:

1.1 What is the prevalence of frailty in elderly with psychiatric disorders?

1.2 Are there gender differences in the prevalence of frailty?
It was hypothesized that a higher prevalence would be found in women, compared to men.

1.3 Are there differences in the prevalence of frailty between the DSM-5 diagnosis groups?
As far as we are aware, the differences per DSM-5 diagnosis group have never been researched in existing frailty studies. Therefore, we will explore these differences, using three diagnosis groups: depressive disorders, bipolar disorders, and psychotic disorders.

The second aim was to examine the association between frailty and cognitive impairment in our sample, using the following research questions:

2.1 What is the prevalence of the co-occurrence of frailty and cognitive impairment?

2.2 Is cognitive impairment a significant predictor of frailty?
It was hypothesized that cognitive impairment is a significant predictor of frailty.

2.3 Is cognitive impairment a significant predictor of weakness?
It was hypothesized that cognitive impairment is a significant predictor of weakness.

2.4 Is cognitive impairment a significant predictor of slowness?
It was hypothesized that cognitive impairment is a significant predictor of slowness.

Research has shown that age and gender may affect frailty, and the relation between frailty and cognitive impairment, therefore these variables were included as covariates (Assis-Faria et al., 2013; Fried et al., 2001; Rockwood et al., 2004).

Methods

Design

We conducted a cross-sectional study in a sample of elderly people with psychiatric disorders, which was part of a longitudinal study. The data-collection of the cross-sectional study started in February 2017 and ended in May 2017. The current study was based on baseline data and data of a pilot study. The pilot study was conducted in 2016 and comprised 12 patients. The measurements of the pilot study overlapped those of the current study, but the current study included a few extra measurements.

Participants

Patients of 65 years and older with a DSM-5 disorder, who were hospitalized at the old age psychiatry department of Parnassia Group in The Hague, the Netherlands, were suitable for inclusion. Patients were excluded if they were non-fluent in Dutch, had a diagnosis of dementia, or refused participation. A few patients (n=3) were untestable due to the severity of their psychiatric condition and therefore excluded. Six patients were already discharged from hospitalization before the measurement was conducted, due to improvement of their psychiatric condition. After applying the in- and exclusion criteria and adding the pilot data, the study sample comprised 50 patients. Figure 1 shows the flowchart of the study.

Procedure

Every new patient who was hospitalized during the time of the data-collection and who met the inclusion criteria was approached to participate in the study. The patients were informed about the study by the researcher or research assistant. When a patient agreed to participate, an appointment was scheduled to complete the measurement. At the start of the appointment, the patients were asked to sign an informed consent form. The measurements were conducted by either the researcher or research assistant, and took approximately 45 minutes to complete. The measurements were conducted in consulting and testing rooms at Parnassia. The Medical Ethics Committee of Leiden University Medical Centre (LUMC) issued a declaration of no objection for this study.

