Practical relevance of frailty assessment in hospitalized older adults

Winters, Marian

DOI:
10.33612/diss.1476791970

Practical relevance of frailty assessment in hospitalized older adults

Marian Winters

ISBN: 978-94-6537-016-3

Cover design by Sabine van Ontwerp met pit.

Layout design by Arina van Londen, Ridderprint

Printing by Ridderprint | www.ridderprint.nl

Printing this thesis was financially supported by Wetenschapsfonds Medisch Specialisten Isala, University of Groningen and the University Medical Center Groningen.

rijksuniversiteit groningen

Practical relevance of frailty assessment in hospitalized older adults

Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. ir. J.M.A. Scherpen
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

woensdag 11 februari 2026 om 12.45 uur

door

Antje Marianne Winters

geboren op 7 augustus 1985

Promotores

Prof. dr. E.J. Finnema
Prof. dr. H.J.G. Bilo

Copromotor

Em. prof. dr. P.F. Roodbol

Beoordelingscommissie

Prof. dr. B.C. van Munster
Prof. dr. H. Vermeulen
Prof. dr. R.C. Oude Voshaar

TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

1.1 FRAILTY IN AN AGEING POPULATION

The Netherlands is undergoing significant demographic shifts, characterized by an increasingly ageing population – a trend that is mirrored globally (1). At the start of 2025, the total population of the Netherlands was 17.9 million. In recent decades, the percentage of the Dutch population 65 years of age and older has increased immensely, from 12.8% in 1990 to 20.5% (3.6 million) in 2024 (2). This percentage is expected to increase further in the coming years. According to current forecasts, in 2050, of the projected population of 19.6 million people, 4.9 million – 25% of the Dutch population – will be at least 65 years of age (3).

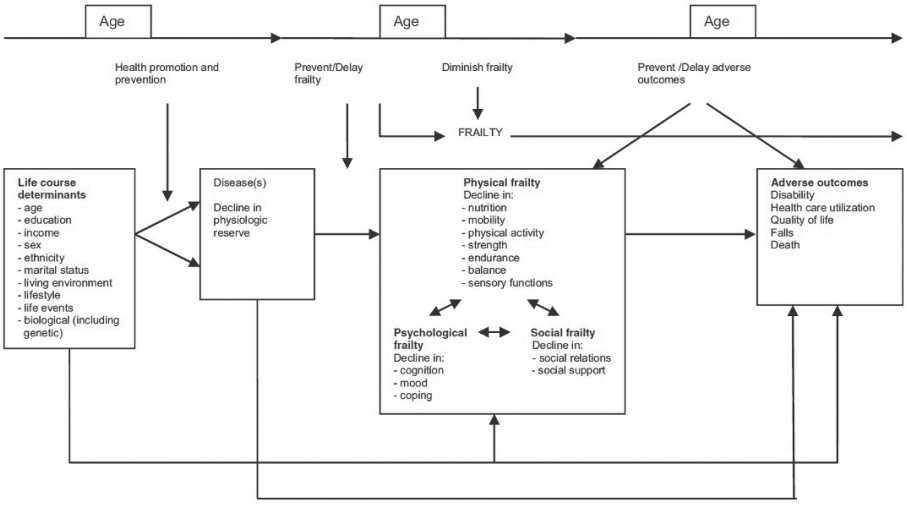
Although ageing is inevitably accompanied by changes in physical and cognitive capacity, it is impossible to capture all older adults in a one-size-fits-all description. Each individual is unique, and age-related changes occur in a large variety, and often at different speeds. Factors shaping the ageing process include environmental influences (e.g. educational level, financial resources), genetic predispositions, and lifestyle choices (including physical activity, smoking, and alcohol consumption). Ageing is also influenced by health conditions and a range of social and psychological factors (1), which together determine whether individuals will remain fit or become frail. It is well known that older adults who are fit tend to maintain a higher degree of independence, experience higher levels of quality of life, and have a lower risk of mortality, as compared to those who are frail. Consequently, frailty has a profound impact on older adults, and global ageing is having a significant effect on the entire healthcare system.

1.2 CONCEPTUALIZATION OF FRAILTY

This thesis applies the following definition of frailty: *'a dynamic condition affecting an individual who is experiencing losses in one or more domains of human functioning (physical, psychological, and/or social) caused by a range of variables and which increases the risk of adverse outcomes'* (4). This definition is reflected in the integral conceptual model of frailty (Figure 1) (5), which was developed in 2010 (4) and updated in 2015 (5). This model describes the pathway from life-course determinants and disease to frailty and, ultimately, to adverse outcomes. According to the model, adverse outcomes are ultimately determined by disease, a decline in physical functioning, and/or physical, psychological, and social frailty. Adverse outcomes include disability, healthcare utilization, falls, lower quality of life, and early death. The integral conceptual model of frailty describes a variety of intervention goals: promoting health

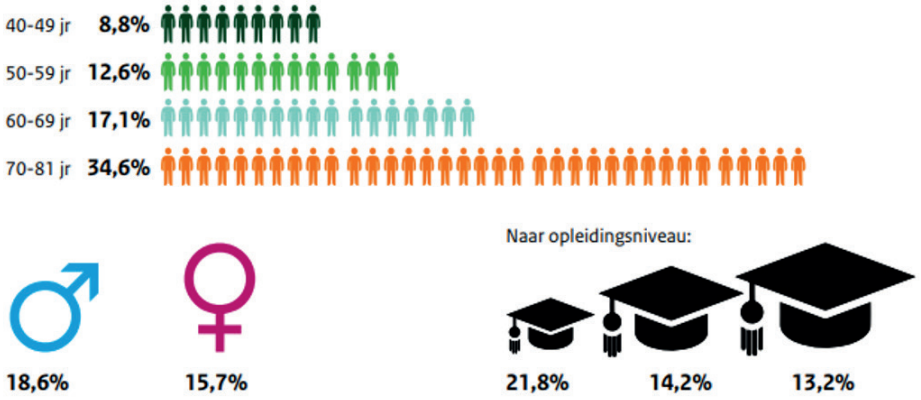
and preventing disease; preventing or delaying frailty; reducing frailty; and preventing or delaying adverse outcomes. It has been validated in community-dwelling people 75 years of age and older (6), as well as in residents of assisted-living facilities (5).

Figure 1: An integral conceptual model of frailty (5)



For the Dutch population, data from the Dutch National Institute for Public Health and the Environment (RIVM) (Figure 2) indicate that the prevalence of frailty increases with advancing age and decreases with higher levels of education (7). According to the most recent data (2019), an estimated 22% of all individuals aged 65 and older in the Netherlands are considered frail (8).

Figure 2: Prevalence of frailty by age, gender, and educational level (7)



A small mortarboard represents a low educational level, and a large mortarboard represents a high educational level.

1.3 FRAILTY IN THE HOSPITAL SETTING

Frail older adults who have been admitted to hospital are at a higher risk of adverse outcomes (e.g. complications, delirium, falls, or prolonged hospital stays), as well as of admission to assisted-living facilities (9). In Dutch hospitals, when older patients are admitted, they are screened to assess the possibility of frailty. Early detection of frailty could increase the possibility of delivering holistic, accessible, and cost-effective care while improving outcomes for older adults. By identifying individuals known to have or be at risk of developing frailty, timely interventions can be implemented to prevent functional decline and promote healthy ageing (10). Examples of such interventions include improving physical function, providing psychological support, and offering nutritional guidance.

If the outcome of the frailty screening points to a suspicion of frailty, a more in-depth evaluation – the Comprehensive Geriatric Assessment (CGA) – can be performed to confirm the diagnosis of frailty and assess the associated risks. Widely accepted as the gold standard for assessing frailty, the CGA is a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities in order to develop a coordinated, integrated plan for treatment and long-term follow-up (11). Ideally, this screening should be conducted by an expert in geriatric medicine, such as a general practitioner, a geriatrician, or a nurse specialist.

In this thesis, frailty assessment refers to screening with a frailty screening instrument and a CGA. The screening is based on a standardized measurement with predetermined cut-off points for determining the diagnosis of frailty.

Despite the existence of general frailty-assessment guidelines, uncertainty remains concerning the adequacy of general advice in enabling the reliability of assessing frailty with a single screening instrument across various situations and settings (e.g. ambulatory, clinical, acute, and long-term care) and diverse patient categories (12). In addition, more than 50 frailty-screening instruments are available. Not all of them have been sufficiently validated, and their prognostic ability has rarely been established (13-16). Furthermore, in practice, screening instruments are deployed in response to mandates from the Dutch Health and Youth Care Inspectorate (IGJ) or decisions made by management.

The identification of frailty is further complicated by the fact that frailty is defined by complex factors (e.g. cognition), as well as by variations in internal and external factors across patients and by variations in frailty management across settings (17). Healthcare providers (HCPs) in hospitals therefore struggle to apply frailty assessment in their daily practice. Nurses, nurse practitioners, and physicians in acute hospital settings have identified several barriers to the effective implementation of frailty screening, even if the instrument is sufficiently valid and reliable. Specific barriers include the insufficiency of follow-up actions and the fact that they have not been integrated into guidelines for clinical management (18). Moreover, nurses tend to focus more on risks relating to falls and delirium rather than on the overall frailty score (19).

Given the situations described above, the added value of the frailty screening instruments used in Dutch hospitals for clinical practice is questionable. For patients scheduled for hospital admission, frailty screening is conducted in the outpatient setting. To our knowledge, however, the experiences of outpatient HCPs in the Dutch setting have not yet been investigated.

Given the infeasibility of investigating all available screening instruments, this study focuses on the screening instruments and patient populations encountered by the author: a nurse practitioner in geriatric care at a hospital in the central region of the Netherlands. In the nurse practitioner's daily practice, the following instruments were applied across various categories of older adults: the Geriatric-8 (G8) (Figure 3) (20), the Groningen Frailty Indicator (GFI) (Figure 4) (21,22), and the VMS frailty score based on three domains, which was developed as part of the Dutch Patient Safety Programme (NPSP; in Dutch, *Veiligheidsmanagementsysteem* or VMS) (Figure 5) (23). Categories of older adults in this practice include patients with a hip fracture and patients with colorectal carcinoma.

Figure 3: The Geriatric-8 measurement (20)

Items	Possible answers	Score
Food intake in the last 3 months	0: severe decrease in food intake 1: moderate decrease in food intake 2: no decrease in food intake	...
Weight loss during the last 3 months	0: weight loss >3 kg 1: does not know 2: weight loss between 1 and 3 kg 3: no weight loss	...
Mobility	0: bed or chair bound 1: able to get out of bed/chair but does not go out 2: goes out	...
Neuropsychological problems	0: severe dementia or depression 1: mild dementia or depression 2: no psychological problems	...
Body Mass Index (BMI)	0: BMI < 19 1: BMI 19 to < 21 2: BMI 21 to < 23 3: BMI 23 and > 23	...
Takes more than 3 medications per day	0: Yes 1: No	...
Self-rated health status (compared to other people of the same age)	0: not as good 0.5: does not know 1: as good 2: better	...
Age (in years)	0: > 85 1: 80–85 2: < 80	...
Total score (0–17) [Cut-off ≤ 14 indicating impairment]		...

The G8 screening tool is a geriatric screening tool consisting of eight questions, with scores for each question, eventually resulting in a total score ranging from 0 to 17. Patients with scores of ≤ 14 are defined as being at risk of frailty (20).

Figure 4: Groningen Frailty Indicator (22)

Items	Yes	No	Sometimes
Are you able to carry out these tasks single-handedly and without any help? (The use of help resources such as a walking stick, walking frame or wheelchair is considered to be independent.)			
1. Grocery shopping	0	1	
2. Walking around outside (around the house or to the neighbours)	0	1	
3. Dressing and undressing	0	1	
4. Going to the toilet	0	1	
5. Do you experience problems in daily life due to poor vision?	1	0	
6. Do you experience problems in daily life due to being hard of hearing?	1	0	
7. During the last 6 months have you lost a lot of weight unwillingly? (3 kg in 1 month or 6 kg in 2 months)	1	0	
8. Do you take 4 or more different types of medicine?	1	0	
9. Do you have any complaints about your memory?	1	0	1
10. Do you sometimes experience emptiness around yourself?	1	0	1
11. Do you sometimes miss people around yourself?	1	0	1
12. Do you sometimes feel abandoned?	1	0	1
13. Have you recently felt downhearted or sad?	1	0	1
14. Have you recently felt nervous or anxious?	1	0	1
15. What mark do you give yourself for physical fitness? (Scale 0 to 10) [0–6 = 1 7–10 = 0]	1	0	
score GFI Total	...		

The GFI consists of 15 questions to determine the level of frailty. It identifies physical, cognitive, social, and psychological impairments and yields a score on a scale from 0 to 15. A GFI-score of 4 or higher suggests frailty (21).

Figure 5: VMS frailty screening tool (three domains)

Question 1:	Do you have cognitive problems/have you experienced an episode of confusion or delirium before?
Question 2:	Did you fall in the last six months?
Question 3:	Did you need help with self-care in the last 24 hours?

The VMS frailty screening tool is implemented in all Dutch hospitals for patients 70 years of age and older upon admission, but variations exist across

hospitals. In the hospital where the author of this thesis is employed, the variant mentioned above is used to assess the presence or the possible risk of three geriatric syndromes: delirium, falls, and functional decline (Figure 4). If a patient shows outcomes that indicate an increased risk, preventive measures should be taken specifically directed towards minimizing the risk that these syndromes will occur (24).

1.4. FOCUS, AIM, AND OUTLINE OF THIS THESIS

Addressing frailty in clinical practice is inherently challenging, particularly in the absence of consensus on the definition of frailty, given that varying approaches are still in use. There are also concerns about the effectiveness of current screening tools in distinguishing frailty levels and customizing treatments accordingly. This situation has given rise to questions regarding the accuracy of the current approach and the instruments used.

This thesis explores the clinical relevance of frailty assessment in the care of older hospitalized patients. In addition to evaluating the predictive value of frailty-screening tools for patient outcomes, it examines the frailty-assessment experiences of HCPs working in the outpatient clinic of a Dutch hospital, the challenges they face in daily practice, and the tools that are utilized to determine the presence and level of frailty. The evaluation of these experiences is essential in order to generate insight into the process and added value of frailty assessment for HCPs.

Overall, this assessment of the clinical relevance of frailty assessment is intended to provide valuable guidance for enhancing the quality of care for older patients who have been admitted to hospital.

The thesis is divided into chapters focusing on these objectives:

Chapter 2 is a literature review focusing on systematic reviews and meta-analyses of frailty-screening tools and tools for predicting shorter life expectancy in acutely hospitalized older adults.

Chapter 3 describes the results of a prospective observational cohort study investigating the predictive value of the GFI and the VMS frailty-screening tool on clinical outcomes amongst patients who have undergone hip-fracture surgery.

Chapter 4 presents the results of a prospective observational cohort study investigating the relationship between orthostatic hypotension (OH), muscle

strength, and the likelihood of successful rehabilitation in hospitalized older patients with hip fractures. The time to successful rehabilitation was defined as the duration needed for an individual to regain the pre-surgery level of functioning and return to the prior living situation. Muscle strength was assessed using handgrip strength, measured in kilograms (kg) with a Jamar hand dynamometer (25). Results indicate that OH and muscle strength have a negative influence on the response to rehabilitation, as do other factors, including advanced age, cognitive impairment, and increased fear of falling (26,27).

Chapter 5 reports on a retrospective cohort study to determine whether the G8 can predict poor short-term health outcomes for older patients undergoing CRC surgery. The G8 is an example of a frailty-screening tool for outpatients. It is widely used for screening frailty in older adults with cancer in Dutch hospitals. The Dutch Inspection for Health Care and Youth (IGJ) has recommended the G8 for identifying individuals who are at greater risk of functional decline, for promoting uniformity across the Netherlands, and for facilitating future data collection (28).

Chapter 6 explores the perspectives of hospital HCPs concerning the value and practice of frailty assessment amongst older patients with CRC.

Finally, **Chapter 7** presents a discussion of the main findings of these studies, in addition to considering their implications for clinical practice regarding appropriate care for older hospitalized adults in the Netherlands.

REFERENCES

1. World Health Organization (WHO). *Ageing and health*. October 2024 [Accessed March 2025]. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
2. Centraal Bureau voor de Statistiek (CBS) [Statistics Netherlands]. Elderly people. [Accessed March 2025]. Available from: https://www.cbs.nl/en-gb/visualisations/dashboard-population/age/elderly-people
3. Centraal Bureau voor de Statistiek (CBS) [Statistics Netherlands]. Bevolking. Bevolkingsomvang [Population. Population size]. November 2024 [Accessed March 2025]. Available from: https://www.vzinfo.nl/bevolking/bevolkingsomvang
4. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community-dwelling older people. Nurs Outlook. 2010;58(2):76-86. doi: 0.1016/j.outlook.2009.09.005.
5. Gobbens RJ, Krans A, van Assen MA. Validation of an integral conceptual model of frailty in older residents of assisted living facilities. Arch Gerontol Geriatr. 2015 Nov-Dec;61(3):400-10. doi: 10.1016/j.archger.2015.06.001.
6. Gobbens RJ, van Assen MA, Luijkx KG, Schols JM. Testing an integral conceptual model of frailty. J Adv Nurs. 2012 Sep;68(9):2047-60. doi: 10.1111/j.1365-2648.2011.05896.x.
7. Rijksinstituut voor Volksgezondheid en Milieu (RIVM) [Dutch National Institute for Public Health and the Environment]. *Ouderen van nu en straks: zijn er verschillen in kwetsbaarheid?* [Elderly people of today and tomorrow: Are there differences in vulnerability?]. December 2015 [Accessed March 2025]. Available from: https://www.rivm.nl/sites/default/files/2018-11/Factsheet%20Ouderen%20van%20nu%20en%20straks.pdf
8. Vektis. June 2020 [Accessed March 2025]. *Factsheet kwetsbare ouderen*. [Factsheet on Frail Elderly People]. Available from: https://www.vektis.nl/intelligence/publicaties/factsheet-kwetsbare-ouderen
9. Age UK Group and/or its National Partners. *Common conditions and frailty*. 2024 [Accessed March 2025]. Available from: https://www.ageuk.org.uk/our-impact/policy-research/frailty-in-older-people/common-conditions-frailty/
10. Rijksinstituut voor Volksgezondheid en Milieu (RIVM) [Dutch National Institute for Public Health and the Environment]. *Factsheet Vroegsignalering* [Factsheet on Early Detection]. 2018 [Accessed March 2025]. Available from: https://www.rivm.nl/sites/default/files/2018-11/010174_111400_Factsheet_Vroegsignalering_TG.pdf
11. Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: A meta-analysis of controlled trials. *Lancet*. 1993;342(8878):1032-6. doi: 10.1016/0140-6736(93)92884-v.
12. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. *Lancet*. 2019 Oct 12;394(10206):1376-1386. doi: 10.1016/S0140-6736(19)31785-4.
13. Warnier RM, van Rossum E, van Velthuijsen E, Mulder WJ, Schols JM, Kempen GI. Validity, reliability, and feasibility of tools to identify frail older patients in inpatient hospital care: A systematic review. J Nutr Health Aging. 2016;20(2):218-30. doi: 10.1007/s12603-015-0567-z.

