

Tiago Filipe Mota Coelho

Modelo Integral de Fragilidade do Idoso
(do constructo à avaliação - *Tilburg Frailty Indicator*)

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Orientadora: Professora Doutora Lia Fernandes
Professora Associada da Faculdade de Medicina da Universidade do Porto.

Co-orientadora: Professora Doutora Constança Paúl

Professora Catedrática do Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto.

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Resumo

Introdução: Fragilidade trata-se de uma síndrome clínica que se refere a um estado de vulnerabilidade aumentada, em que o mínimo fator de stresse pode levar a resultados adversos como incapacidade, institucionalização e morte. Apesar de, ao longo das últimas três décadas, o constructo de fragilidade ter assumido uma crescente relevância ao nível do estudo do envelhecimento, não há consenso sobre a sua caracterização e, consequentemente, sobre a sua avaliação em contexto clínico. Neste sentido, com o intuito de agregar conceptualizações recentes da síndrome, foi desenvolvido o modelo integral de fragilidade. Este modelo afasta-se das visões tradicionais de fragilidade, na medida em que a define como um estado de pré-incapacidade, resultante de perdas em um ou mais domínios do funcionamento humano (físico, psicológico e social).

Objetivo: O presente trabalho visou estudar o modelo integral de fragilidade no contexto português, recorrendo ao instrumento estandardizado que o operacionaliza: o *Tilburg Frailty Indicator* (TFI). Assim, procedeu-se à validação da versão portuguesa do TFI. Posteriormente, como objetivo específico, analisou-se de que forma os determinantes de fragilidade previstos no modelo integral se relacionavam com a manifestação da síndrome nos seus múltiplos domínios. Concomitantemente, para melhor compreender a variância de fragilidade, estudou-se a sua associação independente com outras variáveis clinicamente significativas (medicação e dor). Por fim, comparou-se o TFI e outras duas medidas de fragilidade relativamente à predição de resultados adversos a curto prazo. Paralelamente, adotando a perspetiva multidimensional inerente ao modelo integral e ao TFI, compararam-se os diferentes domínios de fragilidade quanto à predição dos mesmos resultados.

Métodos: Esta investigação iniciou-se com a realização de uma revisão da literatura, de artigos publicados entre Maio de 2004 a 2014. Foram incluídos estudos que descreviam e testavam instrumentos especificamente desenvolvidos para a avaliação/identificação de fragilidade, e que incluíam na sua amostra pessoas com idade ≥ 65 anos. Em seguida, procedeu-se à tradução e adaptação cultural do TFI. Neste processo, de forma a assegurar a sua validade facial e de conteúdo, a versão portuguesa do instrumento foi revista por um painel de peritos. Por sua vez, para se estudar a fiabilidade (consistência interna e fiabilidade teste reteste), validade de constructo (convergente e divergente) e validade de critério da versão portuguesa do TFI, realizou-se um estudo transversal com uma amostra não-probabilística de 252 idosos residentes na comunidade. Paralelamente, foi analisado, na mesma amostra, o contributo independente dos determinantes de fragilidade, do número de medicamentos consumidos diariamente e do nível e impacto da dor para a

explicação da variância de fragilidade. Por fim, numa sub-amostra (com 95 dos participantes), foi feita uma reavaliação dez meses depois, especificamente em relação à utilização de cuidados de saúde, dependência/incapacidade e qualidade de vida.

Resultados: Através da revisão da literatura, foi possível observar que um número considerável de medidas resulta da conceptualização da síndrome como um estado exclusivo ou predominantemente físico e que o TFI foi o único instrumento multidimensional identificado em que a incapacidade e as comorbilidades não são incluídas como componentes de fragilidade. No estudo transversal, a amostra (n=252) apresentou uma média de idades de 79.2 (± 7.3) anos, sendo a maior parte dos participantes do sexo feminino (75.8%). A versão portuguesa do TFI apresentou boa consistência interna (KR-20=0.78), boa fiabilidade teste-reteste ($r=0.91$) e concordância substancial para a maioria dos itens. Os domínios físicos e social do TFI correlacionaram-se com as medidas concorrentes expectáveis, enquanto o domínio psicológico com as medidas físicas e psicológicas. O TFI demonstrou uma capacidade de discriminação entre boa a excelente em relação ao critério de fragilidade (AUC 0.75 a 0.89) e entre razoável e boa relativamente à dependência e utilização de cuidados de saúde (AUC 0.56 a 0.72). Por sua vez, os determinantes explicaram 46% da variância de fragilidade total, assim como 39.8%, 25.3% e 27.7% de fragilidade física, psicológica e social, respetivamente. Idade, sexo, rendimento, morte recente de uma pessoa querida, estilo de vida, satisfação com o ambiente habitacional e comorbilidade foram as variáveis associadas a fragilidade total, enquanto cada um dos domínios se relacionou de forma particular com um conjunto diferente de determinantes. Independentemente do efeito destas variáveis, o número de medicamentos consumidos diariamente relacionou-se com a fragilidade total e física, enquanto a dor se associou a fragilidade total, física e psicológica. Por fim, analisando longitudinalmente a predição de resultados adversos, o TFI destacou-se das restantes medidas de fragilidade por se associar a um maior número de contactos com o médico de família e por contribuir de forma mais significativa para a predição do declínio da qualidade de vida. Por outro lado, comparando os domínios do TFI, verificou-se que a fragilidade física contribuiu mais significativamente para a predição da maioria dos resultados adversos.

Conclusão: O presente trabalho surge como um contributo para o reforço da importância da abordagem holística e biopsicossocial de fragilidade, subjacente ao modelo integral. Além disso, a versão portuguesa do TFI revelou boas propriedades psicométricas, podendo ser utilizada como um instrumento de deteção, particularmente a nível comunitário e dos cuidados de saúde primários. Torna-se, no entanto, necessário levar a cabo mais estudos, dada a importância da prevenção e identificação destas situações de fragilidade, salientando-se a necessidade de se testar diferentes modelos conceptuais, bem como a sua operacionalização em contextos distintos.

Abstract

Introduction: Frailty is a clinical syndrome characterized by an increased vulnerability to minor stressful events, which can lead to adverse outcomes such as disability, institutionalization and death. Over the past three decades, the relevance of the construct of frailty has increased significantly in the study of aging. Nonetheless, there is still no consensus regarding its clinical presentation and assessment. In this regard, in order to aggregate recent conceptualizations of the syndrome, the integral model of frailty was developed. This model departs from the traditional views of the syndrome by defining frailty as a state of pre-disability, resulting from losses in one or more domains of human functioning (physical, psychological and social).

Objective: To study the integral model of frailty in the Portuguese setting, by using its operationalization, the standardized instrument *Tilburg Frailty Indicator* (TFI). Therefore, the Portuguese version was validated. Subsequently, as a specific goal, the relationship between the determinants of frailty, considered in the integral model, and the manifestation of the syndrome in its multiple domains was examined. Concomitantly, to better understand the variance of frailty, its independent association with other clinically significant variables (medication and pain) was studied. Finally, the TFI and other two measures of frailty were compared regarding the prediction of short-term adverse outcomes. Meanwhile, adopting the multidimensional approach subjacent to the integral model and to the TFI, the different domains of frailty were compared with regard to the prediction of the outcomes.

Methods: This research began with a literature review of articles published between May 2004 and 2014. Studies that described and tested instruments specifically developed to assess/identify frailty, and that comprised in their sample individuals with ages ≥ 65 years, were included. Afterwards, the translation and cultural adaptation of TFI was performed. In this process, in order to ensure its face and content validity, the Portuguese version was revised by an expert committee. Subsequently, a cross-sectional study was performed, using a non-probability sample of 252 community-dwelling elderly, in order to examine the reliability (internal consistency and test-retest reliability), construct validity (convergent/divergent) and criterion validity of the Portuguese version of TFI. Meanwhile, the independent contribution of the determinants of frailty, of the amount of daily-consumed medications and of the degree and impact of pain to the explanation of the variance of frailty was analyzed in the same sample. Finally, a sub-sample (95 of the participants) was reassessed 10 months later, specifically regarding healthcare utilization, disability and quality of life.

Results: Through literature review, it was possible to observe that a significant number of measures resulted from the conceptualization of frailty as an exclusive or predominantly physical state. TFI was the only identified multidimensional instrument in which disability and comorbidity were not included as components of frailty. In the cross-sectional study, the mean sample age (n=252) was 79.2 (± 7.3) years, and most of the participants were women (75.8%). The Portuguese version of TFI showed good internal consistency (KR-20=0.78), good test-retest reliability ($r=0.91$) and substantial agreement for most items. TFI physical and social domains correlated as expected with concurrent measures, and the TFI psychological domain showed similar correlations with other psychological and physical measures. The TFI showed good to excellent discrimination ability in regard to frailty criteria (AUC: 0.75-0.89), and fair to good ability to predict disability and healthcare utilization (AUC: 0.56-0.72). In turn, determinants explained 46% of the variance of total frailty, and 39.8%, 25.3%, and 27.7% of physical, psychological, and social frailty respectively. Age, gender, income, death of a loved one in the past year, lifestyle, satisfaction with living environment and self-reported comorbidity predicted total frailty, while each frailty domain was associated with a different set of determinants. Independently of the effect of these variables, the number of medications was associated with total and physical frailty, while pain was correlated with total, physical and psychological frailty. Finally, examining the longitudinal prediction of adverse outcomes, TFI stood out from the other measures of frailty because of its association with a greater amount of contacts with a general practitioner and its higher contribution to the prediction of the decline of quality of life. On the other hand, when comparing TFI domains, physical frailty was the most significant predictor of the outcomes.

Conclusion: The present paper comes across as a contribution to strengthening the importance of the holistic and biopsychosocial approach to frailty, subjacent to the integral model. Furthermore, the Portuguese version of TFI showed good psychometric properties, and it can be used as a screening instrument, particularly in community and primary healthcare settings. It is, however, necessary to carry out further studies, given the importance of prevention and identification of these frailty situations, with emphasis on the need to test different conceptual models, as well as their operationalization, in different contexts.

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1. Introdução

O envelhecimento populacional é um fenómeno global, resultante do declínio progressivo da mortalidade e da fecundidade na maior parte dos países do mundo (United Nations, 2013; World Health Organization, 2012). Este aumento da proporção de pessoas mais velhas na população total tornou-se evidente e exponencial desde meados do século XX (United Nations, 2013). Enquanto que em 2013 se estimava que cerca de 11% da população mundial tivesse 60 ou mais anos de idade, em menos de 40 anos, calcula-se que este valor atinja os 21% (United Nations, 2013). Adicionalmente, espera-se que em 2050 haja 392 milhões de pessoas com 80 ou mais anos de idade, aproximadamente o triplo do que se verifica na atualidade (United Nations, 2013).

Portugal não é exceção a esta tendência global. Para além de possuir uma das mais elevadas proporções de idosos da União Europeia (aproximadamente 19%) (Eurostat, 2014), segundo projeções do Instituto Nacional de Estatística (2014) prevê-se que até 2060 o índice de envelhecimento aumente de 131 para 307 idosos por cada 100 jovens. Estima-se, ainda, que a progressão do envelhecimento demográfico seja uma realidade nos próximos 50 anos (independentemente da recuperação de saldos migratórios positivos e do aumento dos níveis de fecundidade), particularmente devido ao aumento contínuo da esperança média de vida (Instituto Nacional de Estatística, 2009, 2014).

O aumento da longevidade é uma das grandes conquistas da humanidade (Fried, Hogan, & Rowe, 2011; World Health Organization, 2002), no entanto, colocam-se desafios ao nível do planeamento e prestação de cuidados de saúde e sociais, devido à maior prevalência de doenças crónicas e de condições clínicas específicas da velhice (Martín & Brandão, 2012; Olshansky, Beard, & Börsch-Supan, 2011; Ribeiro, Fernandes, Firmino, Simões, & Paúl, 2010). Neste conjunto, a fragilidade merece particular destaque, pelo facto de colocar em risco a manutenção da independência, da qualidade e da dignidade de vida das pessoas mais velhas (Clegg, Young, Iliffe, Rikkert, & Rockwood, 2013; Fried, Walston, & Ferrucci, 2009).

A fragilidade trata-se de uma síndrome clínica que se refere a um estado de vulnerabilidade exacerbada, em que o mínimo fator de stresse pode levar a resultados adversos clinicamente significativos, tais como quedas, *delirium*, incapacidade, institucionalização, hospitalização e morte (Abellan van Kan *et al.*, 2008; Morley *et al.*, 2013; Rockwood & Mitnitski, 2007). Um indivíduo frágil tem menor quantidade de recursos do que uma pessoa não-frágil/robusta e, conseqüentemente, maior dificuldade em lidar com elementos stressantes, internos ou externos (Avila-Funes *et al.*, 2008; Rodriguez-Manas *et al.*, 2013; Zaslavsky *et al.*, 2013). Neste sentido, enquanto um indivíduo idoso

robusto se torna dependente nas atividades diárias em resultado de um fator de stresse *major* (ex.: acidente vascular cerebral, fratura do colo do fêmur ou depressão), um idoso frágil pode ficar dependente em consequência de uma perturbação *minor* da sua homeostasia (ex.: mudança de temperatura, alteração da medicação ou infecção urinária) (Bergman *et al.*, 2007; Clegg *et al.*, 2013; Provencher, Demers, & Gelinas, 2012). Adicionalmente, tal como descreve Clegg *et al.* (2013), uma pessoa frágil tem maior dificuldade em recuperar o seu estado de saúde e funcional após ser confrontado com um fator de stresse, havendo uma grande probabilidade de não se verificar uma recuperação total (ver Figura 1).

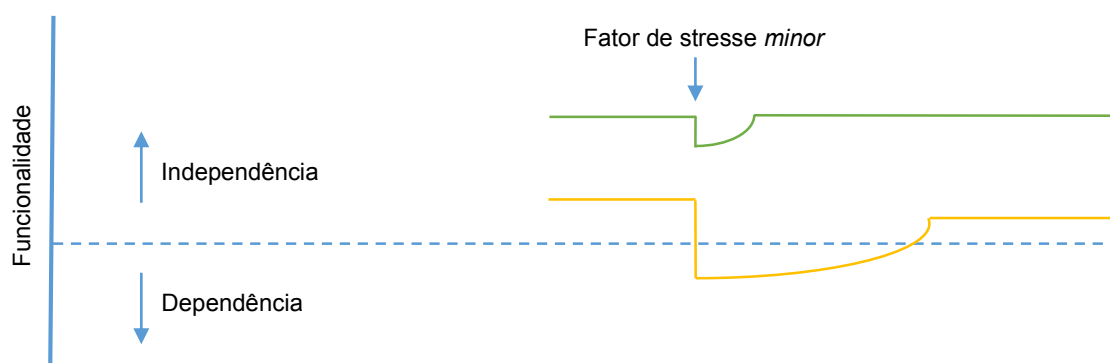


Figura 1: Impacto de um fator de stresse *minor* ao nível da funcionalidade de idosos não frágeis/robustos (linha verde) e de idosos frágeis (linha amarela) – adaptado de Clegg *et al.* (2013).

A condição de fragilidade não se insere num processo de envelhecimento normal. Contudo, na sua base está uma intensificação do declínio da reserva fisiológica, que normalmente acompanha o envelhecimento (Fried *et al.*, 2009; Walston *et al.*, 2006). Por outras palavras, a capacidade funcional de múltiplos sistemas orgânicos, necessária para compensar eficazmente perdas e outros elementos stressantes, está exageradamente diminuída, colocando em causa mecanismos homeostáticos (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004). Esta deterioração resulta de alterações graduais a nível molecular e celular, em função de fatores genéticos, epigenéticos, ambientais e relacionados com o estilo de vida (Clegg *et al.*, 2013; Fried *et al.*, 2009). Concomitantemente, a presença de doença pode precipitar uma situação de fragilidade, na medida em que pode requerer ao organismo que mobilize os recursos disponíveis para dar resposta a essa condição, esgotando a capacidade fisiológica em reserva e, por isso, aumentando a vulnerabilidade do indivíduo (Bergman *et al.*, 2007).

A fragilidade trata-se, portanto, de uma condição específica da população mais envelhecida, particularmente comum em pessoas com 80 ou mais anos de idade (Collard, Boter, Schoevers, & Oude Voshaar, 2012; Morley *et al.*, 2013). Da mesma forma, é mais prevalente no sexo feminino uma vez que, para além da influência de fatores

neuroendócrinos, hormonais e relacionados com o sistema músculo-esquelético, as mulheres sobrevivem mais tempo e com maiores níveis de morbilidade (Puts, Lips, & Deeg, 2005; Rockwood, 2005; Song, Mitnitski, & Rockwood, 2010). Todavia, a prevalência exata de fragilidade na população idosa permanece por determinar, devido ao facto de existirem diferentes perspetivas relativamente aos seus componentes (Collard *et al.*, 2012; Sternberg, Wershof Schwartz, Karunananthan, Bergman, & Mark Clarfield, 2011). Efetivamente, apesar do constructo de fragilidade ter assumido uma crescente relevância ao nível do estudo do envelhecimento e da prestação de cuidados de saúde a pessoas mais velhas ao longo das últimas três décadas, a sua definição e enquadramento clínico não são consensuais (Markle-Reid & Browne, 2003; Sternberg *et al.*, 2011). Existem diversos modelos conceptuais sobre fragilidade, com implicações distintas no que se refere à identificação da síndrome na prática clínica (Abellan van Kan *et al.*, 2008; Hogan, MacKnight, & Bergman, 2003). Não obstante, existem duas conceptualizações geradoras de maior consenso na comunidade científica: o modelo biológico e o modelo de acumulação de défices (Cesari, Gambassi, van Kan, & Vellas, 2014; Morley *et al.*, 2013).

De acordo com o modelo biológico, desenvolvido por Fried *et al.* (2001), a fragilidade expressa-se a nível físico, através da conjugação de uma série de componentes específicos que constituem o fenótipo de fragilidade: fraqueza muscular, lentidão, exaustão, perda de peso involuntária e baixos níveis de atividade física. Nesta perspetiva, a ênfase é colocada na deterioração da capacidade funcional dos sistemas músculo-esquelético, imunológico, hormonal, metabólico e do sistema nervoso central e autónomo, assim como nas suas manifestações corporais, com destaque para a sarcopenia.

Por outro lado, no modelo de acumulação de défices, proposto inicialmente por Mitnitski, Mogilner, MacKnight, e Rockwood (2002), fragilidade é definida como um estado não específico, resultante do efeito cumulativo da conjugação de défices multidimensionais relacionados com o envelhecimento. Nesta linha de pensamento, o pressuposto é que quanto maior a quantidade de problemas, independentemente da sua natureza, maior a probabilidade de estar frágil (Rockwood & Mitnitski, 2007). Assim, em oposição ao modelo de Fried *et al.* (2001), conceptualiza-se que existem diferentes mecanismos que podem aumentar a vulnerabilidade do indivíduo e levar a situações de fragilidade. Segundo este modelo, em alternativa à classificação de um indivíduo como frágil com base na presença de um fenótipo em particular, cabe ao avaliador calcular o índice de fragilidade, que se refere à razão entre os défices presentes e o total de défices considerados numa avaliação clínica. Estes défices referem-se usualmente a doenças e alterações funcionais ao nível das atividades diárias, mas também podem ser sinais e sintomas específicos (Cesari *et al.*, 2014; Rockwood & Mitnitski, 2007; Searle, Mitnitski, Gahbauer, Gill, & Rockwood, 2008).

Apesar da sua predominância na literatura – especialmente em relação à perspectiva biológica (Bouillon *et al.*, 2013) – vários autores colocam objeções a estes modelos (Abellan van Kan *et al.*, 2008; Levers, Estabrooks, & Ross Kerr, 2006; Markle-Reid & Browne, 2003). Efetivamente, para além da sua aplicabilidade prática ser frequentemente discutida (Cesari *et al.*, 2014; Malmstrom, Miller, & Morley, 2014), existem divergências teóricas profundas relativamente a pressupostos basilares de ambas as conceptualizações. Em primeiro lugar, a definição de fragilidade como uma síndrome exclusivamente física é frequentemente criticada, sendo que cada vez mais investigadores defendem a sua natureza multidimensional e biopsicossocial (Bergman *et al.*, 2007; Levers *et al.*, 2006; Markle-Reid & Browne, 2003). A argumentação, nesta perspectiva, relaciona-se com o facto de uma caracterização demasiado estreita de fragilidade não corresponder a uma visão holística do indivíduo e se afastar da conceptualização de saúde enquanto bem-estar físico, psicológico e social (Gobbens, Luijkx, Wijnen-Sponselee, & Schols, 2010a; Markle-Reid & Browne, 2003). Em segundo lugar, a caracterização de fragilidade como o resultado da simples combinação de uma série de condições patológicas e défices funcionais é usualmente contestada (Cesari *et al.*, 2014; Provencher *et al.*, 2012). Com efeito, visões contemporâneas de fragilidade procuram cada vez mais distingui-la de comorbilidade e de incapacidade, reconhecendo, contudo, que existe uma associação entre as diferentes condições (Abellan van Kan *et al.*, 2008; Fried *et al.*, 2004; Sternberg *et al.*, 2011).

Neste contexto, com o intuito de organizar uma conceptualização de fragilidade que traduzisse uma mudança de paradigma relativamente às definições tradicionais da síndrome, foi desenvolvido por Gobbens, Luijkx, Wijnen-Sponselee, e Schols (2010c) o modelo integral de fragilidade. Neste modelo conceptual – apresentado recentemente no seguimento de uma revisão exaustiva da literatura (Gobbens, Luijkx, Wijnen-Sponselee, & Schols, 2010b) e da consulta de peritos (Gobbens, Luijkx, *et al.*, 2010a) – fragilidade é definida como um estado de pré-incapacidade resultante de perdas em um ou mais domínios do funcionamento humano (físico, psicológico e social), sendo causado pela influência de uma gama de variáveis (determinantes do curso de vida, doença(s) e declínio da reserva fisiológica), aumentando o risco de resultados adversos/*outcomes* (incapacidade, utilização de cuidados de saúde e morte). Para além de traduzir uma abordagem holística da pessoa e de definir claramente incapacidade como um potencial resultado de fragilidade, esta conceptualização destaca-se paralelamente pelo facto de pressupor que variáveis como eventos de vida (ex.: morte do cônjuge) ou condições do ambiente habitacional (ex.: mudança para lar) podem influenciar diretamente o estado de fragilidade, além de estarem potencialmente na base de doenças que podem de igual

forma fomentar a vulnerabilidade do indivíduo (Gobbens, van Assen, Luijkx, & Schols, 2012; Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010a) (ver Figura 2).