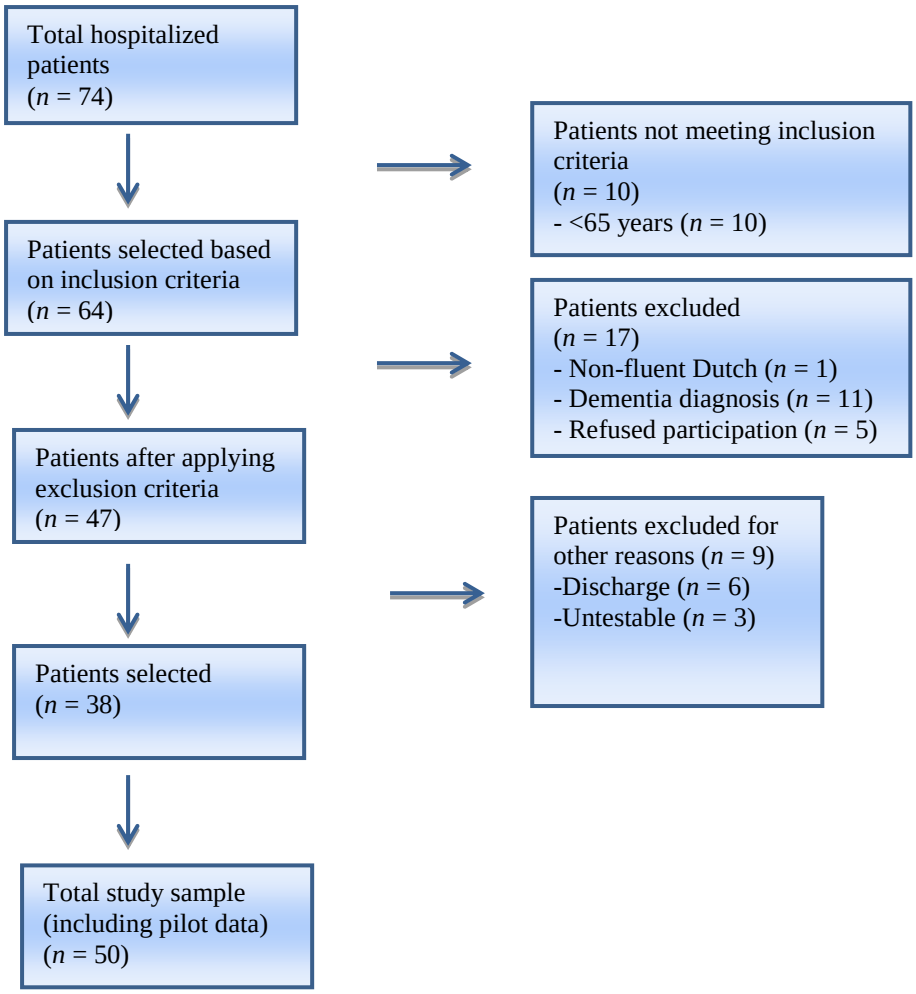

Figure 1. Flowchart of the selection process.

Measures

Frailty was assessed by the five criteria of Fried et al. (2001), operationalized as follows:

The Short Nutritional Assessment Questionnaire (SNAQ) assessed weight loss (Kruizenga, Seidell, de Vet, Wierdsma, & van Bokhorst- de van der Schueren, 2005). If a patient lost 4.5 kilograms or more in the previous year, this criterion was considered present.

A handgrip meter that measured muscle strength assessed weakness. Gender and age-specific cut-off scores were used to evaluate the scores (Mathiowetz et al., 1985). If a patient scored lower than the mean score of the norm group, according to the Mathiowetz et al. (1985) cut-off scores, this criterion was considered present.

Two items of the Center for Epidemiologic Studies Depression Scale (CES-D) assessed exhaustion (Radloff, 1977; Dutch translation: Bouma, Ranchor, Sanderman, & van Sonderen, 1995). If the patient scored high, that is a score of 2 (regularly present) or 3 (mostly or always present) on both of these items, this criterion was considered present.

Walking speed measured slowed gait. Patients were asked to walk 4 meters, with walking aid if necessary. Cut-off scores from the Fried et al. (2001) study were used to evaluate walking speed. If walking speed of a patient was slower than the mean walking speed of the norm group, according to the Fried et al. (2001) cut-off scores, or if it was not possible to walk at all, this criterion was considered present.

Three items of the Netherlands Study of Depression in Older Persons (NESDO study), a study on late-life depression and its course and co-morbidities, assessed low physical activity (Comijs et al., 2011). If the patient scored a total of 0 on these items (no physical activity of any kind), this criterion was considered present.

According to Fried et al. (2001) if three or more of the five criteria were present, a patient was considered frail. In the statistical analyses frailty was evaluated as a dichotomous variable.

The MMSE (Folstein, Folstein, & McHugh,1975; Dutch translation: Kok & Verhey, 2002) and the clock drawing test (Manos & Wu, 1994) assessed cognitive functioning. Both the MMSE (Folstein et al., 1975) and the clock drawing test (Agrell & Dehlin, 1998) are useful screening tests to detect cognitive dysfunction. The clock drawing test is most commonly used as an additional screener to the MMSE (Smits, Koene, Pijnenburg, Scheltens, & van der Flier, 2009). A lower score on both the MMSE (range 0-30) and the clock drawing test (range 0-10) indicates worse cognitive performance. Both scores were combined to measure cognitive impairment. Cut-off points were set at ≤24 for the MMSE (Folstein et al., 1975) and ≤7 for the clock drawing test (Manos, 2006). If the patient scored ≤24 on the MMSE and ≤7 on the clock drawing test, cognitive impairment was considered present. In the statistical analyses, cognitive impairment was evaluated as a dichotomous variable.