14. Buta BJ, Walston JD, Godino JG, Park M, Kalyani RR, Xue QL, et al. Frailty assessment instruments: Systematic characterization of the uses and contexts of highly-cited instruments. Ageing Res Rev. 2016;26:53-61. doi: 10.1016/j.arr.2015.12.003

15. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: A review. Eur J Intern Med. 2016 Jun; 31:3-10. doi: 10.1016/j.ejim.2016.03.007.

16. Faller JW, Pereira DDN, de Souza S, Nampo FK, Orlandi FS, Matumoto S. Instruments for the detection of frailty syndrome in older adults: A systematic review. PLoS One. 2019 Apr 29; 14(4):e0216166. doi: 10.1371/journal.pone.0216166.

17. Carpenter CR, Mooijaart SP. Geriatric screeners 2.0: Time for a paradigm shift in emergency department vulnerability research. J Am Geriatr Soc. 2020;68(7):1402-1405. doi:10.1111/jgs.16502.

18. Liu X, Le MK, Lim AYC, Koh EJ, Nguyen TN, Malik NA, et al. Perspectives on frailty screening, management and its implementation among acute care providers in Singapore: A qualitative study. BMC Geriatr. 2022;58. doi: 10.1186/s12877-021-02686-w.

19. Warnier RMJ, van Rossum E, Du Moulin MFMT, van Lottum M, Schols JMGA, Kempen GIJM. The opinions and experiences of nurses on frailty screening among older hospitalized patients: An exploratory study. BMC Geriatr. 2021 Nov 3;21(1):624. doi: 10.1186/s12877-021-02586-z.

20. Bellera CA, Rainfray M, Mathoulin-Pélissier S, Mertens C, Delva F, Fonck M, et al. Screening older cancer patients: First evaluation of the G-8 geriatric screening tool. Ann Oncol. 2012;23(8):2166-2172. doi: 10.1093/annonc/mdr587

21. Steverink N, Slaets J, Schuurmans H, Van Lis M. Measuring frailty: Developing and testing of the Groningen frailty indicator (GFI). The Gerontologist 2001;41:236-237.

22. Drubbel I, Bleijenberg N, Kranenburg G, Eijkemans RJ, Schuurmans MJ, de Wit NJ, Numans ME. Identifying frailty: Do the Frailty Index and Groningen Frailty Indicator cover different clinical perspectives? A cross-sectional study. BMC Fam Pract. 2013;21;14:64. doi: 10.1186/1471-2296-14-64.

23. Dutch Patient Safety Programme. [Accessed: July 2024]. Available from: https://www.vmszorg.nl/vms-v3iligheidsprogramma/dutch-patient-safety-programme-english/

24. Oud FMM, Meulman MD, Merten H, Wagner C, van Munster BC. Value of the Safety Management System (VMS) frailty instrument as a frailty screener in care for older hospital patients: A systematic review. Eur Geriatr Med. 2024;15(3):609-620. doi: 10.1007/s41999-024-00957-4.

25. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: Towards a standardised approach. Age and ageing. 2011 Jul;40(4):423-9.

26. Di Monaco M, Castiglioni C, De Toma E, Gardin L, Giordano S, Di Monaco R, et al. Handgrip strength but not appendicular lean mass is an independent predictor of functional outcome in hip-fracture women: A short-term prospective study. Arch Phys Med Rehabil. 2014;95(9):1719-24. doi: 10.1016/j.apmr.2014.04.003.

27. Hartog LC, Cizmar-Sweelssen M, Knipscheer A, Groenier KH, Kleefstra N, Bilo HJ, et al. The association between orthostatic hypotension, falling, and successful rehabilitation in a nursing home population. Arch Gerontol Geriatr. 2015;61(2):190-6. doi: 10.1016/j.archger.2015.05.005.

28. Ministerie van Volksgezondheid, Welzijn en Zorg [Dutch Ministry of Health, Welfare and Sport]. Inspectie gezondheidszorg en jeugd (IGJ) [Health and Youth Care Inspectorate]; 2018 Aug; p. 114. [Accessed June 2024] Available from: https://archief23.sitearchief.nl/archives/sitearchief/20190902130808/https://www.igj.nl/binaries/igj/documenten/indicatorensets/2017/01/01/basisset-medisch-specialistische-zorg/IGJ+Basisset+MSZ+2019.pdf.

CHAPTER 2

Frailty and life expectancy assessments are essential in older adults but remain challenging

Published as: Winters AM, Bilo HJG, Roodbol PF and Finnema EJ. Frailty and Life Expectancy Assessments are Essential in Older Adults but Remain Challenging. Gerontology And Geriatric Research. 2022; 4(2):130

ABSTRACT

With more focus on the degree of frailty and life expectancy, in addition to patient characteristics, care could be more tailored, taking into account individual wishes and needs. A valid way of measuring frailty and life expectancy, however, is essential to providing equal treatment and objective judgement. In this short review, the authors aim to provide an insight into the challenges of assessing frailty and life expectancy and of applying the outcomes of such assessments in current healthcare settings. There are several tools, and combinations thereof, that can be used to assess frailty and life expectancy; however, none of the tools are accurate enough for the acute setting. Despite the lack of consensus on which tool or tool combination to use, their importance has been clearly demonstrated. Frailty and life expectancy should be part of identifying patient characteristics before treatment goals can be determined. In addition, the process of making treatment decisions needs to be standardized to support healthcare professionals and patients in making well-considered and well-founded decisions that are focused on the individual.

INTRODUCTION

Especially in older adults, life expectancy and quality of life as essential outcome factors, instead of the possible successful outcomes of technical procedures only, have been considered more frequently when designing care and care structures. Traditionally, treatment is focused on medical conditions and specific diagnoses. These days, a more individualized model is gaining in importance, based on a biopsychosocial approach that considers the degree of frailty and life expectancy to be essential contributing factors in avoiding adverse treatment of or consequences for older adults.

A recently published article shows the usefulness of such an approach (1). In this article, the impact of operative and non-operative management of hip fractures on the quality of life of frail older adults was assessed. Although the short-term mortality in the non-operative management group was higher than in the operative management group, there was no loss of quality of life and health-related quality of life in non-operated patients. Based on these results, the authors concluded that non-operative management could seriously be considered a valid option for frail hospitalized patients with limited life expectancy. Such an approach is an excellent example of focusing on patient characteristics, with treatment choices also depending on life expectancy and patients' quality of life.

In other circumstances, frailty should also be considered in defining treatment goals. Frail older adults with hypertension are at a higher risk of experiencing periods of hypotension when the treatment goal is to lower blood pressure to generally accepted levels (2,3). Hypotension could result in higher risks of depression, falls, hip fractures, and delirium (3). It is also known that for older frail patients with type 2 diabetes mellitus the benefits of intensive blood glucose control diminish with longer diabetes duration and increased age. These patients are more likely to experience hypoglycaemia and that may result in falls, hospitalization, and loss of independence (4). Prescribers should be aware of the impact of standard treatment on frail older adults and, therefore, weigh the benefits of treatment against the harms for each patient.

FRAILTY DEFINITION AND TOOLS

A fundamental question that needs to be addressed first is whether there are sufficient valid instruments to determine the degree of frailty that can be used in such circumstances. There are several tools, and combinations thereof, that can be used to identify frailty but this is complicated by the fact that there are

multiple definitions of frailty and that a gold standard is lacking (5). Whether it will be possible to define a gold standard in due time or whether a consensus-based, generally accepted, and universal compromise is the only option remains an important question. It is quite possible that different settings (e.g. community settings versus hospital or care home settings or chronic versus acute settings) will require different instruments to assess frailty. These topics will be addressed in this short review.

Frailty is most often defined as an ageing-related syndrome of physiological decline, characterized by significant vulnerability to adverse health outcomes (6). Some researchers express frailty as 'the most problematic expression of population ageing' and define frailty as a state of vulnerability to poor resolution of homeostasis after a stressor event that is a consequence of a cumulative decline in many physiological systems during a lifetime (7). These definitions, including an often-used definition by Fried et al. (2001), refer to frailty as a medical concept. In contrast, a multidimensional approach to frailty is increasingly being advocated. It can be defined as a dynamic state, affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, and/or social), which is caused by a range of variables and increases the risk of adverse outcomes (9,10).

We screened the literature for systematic reviews and meta-analyses of frailty screening tools and found two relevant reviews (5,11). Thirty-nine screening tools were included and four were described in both reviews. The populations studied were community-dwelling older adults, aged 60 (5) or 65 years and older (11). One review also included data about frailty tools that were tested in emergency departments and nursing homes (5).

Overall, the researchers agree that a multidimensional frailty tool with a high-accuracy risk prediction of adverse outcomes is desirable if it is sufficiently applicable in a short time frame and validated for a particular setting. Some researchers preferred the Frailty Index, which is based on these properties (5), while others preferred the Tilburg Frailty Index (11). The Frailty Index lists 13-92 health deficits for which patients can be screened, with good criterion and construct validity but poor to moderate discriminatory ability for community-dwelling older adults (12). The Frailty Index accurately predicts adverse outcomes, such as falls, impairment in activities in daily living (ADL), cognitive decline, hospitalization, and mortality. However, various combinations of items were used. The authors also suggest considering the use of simple risk indicators, such as slow gait speed, because of their excellent ability to predict impairment in ADL (5). The Tilburg Frailty Index is a self-administered

questionnaire with 15 items that relate to disability and receiving personal care and that has demonstrated good validity and reliability for primary healthcare settings, (5,11,13). A sensitivity of 0.87 and a specificity of 0.76 were described for frailty related to adverse outcomes, such as disability, hospitalization, and falls (13). For the acute setting or for acutely ill patients, using the frailty tools as described in the reviews is not recommended (5).

TOOLS FOR ESTIMATING LIFE EXPECTANCY

Sometimes, new challenges force us to define aspects of frailty more appropriately. It is known that frailty is associated with shorter life expectancy (14). With the outbreak of the coronavirus pandemic, it became clear that predicting a potentially shorter life expectancy was highly relevant. During the coronavirus pandemic, there was a discussion in the Netherlands about which patients were to be seen as the better candidates to be offered an intensive care (IC) bed or, conversely for which patients the use of IC facilities would not in any way contribute to better outcomes because of the patients' pre-existing poor health (15). Assessing life expectancy as a starting point may contribute to making better-substantiated choices and, ideally, will contribute to allocating appropriate individualized and valuable care. Eventually, age became the official decisive factor in the admission to the intensive care unit (ICU) in case of bed shortages. Therefore, we also wondered whether there are valid instruments to predict life expectancy among older adults in acute settings.

In the literature, we found four reviews of shorter life expectancy predictions among the elderly (16,17,18,19). A variety of settings were described: community-dwelling older adults, elderly individuals undergoing haemodialysis (16), patients with and without cancer (breast cancer in particular) (16,17,19), nursing home patients (17), and elderly individuals who were admitted to the ICU (18). A total of 77 tools were examined to predict mortality within 4 weeks to 10 years. Three tools might be appropriate for the prediction of short-term survival between four weeks and three months for patients with advanced cancer to guide the choice of radiation dose and fraction (19). However, these tools not validated for elderly individuals without cancer. Some other tools have demonstrated moderate to very good accuracy regarding the prediction of mortality between one and seven years. Still, most tools were used and assessed by the researchers who developed them, without examining the external validity (17). The predicting performances of frailty and life expectancy

scores were only assessed for the Frailty Index (5,17). A moderate accuracy of 0.62 has been described to predict a life expectancy of less than 72 months (17). Some researchers suggest that the surprise question 'Would I be surprised if this patient died within one year?' can be used to identify patients at high risk of death and who might benefit from palliative care. In a systematic literature and meta-analysis, the performance characteristics of the surprise question in predicting death has been reviewed (16). For the prediction of mortality within 6 to 18 months, the pooled sensitivity was 0.67 and the specificity 0.80, with a positive predictive value of 37% and a negative predictive value of 93%. For patients with non-cancer illnesses, worse performances were reported. The researchers advised against using the question as a stand-alone prognostic tool (16).

DISCUSSION

None of the tools for predicting frailty and shorter life expectancy were accurate enough to use in an acute setting. Which outcomes are relevant from a patient's perspective regarding screening for risks with these points in mind? Is it essential to know the mortality risk? From a healthcare professional's view, it can be relevant to determine which treatment is valuable and meaningful for patients with a short life expectancy. It is also likely that such a question is appropriate for most patients. Still, it is not necessarily of the same value to everyone because there may also be other issues influencing the eventual judgment of patients (and often their families).

In general, with an approach that focuses on individual needs and wishes, it is possible to initiate advanced care planning and consider stopping any unnecessary life-prolonging treatment, where appropriate. This avoids influencing the quality of life during the short time remaining and timely initiates palliative care, which may contribute to being able to end life with dignity. An approach like this will support patients and families in making appropriate decisions. Still, basing advanced care merely on the outcomes of currently available questionnaires is inappropriate. Predictions and assumptions that are based on such an approach are too unreliable in a considerable minority of patients to be applied as a certainty on an individual basis.

For us as researchers, frailty and mortality are essential patient outcomes. Results from questionnaires, however, apply on a group or population level and are often not sufficiently reliable on an individual level. An approach that combines patient-relevant outcomes and expert-relevant outcomes is

advisable (20). In our opinion, questionnaire outcomes only add to the overall picture but should not dominate in the decision-making process.

Complex decision-making situations

Translating such thoughts as described into practical action remains a challenge. For example, in the Dutch guidelines for older patients with proximal femoral fracture, shared decision-making (SDM) is advised when patients have the explicit wish to receive non-operative management (21). SDM is defined as a process that is taking place in a relationship where there is a partnership between the provider and the patient that is characterized by a collaborative bi-directional mutual exchange of information and discussion involving negotiation that leads to a shared decision (22). In practice, this wish is not always very evident and the process and steps to be taken have not been described in the guidelines. Whether it concerns surgery or admission to the ICU, these are complex medical decision-making situations. A narrative review presented and discussed the ethical frameworks that are used for medically complex situations in older people and recommended the use of frameworks that contain step-by-step plans, moral values, and an approach to balancing the views of all participants (23). Unfortunately, they did not 'identify a single effective framework'. Furthermore, although very important, moral deliberations can be influenced by the cultural background as accepted in a community, by healthcare workers, and by patients and their families. Decision-making that is based on ethical considerations might lead to entirely different outcomes, depending on the cultural setting in which the deliberations take place. This makes generalization a challenge. The process should be as short as possible and be applicable to all healthcare professionals.

CONCLUSION

There is, as yet, no agreement on a standardized frailty assessment and decision-making process for older adults who are admitted to hospital. So far, assessment tools have been validated and a standardized approach is accepted

as part of guidelines. An alternative might be to address a set of fundamental questions when considering new interventions in the acute setting:

1. Does this intervention improve wellbeing or contribute to maintaining an acceptable state of wellbeing?
2. Does this intervention improve prognosis regarding morbidity and mortality, with the explicit understanding that wellbeing will be either improved or maintained at the pre-intervention level?
3. When therapeutic interventions are considered not meaningful, when judged in the light of bullet point 2, are any interventions possible to alleviate symptoms and suffering in the frail older adult?

Although a treatment decision is nearly always initiated by healthcare professionals, it will, of course, always be the result of deliberations by the frail person, their family, and healthcare professionals. Such a process will never be easy but our patients deserve a well-considered and well-founded decision that is focused on the individual.

REFERENCES

1. Loggers SAI, Willems HC, Van Balen R, Gosens T, Polinder S, et al. FRAIL-HIP Study Group. Evaluation of Quality of Life After Nonoperative or Operative Management of Proximal Femoral Fractures in Frail Institutionalized Patients: The FRAIL-HIP Study. *JAMA Surg*. 2022, Mar 2:e220089.
2. Hateren van KJJ, Hendriks SH, Gronier KH, Bakker SJL, Bilo HJG, et al. Frailty and the relationship between blood pressure and mortality in elderly patients with type 2 diabetes (Zwolle Outpatient Diabetes project Integrating Available Care-34) *Journal of hypertension*. 2015. Volume 33, nr. 6, p. 1162-6.
3. Franz H Messerli, Sven Streit, Tomasz Grodzicki, The oldest old: does hypertension become essential again?, *European Heart Journal*. 2018. Volume 39, Issue 33, Pages 3144–3146.
4. Verenso 2011. Multidisciplinaire Richtlijn Diabetes [multidisciplinary guideline diabetes] https://www.verenso.nl/_asset/_public/Richtlijnen_kwaliteit/richtlijnen/VER_Richtlijn_Diabetes_Deel1_2011_web.pdf Assessed at 4th of April 2022
5. Apóstolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, et al. Predicting risk and outcomes for frail older adults: an umbrella review of frailty screening tools. *JBI Database System Rev Implement Rep*. 2017 Apr;15(4):1154-1208.
6. British Geriatrics Society. https://www.bgs.org.uk/resources/introduction-to-frailty Assessed at 4th of April 2022
7. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet.* 2013 Mar 2;381(9868):752-62.
8. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, et al. Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001 Mar;56(3):M146-56.
9. Slaets JPJ. Vulnerability in the Elderly: Frailty. *Medical Clinics of North America*. 2006. Volume 90, Issue 4, Pages 593-601.
10. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community dwelling older people. *Nurs Outlook*. 2010. 58(2):76–86.
11. Gilardi F, Capanna A, Ferraro M, Scarcella P, Marazzi MC, et al. Frailty screening and assessment tools: a review of characteristics and use in Public Health. *Ann Ig.* 2018. Mar-Apr;30(2):128-139.
12. Drubbel I, Numans ME, Kranenburg G, Bleijenberg N, de Wit NJ, Schuurmans MJ. Screening for frailty in primary care: a systematic review of the psychometric properties of the frailty index in community-dwelling older people. *BMC geriatrics*. 2014. *14*, 27.
13. Gobbens RJ, Boersma P, Uchmanowicz I,Santiago LM. The Tilburg Frailty Indicator (TFI): New Evidence for Its Validity. *Clinical interventions in aging*. 2020. Vol. 15, 265–274.
14. Herr M, Arvieu JJ, Ankri J, Robine JM. What is the duration of life expectancy in the state of frailty? Estimates in the SIPAF study. *European journal of ageing*. 2017. Vol. *15*(2), 165–173.
15. Vincent JL, Creteur J. Appropriated care for the elderly in the ICU. *J Intern Med.* 2022;291:458-468

16. Downar J, Goldman R, Pinto R, Englesakis M, Adhikari NK. The "surprise question" for predicting death in seriously ill patients: a systematic review and meta-analysis. *CMAJ*. 2017 Apr 3;189(13):E484-E493.