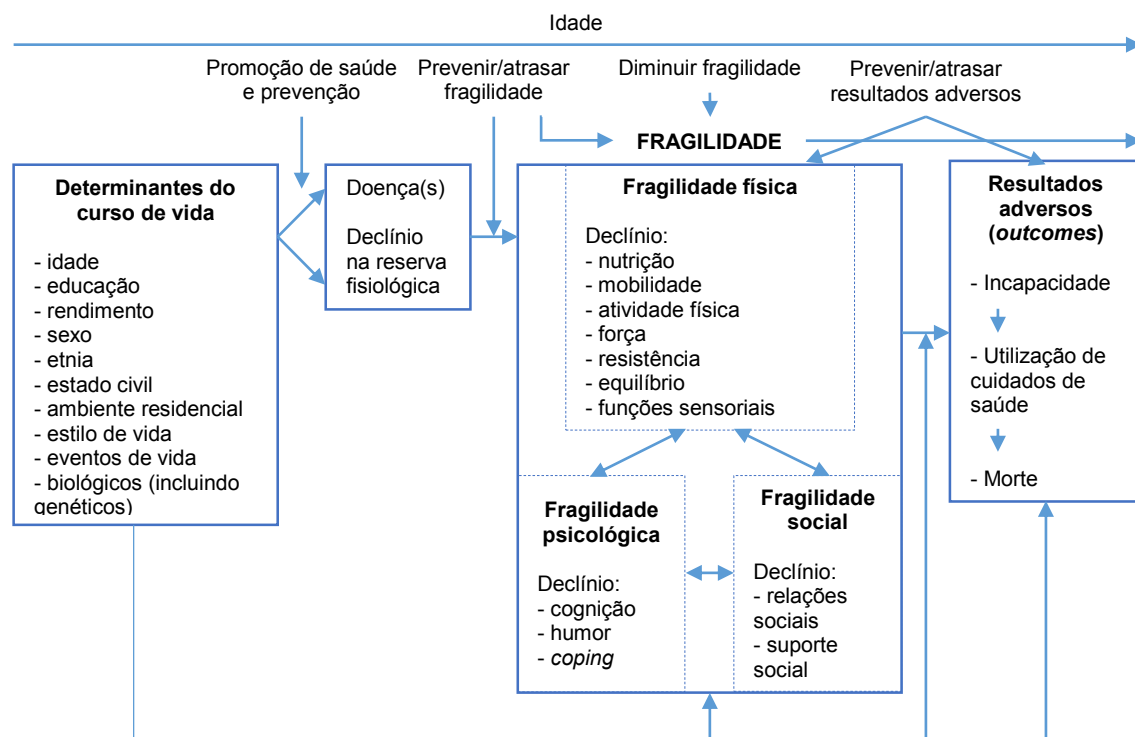


Figura 2: Modelo integral de fragilidade de Gobbens, Luijkx, et al. (2010c).

Independentemente da conceptualização de fragilidade, parece consensual na literatura que, na ausência de intervenção, o estado de saúde e funcional de um indivíduo frágil tende a piorar com o tempo (Clegg *et al.*, 2013; Morley *et al.*, 2013). Porém, há evidência de que a vulnerabilidade associada à síndrome pode ser prevenida, atenuada ou revertida, destacando-se, assim, a importância da sua deteção atempada, particularmente nos contextos dos cuidados de saúde primários e comunitários (Bergman *et al.*, 2007; Sternberg *et al.*, 2011). Com efeito, a diminuição da severidade e prevalência de fragilidade terão indubitavelmente claros benefícios não só a nível individual e familiar, mas também ao nível da sociedade (Clegg *et al.*, 2013; Vermeulen, Neyens, van Rossum, Spreeuwenberg, & de Witte, 2011). Todavia, para que se possam desenvolver programas de prevenção/intervenção eficazes, torna-se necessário compreender qual a definição de fragilidade mais apropriada a diferentes contextos, e qual a forma mais eficiente de a avaliar (Bergman *et al.*, 2007; Clegg *et al.*, 2013; Pialoux, Goyard, & Lesourd, 2012). Por outras palavras, é fundamental perceber quais os modelos conceptuais de fragilidade cuja operacionalização permita identificar adequadamente as pessoas idosas em risco, em diferentes contextos e situações.

Neste âmbito, o presente trabalho teve como principal objetivo estudar a aplicabilidade e pertinência do modelo integral de fragilidade no contexto português. Desta forma, analisou-se essencialmente a relação entre determinantes, fragilidade (física, psicológica e social) e resultados adversos, num grupo de idosos residentes na comunidade. Para tal, recorreu-se ao instrumento estandardizado *Tilburg Frailty Indicator* (TFI) (Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010b), que permite a operacionalização clínica do modelo de Gobbens, Luijkx, *et al.* (2010c). Procedeu-se, assim, ao processo de validação do TFI para a população portuguesa, com o estudo das respetivas propriedades psicométricas. Paralelamente, foi estudada a associação entre fragilidade e outras variáveis clinicamente relevantes (medicação e dor), de modo a melhor compreender esta síndrome na população idosa.

Consequentemente, este trabalho é composto pelos seguintes artigos científicos:

1. **Avaliação de fragilidade em pessoas idosas. Coelho T, Paúl C, Fernandes L. *Revista Portuguesa de Enfermagem de Saúde Mental* (submetido).**

Objetivo: Identificar os instrumentos de avaliação de fragilidade em idosos desenvolvidos nos últimos dez anos, para analisar como diferentes autores operacionalizam a medição da síndrome.

2. ***Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation.* Coelho T, Santos R, Paúl C, Gobbens RJJ, Fernandes L. *Geriatrics & Gerontology International*, 2014.**

Objetivo: Desenvolver a versão portuguesa do TFI e estudar as suas propriedades psicométricas (inclui a análise da associação de fragilidade com medidas alternativas dos seus componentes e com indicadores de resultados adversos).

3. ***Determinants of frailty: the added value of assessing medication.* Coelho T, Paúl C, Gobbens RJJ, Fernandes L. *Frontiers in Aging Neuroscience* (submetido).**

Objetivos: (1) Analisar como os determinantes previstos no modelo integral se relacionam com fragilidade; (2) Estudar a associação entre o número de medicamentos consumidos diariamente e fragilidade, independentemente do efeito dos determinantes.

4. ***Multidimensional frailty and pain in community dwelling elderly.* Coelho T, Paúl C, Gobbens RJJ, Fernandes L. *Pain Medicine* (submetido).**

Objetivo: Investigar de que forma a presença de dor permite explicar a variância de fragilidade, independentemente do efeito dos determinantes previstos no modelo de Gobbens, Luijkx, *et al.* (2010c).

- 5. *Frailty as a predictor of short-term adverse outcomes.* Coelho T, Paúl C, Gobbens RJJ, Fernandes L. *Journal of Nutrition, Health and Aging* (submetido).**

Objetivos: (1) Comparar o TFI e outras duas medidas de fragilidade relativamente à associação com resultados adversos numa reavaliação dez meses depois; (2) Comparar fragilidade física, psicológica e social relativamente à predição dos *outcomes*.

2. Enquadramento teórico

2.1. Avaliação de fragilidade em pessoas idosas

Autores: Tiago Coelho, Constança Paúl, Lia Fernandes

Revista Portuguesa de Enfermagem de Saúde Mental (em processo de revisão)

Indexação: *CINAHL Complete*; *Consejo Iberoamericano de Editores de Revistas de Enfermería y Afines (CIBERE)*; *EBSCO Discovery Service*; *Latindex*; *REV@Enf - Biblioteca Virtual em Saúde – Enfermagem*; *SciELO Citation Index - Thomson Reuters*; *SciELO Portugal*;

Resumo

Contexto: Fragilidade refere-se a um estado de vulnerabilidade aumentada que se traduz num elevado risco de incapacidade, institucionalização e morte. Trata-se de uma síndrome sobre a qual não há consenso, nomeadamente em relação à sua conceptualização e operacionalização.

Objetivo: Analisar os instrumentos de avaliação de fragilidade em idosos, desenvolvidos nos últimos dez anos.

Metodologia: Revisão não-sistemática da literatura, de artigos publicados entre Maio de 2004 a 2014, disponíveis na *PubMed*. Foram incluídos estudos que descreviam e testavam instrumentos especificamente desenvolvidos para a avaliação/identificação de fragilidade, e que incluíam na sua amostra pessoas com idade ≥ 65 anos. Artigos não escritos em inglês e/ou português foram excluídos.

Resultados: Foram analisados 14 artigos. Verificou-se um crescente interesse a nível europeu para o desenvolvimento de medidas de avaliação de fragilidade. A administração de oito dos instrumentos identificados envolvia a realização de uma avaliação clínica, enquanto os restantes se baseavam maioritariamente na autoavaliação. Um número significativo de instrumentos resulta da conceptualização de fragilidade como um estado exclusivo ou predominantemente físico. Os componentes mais comuns relacionavam-se com a mobilidade/desempenho motor, a nutrição e a exaustão/fadiga, seguidos de fatores relacionados com a cognição e com o suporte e rede social do idoso. A prevalência de fragilidade variou entre 5% e 51%.

Conclusões: A importância da deteção atempada de situações de fragilidade salienta a necessidade de se testar a aplicabilidade, a fiabilidade e a validade dos instrumentos existentes, particularmente em Portugal, com poucos estudos, ainda, sobre esta temática.

PALAVRAS-CHAVE: fragilidade; idosos; avaliação; instrumentos

Resumen

Introducción: Fragilidad se refiere a un estado de mayor vulnerabilidad que se traduce en un mayor riesgo de discapacidad, de institucionalización y de muerte. Es un síndrome para el cual no existe un consenso, sobre todo cuanto a su conceptualización y operacionalización.

Objetivo: Analizar los instrumentos de evaluación de fragilidad en los ancianos, desarrollado en los últimos diez años.

Metodología: Revisión no sistemática de la literatura de artículos publicados entre mayo 2004-2014, disponible en PubMed. Se incluyeron los estudios que describían y estaban probando instrumentos desarrollados específicamente para la evaluación/identificación de fragilidad, y que se incluyen en su muestra personas de edad ≥ 65 años. Se excluyeron los artículos no escritos en inglés y/o portugués.

Resultados: Fueron analizados 14 artículos. Hubo un creciente interés europeo en el desarrollo de medidas de evaluación de fragilidad. La administración de ocho de los instrumentos identificados involucró la realización de una evaluación clínica, mientras que los restantes se basaron en gran medida en la autoevaluación. Un número significativo de instrumentos resulta de la conceptualización de fragilidad como un estado exclusivo o predominantemente físico. Los componentes más comunes estaban relacionados con la movilidad/desempeño motor, la nutrición y el cansancio/fatiga, seguido de los factores relacionados con la cognición y el soporte y red social de los ancianos. La prevalencia de fragilidad varió entre 5% y 51%.

Conclusiones: La importancia de la detección temprana de las situaciones de fragilidad hace hincapié en la necesidad de probar la factibilidad, fiabilidad y validez de los instrumentos existentes, en particular en Portugal, donde aún hay pocos estudios sobre este tema.

DESCRIPTORES: fragilidad; ancianos; evaluación; instrumentos

Abstract

Background: Frailty is a state of increased vulnerability that entails a high risk of disability, institutionalization and death. It is a syndrome about which there is no consensus, particularly regarding its conceptualization and operationalization.

Aim: To analyze the assessment instruments of frailty in the elderly, developed in the last ten years.

Methods: Non-systematic literature review of articles published between May of 2004 to 2014, available on PubMed. Studies that described and tested instruments specifically developed to assess/identify frailty, and that comprised in their sample individuals with ages ≥ 65 years, were included. Articles not written in English and/or Portuguese were excluded.

Results: In the present study, 14 articles were analyzed. A growing European interest in the development of frailty assessment measures was found. The administration of eight of the identified instruments involved conducting a clinical evaluation, while the remaining were based largely on self-report. A significant number of instruments results from the

conceptualization of frailty as an exclusive or predominantly physical state. The most common components were related to mobility/motor performance, nutrition, and exhaustion/fatigue, followed by factors related to cognition and social support/network of the elderly. The prevalence of frailty varied between 5% and 51%.

Conclusions: The importance of early detection of frailty situations stresses the need to test the feasibility, reliability and validity of existing instruments, particularly in Portugal, where few studies on this topic exist.

KEY-WORDS: frailty; elderly; assessment; instruments

Introdução

O aumento da longevidade é uma das grandes conquistas da humanidade. No entanto, o crescimento do número de pessoas idosas é acompanhado pelo incremento de situações de fragilidade (Collard, Boter, Schoevers, & Oude Voshaar, 2012).

A fragilidade trata-se de uma síndrome clínica que se refere a um estado de vulnerabilidade aumentada, em que o mínimo fator de stresse pode levar a resultados adversos clinicamente significativos, tais como quedas, incapacidade, institucionalização, hospitalização e morte (Morley *et al.*, 2013). É uma condição específica da população mais envelhecida – particularmente comum em pessoas com 80 ou mais anos de idade – mas que não se insere num processo de envelhecimento normal, podendo ser prevenida, atenuada ou revertida (Abellan van Kan *et al.*, 2008). Neste sentido, destaca-se a importância da sua deteção atempada, particularmente nos contextos dos cuidados de saúde primários e comunitários.

Apesar de, ao longo das últimas três décadas, o constructo de fragilidade ter assumido uma crescente relevância ao nível do estudo do envelhecimento e da prestação de cuidados de saúde a pessoas mais velhas, a sua definição e enquadramento clínico não são consensuais (Sternberg, Wershof Schwartz, Karunananthan, Bergman, & Mark Clarfield, 2011). Efetivamente, existem diversos modelos conceptuais sobre fragilidade, com implicações distintas no que se refere à identificação da síndrome na prática clínica. O modelo biológico e o modelo de acumulação de défices são as conceptualizações geradoras de maior consenso na comunidade científica (Morley *et al.*, 2013).

De acordo com o modelo biológico, desenvolvido por Fried *et al.* (2001), a fragilidade trata-se de uma condição exclusivamente física, resultante essencialmente de um declínio exacerbado da reserva fisiológica a nível multi-sistémico (músculo-esquelético, imunológico, hormonal, inflamatório, metabólico e do sistema nervoso central e autónomo) e das suas manifestações corporais, com destaque para a sarcopenia. Nesta linha de pensamento, é proposta uma apresentação clínica da síndrome – designada como o Fenótipo de Fragilidade – e que inclui: fraqueza, lentidão, exaustão, perda de peso involuntária e baixos níveis de atividade física. A operacionalização deste modelo – também identificado na *Cardiovascular Health Study (CHS) Scale*, em referência ao estudo em que foi desenvolvido – implica a avaliação dos componentes do Fenótipo, sendo a presença de três ou mais elementos, indicativa de um estado de fragilidade, e, de um a dois, de pré-fragilidade.

Por sua vez, no modelo de acumulação de défices, proposto por Mitnitski, Mogilner, MacKnight, e Rockwood (2002), fragilidade é definida como uma síndrome

multidimensional, resultante da conjugação de défices relacionados com o envelhecimento, cujo incremento implica uma diminuição das reservas e um aumento da vulnerabilidade. Estes défices podem ser sinais, sintomas, doenças e alterações funcionais ao nível das atividades diárias. No entanto, a natureza e quantidade exatas destes fatores não são pré-definidas no modelo. Em alternativa, os autores sugerem o cálculo do Índice de Fragilidade, que se refere à razão entre os défices presentes e o total de défices considerados numa avaliação clínica. Tradicionalmente, são tidos em conta entre 20 a 70 défices, incluindo na sua maioria comorbilidades e dificuldades ao nível do desempenho de atividades de vida diária.

Apesar da sua predominância, vários autores colocam objeções a estes modelos, seja a nível conceptual, seja a nível operacional (Abellan van Kan *et al.*, 2008; Sternberg *et al.*, 2011). Em primeiro lugar, a definição da síndrome como exclusivamente física é frequentemente criticada, sendo que cada vez mais investigadores defendem a sua natureza multidimensional e biopsicossocial. A argumentação, nesta perspetiva, relaciona-se com o facto de uma caracterização demasiado estreita de fragilidade não corresponder a uma visão holística do indivíduo e se afastar da conceptualização de saúde enquanto bem-estar físico, psicológico e social. Em segundo lugar, a ênfase excessiva dada às comorbilidades e à incapacidade, no modelo de Mitnitski *et al.* (2002), é usualmente contestada, uma vez que visões contemporâneas de fragilidade procuram cada vez mais distingui-la como uma síndrome específica, mais complexa do que o resultado da combinação de condições patológicas e défices funcionais. De facto, vários autores preferem considerar estes dois aspetos, respetivamente, como potenciais causas e resultados de um estado de fragilidade. Por outro lado, é possível identificar limitações ao nível da aplicabilidade clínica da avaliação do Fenótipo de Fragilidade e do cálculo do Índice de Fragilidade. Com efeito, se refletirmos que a CHS *scale* envolve a realização de medições (força manual/fraqueza e velocidade da marcha/lentidão) e que a elaboração do Índice envolve uma avaliação clínica detalhada que permita a identificação de uma grande quantidade de défices, será fácil de compreender a dificuldade em implementar a avaliação de fragilidade ao nível dos cuidados de saúde. Para além disso, muitos autores questionam se estas ferramentas são suficientemente sensíveis e específicas para identificar os indivíduos verdadeiramente frágeis.

Neste sentido, considerando a falta de consenso em torno da conceptualização e subsequentemente da avaliação de fragilidade, o presente estudo tem como objetivo identificar e analisar os instrumentos de avaliação de fragilidade em idosos, desenvolvidos nos últimos dez anos.

Metodologia

No presente estudo procede-se a uma revisão de artigos publicados entre Maio de 2004 e Maio de 2014, disponíveis na base de dados eletrónica *PubMed*, combinando os termos “*elderly*”, “*older*” ou “*aged*”, com “*frailty*” ou “*frail*”, e com “*assessment*”, “*screening*”, “*tool*”, “*instrument*”, “*scale*”, “*measure*” ou “*diagnosis*”. Foram incluídos estudos empíricos que descreviam e testavam a operacionalização de instrumentos (ex.: questionários, escalas, índices) especificamente desenvolvidos para a avaliação/identificação da síndrome de fragilidade, e que incluíssem na sua amostra (na *baseline*) pessoas com idade igual ou superior a 65 anos. Por sua vez, foram excluídos artigos não escritos em inglês e/ou português, estudos de caso, artigos referentes a utilizações subsequentes de instrumentos de avaliação de fragilidade previamente aplicados a pessoas idosas e estudos em que a fragilidade é medida através da avaliação de diversos fatores não integrados num instrumento com uma designação específica.

A pesquisa inicial envolveu a avaliação dos resumos dos artigos identificados por parte de dois dos autores do presente estudo, de forma independente e cega, obedecendo rigorosamente aos critérios de inclusão e exclusão previamente definidos. A análise dos artigos na íntegra foi realizada nos casos em que os resumos não eram suficientemente esclarecedores. Os estudos foram examinados considerando as seguintes características: objetivo, desenho de estudo, amostra, contexto, critérios de inclusão e exclusão, medidas recrutadas para a avaliação de fragilidade e principais resultados.

Por fim, foi efetuada uma análise da bibliografia dos artigos selecionados com o objetivo de potencialmente identificar outros estudos a incluir na presente revisão.

Resultados

A pesquisa inicial permitiu identificar 4079 artigos, dos quais 14 foram selecionados e incluídos na análise. Não foram identificados estudos adicionais com base na análise bibliográfica dos artigos selecionados. Os principais dados relativos aos estudos selecionados e aos instrumentos utilizados estão sumariados na tabela 1.

