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Detection of frailty in elderly cancer patients: Improvement of the G8 screening test

Aurélie Petit-Monéger[a,b,c,*], Muriel Rainfray[c,d], Pierre Soubeyran[c,e], Carine A. Bellera[a,b], Simone Mathoulin-Pélissier[a,b,c]

[a]Clinical and Epidemiological Research Unit, Institut Bergonié, Comprehensive Cancer Centre, 229 cours de l'Argonne, F-33000 Bordeaux, France
[b]INSERM, ISPED, Centre INSERM U897-Epidemiologie-Biostatistique, Clinical Epidemiology and Clinical Investigation Centre CIC-1401, Clinical Epidemiology Module, F-33000 Bordeaux, France
[c]Bordeaux University, 146 rue Léo Saignat, F-33000 Bordeaux, France
[d]Department of Clinical Gerontology, Bordeaux University Hospital, F-33604 Pessac, France
[e]Department of Medical Oncology, Institut Bergonié, Comprehensive Cancer Centre, 229 cours de l'Argonne, F-33000 Bordeaux, France

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ABSTRACT

Objective: The G8 is a screening test to identify frail elderly patients with cancer. Objectives were to design and evaluate the performance of alternative tests taking into account other predictive domains for frailty.

Methods: We conducted a literature review to identify predictive factors of frailty. Using a Delphi consensus, we collected 24 European experts' opinions to validate the most relevant items to improve the G8. Alternative tests were created and performance assessed on a development population (ONCODAGE cohort). The highest performing test was compared to the G8, and validated through both an internal and an external population validation (Aquitaine Geriatric Oncology cohort).

Results: The study population consisted of 1435 patients (ONCODAGE cohort) and 364 patients (Aquitaine Geriatric Oncology cohort). Twenty-three experts validated two items with a strong consensus (>75%): modification of the threshold for the G8 polypharmacy item to six drugs per day and replacement of the G8 item on neuropsychological problems by four Instrumental Activities of Daily Living (IADL) items predictive of incident dementia, creating three modified G8 tests (addition of either item, or both). Only the G8 IADL-modified test had better performance than the G8 when tested on the ONCODAGE cohort: sensitivity = 77%, specificity = 67%. This test was validated on the internal (sensitivity = 78%, specificity = 71%) and external (sensitivity = 88%, specificity = 69%) validation populations.

* Corresponding author at: Bordeaux University, 146 rue Léo Saignat, F-33000 Bordeaux, France. Tel.: +33 5 57 57 13 93; fax: +33 5 56 93 05 72.
E-mail addresses: aurelie.petit-moneger@isped.u-bordeaux2.fr (A. Petit-Monéger), muriel.rainfray@chu-bordeaux.fr (M. Rainfray), p.soubeyran@bordeaux.unicancer.fr (P. Soubeyran), c.bellera@bordeaux.unicancer.fr (C.A. Bellera), s.mathoulin@bordeaux.unicancer.fr (S. Mathoulin-Pélissier).

Conclusion: Adding the four IADL items improves the performance of the G8. We have developed and validated a G8-modified test that is more specific than the G8 to detect frail elderly, while still sensitive and feasible in less than 10 min.

1. Introduction

The risk of cancer increases with age and 55% of new cancer cases are diagnosed in patients over 65 years.[1] Although elderly patients are a heterogeneous population, they are often excluded from clinical trials due to restrictive inclusion criteria.[2,3] Chronological age is not sufficient to characterize the heterogeneity of the elderly, and it is important to identify frail patients who need an adapted treatment plan.[4]

Frailty is a clinical syndrome representing a state of reduced homeostasis and stress resistance, together with an increase of vulnerability of patients and the risk of adverse events such as falls, disability, hospitalization or death.[5] Cancers and their treatment represent potential stressors that reduce physiological reserves and frailty is particularly relevant to the elderly with cancer. This clinical syndrome is potentially reversible, which justifies the need for early detection and treatment in elderly patients with cancer.