Statistical analyses

Descriptive analyses were used to study the prevalence of frailty and the prevalence of the co-occurrence of frailty and cognitive impairment, answering research question 1.1 and 2.1. Chi-squared (χ^2) tests were performed to test the gender and DSM-5 diagnosis differences, answering research question 1.2 and 1.3. In the χ^2 tests frailty and gender were dichotomous variables and DSM-5 diagnosis categorical. DSM-5 diagnoses have been categorized in three diagnosis groups: depressive disorders, bipolar disorders, and psychotic disorders, as these three diagnosis groups are most common at this old age department.

Logistic regression was performed to examine the association between frailty and cognitive impairment, answering research question 2.2. In this regression cognitive impairment (dichotomous) was the independent variable and frailty (dichotomous) the dependent variable. Logistic regression was also performed to examine the association between weakness/slowness and cognitive impairment, answering research question 2.3 and 2.4. In these regression analyses weakness and slowness (both dichotomous) were the dependent variables and cognitive impairment (dichotomous) the independent variable. All three logistic regression analyses were performed stepwise; first without, and second with covariates age and gender. In this study, we were interested in the adjusted results, the unadjusted results have been added for sensitivity analyses.

To perform the statistical analyses IBM SPSS statistics version 23 was used. The significance threshold was set on $p = .05$.

Both assumptions for the Chi-squared tests (independence of data and expected frequencies) were met. Two assumption for the logistic regressions (independence of errors and multicollinearity) were also met, the assumption of linearity did not apply to our data. Independence of errors was checked with the Durbin-Watson. Multicollinearity was checked with tolerance and VIF statistics.

Results

Prevalence

The study sample comprised 50 patients, of which 20.0% were male. The average age of the sample was 74.9 years (*SD* = 7.1). Table 1 shows the characteristics of the sample. A total of 18 patients were considered to be frail, meaning that the prevalence of frailty in this sample was 36.0%. We found no significant gender differences in the prevalence of frailty ($\chi^2(1) = 1.389$ $p = .239$). There was also no significant difference in frailty prevalence between the DSM-5 diagnosis groups ($\chi^2(2) = 0.820$ $p = .664$). A total of 8 patients were considered to be both frail and cognitively impaired, meaning that the prevalence of the co-occurrence of frailty and cognitive impairment was 16.7% in this sample.

Table 1. Baseline characteristics

	Total *n* = 50	**Frail** *n* = 18	**Non frail** *n* = 32
Gender, *n* (%)			
Female	40 (80.0%)	16 (88.9%)	24 (75.0%)
Male	10 (20.0%)	2 (11.1%)	8 (25.0%)
Age, *M (SD)*	74.9 (7.1)	75.3 (7.4)	74.6 (7.0)
MMSE, *M (SD)*	24.6 (4.2)	23.3 (3.2)	25.3 (4.5)
Clock drawing test, *M (SD)*	6.1 (3.4)	4.3 (3.7)	7.1 (2.9)
Cognitive impairment, *n (%)*	14 (28.0%)	8 (44.4%)	6 (18.8%)
Weight loss, *n (%)*	22 (44.0%)	13 (72.2%)	9 (28.1%)
Weakness, *n (%)*	29 (58.0%)	17 (94.4%)	12 (37.5%)
Exhaustion, *n (%)*	24 (48.0%)	17 (94.4%)	7 (21.9%)
Slowness, *n (%)*	15 (30.0%)	12 (66.7%)	3 (9.4%)
Physical inactivity *n (%)*	5 (10.0%)	5 (27.8%)	0 (0.0%)
DSM-5 diagnosis *n (%)*			
Depressive disorder	24 (48.0%)	10 (55.6%)	14 (43.8%)
Bipolar disorder	9 (18.0%)	4 (22.2%)	5 (15.6%)
Psychotic disorder	14 (28.0%)	4 (22.2%)	10 (31.3%)

Note. MMSE = Mini Mental State Examination, DSM = Diagnostic and Statistical Manual of Mental Disorders

Association frailty and cognitive impairment

Cognitive impairment was found to be a significant predictor of frailty. Table 2 shows the unadjusted and adjusted associations between frailty and cognitive impairment. Cognitively impaired patients were, after adjusting for age and gender, over 5 times more likely to be frail than cognitively intact patients. Cognitive impairment was also a significant predictor of the frailty component weakness. Cognitively impaired patients were, after adjusting for age and gender, almost 9 times more likely to have low muscle strength than cognitively intact patients. Cognitive impairment was also a significant predictor of the frailty component slowness. Cognitively impaired patients were, after adjusting for age and gender, almost 7 times more likely to have slow walking speed than cognitively intact patients.