Tabela 1: Descrição dos estudos analisados

Instrumento e referência	Descrição do instrumento e componentes de fragilidade	Desenho de estudo	Contexto e amostra	% fragilidade *
Frailty Index - Comprehensive Geriatric Assessment (FI-CGA) Jones, Song, & Rockwood, 2004	Índice constituído por 11 défices/componentes de fragilidade e pontuado com base numa avaliação clínica: Défices a nível da cognição, da mobilidade, do equilíbrio, da comunicação (incluindo visão e audição), da nutrição, da função intestinal e da função vesical, perturbação do humor, dependência nas atividades diárias, necessidade de apoio social e presença de comorbilidades. Pontuação total obtida através da soma de cada item (pontuado de 0 a 2 consoante a gravidade) com metade do número total de comorbilidades. 0-7 = fragilidade ligeira. 7-13 = fragilidade moderada. >13 = fragilidade severa.	Longitudinal	Canadá <i>(Mobile Geriatric Assessment Team trial)</i> n = 182 (≥65 anos; residentes na comunidade; previamente identificados como frágeis)	Ligeira: 17% Moderada: 58% Severa: 25%
Clinical Global Impression of Change in Physical Frailty instrument (CGIC-PF instrument) Studenski et al., 2004	Escala constituída por 6 componentes e 7 consequências de fragilidade, pontuada com base em avaliações clínicas sucessivas: Componentes – limitações da mobilidade, força, equilíbrio, resistência, nutrição e desempenho neuromotor; Consequências – utilização de cuidados de saúde, dependência nas atividades diárias, complexidade clínica e alterações ao nível da aparência, auto-perceção da saúde, interação social e do estado emocional. Cada item pontuado de 1 (declínio evidente) a 7 (melhoria evidente) com base na mudança verificada entre avaliações.	Transversal	Estados Unidos da América n = 24 (≥70 anos)	Não aplicável (NA)

Clinical Frailty Scale (CFS) Rockwood et al., 2005	Escala classificada de 1 a 7 com base numa apreciação clínica: 1 – Completamente em forma, robusto e pratica atividade física com frequência; 2 – Saudável mas numa forma menor do que na categoria 1; 3 – Em bom estado, com comorbilidades mas com sintomas bem controlados; 4 – Aparentemente vulnerável e com alguns sintomas de doenças; 5 – Ligeiramente frágil, dependendo de outros ao nível das atividades de vida diária instrumentais; 6 – Moderadamente frágil, necessitando de ajuda em atividades instrumentais e básicas; 7 – Severamente frágil, sendo completamente dependente de outros nas atividades diárias.	Longitudinal	Canadá (<i>Canadian Study of Health and Aging</i>) n = 2305 (≥65 anos)	43%
Edmonton Frail Scale (EFS) Rolfson, Majumdar, Tsuyuki, Tahir, & Rockwood, 2006	Escala com 9 componentes de fragilidade, pontuada com base no auto-reporte do participante e na realização de testes: Défice cognitivo (teste do relógio), limitações da mobilidade funcional (teste <i>Timed Up and Go</i>), humor depressivo, dependência nas atividades diárias, perda de peso, necessidade de apoio social, consumo de ≥5 medicamentos, incontinência, pobre estado de saúde. Pontuação total obtida através da soma de cada item (pontuado de 0 a 1 ou de 0 a 2 consoante a gravidade).	Transversal	Canadá n = 158 (≥65 anos)	NA

Study of Osteoporotic Fractures index (SOF index) Ensrud et al., 2008	Escala com 3 componentes de fragilidade, pontuada com base no auto-reporte do participante e realização de um teste: Perda de peso, auto-reporte de baixos níveis de energia e incapacidade de levantar de uma cadeira 5 vezes seguidas sem usar os braços. 1 componente = pré-fragilidade. ≥2 componentes = fragilidade.	Longitudinal	Estados Unidos da América <i>(Study of Osteoporotic Fractures)</i> n = 6701 (≥69 anos; mulheres)	17%
Marigliano-Cacciafesta Polypathological Scale (MCPS) Amici et al., 2008	Escala com 11 componentes de fragilidade, pontuada com base em avaliação clínica: Doenças neurológicas, cardiovasculares, respiratórias, renais, gastrointestinais, metabólicas, oftalmológicas e auditivas, cancerígenas, do aparelho locomotor, do sistema vascular periférico, e relacionadas com o estado cognitivo e humor. Pontuação final obtida pelo somatório da classificação de cada componente (cotados de forma distinta). <15 = ligeira. 15-24 = moderada. 25-49 = moderada/severa 50-74 = severa >75 = muito severa.	Transversal	Itália n = 180 (≥65 anos)	Moderada/severa: 52% Severa: 15% Muito severa: 2%

Tilburg Frailty Indicator (TFI) Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010	Questionário destinado ao auto-reporte constituído por 10 determinantes de fragilidade (características sociodemográficas, eventos de vida no último ano, estilo de vida, satisfação com o ambiente habitacional e comorbilidades) e 15 componentes de fragilidade, divididos em 3 domínios: Domínio físico – pobre saúde física, perda de peso involuntária, dificuldade em andar e em manter o equilíbrio, problemas de audição e de visão, falta de força nas mãos e fadiga; Domínio psicológico – problemas de memória, sintomatologia depressiva e ansiosa, e dificuldades em lidar com os problemas (<i>coping</i>); Domínio social – viver sozinho, insatisfação com relações e suporte social. ≥5 componentes = fragilidade.	Transversal	Holanda n = 479 (≥75 anos; residentes na comunidade)	47%
SHARE Frailty Instrument (SHARE-FI) Romero-Ortuno, Walsh, Lawlor, & Kenny, 2010	Escala com 5 componentes de fragilidade, pontuada com base no auto-reporte do participante e realização de uma medição: Diminuição do apetite, limitação da mobilidade, exaustão, baixos níveis de atividade física e fraqueza muscular (medida com dinamómetro). Pontuação calculada com base em fórmulas ajustadas ao sexo e baseadas na predição de mortalidade na população estudada.	Longitudinal	Alemanha, Áustria, Bélgica, Dinamarca, Espanha, França, Grécia, Israel, Itália, Holanda, Suécia, Suíça (<i>Survey of Health, Aging and Retirement in Europe</i>) n = 28361 (≥50 anos; residentes na comunidade)	Pré-frágil: 21% Frágil: 5%

Comprehensive Assessment of Frailty test (CAF test) Sundermann et al., 2011	Escala com 11 componentes de fragilidade, pontuada com base numa avaliação clínica (incluindo a realização de testes laboratoriais e aplicação de outros instrumentos standardizados): Fraqueza muscular, exaustão auto-reportada, lentidão de marcha, baixos níveis de atividade física, défices nutritivos, problemas de equilíbrio, dificuldades na execução motora de tarefas simples, défices ao nível da função respiratória, cardíaca, renal e hepática. Cada item é pontuado entre 0 a 1 ou 0 a 4, com base na gravidade do défice. Pontuação final produzida através do somatório da cotação de cada item e da pontuação obtida na aplicação paralela da CFS. 1-10 = não frágil. 11-25 = moderadamente frágil. ≥26 = severamente frágil.	Longitudinal	Estados Unidos da América n = 400 (≥74 anos; hospitalizados a aguardar cirurgia cardíaca)	Moderadamente frágil: 43% Severamente frágil: 8%
FRAIL scale Hyde et al., 2010	Questionário destinado ao auto-reporte constituído por 5 componentes de fragilidade: Fadiga, baixa resistência, dificuldade em caminhar, ter ≥5 doenças e perda de peso. 1-2 componentes = pré-fragilidade. ≥3 componentes = fragilidade.	Longitudinal	Austrália (<i>Health in Men Study</i>) n = 3616 (≥70 anos; homens, residentes na comunidade)	Pré-frágil: 46.2% Frágil: 15.2%

Comprehensive Frailty Assessment Instrument (CFAI) De Witte et al., 2013	Questionário destinado ao auto-reporte constituído por 23 componentes de fragilidade, divididos em 4 domínios: Domínio físico – limitações funcionais em atividades diárias pouco exigentes, dificuldade em levantar objetos, em subir escadas e em fazer caminhadas; Domínio psicológico – sentimento geral de infelicidade, pressão, vazio, falta de valor e falta de autoconfiança, incapacidade de lidar com problemas, sentir falta de pessoas à sua volta, sentir-se rejeitado; Domínio social – reduzida quantidade de pessoas próximas, de confiança e que ajudem a resolver problemas, assim como número reduzido de pessoas em 3 níveis da rede de suporte social. Domínio ambiental – más condições gerais da habitação, problemas ao nível do aquecimento da habitação, falta ou inexistência de conforto na habitação e má vizinhança. Pontuação final obtida pelo somatório da classificação de cada componente (cotados de forma distinta).	Transversal	Bélgica (<i>Belgian Ageing Studies</i>) n = 33629 (≥60 anos; residentes na comunidade)	NA
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Easycare Two-step Older persons Screening (Easycare-TOS) van Kempen et al., 2013	Inventário que constitui o 1º passo da avaliação é formado por 14 componentes de fragilidade a serem considerados numa avaliação clínica: Número de comorbilidades e medicamentos, défices cognitivos, visuais e auditivos, dependência em atividades diárias, limitações da mobilidade, historial de quedas, necessidade de cuidado pessoal, solidão, rede social reduzida, sintomatologia depressiva e ansiosa, queixas somáticas e outras perturbações psiquiátricas. Com base no estado geral do indivíduo, considerando os componentes do 1º passo, o clínico geral é responsável por classificar o indivíduo como não frágil ou frágil. Em caso de dúvida ou de ser identificada uma situação de fragilidade, o indivíduo é encaminhado para o 2º passo, que consiste de uma avaliação detalhada com o instrumento <i>EASY-Care</i>.	Transversal	Holanda n = 151 (≥70 anos; residentes na comunidade)	24%
Gerontopole Frailty Screening Tool (GFST) Vellas et al., 2013	Inventário formado por 6 componentes de fragilidade a serem considerados numa avaliação clínica: Perda de peso involuntária, fadiga, viver sozinho, problemas de memória, lentidão da marcha, dificuldades na mobilidade. Com base no estado geral do indivíduo, considerando os componentes de fragilidade, o clínico geral é responsável por classificar o indivíduo como não frágil ou frágil	Transversal	França n = 442 (≥65 anos; residentes na comunidade)	NA

	Escala com 7 componentes de fragilidade, pontuada com base numa avaliação clínica (incluindo a realização de testes laboratoriais e aplicação de outros instrumentos standardizados): Frailty Trait Scale (FTS) Reduzida atividade física, desequilíbrio energético e défices nutritivos, fraqueza muscular, baixa resistência, lentidão, défices no funcionamento do sistema nervoso (equilíbrio e cognição) e do sistema vascular. Cada item é pontuado entre 0 a 4 ou 0 a 5, com base na gravidade do défice. Pontuação final produzida através do rácio entre somatório da cotação de cada item e cotação máxima da escala.	Longitudinal	Espanha (<i>Toledo Study for Healthy Aging</i>) n = 1972 (≥64 anos)	NA
Garcia-Garcia et al., 2014				

* No caso dos estudos longitudinais a prevalência de fragilidade é relativa à *baseline*.

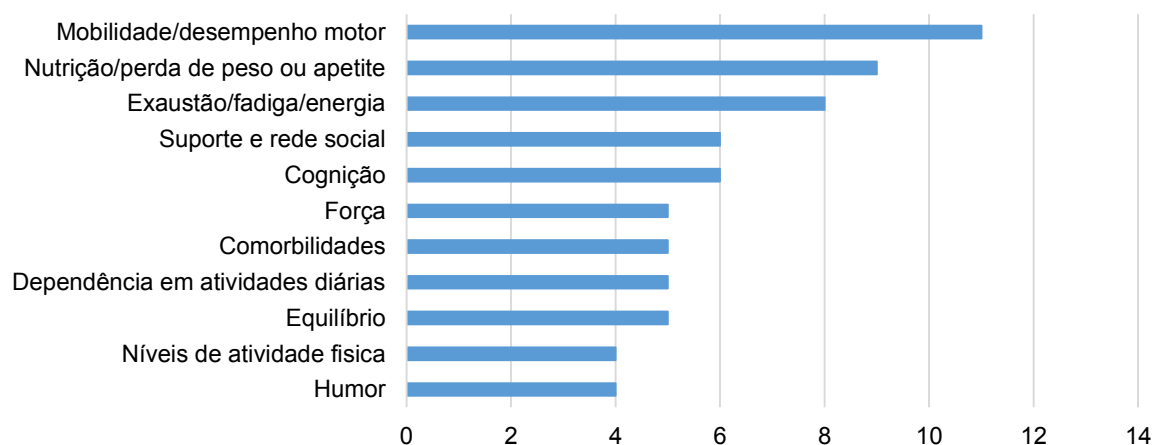
Incluíram-se sete estudos transversais (Amici *et al.*, 2008; De Witte *et al.*, 2013; Gobbens *et al.*, 2010; Rolfson *et al.*, 2006; Studenski *et al.*, 2004; van Kempen *et al.*, 2013; Vellas *et al.*, 2013) e sete estudos longitudinais (Ensrud *et al.*, 2008; Garcia-Garcia *et al.*, 2014; Hyde *et al.*, 2010; Jones *et al.*, 2004; Rockwood *et al.*, 2005; Romero-Ortuno *et al.*, 2010; Sundermann *et al.*, 2011). Sete estudos foram realizados a nível europeu (Amici *et al.*, 2008; De Witte *et al.*, 2013; Garcia-Garcia *et al.*, 2014; Gobbens *et al.*, 2010; Romero-Ortuno *et al.*, 2010; van Kempen *et al.*, 2013; Vellas *et al.*, 2013), seis estudos na América do Norte (Ensrud *et al.*, 2008; Jones *et al.*, 2004; Rockwood *et al.*, 2005; Rolfson *et al.*, 2006; Studenski *et al.*, 2004; Sundermann *et al.*, 2011) e um estudo na Oceânia (Hyde *et al.*, 2010). Na globalidade, verificou-se que os estudos europeus eram mais recentes que os norte-americanos.

Relativamente à administração dos instrumentos de avaliação identificados, três baseiam-se exclusivamente na autoaplicação (TFI, FRAIL *scale* e CFAI), três na autoaplicação e na realização de medições/testes (EFS, SOF *index* e SHARE-FI), enquanto os restantes se baseiam em avaliações clínicas. Deste último grupo destaca-se a eventual necessidade de complementar o *Easycare-TOS* com a administração de outro instrumento standardizado, assim como a obrigatoriedade de realização de testes laboratoriais e aplicação de outras medidas standardizadas para pontuar o CAF *test* e a FTS.

Por sua vez, quanto aos componentes de fragilidade avaliados, os instrumentos CGIC-PF *instrument*, SOF *index*, SHARE-FI e o CAF *test* incluem apenas fatores físicos/biológicos. A esses aspetos biocomportamentais, o GFST e a FTS acrescentam um componente cognitivo, enquanto a FRAIL *scale* acrescenta um componente relacionado com a presença de comorbilidades. Por outro lado, o MCPS avalia fragilidade exclusivamente como a conjugação de uma série de doenças, e a CFS classifica indivíduos como frágeis essencialmente com base em défices funcionais e comorbilidades. As restantes medidas podem ser consideradas como multidimensionais, destacando-se o TFI por ser a única ferramenta a não incluir componentes diretamente relacionados com dificuldades no desempenho de tarefas diárias/incapacidade e com condições patológicas.

Os fatores mais frequentemente identificados como componentes de fragilidade foram os relacionados com a mobilidade/desempenho motor, nutrição e exaustão/fadiga. A frequência dos diferentes componentes encontra-se sumarizada no gráfico 1.

Gráfico 1: Frequência absoluta dos componentes de fragilidade incluídos na totalidade dos instrumentos analisados*



* Incluídos apenas os componentes presentes em mais de 25% (≥ 4) dos instrumentos.

Por fim, considerando apenas os instrumentos com pontos de corte que permitissem distinguir indivíduos frágeis de não-frágeis, verificou-se que a prevalência de fragilidade variava entre 5% (Romero-Ortuno *et al.*, 2010) e 51% (Sundermann *et al.*, 2011).

Discussão

A presente revisão permitiu identificar e analisar uma quantidade considerável de instrumentos de avaliação de fragilidade. Estas ferramentas foram desenvolvidas em

contextos diferentes e representam definições distintas de fragilidade. Os autores dos artigos selecionados e incluídos correspondem aos autores dos instrumentos, à exceção da *FRAIL scale* que, apesar da sua aplicação ter sido testada pela primeira vez em pessoas idosas no estudo de Hyde *et al.* (2010), foi originalmente proposta por Abellan van Kan *et al.* (2008).

Verificou-se que os instrumentos mais recentemente desenvolvidos eram maioritariamente europeus, o que poderá resultar de um incremento do interesse da comunidade científica destes países relativamente ao tema de fragilidade e à validação de medidas para os respetivos grupos populacionais (Romero-Ortuno *et al.*, 2010).

Por sua vez, a prevalência de fragilidade reportada nos estudos apresentou uma grande variabilidade. Este aspeto estará forçosamente relacionado com os componentes de fragilidade avaliados, assim como com as características das amostras analisadas (Collard *et al.*, 2012). Efetivamente, estudos recentes demonstram que indivíduos mais velhos, do sexo feminino e com doença crónica, têm maior probabilidade de se tornarem frágeis (Collard *et al.*, 2012; Morley *et al.*, 2013). Em concordância, verificou-se que a prevalência mais baixa foi detetada numa amostra de indivíduos com 50 ou mais anos de idade e residentes na comunidade (Romero-Ortuno *et al.*, 2010), enquanto que a prevalência mais elevada se verificou numa amostra de indivíduos com 74 ou mais anos e com doença cardiovascular grave (a aguardar cirurgia) (Sundermann *et al.*, 2011).

A heterogeneidade entre os componentes de fragilidade avaliados espelha a falta de consenso em torno desta temática (Sternberg *et al.*, 2011). Contudo, um número considerável de instrumentos focou-se exclusivamente em aspetos físicos/biológicos do funcionamento humano. Para além disso, fatores relacionados com o Fenótipo de Fragilidade (Fried *et al.*, 2001) foram dos componentes mais incluídos nas medidas analisadas, referindo-se, inclusivamente, aos três mais utilizados (lentidão/mobilidade, perda de peso/nutrição e exaustão/fadiga). Estas constatações traduzem a tendência da maior parte dos autores para desenvolver a sua definição de fragilidade baseada no modelo biológico (Collard *et al.*, 2012; Sternberg *et al.*, 2011). Neste sentido, as novas propostas de avaliação da síndrome surgem com os objetivos de facilitar a sua execução na prática clínica, de desenvolver medidas com maior poder preditivo e/ou para superar divergências teóricas. Por exemplo, no caso do *SOF index* (Ensrud *et al.*, 2008), a intenção dos autores foi essencialmente simplificar a avaliação de fragilidade e promover a deteção da síndrome em vários contextos, tendo selecionado e adaptado os três itens do Fenótipo que apresentaram maior validade preditiva em estudos anteriores. Por sua vez, o *SHARE-FI* (Romero-Ortuno *et al.*, 2010) resultou de uma subtil alteração na avaliação do Fenótipo para tornar a sua aplicação mais rápida, destaca-se por apresentar uma pontuação específica, baseada em fórmulas ajustadas ao sexo e à predição de mortalidade na

amostra estudada (representativa de vários países europeus). Por outro lado, o TFI (Gobbens *et al.*, 2010) espelha uma diferente conceptualização teórica de fragilidade (modelo integral de fragilidade) e, apesar de incluir quatro componentes do Fenótipo, distancia-se das visões tradicionais da síndrome uma vez que inclui fatores psicológicos e sociais.

Concomitantemente, alguns instrumentos [ex.: FI-CGA (Jones *et al.*, 2004), CFS (Rockwood *et al.*, 2005) e MCPS (Amici *et al.*, 2008)] aproximam-se mais do Índice de Fragilidade (Mitnitski *et al.*, 2002), pela valorização de fatores relacionados com doenças e défices funcionais em atividades diárias. De facto, apesar da maioria dos autores concordar que fragilidade, comorbilidade e incapacidade são condições relacionadas mas distintas (Morley *et al.*, 2013; Sternberg *et al.*, 2011), algumas das medidas analisadas não fazem essa diferenciação.

Verificou-se, porém, que os componentes mais frequentemente incluídos nas medidas analisadas foram relativamente semelhantes aos identificados como mais prevalentes numa revisão recente (Sternberg *et al.*, 2011), sobre as diferentes definições de fragilidade propostas entre 1997 e 2009. Efetivamente, se analisarmos as principais diferenças nos dados obtidos, é possível afirmar que houve uma maior frequência de componentes relacionados com a fadiga/exaustão/energia e com o suporte e rede social do idoso, tendo-se verificado uma menor proporção de fatores relacionados com os níveis de atividade física.

Conclusões

A presente revisão surge como um contributo para uma melhor compreensão do estado da arte sobre fragilidade e a sua avaliação, na medida em que existem, ainda, poucas publicações em Portugal sobre o tema. No entanto, deve salientar-se que os resultados apresentados devem ser analisados tendo em consideração os critérios de inclusão e exclusão pré-definidos. Como principal limitação desta revisão destaca-se a não inclusão de artigos relativos a constructos intrinsecamente associados a fragilidade, como por exemplo a vulnerabilidade.

A escolha do instrumento de avaliação de fragilidade deve ter em conta o modelo conceptual na sua base, a sua forma de administração, a adequabilidade ao contexto e, entre outras propriedades, a sua capacidade preditiva. Neste sentido, justifica-se a realização de estudos – idealmente longitudinais – para determinar quais as medidas que mais se ajustam às características da população idosa e dos cuidados de saúde e sociais.

A fragilidade deve ser encarada como uma questão de saúde pública, sendo a sua detecção atempada fundamental para a manutenção da qualidade de vida dos mais velhos.

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3. Investigação empírica

3.1. Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation

Autores: Tiago Coelho, Rubim Santos, Constança Paúl, Robbert J. J. Gobbens, Lia Fernandes

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Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation

Tiago Coelho,^{1,2} Rubim Santos,³ Constança Paúl,² Robbert JJ Gobbens⁴ and Lia Fernandes⁵

¹School of Allied Health Sciences, Porto Polytechnic Institute, ³Activity and Human Movement Study Center, School of Allied Health Sciences, Porto Polytechnic Institute, Vila Nova de Gaia, ²UNIFAI/ICBAS, University of Porto, ⁵UNIFAI/CINTESIS – Faculty of Medicine, University of Porto, Porto, Portugal; and ⁴Research & Development Center Innovations in Care, Rotterdam University of Applied Sciences, Rotterdam, the Netherlands

Aim: To present the translation and validation process of the Portuguese version of the Tilburg Frailty Indicator (TFI).

Methods: A cross-sectional study was designed using a non-probability sample of 252 community-dwelling older adults. Preliminary studies were carried out for face and content validity assessment. Internal consistency, test–retest reliability, construct (convergent/divergent) and criterion validity were subsequently analyzed.

Results: The sample was mainly women (75.8%), with a mean age of 79.2 ± 7.3 years. TFI internal consistency was good (KR-20 = 0.78). Test–retest reliability for the total was also good ($r = 0.91$), with kappa coefficients showing substantial agreement for most items. TFI physical and social domains correlated as expected with concurrent measures, whereas the TFI psychological domain showed similar correlations with other psychological and physical measures. The TFI showed a good to excellent discrimination ability in regard to frailty criteria, and fair to good ability to predict adverse outcomes.

Conclusions: The psychometric properties of the TFI seem to be consistently good. These findings provide initial evidence that the Portuguese version is a valid and reliable measure for assessing frailty in the elderly. *Geriatr Gerontol Int* 2014; ●●: ●●–●●.

Keywords: elderly, frailty, Tilburg Frailty Indicator, validation study.