17. Thomas R, Pieri A, Cain H. A systematic review of generic and breast cancer specific life expectancy models in the elderly. *Eur J Surg Oncol*. 2017 Oct;43(10):1816-1827

18. Keuning BE, Kaufmann T, Wiersema R, Granholm A, Pettilä V, et al. HEALICS consortium. Mortality prediction models in the adult critically ill: A scoping review. *Acta Anaesthesiol Scand.* 2020. Apr;64(4):424-442.

19. Pobar I, Job M, Holt T, Hargrave C, Hickey B. Prognostic tools for survival prediction in advanced cancer patients: A systematic review. *J Med Imaging Radiat Oncol*. 2021. Oct;65(6):806-816.

20. Kersting C, Kneer M, Barzel A. Patient-relevant outcomes: what are we talking about? A scoping review to improve conceptual clarity. *BMC Health Serv Res.* 2020. Jun 29;20(1):596.

21. Federatie Medisch specialisten (2016). 'Richtlijn Proximale femurfracturen' [Guideline proximal femoral fractures] https://richtlijnendatabase.nl/richtlijn/proximale_femurfracturen/proximale_femurfracturen_-_startpagina.html, assessed at 4th of April 2022.

22. Charles C, Gafni A, Whelan T. Shared decision-making in the medical encounter: what does it mean? (or it takes at least two to tango). *Soc Sci Med.* 1997. Mar;44(5):681-92.

23. van Bruchem-Visser RL, van Dijk G, de Beaufort I, Mattace-Raso F. Ethical frameworks for complex medical decision making in older patients: A narrative review. *Arch Gerontol Geriatr.* 2020. Sep-Oct;90:104160

CHAPTER 3

Relationship between clinical outcomes and Dutch frailty score among elderly patients who underwent surgery for hip fracture

Published as: Winters AM, Hartog LC, Roijen H, Brohet RM, Kamper AM. Relationship between clinical outcomes and Dutch frailty score among elderly patients who underwent surgery for hip fracture. Clin Interv Aging. 2018 Dec 5;13:2481-2486. doi: 10.2147/CIA.S181497. PMID: 30584288; PMCID: PMC6287424.

ABSTRACT

Background: Frailty is a geriatric condition that is associated with an increased risk of mortality and functional decline. To date, mainly the Groningen Frailty Indicator (GFI) and Hospital Safety Management (VeiligheidsManagementSysteem [VMS]) frailty score are used to determine frailty in several hospitals in the Netherlands. However, it is yet unknown, which method has the best predictive value on clinical outcomes.

Objective: The aim of this study was to investigate the predictive value of GFI and VMS on clinical outcomes among patients who underwent hip fracture surgery.

Design: This is a prospective observational cohort study.

Methods: We selected all patients aged 70 years or higher, who underwent hip fracture surgery in our general hospital, between November 2014 and November 2015. Among all patients, VMS, GFI and Barthel-20 index (BI) were assessed. McNemar's paired test and Cohen's κ were used to examine the difference and the level of agreement between the two scoring methods. Kaplan–Meier and multivariable regression analyses were performed to determine overall survival and mortality, respectively, 3 years and 30 days after surgery.

Results: A total of 280 patients were included in the study. The median follow-up was 25 months. No systematic difference was found between the two methods (P=0.237), while a fair level of agreement could be measured (κ=0.363 [95% CI =0.23–50]). VMS showed a statistically significant difference in overall survival as compared to nonfrail patients (57 vs 80%, respectively [$P_{logrank}$ <0.001] with an HR of 3.5 [95% CI =2.1–5.7; P<0.001]). Classification according to GFI yielded a lower but still significant HR 2.3 (95% CI =1.2–4.1; P=0.008).

Conclusion: VMS can be used in classifying frailty, whereby VMS frailty score is associated with clinical outcomes as overall survival mortality in older patients with hip fracture and who underwent surgery.

INTRODUCTION

The number of elderly people is rising in the Netherlands, from 2.9 million people aged above 65 years in 2017 to 4.8 million in 2040 (1). Hip fractures are a leading cause of morbidity and mortality in elderly, an incidence of 18,000 patients above the age of 50 years in the Netherlands has been described (2). Among others, the overall outcome of hip fracture patients reflects the prefracture condition of the patient and is a summation of many factors. Identification of these factors can be used to identify patients who are frailer and might need a different approach during and after hospital stay. Frailty is a geriatric condition characterized by an increase in vulnerability to external stressors (3,4) and has shown to be predictive for adverse postoperative outcomes in patients with hip fracture (5,6).

In the Netherlands, a proven feasible, valid, and reliable instrument for measuring frailty is the Groningen Frailty Indicator (GFI) (7,8). The internal consistency is 0.68–0.81. The GFI consists of 15 questions to determine the level of frailty; it establishes physical, cognitive, social, and psychological impairments and gives a score at a scale of 0–15. A GFI score of 4 or higher suggests frailty (9). An alternative for scoring frailty in the Netherlands is the Hospital Safety Management (VeiligheidsManagementSysteem [VMS]) frailty score (10). VMS was based on the following three questions: one about cognitive impairment or confusion during earlier admissions, one about falls in the last 6 months, and one question about physical impairments (10). When falling and another question scored yes, frailty was assumed. It is already known that VMS frailty score is correlated with mortality (11).To our knowledge, no previous studies investigated the predictive value of the GFI and VMS frailty scores on 30-day mortality or functional decline in patients with hip fracture. We performed a study in which we aimed to investigate the predictive value on adverse outcome of the GFI and VMS frailty scores in older patients with hip fracture and who underwent surgery.

METHODS

Study population

This prospective observational cohort study was performed in a general hospital. All patients at the age of 70 years or older, who were admitted to our hospital with a primary proximal hip fracture and underwent surgery, were recruited. Recruitment and data collection were carried out between November 2014 and December 2015. Exclusion criteria were fractures distal

from subtrochanteric fracture, periprosthetic fractures, pathological fractures, and admission to another department than the orthopedics/surgical or internal medicine/geriatric department.

Data collection

Baseline data involved demographic characteristics, multi-morbidity, medication use, nutritional status, functional status, surgical treatment, anesthesia technique, delirium during admission, date of admission, and date of surgery. Delirium was considered to be present, when delirium was reported by a member of the geriatric team or when the Delirium Observation Screening (DOS) scores were at least three times above three and were fluctuating during the day (12). Data of mortality were collected from the municipality population register at one point after about 3 years after surgery. Morbidities were classified into the following five categories: diabetes mellitus, cardiovascular disease (heart disease, cerebrovascular accident, transient ischemic attack, renal failure, or hypertension), neurodegenerative disease (dementia and Parkinson's disease), chronic obstructive pulmonary disease (COPD; asthma, or fibrosis), and cancer. We combined medication with identical ATC3 codes, with polypharmacy defined as the use of five or more prescriptions with different ATC3 codes at admission.

Frailty was determined with two instruments, such as the GFI and the VMS, at admission or within 24 hours after admission.

Nutritional status was determined with the Short Nutritional Assessment Questionnaire (SNAQ). A SNAQ score of two or more is assumed to be related to a moderate-to-severe risk of malnourishment (13). Daily living activities were measured with the Barthel-20 index (BI) (14). at the day of admission to evaluate prefracture functional status. Degree of functional status change was based on assessing the difference in BI scores between baseline and 2 months after surgery.

All tests were part of the usual clinical care. Four trained medical staff members performed all tests to reduce interobserver disagreement. It was intended that all tests on a patient were taken by one and the same medical staff member.

Statistical analyses

Descriptive statistics was used to describe the baseline characteristics of the population and the outcome variables. Because of the lack of a golden standard to use as a reference, no sensitivity and specificity analyses were performed. McNemar's paired test was used to determine whether there was

a systematic difference between the two frailty scoring methods. Cohen's κ was used to measure the level of agreement between the two methods. Univariate analyses were performed with the Pearson chi-squared or Fisher's exact tests for dichotomous variables and the parametric independent *t*-test or nonparametric Mann–Whitney *U* test for continuous variables. Spearman and Pearson correlations were used to determine the correlation between the potential independent variables. In a multivariate logistic regression model, the predictive value of the frailty scoring methods and other patient characteristics on functional decline and mortality was determined. Stepwise regression analyses were performed to determine potential independent predictive variables for mortality and survival. These included logistic regression to examine 30-day mortality and Cox regression to examine overall survival as clinical outcome. Kaplan–Meier analysis was used to examine the difference in overall survival between frail and nonfrail patients classified by VMS and GFI. Potential confounders were age in two groups, smoking, gender, classification of frail by GFI or VMS, malignancy, and multimorbidity at baseline, such as chronic pulmonary diseases, cardiovascular disease, and living in a nursing home. Receiver operating characteristic curve analysis was not performed, since this would only consider the occurrence of events and not time to event. A *P*-value of <0.05 was considered as statistically significant. SPSS (Version 24) was used for the analysis.

Ethical approval

The study protocol was approved by the local medical ethics committee (Medisch Ethische Toetsingscommissie, Zwolle; study number 14.0110). Written informed consent was obtained from all patients by the participating medical doctor or nurse. All data were analyzed anonymously. The study protocol was registered prior to the start of the study at trailregister.nl (NTR5058). The "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) statement was used to describe this observational cohort study (15).

RESULTS

A total of 286 patients were included in the study. The median follow-up was 25 months. The characteristics are presented in Table 1. The mean age was 83 years, and 75% of the patients were female. Prevalence of delirium during admission was 21%, 9% of the patients died within 30 days after surgery, and 26% of the patients died within 1 year after surgery. Multimorbidity, polypharmacy, and living in a nursing home before admission were associated with an increased 1-year mortality risk.

Table 1. Characteristics and outcome measures

	Total N=286
Mean age (SD)	83.0 (6.6)
Gender	
Male	71 (25%)
Female	215 (75%)
Multimorbidity	
cardiovascular disease	206 (72%)
neurodegenerative disease	75 (26%)
chronic pulmonary disease	32 (11%)
diabetes mellitus	63 (22%)
Cancer	17 (9%)
Polypharmacy[a]	186 (65%)
Living in a nursing home	38 (13%)
Dependency in ADL[b]	33 (18%)
Risk for malnutrition[c]	32 (14%)
Frail by VMS[d]	160 (58%)
Frail by GFI[e]	113 (60%)
Operation technique	
(hemi) arthroplasty	126 (44%)
internal fixation	160 (56%)
General analgesia	145 (51%)
Delirium	57 (21%)
Functional decline[f]	22 (8%)
30-days mortality	25 (9%)
1-year mortality	75 (26%)

[a]Polypharmacy was defined as the use of 5 or more prescriptions with different ATC3-code at admission. [b]Dependency in activities of daily living (ADL) = score <15 on BI; [c]Based on Short Nutritional Assessment Questionnaire (SNAQ) = ≥ 1; [d]Frail according to VMS (Hospital Safety Management) was defined as two or more questions scored yes; [e]Frail according to GFI (Groninger Frailty Index) when the total score was four or higher; [f]Decline in Barthel-20 Index score two months after surgery.

Frailty

A total of 277 patients completed the VMS, and 189 patients completed the GFI. Both tests were completed by 185 patients. A total of 76 (41%) patients were identified as frail according to both instruments, whereas 51 (28%) patients were identified as nonfrail in both instruments. A total of 24 patients scored frail in the VMS and not in the GFI, and 34 patients scored frail in the GFI and not in the VMS. Paired analysis showed that there was no difference between the two diagnostic tools (P=0.237) in addition to a fair level of agreement (κ=0.363 [95% CI =0.23–50]). In the group patients without GFI scores, fewer patients stayed in a nursing home before admission (9 vs 22%) and fewer patients were known with neurodegenerative disease (17 vs 44%). Other variables were comparable. An increase in positive answers on the VMS questionnaire was associated with an increase in mortality, polypharmacy, malnutrition, and living in a nursing home before admission.

Functional decline

For 62% of all patients, the BI scores were assessed at two moments. In 8% of the patients, functional decline was found (Table 1). The mean age of the patients with functional decline was 86 years, of whom 86% was female. The prevalence of frailty was 68 and 71% according to VMS frailty score and GFI, respectively. Functional decline was significantly associated with VMS (P=0.003) and (hemi) arthroplasty operation technique (P=0.015) (Table 2). Unfortunately, multivariate logistic regression analysis with functional decline as outcome was not possible due to the high number of missing BI scores.

Table 2 includes patients' characteristics and their possible association or relation with patient outcomes as functional decline, 30-day mortality, and overall mortality.

Table 2. Characteristics and univariate analyses by patient outcome

	Functional decline[c] N=22 (%)	Sign.	30-days mortality N=25 (%)	Sign.	Overall mortality[d] N=105 (%)	Sign.
Mean age (SD)	86.0 (6.0)		85.0 (6.0)		85 (6.0)	
Gender [male]	3 (14)	0.269[b]	11 (44)	**0.020**	29 (28)	0.405
Cardiovascular disease	18 (82)	0.200[b]	24 (96)	**0.004[b]**	86 (82)	**0.005**
Neuro-degenerative disease	5(23)	0.165	9 (36)	0.245	41 (39)	**0.000**
Chronic pulmonary disease	1 (5)	-	5 (20)	0.143	16 (15)	0.098
Diabetes mellitus	4 (18)	-	8 (32)	0.208	30 (29)	**0.042**
Polypharmacy[e]	18 (82)	0.081[b]	21 (84)	**0.047[b]**	76 (72)	**0.047**
Living in a nursing home	0	-	5 (20)	0.301	23 (22)	**0.001**
Risk for malnutrition[f]	4 (18)	0.074[b]	5 (33)	**0.029**	22 (21)	**0.000**
Frail by VMS[g]	15 (68)	**0.003**	20 (91)	**0.001[b]**	80 (76)	**0.000**
Frail by GFI[h]	15 (71)	0.063	11 (79)	0.165[b]	47 (45)	**0.001**
Operation technique [(hemi) arthroplasty]	4 (18)	**0.015[b]**	14 (56)	0.208	45 (43)	0.756
Delirium	2 (9)	0.732[b]	10 (18)	**0.008**	34 (60)	**0.000**

Values are number (percentage) of patients. SD: standard deviation; [a]Pearson Chi-Square test; [b]Fisher's exact test; [c]Decline in Barthel-20 Index score two months after surgery; [d]Data of mortality were collected from the population register at one point after two till three years after surgery; [e]Polypharmacy was defined as the use of 5 or more prescriptions with different ATC3-code at admission; [f]Based on Short Nutritional Assessment Questionnaire (SNAQ) = ≥ 1; [g]Frail according to VMS (Hospital Safety Management) was defined as two or more questions scored yes; [h]Frail according to GFI (Groninger Frailty Index) when the total score was four or higher;

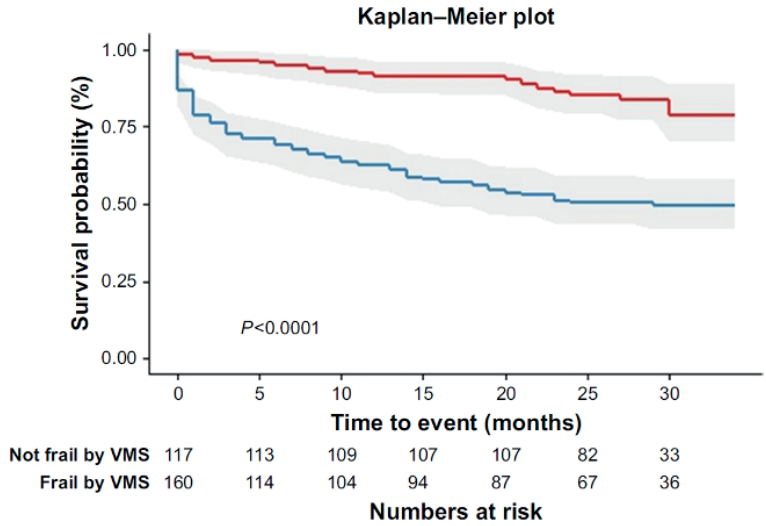
Mortality

Nine percentage of all patients died within 30 days after surgery (Table 1). The median age was 85 years, and 56% of the patients were female (Table 2). The prevalence of frailty was 91 and 79% according to VMS and GFI, respectively. Of these patients, 84% had polypharmacy and 96% of them suffered from cardiovascular disease. In the univariate analysis, VMS was significantly associated with 30-day mortality and overall mortality. Other factors associated with mortality were being male, delirium during hospitalization, polypharmacy, presence of cardiovascular disease, and malnutrition.

Figure 1 shows the Kaplan–Meier curves of the overall survival among patients with a hip fracture classified as frail (blue line) and not frail (red line) by VMS. Patients who were classified as frail with VMS showed a

significantly worse survival than nonfrail patients (overall survival: 57 vs 80%, respectively; $P_{logrank}$ <0.001). These results were similar when patients were classified according to the GFI method (58 and 81%) (data not shown). The corresponding hazards of death were statistically significant (HR_{VMS} =3.5; 95% CI =2.1–5.7, *P*<0.001, and HR_{GFI} =2.3; 95% CI =1.2–4.1, *P*=0.008). Other independent variables of survival in the regression model were age higher than 83 years (HR =2.6; 95% CI =1.5–4.2, *P*<0.001) and presence of chronic pulmonary disease (HR =0.46; 95% CI =0.2–0.9, *P*=0.013).