Table 2. logistic regression with cognitive impairment as predictor of frailty

	Unadjusted			**Adjusted***		
	B [SE]	OR [95% CI]	*p*	B [SE]	OR [95% CI]	*p*
frailty	1.47 [0.68]	4.33 [1.16-16.26]	.030	1.73 [0.74]	5.45 [1.33-23.94]	.019
weakness	2.02 [0.84]	7.60 [1.47-39.29]	.016	2.19 [0.87]	8.89 [1.62-48.86]	.012
slowness	1.35 [0.68]	3.86 [1.01-14.69]	.048	1.92 [0.83]	6.81 [1.35-34.38]	.020

* adjusted for age and gender

Discussion

The first aim of this study was to describe the prevalence of frailty, and gender and DSM-5 differences in this prevalence. The second aim was to examine the relationship between frailty and cognitive impairment in our sample of elderly with psychiatric disorders. Frailty was assessed with the five Fried et al. (2001) criteria (unintentional weight loss, weakness, exhaustion, slowed gait, and low physical activity level) and cognitive functioning was assessed with the MMSE and clock drawing test. We found both a high prevalence of frailty and a high prevalence of the co-occurrence of frailty and cognitive impairment. Furthermore, we found a strong association between cognitive impairment and frailty, and between cognitive impairment and two of the frailty components. Examining frailty and the relationship between frailty and cognitive impairment in this group of elderly is important because it could lead to evidence-based interventions, which in turn could lead to a reduction in healthcare costs (Butler et al., 2016; Collard & Oude Voshaar, 2012).

The prevalence of frailty was 36.0% in this study, which is much higher than the frailty prevalence of 6.9% found in community dwelling elderly (Fried et al. 2001). This suggests that frailty may be more prevalent in elderly with psychiatric disorders than in elderly without psychiatric disorders. One possible explanation for this could be the overlap between frailty and psychiatric disorders (Collard & Oude Voshaar, 2012). Depression, for example, shares risk factors (e.g., low grade inflammation), common symptoms (e.g., exhaustion), and adverse health outcomes (e.g., mortality) with frailty (Buigues et al., 2014). However, the overlap between frailty and psychiatric disorders in general remains unclear, and should be further investigated in future research. Another possible explanation, at least in part, for the high frailty prevalence we found, compared to that of Fried et al. (2001), is the higher proportion (80.0%) of female participants in our sample, as opposed to the 57.9% of Fried et al. (2001). However, we found no significant gender differences in the prevalence of frailty in our sample. This is not in line with our hypothesis or with previous research, as the majority of existing frailty studies found a significantly higher prevalence in women compared to men (Fried et al., 2001; Rockwood et al., 2004). One possible explanation for not finding a significant gender difference in our sample could be the small sample size, which could have led to type II error. We also found no significant differences in the prevalence of frailty between the three DSM-5

diagnosis groups (depressive disorders, bipolar disorders, and psychotic disorders). This could indicate that the type of DSM-5 diagnosis does not influence the chance of being frail. Hypothetically, considering the high frailty prevalence in our sample, it could indicate an underlying vulnerability of having a psychiatric conditioning in itself that causes a higher chance to be frail, instead of one type of DSM-5 diagnosis being at higher risk. However, it is also possible that the nonsignificant result was a consequence of the small sample size, which could have led to type II error. More research is needed to investigate these possibilities, as potential differences in frailty per DSM-5 diagnosis could be important to offer different patient groups appropriate treatment.