Van Iersel et al. estimated the prevalence of frailty ranged from 36% to 88% depending on the definition of frailty used in a population of elderly hospitalized patients.[6] However, there is currently no consensus regarding the definition of frailty.[7] In 2005, the International Society of Geriatric Oncology (SIOG) recommended that geriatric assessment of older patients with cancer should include, at least, functional status, cognitive status and mood assessments[8]; other authors suggested that criteria on aspects that could lead to a drop in physiological reserves such as mood, cognitive state and biological markers should be included.[9–11] Rodriguez-Manas et al. conducted an international modified Delphi process to develop a concrete definition of frailty.[11] However, additional work is needed to identify the specific combination of clinical and laboratory biomarkers that can be used for the diagnosis of frailty.

The Comprehensive Geriatric Assessment (CGA) has demonstrated its value for elderly patients with cancer[12,13] and there is a strong consensus of the SIOG and geriatric oncology experts to recommend any geriatric assessment in elderly patients with cancer.[14,15] However, the classic CGA is time- and resource-consuming and as such is not feasible for every patient. This justifies to develop a rapid geriatric screening test to detect frail elderly patients with cancer for whom the classic CGA will be more strongly relevant.[16] To date, research has been focused on the development of rapid geriatric screening tests to identify elderly patients for standard cancer treatment[17–24] and frail elderly patients are required to undergo a CGA to establish a treatment plan best suited to their health status.[23] The SIOG recommended a baseline assessment to be carried out in two stages for elderly patients with cancer[8]: the first step involves a rapid geriatric screening test to identify frail elderly patients for whom standard treatment is not suitable, and in case of a positive test, the second step is to provide a CGA to determine the most appropriate treatment plan.[23,24]

Several rapid geriatric screening tests that take only a few minutes to complete have been developed,[23] including the Vulnerable Elders Survey (VES-13)[25] and the G8.[26] The validation of the G8 in the ONCODAGE study showed a good sensitivity (primary outcome) but only moderate specificity.[27] Even if these results compare favorably to the other screening tests,[28] there is a necessity to develop more accurate and rapid geriatric screening tests.[29,30]

Some studies reported that oncogeriatric screening tests should integrate frailty markers to improve performance: (i) mobility disorders such as history of falls, an alteration of the Timed Get Up and Go (TGUG) test, or low physical activity[31]; (ii) patients' medical history (such as polypharmacy[32] or comorbidities[33]) or socio-economic conditions (such as social support or adequate financial resources[34]).

The main objective of this study was to design alternative G8 tests based on a literature review and a Delphi consensus, and then to evaluate the performance of these alternative tests taking into account other domains associated with frailty to identify patients requiring CGA. Secondary objectives were to compare classification performances (sensitivity and specificity) of the highest performing alternative test to the original G8, and to conduct internal and external validations.

2. Materials and Methods

2.1. Proposition of Alternative G8 Tests

2.1.1. Literature Review
A literature review was conducted to identify factors of frailty. We identified 810 articles published between 2002 and 2012 using the following Medline algorithm: (*"neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields]) OR "oncology"[All Fields]) AND ("geriatric assessment"[All Fields] OR "frail elderly") AND ("2002/09/10"[PDAT]: "2012/09/30"[PDAT] AND (English[lang] OR French[lang]))*. Thirty two articles were selected for full text reading. Two were discarded — one published as an abstract only and one as a letter to the editor (Appendix A). The thirty articles that were included in the literature review are listed in (Appendix B).

Twelve potential factors related to medical history, social conditions, or dependence of patients were identified as important to detect frailty by the study's steering committee (APM, MR, PS, CB and SMP) (Table 1). We did not retain biological factors, comorbidity items using a comorbidity scale, and the TGUG, as the inclusion of these items would not allow us to carry out the test in less than ten minutes.

2.1.2. Delphi Consensus
As per recommended practices,[35] a Delphi process[36,37] in three rounds was set up to validate the 12 items that could be included in an alternative G8 to potentially improve performance (Appendix C). These items could be items to add to the G8, or G8 items to modify, delete or replace. During each of the