Figure 1. Overall survival analysis for patients with a hip fracture classified as frail and non-frail with the VMS scoring method



VMS (Hospital Safety Management) was defined as two or more questions scored yes; Red line is not frail by VMS, the blue line is frail by VMS.

DISCUSSION

In this study, we showed that elderly patients who underwent surgery for hip fracture classification as frail by VMS and GFI are associated with a significantly decreased overall survival. Other independent risk factors for survival were higher age and presence of chronic pulmonary disease. In addition, classification as frail according to VMS was significantly associated with a functional decline after surgery and with 30-day mortality.

VMS

The results of this study are generally consistent with the sparse literature on VMS frailty and outcomes in patients with hip fracture. Patients classified by the VMS as "frail older people" had a higher risk of dying (11). Another study in elderly patients stated that the best predictive power for adverse outcome was found by identifying patients at risk aged 70–80 years and scoring positive on three or four VMS domains or aged >80 years and scoring positive on one or more of the VMS domains (16). The fourth domain in that study was undernutrition. We used three VMS questions about cognitive impairment or confusion during earlier admission periods, activities of daily living (ADL) limitations, and falling. We found that VMS frailty (scoring positive on one of the other questions than falling) was predictable for 30-day mortality, overall mortality, and functional decline. The only study that studied VMS frailty in a population elderly with hip fracture showed that VMS score for delirium risk was predictive for clinical outcome (17).

GFI

The existence of higher numbers of missing scores on the GFI frailty score was probably explained by the usability of this questionnaire. The GFI was more difficult to complete than was expected beforehand. During data collection, researchers experienced problems in answering the questions in patients with decline in cognitive functioning and, sometimes, they scored themselves less frail than they actually were.

Another explanation for the missing scores is the inaccurate computer system for selecting eligible patients.

Only one study assessed GFI in patients with hip fractures (N=30). The main study was conducted for vertebral fracture patients. A frailty score of 67% was mentioned only for the total study population (18). Previous studies about the GFI have reported good internal consistency with adequate validity (7,8,11,19). In the present study, GFI was not able to predict 30-day mortality and 1-year mortality. There was an association between GFI and functional decline; however, due to high numbers of missing BI scores, we could not accurately carry out the analyses. Previous studies compared GFI frailty scores only with other frailty measurements, not with patients' outcomes such as mortality, functional decline, delirium, length of stay, and quality of life.

In this study, chronic pulmonary disease seemed to be protecting with regard to overall mortality. This is inconsistent with earlier studies. Earlier studies in patients with hip fracture showed that patients with chronic pulmonary

disease have higher risk of passing away than those without chronic pulmonary disease (20,21). In these studies, patients above the age of 40 or 65 years were included. A similar study, as ours, did not describe pulmonary disease separately but used the Charlson comorbidity index for counting comorbidity (17).

Strengths and limitations

The present study has several strengths. It was performed in a general hospital, few exclusion criteria were used, and our study population is a representative group of older patients with hip fracture. To our knowledge, no previous studies investigated the predictive value on adverse outcome of GFI and VMS frailty scores in patients with hip fracture.

There were also limitations in this study. Functional decline by Barthel-20 index is probably not the most relevant outcome of patients after hip fracture. Researchers noticed, during data collection, that in most cases, several months after surgery, the maximum scores on mobility were reached when patients still experienced decline in mobility. Our population was too small for exploring predictive values for 30-day mortality in multivariate analyses. Frailty scoring by VMS and the cutoff point were based on clinical expertise in elderly patients of the geriatric specialists/researchers. The VMS frailty score is based on a commonly accepted guideline in the Netherlands but applied in different ways.

Implications for practice

Frailty should be assessed by VMS in every patient aged 70 years or higher with hip fracture. VMS frailty score is easier to complete than GFI and is also statistically comparable with GFI. When two or more questions are answered with yes, the patient with hip fracture should be documented as frail. For the outcomes assessed in the study, the VMS might be more appropriate than the GFI.

Further research

Further research is necessary to explore which values predict 30-day mortality and to explore the predictive value of frailty on adverse outcome in patients as duration of stay, delirium, functional decline, and quality of life. When knowing these predictive values, it is crucial to explore in what way we can improve adverse outcome in patients with hip fracture in order to realize the main goal of these patients; returning to prefracture functional level.

Furthermore, especially in frail patients, the situation before admission is relevant for decision making, in choosing surgery or not and setting other treatment goals. Therefore, a geriatric comprehensive assessment including GFI probably is relevant for other purposes. Moreover, in this study, frailty was assessed during hospital stay but might also be suitable in the situation before admission. These elements should also be the focus of further research.

CONCLUSION

VMS frailty scores can be used in establishing frailty and thereby adverse outcome as overall survival and 30-day mortality in older patients with hip fracture.

REFERENCES

1. van Duin C, Stoeldraijer L. Bevolkingsprognose 2014-20160: groei door migratie. CBS, bevolkingstrends 2014(17-18).
2. Lotters FJ, van den Bergh JP, de Vries F, Rutten-van Molken MP. Current and Future Incidence and Costs of Osteoporosis-Related Fractures in The Netherlands: Combining Claims Data with BMD Measurements. *Calcif Tissue Int* 2016 Mar;98(3):235-243.
3. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001 Mar;56(3):M146-56.
4. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013 Jun;14(6):392-397.
5. Kistler EA, Nicholas JA, Kates SL, Friedman SM. Frailty and Short-Term Outcomes in Patients With Hip Fracture. *Geriatr Orthop Surg Rehabil* 2015 Sep;6(3):209-214.
6. Farhat JS, Velanovich V, Falvo AJ, et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. *J Trauma Acute Care Surg* 2012 Jun;72(6):1526-30; discussion 1530-1.
7. Peters LL, Boter H, Buskens E, Slaets JP. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. *J Am Med Dir Assoc* 2012 Jul;13(6):546-551.
8. Bielderman A, van der Schans CP, van Lieshout MR, et al. Multidimensional structure of the Groningen Frailty Indicator in community-dwelling older people. *BMC Geriatr* 2013 Aug 22;13:86-2318-13-86.
9. Steverink N, Slaets J, Schuurmans H, Van Lis M. Measuring frailty: developing and testing of the Groningen frailty indicator (GFI). *The Gerontologist* 2001;41:236-237.
10. VMS. Praktijkgids kwetsbare oudere. 2009; Available at: http://www.vmszorg.nl/_library/5540/web_2009.0104_praktijkgids_kwetsbare_ouderen.pdf. Accessed april, 2017.
11. Oud FM, de Rooij SE, Schuurman T, Duijvelaar KM, van Munster BC. Predictive value of the VMS theme 'Frail elderly': delirium, falling and mortality in elderly hospital patients. *Ned Tijdschr Geneeskd* 2015;159:A8491.
12. Schuurmans MJ, Early recognition of delirium, Vroegtijdig herkenning van het delirium, proefschrift, Amsterdam, 2001
13. Kruizenga HM, Seidell JC, de Vet HC, Wierdsma NJ, van Bokhorst-van der Schueren MA. Development and validation of a hospital screening tool for malnutrion: the short nutritional assessment questionnaire (SNAQ). *Clin Nutr* 2005;24 (1):75-82.
14. Wade DT, Hewer RL. Functional abilities after stroke: measurement, natural history and prognosis. *J Neurol Neurosurg Psychiatry* 1987 Feb;50(2):177-182.
15. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014 Dec;12(12):1495-1499.
16. Heim N, van Fenema EM, Weverling-Rijnsburger AW, et al. Optimal screening for increased risk for adverse outcomes in hospitalised older adults. *Age Ageing* 2015 Mar;44(2):239-244.

17. Folbert EC, Hegeman JH, Gierveld R, et al. Complications during hospitalization and risk factors in elderly patients with hip fracture following integrated orthogeriatric treatment. *Arch Orthop Trauma Surg* 2017 Apr;137(4):507-515.

18. Walters S, Chan S, Goh L, Ong T, Sahota O. The Prevalence of Frailty in Patients Admitted to Hospital with Vertebral Fragility Fractures. *Curr Rheumatol Rev* 2016;12(3):244-247.

19. Metzelthin SF, Daniels R, van Rossum E, de Witte L, van den Heuvel WJ, Kempen GI. The psychometric properties of three self-report screening instruments for identifying frail older people in the community. *BMC Public Health* 2010 Mar 31;10:176-2458-10-176.

20. Roche JJW, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ*, 2005 Nov 18.

21. Luise, de, C, Brimacombe, M, Pedersen, L, Toft Sorensen, H. Chronic obstructive pulmonary disease and mortality following hip fracture: a population-based cohort study. 2008 *European Journal of Epidemiology,* 2008. Volume 23, issue 2, pp115-122.

CHAPTER 4

The association between orthostatic hypotension and handgrip strength with successful rehabilitation in elderly hip fracture patients

Published as: Hartog LC, Winters AM, Roijen H, Kamper AM, Inia H, Kleefstra N, Bilo HJG, van Hateren KJJ. Association Between Orthostatic Hypotension and Handgrip Strength With Successful Rehabilitation in Elderly Hip Fracture Patients. Arch Phys Med Rehabil. 2017 Aug;98(8):1544-1550.e3. doi: 10.1016/j.apmr.2016.11.009. Epub 2016 Dec 16. PMID: 27993582.

ABSTRACT

Objective: To investigate the relationship between orthostatic hypotension (OH) and muscle strength versus time to successful rehabilitation within elderly patients with hip fracture.

Design: A prospective, observational cohort study. Handgrip strength was measured at the day of admission and OH as soon as possible after surgery. Cox proportional hazard modeling was used to investigate the relationship between OH or handgrip strength (kg) and time to successful rehabilitation, expressed as hazard ratios (HRs). OH was defined as a decrease in systolic blood pressure of ≥20mmHg or diastolic blood pressure of ≥10mmHg after postural change (dichotomous). Handgrip strength was measured with a hand dynamometer (continuous).

Setting: General hospital.

Participants: Patients (N=116) aged ≥70 years with a hip fracture were recruited on the day of hospital admission.

Interventions: Not applicable.

Main outcome measures: Primary outcome was time to successful rehabilitation, which was defined as discharge to patients' own homes.

Results: During a median follow-up period of 36 days (interquartile range, 9-57d), 103 patients (89%) were successfully rehabilitated. No statistically significant relationships were found between OH and time to successful rehabilitation (HR=1.05; 95% confidence interval [CI], .67-1.66). Also, handgrip strength and successful rehabilitation were not statistically significantly related (HR=1.03; 95% CI, .99-1.06).

Conclusions: OH measured during the first days of hospitalization is not related to time to successful rehabilitation in patients with hip fracture who have undergone surgery. Although no significant relationship was seen in the present study, the width of the CIs does not exclude a relevant relationship between handgrip strength and time to successful rehabilitation.

INTRODUCTION

Hip fractures are a common cause of hospitalization and rehabilitation in elderly patients [1, 2]. The main purpose of rehabilitation in these patients is to regain their prefracture health status as much as possible [3, 4]. Dependence on medical care, decline in functional outcome, or admission to a nursing home may be the consequence when rehabilitation fails. The outcome of rehabilitation reflects the condition of the elderly patient and is a summation of many factors, including both physical and mental parameters [3-11]. The definition of successful rehabilitation or recovery varied widely; from regaining prior functional and/or mobility status, to functional independence leading to discharge to patients own home [4, 7, 9, 10, 12].

Examples of the numerous factors that negatively influence the response to rehabilitation are high age, presence of cognitive impairment or coexisting diseases, and high fear of falling (FOF) [3-5, 9, 13].

Also, orthostatic hypotension (OH) and muscle strength are amongst the factors that have been found to influence rehabilitation in elderly patients [7] [8, 10]. As the prevalence of OH and impaired muscle strength is high in elderly patients and are considered as important risk factors for falling and frailty, these variables are likely to negatively influence successful rehabilitation [14-20].

A previous study observed the counterintuitive finding that patients with OH were found to have a higher risk of successful rehabilitation compared to patients without OH [7]. Another study found no difference in functional outcome between stroke patients with and without OH [21]. Muscle strength is considered to be a strong positive predictor for functional outcome after rehabilitation in elderly hip fracture patients [8, 10]. OH and muscle strength separately influence outcome, but it is likely that these factors are also interrelated. Several causes of OH, such as the use of different medications, hypovolemic disorders, and bed rest, are potentially related to muscle strength [22-25].

As muscle strength and OH are both related to successful rehabilitation, and possibly also interrelated, these factors should be combined (and adjusted for) in analysing the association with rehabilitation. As far as we are aware, no previous studies investigated these combined associations. Therefore, we performed a study in which we aimed to investigate the relation between OH and muscle strength with time to successful rehabilitation within elderly hip fracture patients. We hypothesized that the presence of OH or low muscle

strength would negatively influence the time to successful rehabilitation. Furthermore, we hypothesized that the relationship between OH and time to successful rehabilitation would be influenced by muscle strength.

METHODS

Study population

This prospective observational cohort study was performed in a general hospital (the Isala hospital, Zwolle, the Netherlands). All patients of 70 years of age or older, admitted to the hospital with a hip fracture and treated by surgery, were recruited.

Recruitment and all study procedures took place between November 2014 and December 2015. Exclusion criteria were a life expectancy of less than 3 months, unable to mobilize before hospitalization, and being institutionalized in a nursing home facility before hospitalization. By performing a prospective study in a general hospital we tried to minimize the chance of selection bias.

Data collection

Baseline data involved demographic characteristics, a full medical history including a history of cardiovascular disease (CVD), diabetes mellitus (DM), hypertension, FOF, and medication use. Patients were considered to have cardiovascular disease when they had a history of angina pectoris, myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, stroke or transient ischaemic attack.

Blood pressure was measured following a standardized protocol, using an automated sphygmomanometer (A&D UA-767 Plus) [26]. If the automated sphygmomanometer displayed an error message, blood pressure was manually measured with a Heine Gamma XXL-T sphygmomanometer [27]. Blood pressure was measured two times in supine position after 5 minutes of rest, and two times each at 1 and 3 minutes after postural change. The forearm of the patient was supported at heart level during the measurements in upright position [28]. The postural change was from supine to standing position, or from supine to sitting position for patients who were unable to stand. Blood pressure was measured as soon as possible after surgery. OH was defined as a drop in systolic blood pressure (SBP) of $\geq$ 20 mmHg or diastolic blood pressure (DBP) of $\geq$ 10 mmHg after postural change compared to the mean value of the baseline measurements in supine position [29]. Characteristic symptoms

of OH like light-headedness, syncope, or dizziness after postural change were questioned and the combination of OH and orthostatic complaints was described as symptomatic OH.

Handgrip strength was measured with a Jamar hand dynamometer [30] in kilogram (kg) within 2 days of hospital admission, preferably at the day of admission. When a patient was operated on the day of admission, the handgrip strength was measured postoperatively but always within two days after admission.

Testing was performed with the participant in a comfortable sitting position in the hospital bed. The forearms were resting with the elbow flexed at 90□, the forearm in neutral position, and thumbs facing up. Both dominant and non-dominant hand was tested, both 3 times. The best of 6 attempts of maximal voluntary contraction was used for statistical analysis [30]. OH was expressed as dichotomous (OH vs no OH) and handgrip strength as a continuous variable.

To measure FOF, a numeric scale (1-10) was used, with 1 representing no FOF and with 10 representing an extreme FOF [31]. The FOF was measured at the day of admission.

Activities of daily living were measured with the Barthel-20 index at the day of admission [32] to evaluate prefracture status.

Body mass index was calculated by measuring body weight and height.

All tests were part of usual clinical care. Four trained medical staff members performed all tests to reduce the change on inter-observer disagreement. It was intended to measure all variables per patient by the same medical staff member. Primary outcome was time to successful rehabilitation, which was defined as discharge to patients' own homes, where they functioned self-reliant and lived by themselves. Time to successful rehabilitation started on the day of OH blood pressure measurements, which were performed as soon as possible after surgery. Patients were considered as self-reliant if a patient regained his or her prefracture health status. As a consequence, patients with an already highly adapted home environment (e.g. stairlift, homecare, meal service) may be sent home earlier than others.

In the trial register, successful rehabilitation was predefined as having the same functional status compared to the prefracture status, evaluated by using the mobility component of the Barthel index. Because all patients reached the prefracture mobility score on the Barthel index in a few days after surgery (despite the fact they were not discharged home, but had to be admitted to

a rehabilitation facility), we evaluated this definition and decided to change it into the current clinically more relevant definition.

Statistical analyses

Continuous variables are presented as mean and standard deviation for normally distributed variables, or as median and interquartile range for non-normally distributed variables. Cox proportional hazard modelling was used to investigate the relation between OH, orthostatic complaints, symptomatic OH, or handgrip strength and time to successful rehabilitation. Two separate cox proportional hazard analyses were performed; one regarding the relationship between OH and successful rehabilitation and one between muscle strength and successful rehabilitation. We used three different models. In model 1, unadjusted analyses were performed. In model 2, only age and gender were taken into account as possible confounders. In model 3, regarding the relationship between OH and rehabilitation, we additionally adjusted for the following variables: body mass index (BMI), a history of diabetes mellitus, the score on the Barthel index, previous macrovascular complications, mean systolic blood pressure, the use of antihypertensive medication, and baseline handgrip strength. For the analyses regarding the relationship between handgrip strength and rehabilitation, we adjusted for age, gender, BMI, the score of the Barthel index, previous macrovascular complications, and OH. These confounders were chosen based on clinical grounds, since all confounders were likely to be related to successful rehabilitation and OH or handgrip strength. By adjusting for potential confounding factors the risk of confounding bias was reduced.

The confounding effect of FOF on the relationship between OH, handgrip strength and successful rehabilitation was explored by adding FOF to model 3 in both analyses. FOF was added separately because of missing values (n=8). There were missing values of FOF (n=8), BMI (n=6), and Barthel index (n=2). The hazard ratios (HRs) regarding systolic blood pressure refer to a pressure increase in steps of 10 mmHg.

The Schoenfeld residual plots were inspected for each predictor variable to check the assumption of proportional hazards.

P-values less than 0.05 were considered statistically significant. Collinearity diagnostics were tested for each confounder; co-variables are considered to be highly correlated with a variance inflation factor (VIF) of 10 or more [33, 34]. When necessary, interaction was tested between different variables. Interaction was considered to be significant, with a p value less than 0.05.