We found a prevalence of the co-occurrence of frailty and cognitive impairment of 20.8%. This combined prevalence is much higher than the 2.7% found by Shimada et al. (2013) in a Japanese sample of community dwelling elderly. This result could be explained by the high frailty prevalence we found in our sample, 36.0% compared to 11.3% found by Shimada et al. (2013). Hypothetically, another explanation could be that elderly with psychiatric disorders are in fact more likely to be both frail and cognitively impaired than non-psychiatric elderly, which in turn could be explained by the fact that cognitive impairment is more common in patients with psychiatric disorders, e.g., bipolar disorder (Coffman, Bornstein, Olson, Schwarzkopf, & Nasrallah, 1990) and schizophrenia (Taylor and Abrams, 1984). However, future research should point out whether there are significant differences between non-psychiatric and psychiatric elderly patients in this combined prevalence, as potential differences between these groups could be important in the diagnostic and treatment phases.

Cognitive impairment was found to be a significant predictor of frailty in our sample, which is in line with our hypothesis and previous research (Jacobs et al., 2011; Han et al., 2014). The cognitively impaired patients in our sample were over five times more likely to be frail than cognitively intact patients. This relationship between cognitive impairment and frailty could possibly be explained by the shared underlying mechanisms, e.g., neuropathological mechanisms, chronic inflammation, hormonal mechanisms, cardiovascular disease, and nutrition (Buchman et al., 2008; Kang et al., 2016; Robertson et al., 2013). It seems that having a psychiatric condition is causing the relationship between cognitive impairment and frailty to be even stronger, as we found a higher OR in our sample than Han et al. (2014) in their sample

of non-psychiatric elderly. They found that cognitively impaired participants were twice as likely to be frail than cognitively intact participants. This assumption is in line with the findings of Robertson et al. (2013), who found that mood disorders have an amplifying influence on the relationship between frailty and cognitive impairment. However, the high odds ratio could also be caused by the high frailty prevalence we found in our study. Cognitive impairment was also a significant predictor of weakness, one of the frailty components, in our sample, which is in line with our hypothesis and previous research (Alvaro-Acha et al., 2006; Houles et al., 2012). The cognitively impaired patients in our sample were almost nine times more likely to have low muscle strength than cognitively intact patients. A possible explanation for this relationship could be that loss of muscle strength and cognitive decline share the same underlying mechanisms (e.g., chronic inflammation), causing a general decline in brain structure and function (Alfaro-Acha et al., 2006). Cognitive impairment was also a significant predictor of slowness, one of the frailty components, in our sample, which is in line with our hypothesis and previous research (Abellan van Kan et al., 2009; Houles et al., 2012). The cognitively impaired patients in our sample were almost seven times more likely to have slow walking speed than cognitively intact patients. A possible explanation for this relationship could be that in order to walk, several cognitive functions (e.g., attention, executive functioning, visuospatial functioning) are needed, thus slow gait speed and cognitive impairment may also share the same underlying mechanisms (Buracchino, Dodge, Howieson, Wasserman, & Kaye, 2010). Considering these results, it is possible that of all frailty components, weakness and slowed gait show the strongest relation with cognitive impairment, which is in line with previous research (Buchman et al. 2014; Robertson et al., 2014). However, future research should investigate which of all five frailty components show the strongest relation with cognitive impairment in psychiatric elderly patients.

Strengths of our study are the high participation rate, implying our sample should be an adequate representation of the elderly psychiatric inpatient population. Furthermore, we used valid and reliable measures, e.g., the five Fried et al. (2001) criteria which are used by over 300 other studies. This makes our study easily comparable to other studies on the topic. Despite the strengths of this study, there are some limitations that should be considered when interpreting the findings. First, because of our cross-sectional study design, we cannot show a causal relationship between frailty and cognitive impairment in our sample. Previous longitudinal

research has shown an interrelationship between frailty and cognitive impairment in community dwelling elderly (Ávila-Funes et al., 2012; Samper-Ternent et al., 2008; Solfrizzi et al., 2013), and multiple possible underlying mechanisms have been suggested to explain this interrelationship. However, future longitudinal research should indicate whether this interrelationship also exists in elderly with psychiatric disorders. Second, our sample size of 50 patients was small, which may have led to type II error. The small sample size could also be an explanation for the wide 95% confidence intervals in the regression analyses. Also, our study sample comprised more women than men, which could have caused bias. However, in the psychiatric hospital where the current study was conducted, it is the standard that more women are hospitalized than men. Thus, the skewed gender distribution of our sample should actually be an adequate representation of their inpatient population. This is in line with the existing literature about gender differences in psychiatric disorders, as for example mood disorders, which are highly present in this psychiatric hospital, have been found to be more prevalent in women compared to men (ten Have, Schoemaker, & Volleberg, 2002; Nolen-Hoeksema, 1987). The third limitation to our study was that we only included inpatients which may have led to selection bias, as it is possible that frail patients get hospitalized more than non-frail patients. The fourth limitation of our study is that cognitive functioning has been measured by only two screening instruments. Ideally, a complete neuropsychological test-battery should assess cognitive functioning, as a neuropsychological test-battery will give a more valid representation of cognitive functioning and it will allow investigating the different domains of cognition.