Introduction

Portugal is no exception to the worldwide trend of population aging, with one of the highest proportions (19%) of elderly in the European Union.¹ As life expectancy increases, so does the need to maintain health and independence during a longer life. Despite the heterogeneity of functional decline with chronological age, frailty is considered to be highly prevalent in elderly individuals.^{2,3}

Over the past three decades, the relevance of the concept of frailty has increased significantly in the study of aging and the clinical care of older adults.^{4–6} Frailty is

generally recognized as a state of increased vulnerability that entails a high risk of clinically significant adverse outcomes, such as falls, disability, hospitalization, institutionalization and mortality.^{7–9} However, there is no agreed definition.^{2,10,11} Although frailty is commonly accepted as a clinically observable syndrome that results from a significantly diminished physiological reserve and its interplay with life course determinants and/or disease(s), which affect the individual's ability to maintain homeostasis when facing stressors, the same cannot be said about its outcomes and, especially, its components.^{12–14} A recent literature review shows that despite some factors, there has been a greater number in differing approaches regarding the components and the adverse outcomes of frailty (e.g. physical function and death), over which there is still a lot of controversy.¹⁵ Nevertheless, two major trends in the conceptualization of frailty have been identified. An increasing number of authors state that disability is an outcome of frailty rather than a component of the syndrome. Disability,

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Correspondence: Dr Tiago Coelho OTR MSc, School of Allied Health Sciences, Porto Polytechnic Institute, Occupational Therapy Department, Rua Valente Perfeito, 322, 4400-330, Vila Nova de Gaia, Portugal. Email: tfc@eu.ipp.pt

such as morbidity and the normal process of aging, is not synonymous with frailty.^{4,5,16,17} Progressively more studies emphasize the need for including psychosocial factors in the definition of frailty, instead of conceptualizing it as consisting of exclusively physical conditions.^{6,7,15,18}

Traditional approaches of frailty emphasize physical losses that result from functional decline across multiple physiological systems (e.g. musculoskeletal, immune, hormonal, inflammatory, autonomic/central nervous system) and its physical manifestations (e.g. sarcopenia).^{13,19–21} From these approaches, a consensus has been reached on the operationalization of frailty that is known as the frailty phenotype, in which the clinical presentation of the syndrome refers to the presence of three or more of the following components: unintentional weight loss, low physical activity, exhaustion, slow walking speed and weakness.³ However, there is an increasing number of researchers with a more integrative, multidimensional and health-based perspective, avoiding the fragmentation of care for older adults.^{2,6,22–27} In order to make sense of a multidimensional approach to frailty and, at the same time, to clearly differentiate frailty from disability, an integral conceptual model has been developed, resulting from an exhaustive literature review and expert consultation.^{5,18,26,28} The need to identify frailty according to this conceptualization has led to the development of the Tilburg Frailty Indicator (TFI).²⁹

Considering that most researchers agree that frailty and its adverse outcomes can be prevented, the ability to effectively assess frailty should be of great relevance, from a social and public health perspective.² In this context, TFI allows the screening of frailty in community-dwelling older people, according to the more recent approaches.²⁹ Taking into account that there is no Portuguese version of TFI, the present study aimed to translate and validate this instrument.

Methods

Sample

From May to September 2013, a non-probability sample of 252 elderly volunteers from three northern Portuguese cities (Maia, Porto, Vila Nova de Gaia) was recruited. These persons, users of institutions, such as social, recreation and day care centers, and senior academies, were interviewed. The inclusion criteria was community dwellers aged ≥65 years. Individuals with severe cognitive impairment or unable to speak Portuguese were excluded. Data collection was carried out by nine trained researchers. For test–retest reliability, the first 74 available participants were assessed twice with TFI within a 12–16-day period (mean 14 days). The

study was approved by institutional review boards, and all participants gave their written informed consent.

Description of TFI

TFI is a brief self-report questionnaire for screening frail community-dwelling older adults with two subscales: part A-10 items about determinants of frailty (e.g. age, sex, education and income); and part B-15 questions divided into three domains (physical, psychological and social), and focuses exclusively on components of frailty. The part B set of items inform frailty total and each domain score as follows. A total of 11 items have two response categories (yes/no), while four items have three (yes/no/sometimes). Nevertheless, all items are scored zero or one. The TFI physical domain includes eight questions about physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, hearing problems, vision problems, lack of strength in hands and physical tiredness. The psychological domain comprises four items related to cognition, depressive/anxiety symptoms and coping mechanisms. The social domain includes three items: living alone, social relations and social support. The originally proposed cut-off for frailty was 5.²⁹

For screening purposes, TFI can be administered alone, without supplementary assessment tools. This possibility is supported by the observed association of TFI domains with concurrent measures.²⁹ Furthermore, previous studies have shown that TFI is sufficient to predict healthcare utilization, 1 and 2 years later.³⁰ Nevertheless, to better predict disability, the use of both TFI and the Timed Up and Go test (TUG)³¹ is recommended.³⁰ Also, a previous screening of severe cognitive deficit might be advised, because of the self-reporting nature of TFI.

TFI was recently developed with tested psychometric properties in the Netherlands.²⁹ An English version was promptly made available by the authors, resulting from a translation and back-translation process. Since then, a valid and cross-culturally adapted version was prepared in Brazil^{32,33} and Denmark.³⁴ Furthermore, studies carried out by different researchers^{35,36} highlighted TFI psychometric properties in comparison with other frailty measures.

Translation and cultural adaptation process

This process was carried out according to the guidelines of the International Society for Pharmacoeconomics and Outcomes Research, beginning with permission to use the TFI and inviting the main author of the questionnaire to be involved in the research.³⁷ Forward translation from English into Portuguese was carried out by three authors of this research, who are fluent in English. After the forward translations had been

analyzed, and a single forward translation agreed on, the back translation was carried out by two professional English translators. The back translation results were reviewed, and a harmonization of all versions was sought to detect and deal with any discrepancies that could have arisen between different language versions, ensuring conceptual equivalence. To assess the level of comprehensibility of the translation, a cognitive debriefing was carried out, involving a pretest with six participants that would be eligible for this research. Additionally, a multidisciplinary committee (five experts regarding geriatric research) was consulted to provide their opinion on the face and content validity of the preliminary version. Pretest results along with multidisciplinary group feedback suggested good face and content validity. The final version was proofread and then used for psychometric testing.

Additional measures

To examine the construct validity of TFI, the following measures of physical, psychological and social frailty components were used: body mass index (BMI), TUG,³¹ handgrip strength, center of pressure (COP) sway analysis, Mini-Mental State Examination (MMSE),^{38,39} Geriatric Depression Scale (GDS),⁴⁰ Geriatric Anxiety Inventory (GAI)^{41,42} and Social Support Satisfaction Scale (SSSS).⁴³

To study the criterion validity, frailty was also identified through alternative frailty specific measures: the Groningen Frailty Indicator (GFI) and an operationalization of the frailty phenotype.^{44,45} Adverse outcomes (disability and healthcare utilization) and quality of life were equally assessed for the same purpose. Disability in basic activities of daily living (ADL) was measured with the Barthel Index,^{46,47} and in instrumental ADL with the Lawton and Brody Scale.^{48,49} Quality of life was assessed with EUROHIS Quality of Life 8-item index (EUROHIS-QOL-8),^{50,51} and World Health Organization Quality of Life – Old Module (WHOQOL-OLD).^{52,53}

Hand strength was measured with a GRIP-D Takei Hand Grip Dynamometer (T.K.K. 5401; Takei Scientific Instruments, Tokyo, Japan) and considering a proposed standardized approach.⁵⁴ COP sway, which is usually measured to assess postural control and balance, was analyzed with an Emed-AT25D pressure platform (Novel, Munich, Germany).⁵⁵ The parameters measured were maximum velocity and maximum range in medial/lateral/COP_x and anterior/posterior/COP_y axis, during two tasks carried out while standing (eyes open/eyes closed). In regard to frailty phenotype components: unintentional weight loss was considered if answered “yes” to TFI question 12, “Have you lost a lot of weight recently without wishing to do so?”. Low physical activity and exhaustion were detected using two

questions based on previous studies.⁵⁶ Slow walking speed was detected if the participant took more than 20 s to complete the TUG. Weakness was identified if the participant’s hand strength was below the cut-off determined by Fried *et al.* stratified by sex and BMI.³ Frailty was identified if the participant had ≥ 3 components, and prefrailty if one or two components were present. Healthcare utilization was assessed with a set of questions previously used in other studies and referred only to the last year.^{28,29,57}

See Supporting Information for more details about the additional measures used.

Statistical analysis

Internal consistency was assessed using the Kuder–Richardson formula (KR-20), which is equivalent to Cronbach’s alpha, but used for dichotomous measures. Test–retest reliability was measured by calculating the Pearson correlation coefficient for each domain and for total score, and by assessing simple agreement and Cohen’s kappa coefficient for each TFI item.

Construct validity was determined by the Spearman correlations between TFI domains score and other measures. It was expected that each score would show higher correlations with measures of the same domain of human functioning, and lower correlations with measurements of other domains (convergent/divergent validity).

Criterion validity was primarily assessed by carrying out receiver operating characteristic (ROC) analysis applied to the criteria of frailty and adverse outcomes: disability and healthcare utilization. Criterion validity was also assessed by multiple regression analysis in order to ascertain if TFI multiple domains predict quality of life, as evidenced in other studies.^{29,57,58} The association of quality of life with frailty domains, after controlling for the effect of the other domains, was also analyzed.

Two-tailed tests were used, and a $P < 0.05$ was considered statistically significant. For statistical analysis, IBM SPSS Statistics 22.0 (IBM, Armonk, NY, USA) was used.

Results

Sample

The sample comprised 252 participants (75.8% women, 55.6% widowed), aged 65–99 years (mean 79.2 ± 7.3 years) and with low education level (63.9%). The mean TFI total was 6.0 (SD 3.4), and frailty components with the highest prevalence were “feeling nervous or anxious” (69.0%), “feeling down” (64.3%) and “miss having people around” (59.9%). Detailed information is presented in Table 1.

Table 1 Participant characteristics

Characteristic	<i>n</i> (%)	Characteristic	<i>n</i> (%)
Sociodemographic characteristics		COP sway (eyes closed) [‡]	
Mean age (years)	79.2 ± 7.3	Mean COP _X maximum velocity (cm/s)	3.1 ± 2.0
65–74	68 (27.0)	Mean COP _Y maximum velocity (cm/s)	4.0 ± 2.5
75–84	116 (46.0)	Mean COP _X maximum range (cm)	2.0 ± 1.1
≥85	68 (27.0)	Mean COP _Y maximum range (cm)	2.3 ± 0.9
Sex (women)	191 (75.8)	Mean MMSE (0–30)	23.6 ± 4.9
Marital status		Cognitive deficit	132 (52.4)
Married/living with partner	49 (19.4)	Mean GDS (0–15)	5.4 ± 3.9
Unmarried	24 (9.5)	Depression	113 (44.8)
Separated/divorced	39 (15.5)	Mean GAI (0–20)	9.5 ± 6.3
Widow/widower	140 (55.6)	Severe anxiety symptoms	130 (51.6)
Mean education (years)	4.4 ± 3.6	Mean SSSS (15–75)	53.0 ± 11.2
0	36 (14.3)	Mean GFI (0–12)	4.6 ± 2.7
1–4	161 (63.9)	Frailty	132 (52.4)
≥5	55 (21.9)	Frailty phenotype components	
Monthly household income (EUR)		Weight loss	40 (15.9)
≤500	103 (40.9)	Low physical activity	109 (43.3)
≥501	149 (59.1)	Exhaustion	130 (51.6)
Frailty assessed with TFI		Slowed performance	58 (23.0)
Mean TFI total score (0–15)	6.0 ± 3.4	Weakness	161 (63.9)
Mean TFI physical domain score (0–8)	2.9 ± 2.2	Mean frailty phenotype	2.0 ± 1.4
TFI Q11: Poor physical health	98 (38.9)	0 (non-frail/robust)	39 (15.5)
TFI Q12: Unintentional weight loss	40 (15.9)	1–2 (prefrail)	121 (48.0)
TFI Q13: Difficulty in walking	126 (50.0)	3–5 (frail)	92 (36.5)
TFI Q14: Difficulty in maintaining balance	105 (41.7)	Adverse outcomes	
TFI Q15: Poor hearing	69 (27.4)	Mean Barthel Index (0–20)	19.0 ± 1.5
TFI Q16: Poor vision	81 (32.1)	Mean Lawton and Brody Scale (0–23)	17.5 ± 5.6
TFI Q17: Lack in hand strength	68 (27.0)	Healthcare utilization	
TFI Q18: Physical tiredness	141 (56.0)	Contact with general practitioner	
Mean TFI psychological domain score (0–4)	1.7 ± 1.1	0	11 (4.4)
TFI Q19: Problems with memory	61 (24.2)	1–2	115 (45.6)
TFI Q20: Feeling down	162 (64.3)	3–4	83 (32.9)
TFI Q21: Feeling nervous or anxious	174 (69.0)	5–6	23 (9.1)
TFI Q22: Unable to cope with problems	36 (14.3)	≥7	20 (7.9)
Mean TFI social domain score (0–3)	1.4 ± 1.0	Contact with healthcare professionals	180 (71.4)
TFI Q23: Living alone	131 (52.0)	Hospitalization	62 (24.6)
TFI Q24: Miss having people around	151 (59.9)	Professional personal care	17 (6.7)
TFI Q25: Not receiving enough support	68 (27.0)	Nursing care	70 (27.8)
Alternative measurements of frailty		Informal care	48 (19.0)
Mean BMI (kg/m ²)	28.6 ± 5.4	Other healthcare or residential care institutions	28 (11.1)
<18.5 (underweight)	1 (0.4)	Quality of life	
18.5–24.9 (normal)	64 (25.4)	Mean EUROHIS-QOL-8 (8–40)	27.9 ± 5.0
25–29.9 (overweight)	99 (39.3)	Mean WHOQOL-OLD (28–140)	98.4 ± 15.7
>30 (obese)	88 (34.9)	Mean sensory abilities	15.4 ± 4.0
Mean TUG test (s) [†]	15.8 ± 8.8	Mean autonomy	14.0 ± 3.0
Mean handgrip strength (kg)	19.9 ± 8.4	Mean past, present and future activities	13.4 ± 3.0
COP sway (eyes open) [‡]		Mean social participation	14.9 ± 2.8
Mean COP _X maximum velocity (cm/s)	2.4 ± 1.5	Mean death and dying	13.0 ± 4.3
Mean COP _Y maximum velocity (cm/s)	3.0 ± 1.5	Mean intimacy	13.2 ± 3.9
Mean COP _X maximum range (cm)	1.8 ± 0.9	Mean family/family life	14.5 ± 4.2
Mean COP _Y maximum range (cm)	1.9 ± 0.7		

n = 252. [†]Two cases were missing. [‡]Three cases were missing. BMI, body mass index; COP, center of pressure; EUROHIS-QOL, EUROHIS Quality of Life 8-item index; GAI, Geriatric Anxiety Inventory; GDS, Geriatric Depression Scale; GFI, Groningen Frailty Indicator; MMSE, Mini-Mental State Examination; SSSS, Social Support Satisfaction Scale; TFI, Tilburg Frailty Indicator; WHOQOL-OLD, World Health Organization Quality of Life – Old Module.

Table 2 Simple agreement and Cohen's kappa coefficients of Tilburg Frailty Indicator items

TFI items	Agreement	Kappa (95% CI)
Physical domain		
Physical health	0.81	0.61 (0.43–0.79)
Nutrition	0.95	0.69 (0.39–0.99)
Mobility	0.85	0.70 (0.54–0.86)
Balance	0.87	0.72 (0.56–0.88)
Hearing	0.91	0.76 (0.60–0.93)
Vision	0.88	0.71 (0.52–0.89)
Strength	0.83	0.57 (0.36–0.78)
Endurance	0.81	0.62 (0.44–0.80)
Psychological domain		
Cognition	0.84	0.52 (0.28–0.77)
Mood	0.78	0.54 (0.34–0.74)
Anxiety	0.78	0.53 (0.33–0.74)
Coping	0.93	0.76 (0.56–0.96)
Social domain		
Living alone	0.97	0.95 (0.87–1.00)
Social relations	0.84	0.66 (0.49–0.84)
Social support	0.88	0.73 (0.56–0.89)

TFI, Tilburg Frailty Indicator.

Feasibility

The researchers' training process was easy, and the administration of TFI was remarkably quick and simple. Completing TFI took on average 10 min (SD 4.1). All part B items were easily understood by the elderly individuals. In regard to part A, some participants with a lower educational level required a brief explanation about the description of a healthy lifestyle (including among other aspects, eating a prudent diet, exercising frequently and not drinking excessively or smoking).

Reliability

The KR-20 was 0.78 for frailty, and 0.75, 0.48, 0.49 for physical, psychological and social domains, respectively. The test-retest reliability was 0.91 (95% CI 0.86–0.94) for TFI total, 0.87 (95% CI 0.80–0.91) for physical, 0.75 (95% CI 0.62–0.83) for psychological and 0.87 (95% CI 0.80–0.91) for social domains. Simple agreement was observed for all items (78–97%), and regarding kappa coefficients, values ranged from 0.52 to 0.95 (Table 2). No statistically significant differences were found, between the total and the subsample for retest, in regard to sociodemographic characteristics and components of frailty.

Construct validity

The TFI physical domain score showed the highest correlations with BMI, TUG test, handgrip strength and

most parameters regarding COP sway, whereas TFI social domain score correlated better with SSSS. In contrast, similar correlations were obtained between GDS and TFI physical and psychological domains, whereas MMSE and GAI showed the highest correlations with TFI physical domain, although not very different from the correlations obtained with the psychological domain (Table 3).

Criterion validity

To examine the criterion validity of TFI total, the area under the curve (AUC) with 95% CI for adverse outcome and alternative frailty measures was calculated, as well as the sensitivity and specificity for one or two cut-off points that gave the best results. The AUC obtained by using the GFI and the frailty phenotype as criteria was 0.89 and 0.75, respectively. In regard to the adverse outcomes, the AUC ranged from 0.56 to 0.72 (Table 4). In the absence of an optimal cut-off point, 6 was chosen, because it showed better sensitivity and specificity.

TFI domains predicted 38.7% of quality of life variance, measured by EUROHIS-QOL-8 and 42.1% by WHOQOL-OLD. Although each domain contributed to the prediction of quality of life, TFI physical had the largest contribution ($R^2 = 13.7\%$ EUROHIS-QOL-8, $R^2 = 11.6\%$ WHOQOL-OLD). After controlling for the effect of the other two TFI domains, each one had higher correlations than the others in regard to at least two WHOQOL-OLD facets: the TFI physical domain unique contribution was stronger for "sensory abilities", "social participation" and "death and dying"; psychological domain for "autonomy" and "past, present and future activities"; whereas social domain's contribution was higher for "intimacy" and "family/family life" (Table 5).

Discussion

The present study developed a culturally adapted version of the TFI, which showed good reliability and validity when applied to a Portuguese community-dwelling sample. This sample's sociodemographic characteristics approximately resemble those of the elderly population in Portugal, in which there is an increasingly larger proportion of women, low education levels and widows in older groups.⁵⁹

Internal consistency was good for frailty and for the physical domain, but rather low for psychological and social domains. These results approximately resemble the values obtained in the original and Brazilian studies.^{29,32} The low values can be explained by the reduced number of items in the psychological and social domains (four and three, respectively). Gobbens *et al.*

Table 3 Spearman correlations between Tilburg Frailty Indicator domains and alternative frailty measurements

Alternative measurements of frailty	TFI physical domain	TFI psychological domain	TFI social domain
Physical domain			
BMI	0.16*	0.07	0.00
TUG test	0.48***	0.21***	0.12
Hand grip strength	-0.34***	-0.28***	-0.19**
COP sway (eyes open)			
COP _X maximum velocity	0.17**	0.02	0.03
COP _Y maximum velocity	0.13*	-0.06	-0.08
COP _X maximum range	0.17**	0.03	0.08
COP _Y maximum range	0.15*	0.00	-0.07
COP sway (eyes closed)			
COP _X maximum velocity	0.09	-0.02	0.01
COP _Y maximum velocity	0.07	0.01	-0.02
COP _X maximum range	0.18**	0.06	0.04
COP _Y maximum range	0.07	0.10	0.02
Psychological domain			
MMSE	-0.26***	-0.22***	-0.06
GDS	0.58***	0.58***	0.41***
GAI	0.58***	0.56***	0.29***
Social domain			
SSSS	-0.35***	-0.37***	-0.43***

* $P < 0.05$. ** $P < 0.01$. *** $P < 0.001$. Highest significant correlation of each row printed in bold. BMI, body mass index; COP, center of pressure; GAI, Geriatric Anxiety Inventory; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; SSSS, Social Support Satisfaction Scale; TFI, Tilburg Frailty Indicator.

Table 4 Receiver operating characteristic analysis of Tilburg Frailty Indicator total score in regard to criteria of frailty and adverse outcomes

Measure/criterion	TFI cut-point	Sensitivity	Specificity	AUC (95%CI)
Alternative frailty measures				
GFI	≥5	0.84	0.78	0.89 (0.85–0.93)
	≥6	0.74	0.86	
Frailty phenotype	≥5	0.78	0.59	0.75 (0.68–0.81)
	≥6	0.71	0.69	
Disability				
Barthel Index	≥5	0.70	0.60	0.72 (0.66–0.78)
	≥6	0.64	0.73	
Lawton and Brody Scale	≥4	0.65	0.56	0.63 (0.53–0.72)
	≥5	0.58	0.58	
Healthcare utilization				
Contact with general practitioner	≥6	0.63	0.58	0.64 (0.56–0.73)
	≥7	0.54	0.67	
Contact with healthcare professionals	≥5	0.58	0.54	0.57 (0.49–0.65)
Hospitalization	≥6	0.57	0.58	0.60 (0.51–0.68)
Professional personal care	≥6	0.65	0.56	0.63 (0.49–0.77)
	≥7	0.59	0.64	
Nursing care	≥6	0.51	0.57	0.56 (0.49–0.64)
Informal care	≥6	0.58	0.58	0.60 (0.52–0.68)
Other healthcare or residential care institutions	≥6	0.57	0.56	0.59 (0.48–0.69)
	≥7	0.50	0.64	

Optimal cut-points of each criterion printed in bold. GFI, Groningen Frailty Indicator; TFI, Tilburg Frailty Indicator.