All statistical analyses were performed using SPSS software (version 22).

The 'Strengthening the Reporting of Observational studies in Epidemiology' (STROBE) statement was used to describe this observational cohort study [35].

Ethical approval and Clinical Trial registration

This study was performed in accordance with the Declaration of Helsinki. According to Dutch guidelines this study did not fall under the scope of the Medical Research Involving Human Subjects Act, and therefore this study did not need a formal approval of an accredited medical ethics committee. Written informed consent was obtained for all patients by the participating medical doctor or nurse. All data were analysed anonymously. The study was registered on Trialregister.nl (NTR4940).

RESULTS

A total of 116 patients was included in this cohort. The baseline characteristics are presented in table 1. Median age of the total study population was 82 (IQR (interquartile range) 76-86) years. Various surgical techniques were used to treat the hip fractures; 37% intramedullary nail, 50% hemi- or total hip arthroplasty, 13% (sliding) hip screws. 39 patients (34%) were discharged to their own homes and 77 patients (66%) to a nursing home facility for further rehabilitation. During a median follow-up period of 36 days (IQR 9-57), 103 (89%) patients were successfully rehabilitated. Three patients died during rehabilitation. Ten patients could not return home and stayed at a long-term nursing home facility. Patients who did not successfully rehabilitate were found to have a higher prevalence of macrovascular disease and hypertension compared to patients who were successfully rehabilitated.

Table 1. Baseline characteristics total population

Characteristic	Total Baseline *N=116*
Demographics	
Age (years)	82 (76-86)
Female gender	86 (74)
Mean body mass index (kg/m^2)	25 (23-28)
Hypertension	77 (66)
History of CVD	27 (23)
Diabetes mellitus	23 (20)
Current smoker	17 (15)
Measurements	
Consumption meal or drink[a]	113 (97)
No. Days between operation and BPM	2 (1-3)
Mean SBP lying (mmHg)	130 (22)
Mean DBP lying (mmHg)	65 (11)
Mean pulse frequency (beats/min)	81 (18)
Orthostatic hypotension	39 (34)
Orthostatic complaints	22 (19)
Symptomatic hypotension	16 (14)
Percentage postoperative handgrip strength measurement	21 (18)
Handgrip Strength (kg)	20 (15-26)
Score Barthel index	19 (17-20)
Fear of Falling[b]	1 (1-4)
Medication during admission	
Mean number of agents	6 (3-9)
Antihypertensive medication	70 (60)
• Diuretics	40 (35)
• Beta blockers	31 (27)
• Calcium channel blockers	17 (15)
• ACE inhibitors	44 (38)
Benzodiazepines	22 (19)
Antipsychotics	3 (3)
Antidepressants	12 (10)

Data are means (± SD), medians (interquartile range) or n (%). BPM = blood pressure measurement. MSM = muscle strength measurement. SBP = systolic blood pressure. DBP = diastolic blood pressure. [a] Meal < 2 hours or drink < 1 hour prior to the measurements. [b] Missing values in 8 patients.

OH and Successful rehabilitation

OH was present in 39 out of 116 patients, resulting in a prevalence of 34% (95% confidence interval (CI) 25-43%). The postural change was performed mostly from lying to sitting (n=114 (98%)) due to decreased mobility; only 2% of the tested population could perform postural change from lying to standing position. Blood pressure measurement took place with a median of 2 (IQR 1-3) days after surgery.

Table 2 presents the results of the Cox regression analyses regarding the relationship between OH and successful rehabilitation. In the present study no statistically significant relationships were seen between OH (HR 1.05 (95%CI 0.67-1.66)) and time to rehabilitation. The confounders systolic blood pressure (HR 1.01 (95%CI 1.00-1.03)), diabetes mellitus (HR 0.47 (95%CI 0.26-0.85)), and handgrip strength (HR 1.05 (95%CI 1.01-1.08)) were statistically significantly related to time to successful rehabilitation. Adding FOF to the multivariate model did not change the association between OH and time to rehabilitation. The hazard ratio of FOF was 0.87 (95%CI 0.79-0.97). Orthostatic complaints (HR 1.06 (95%CI 0.62-1.83)) and symptomatic OH (HR 1.15 (95%CI 0.62-2.13)) were also not related to time to successful rehabilitation in the multivariate analyses.

As blood pressure may be a marker of frailty in old age [36], we performed analyses in which we tested for interaction between systolic blood pressure and OH. No statistically significant interaction was seen.

The plots of the Schoenfeld residuals showed that the assumptions of proportional hazards were met (see supplemental data for Schoenfeld residual plots). Collinearity was tested and no serious multicollinearity was seen, because the mean VIF value was 1.37 (range 1.01-2.22).

Table 2. Hazard ratios of OH for successful rehabilitation (n=116)

	Model 1	Model 2	Model 3
	HR (95% CI)	HR (95% CI)	HR (95% CI)
OH	1.35 (0.90-2.05)	1.28 (0.85-1.94)	1.05 (0.67-1.66)
Age	-	**0.96 (0.93-0.99) (p=0.02)**	0.99 (0.96-1.03)
Gender, female vs male	-	0.99 (0.63-1.54)	0.61 (0.31-1.18)
BMI	-	-	0.99 (0.95-1.05)
Score Barthel Index	-	-	1.05 (0.94-1.18)
Antihypertensive medication	-	-	0.90 (0.58-1.40)
History of CVD disease	-	-	0.64 (0.37-1.11)
DM, DM vs control	-	-	**0.47 (0.26-0.85) (p=0.01)**
Mean SBP lying [a]	-	-	**1.01 (1.00-1.03) (p=0.01)**
Handgrip Strength	-	-	**1.05 (1.01-1.08) (p<0.01)**

Hazard ratios for successful rehabilitation. Model 1 unadjusted. Model 2 adjusted for age and gender. Model 3 adjusted for age, gender, BMI, score Barthel index, the number of antihypertensive medications, previous macro vascular complications, diabetes mellitus, mean SBP lying, and Handgrip Strength. OH = orthostatic hypotension. BMI = Body mass index. CVD = Cardio vascular disease. DM = Diabetes Mellitus. SBP = systolic blood pressure. [a] The hazard ratio refers to a pressure increase of 10 mmHg.

Handgrip strength and Successful rehabilitation

Median handgrip strength of the dominant arm was 20 kilograms (IQR 15-26). All handgrip strength measurements were performed within 2 days of admission. For the majority (82%) of the patients the handgrip strength measurements were performed preoperatively.

Table 3 present the results of the Cox regression analyses regarding the relationship between muscle strength and time to successful rehabilitation. None of the models showed a significant relationship between handgrip strength and time to successful rehabilitation. The confounder CVD was related to time to successful rehabilitation (HR 0.57 (95%CI 0.33-0.99).

Adding FOF to the multivariate model did not change the association of handgrip strength with rehabilitation (HR 1.03 (95%CI 0.99-1.06)). As a confounder, FOF was significantly related to time to successful rehabilitation (HR 0.87 (95%CI 0.78-0.97)).

Table 3. Hazard ratios of handgrip strength for successful rehabilitation (n=116).

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Handgrip strength	1.02 (1.00-1.04)*	1.02 (0.99-1.05)	1.03 (0.99-1.06)
Age	-	0.97 (0.94-1.00)	0.99 (0.95-1.02)
Gender, female vs male	-	0.72 (0.39-1.33)	0.83 (0.44-1.57)
BMI	-	-	0.97 (0.93-1.02)
Score Barthel Index	-	-	1.09 (0.98-1.21)
History of CVD disease	-	-	0.57 (0.33-0.99)
OH	-	-	1.09 (0.71-1.68)

Hazard ratios for successful rehabilitation. Model 1 unadjusted. Model 2 adjusted for age and gender. Model 3 adjusted for age, gender, BMI, score Barthel index, previous macro vascular complications, and OH. CVD = Cardio vascular disease. OH = orthostatic hypotension. * p=0,054

DISCUSSION

OH, measured in the immediate postoperative phase, was not related to time to successful rehabilitation in hospitalized elderly with a hip fracture. Although increased muscle strength was not significantly related to time to successful rehabilitation in the present study, the width of the confidence interval does not exclude a relevant relationship between handgrip strength and time to successful rehabilitation. Besides, muscle strength as a confounder, in the model with OH as the variable of interest, was significantly related to time to successful rehabilitation.

OH and successful rehabilitation

In contrast to the current study, a previous study performed by the same authors showed that patients with OH were found to have a higher hazard of successful rehabilitation compared to patients without OH [7]. Although our previous study reported a positive relation between OH and time to successful rehabilitation, we hypothesized prior to the present study that the presence of OH would negatively influence the time to successful rehabilitation. The prevalence of OH and successful rehabilitation was similar in both studies. When comparing both study populations, patients of the present study seemed to have less comorbidity, used less medication, and baseline blood pressure was lower, which reflects the setting of the previous study (nursing home).

The high prevalence of OH in the present study could be partially caused by hip fracture or hospital admission-related factors like bed rest, surgery, effects of anaesthesia, inadequate water intake, and blood loss. In these circumstances, OH may very well be a temporarily phenomenon and therefore not a predictor for an outcome such as time to successful rehabilitation [23]. In the study of Weiss et al., the impact of OH in hospitalized patients on mortality was described, and they advised to divide patients in 2 groups; patients with episodic OH, as is seen during hospitalization, and established OH (repeated measurements) [22]. Measuring OH in the first week of rehabilitation within a nursing home might possibly be a more accurate predictor for successful rehabilitation.

Analogous to the association with mortality, as assessed in the study by Weiss et al., one may hypothesize that episodic and sustained OH have different associations with rehabilitation. Episodic OH may have no consequences for chances of rehabilitation, whereas sustained OH may be much more relevant.

The confounders DM, SBP, handgrip strength and FOF were significantly related to time to successful rehabilitation. The hazard of successful rehabilitation in patients with DM was lower than patients without DM, as was also seen in the previous (mentioned) study [7]. The hazard of successful rehabilitation increased by 15% (95%CI 3-28%) for every 10 mmHg increase in SBP. In a previous study, higher blood pressure in frail patients was related to lower all-cause mortality while the opposite relationship was seen in non-frail patients [37]. Therefore, it was not unexpected that higher SBP is associated with a higher hazard of successful rehabilitation.

Poor muscle strength and FOF are frequently seen in elderly patients, and these factors are also related with the level of frailty [14-16]. Successful rehabilitation increased by 5% (95% CI 1-8) for every 1 kg increase in handgrip strength measurement. The relationship between handgrip strength and rehabilitation will be discussed in 4.2.

Time to successful rehabilitation decreased by 13% (95% CI 3-22%) for every 1-point increase on the VAS-FOF scale. These results support previous studies regarding the impact of FOF on functional outcome [11, 38], which describes an association between FOF with negative outcomes as falling and functional impairment (e.g. IADL). In the study by Oude Voshaar et al. FOF seems to be an important predictor for functional recovery after hip fracture surgery [9]. Previous studies described that fear after falling may restrict physical activity, which causes immobility and further loss of functional independence and risk of falling [39, 40]. FOF can be divided into three components; physiological,

behavioural, and cognitive [11]. Prevention and treatment of FOF by intervening all of those three components is an important clinical treatment goal.

Handgrip strength and successful rehabilitation

Although increased muscle strength was not significantly related to time to successful rehabilitation in the present study, a relationship cannot be excluded based on the width of the confidence interval. In the model with OH as the variable of interest, a statistically significant association was observed. Previous studies also observed positive relationships between handgrip strength and rehabilitation [8] [41]. Di Monaco et al. described a significant relationship between handgrip strength and functional outcome in hip fracture patients [8]. Another study showed a relationship between handgrip strength during hospital admission and walking independently [41]. An important difference between the study of Di Monaco and the present study is the timing of the handgrip strength measurement; at the rehabilitation division after discharge from the hospital versus preoperatively in the present study. Measuring handgrip strength preoperatively reflects the baseline condition of a patient and is a predictor for complications or length of stay [42, 43]. Therefore, handgrip strength measurement can be used to identify those patients who are frailer and need a different approach during hospital admission [42].

Study Strengths and Limitations

As the present study took place in a general hospital, and only a few exclusion criteria were used, our study population is a representative group of elderly patients with a hip fracture. The timing of inclusion and the homogenous study population of the present study were major strengths compared to our previous study [7]. Recruitment and testing took place within 2 days after admission to the hospital, preferably at the day of admission.

The current study has also some limitations. The main limitation was that 18% of the handgrip strength measurements were not measured preoperatively. However, we performed the same analyses in the group of patients with preoperatively measured handgrip strength, and the results did not relevantly change (data not shown). Although OH should be measured from lying to standing, this was not possible in 98% of patients. It is very likely that the actual number of patients with OH was higher. Furthermore, OH was only measured once during the follow-up period, which probably biased the results. By repeated OH measurements not only episodic OH but also established OH would have been diagnosed. Future studies are needed to evaluate the clinical implications of sustained OH on rehabilitation.

Another limitation is the definition of successful rehabilitation; in our study, this was defined as discharge to patients' own homes. Patients with a worse outcome after rehabilitation but with a highly adapted home environment may be sent home earlier than others.

CONCLUSIONS

In conclusion, this study showed that orthostatic hypotension measured during the first days of hospitalization was not related to time to successful rehabilitation. Although no significant relationship was seen in the present study, the width of the confidence interval does not exclude a relevant relationship between handgrip strength and time to successful rehabilitation.

REFERENCES

1. Peeters CM, Visser E, Van de Ree CL, et al. Quality of life after hip fracture in the elderly: A systematic literature review. LID - S0020-1383(16)30119-X [pii] LID - 10.1016/j.injury.2016.04.018 [doi]. 20160514(1879-0267 (Electronic)).
2. Polinder S, Haagsma J, Panneman M, et al. The economic burden of injury: Health care and productivity costs of injuries in the Netherlands. 20160513(1879-2057 (Electronic)).
3. Lieberman D, Friger M, Lieberman D. Inpatient rehabilitation outcome after hip fracture surgery in elderly patients: a prospective cohort study of 946 patients. Archives of physical medicine and rehabilitation. 2006 Feb;87(2):167-71.
4. Koot VC, Peeters PH, de Jong JR, Clevers GJ, van der Werken C. Functional results after treatment of hip fracture: a multicentre, prospective study in 215 patients. The European journal of surgery = Acta chirurgica. 2000 Jun;166(6):480-5.
5. Clague JE, Craddock E, Andrew G, Horan MA, Pendleton N. Predictors of outcome following hip fracture. Admission time predicts length of stay and in-hospital mortality. Injury. 2002 Jan;33(1):1-6.
6. Muir SW, Yohannes AM. The impact of cognitive impairment on rehabilitation outcomes in elderly patients admitted with a femoral neck fracture: a systematic review. Journal of geriatric physical therapy (2001). 2009;32(1):24-32.
7. Hartog LC, Cizmar-Sweelssen M, Knipscheer A, et al. The association between orthostatic hypotension, falling and successful rehabilitation in a nursing home population. LID - S0167-4943(15)00074-6 [pii] LID - 10.1016/j.archger.2015.05.005 [doi]. 20150531(1872-6976 (Electronic)).
8. Di Monaco M, Castiglioni C Fau - De Toma E, De Toma E Fau - Gardin L, et al. Handgrip strength is an independent predictor of functional outcome in hip-fracture women: a prospective study with 6-month follow-up. 20150214 DCOM- 20150423(1536-5964 (Electronic)).
9. Oude Voshaar RC, Banerjee S Fau - Horan M, Horan M Fau - Baldwin R, et al. Fear of falling more important than pain and depression for functional recovery after surgery for hip fracture in older people. 20061016 DCOM- 20070206(0033-2917 (Print)).
10. Di Monaco M, Castiglioni C, De Toma E, et al. Handgrip strength but not appendicular lean mass is an independent predictor of functional outcome in hip-fracture women: a short-term prospective study. 20140830 DCOM- 20141021(1532-821X (Electronic)).
11. Visschedijk JH, Caljouw MA, Bakkers E, van Balen R, Achterberg WP. Longitudinal follow-up study on fear of falling during and after rehabilitation in skilled nursing facilities. 20151205(1471-2318 (Electronic)).
12. Vaughan L, Leng X, La Monte MJ, et al. Functional Independence in Late-Life: Maintaining Physical Functioning in Older Adulthood Predicts Daily Life Function after Age 80. 20160209 DCOM- 20160613(1758-535X (Electronic)).
13. Marottoli RA, Berkman LF, Leo-Summers L, Cooney LM, Jr. Predictors of mortality and institutionalization after hip fracture: the New Haven EPESE cohort. Established Populations for Epidemiologic Studies of the Elderly. American journal of public health. 1994 Nov;84(11):1807-12.
14. Fried LP, Tangen Cm Fau - Walston J, Walston J Fau - Newman AB, et al. Frailty in older adults: evidence for a phenotype. 20010316 DCOM- 20010329(1079-5006 (Print)).

15. O'Connell MD, Savva GM, Fan CW, Kenny RA. Orthostatic hypotension, orthostatic intolerance and frailty: The Irish Longitudinal Study on Aging-TILDA. 20150413 DCOM-20151117(1872-6976 (Electronic)).

16. Rockwood K, Abeysundera Mj Fau - Mitnitski A, Mitnitski A. How should we grade frailty in nursing home patients? 20071113 DCOM- 20071213(1538-9375 (Electronic)).

17. Angelousi A, Girerd N, Benetos A, et al. Association between orthostatic hypotension and cardiovascular risk, cerebrovascular risk, cognitive decline and falls as well as overall mortality: a systematic review and meta-analysis. Journal of hypertension. 2014 Aug;32(8):1562-71; discussion 71.

18. Shaw BH, Claydon VE. The relationship between orthostatic hypotension and falling in older adults. Clinical autonomic research : official journal of the Clinical Autonomic Research Society. 2014 Feb;24(1):3-13.

19. Scheffer AC, van Hensbroek PB, van Dijk N, et al. Risk factors associated with visiting or not visiting the accident & emergency department after a fall. BMC health services research. 2013;13:286.

20. Moreland JD, Richardson Ja Fau - Goldsmith CH, Goldsmith Ch Fau - Clase CM, Clase CM. Muscle weakness and falls in older adults: a systematic review and meta-analysis. 20040622 DCOM- 20050405(0002-8614 (Print)).

21. Kong KH, Chuo AM. Incidence and outcome of orthostatic hypotension in stroke patients undergoing rehabilitation. Archives of physical medicine and rehabilitation. 2003 Apr;84(4):559-62.