In conclusion, this study investigated frailty and the relationship between frailty and cognitive impairment in elderly with psychiatric disorders, which has received little attention in the existing literature. The current study contributes and adds to the knowledge on this topic. We found that both frailty and the co-occurrence of frailty and cognitive impairment are highly prevalent in elderly with psychiatric disorders (36.0% and 20.8%, respectively). Additionally, cognitive impairment predicted frailty, and particularly the two frailty components grip strength and walking speed. Therapists should be aware of the higher chance of a cognitively impaired patient to also be frail. When aware of this, therapists can take precautionary actions and commence intervention. Future research, especially longitudinal, is needed to examine the interrelationship between frailty and cognitive impairment, the

underlying mechanisms (e.g., cardiovascular disease, nutrition), the different domains of cognition and the possible interventions (e.g., special diet, physiotherapy) in this population of patients with psychiatric disorders. Also, future research should include psychiatric patients who are not hospitalized but receive outpatient treatment for their psychiatric condition. This could lead to a more adequate representation of the total population of elderly with psychiatric disorders, and in turn lead to more generalizable conclusions.

References

Abellan van Kan, G., Rolland, Y., Andrieu, S., Bauer, J., Beauchet, O., Bonnefoy, M., . . . Vellas, B. (2009). Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people, an International Academy on Nutrition and Aging (IANA) Task Force. *The Journal of Nutrition, Health & Aging, 13*, 881-889.

Agrell, B. & Dehlin, O. (1998). The clock-drawing test. *Age and Ageing, 27*, 399-403.

Alfaro-Acha, A., al Snih, S., Raji, M.A., Kuo, Y.F., Markides, K.S., & Ottenbacker, K.J. (2006). Handgrip strength and cognitive decline in older Mexican Americans. *Journal of Gerontology, 61*, 859-865.

Assis-Faria, C., Lourenço, R.A., Ribeiro, P.C.C., & Lopes, C.S. (2013). Cognitive performance and frailty in older adult clients of a private care plan. *Revista de Saúde Pública, 47*(5), 1-8.

Ávila-Funes, J.A., Helmer, C., Amieva, H., Barberger-Gateau, P., Le Goff, M., Ritchie, K., . . . Dartigues, J. (2008). Frailty among community-dwelling elderly people in France: The Three-City study. *Journal of Gerontology, 63A*(10), 1089-1096.

Ávila-Funes, J.A., Amieva, H., Barberger-Gateau, P., Le Goff, M., Raoux, N., Ritchie, K., . . . Dartigues, J. (2009). Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: The Three-City Study. *Journal of the American Geriatrics Society, 57*, 453-461.

Ávila-Funes, J.A., Carcaillon, L., Helmer, C., Carriere, I., Ritchie, K., Raoud, O., . . . Amieva, H. (2012). Is frailty a prodromal stage of vascular dementia? Results from the three-city study. *Journal of the American Geriatrics Society, 60*, 1708-1712.

Auyeung, T.W., Lee, J.S.W., Kwok, T., & Woo, J. (2011). Physical frailty predicts future cognitive decline – a four-year prospective study in 2737 cognitively normal older adults. *The Journal of Nutrition, Health & Aging, 15*(8), 690 694.

Bouma, J., Ranchor, A.V., Sanderman, R., & van Sonderen, E. (1995). *Het meten van symptomen van depressie met de CES-D: een handleiding.* Groningen:

Noordelijk centrum voor gezondheidszorgvraagstukken, Rijksuniversiteit Groningen.

Buchman, A.S., Schneider, J.A., Leurgans, S., & Bennett, D.A. (2008). Physical frailty in older persons is associated with Alzheimer disease pathology. *Neurology, 71,* 499-504.

