ACTA ONCOLOGICA, 2016
VOL. 55, NO. 5, 644–646
http://dx.doi.org/10.3109/0284186X.2015.1096022

Taylor & Francis
Taylor & Francis Group

LETTER TO THE EDITOR

Frailty Index and Frailty Phenotype in elderly patients with cancer

Floor J. van Deudekom[1], Marijke van de Ruitenbeek[2], Wilma te Water[3], Jitty M. Smit[2] and Barbara C. van Munster[3,4]

[1]Department of Geriatric Medicine, Slotervaartziekenhuis, The Netherlands, [2]Department of Internal Medicine, Gelre Hospitals Apeldoorn, The Netherlands, [3]Department of Geriatric Medicine, Gelre Hospitals Apeldoorn, The Netherlands, and [4]Department of Internal and Geriatric Medicine, University Medical Center, Groningen, The Netherlands.

Dear Editor,

With the population ageing and improved medical care, there are an increasing number of elderly patients with cancer. In Europe and the USA 60% of all cancers are diagnosed in patients over 65 years of age and this amount is expected to rise up to 70% in the next 30 years [1,2]. Due to the heterogeneity within the elderly population, with its variation in physiological reserves, comorbidity and geriatric conditions, differences in (side) effects of therapy can be expected. Therefore, tailoring of care is needed, based on a thorough evaluation of the patient's overall health status in addition to tumour characteristics.

Recently the concept of frailty, a state of low homeostatic reserve leading to a high vulnerability for sudden adverse health changes, emerged as a possible good predictor for an increased risk of chemotherapy intolerance, postoperative complications and mortality [3].

In the general population approximately 10% of people older than 65 years are classified as frail, increasing to 25–50% of people older than 85 years [4]. As both cancer and treatment are potential stressors and can challenge physiological reserve, this percentage will probably be higher in patients with cancer.

To detect disabilities and geriatric conditions that can contribute to frailty in geriatric oncology a comprehensive geriatric assessment (CGA) can be done. The CGA is a time consuming process and therefore research is focussing on screening assessments to discriminate between patients who are able to receive standard care and frail patients who should receive a CGA to guide tailoring of their treatment [5]. However, there is no clear consensus about the exact definition of frailty and multiple frailty assessment instruments are implemented [6,7].

Frailty was originally operationalised by Fried and colleagues as physical weakness and wasting [8]. Subsequently Rockwood et al. developed the Frailty Index (FI) based on a count of accumulated deficits [9]. Both approaches to measure frailty are frequently used for scientific purposes but it is unclear if they would both define the same patients as frail in an elderly population with cancer. The aim of this study is to establish the prevalence of frailty measured with two validated assessment instruments, the Frailty Phenotype (FP) and the FI and to determine if they capture the same population at risk for adverse events.

Methods

Study population

This cross-sectional study was conducted in the oncology outpatient department in Gelre Hospitals in Apeldoorn, the Netherlands, from January 2014 until March 2014 in patients aged older than 65 with cancer and who were eligible for treatment with chemotherapy.

The Medical Ethics Committee (METC) of the Academic Medical Center Amsterdam reviewed the study and written informed consent was obtained from all participants.

Data collection

At enrolment, trained research staff collected medical information from the medical charts, including diagnosed comorbidities according to the Charlson comorbidity index and the Karnofsky score [10].

Frailty was established according to the FI [11] and the FP [8]. For the FI we used 38 variables and cut-off points as used by Searle et al. [12] consisting of physical, psychological, social and cognitive items and documented comorbidity and excluding shoulder strength and peak flow measurement. The FI was the total deficits as a proportion of those counted, and was graded in three categories equivalent to the FP. A FI of $\leq$0.08 was considered as non-frail, a FI of $>$0.08 and $<$0.25 as pre-frail and a FI of $\geq$0.25 as frail [4]. The FP measures five components of frailty: weight loss, exhaustion, weakness, slow walking speed and low physical activity. Score range from 0 to 5, a score 1–2 was considered as pre-frail, and a score above 3 as frail. Additional information about the exact scoring can be derived from the authors.

Correspondence: B. C. van Munster, b.van.munster@gelre.nl, Department of Geriatric Medicine, Gelre Hospitals, PO Box 9014, 7300 DS Apeldoorn, The Netherlands. Tel: +31 55 5818395.

Table I. Patient characteristics: frailty status according to Frailty Index.

Characteristic	Non-frail ($n = 33$)	Frail ($n = 13$)	p-Value
Male, n (%)	21 (64)	4 (31)	0.04
Age	73.9 (±6.4)	77.0 (±5.8)	0.13
Tumour, n (%)			
Gastrointestinal	11 (33)	5 (40)	–
Haematologic	10 (30)	1 (8)	
Urologic	5 (15)	3 (23)	
Breast	2 (6)	2 (15)	
Lung	3 (9)	1 (8)	
Other	2 (6)	1 (8)	

Table II. Comparison of frailty assessment instruments.

		Frailty Index		
		Non-frail ($n = 4$)	Pre-frail ($n = 29$)	Frail ($n = 13$)
Frailty Phenotype	Non-frail ($n = 13$)	2 (15.4)	8 (61.5)	3 (23.1)
	Pre-frail ($n = 27$)	2 (7.4)	20 (74.1)	5 (18.5)
	Frail ($n = 6$)	0 (0)	1 (16.7)	5 (83.3)

Statistical analysis

We tested for differences in characteristics in patients with and without frailty using t-tests, Mann-Whitney tests and χ^2-tests.