22. Weiss A, Beloosesky Y, Kornowski R, et al. Influence of orthostatic hypotension on mortality among patients discharged from an acute geriatric ward. J Gen Intern Med. 2006 Jun;21(6):602-6.

23. Feldstein C, Weder AB. Orthostatic hypotension: a common, serious and underrecognized problem in hospitalized patients. Journal of the American Society of Hypertension : JASH. 2012 Jan-Feb;6(1):27-39.

24. Spruit MA, Sillen MJ, Groenen MT, Wouters EF, Franssen FM. New normative values for handgrip strength: results from the UK Biobank. Journal of the American Medical Directors Association. 2013 Oct;14(10):775 e5-11.

25. Dodds RM, Syddall HE, Cooper R, et al. Grip strength across the life course: normative data from twelve British studies. PloS one. 2014;9(12):e113637.

26. Rogoza AN, Pavlova TS, Sergeeva MV. Validation of A&D UA-767 device for the self-measurement of blood pressure. Blood pressure monitoring. 2000 Aug;5(4):227-31.

27. Dorigatti F, Bonso E, Zanier A, Palatini P. Validation of Heine Gamma G7 (G5) and XXL-LF aneroid devices for blood pressure measurement. Blood pressure monitoring. 2007 Feb;12(1):29-33.

28. Mariotti G, Alli C, Avanzini F, et al. Arm position as a source of error in blood pressure measurement. Clinical cardiology. 1987 Oct;10(10):591-3.

29. Lahrmann H, Cortelli P, Hilz M, et al. EFNS guidelines on the diagnosis and management of orthostatic hypotension. European journal of neurology : the official journal of the European Federation of Neurological Societies. 2006 Sep;13(9):930-6.

30. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age and ageing. 2011 Jul;40(4):423-9.

31. Scheffer Ac Fau - Schuurmans MJ, Schuurmans Mj Fau - vanDijk N, vanDijk N Fau - van der Hooft T, van der Hooft T Fau - de Rooij SE, de Rooij SE. Reliability and validity of the visual analogue scale for fear of falling in older persons. 20101108 DCOM- 20101202(1532-5415 (Electronic)).

32. Sainsbury A, Seebass G, Bansal A, Young JB. Reliability of the Barthel Index when used with older people. Age and ageing. 2005 May;34(3):228-32.

33. G. D. The little handbook of statistical practice.: Amazon digital services; 2002.

34. Tu YK, Kellett M Fau - Clerehugh V, Clerehugh V Fau - Gilthorpe MS, Gilthorpe MS. Problems of correlations between explanatory variables in multiple regression analyses in the dental literature. 20051010 DCOM- 20051114(0007-0610 (Print)).

35. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies. International journal of surgery. 2014 Jul 18.

36. van Hateren KJ, Landman GW, Kleefstra N, et al. Lower blood pressure associated with higher mortality in elderly diabetic patients (ZODIAC-12). Age and ageing. 2010 Sep;39(5):603-9.

37. van Hateren KJ, Hendriks SH, Groenier KH, et al. Frailty and the relationship between blood pressure and mortality in elderly patients with type 2 diabetes (Zwolle Outpatient Diabetes project Integrating Available Care-34). Journal of hypertension. 2015 Jun;33(6):1162-6.

38. Lach HW, Parsons JL. Impact of fear of falling in long term care: an integrative review. 20130805 DCOM- 20131213(1538-9375 (Electronic)).

39. Myers AM, Powell LE, Maki BE, et al. Psychological indicators of balance confidence: relationship to actual and perceived abilities. The journals of gerontology Series A, Biological sciences and medical sciences. 1996 Jan;51(1):M37-43.

40. Tinetti ME, Powell L. Fear of falling and low self-efficacy: a case of dependence in elderly persons. Journal of gerontology. 1993 Sep;48 Spec No:35-8.

41. Savino E, Martini E Fau - Lauretani F, Lauretani F Fau - Pioli G, et al. Handgrip strength predicts persistent walking recovery after hip fracture surgery. 20131122 DCOM- 20140113(1555-7162 (Electronic)).

42. Shyam Kumar AJ, Beresford-Cleary N Fau - Kumar P, Kumar P Fau - Barai A, et al. Preoperative grip strength measurement and duration of hospital stay in patients undergoing total hip and knee arthroplasty. 20130619 DCOM- 20140313(1633-8065 (Print)).

43. Webb AR, Newman La Fau - Taylor M, Taylor M Fau - Keogh JB, Keogh JB. Hand grip dynamometry as a predictor of postoperative complications reappraisal using age standardized grip strengths. 19890502 DCOM- 19890502(0148-6071 (Print)).

CHAPTER 5

Prognostic value of Geriatric-8 for adverse outcomes within 30 days of surgery in older adults with colorectal cancer: a retrospective cohort study

Published as: Winters AM, Bakker J, ten Hoor J, Bilo HJG, Roodbol PF, Edens MA, Finnema EJ. (2024) Prognostic value of Geriatric-8 for adverse outcomes within 30 days of surgery in older adults with colorectal cancer: a retrospective cohort study. European Journal of oncology nursing. Volume 70, 102591, ISSN 1462-3889, https://doi.org/10.1016/j.ejon.2024.102591

ABSTRACT

Purpose: It is unclear whether the Geriatric-8 (G8) has the accuracy to preselect patients for complete geriatric assessment, and has the ability to predict adverse outcomes in patients with colorectal cancer (CRC). We therefore aimed to determine whether the G8, or other variables present in the medical record, are applicable in predicting 30-day adverse outcomes in older patients undergoing surgery for CRC.

Methods: We performed a retrospective cohort study involving patients ≥70 years who had surgery for CRC between 2018 and 2020 in a general hospital in the Netherlands. The primary outcome was adverse outcome(s), which is a composite of surgical and non-surgical complications, readmission and mortality, all within 30 days of surgery. The secondary endpoints were the individual components, such as delirium, infection and ileus. We explored potential prognostic factors using multivariable logistic regression analysis. Data were collected from the Dutch ColoRectal Audit (DRCA) and medical records.

Results: The study included 200 patients (mean age 78.9 years: 50% female), with 36.5% having adverse outcomes in the first 30 days of surgery. In neither univariate nor multivariable analysis were G8 scores associated with adverse outcomes. Factors with higher odds of adverse outcomes were male gender, and having cognitive decline or previous delirium.

Conclusion: This study confirms that G8 scores have no prognostic value for adverse outcomes, complications and mortality within 30 days of surgery among older adults with CRC. Therefore, the G8 should not be the tool for short-term risk prediction of adverse outcomes in these patients.

Highlights:

- G8 scores do not predict adverse outcomes within 30 days after surgery among older adults with CRC.
- Male gender, and problems in cognitive functioning are important prognostic factors and should be included in the frailty screening process before surgery.
- Further studies need to focus on the development of new frailty screening procedures and their impact on patient and clinical outcomes

INTRODUCTION

In 2021, the total Dutch population was 17.4 million individuals, with more than 50% aged over 50 years. In that year, more than 12.9 thousand new colorectal cancer (CRC) cases were identified among individuals aged 55 years or older, and more than 35% of these cases were diagnosed among individuals aged 75 years and older (1).

Within five years of surgery for CRC, 27% have postoperative complications (2), with higher mortality rates, increased healthcare costs, and decreased health-related quality of life (3). Immediate postoperative complications that often occur are hemorrhage, venous thromboembolism, infections, anastomotic leakage, ileus, colon ischemia (4,5), delirium (6), and even death.

Among frail older patients, the complication rate is even higher (76%) (3). Frailty can be defined as a dynamic state affecting an individual who experiences loss in one or more domains of human functioning (physical, psychological, social), which is caused by the influence of a range of variables and increases the risk of adverse outcomes (7,8). The International Society of Geriatric Oncology (SIOG) recommends a Clinical Geriatric Assessment (CGA) for older patients to detect and define the extent of frailty (9). With a finding of frailty, appropriate attention can be paid to geriatric syndromes and prevention of risks. A CGA is a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long-term follow-up. The domains recommended to be evaluated are functional status, comorbidity, cognition, mental health status, fatigue, social status and support, nutrition, and geriatric syndromes. The strength of the CGA is its ability to detect impairment that is not assessed through routine history or physical examination. Furthermore, the CGA can predict institutionalization and overall survival and has the potential ability to influence treatment choice (10,11,12). However, a CGA is time-consuming (>1 hour) and is therefore not recommended for every older patient. As an alternative, a screening tool to detect patients at increased risk for surgical and non-surgical complications is recommended for daily practice. After an abnormal screening result, a CGA should follow (13).

The Dutch Inspection for Health Care and Youth (IGJ) recommends the ISAR-HP or the Geriatric-8 (G8) as screening tools for patients undergoing surgery for CRC (14). In Isala Hospital, located in Zwolle, the Netherlands, the G8 has been used as a screening instrument in the outpatient clinic of the oncology department since 2019, before which the Groningen Frailty Indicator (GFI)

was used (15). The accuracy of the G8 as a tool for detecting frailty or predicting adverse outcomes is being questioned by experts, partly because suddenly many more patients are being referred for a CGA than were identified as potentially frail by the GFI.

The predictive performance of the G8 has been evaluated among patients with multiple types of cancer in several studies (16-20,9,21). Approximately 30% of the populations included in these studies were patients with CRC. In a systematic review of the use of the G8 screening tool by van Walree et al., (2019), only two studies included postoperative complications after colorectal surgery (22,23). Moreover, a sensitivity of approximately 0.8 and a moderate specificity (0.3-0.6) were described for adverse and CGA outcomes, respectively (16-18,9,21). A lower result on the G8 was also associated with functional decline and overall survival (19). Furthermore, in univariate analysis among older patients with colorectal carcinoma, a G8 score ≤14 was associated with a higher risk of 30-day postoperative complications, however in multivariate analysis the significance was not maintained (22).

In contrast, a multicenter cohort study involving two hospitals in the Netherlands, which aimed to evaluate the prognostic value of G8 and ISAR-HP for 30-day complications, concluded that the G8 had no predictive value as a separate screening tool in contrast to ISAR-HP (23). Finally, in a study where the prognostic value of G8 was compared with a modified G8 (six items) among patients with multiple types of cancer, an association was found between scores on both tools and overall three-year survival for patients with CRC (24).

The primary aim of this study is to determine if the results of the G8 are associated with 30-day adverse outcomes for older patients (aged ≥70) undergoing surgery for colorectal cancer. Furthermore, we explored whether other variables present in the medical record are associated with adverse outcomes, aiming to improve current methods for identifying frail patients with CRC.

METHODS

The reporting of this study is in line with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines (25).

Study design

We performed a retrospective cohort study on the potential prognostic factors for postoperative adverse outcomes among older adults (≥70 years) undergoing surgery for colorectal carcinoma.

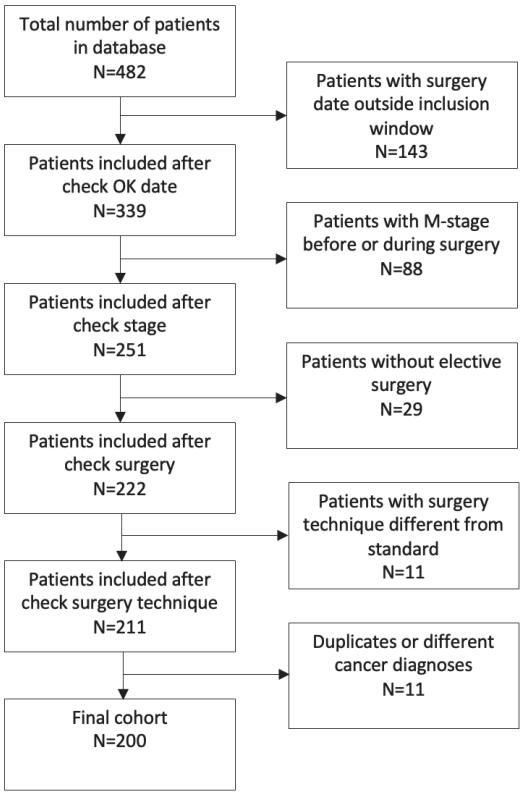
Setting

We used data from the medical records of patients admitted to the outpatient clinic between April 2018 and April 2020 in Isala Hospital, Zwolle, the Netherlands. Isala is a general teaching hospital with a large affiliation area.

Participants

Inclusion criteria were: (a) admitted to the outpatient clinic (b) 70 years or older, (c) diagnosed with CRC without metastasis, based on pathological TNM stage (Figure 1), and (d) patients undergoing elective surgery. Patients undergoing emergency surgery (e.g., when an ileus or blow-out was presented) were excluded.

Figure 1: Flow diagram of the patients included



Data sources

We used two data sources for this study: the Dutch ColoRectal Audit (DRCA) and medical records found in the electronic patient files of Isala Hospital (HiX). Part of the latter data was also available in structured form in the DRCA. The DRCA registered indicators and outcomes and gave insight into the development and quality of colorectal surgery. We used structured data from the DRCA.

Data concerning complications were available in the medical records and the DRCA data. When there were differences between the sources, data within the medical records were prioritized. This occurred in less than 5% of the patients.

Outcomes

The primary endpoint was adverse outcome(s), which is a composite of surgical and non-surgical complications, readmission and mortality, all within 30 days of surgery. Secondary endpoints consisted of individual components, which are described as distinct complications below.

For the components, we collected data on surgical complications and non-surgical complications. Surgical complications included postoperative bleeding, anastomotic leakage, ileus, wound dehiscence, intestinal perforation, infection, and urinary leak. Non-surgical complications were registered as cardiac, pulmonary, delirium, and infectious (other than wound and pulmonary infection). Delirium was considered present if it was reported by a member of the geriatric team and/or if the Delirium Observations Screening (DOS) score was greater than three on least three moments and fluctuated throughout the day (26).

Variables

The primary variable of interest was the G8 score. The G8 is a geriatric screening tool that consists of eight questions, with individual scores resulting in a total score between 0 and 17. It consisted of a total score and a dichotomized score distinguishing frailty from non-frailty, with ≤14 as the cut-off point (16). Other potential predictors were based on the literature and consisted of patient characteristics and patient data from medical records. These are described in the data collection section below.

DRCA

The variables collected from the DRCA were gender, age at the moment of surgery, TNM-stage known after surgery (classified into the different

AJCC stages, 8th version) (27), the American Society of Anesthesiologists (ASA) grading scale (28), type of surgery, and postoperative complications. Furthermore, the DRCA contained data about readmission within 30 days after surgery (yes/no) and mortality within 30 days (yes/no).

Medical records

The variables collected manually from medical records were: living in a nursing/care home (yes/no), using formal or informal care (yes/no), and living alone (yes/no). Drinking alcohol was classified as a drinker or non-drinker and further specified in units of alcohol consumed per day. Smoking was classified into smoker, non-smoker, and previous smoker. Anemia was scored "yes," when the level of hemoglobin before surgery was ≤6.5 for women or ≤7.0 for men, in accordance with DRCA criteria.

In addition to the G8, two other questionnaires were available in the medical records. First, another frailty score is part of the National Patient Safety Program (NPSP: in Dutch, Veiligheidsmanagementsysteem = VMS). Data from this NPSP tool was used because it contained information about the history of delirium and cognitive decline, which are risk factors for developing delirium after surgery. It was initially developed to prevent adverse events in geriatric care in Dutch hospitals (29). NPSP sensitivity rates regarding discharge destination, readmission, and mortality varied from 55% to 91%, and specificity rates from 47% to 52% (30). Second, the specific risk of malnutrition was assessed by scores on the Short Nutritional Assessment Questionnaire (SNAQ), a 5-item questionnaire. The SNAQ total score ranges from 0 to 7, where a score of ≥1 is suggestive of malnutrition (31). In addition, weight loss in the past month was scored yes/no, and Body Mass Index (BMI) was calculated.

Ethical considerations

The Daily Board of the Medical Ethics Committee Isala, Zwolle, the Netherlands, reviewed the research proposal (no. 200622). As a result of this review, the Committee concluded that rules laid down in the Medical Research Involving Human Subjects Act (also known by its Dutch abbreviation WMO) did not apply to this research proposal.

Data analysis

Descriptive analysis

Categorical data were summarized using n (%). Quantitative data were summarized using mean (standard deviation) (SD) or median (interquartile range) (IQR), depending on the distribution.

Inferential statistics

Categorical data were compared using Fisher's exact test. Quantitative data were compared using the independent t-test or Mann-Whitney U test, depending on the distributions.

To investigate prognostic factors for the adverse outcome(s), a multivariable logistic regression analysis was performed. Both numeric and dichotomous variables were included in the analysis. The numeric variables were: mean age, BMI, ASA, chronic conditions, tumor stage, tumor location, G8 total score, and NPSP total score. The dichotomous variables were: age (with cut-off point of ≤80 years), gender, living situation, receiving care, familiar CRC, anemia, type of surgery, G8 (with cut-off point of ≤14), NPSP, and SNAQ. Adverse outcomes, which included surgical and non-surgical, and individual complications, were also dichotomous variables.

Odds with 95% confidence intervals (CI) were calculated for the association between the variables, including G8 scores, and adverse outcomes. Variables with a P-value ≤0.1 by univariate analysis were then studied by multivariable analysis using backward selection. The variable with the largest *p*-value was removed until significant variables remained (32). Furthermore, we visualized the discriminative value of the univariate G8 frailty score for complication(s) using a ROC curve. SPSS version 26 was used for the data analyses to that point.

Sensitivity and specificity were also computed (34). In addition, we calculated the positive predictive value (PPV) and the negative predictive value (NPV) for both of frailty screening tools. The PPV is the probability that frailty is present when the test is positive and the NPV is the probability that frailty is not present when the test is negative (34). MedCalc (v20.009) was used for ROC analyses. A *p*-value of <0.05 was considered statistically significant.

RESULTS

Patient characteristics

Of the 200 patients included in the study, 50% were female and 50% male (Figure 1). Their mean age was 78.1 years (SD: 5.3) (Table 1). Almost 30% of the patients lived alone before admission, and 45% received care from relatives or healthcare professionals. In 20% of the patients with colorectal carcinoma, another form of cancer had been diagnosed in previous years. Some patients had a history of cerebrovascular events (20%) or myocardial infarct (13%), and 25% were classified as ASA 3. The patients had AJCC stages between 0 and IV at the time of surgery. Stage I was diagnosed in 28.5% of the patients, Stage II in 39%, and Stage III in 25%.