Buchman, A.S., Yu, L., Wilson, R.S., Boyle, P.A., Schneider, J.A., & Bennet, D.A. (2014). Brain pathology contributes to simultaneous change in physical frailty and cognition in old age. *Journal of Gerontology, 69*(12), 1536-1544.

Buigues, C., Padilla-Sánchez, C., Garrido, J.F., Navarro-Martínez, R., Ruiz-Ros, V., & Cauli, O. (2015). The relationship between depression and frailty syndrome: a systematic review. *Aging and Mental Health, 19*(9), 762-772.

Buracchino, T., Dodge, H.H., Howieson, D., Wasserman, D., & Kaye, J. (2010). The trajectory of gait speed preceding mild cognitive impairment. *Archives of Neurology,* 67, 980-986.

Butler, A., Gallagher, D., Gillespie, P, Crosby, L., Ryan., D, Lacey, L., . . . Lawlor, B. (2016). Frailty: a costly phenomenon in caring for elders with cognitive impairment. *International Journal of Geriatric Psychiatry, 31,* 161-168.

Clegg, A., Rogers, L., & Young, J. (2014). Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. *Age and Ageing, 44,* 148-152.

Coffman, J.A., Bornstein, R.A., Olson, S.C., Schwarzkopf, S.B., & Nasrallah, H.A. (1990). Cognitive impairment and cerebral structure by MRI in bipolar disorder. *Biological Psychiatry, 27*(11), 1188-1196.

Collard, R.M. & Oude Voshaar, R.C. (2012). Frailty: een kwetsbaar begrip. *Tijdschrift voor Psychiatrie, 54*(1), 59-69.

Comijs, H.C., van Marwijk, H.W., van der Mast, R.C., Naarding, P., Oude Voshaar, R.C., Beekman, A.T.F., . . . Smit, J.H. (2011). The Netherlands study of depression in older persons (NESDO); a prospective cohort study. *BMC Research Notes, 4*(524), 1-10.

Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189-198.

Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., . . . McBurnie, M.A. (2001). Frailty in older adults: evidence for a phenotype. *Journal of Gerontology, 56A*(3), M146-M156.

Han, E.S., Lee, Y., & Kim, J. (2014). Association of cognitive impairment with frailty in community-dwelling older adults. *International Psychogeriatrics, 26*(1), 155-163.

Ten Have, M., Schoemaker, C., & Vollebergh, W. (2002). Genderverschillen in psychische stoornissen, consequenties en zorggebruik: resultaten van de Netherlands Mental Health Survey and Incidence Study (nemesis). *Tijdschrift voor psychiatrie, 44*(6), 367-375.

Houles, M., Canevelli, M., Abellan van Kan, G., Ousset, J., Cesari, M., & Vellas, B. (2012). Frailty and cognition. *The Journal of Frailty and Aging, 1*(2), 56-63.

Jacobs, J.M., Cohen, A., Ein-mor, E., Maaravi, Y., & Stessman, J. (2011). Frailty, cognitive impairment and mortality among the oldest old. *The Journal of Nutrition, Health & Aging, 15*(8), 678-682.

Jurschik, P., Nunin, C., Botigue, T., Escobar, M.A., Lavedan, A., & Viladrosa, M. (2012). Prevalence of frailty and factors associated with frailty in the elderly population of Lleida, Spain: The FRALLE survey. *Archives of Gerontology and Geriatrics 55,* 625–631.

Kang, J.Y., Kim, C.H., Sung, E.J., Shin, H.C., Shin, W.J., & Jung, K.H. (2016). The association between frailty and cognition in elderly women. *Korean Journal of Family Medicine, 37,* 164-170.

Kok, R.M. & Verhey, F.R.J. (2002). Gestandaardiseerde MMSE. Zeist, Nederland: Altrecht GGz.

Kruizenga, H.M., Seidell, J.C., de Vet, H.C.W., Wierdsma, N.L., & van Bokhorst- de van der Schueren, M.A.E. (2005). Development and validation of a hospital screening tool for malnutrition: the short nutritional assessment questionnaire (SNAQr). *Clinical Nutrition, 24,* 75-85.

Langlois, F., Vu, T.T.M., Kergoat, M.-J., Chassé, K., Dupuis, G., & Bherer, L. (2012). The multiple dimensions of frailty: physical capacity, cognition, and quality of life. *International Pychogeriatrics, 24*(9), 1429-1436.