Table 5 Prediction of quality of life with Tilburg Frailty Indicator domains

Quality of life measures	TFI physical domain			TFI psychological domain			TFI social domain			TFI r	R^2 (%)	P -value
	β	r	P -value	β	r	P -value	β	r	P -value			
EUROHIS-QOL-8	-0.43	-0.37	<0.001	-0.22	-0.18	<0.001	-0.11	-0.10	<0.05	-0.62	38.7	<0.001
WHOQOL-OLD	-0.40	-0.34	<0.001	-0.26	-0.22	<0.001	-0.14	-0.13	<0.01	-0.65	42.1	<0.001
Sensory abilities	-0.58	-0.49	<0.001	-0.16	-0.13	<0.01	0.07	0.06	0.12	-0.65	42.5	<0.001
Autonomy	-0.26	-0.22	<0.001	-0.31	-0.26	<0.001	0.03	0.03	0.59	-0.49	23.5	<0.001
Past, present and future activities	-0.21	-0.18	<0.01	-0.24	-0.20	<0.001	-0.08	-0.07	0.20	-0.43	18.4	<0.001
Social participation	-0.28	-0.24	<0.001	-0.19	-0.16	<0.01	-0.08	-0.08	0.18	-0.45	20.6	<0.001
Death and dying	-0.17	-0.14	<0.05	-0.12	-0.10	0.12	-0.05	-0.05	0.46	0.27	7.2	<0.001
Intimacy	-0.13	-0.11	0.07	-0.07	-0.06	0.36	-0.22	-0.20	<0.001	0.32	10.5	<0.001
Family/family life	-0.14	-0.12	<0.05	-0.13	-0.11	0.07	-0.26	-0.24	<0.001	0.41	17.0	<0.001

Standardized regression coefficient (β), semi-partial correlation coefficient (r) and P -value for each Tilburg Frailty Indicator (TFI) domain (highest r printed in bold), and correlation coefficient (r), coefficient of determination (R^2) and P -value for all three domains inserted in the regression model. EUROHIS-QOL, EUROHIS Quality of Life 8-item index; WHOQOL-OLD, World Health Organization Quality of Life – Old Module.

recognized this, but preferred to value the benefits of assessing these domains with the fewest possible questions.²⁹

Regarding kappa coefficients, it was observed that four items showed moderate agreement (0.41–0.60), 10 showed substantial agreement (0.61–0.80) and one showed nearly perfect agreement (0.81–1.00) according to the Landis and Koch classification.⁶⁰ The TFI total and each domain score obtained in both assessments were also found to be highly correlated. In accordance with other TFI validation studies, these results showed a good test–retest reliability.^{29,32}

TFI also showed good construct validity (convergent/divergent) in regard to its physical and social domains, as each correlated as expected with alternative physical and social measures. The same cannot be said regarding TFI psychological domain's divergent validity, as other psychological measures correlated equally or slightly better with the physical domain than with the psychological one. Gobbens *et al.*²⁹ had already drawn similar results regarding MMSE, whereas Santiago *et al.*³² also struggled to find alternative psychological measures that correlated better with the TFI psychological domain. These results can be explained by the well-documented relationship between cognitive and physical performance,⁶¹ and between depression⁶² and anxiety⁶³ and self-reported physical function.

ROC analysis used to assess TFI criterion validity showed that its discrimination ability was excellent regarding the identification of those classified as frail by GFI, and good for frailty detected by the frailty phenotype. The prediction of disability in ADL was good and fair for the remaining adverse outcomes (dependence on instrumental ADL and healthcare utilization). Choosing 6 as a cut-off for frailty, 54.8% of the participants were identified as frail. This prevalence is remarkably similar to the proportion of frail participants identified in our sample by GFI (52.4%), larger than the prevalence of frailty detected by this operationalization of its phenotype (36.5%), and higher than observed in other studies that used the TFI in a community setting. Values from 31.7%³² to 47.1%²⁹ have been reported. One possible explanation for the substantial difference observed between the Brazilian study³² and this research could be the age of participants (significantly younger in the first one).

The good criterion validity of the TFI was also supported by its ability to predict quality of life. Besides assuming a primary role in predicting EUROHIS-QOL-8 and WHOQOL-OLD totals, the TFI physical domain also had the highest correlation of the three domains with the largest number of WHOQOL-OLD facets. The highest contribution of the physical domain for the explanation of quality of life emphasizes its importance in the conceptualization of frailty, but the

value added by the other domains provides robust evidence for an integral definition of the syndrome.

The rigorous process of translation and cultural adaptation, and thorough study of several psychometric properties were the main strengths of this research. Nevertheless, some limitations should be highlighted. First, test-retest reliability reported only on a second application of TFI 2 weeks after the first inquiry, and that difference could provide different results. Second, the correlations between each TFI item and correspondent other validated measures were not examined, which could provide additional evidence about construct validity. The cross-sectional nature of the present study can also be considered as a limitation, as it does not allow understanding of the temporal continuum between frailty and adverse outcomes. Finally, the non-probability sampling method could have limited these findings regarding the generalization of results. Nevertheless, considering that the psychometric properties of this version resemble those obtained in other validation studies, these results are promising.

Longitudinal studies should be carried out to better examine how frailty, and each domain, predicts adverse outcomes in the short, medium and long term. Likewise, understanding which variables/determinants (e.g. sociodemographic characteristics, life events, lifestyle) can effectively predict frailty in general, and each domain in particular, is essential to implement timely and targeted interventions in order to prevent the syndrome and its adverse outcomes. Although benefits can be drawn by measuring frailty with the multidimensional TFI, further research should be carried out to better understand which frailty definition and operationalization concept should be chosen. Also, further research about the TFI cut-off for frailty and its application in other contexts (e.g. hospital, primary care, nursing home) should be carried out.

In conclusion, this research provides robust evidence that this TFI version is a valid and reliable measure for assessing frailty in Portuguese older adults. Consequently, it provided a simple, but invaluable, tool for health/social care providers and for researchers that effectively identifies highly vulnerable older persons in a multidimensional perspective, allowing more focused and efficient interventions to prevent adverse outcomes.

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Disclosure statement

No potential conflicts of interest were disclosed.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Description of the additional measures.

English and Portuguese versions of the Tilburg Frailty Indicator.

3.2. Determinants of frailty: the added value of assessing medication

Autores: Tiago Coelho, Constança Paúl, Robbert J. J. Gobbens, Lia Fernandes

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Abstract

This study aims to analyze which determinants predict frailty in general and each frailty domain (physical, psychological, and social), considering the integral conceptual model of frailty, and particularly to examine the contribution of medication in this prediction. A cross-sectional study was designed using a non-probabilistic sample of 252 community-dwelling elderly from three Portuguese cities. Frailty and determinants of frailty were assessed with the Tilburg Frailty Indicator. The amount of different daily-consumed medicines was also examined. Hierarchical regression analysis were conducted. The mean age of the participants was 79.2 years (± 7.3), and most of them were women (75.8%), widowed (55.6%) and with a low educational level (0-4 years: 63.9%). In this study, determinants explained 46% of the variance of total frailty, and 39.8%, 25.3%, and 27.7% of physical, psychological, and social frailty respectively. Age, gender, income, death of a loved one in the past year, lifestyle, satisfaction with living environment and self-reported comorbidity predicted total frailty, while each frailty domain was associated with a different set of determinants. The number of medications independently predicted an additional 2.5% of total frailty and 5.3% of physical frailty. The adverse effects of polymedication and its direct link with the amount of comorbidities could explain the independent contribution of this variable to frailty prediction. In the present study, a significant part of frailty was predicted, and the different contributions of each determinant to frailty domains provided additional evidence of the integral model of frailty's relevance. The added value of a simple assessment of medication was considerable, and it should be taken into account for effective identification of frailty.

Keywords: elderly, frailty, determinants, comorbidity, medication.

Introduction

As age increases, physiological reserves inevitably decrease in multiple systems, and comorbidities become more prevalent (WHO, 1999). Nonetheless, chronological age is not a precise indicator of functional decline (Bergman et al., 2007). The changes that accompany aging depend on genetic and environmental factors, and are lifestyle and life event related (WHO, 1999). Therefore, while some may remain healthy and resilient in later life, others may become increasingly vulnerable to internal and external stressors. The latter refers to a state of frailty.

Frail individuals are at greater risk of clinically significant adverse outcomes such as hospitalization, institutionalization and mortality (Abellan van Kan et al., 2008; Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Fried, Walston, & Ferrucci, 2009). Although frailty is generally considered a clinical syndrome separate from the normal aging process, there are different perspectives about its definition (Bergman et al., 2007; Hogan, MacKnight, & Bergman, 2003; Markle-Reid & Browne, 2003; Sternberg, Wershof Schwartz, Karunanathan, Bergman, & Mark Clarfield, 2011). More traditional approaches to the concept describe frailty as an exclusively physical condition (presence of three or more of the following components: weight loss, low physical activity, exhaustion, slowed performance and weakness) (Fried et al., 2001), or as a result of the accumulation of multidimensional deficits (e. g. disabilities, symptoms, signs, diseases) (Rockwood & Mitnitski, 2007). On the other hand, following the more current trends in frailty definition, the recently described integral conceptual model specified frailty as dynamic pre-disability state that includes losses in physical, psychological and/or social domains (Gobbens, Luijkx, Wijnen-Sponselee, & Schols, 2010a, 2010b, 2010c).

A broader definition of frailty also involves that the factors considered as underlying a state of increased vulnerability are beyond the decline of physiological reserve and comorbidity. In fact, according to the integral conceptual model of frailty, life course determinants such as sociodemographic characteristics and lifestyle, life event and environment-related factors can influence frailty directly, besides influencing the onset of diseases which can also lead to frailty (Gobbens, Luijkx, et al., 2010c; Gobbens, van Assen, Luijkx, & Schols, 2012; Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010a). From this standpoint, as multiple circumstances may impact the onset of frailty in older persons, researchers should focus on ascertaining which elements are associated with frailty in different contexts.

This study's main objective was to analyze which determinants – described in the integral conceptual model of frailty – contribute to the prediction of frailty in general and of

each frailty domain (physical, psychological, and social), in a sample of Portuguese community dwelling individuals aged 65 years and over. Furthermore, the present study examined if a simple and objective measurement, such as assessing the number of daily-consumed medications, could help to explain frailty variance, after controlling for the effect of the determinants. It is hypothesized that a higher medication consumption is independently associated with increased frailty levels.

Materials and methods

Study Design and Participants

A cross-sectional study was designed with a non-probabilistic sample of 252 community dwelling elderly (aged 65 years and over), in three northern Portuguese cities (Maia, Porto and Vila Nova de Gaia).

Exclusion criteria were severe cognitive impairment (screened with Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975)) and being unable to speak Portuguese.

Participants were interviewed in 16 local community institutions, such as social, recreation and day care centers, as well as universities of the third age. Trained researchers conducted the personal interviews from May to September 2013, using structured questionnaires. The study was approved by institutional review boards and written informed consent was obtained.

Measurements

Frailty and determinants of frailty were assessed with the Tilburg Frailty Indicator (TFI) (Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010b), which is an operationalization of the integral conceptual model of frailty. This brief self-report questionnaire comprises two subscales (parts A and B). Part A is composed of 10 questions about determinants of frailty: sociodemographic characteristics (age, sex, marital status, nationality, level of education, income); life events in the last year (death of a loved one, serious illness, serious illness in a loved one, divorce or end of an important relationship, traffic accident, crime); assessment of how healthy the respondent's lifestyle is; satisfaction with home living environment; and presence of two or more chronic diseases. Part B measures frailty in three domains: physical (physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, hearing problems, vision problems, lack of strength in hands, and physical tiredness), psychological (cognition, depression and anxiety symptoms, and coping), and social (living alone, social relations and support). All

items are rated dichotomously (0-1), with higher scores meaning higher frailty. Scores for each frailty domain and a total frailty score (0-15) are produced. The Portuguese version of TFI (Coelho, Santos, Paúl, Gobbens, & Fernandes, 2014) was used. This tool has a good internal consistency (KR-20=0.78) and test-retest reliability ($r=0.91$) for total frailty, and there is encouraging evidence in regard to its construct and criterion validity (Coelho et al., 2014).

Medication was assessed in terms of the number of different daily-consumed drugs. In order to prevent recall bias during the interview, participants were previously asked to bring their medication or prescriptions to the interview.

Statistical Analysis

Descriptive statistical analysis was performed using proportions and measures of central tendency and dispersion, according to the nature of the variables.

Linear regressions were conducted to ascertain how each determinant predicts frailty total score/each domain. Multiple regression analysis were hierarchical, consisting of four steps: in the first one, sociodemographic characteristics and life events were entered as predictors; second, assessment of lifestyle and satisfaction with living environment; third, self-reported comorbidity; and fourth, number of daily-consumed medicines.

As in previous studies (Gobbens et al., 2012; Gobbens, van Assen, et al., 2010a), life event “serious illness in the last year” was excluded from the analysis because it overlaps with comorbidity. Likewise, marital status was not considered for the prediction of total frailty and social frailty because it is closely linked with the TFI item “living alone”. Variables that revealed low frequencies (<5%) in the descriptive analysis were excluded in the regression models.

Two-tailed tests were used throughout all analysis and a $p\text{-value}<0.05$ was considered statistically significant. All statistical analysis were conducted using IBM SPSS Statistics 22.0 (SPSS, Inc., Chicago, IL, USA).

Results

Descriptive Analysis

The mean age of the participants was 79.2 years (± 7.3), mostly women (75.8%), widowed (55.6%), and low education level (63.9%). The most common monthly household income was 251 to 500 euros (32.9%). The most shared life event (28.2%) was serious illness in a loved one, most described their lifestyle as healthy (54.4%), and were satisfied

with their home living environment (79.0%). These elderly reported the presence of two or more chronic illnesses (53.2%), and the mean number of different daily-consumed medications was 5.3 (± 3.1). The mean frailty total score was 6.0 (± 3.4), and 2.9 (± 2.2), 1.7 (± 1.1), and 1.4 (± 1.0) for the physical, psychological and social domains respectively. See table 1 for more details about the participants' characteristics.

Table 1. Characteristics of the Participants (n=252) in regard to Determinants of Frailty, Frailty, Medication

Characteristics	n (%)
Determinants of frailty (TFI part A)	
Age (years), mean $\pm$ SD	79.2 $\pm$ 7.3
65-74	68 (27.0)
75-84	116 (46.0)
≥ 85	68 (27.0)
Sex (women)	191 (75.8)
Nationality (Portuguese)	251 (99.6)
Marital status	
Married/living with partner	49 (19.4)
Unmarried	24 (9.5)
Separated/divorced	39 (15.5)
Widow/widower	140 (55.6)
Education (years), mean $\pm$ SD	4.4 $\pm$ 3.6
0	36 (14.3)
1-4	161 (63.9)
≥ 5	55 (21.9)
Monthly household income (euros)	
≤ 250	20 (7.9)
251-500	83 (32.9)
501-750	50 (19.8)
751-1000	44 (17.5)
1001-1500	25 (9.9)
1501-2000	22 (8.7)
≥ 2001	8 (3.2)
Life events	
Death of a loved one	55 (21.8)
Serious illness	56 (22.2)
Serious illness in a loved one	71 (28.2)
End of important relationship	8 (3.2)
Traffic accident	1 (0.4)
Crime	14 (5.6)
Lifestyle self-assessment	
Healthy	137 (54.4)
Not healthy, not unhealthy	92 (36.5)
Unhealthy	23 (9.1)

Satisfaction with living environment	199 (79.0)
Self-reported comorbidity	134 (53.2)
Frailty (TFI part B)	
TFI total score (0-15), mean $\pm$ SD	6.0 $\pm$ 3.4
TFI physical domain score (0-8), mean $\pm$ SD	2.9 $\pm$ 2.2
TFI psychological domain score (0-4), mean $\pm$ SD	1.7 $\pm$ 1.1
TFI social domain score (0-3), mean $\pm$ SD	1.4 $\pm$ 1.0
Medication	
Number of daily-consumed medication, mean $\pm$ SD	5.3 $\pm$ 3.1

Regression Analysis

First, due to the low percentage of non-Portuguese individuals, nationality was excluded from the regression analysis. Likewise, life events “divorce or end of important relationship” and “traffic accident” were left out. Also resulting from the descriptive analysis, the last two categories of income “1501-2000” and “ ≥ 2001 ” were regrouped in the single category “ ≥ 1501 ” before inclusion in the regression models. On the other hand, a dummy variable “cohabit” (“1” for married/living with partner and “0” for unmarried, separated/divorced and widow/widower) was created as an alternative to marital status. A dummy variable for sex was also created (“1” for women and “0” for men), and lifestyle was rated “1” for “healthy”, “2” for “not healthy, not unhealthy”, and “3” for “Unhealthy”. Preliminary analysis showed that the effects of education, income and lifestyle were linear, whereas the effects of age were both linear and quadratic. Consequently, age was squared and centered to allow the analysis of both effects on the regression models.

Table 2 presents the effects of the determinants on TFI total score and their significance in the four steps of the hierarchical regression. The first one showed that age had a quadratic effect on frailty, with the youngest and oldest participants having less frailty. Women were, on average, frailer than men, as well as those who experienced the death of a loved one in the last year. On the other hand, as monthly income increases, the degree of frailty decreases. Education and life events “serious illness in a loved one” and “crime” had no effect on frailty. A total of 17.2% of frailty was predicted in the first step. In the second step, an additional 22.9% was predicted. Unhealthy lifestyle and dissatisfaction with living environment were associated with higher frailty. By including self-reported comorbidity in the third step, 5.9% of the variance of frailty was further predicted, with the presence of comorbidity being associated with a higher degree of frailty. Finally, by adding the amount of daily-consumed medication, an additional 2.5% of frailty was predicted, while the effect of age on frailty was no longer significant. As hypothesized, a higher number of medications was associated with higher frailty levels.

Table 2. Results of Hierarchical Regression Analysis on Frailty

Determinants	Model 1			Model 2			Model 3			Model 4		
	b	95%CI	r	b	95%CI	r	b	95%CI	r	b	95%CI	r
Age												
Linear effect	0.02	-0.04; 0.08	0.03	0.02	-0.03; 0.07	0.05	0.04	-0.01; 0.09	0.08	0.04	-0.01; 0.09	0.07
Quadratic effect	-0.01**	-0.02; 0.00	0.16	-0.01*	-0.01; 0.00	-0.13	-0.01*	-0.01; 0.00	-0.10	-0.01	-0.01; 0.00	-0.08
Sex (women vs. men)	1.41**	0.46; 2.35	0.17	1.25**	0.43; 2.06	0.16	0.95*	0.17; 1.74	0.11	1.03**	0.26; 1.80	0.12
Education	-0.11	-0.24; 0.01	-0.10	-0.09	-0.20; 0.02	-0.09	-0.06	-0.16; 0.04	-0.05	-0.03	-0.14; 0.07	-0.03
Monthly household income	-0.43**	-0.71; -0.15	-0.18	-0.35**	-0.59; -0.11	-0.15	-0.31**	-0.54; -0.08	-0.13	-0.32**	-0.55; -0.10	-0.13
Life events												
Death of a loved one	1.15*	0.15; 2.14	0.13	1.01*	0.16; 1.86	0.12	1.08**	0.27; 1.90	0.13	1.05**	0.26; 1.85	0.12
Serious illness in a loved one	0.30	-0.61; 1.22	0.04	0.20	-0.58; 0.99	0.03	0.15	-0.60; 0.89	0.02	0.07	-0.66; 0.80	0.01
Crime	0.25	-1.49; 2.00	0.02	0.31	-1.18; 1.80	0.02	0.06	-1.36; 1.48	0.00	-0.02	-1.41; 1.37	-0.00
Lifestyle				1.73***	1.18; 2.28	0.31	1.48***	0.95; 2.01	0.26	1.41***	0.90; 1.93	0.25
Satisfaction living environment				-2.35***	-3.22; -1.49	-0.27	-1.96***	-2.80; -1.12	-0.22	-2.01***	-2.83; -1.19	-0.22
Self-reported comorbidity							1.82***	1.11; 2.52	0.24	1.39***	0.66; 2.12	0.17
Medication										0.20***	0.08; 0.31	0.16
ΔR^2 (%) (p-value)		17.2 (<0.001)			22.9 (<0.001)			5.9 (<0.001)			2.5 (<0.001)	

Regression coefficient (b), semi-partial correlation coefficient (r) and p-value for each determinant, and coefficient of determination change (ΔR^2) and p-value for each model.

* p<0.05. ** p<0.01. ***p<0.001.

In regard to physical frailty, a total of 45.1% of TFI physical domain score was predicted (step 1: $\Delta R^2=14.2\%$; step 2: $\Delta R^2=19.7\%$; step 3: $\Delta R^2=5.9\%$; step 4: $\Delta R^2=5.3\%$). In the last model, physical frailty was associated with age (positive linear effect), death of a loved one in the last year, unhealthy lifestyle, dissatisfaction with living environment, self-reported comorbidity and a higher amount of medication. The quadratic effect of age was no longer significant after adding lifestyle and satisfaction with living environment, whereas sex and education no longer contributed to frailty prediction after adding self-reported comorbidity. Income, serious illness in a loved one, crime and cohabitation had no effect on physical frailty.

Psychological frailty was significantly higher in women, in participants who had experienced the death of a loved one in the last year, had unhealthy lifestyle, weren't satisfied with living environment and reported comorbidity. The effect of education was only significant in the first step, whereas the contribution of age, income, cohabitation, the remainder life events and number of medications was always non-significant. A total of 25.3% of TFI psychological domain score was predicted in the first three models (step 1: $\Delta R^2=10.8\%$; step 2: $\Delta R^2=11.9\%$; step 3: $\Delta R^2=2.6\%$).

Likewise, the amount of daily-consumed medication did not contribute to the prediction of social frailty. Remarkably, neither did self-reported comorbidity. A total of 27.7% was predicted in the first two steps (step 1: $\Delta R^2=19.3\%$; step 2: $\Delta R^2=8.4\%$). Social frailty was associated with age (quadratic effect), being female, higher levels of education, lower income, lifestyle and satisfaction with living environment.

Discussion

A significant proportion of frailty was predicted by life course determinants and by comorbidity. It was also possible to ascertain that each determinant played a different role in the prediction of frailty in general and in each domain. This provides robust evidence to support the integral conceptual model of frailty. The number of daily-consumed drugs was independently associated with total and physical frailty.

The observed effect of age on frailty was complex. As in other studies (Avila-Funes et al., 2008; Collard, Boter, Schoevers, & Oude Voshaar, 2012; Gobbens, van Assen, et al., 2010a), physical frailty was associated with an increase in age. This result was expected considering the physical toll of aging (Fried et al., 2009). However, total frailty was highest in participants aged between 75 and 84 years old, mainly because of the higher social frailty observed in this group. In fact, most of the participants who lived alone were included in this

age group, possibly due to the fact that most of the younger participants still lived with their spouses, and that many older and widowed individuals lived with younger family members in order to receive the support needed to overcome their physical impairments. Nonetheless, the fact that age was no longer significant in frailty prediction after adding medication to the regression analysis, indicates that other determinants, including comorbidity, better explain the variance of frailty.