Results

A total of 46 patients with a mean age of 74.8 years [standard deviation (SD) ± 6.3] participated in this study, mostly diagnosed with gastrointestinal, hematologic or urologic cancer. According to the FI, frailty patients were significant less male 31% versus 64% ($p = 0.04$) and had a lower Karnofsky score (70 vs. 90, $p = 0.001$). More frail patients are treated curative: nine of 14 frail patients and 11 of 33 non-frail patients (64% vs. 33%, $p = 0.03$) (Table I).

Prevalence of frailty in this population according to the FI was 28.3%, compared with a prevalence of 13% according to the FP, 63% was pre-frail according to the FI and 58.7% according to the FP. Twenty-seven of the 46 participants (27/46 = 58.7%) were categorised in the same phenotype category (Table II).

Discussion

In this cross-sectional study of elderly patients with cancer and eligible for chemotherapy, the prevalence of frailty, according to the FI, was 28.3%. There was a substantial difference in prevalence of frailty (28% vs. 13%) depending on the instrument used. To our knowledge this is the first study in elderly with cancer that measured frailty by the FI and compared the prevalence by the FI and the FP.

The prevalence of frailty, according to the FI, in this population of 28.3% seems higher than the prevalence of 22.7% measured by the FI in a community dwelling population with mean age of 74.0 years (SD ± 6.6) [4]. In previous studies in older cancer patients the median prevalence of frailty across studies that identified frailty using CGA was 43% (range 7–68), compared to a median frailty prevalence of 13% (range 6–86) for studies that applied the phenotype model [3]. The higher prevalence of frailty in this oncological population compared to the general population was to be expected based on the impact of cancer, risk factor for cancer and its therapies.

In our study, only 58.7% of all participants were categorised in the same phenotype category. To our knowledge no studies compared the FI and the FP in the oncological population before. The FI prevalence estimate in our population was more than 2.0 times higher than the prevalence estimated by the FP, which is in concordance with results found in the general population [4,13,14]. Studies with large study samples of community dwelling adults proposed that these two frailty models capture different, but overlapping, groups of older adults and that they cover different sides of the spectrum of frailty [15,16]. In the community dwelling population it seems that the FI could define risk of adverse outcomes, including mortality, more precisely than the FP does [13,14]. This may be promising for the use of the FI in elderly with cancer, who need chemotherapy or other treatment, in the estimation of frailty, but further research in comparison with other frailty instruments should be done.

Strength of this cross-sectional study included measurements of a validated construct of frailty. Due to the single centre study of 46 participants, limitations in statistical power to detect small subgroup effect and generalisability for oncology in elderly have to be taken into account. However, the high incidence of frailty and the large difference in frailty prevalence measured by two different scales are remarkable even in this small population and cannot be ignored.

As the population elderly with cancer is growing, frailty becomes important in clinical care. Frailty is associated with poor clinical outcomes, falls, disability and mortality [4,8], so it is important to identify those who are at risk in order to improve care and outcomes. Standardisation of the scientific definition of frailty is desperately needed for comparability of studies aimed at evaluating individual adjusted therapy regimes.

References

1. Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: Burdens upon an aging, changing nation. J Clin Oncol 2009;27:2758–65.
2. Arnold M, Karim-Kos HE, Coebergh JW, Byrnes G, Antilla A, Ferlay J, et al. Recent trends in incidence of five common cancers in 26 European countries since 1988: Analysis of the European Cancer Observatory. Eur J Cancer 2015;51:1164–87.
3. Handforth C, Clegg A, Young C, Simpkins S, Seymour MT, Selby PJ, et al. The prevalence and outcomes of frailty in older cancer patients: A systematic review. Ann Oncol 2015;26:1091–101.
4. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. J Am Geriatr Soc 2010;58:681–7.
5. Maas HA, Janssen-Heijnen ML, Olde Rikkert MG, Machteld Wymenga AN. Comprehensive geriatric assessment and its clinical impact in oncology. Eur J Cancer 2007;43:2161–9.

6. Bouillon K, Kivimaki M, Hamer M, Sabia S, Fransson EI, Singh-Manoux A, et al. Measures of frailty in population-based studies: An overview. BMC Geriatr 2013;13:64.
7. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet 2013;381:752–62.
8. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146–56.
9. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. Can Med Ass J 2005;173:489–95.
10. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 1987;40:373–83.
11. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. Sci World J 2001;1:323–36.
12. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BMC Geriatr 2008;8:24.
13. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. J Gerontol A Biol Sci Med Sci 2007;62:738–43.
14. Kulminski AM, Ukraintseva SV, Kulminskaya IV, Arbeev KG, Land K, Yashin AI. Cumulative deficits better characterize susceptibility to death in elderly people than phenotypic frailty: Lessons from the Cardiovascular Health Study. J Am Geriatr Soc 2008;56:898–903.
15. Cigolle CT, Ofstedal MB, Tian Z, Blaum CS. Comparing models of frailty: The Health and Retirement Study. J Am Geriatr Soc 2009;57:830–9.
16. Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: Different instruments for different purposes. Age Ageing 2014;43:10–12.