Table 1. Patient and clinical characteristics

Variables	Mean (SD)	N (%)	Missing N
Age in years	78.1 (5.3)		0
Age <80 years		124 (62)	0
Age ≥80 years		76 (38)	
Gender			0
Male		100 (50)	
Female		100 (50)	
Body Mass Index (BMI)	26.7 (4.7)		0
Living situation			0
Living alone		59 (29.5)	
Living with a partner or relative(s)		141 (70.5)	
Care			2
Receiving informal care and/or formal care		77 (38.5)	
No care		121 (60.5)	
Chronic conditions			0
Other cancer		42 (21)	
Cerebrovascular events		40 (20)	
Myocardial infarct		26 (13)	
Diabetes Mellitus		25 (12.5)	
Pulmonary Disease		11 (5.5)	
Mixed connective tissue diseases		10 (5)	
Others		18 (9)	
ASA			0
0-1		24 (12)	
2		126 (63)	
3		50 (25)	
Familiar colorectal cancer			50
[yes]		39 (26)	
[no]		111 (74)	
Anemia			9
[yes]		32 (16.8)	
[no]		159 (83.2)	
Tumor stage (AJCC)			0
No residual tumor*		3 (1.5)	
I		57 (28.5)	
IIA		69 (34.5)	
IIB		7 (3.5)	
IIC		3 (1.5)	
IIIA		11 (5.5)	
IIIB		34 (17.0)	
IIIC		16 (8.0)	
Tumor location			0
Right-sided		122 (61)	
Left-sided		13 (6.5)	
Rectum		3 (1.5)	
Transverse colon		34 (17.0)	
Low anterior		11 (5.5)	
Overlapping or not otherwise specified		17 (8.5)	

Variables	Mean (SD)	N (%)	Missing N
Type of surgery			0
Laparoscopic		194 (97)	
Open		6 (3)	
G8			7
Total score G8	14 (2.2)		
Frail (score 14 or lower)		92 (47.7)	
Non-frail (score 15-17)		101 (52.3)	
NPSP			0
Cognitive problems/delirium before admission		26 (13.0)	
History of falling		21 (10.5)	
Receiving aid in the last 24 hours before admission		20 (10)	
Frail (score 1-3)		44 (22)	
Non-frail		156 (78)	
SNAQ			1
Loss of weight last month		32 (16)	
No loss of weight last month		167 (84)	
Complications directly related to surgery		32 (16)	0
Ileus		20 (10)	
Other complications			
Delirium		18 (9)	
Pulmonary complication		10 (5)	
Cardiac complication		10 (5)	
Infectious complication		13 (6.5)	
Readmission		23 (11.5)	0
Re-intervention		13 (6.5)	0
Mortality within 30 days after surgery		6 (3.0)	0
Adverse outcomes within 30 days of surgery		73 (36.5)	0
Patients with two or more adverse outcomes		20 (10)	0

SD: standard deviation; Informal/Formal care is defined as receiving any kind of help/support in daily living from a relative or health professional; ASA: American Society of Anesthesiology classification system; AJCC: Cancer staging by The American Joint Committee on Cancer; Anemia was scored yes when the level of hemoglobin before surgery was ≤6.5 for women and ≤7.0 for men; G8: Geriatric 8, geriatric screening tool; NPSP: National Patient Safety Program (in Dutch: Veiligheidsmanagementsysteem [VMS]); SNAQ: Short Nutritional Assessment Questionnaire; *After (neo)adjuvant treatment no residual tumor was found during surgery.

Primary endpoint

Of all the patients included in this study, 36,5% had an adverse outcome (Table 1) within 30 days of surgery (95%CI= [30%-43%]). Their mean age was 78.7 years (SD 5.3), and 63% were male and 37% were female. The most common complications were delirium (9.0%), ileus (10%), and infection (other than wound and pulmonary infection) (6.5%). Readmission was necessary for 11.5% of all patients, and 3% died within 30 days after surgery. As only 6 patients had

died within 30 days, mortality was not studied as a separate endpoint, but was included in the composite endpoint of adverse outcome(s).

Predictive value of G8

The degree of frailty was assessed with G8 and NPSP before surgery. The G8 identified 47.5% of patients as frail, while the NPSP identified 22% of patients as frail (Table 1). According to both questionnaires, 34 patients were frail, and 95, were not. Table 2 shows that G8 was not associated with adverse outcomes in univariate analysis. The association of NPSP with adverse outcomes was also not significant (data not shown).

In univariate analysis, G8 was not significantly associated with individual complications, readmission, or mortality (data not shown).

Table 2: Univariate association of G8 and adverse outcome(s) 30-days of surgery

	No adverse outcome N=127	Adverse outcomes N=73	P-value
G8 total score: mean (SD)	14.2 (2.0)	13.9 (2.4)	0.471[a]
G8			
Frail (score 14 or lower)	57	35	0.766[b]
Non-frail (score 15-17)	65	36	
Missing	5	2	

SD: standard deviation; [a]Independent samples t-test; [b]Fisher's exact test;

To demonstrate the prognostic value of frailty assessed with the G8 and NPSP, we also calculated sensitivity, specificity, PPV, and NPV (Table 3). The sensitivity and specificity of the G8 were both approximately 0.5 for adverse outcome(s). The area under the curve (AUC) for G8 was 0.48 (95%CI= [0.4-0.6]).

Table 3: Prognostic evaluation of G8 and NPSP for the development of adverse outcomes

Screening	Sensitivity	Specificity	PPV	NPV
G8 [frail: score ≤14]	0.49	0.53	38%	64%
NPSP [frail: score 1-3]	0.27	0.81	45%	66%

Dichotomized G8: Geriatric 8, geriatric screening tool; Dichotomized NPSP: National Patient Safety Program (in Dutch: Veiligheidsmanagementsysteem [VMS]); PPV: positive predictive value. NPV: negative predictive value.

Multivariable analyses

Table 4 presents the multivariable logistic regression analysis results to explore prognostic factors for adverse outcomes within 30 days after surgery

in patients with CRC. Factors with higher odds for adverse outcomes were male patients (Odds Ratio (OR)=2.3; 95%CI= [1.3-4.1]; P=0.007), and the NPSP question about cognitive decline or previous delirium (OR=2.2; 95%CI= [0.9-5.1]; P=0.072).

Probabilities for developing adverse outcome(s) were 25.8% (17.4%-36.4%), 66.7% (38.7%-87.0%), 36.4% (12.4% – 68.4%), and 42.4% (31.9 – 53.5%), for women without cognition problem, men with cognition problem, women with cognition problem, and men without cognition problem, respectively.

Table 4. Multivariable logistic regression on adverse outcomes within 30 days of surgery

	Odds Ratio	95% CI.	P-value
Gender [male]	2.26	1.25-4.10	**0.007**
NPSP question: Cognitive decline or previous delirium	2.18	0.93-5.11	0.072

Variables added in step 1 of the 'backward' procedure: NPSP frail versus not frail, gender, G8 frail versus not frail, total G8 score, NPSP question about cognitive decline or previous delirium. Adverse outcome yes = 1, no = 0. Independent variables: male = 1, female = 0, NPSP frail = 1, NPSP non-frail = 0, G8 score <15 = 1 and G8 score non-frail = 0. No cognitive decline or previous delirium = 0, cognitive decline or previous delirium = 1. CI: Confidence Interval. NPSP: National Patient Safety Program (in Dutch: Veiligheidsmanagementsysteem [VMS]). Bold text indicates a statistically significant difference (P<0.05).

Factors associated with delirium, infection, and ileus

Only the NPSP question about cognitive decline or previous delirium was significantly associated with delirium and infection during admission. An OR=7.4 (95%CI= [2.6-21.4]; P<0.001) was found for the outcome of delirium, and an OR=4.9 (95%CI= [1.4-16.0]; P=0.032) for infection.

There were surgical complications in 27% of males and 9% of females. In multivariable analysis, the male patients had significantly higher odds of surgical complications than women (OR 4.4; 95%CI= [1.8-10.8]; P<0.001). Men were more likely to develop complications directly related to surgery, such as ileus, compared to women (OR [ileus] 3.4; 95%CI= [1.2-9.6]; P=0.024). Ileus incidence was 15% among males and 5% among females.

DISCUSSION

The primary aim of this study was to determine whether the results of the G8 are associated with adverse outcome(s) in older patients (aged 70 or above) within 30 days of surgery for CRC. Based on the results of this study, we can conclude that the G8 geriatric screening tool is not associated with adverse outcomes, nor with readmissions within 30 days and separate complications such as delirium, infection, or ileus. This is in line with the studies of Fagard et al., (2017) and Souwer et al., (2018), which were also conducted in the Netherlands on a comparable population. However, the numbers for open surgery differed: 40% open surgery in their studies versus 3% open surgery in the current study. As of 2019, laparoscopy has become the method of first choice and is considered less invasive (35).

The percentage of adverse outcomes (36.5%) in our study is comparable to the results of Warps et al. (2022). For frail older patients, the number of adverse outcomes might be higher (76%), as Fagard et al. (2017) stated. However, these studies are not entirely comparable, given developments in surgical techniques.

In the prognostic evaluation of the G8, we found a sensitivity of 0.49 and a specificity of 0.53. Fagard et al. (2017) described a sensitivity of 0.71 and a specificity of 0.46. We may assume good inter-rater reliability, demonstrated by other researchers (36). We should note here that the G8 was developed initially as a frailty screening tool and was not intended to be a prognostic tool (16). Thus, it might be more valuable to investigate the prognostic value of separate components of the CGA since screening tools showed low to moderate sensitivity and specificity rates on patient outcomes.

Furthermore, we explored the possible prognostic value of other potential predictors based on medical records associated with the primary and secondary endpoints. In predicting adverse outcomes within 30 days after surgery, we found that male patients, and cognitive decline or previous delirium had higher odds. Being a man in often described as a risk factor for complications after surgery for CRC (37,6,5). The relationship between the development of delirium after surgery and a history of delirium or cognitive decline has been previously reported in the literature (37,6), as has the higher risk of adverse outcomes among older patients with cognitive impairment during hospitalization (38).

Since we have not examined longer-term complications, we cannot draw conclusions on this aspect based on our study. Several studies have shown a positive association between G8 scores and adverse outcomes of CGA tests

(16,17,21) and the predictive performances of the G8 tool for long-term survival (24).

Some limitations of this study should be considered. First, the study design was a retrospective cohort study from a single institution with a heterogeneous study population. Consequently, some caution must be exercised in interpreting outcomes and generalizability. Second, in about 5% of the data, there was a discrepancy in the complications scored in the DRCA and what was described in the medical records. We could only resolve this by prioritizing the medical records. Third, unfortunately, we did not have information about the patients' objective functional and psychological status, nor data about functional outcomes, which, especially in older patients, are relevant.

The strength of this study is that it was based on a demand from clinical practice and can contribute to improving care for patients with CRC. It gives credence to the concerns of professionals, and supports the need to evaluate the entire process of providing appropriate care so that we do no more and no less than necessary. As the G8 alone cannot prognostic value of CGA components or the added value of artificial intelligence.

Based on our results, we found that the NPSP question about cognitive decline or a history of delirium was associated with adverse outcomes and may therefore be valuable as signals indicating the need for increased awareness of the risk of complication. In current practice, the NPSP question about cognitive decline or previous delirium is only posed on admission day. Still, it might be asked and discussed several weeks before admission so that not only nurses but also patients, family, and other professionals consider this outcome.

It is often difficult to assess cognitive function in a short interview. As an alternative, we would recommend that nurses use some objective questions, such as the 6-item Cognitive Impairment Test (CIT) score (39) or the Mini-Cog (40), and pay more attention to older patients with a history of delirium. Subsequently, it is essential to refer the right patients for CGA based on frailty screening so that appropriate treatment decisions can be made and precautions taken, also taking into account the increasing number of older adults.

CONCLUSION

This study suggests that G8 scores do not predict adverse outcomes within 30 days of surgery in older adults with CRC. Therefore, the G8 alone should not be used as a tool to predict adverse outcomes. The presence of cognitive decline or a history of delirium should play a greater role in preoperative screening. Currently, we do not have a sufficient procedure for obtaining a complete picture of patients starting the CRC pathway after being diagnosed with colorectal carcinoma, but this is of utmost importance to provide appropriate care. Further studies need to focus on the development of new frailty screening procedures and their impact on patient and clinical outcomes.

REFERENCES

1. Integraal kankercentrum Nederland (IKNL). 'Incidentie dikke darmkanker en endeldarmkanker'. Available at: https://iknl.nl/nieuws/2022/kerncijfers-darmkanker-12900-diagnoses-in-2021 [Accessed: June 2023].
2. Warps, A.K., Tollenaar, R.A.E.M., Tanis, P.J. et al. (2022)' Postoperative complications after colorectal cancer surgery and the association with long-term survival', *European Journal of Surgical Oncology,* Volume 48, Issue 4,Pages 873-882,ISSN 0748-7983. DOI: https://doi.org/10.1016/j.ejso.2021.10.035
3. Kristjansson, S.R., Nesbakken, A., Jordhøy, M.S. et al. (2010) 'Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: A prospective observational cohort study', *Critical Reviews in Oncology/Hematology*, 76(3), 208–217. DOI: https://doi.org/10.1016/j.critrevonc.2009.11.002
4. Climent, M., Martin, S.T. (2018) 'Complications of laparoscopic rectal cancer surgery', *Mini-invasive Surg*, 2:45. DOI: http://dx.doi.org/10.20517/2574-1225.2018.62
5. Pak, H., Maghsoudi, L.H., Soltanian, A. et al. (2020) 'Surgical complications in colorectal cancer patients', *Annals of medicine and surgery,* 11; *55*, 13–18. DOI: https://doi.org/10.1016/j.amsu.2020.04.024
6. Lee, S.H., Lim, S.W. (2020) 'Risk factors for postoperative delirium after colorectal surgery: a systematic review and meta-analysis', *Int J Colorectal Dis*, 35(3):433-444. DOI: https://doi.org/10.1007/s00384-019-03498-6
7. Slaets, J.P.J. (2006) 'Vulnerability in the Elderly: Frailty', *Medical Clinics of North America,* Volume 90, Issue 4. Pages 593-601. DOI: https://doi.org/10.1016/j.mcna.2006.05.008
8. Gobbens, R.J., Luijkx, K.G., Wijnen-Sponselee, M.T. et al. (2010) 'Toward a conceptual definition of frail community dwelling older people', *Nurs Outlook*, 58(2):76–86. DOI: https://doi.org/10.1016/j.outlook.2009.09.005
9. Papamichael, D., Audisio, R.A., Glimelius, B. et al. (2015) 'Treatment of colorectal cancer in older patients: International Society of Geriatric Oncology (SIOG) consensus recommendations 2013', *Annals of Oncology*, Volume 26, Issue 3, Pages 463-476, ISSN 0923-7534. DOI: https://doi.org/10.1093/annonc/mdu253
10. Puts, M.T.E., Hardt, J., Monette, J. et al. (2012) 'Use of geriatric assessment for older adults in the oncology setting: A systematic review', *J Natl Cancer Inst,* 8; 104(15): 1133-63. DOI: 10.1093/jnci/djs285
11. Wildiers, H., Heeren, P., Puts, M. et al. (2014) 'International Society of geriatric oncology consensus on geriatric assessment in older patients with cancer', *J Clin Oncol*, 20; 32(24): 2595-603. DOI: 10.1200/JCO.2013.54.8347
12. Ellis, G., Gardner, M., Tsiachristas, A. et al. (2017) 'Comprehensive geriatric assessment for older adults admitted to hospital', *Cochrane Database Sys Rev,* 12; 9(9): CD006211. DOI: 10.1002/14651858.CD006211
13. Decoster, L., Van Puyvelde, K., Mohile, S. et al. (2015) 'Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: An update on SIOG recommendations', *Ann Oncol*, 26(2): 288-300. DOI: https://doi.org/10.1093/annonc/mdu210

14. Inspectie Gezondheidszorg en Jeugd (IGJ). 'Basisset Medisch Specialistische Zorg 2019'. Available at: https://www.igj.nl/documenten/indicatorensets/2017/01/01/basisset-medisch-specialistische-zorg [Accessed: June 2020].

15. Metzelthin, S.F., Daniels, R., van Rossum, E. et al. (2011) 'Psychometrische eigenschappen van drie screeningsinstrumenten voor kwetsbaarheid bij thuiswonende ouderen [The psychometric properties of three self-report screening instruments for identifying frail older people in the community]', *Tijdschr Gerontol Geriatr*, 42(3):120-30. Dutch. DOI: https://doi.org/10.1007/s12439-011-0022-5

16. Soubeyran, P., Bellera, C., Goyard, J. et al. (2011) 'Validation of the G8 screening tool in geriatric oncology: the ONCODAGE project', *J Clin Oncol*, 29(15 suppl). DOI: https://doi.org/10.1016/j.jgo.2020.10.017

17. Bellera, C.A., Rainfray. M., Mathoulin-Pélissier, S. et al. (2012) 'Screening older cancer patients: first evaluation of the G-8 geriatric screening tool', *Ann Oncol,* 23(8): 2166-2172. DOI: https://doi.org/10.1093/annonc/mdr587

18. Hamaker, M.E., Jonker, J.M., De Rooij, S.E. et al. (2012) 'Frailty screening methods for predicting the outcome of a comprehensive geriatric assessment in elderly patients with cancer: A systematic review', *Lancet Oncol,* 13(10):437-44. DOI: https://doi.org/10.1016/s1470-2045(12)70259-0

19. Liuu, E., Canouï-Poitrine, F., Tournigand, C. et al. (2014) 'Accuracy of the G-8 geriatric-oncology screening tool for identifying vulnerable elderly patients with cancer according to tumour site: The ELCAPA-02 study', *J Geriatr Oncol,* 5(1):11-9. DOI: https://doi.org/10.1016/j.jgo.2013.08.003

20. Walree, van I.C., Scheepers, E., van Huis-Tanja, L. et al. (2019) 'A systematic review on the association of the G8 with geriatric assessment, prognosis and course of treatment in older patients with cancer', *J Geriatr Oncol,* 10(6): 847-858. DOI: https://doi.org/10.1016/j.jgo.2019.04.016

21. Fagard, K., Casaer, J., Wolthuis, A. et al. (2017) 'Value of geriatric screening and assessment in predicting postoperative complications in patients older than 70 years undergoing surgery for colorectal cancer', *J Geriatr Oncol,* 8(5): 320-327. DOI: https://doi.org/10.1016/j.jgo.2017.07.008

22. Souwer, E.T.D., Verweij, N.M., Van den Bos, F. et al. (2018) 'Risk stratification for surgical outcomes in older colorectal cancer patients using ISAR-HP and G8 screening tools', *J Geriatr Oncol,* 9(2): 110-114. DOI: https://doi.org/10.1016/j.jgo.2017.09.003

23. Martinez-Tapia, C., Paillaud, E., Liuu, E. et al. (2017) 'Prognostic value of the G8 and modified-G8 screening tools for multidimensional health problems in older patients with cancer', *Eur J Cancer*, 83: 211-219. DOI: https://doi.org/10.1016/j.ejca.2017.06.027

24. Elm, von E., Altman, D.G., Egger, M. et al. (2007) 'The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies', *Prev Med,* 45(4):247-51. DOI: https://doi.org/10.1016/j.ijsu.2014.07.014

25. Schuurmans, M.J., Duursma, S.A., Shortridge-Baggett, L.M. (2001) 'Early recognition of delirium: review of the literature', *J Clin Nurs,* 10(6):721-9. DOI: https://doi.org/10.1111/j.1365-2702.2001.00548.x

26. Weiser, M.R. (2018) 'AJCC 8th Edition: Colorectal Cancer', *Ann Surg Oncol,* **25,** 1454–1455 DOI: https://doi.org/10.1245/s10434-018-6462-1

27. ASA: American Society of Anesthesiologists (2020). Available at: file:///F:/Downloads/asa-physical-status-classification-system.pdf [Accessed: May 2022].