Similarly to previous research (Collard et al., 2012; Puts, Lips, & Deeg, 2005; Song, Mitnitski, & Rockwood, 2010), women were frailer than men. It has been shown that elderly men have a greater likelihood of dying suddenly, while women more often show a steady progressive decline, associated with an increase in morbidity (Puts et al., 2005). This fact can explain the present findings, including why the sex-based difference in physical frailty disappeared after controlling for comorbidity.

As expected (Avila-Funes et al., 2008; Fried et al., 2001; Woo, Goggins, Sham, & Ho, 2005), frailty was also associated with lower income. On the other hand, education had a remarkably positive linear effect on the social frailty domain. This result was surprising considering that in previous research the association of education with frailty was either non-significant (Garcia-Garcia et al., 2011; Gobbens, van Assen, et al., 2010a), or negative (Barreto Pde, Greig, & Ferrandez, 2012; Fried et al., 2001; Woo et al., 2005), with lower education levels predicting higher frailty. The present finding may be explained by different views and expectations of social support and relationship quality, from individuals with distinct education levels.

Death of a loved one was the only life event associated with frailty. Considering the well-documented physical and psychological impact of bereavement (Stroebe, Schut, & Stroebe, 2007), it is understandable that this event could lead to frailty. Concomitantly, unhealthier lifestyle and dissatisfaction with living environment predicted frailty in general and in each domain. This provides further evidence of the previously described importance of health-related behavior (Avila-Funes et al., 2008; Fried et al., 2009; Gobbens, van Assen, et al., 2010a) and environmental factors (Bergman et al., 2007; Hogan et al., 2003; Markle-Reid & Browne, 2003) in precipitating frailty.

Self-reported comorbidity, as in previous research (Gobbens, van Assen, et al., 2010a), predicted frailty in general, as well as physical and psychological frailty. Most authors agree that comorbidity can lead to the onset of frailty (Bergman et al., 2007; Fried et al., 2009; Morley et al., 2013). Nonetheless, as described in other studies (Kriegsman, Penninx, van Eijk, Boeke, & Deeg, 1996), assessing comorbidity through self-report may be susceptible to bias, mainly because of its dependence on the participants' insight regarding chronic disease. Consequently, as it is directly linked with the amount of comorbidities, the assessment of the number of daily-consumed drugs might have been a more precise

indicator of the participants' health status. Moreover considering that self-reported comorbidity was rated dichotomously (yes/no), to assess the amount of consumed medicines leads to a more accurate view of the heterogeneity of the participants' comorbidity burden.

In fact, as hypothesized, the assessment of medication allowed the prediction of an additional variance of frailty, mainly because of the higher physical frailty of individuals who take greater levels of medication. It can be discussed that assessing medication, a less subjective measure than self-reported comorbidity, was associated with the less subjective domain of frailty. Nonetheless, one should consider that these findings may also be linked with the adverse outcomes of poly medication and its association with frailty (Gnjidic, Hilmer, Blyth, Naganathan, Cumming, et al., 2012; Gnjidic, Hilmer, Blyth, Naganathan, Waite, et al., 2012).

The main strengths of the present study are the statistical procedures used, the reinforcement of the current evidence supporting the multidimensional definition of frailty and of its predictors, and the findings in regard to increasing the prediction of frailty with an objective, easy to execute, assessment of medication. It is also the first study to analyze the determinants considered in the integral conceptual model of frailty in elderly individuals from a southern European country. Some limitations of this study should be noted. First, the non-probabilistic sampling method could have limited these findings namely in regard to generalization. Furthermore, correlation coefficient values were somewhat low, possibly due to the small sample size. Also, the cross-sectional design does not allow the examination of the temporal continuum between determinants, comorbidity and frailty, in order to conclude causality. Finally, the self-report nature of TFI can be considered a limitation because of the inherent subjectivity. Nonetheless, TFI items correlated as expected with corresponding standardized measures in previous research (Coelho et al., 2014; Gobbens, van Assen, et al., 2010b).

Several directions for future research can be suggested. Longitudinal studies should be conducted to better examine how life course determinants and comorbidity predict frailty in the short, medium and long term. Also, further studies should focus on the association of comorbidity and medications with the psychological and social domains of frailty. Likewise, the association between level of education and each frailty domain should be thoroughly analyzed, especially considering the findings of this study in regard to social frailty.

In conclusion, this research provides important information about which factors may precipitate states of high vulnerability in the present elderly sample. Furthermore, the added value of a brief assessment of medication was significant, and should be considered as supplementary to TFI. These findings should be taken into account for more effective

identification of frailty, and to implement timely and targeted interventions in order to treat this syndrome and prevent adverse outcomes.

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Conflict of interest statement

Authors declare no conflict of interest.

Author contributions

TC, CP and LF designed the study. TC was responsible for data collection, carried out the statistical analysis, and drafted the paper. CP and LF supervised the whole research and assisted with interpreting data and writing the article. RG provided advice and aided in the preparation of the final manuscript. All authors reviewed and provided valuable contributions to the whole manuscript.

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3.3. Multidimensional frailty and pain in community dwelling elderly

Autores: Tiago Coelho, Constança Paúl, Robbert J. J. Gobbens, Lia Fernandes

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Abstract

Objective. To examine the relationship between frailty and pain, particularly to analyze whether pain predicts physical, psychological and social frailty, after controlling for the effects of life-course determinants and comorbidity.

Design. Cross-sectional.

Methods. A non-probabilistic sample of 252 community dwelling elderly was recruited. Frailty and determinants of frailty were assessed with the Tilburg Frailty Indicator and pain was measured with the Pain Impact Questionnaire. Hierarchical regression analysis was conducted.

Results. In this study, 52.4% of the participants were aged 80 years and over, and 75.8% were women. Pain and frailty were higher in women, and physical frailty was higher in those aged ≥ 80 years. Greater pain was associated with higher frailty levels. After controlling for the effects of the determinants and comorbidity, pain predicted 5.8% of the variance of frailty, 5.9% of the variance of physical frailty, and 4.0% of the variance of psychological frailty, while the prediction of social frailty was non-significant.

Conclusion. Frailty was independently predicted by pain, emphasizing the importance of its treatment, contributing for the prevention of vulnerability, dependency and mortality. Nonetheless, longitudinal studies are required in order to better understand the association between pain and frailty.

Key words: Elderly, frailty, pain.

Introduction

Frailty is the term used in geriatrics to describe a clinical syndrome in which the individual is in a state of increased vulnerability to stressors, which entails a high risk of adverse outcomes, such as functional deterioration, hospitalization, institutionalization and death [1-5]. Although it is generally recognized that the prevalence of frailty increases with age, particularly affecting persons older than 80 years, the precise prevalence rates depend of the definition of frailty [4, 6]. In fact, there are different approaches regarding the specific components of frailty [7-10]. The presence of exclusively physical manifestations (weight loss, low physical activity, exhaustion, slowed performance and weakness) that constitute the Frailty Phenotype [11], and the accumulation of various deficits (e. g. disabilities, symptoms, signs, diseases) that create a Frailty Index [2], are the most popular approaches. Currently, some definitions of frailty tend to include psychological and social components in addition to physical components, and exclude disability as part of frailty [1, 7, 8, 12, 13].

Frailty can occur as the result of the interplay between a significantly diminished physiological capacity, life-course determinants and medical conditions [5, 14, 15]. These conditions, particularly chronic illnesses such as cancer and osteoarticular diseases, are likewise documented as an evident source of pain in the elderly [16, 17]. In fact, pain is also highly prevalent in older populations, and its interference with everyday life increases significantly with age [18-20]. Furthermore, if untreated, pain may have a severe impact on the physical, psychological and social domains of functioning [17, 21-24]. Therefore, it seems reasonable to hypothesize that pain and frailty may be linked, particularly that pain, in older individuals who most likely already suffer from chronic illness, can expand their vulnerability and lead to frailty situations.

To our knowledge, Blyth *et al.* [25] published the first study focused on specifically examining the relationship between frailty and pain, and found that those already frail (with ≥ 3 components of the Frailty Phenotype) were more likely to report pain. Since then, several studies have corroborated the hypothesis of frailty being positively associated with pain [26-29]. Although the direction of the association has not yet been established, the hypothesis of pain diminishing the physiological reserves needed to maintain homeostasis when faced with biological, psychological or social stressors, and precipitating frailty, proposed by Shega *et al.* [29] based on the concept of pain homeostenosis [30], seems to be well supported.

Considering the conceptualized relationship between pain and frailty, and that in previous research, frailty has only been measured according to more traditional approaches to the concept (as a physical syndrome/Frailty Phenotype or as a result of the accumulation

of deficits/Frailty Index), undervaluing the importance of psychosocial components, the present study aims to examine whether pain predicts multidimensional frailty (physical, psychological and social) in a sample of community dwelling elderly individuals.

Methods

Study design and sample

A cross-sectional study was designed using a non-probabilistic sample of 252 elderly persons from the district of Porto, Portugal. The participants were community dwellers aged 65 years and over. Individuals who were unable to speak Portuguese, or with severe cognitive impairment (screened with the Mini Mental State Examination [31]), were excluded due to the self-report nature of the measures used.

Participants were interviewed in 16 local community institutions, such as social, recreation and day care centers, as well as universities of the third age. Data collection was carried out from May to September 2013 by trained researchers. The study was approved by the institutional reviewer board and all participants gave their written informed consent.

Measures

Frailty and determinants of frailty were assessed with the Tilburg Frailty Indicator (TFI) [32]. The TFI is an operationalization of the Integral Conceptual Model of Frailty [12, 33-35], which defines it as a dynamic pre-disability state resulting from losses in physical, psychological and/or social domains. It consists of a brief self-report screening questionnaire divided in two subscales. The first subscale (10 items) assesses the determinants of frailty proposed in the model: sociodemographic characteristics (age, gender, marital status, ethnicity, level of education, income); life events in the last year (death of a loved one, serious illness, serious illness in a loved one, divorce or end of an important relationship, traffic accident, crime); assessment of how healthy the respondent's lifestyle is; satisfaction with their home environment; and the presence of two or more chronic diseases. The second subscale (15 items) measures physical frailty (physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, hearing problems, vision problems, lack of strength in hands, and physical tiredness), psychological frailty (cognition, depression and anxiety symptoms and coping), and social frailty (living alone, social relations and social support). All items are rated dichotomously (0-1), and scores for each frailty domain and a total frailty score are produced. Higher scores

refer to higher frailty. In the present study, the Portuguese version of TFI [36] was used (internal consistency = 0.78).

Pain was measured with the Pain Impact Questionnaire (PIQ-6) [37]. PIQ-6 is a brief (6-item) self-report questionnaire, rated with 6 or 5 point Likert scales. It measures the presence/severity of pain (1 item), and its impact on functional status (3 items) and emotional well-being (2 items), within a 4-week recall period. The total score is calculated by a conversion of the scores of each item and by the sum of the weighted responses, ranging from 40-78 points. A higher impact of pain translates into higher scores. The Portuguese version of PIQ-6 [38] was used (internal consistency = 0.92).

Statistical analysis

Descriptive statistical analysis was performed using proportions and measures of central tendency and dispersion, according to the variables' nature. Independent sample t-tests were performed to compare frailty and pain, according to age and gender. Hierarchical regression analysis were conducted in order to ascertain whether pain (independent variable) predicted frailty in general and each frailty domain (dependent variables), after controlling for the effect of determinants of frailty (covariates) in frailty variance. Age, gender, marital status, ethnicity, level of education, income, life events, lifestyle, living environment and comorbidity were included in the first step of the regression, and pain in the second, for each frailty score. As in previous studies [35, 39], life event "serious illness in the last year" was excluded from the analysis because it overlaps with comorbidity. Likewise, marital status was not considered for the prediction of total frailty and social frailty because it is closely linked with the TFI item "living alone". Two-tailed tests were used throughout all analysis and a p-value <0.05 was considered statistically significant. All statistical analysis were conducted using IBM SPSS Statistics 22.0 (SPSS, Inc., Chicago, IL, USA).

Results

In the present study, 52.4% of the participants were aged 80 years and over (mean=79.2±7.3), and 75.8% were women. Most of the individuals were Portuguese (99.6%), widowed (55.6%), and had ≤4 years of education (78.2%) and low (≤500 euros) household income (40.9%). Serious illness of a loved one, serious illness and death of a loved one were the most often reported life events (28.2%, 22.2% and 21.8%, respectively). In the sample, 54.4% described their lifestyle as healthy, 79.0% were satisfied with their

living environment, and 53.2% reported the presence of two or more chronic illnesses. The mean pain impact score was 53.8 (± 10.7). The mean frailty total score was 6.0 (± 3.4), and 2.9 (± 2.2), 1.7 (± 1.1), and 1.4 (± 1.0) for physical, psychological and social frailty respectively.

There were statistically significant differences between participants aged 65-79 years and those aged ≥ 80 years in physical frailty scores, although not in psychological, social and total frailty, and in pain. On the other hand, there were significant differences between men and women in regard to total frailty, physical frailty, psychological frailty, social frailty, and pain. Frailty and pain impact was higher in women. See Table 1 for additional details regarding t-test results.

Table 1: Results of t-tests and descriptive statistics of frailty and pain scores by age group and gender

Measure	Age group				95%CI for Mean Difference	t	df
	65-79 years		≥80 years				
	M	SD	M	SD			
Frailty	5.6	3.6	6.4	3.3	-1.7, 0.0	-1.94	250
Physical frailty	2.5	2.3	3.2	2.2	-1.3, -0.2	-2.55*	250
Psychological frailty	1.6	1.1	1.8	1.1	-0.4, 0.1	-1.07	250
Social frailty	1.4	1.0	1.4	1.0	-0.2, 0.3	0.16	250
Pain impact	53.1	11.0	54.4	10.5	-4.0, 1.3	-1.01	250
	Gender						
	Men		Women				
Frailty	4.8	3.2	6.4	3.4	-2.6, -0.7	-3.30**	250
Physical frailty	2.3	2.1	3.1	2.2	-1.4, -0.1	-2.34*	250
Psychological frailty	1.4	1.1	1.8	1.1	-0.8, -0.2	-3.01**	250
Social frailty	1.1	1.0	1.5	1.0	-0.7, -0.1	-2.76**	250
Pain impact	48.1	9.1	55.6	10.6	-10.4, -4.5	-4.95***	250

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Regarding the regression analysis, variables that revealed low frequencies ($< 5\%$) were excluded: ethnicity (due to the low percentage of non-Portuguese individuals) and life events “divorce or end of important relationship” and “traffic accident”. A dummy variable “cohabit” (“1” for married/living with partner and “0” for unmarried, separated/divorced and widow/widower) was created as an alternative to marital status. Gender was rated “1” for women and “0” for men, while lifestyle was rated “1” for “healthy”, “2” for “not healthy, not unhealthy”, and “3” for “Unhealthy”.

The results of the regression indicated that after controlling for the effects of determinants of frailty, pain predicted 5.8% of the variance of frailty, 5.9% of the variance of physical frailty, and 4.0% of the variance of psychological frailty, while the prediction of

social frailty was non-significant. Regression coefficients indicate that an increase in pain impact would imply an increase in frailty scores. See Table 2 for additional details regarding the regression analysis.

Table 2: Hierarchical regression of life-course determinants and comorbidity (step 1), and pain (step 2), predicting total frailty, physical frailty, psychological frailty, and social frailty.

Step	Frailty				
	ΔR^2	ΔF	df	b	95%CI
Step 1: determinants^a	0.460	18.59***	(11, 240)	-	-
Step 2: pain	0.058	28.92***	(1, 239)	0.09	0.06; 0.13
Physical frailty					
Step 1: determinants^b	0.398	13.15***	(12, 239)	-	-
Step 2: pain	0.059	25.77***	(1, 238)	0.06	0.04; 0.09
Psychological frailty					
Step 1: determinants^b	0.253	6.76***	(12, 239)	-	-
Step 2: pain	0.040	13.32***	(1, 238)	0.02	0.01; 0.04
Social frailty					
Step 1: determinants^a	0.287	8.78***	(11, 240)	-	-
Step 2: pain	0.005	1.59	(1, 239)	0.01	0.00; 0.02

^a Age, gender, education, income, life events (death of a loved one, serious illness in a loved one and crime), lifestyle, living environment and comorbidity.

^b Age, gender, cohabitation, education, income, life events (death of a loved one, serious illness in a loved one and crime), lifestyle, living environment and comorbidity.

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Discussion

More severe pain with interference in daily life and well-being was independently associated with higher frailty, particularly with physical and psychological frailty. Although the present study cannot explain the causal direction of this association, these findings provide important evidence to support the hypothesis that pain can precipitate and/or worsen frailty in elderly populations.

The present study strengthens the current body of evidence regarding the relationship between frailty and pain, for two major reasons: first, a well-validated 6-item tool, the PIQ-6 [37], was used to measure the severity of pain and its impact within a 4-week recall period, while in previous studies a single question was used to assess either the severity of pain (e.g. "How much bodily pain have you had during the past 4 weeks?" [26, 29]), or its interference with function (e.g. "During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)" [25]). The

second reason underlined that in previous studies frailty was assessed as a whole (with individuals being categorized as frail, pre-frail and not frail), and considered exclusively as a physical condition [25, 27, 28] or as an accumulation of deficits mainly related to function and comorbidity [26, 29], in this study it was shown that pain has a different association with the overall scores of distinct domains of frailty: physical, psychological and social.

Particularly, the present study showed that pain could predict physical frailty. This can be explained by the well-documented impact of pain on physical function. In fact, pain has been connected with mobility limitations, fatigue, and decreased nutritional intake [24, 40-42], which are components of physical frailty, or directly linked to them. Evidence also shows that pain can lead to sleep disturbances [17, 23, 24, 42], which in turn have been associated with higher physical frailty [43, 44].

This study also demonstrated that pain independently predicts psychological frailty. This was expected considering the robust evidence supporting the complex bi-directional relationship between psychological factors and pain [22, 45, 46]. Previous research provides evidence of fewer complaints of pain in elderly individuals with good coping strategies and without depression [22]. On the other hand, some authors highlight that persistent pain can precipitate anxiety and depressive symptoms, as well as cognitive dysfunction [17, 18, 22, 47].

Finally, the present study found no association between pain and the components of social frailty (living alone, missing having people around, and not receiving enough social support), although some authors state that persistent pain can have a negative effect on socialization [22]. The social impact of pain, while certainly related to its physical and psychological consequences, seems therefore less evident. In fact, a previous study shows that there are no significant differences in the social networks of elderly whether or not they are in pain [42].

The evidence provided by this study highlights the importance of the effective treatment of pain in order to prevent, attenuate or reverse frailty in the elderly. There is a vast array of pharmacological and nonpharmacological strategies that contribute to the relief of pain, particularly when individually tailored after a comprehensive assessment of the patient [22, 48]. The most common strategy employed is the prescription of analgesic drugs (nonopioids, opioids and adjuvant drugs) [22]. There is some evidence of the usefulness of other medications in pain management, such as vitamin D supplement [17, 21], which is also considered to have a positive effect on physical frailty [4]. On the other hand, effective nonpharmacological approaches are reckoned to be adequate, including physical and occupational therapy, cognitive behavioral therapy and patient and caregiver education programs [21, 22, 29].

The main strengths of the present study are the robust statistical procedures performed, and the bolstering of the current evidence supporting the association between pain and frailty, especially by analyzing its relationship to each domain of frailty and measuring it precisely. Nonetheless, some limitations should be noted. First, the non-probabilistic sampling method could limit the generalization of the findings. Second, the cross-sectional design does not allow the examination of the causality between frailty and pain. Third, pain was not categorized as persistent or acute, since it was measured only over a 4-week recall period (persistent pain is only present when the painful sensation lasts for at least 3 months [21]). Considering the potentially cumulative impact of persistent pain over time, the association with frailty could have been different.

Future research including longitudinal studies will be needed in order to determine the causality between frailty and pain. The influence of the duration of the painful experience on frailty and each domain, its social impact as well as its association with the physical and psychological consequences of persistent pain, should also be examined.

In conclusion, this research provides significant evidence to support the importance of the assessment and management of pain to prevent frailty in the elderly.

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3.4. Frailty as a predictor of short-term adverse outcomes

Autores: Tiago Coelho, Constança Paúl, Robbert J. J. Gobbens, Lia Fernandes

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Abstract

Objectives: To compare how different frailty measures (Frailty Phenotype/FP, Groningen Frailty Indicator/GFI and Tilburg Frailty Indicator/TFI) predict short-term adverse outcomes. Secondly, adopting a multidimensional approach to frailty (integral conceptual model – TFI), this study aims to compare how physical, psychological and social frailty predict the outcomes. **Design:** Longitudinal study. **Setting:** Community. **Participants:** 95 elderly individuals (≥ 65 years). **Measurements:** Participants were assessed at baseline for frailty, determinants of frailty, and adverse outcomes (healthcare utilization, quality of life, disability in basic and instrumental activities of daily living/ADL and IADL). Ten months later the outcomes were assessed again. **Results:** The participants' mean age was 78.5 ± 6.2 years, and most were women (67.4%). Frailty was associated with specific healthcare utilization indicators: the FP with a greater utilization of informal care; GFI with an increased contact with healthcare professionals; and TFI with a higher amount of contacts with a general practitioner. After controlling for the effect of life-course determinants, comorbidity and adverse outcome at baseline, GFI predicted IADL disability and TFI predicted quality of life. The effect of the FP on the outcomes was not significant, when compared with the other measures. However, when comparing TFI's domains, the physical domain was the most significant predictor of the outcomes, even explaining part of the variance of ADL disability. **Conclusions:** Frailty at baseline was associated with adverse outcomes at follow-up. However, the relationship of each frailty measure (FP, GFI and TFI) with the outcomes was different. In spite of the role of psychological frailty, TFI's physical domain was the determinant factor for predicting disability and most of the quality of life. **Key words:** Frailty; Adverse outcomes; Frailty Phenotype; Groningen Frailty Indicator; Tilburg Frailty Indicator.