Macuco, C.R., Batistoni, S.S., Lopes, A., Cachioni, M., da Silva Falcao, D.V., Neri, A.L., & Yassuda, M.S. (2012). Mini-Mental State Examination performance in frail, pre-frail, and non-frail community dwelling older adults in Ermelino

Matarazzo, Sao Paulo, Brazil. *International Psychogeriatrics*, *24*(11), 1725-1731

Manos, P.J. & Wu, R. (1994). The ten point clock test: a quick screen and grading method for cognitive impairment in medical and surgical patients. *International Journal of Psychiatry in Medicine, 24*(3), 229-244.

Manos, P.J. (2006). 10-Point Clock Test Screens for Cognitive Impairment in Clinic and Hospital Settings**.** *Psychiatric Times, 15*(10), 1-3.

Mathiowetz, V., Kashman, N., Volland, G., Weber, K., Dowe, M., & Rogers, S. (1985). Grip and pinch strength: normative data for adults. *Archives of Physical Medicine and rehabilitation, 66*(2), 69-74.

Morley, J.E. (2015). Cognitive frailty: a new geriatric syndrome? *European Geriatric Medicine, 6,* 408-411.

Nolen-Hoeksema, S. (1987). Sex differences in unipolar depression: evidence and theory. *Psychological Bulletin, 101*(2), 259-282.

Ottenbacher, K.J., Ostir, G.V., Peek, M.K., Snih, S.A., Raji, M.A., & Markides, K.S. (2005). Frailty in older Mexican Americans. *Journal of the American Geriatrics Society, 53,* 1524-1531.

Radloff, L.S. (1977). The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement, 1,* 385-401.

Robertson, D.A., Savva, G.M., & Kenny, R.A. (2013). Frailty and cognitive impairment- a review of the evidence and causal mechanisms. *Ageing Research Review, 12,* 840-851.

Robertson, D.A., Savva, G.M., Coen, R.F., & Kenny, R.A. (2014). Cognitive function in the prefrailty and frailty syndrome. *Journal of the American Geriatrics Society, 62*(11), 2118-2124.

Rockwood, K., Howlett, S.E., MacKnight, C., Beattie, B.L., Bergman, H., Hébert, R., . . . Mcdowell, I. (2004). Prevalence, attributes, and outcomes of fitness and frailty in community-dwelling older adults: report from the Canadian Study of Health and Aging. *Journal of Gerontology, 59*(12), 1310-1317.

Samper-Ternent, R., Al Snih, S., Raji, M.A., Markides, K.S., & Ottenbacher, K.J. (2008) Relationship between frailty and cognitive decline in older Mexican Americans. *Journal of the American Geriatrics Society 56,* 1845–1852.

Shimada, H., Makizako, H., Doi, T., Yoshida, D., Tsutsumimoto, K., Anan, Y., . . . Suzuki, T. (2013). Combined prevalence of frailty and mild cognitive

impairment in a population of elderly Japanese people. *Journal of the American Medical Directors Association, 14*, 518-524.

Smits, L.L., Koene, T., Pijnenburg, Y.A.L., Scheltens, P., & van der Flier, W.M. (2009). De Klokkentest: Bespreking van de literatuur en voorbeelden uit de praktijk. *Tijdschrift voor Neuropsychologie, 3*, 1-14.

Solfrizzi, V., Scafato, E., Frisardi, V., Seripa, D., Logroscino, G., Maggi, S., . . . Panza, F. (2013). Frailty syndrome and the risk of vascular dementia. The Italian Longitudinal Study on Aging. *Alzheimer's & Dementia, 9*, 113–122.

Taylor, M.A. & Abrams, R. (1984). Cognitive impairment in schizophrenia. *The American Journal of Psychiatry, 141*(2), 196-201.

Theou, O., O'Connell, M.D.L., King-Kallimanis, B.L., O'Hollaran, A.M.O., Rockwood, K., & Kenny, R.A. (2015). Measuring frailty using self-report and test-based health measures. *Age and Ageing, 44*, 471-477.

World Health Organization. (2015). *Ageing and Health* (fact sheet No. 404). Retrieved from http://www.who.int/mediacentre/factsheet/fs404/en/.