Introduction

As the number of elderly people increases worldwide, so does the prevalence of frailty.^{1, 2} This geriatric syndrome, particularly common in individuals older than 80 years, entails an increased risk of clinically significant adverse outcomes.³⁻⁵ Frail individuals are highly vulnerable, and minor stressful events can cause disability, institutionalization, hospitalization or even death.^{2-4, 6} Therefore, screening for frailty in the contexts of primary and community healthcare is fundamental to ensure the dignity and quality of life of older persons.^{2, 3}

There are different approaches regarding the conceptualization and operationalization of frailty.^{3, 6-8} The assessment based on the presence of the components that make up the Frailty Phenotype/FP⁹ (unintentional weight loss, low physical activity, exhaustion, slow walking speed and weakness) has gained wide attention in the scientific community.^{8, 10-12} This approach stems from a biological model, in which frailty is defined as an exclusively physical condition, caused by energy dysregulation and functional decline across multiple physiological systems.^{9, 13}

On the other hand, some authors argue that psychosocial factors can also increment vulnerability and lead to frailty.^{4, 10, 14, 15} Furthermore, a biopsychosocial approach of a clinical syndrome such as frailty is more in line with the definition of health as physical, psychological and social well-being.^{6, 14, 16} Consequently, multidimensional measures, such as the Groningen Frailty Indicator/GFI^{17, 18} and the Tilburg Frailty Indicator/TFI,¹⁹ have been developed as alternatives to the traditional physical operationalization. However, GFI and TFI present different pictures of frailty. In fact, while GFI includes functional performance/disability as components of the syndrome, in the integral conceptual model^{16, 20-22} (on which TFI is based) disability is regarded as a potential outcome of frailty. The clear distinction between frailty and disability is in consonance with a growing consensus in regard to frailty conceptualization.^{10, 23, 24}

Considering that there are different frailty measures, and that the prevention of frailty and its' adverse effects is of the utmost importance from a social and public health perspective, research should focus on ascertaining which measures are most effective in detecting the syndrome and predicting outcomes in different populations.^{2, 6, 25, 26} Therefore, the present study aims to compare how three well-known³ tools (the FP, GFI and TFI) predict short-term adverse outcomes in a sample of community-dwelling elderly, particularly by analyzing whether the measures are associated with greater healthcare utilization and disability, and lower quality of life, in a 10-month follow-up. Additionally, assuming a multidimensional approach to frailty inherent to Gobbens *et al.*²¹ integral conceptual model,

the secondary objective of this study is to examine which TFI's domain (physical, psychological or social) is the most significant predictor of disability and quality of life. This model was chosen to assess frailty domains because it results from a recent and an exhaustive research^{16, 21, 22}. Furthermore, studies have shown that TFI has a good predictive validity,^{20, 27, 28} and better psychometric properties than other multidimensional frailty questionnaires.^{25, 29}

Methods

Sample

From May to September 2013, a non-probabilistic sample of 252 community-dwelling elderly individuals (aged 65 years and over) was recruited from three northern Portuguese cities (Maia, Porto, V.N. Gaia). Exclusion criteria were severe cognitive impairment (screened with Mini Mental State Examination³⁰) and inability to speak Portuguese, due to the self-report nature of most measures. The participants, users of local community institutions (e.g. social, recreation and day care centers), were interviewed by nine trained researchers. Among other measurements, the individuals were assessed for life-course determinants of frailty, comorbidity, frailty and adverse outcomes (disability, quality of life and healthcare utilization). In 2014, 10 months later, the first 118 participants (47%), who lived in V.N. Gaia, were selected for a follow-up assessment, regarding the same adverse outcomes. From this group, only 95 individuals (38%) were included in the present study. After the first assessment, two participants died, five were admitted to a nursing home, two were hospitalized, one was ineligible due to severe cognitive impairment (severe dementia), nine could not be contacted, and four refused to participate. The follow-up interviews were conducted by three of the researchers that performed the first assessment. The study was approved by institutional review boards and written informed consent was obtained.

Measures

Part A of TFI^{19, 31} was used to assess life-course determinants of frailty and comorbidity, while the FP,⁹ GFI^{17, 18, 32} and part B of TFI^{19, 31} were used to measure frailty. Disability in activities of daily living/ADL and in instrumental activities of daily living/IADL were measured with the Barthel Index^{33, 34} and with the Lawton and Brody Scale,^{35, 36} respectively. Finally, quality of life was evaluated with EUROHIS-QOL-8^{37, 38} and WHOQOL-OLD,^{39, 40} whereas healthcare utilization was assessed with a set of questions previously used in other studies.^{19, 20, 27, 28, 31}

TFI consists of a self-report questionnaire divided into two parts. Part A (10 items) assesses determinants of frailty: sociodemographic characteristics (age, gender, marital status, ethnicity/nationality, education, income); life events in the last year (death of a loved one, serious illness, serious illness in a loved one, divorce or end of an important relationship, traffic accident, crime); assessment of how healthy the respondent's lifestyle is; satisfaction with home living environment; and presence of two or more chronic diseases. Part B (15 items) measures physical frailty (physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, hearing problems, vision problems, lack of strength in hands, and physical tiredness), psychological frailty (cognition/memory, depression and anxiety symptoms, and coping), and social frailty (living alone, social relations and support). All items are rated dichotomously (0-1), and scores for each frailty domain and a total frailty score are produced. Higher scores refer to higher frailty, and the Portuguese version³¹ has a cut-off of 6.

GFI is also a questionnaire that aims to measure frailty in different domains: physical (difficulties in shopping, walking around outside, dressing and undressing, and going to the toilet, vision problems, and consumption of four or more medicines), cognition (complaints about memory), psychological (depressed mood and feelings of anxiety), and social (three items about emotional isolation). The Portuguese version³² has only 12 items, excluding three items from the original (physical fitness, hearing problems and weight loss). As for TFI, all items are rated dichotomously and scores refer to higher frailty. A cut-off point of 5 was considered.³²

In regard to the assessment of the FP, unintentional weight loss was considered if the participant answered "yes" to TFI's question 12 "Have you lost a lot of weight recently without wishing to do so?". Low physical activity and exhaustion were detected using two questions based on previous studies.⁴¹ Slow walking speed was detected if the participant took more than 20 seconds to complete the Timed Up and Go/TUG test.⁴² Weakness was identified if the participant's hand strength was below the cut-off determined by Fried *et al.*⁹ stratified by gender and BMI. In this regard, a GRIP-D Takei Hand Grip Dynamometer was used and a standardized approach for assessing hand strength was considered.⁴³ Frailty was identified if the participant had ≥ 3 components, and pre-frailty if one or two components were present.

The Barthel Index (10 items) and the Lawton and Brody Scale (8 items) are measures widely used to assess ADL and IADL disability, respectively, and, in both cases, lower scores refer to higher dependence. Regarding quality of life, the EUROHIS-QOL-8 is an 8-item generic assessment instrument and the WHOQOL-OLD is a more extensive tool, of which the Portuguese version³⁹ has 28 items distributed by 7 facets: sensory abilities; autonomy; past, present and future activities; social participation; death and dying; intimacy;

family/family life. In both measures, higher scores indicate better quality of life. Finally, healthcare utilization was assessed in regard to the last year and with items regarding: contact with a general practitioner and with other healthcare professionals, hospitalization and different care support (professional personal, nursing, informal and in other healthcare or residential institutions). All answers were dichotomous (yes/no), except for contact with a general practitioner (0, 1-2, 3-4, 5-6 or ≥ 7 contacts). This item was later dichotomized for statistical analysis, and only ≥ 5 contacts were considered.

Statistical Analysis

Data is described using proportions, mean values and standard deviations, according to the nature of the variables. Independent samples t-test, chi-square test and Fisher's exact test were used to compare the baseline characteristics (determinants of frailty, frailty, disability, quality of life, and healthcare utilization) of participants interviewed in the follow-up with those not reassessed. The comparison of the adverse outcomes at baseline and 10 months later was performed using paired samples t-test and McNemar test. The association between healthcare utilization reported at follow-up with frailty at baseline was examined with chi-square test or Fisher's exact test. Hierarchical regressions were conducted to analyze whether frailty at baseline predicted quality of life and disability in ADL and IADL at the 10-month reassessment, while controlling for the effect of life-course determinants, comorbidity and the same adverse outcome at baseline. Life-course determinants and comorbidity were included in the first step of the regression, and the same adverse outcome at baseline in the second. For these steps, the "enter" method was used. Variables that revealed low frequencies ($<5\%$) were not included, neither was the life event serious illness because it overlaps comorbidity.^{27, 44} Dummy variables were created for gender, marital status and life events. Lifestyle was classified as healthy (1), not healthy, not unhealthy (2) and unhealthy (3). The baseline scores of each frailty measure were included in the third step (step 3a). The "stepwise" method was used in order to ascertain which frailty measure improved prediction of the outcomes. The same procedure was used to examine which frailty domain improved the prediction of adverse outcomes at follow-up. In this case, while the first two steps were similar to the previous analysis, the third step (step 3b) consisted of including the scores obtained by TFI regarding physical, psychological and social frailty. Two-tailed tests were used throughout all analysis and a $p\text{-value} < 0.05$ was considered statistically significant. All statistical analysis were conducted using IBM SPSS Statistics 22.0 (SPSS, Inc., Chicago, IL, USA).

Results

There were no statistically significant differences between the individuals reassessed at follow-up and those who were not, except for gender and mean education years (Table 1). At baseline, the mean age of the participants (n=95) was 78.5 years (± 6.2). Most of them were women (67.4%), widowed (55.8%) and with a low educational level (0-4 years: 68.4%). The prevalence of frailty in this group ranged from 29.5% (detected with the FP) to 48.4% (measured with GFI and TFI).

Table 1. Baseline characteristics (life course-determinants, self-reported comorbidity and frailty) of the individuals that were reassessed at follow-up and those who weren't.

	Participants		P-value
	Assessed at follow-up (n=95)	Not assessed at follow-up (n=157)	
Life-course determinants and comorbidity	n (%)	n (%)	
Age (years), mean $\pm$ SD	78.5 $\pm$ 6.2	79.6 $\pm$ 7.9	0.22 ^a
65-74	24 (25.3)	44 (28.0)	
75-84	52 (54.7)	64 (40.8)	0.07 ^b
≥ 85	19 (20.0)	49 (31.2)	
Gender (women)	64 (67.4)	127 (80.9)	<0.05 ^b
Nationality (Portuguese)	95 (100)	156 (99.4)	1.00 ^c
Marital status			
Married/living with partner	23 (24.2)	16 (16.6)	
Unmarried	9 (9.5)	15 (9.6)	0.24 ^b
Separated/divorced	10 (10.5)	29 (18.5)	
Widow/widower	53 (55.8)	87 (55.4)	
Education (years), mean $\pm$ SD	3.6 $\pm$ 2.6	4.9 $\pm$ 4.1	<0.01 ^a
0	15 (15.8)	21 (13.4)	
1-4	65 (68.4)	96 (61.1)	0.19 ^b
≥ 5	15 (15.8)	40 (25.5)	
Monthly household income (euros)			
≤ 500	48 (40.0)	65 (41.4)	
501-750	28 (29.5)	22 (14.0)	0.09 ^b
≥ 751	14 (30.5)	70 (44.6)	
Life events			
Death of a loved one	15 (15.8)	40 (25.5)	0.07 ^b
Serious illness	25 (26.3)	31 (19.7)	0.22 ^b
Serious illness in a loved one	29 (30.5)	42 (26.8)	0.52 ^b
End of important relationship	3 (3.2)	5 (3.2)	1.00 ^c
Traffic accident	1 (1.1)	0 (0.0)	0.38 ^c
Crime	6 (6.3)	8 (5.1)	0.68 ^b

Lifestyle self-assessment			
Healthy	59 (62.1)	78 (49.7)	
Not healthy, not unhealthy	30 (31.6)	62 (39.5)	0.13 ^b
Unhealthy	6 (6.3)	17 (10.8)	
Satisfaction with living environment	78 (82.1)	121 (77.1)	0.34 ^b
Self-reported comorbidity	49 (51.6)	85 (54.1)	0.69 ^b
Frailty			
TFI total score (0-15), mean ± SD	5.6 ± 3.5	6.2 ± 3.4	0.18 ^a
≥6 (Frailty)	46 (48.4)	92 (58.6)	0.12 ^b
TFI physical domain score (0-8), mean ± SD	2.7 ± 2.2	3.0 ± 2.2	0.19 ^a
TFI psychological domain score (0-4), mean ± SD	1.6 ± 1.1	1.8 ± 1.1	0.14 ^a
TFI social domain score (0-3), mean ± SD	1.4 ± 1.1	1.4 ± 1.0	0.90 ^a
GFI (0-12), mean ± SD	4.4 ± 2.4	4.7 ± 2.8	0.31 ^a
≥5 (Frailty)	46 (48.4)	86 (54.8)	0.33 ^b
FP, mean ± SD	1.8 ± 1.3	2.1 ± 1.4	0.09 ^a
0 (Non-frailty/robustness)	15 (15.8)	24 (15.3)	
1-2 (Pre-frailty)	52 (54.7)	69 (43.9)	0.17 ^b
≥3 (Frailty)	28 (29.5)	64 (40.8)	

^a Independent samples t-test; ^b Chi-square test; ^c Fisher's exact test.

Regarding the comparison of the outcomes at baseline and at follow-up, only IADL disability, the autonomy facet of quality of life and three indicators of healthcare utilization (contact with healthcare professionals, hospitalization and nursing care) showed significant differences (Table 2).

Table 2. Adverse outcomes at baseline and 10 months after

Outcome	Baseline		Follow-up		Δ (difference)		P-value ^a
	M	SD	M	SD	M	SD	
Quality of life							
EUROHIS-QOL-8	27.7	4.8	27.4	4.7	-0.4	4.1	0.40
WHOQOL-OLD	99.2	16.1	99.2	15.3	0.0	9.4	1.00
Sensory Abilities	15.6	4.0	16.1	3.6	0.5	3.3	0.12
Autonomy	14.1	3.2	14.9	3.0	0.8	2.9	<0.05
Past, Present and Future Activities	13.5	3.9	13.2	2.7	-0.2	2.7	0.42
Social Participation	15.0	2.9	14.8	2.8	-0.3	2.5	0.27
Death and Dying	12.6	4.5	13.1	4.1	0.4	3.9	0.31
Intimacy	13.4	4.0	12.6	4.1	-0.8	4.2	0.08
Family/Family life	15.0	4.0	14.5	3.5	-0.4	2.6	0.10
ADL disability							
Barthel Index	19.2	1.3	19.0	1.4	-0.2	1.4	0.23

IADL disability

Lawton and Brody Scale	18.0	5.2	15.1	6.4	-2.9	3.7	<0.001
	n	%	n	%	%		P-value^b
Healthcare utilization							
Contact with general practitioner (≥5)	17	17.9	11	11.6	-6.3		0.21
Contact with healthcare professionals	69	72.6	55	57.9	-14.7		<0.05
Hospitalization	24	25.3	11	11.6	-13.6		<0.01
Professional personal care	9	9.5	6	6.3	-3.2		0.55
Nursing care	29	30.5	10	10.5	-20.0		<0.001
Informal care	19	20.0	19	20.0	0.0		1.00
Other healthcare/residential institutions	10	10.5	4	4.2	-6.3		0.11

^a Paired samples t-test; ^b McNemar test.

There was a significant relationship between being classified as frail at baseline and indicators of healthcare utilization at follow-up (Table 3). Each measure of frailty was associated with one specific indicator: the FP with a greater utilization of informal care; GFI with increased contact with healthcare professionals; and TFI with a greater contact with a general practitioner.

Table 3. Frailty and healthcare utilization.

Healthcare utilization		FP		P-value	GFI		P-value*	TFI		P-value
		Non-frail	Frail		Non-frail	Frail		Non-frail	Frail	
		n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
Contact with general practitioner (≥5)	Yes	8 (72.7)	3 (27.3)	1.00 ^b	4 (36.4)	7 (63.6)	0.28 ^a	2 (18.2)	9 (81.8)	<0.05 ^a
	No	59 (70.2)	25 (29.8)		45 (53.6)	39 (46.4)		47 (56.0)	37 (44.0)	
Contact with healthcare professionals	Yes	39 (70.9)	16 (29.1)	0.92 ^a	22 (40.0)	33 (60.0)	<0.01 ^a	24 (43.6)	31 (56.4)	0.07 ^a
	No	28 (70.0)	12 (30.0)		27 (67.5)	13 (32.5)		25 (62.5)	15 (37.5)	
Hospitalization	Yes	6 (54.5)	5 (45.5)	0.29 ^b	3 (27.3)	8 (72.7)	0.08 ^a	3 (27.3)	8 (72.7)	0.09 ^a
	No	61 (72.6)	23 (27.4)		46 (54.8)	38 (45.2)		46 (54.8)	38 (45.2)	
Professional personal care	Yes	3 (50.0)	3 (50.0)	0.36 ^b	2 (33.3)	4 (66.7)	0.43 ^b	2 (33.3)	4 (66.7)	0.36 ^b
	No	64 (71.9)	25 (28.1)		47 (52.8)	42 (47.2)		47 (52.8)	42 (47.2)	
Nursing care	Yes	6 (60.0)	4 (40.0)	0.47 ^b	6 (60.0)	4 (40.0)	0.74 ^b	4 (40.0)	6 (60.0)	0.52 ^b
	No	61 (71.8)	24 (28.2)		43 (50.6)	42 (49.4)		45 (52.9)	40 (47.1)	
Informal care	Yes	7 (36.8)	12 (63.2)	<0.001 ^a	7 (36.8)	12 (63.2)	0.15 ^a	7 (36.8)	12 (63.2)	0.15 ^a
	No	60 (78.9)	16 (21.1)		42 (55.3)	34 (44.7)		42 (55.3)	34 (44.7)	

Other healthcare/ residential institutions	Yes	2 (50.0)	2 (50.0)	0.58 ^b	2 (50.0)	2 (50.0)	1.00 ^b	1 (25.0)	3 (75.0)	0.35 ^b
	No	65 (71.4)	26 (28.6)		47 (51.6)	44 (48.4)		48 (52.7)	43 (47.3)	

^a Chi-square test; ^b Fisher's exact test.

Regarding the regression analysis (Table 4) ethnicity/nationality was not included because all participants were Portuguese. Life events: divorce or end of an important relationship and traffic accidents, were also excluded because of their low frequency.

Frailty measures explained from 29.3% to 73.4% of the variances of the disability and quality of life scores. After controlling for the effect of life-course determinants, comorbidity and the same adverse outcome at baseline, the TFI was most often selected as the measure that better predicted the outcomes. After the TFI was inserted in the regression models, an additional 4.4% of quality of life variance (measured by EUROHIS-QOL-8) and 2.4% (measured by WHOQOL-OLD), was explained. The TFI also predicted three quality of life (WHOQOL-OLD) facets: sensory abilities (3.3%), intimacy (4.4%) and family/family life (4.4%). On the other hand, GFI was the measure that most significantly increased the prediction of IADL disability (1.4%) and two quality of life facets: past, present and future activities (8.6%) and social participation (7.2%). The effect of the FP on the outcomes was not significant, when compared to the other measures. Concomitantly, neither of the frailty measures predicted ADL disability and quality of life facets: autonomy, and death and dying. In summary, an increment in frailty was associated with a decrease in quality of life and an increase in disability.

When comparing TFI's frailty domains, physical frailty contributed to the prediction of most of the adverse outcomes: ADL disability (3.3%), IADL disability (2.2%), global quality of life (EUROHIS-QOL-8: 4.7%; WHOQOL-OLD: 2.9%) and quality of life facets: sensory abilities (4.5%), social participation (5.6%), death and dying (3.0%) and family/family life (2.8%). On the other hand, TFI's psychological domain predicted past, present and future activities (7.2%) and intimacy (4.0%), whereas the effect of social frailty was not significant.

Table 4. Prediction of outcomes (disability and quality of life) in a 10-month follow-up by life-course determinants and comorbidity (step 1), by the same outcome at baseline (step 2), by the Frailty Phenotype/FP, Groningen Frailty Indicator/GFI and the Tilburg Frailty Indicator/TFI (step 3a), and by physical, psychological and social frailty measured by TFI (step 3b).

Predictors	Barthel Index	Lawton and Brody Scale	EUROHIS-QOL-8	WHOQOL-OLD							
				Total	Sensory Abilities	Autonomy	Past, Present and Future Activities	Social Participation	Death and Dying	Intimacy	Family/Family life
Step 1 (enter)											
Age (years)	-0.06*	-0.26*	0.12	0.17	-0.05	0.00	0.08	0.04	-0.12	0.07	0.16*
Gender (women/men)	-0.41	-0.67	0.68	0.49	0.25	-0.11	0.45	0.22	-0.56	-0.68	0.92
Education (years)	-0.05	0.05	0.25	0.15	0.16	0.16	-0.02	-0.12	-0.09	-0.05	0.10
Marital status (married/unmarried) ^a	-0.21	-2.65	-0.01	1.64	0.08	-1.01	0.09	0.03	-1.11	2.85*	0.76
Household income	0.12	-0.53	-0.33	0.29	0.27	0.06	0.16	0.05	0.04	-0.19	-0.09
Life events (yes/no) ^b	-0.13	0.00	-0.84	-1.34	-0.20	-0.68	-0.38	-0.34	-0.54	-0.09	0.89
Lifestyle self-assessment	-0.08	-1.01	-2.15**	-9.24***	-0.88	-1.99***	-1.01*	-1.21*	-1.79*	-0.74	-1.64**
Satisfaction living environment (yes/no)	-0.33	-2.35	1.52	8.80*	1.36	0.27	1.60*	1.01	1.00	2.47*	1.04
Self-reported comorbidity (yes/no)	-0.18	1.45	-2.33*	-0.03	-0.13	0.60	0.06	0.19	-1.35	0.51	0.08
ΔR ² (%)	9.8	17.0	24.9**	22.0**	8.5	17.3	18.7*	13.7	15.7	18.2*	21.5*
Step 2 (enter)											
Outcome at baseline	0.51***	1.00***	0.53***	0.82***	0.58***	0.51***	0.43***	0.62***	0.49***	0.41***	0.70***
ΔR ²	19.5***	55.0***	21.4***	47.2***	33.9***	22.8***	17.1***	28.6***	22.7***	12.5***	41.1***
Step 3a (stepwise)											
FP	-	-	-	-	-	-	-	-	-	-	-
GFI	-	-0.39*	-	-	-	-	-0.39***	-0.39***	-	-	-
TFI	-	-	-0.42**	-1.09**	-0.29*	-	-	-	-	-0.32*	-0.27**
ΔR ² (%)	-	1.4*	4.4**	2.4**	3.3*	-	8.6***	7.2***	-	4.4*	4.4**
R ² (%) total	29.3***	73.4***	50.7***	71.5***	45.7***	40.1***	44.4***	49.5***	38.4***	35.2***	66.9***
Step 3b (stepwise)											
Physical frailty	-0.15*	-0.55**	-0.60**	-1.65**	-0.49	-	-	-0.38**	-0.39*	-	-0.32*
Psychological frailty	-	-	-	-	-	-	-0.79**	-	-	-0.87*	-
Social frailty	-	-	-	-	-	-	-	-	-	-	-
ΔR ² (%)	3.3*	2.2**	4.7**	2.9**	4.5**	-	7.2**	5.6**	3.0*	4.0*	2.8*
R ² (%) total	32.6***	74.2***	51.0***	72.1***	46.9***	40.1***	42.9***	47.8***	41.4***	34.8***	65.4***

^a Marital status ("1" for married/living with partner and "0" for unmarried, separated/divorced and widow/widower); ^b Life events ("1" for death and/or serious illness in a loved one, and "0" for absence of these life events).

Regression coefficients (b) are displayed. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Discussion

In general, frailty at baseline was associated with the adverse outcomes at follow-up. The TFI predicted global quality of life, the GFI predicted disability, while the FP was not relevant after controlling for comorbidity and the remaining frailty measures. On the other hand, when comparing TFI's frailty domains, physical frailty was the most significant predictor of the outcomes, even explaining part of the variance of ADL disability.

As described by Rockwood⁴⁵, a successful operationalization of frailty, among other factors, implies that it is easy to use in a busy clinical setting, and allows the prediction of adverse outcomes. From this standpoint, the assessment of the FP is immediately at disadvantage, as it seems less practical than administering GFI or TFI, due to requiring the measurement of grip strength and gait speed.^{7, 11} Furthermore, in the present study, despite being associated with increased utilization of informal care, the FP's contribution to the prediction of disability and quality of life was inferior when compared with the other measures. This does not mean that the FP would not be able to predict outcomes in different time periods (i.e. medium and-long term), or other adverse outcomes. In fact, several studies^{9, 46-49} have shown that it predicts outcomes such as falls, disability, hospitalization and mortality, in different time frames. The present study shows that multidimensional measures of frailty assessment were better predictors of the selected outcomes in a 10-month follow-up than an exclusively physical one. This may be related not only to the components of the GFI and the TFI, but also to the amplitude of their scores, since measures with continuous scores seem to discriminate better between frail and non-frail individuals.^{2, 11, 50}

Indeed, besides being associated with increased contact with healthcare professionals, the GFI explained the variance of IADL disability. However, the fact that its contribution to the prediction of disability is greater than the other measures (which is consistent with another study⁵¹) may simply be justified by the inclusion of four disability related questions in the GFI itself. Nevertheless, there is some evidence⁷ that by including the assessment of comorbidity there is a relevant increase in the prediction of disability. Moreover the GFI comprises a question about the consumption of four or more medicines, which is directly related to the presence of multiple diseases. On the other hand, the TFI was associated with a greater contact with a general practitioner and independently predicted global quality of life, which is consistent with previous studies.^{20, 27, 28, 52, 53} The prediction of an intricate concept such as quality of life emphasizes the relevance of a holistic definition of frailty and of the TFI's components.^{52, 53}

In regard to the comparison of TFI's frailty domains, similarly to prior research,^{20, 27, 28, 52, 53} the physical domain provided the most important contribution for the explanation of the variance of the adverse outcomes. Nevertheless, while it has been previously observed^{20, 28, 52, 53} that the TFI's psychological and social domains also predicted disability and quality of life, in the present study, only the contribution of psychological frailty was significant, as it was independently associated with two quality of life facets. These results highlight the relevance of physical factors, but also the importance of including at least psychological components in the definition of frailty.

On the other hand, it should be emphasized that the TFI's physical domain explained ADL disability and the death and dying facet of quality of life, whereas other global frailty measures were unable to do so. First, this may suggest that the components of the TFI's physical domain circumscribed physical frailty more precisely than the FP's components (i.e. the components of the FP might have been insufficient to predict the outcomes). Second, it may indicate that the TFI's psychological and/or social domains include items that were detrimental to the prediction of these specific outcomes. Nonetheless, the fact that, in some cases, the contribution of the TFI's psychological domain was more important than the physical one, and that in previous studies^{20, 28, 52, 53} the social domain explained some of the outcomes' variance, justify TFI's multidimensional structure.

The main strengths of the present study are related to its longitudinal design and to the fact that the prediction of disability and quality of life was examined after controlling for the effect of life-course determinants, comorbidity and the same adverse outcome at baseline. Nonetheless, some limitations should be noted. First, the non-probabilistic sampling method could limit the generalization of results. Second, the relatively small sample size limited the analysis of the prediction of dichotomous variables such as the healthcare utilization indicators, after adjusting for baseline characteristics, as it was done for scale scores (disability and quality of life). Third, outcomes were only assessed through self-report, which in part might explain why they were mainly associated with the exclusively self-report measures (to the detriment of the FP, which included objective measurements). Finally, the selected operationalization of the FP was different from other studies^{7, 9, 41}, which limits the comparability of the results. Furthermore, the hand strength cut-off points used were based on the original study regarding the FP.

Several directions for future research can be suggested. Studies should focus on examining the prediction of outcomes in different time frames (medium and long-term). Other outcomes such as falls, institutionalization and mortality should also be analyzed. Likewise, the association between physical, psychological and social frailty components and different adverse outcomes should be better examined in order to improve the understanding of the multidimensional nature of frailty.

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Disclosure statement

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4. Discussão e conclusão

O presente estudo visou analisar a aplicabilidade e pertinência do modelo integral de fragilidade no contexto português, procurando, acima de tudo, contribuir para a compreensão do constructo de fragilidade e das suas implicações clínicas.

Em Portugal, a fragilidade não faz parte do vocabulário de muitos prestadores de cuidados de saúde/sociais a idosos, existindo ainda, poucas publicações sobre o tema. Para além disso, não há planos de ação especificamente estruturados para a identificação de fragilidade a nível comunitário e dos cuidados de saúde primários, nem programas de prevenção e intervenção estruturados com base em conceptualizações contemporâneas de fragilidade. Assim, a importância deste trabalho é salientada, especialmente por ter permitido a adaptação e validação do TFI, de forma estandardizada e obedecendo às linhas orientadoras internacionalmente definidas para a investigação neste âmbito.

O facto de a versão portuguesa do TFI ser fiável, válida e de fácil aplicação, evidencia, por sua vez, a possibilidade de operacionalizar o modelo integral de fragilidade neste contexto. Contudo, enquanto se pode apontar como limitação a esta ferramenta a não avaliação dos resultados adversos de fragilidade, existem vários instrumentos estandardizados e validados – igualmente de fácil utilização – que permitem complementar o TFI neste âmbito. Adicionalmente, a aplicabilidade deste modelo conceptual no contexto português é reforçada pelo facto de se terem observado as relações principais previstas no modelo, entre determinantes, fragilidade e *outcomes*. Com efeito, foi possível verificar que os determinantes explicaram uma parcela significativa da fragilidade exibida pelos idosos, enquanto níveis superiores de fragilidade foram responsáveis por piores *outcomes*.

Concomitantemente, a pertinência desta conceptualização e consequente operacionalização de fragilidade não reside apenas no pressuposto teórico de uma avaliação biopsicossocial corresponder a uma abordagem mais holística, permitindo que sejam desenvolvidas intervenções focadas no(s) domínio(s) do funcionamento humano onde se verificam perdas que aumentam a vulnerabilidade individual. Tal como foi possível observar através do presente estudo, a importância deste modelo é igualmente destacada através de dados empíricos, que devem ser tidos em consideração para o planeamento de cuidados de saúde e sociais. Neste âmbito destaca-se, especialmente, a particular associação de fragilidade, medida através do TFI, com o declínio da qualidade de vida e com um maior número de contactos com o médico de família.

Por outro lado, considerando o papel principal do domínio físico do TFI para a predição de resultados adversos, seria possível colocar em causa a relevância da divisão de fragilidade em três domínios. Contudo, tendo em conta que as variáveis que podem

estar na base de um aumento da vulnerabilidade física, psicológica e social são distintas, o cariz multidimensional desta definição de fragilidade é justificado. Efetivamente, a compreensão dos fatores que podem precipitar situações de risco a diferentes níveis é fundamental para o desenvolvimento de programas preventivos.

Finalmente, importa salientar que o presente trabalho teve pontos fortes e fracos, devidamente identificados em cada um dos estudos que o constitui. Destes, merecem particular destaque, respetivamente, o cariz inovador do estudo (por ser a primeira investigação em Portugal a estudar o modelo integral de fragilidade e a utilizar o TFI) e o reduzido tamanho amostral (que impossibilita a generalização dos resultados obtidos à população idosa portuguesa).

Paralelamente, são sugeridos trabalhos futuros, especialmente relacionados com o estudo da natureza psicológica e social da síndrome de fragilidade, assim como com o acompanhamento longitudinal dos idosos. A continuação da investigação relacionada com a fragilidade será fundamental para definir com precisão as medidas necessárias para promover a sua prevenção e dos seus resultados adversos, nos mais variados contextos. Este aspeto será fundamental para garantir que o aumento da longevidade é acompanhado pelo incremento do número de anos em que é possível viver com dignidade e qualidade de vida.

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Anexos

Anexo I: *Description of the additional measures used to examine the construct and criterion validity of the Portuguese version of the Tilburg Frailty Indicator*

Anexo II: *English version of Tilburg Frailty Indicator*

Anexo III: *Versão portuguesa do Tilburg Frailty Indicator*

Description of the additional measures used to examine the construct and criterion validity of the Portuguese version of the Tilburg Frailty Indicator (TFI)

To examine the construct validity of the Portuguese version of TFI, other measures of physical, psychological, and social frailty components were used. Physical measures included Body Mass Index (BMI), Timed Up and Go (TUG) test, hand grip strength, and center of pressure (COP) sway analysis, psychological measures encompassed Mini Mental State Examination (MMSE), Geriatric Depression Scale (GDS), Geriatric Anxiety Inventory (GAI), while Social Support Satisfaction Scale (SSSS) was used as a social measure.

The BMI is an indicator of nutritional status and it is calculated by dividing weight in kilograms by the square of height in meters. The TUG test assesses mobility by measuring the time it takes a person to get up from a chair, walk three meters at their usual pace and return to the chair and sit down again. Performances exceeding 10 seconds are usually considered to indicate some mobility impairment, while performances over 20 seconds typically show evident mobility limitations and some dependence of gait aids and/or personal assistance. Hand grip strength was assessed with a GRIP-D Takei Hand Grip Dynamometer (T.K.K. 5401, Takei Scientific Instruments Co., LTD, Tokyo, Japan), measuring strength three times per hand, alternating side between measurements, with the participant sitting comfortably, and using the highest value obtained. COP sway, which reflects the trajectory of the center of mass and the magnitude of force applied at the support surface to control body-mass acceleration, is usually measured to assess postural control and balance. COP sway was analyzed with a pressure platform (Emed-AT25 D, Novel Inc., Munich, Germany), which contains 4000 capacitive sensors within a sensing area of 380x240 mm² (sensor resolution of two sensors/cm²), and has a 25 Hz recording frequency. Participants were asked to stand 60 seconds on the platform, barefoot and in a self-selected comfortable upright position. The subjects were asked to execute the task twice, one with their eyes open, looking directly at a target placed two meters away at the height of the participants' eyes, and another with their eyes closed. The order in which the test was performed was random to avoid possible fatigue and learning effect and, considering that balance in this position depends on the base of support area, all parameters correlated with TFI domains were first normalized by a projection of that area, which was calculated after measuring the distance between the lateral borders of the feet and their length, as detected by the platform. The COP sway parameters measured for this study were maximum sway velocity and maximum sway range in medial/lateral (COPX) and

anterior/posterior (COPY) axis, and they were analyzed based on the most stable 30 second period of each test. It was considered that lower values in regard to COP sway would represent a better ability to maintain balance. MMSE assesses different cognitive domains (i.e. spatial and time orientation, memory, attention and calculation, and language) and allows for the detection of cognitive deficit with cut-off for different education levels: ≤ 22 for 0-2 years of literacy; ≤ 24 for 3-6 years; and ≤ 27 for ≥ 7 years. In regard to GDS, which is a scale specifically used to identify depression in older persons, the 15-item version was used, which has a cut-off of 5. GAI is a 20-item scale that measures anxiety in older adults and the presence of severe anxiety symptoms was considered if the participant scored ≥ 9 . The SSSS evaluates perception of social support in 15 questions, specifically related with satisfaction with friends and family, intimacy and social activities. Higher scores translate a better satisfaction with social support.

To study the criterion validity of this version of TFI, frailty was also identified through alternative frailty specific measures: the Groningen Frailty Indicator (GFI) and an operationalization of the frailty phenotype. Adverse outcomes (disability and health care utilization) and quality of life were equally assessed for the same purpose.

GFI allows for a multidimensional assessment of frailty (including disability), and its Portuguese version has 12 items and a cut-off point of 5. In regard to frailty phenotype components: unintentional weight loss was considered if the participant answered “yes” to TFI question 12 “Have you lost a lot of weight recently without wishing to do so? (‘a lot’ is: 6 kg or more during the last six months, or 3 kg or more during the last month)”. Low physical activity was detected if the participant answered “one to three times a month” or “hardly ever or never” to the question “How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car/house, or going for a walk?”. Exhaustion was identified if the participant answered “yes” to the question “In the last month, have you had too little energy to do things you wanted to do?”. Slow walking speed was detected if the participant took more than 20 seconds to complete the TUG (if the participant wasn’t able to perform TUG due to mobility limitations, they were considered to have a slow walking speed). Weakness was identified if the participant’s hand grip strength was below the previously established cut-off, stratified by sex and BMI. Frailty was identified if the participant had at least three of the components, and pre-frailty if one or two components were present.

Disability in activities of daily living was measured with the Barthel Index and in instrumental activities of daily living with the Lawton and Brody Scale. Higher scores in both scales reflect total independence, and lower scores show some degree of dependence. Healthcare utilization was assessed regarding only to the last year. These items comprised: contact with general practitioner; contact with other healthcare professionals;

hospitalization; professional personal care; nursing care; informal care; and receiving care in other healthcare or residential care institutions. All answers were dichotomous (yes/no), except for contact with general practitioner, in which the participants could specify if they had none, 1-2, 3-4, 5-6 or ≥ 7 contacts. Nonetheless, this item was later dichotomized for statistical analysis, and only ≥ 5 contacts were considered.

Quality of life was assessed with EUROHIS-QOL-8, which is an 8-item generic assessment of quality of life, and WHOQOL-OLD, which is a more extensive instrument with several facets. The WHOQOL-OLD experimental Portuguese version used in this research had 28 items and comprised 7 facets: sensory abilities; autonomy; past, present and future activities; social participation; death and dying; intimacy; family/family life. In both measures, higher scores indicate better quality of life.

English version of Tilburg Frailty Indicator (TFI) *

Gobbens, R. J., van Assen, M. A., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). The Tilburg Frailty Indicator: psychometric properties. *J Am Med Dir Assoc*, 11(5), 344-355. doi: 10.1016/j.jamda.2009.11.003

Part A Determinants of frailty

1. Which sex are you?

☐ male ☐ female

2. What is your age?

..... years

3. What is your marital status?

☐ married/living with partner

☐ unmarried

☐ separated/divorced

☐ widow/widower

4. In which country were you born?

☐ The Netherlands

☐ Former Dutch East Indies

☐ Suriname

☐ Netherlands Antilles

☐ Turkey

☐ Morocco

☐ Other, namely.....

5. What is the highest level of education you have completed?

☐ none or primary education

☐ secondary education

☐ higher professional or university education

6. Which category indicates your net monthly household income?

☐ €600 or less

☐ €601 - €900

☐ €901 - €1200

☐ €1201 - €1500

☐ €1501 - €1800

☐ €1801 - €2100

☐ €2101 or more

7. Overall, how healthy would you say your lifestyle is?

0 healthy

0 not healthy, not unhealthy

0 unhealthy

8. Do you have two or more diseases and/or chronic disorders?

0 yes 0 no

9. Have you experienced one or more of the following events during the past year?

- the death of a loved one 0 yes 0 no

- a serious illness yourself 0 yes 0 no

- a serious illness in a loved one 0 yes 0 no

- a divorce or ending of an important intimate relationship 0 yes 0 no

- a traffic accident 0 yes 0 no

- a crime 0 yes 0 no

10. Are you satisfied with your home living environment?

0 yes 0 no

Part B Components of frailty

B1 Physical components

11. Do you feel physically healthy?

0 yes 0 no

12. Have you lost a lot of weight recently without wishing to do so? ('a lot' is: 6 kg or more during the last six months, or 3 kg or more during the last month)

0 yes 0 no

Do you experience problems in your daily life due to:

13. difficulty in walking?

0 yes 0 no

14. difficulty maintaining your balance?

0 yes 0 no

15. poor hearing?

0 yes 0 no

16. poor vision?

0 yes 0 no

17. lack of strength in your hands?

0 yes 0 no

18. physical tiredness?

0 yes 0 no

B2 Psychological components

19. Do you have problems with your memory?

0 yes 0 sometimes 0 no

20. Have you felt down during the last month?

0 yes 0 sometimes 0 no

21. Have you felt nervous or anxious during the last month?

0 yes 0 sometimes 0 no

22. Are you able to cope with problems well?

0 yes 0 no

B3 Social components

23. Do you live alone?

0 yes 0 no

24. Do you sometimes miss having people around you?

0 yes 0 sometimes 0 no

25. Do you receive enough support from other people?

0 yes 0 no

* The TFI was translated into English using the method of back-translation

Scoring Part B Components of frailty (range: 0 – 15)

Question 11: yes = 0, no = 1

Question 12 – 18: no = 0, yes = 1

Question 19: no and sometimes = 0, yes = 1

Question 20 and 21: no = 0, yes and sometimes = 1

Question 22: yes = 0, no = 1

Question 23: no = 0, yes = 1

Question 24: no = 0, yes and sometimes = 1

Question 25: yes = 0, no = 1

Cutpoint: 5

Versão portuguesa do *Tilburg Frailty Indicator* (TFI)

Coelho, T., Santos, R., Paúl, C., Gobbens, R. J. J., & Fernandes, L. (2014). Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation. *Geriatr Gerontol Int*, n/a-n/a. doi: 10.1111/ggi.12373

Parte A: Determinantes de fragilidade

1. Qual é o seu sexo?

☐ masculino ☐ feminino

2. Qual é a sua idade?

_____ anos

3. Qual é o seu estado civil?

☐ casado(a)/vive com um parceiro(a)

☐ separado(a)/divorciado(a)

☐ solteiro(a)

☐ viúvo(a)

4. Em que país nasceu?

5. Quantos anos de escolaridade completou?

_____ anos

6. Em que categoria inclui o rendimento mensal do seu agregado familiar?

☐ 250€ ou menos

☐ 501€ a 750€

☐ 1001€ a 1500€

☐ 2001€

☐ 251€ a 500€

☐ 751€ a 1000€

☐ 1501€ a 2000€

ou mais

7. Globalmente, em que medida diria que o seu estilo de vida é saudável?

☐ Saudável

☐ nem muito nem pouco saudável

☐ não saudável

8. Tem duas ou mais doenças e/ou perturbações crónicas?

☐ sim ☐ não

9. Aconteceu-lhe uma ou mais das seguintes situações durante o ano passado?

- a morte de uma pessoa querida ☐ sim ☐ não

- uma doença grave em si próprio ☐ sim ☐ não

- uma doença grave numa pessoa querida ☐ sim ☐ não

- um divórcio ou o fim de uma relação íntima importante ☐ sim ☐ não

- um acidente de viação ☐ sim ☐ não

- um crime ☐ sim ☐ não

10. Está satisfeito com o ambiente em sua casa?

☐ sim ☐ não

Parte B: Componentes de fragilidade

B1: Componentes físicos

11. Sente-se fisicamente saudável?	☐ sim ☐ não
12. Perdeu muito peso recentemente sem desejar fazê-lo? ('muito' é: 6 kg ou mais, durante os últimos seis meses, ou 3 kg ou mais, durante o último mês)	☐ sim ☐ não
Tem problemas na sua vida diária devido a:	
13. dificuldade em andar?	☐ sim ☐ não
14. dificuldade em manter o seu equilíbrio?	☐ sim ☐ não
15. dificuldade de audição?	☐ sim ☐ não
16. dificuldade de visão?	☐ sim ☐ não
17. falta de força nas suas mãos?	☐ sim ☐ não
18. cansaço físico?	☐ sim ☐ não
B2: Componentes psicológicos	
19. Tem problemas com a sua memória?	☐ sim ☐ por vezes ☐ não
20. Tem-se sentido em baixo durante o ultimo mês?	☐ sim ☐ por vezes ☐ não
21. Tem-se sentido nervoso ou ansioso durante o ultimo mês?	☐ sim ☐ por vezes ☐ não
22. É capaz de lidar bem com os problemas?	☐ sim ☐ não
B3: Componentes Sociais	
23. Vive sozinho?	☐ sim ☐ não
24. Por vezes, sente falta de ter pessoas à sua volta?	☐ sim ☐ por vezes ☐ não
25. Recebe suficiente apoio de outras pessoas?	☐ sim ☐ não

Pontuação da Parte B: Componentes de fragilidade (varia: 0 – 15)	
Questão 11: sim = 0, não = 1 Questão 12 – 18: não = 0, sim = 1 Questão 19: não e por vezes = 0, sim = 1 Questão 20 e 21: não = 0, sim e por vezes = 1	Questão 22: sim = 0, não = 1 Questão 23: não = 0, sim = 1 Questão 24: não = 0, sim e por vezes = 1 Questão 25: sim = 0, não = 1
Pontuação final: _____ Pontuação B1 (domínio físico): _____	Pontuação B2 (domínio psicológico): _____ Pontuação B3 (domínio social): _____

Ponto de corte: 6