28. Oud, F.M., Wolzak, N.K., Spies, P.E. et al. (2015) 'Predictive value of the VMS theme 'Frail elderly': delirium, falling and mortality in elderly hospital patients'. *Nederlands Tijdschrift voor Geneeskunde*, 159:A8491. DOI: https://doi.org/10.1016/j.archger.2021.104514

29. Warnier, R.M.J., van Rossum, E., van Kuijk, S.M.J. et al. (2020) 'Frailty screening in hospitalised older adults: How does the brief Dutch National Safety Management Program perform compared to a more extensive approach?', *J Clin Nurs,* 29(7-8):1064-1073. DOI: https://doi.org/10.1111/jocn.15148

30. Kruizenga, H.M., Seidell, J.C., de Vet, H.C.W. et al. (2005) 'Development and validation of a hospital screening tool for malnutrition: the short nutritional assessment questionnaire (SNAQ)', *Clinical Nutrition,* 24:75-82. DOI: https://doi.org/10.1016/j.clnu.2004.07.015

31. Twisk, J.W.R. (2017). *Inleiding in de toegepaste biostatistiek.* 2nd edn. Amsterdam: Reed Business.

32. Akobeng, A.K. (2007a) 'Understanding diagnostic tests 1: sensitivity, specificity and predictive values', *Acta Paediatr,* 96(3):338-41. DOI: https://doi.org/10.1111/j.1651-2227.2006.00180.x

33. Akobeng, A.K. (2007b) 'Understanding diagnostic tests 3: Receiver operating characteristic curves', *Acta Paediatr,* 96(5):644-7. DOI: https://doi.org/10.1111/j.1651-2227.2006.00178.x

34. Richtlijn colorectale chirurgie. (2019) Available at: [Accessed: May 2022]. https://www.mdl.nl/files/richlijnen/Richtlijn%20Colorectaal%20Carcinoom.pdf

35. Cavusoglu, C., Tahtaci, G., Dogrul, R.T. et al. (2021) 'Predictive ability of the G8 screening test to determine probable sarcopenia and abnormal comprehensive geriatric assessment in older patients with solid malignancies', *BMC Geriatr,* **21**, 574. DOI: https://doi.org/10.1186/s12877-021-02544-9

36. Kim, Y., Kim, I.Y. (2016) 'Factors associated with postoperative complications and 1-year mortality after surgery for colorectal cancer in octogenarians and nonagenarians', *Clin Interv Aging*, 11:689-697 DOI: https://doi.org/10.2147/cia.s104783

37. Fogg, C., Griffiths, P., Meredith, P. et al. (2018) 'Hospital outcomes of older people with cognitive impairment: An integrative review', *Int J Geriatr Psychiatry*, 26;33(9):1177–97. DOI: https://doi.org/10.1002%2Fgps.4919

38. Brooke, P., Bullock, R. (1999) 'Validation of a 6 item cognitive impairment test with a view to primary care usage', *Int J Geriatr Psychiatry*, 14(11):936-40. DOI: https://doi.org/10.1002/(SICI)1099-1166(199911)14:11%3C936::AID-GPS39%3E3.0.CO;2-1

39. Borson, S., Scanlan, J.M., Chen, P.J. et al. (2003) 'The Mini-Cog as a screen for dementia: Validation in a population-based sample', *J Am Geriatr Soc,* 51:1451–1454. DOI: https://doi.org/10.1046/j.1532-5415.2003.51465.x

CHAPTER 6

Perspectives of healthcare professionals on frailty assessment among older patients with colorectal cancer: a qualitative study

Published as: Winters M, Bakker J, Ardesch V, van der Zwaag S, Kamper A, Bilo H, Roodbol P, Finnema E. Perspectives of healthcare professionals on frailty assessment among older patients with colorectal cancer: A qualitative study. Eur J Oncol Nurs. 2025 Apr;75:102827. doi: 10.1016/j.ejon.2025.102827.

ABSTRACT

Aim: Exploring the perspectives of healthcare professionals (HCPs) working at the outpatient clinic on the value and practice of standardized frailty assessment in older adults with colorectal cancer (CRC). In current practice, frailty assessment comprises initial frailty screening using the G8 measurement, followed by a comprehensive geriatric assessment (CGA) to further evaluate frailty detected during screening.

Methods: This is a qualitative study involving semi-structured interviews with 17 HCPs, conducted from February to July 2023. Physicians specializing in oncology, surgery, gastroenterology, and geriatrics were asked to participate as well as nurses and nurse practitioners at the outpatient clinic of a large teaching hospital involved in frailty assessment of patients with CRC.

Results: Two main themes emerged: 1) the perceived value of the G8 measurement for frailty screening and 2) the perceived value of the CGA. The moment, content, and outcome of the G8 and CGA were discussed. Other issues discussed were the complexity of frailty appreciation and collaboration between HCPs. The integration of perspectives proved important to the overall added value of frailty assessment. The CGA is considered most beneficial in patients with suspected cognitive impairment or if there is uncertainty about the degree of frailty or about the optimal treatment.

Conclusion: We conclude that the G8 is not an appropriate screening instrument for this patient population. CGA adds value in a specific subset of patients if it is conducted before treatment decisions are made and integrated into an efficient, multidisciplinary pathway, focusing on collaborative decision-making, including with the patient.

HIGHLIGHTS

- According to HCPs, the G8 is not suitable for reliable identification of frail patients with CRC who might benefit from CGA.
- HCPs argued that a CGA would add value to the care of older patients with CRC in complex cases, such as suspected cognitive impairment or differing assessments of frailty.
- HCPs emphasized that collaboration among HCPs is essential to combining different perspectives on the patient to benefit from the added value of frailty assessment.
- Improving HCP' knowledge of older patients, and improving shared decision-making processes should contribute personalized care.

INTRODUCTION

In 2021, the Dutch population comprised 17.4 million people. In that year, more than 12,900 new colorectal cancer (CRC) cases were identified among individuals aged 55 years and over, and more than 35% of these cases were diagnosed among individuals aged 75 years and over (IKNL, 2022). In 2014, a colorectal cancer screening programme was introduced, which involves inviting people aged 55 to 75 to be screened every two years.

About 25% of older patients (aged ≥ 75 years) with CRC had a complication within five years of surgery for CRC. Possible complications, such as perforation, ileus, bleeding, delirium, and infection, have a large impact on patients' level of functioning and survival (Warps et al., 2022). Among frail older patients, the complication rate is higher (62%) than in patients who are in good condition (Kristjansson et al., 2010). Frailty is a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, and/or social), which is caused by a range of variables and increases the risk of adverse outcomes (Sleats, 2006; Gobbens et al., 2010a). The Dutch Health and Youth Care Inspectorate (IGJ) recommends pre-screening for frailty by nurses (i.e. nurses and nurse practitioners) in older patients with CRC, using the Geriatric-8 (G8) questionnaire as a standardized assessment tool, and in case of a poor G8 score, to complement the assessment with a comprehensive geriatric assessment (CGA). The involvement of an expert in geriatric medicine is intended to ensure that only those older people will be operated on whose chances are highest and where such an intervention will add value in terms of quality of life, longevity, and/or improved functioning (IGJ, 2019).

The G8 contains eight items comprising multiple geriatric domains, including patients' age (>85, 80-85, or <80), nutritional status (appetite changes, weight loss, and body mass index), mobility, neuropsychological condition, self-rated health, and polypharmacy (Appendix 1). The total G8 score lies between 0 and 17. A higher score is considered to be associated with a better health status. A score of 14 or lower is considered to be indicative of frailty (Bellera et al., 2012).

In Dutch hospitals, there are variations with regard to the screening with the G8 questionnaire and the referral policy after a poor result (IGJ, 2020). At Isala Hospital (a 1275-bed teaching hospital, in the north of the Netherlands), the G8 is part of the frailty assessment process (Figure 1). All patients with CRC and who are over 70 are screened for frailty using the G8. If they are found to be at risk, the policy is to refer these patients to the geriatric department

for a CGA. However, in reality, only 50% of patients identified as at risk for frailty were referred to the geriatric department; no specific reason could be identified for the failure to refer patients (Winters et al., 2024). Also, this previous study in our hospital examined the association between G8 scores and adverse outcomes within 30 days of surgery for CRC and concluded that the G8 score has no prognostic value for adverse outcomes within 30 days of surgery in older adults with CRC.

The perspectives and attitudes of healthcare professionals (HCPs) regarding several frailty screening tools have been studied before (Van Damme et al., 2020; Liu et al., 2022; Warnier et al., 2021). These include a 13-item RISK scale, based on the Dutch National Safety Management Programme for the screening of frail hospitalized older patients (in Dutch abbreviated as 'VMS') (VMS, 2009); the 15-item Groningen Frailty Indicator (GFI) (Peters et al., 2012); the Maastricht Frailty Screening Tool for Hospitalized Patients (MFST-HP) (Warnier et al., 2017); Fried's Frailty Phenotype (Fried et al., 2001); Frailty Index (Rockwood et al., 2005); FRAIL scale (Morley et al., 2012); Clinical Frailty Scale (CFS) (Rockwood et al., 2005); Edmonton Frail Scale (Rolfson et al., 2006); Tilburg Frailty Indicator (Gobbens et al., 2010b); and the Seniors Fitness Test (SFT) (Rikli and Jones, 1999). According to nurses working in inpatient environments (general medical and surgical wards) in three Dutch hospitals, frailty screening contributes to proactive work and creating awareness of potential risks. However, standardized screening must be better integrated into daily routines (Warnier et al., 2021). A qualitative study of nurses and doctors working in a range of hospital wards (Accident & Emergency, Anaesthesia, General Surgery, and Orthopaedics) found that understanding of frailty varied due to barriers such as lack of resources (time and manpower), but also due to the lack of an appropriate and more generally accepted definition of frailty (Liu et al., 2022). Van Damme et al., (2020) stated that HCPs agreed with older adults that frailty is multidimensional and dynamic and needs to be tailored to each individual older adult. However, HCPs lacked involvement in implementing frailty screening in the acute care setting and experienced an absence of the context of the screening and inconsistency in its application (12).

Perspectives on the significance and implementation of the G8 frailty screening and assessment by HCPs who are involved in frailty evaluations in the outpatient clinic have so far not been investigated.

Therefore, this study aims to explore the perspectives of HCPs at the outpatient clinic on the significance and implementation of frailty assessment in older adults with colorectal carcinoma (CRC).

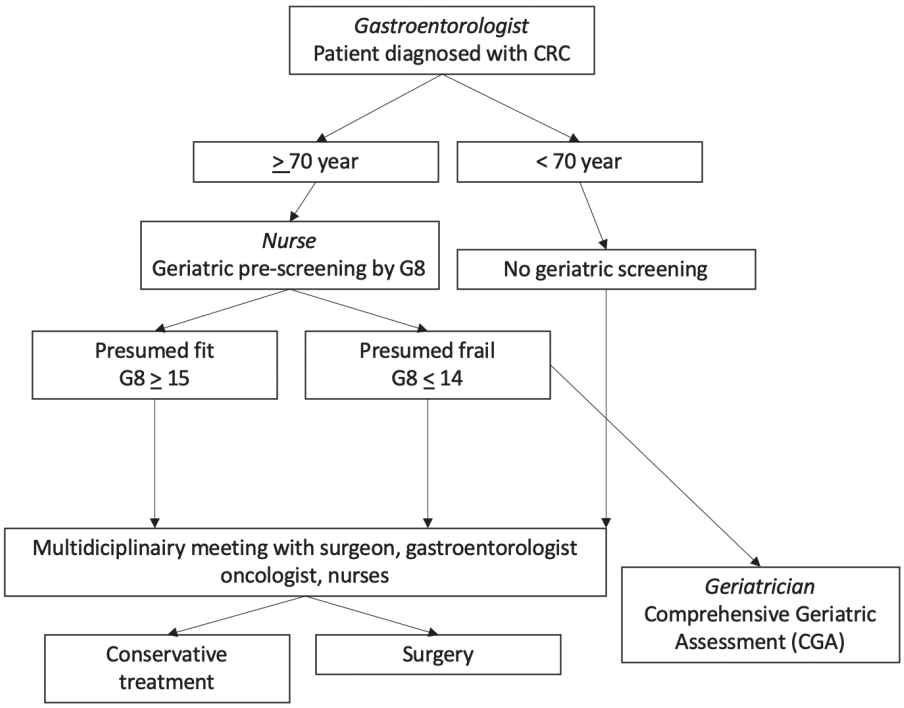
METHODS

We conducted an explorative qualitative study with semi-structured interviews. To ensure comprehensive and transparent reporting, the reporting was carried out according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist (Tong et al., 2007). The study is based on an inductive approach, searching for meaning without preconceptions or expectations (Creswell and Creswell, 2017).

Setting

The individuals participating in this study comprised HCPs working with older patients with CRC in the outpatient clinic of a large teaching hospital in the northern parts of the Netherlands. Different categories of HCPs are involved in the care of patients with CRC. The gastroenterologist arranges diagnostics, such as blood tests and a colonoscopy with biopsy, if necessary. Once the diagnosis has been communicated, frailty screening with the G8 is arranged by nurses or nurse practitioners in the outpatient clinic (Figure 1). Patients are referred to a geriatrician for a CGA if the outcome suggests frailty. Feedback from geriatricians is usually provided in writing and subsequently addressed by the nursing department. Sometimes, the principally responsible physician is contacted by telephone to discuss the proposed decisions. During a multidisciplinary consultation session, patients are seen by a surgeon to discuss any further results and proposed treatment. If there are metastases, an oncologist will also see the patient. In our working environment, only the geriatricians and geriatric nurses are trained to perform a proper geriatric assessment of older people. The other nurses and doctors have received training in geriatrics during their studies in medicine or nursing, or in the oncology specialization. They did not receive additional specific training from the research team.

Figure 1: Procedure for patients with CRC, from diagnosis to treatment decision



Recruitment

The HCPs were recruited through a total population sample, a purposive sampling technique. All HCPs (eleven doctors, five nurses, three nurse practitioners) from the outpatient department were emailed by the researcher M.W. and asked to make an appointment. Participants received oral and written information about the study before the interview.

Data collection

All interviews were held in the period from February to July 2023. Interviews were conducted in Dutch using an interview guide (Appendix 2). This interview guide contained 10 questions, including 5 optional questions, related to the HCP's perspective on frailty screening and assessment of patients with CRC. The optional questions were asked if the participants did not provide this information themselves. The questions were defined in consultation with the research team. The interview guide was especially developed for this project and evaluated during the iterative data collection and analysis process (M.W.,

V.A., J.B.). No major changes were made to the interview guide. Demographic data on gender, age, job title, and work experience were requested at the start of the interview.

All interviews were conducted by M.W., a researcher and nurse practitioner on the geriatric team who has not been involved in caring for such patients for the past five years. She followed a two-day training course in conducting interviews. Participants were interviewed in a quiet and closed area within the hospital. A telephone interview was only considered if it proved very difficult to arrange a meeting. The interviews lasted between 25 and 55 minutes. The interviewer, M.W., described the notes on observations and reflections directly after the interview, which assisted in the data analyses, interpretation, and writing process. Member checking was carried out at the end of the interviews, with the interviewer providing a brief summary of the interview. This allowed the nurses or doctors to make any additions or changes (Holloway and Galvin, 2017). No changes were made since no suggestions for change were made by the interviewees, but many respondents elaborated on their experiences. Data collection stopped when all HCPs who agreed to participate were interviewed.

Data analysis

All interviews were audio-recorded and transcribed verbatim directly after the interview. Coding and data analysis were conducted systematically following the six steps of reflective thematic analysis (Braun and Clarke, 2006).

First, the interviewer (M.W.) listened to, read, and reread the transcribed interview to familiarize herself with the data. Second, initial codes were assigned to important segments of the transcripts. Five interviews were independently coded by three researchers (J.B., V.A., and S.Z.) and their generated codes (see Appendix 3) were discussed and compared with those of the main researcher (M.W.). As consensus was high, all subsequent transcripts were coded by one researcher (M.W.). Third, codes were sorted and grouped into potential themes by three research group members (J.B., V.A., and M.W.) in collaborative meetings. Fourth, the potential themes were tested and modified by checking against the full dataset. The potential themes were shared with the research team, who provided written feedback. The fourth step was repeated three times, resulting in this study's final themes. Finally, appropriate quotations were extracted from the transcripts to support the themes.

The software program ATLAS.ti. 22 was used to store, organize, and analyse the data.

Ethical considerations

This study was conducted according to the principles of the Declaration of Helsinki (World Medical Association, 2013) and does not fall under the scope of the Medical Research Involving Human Subjects Act (WMO). Therefore, it does not require approval from an accredited medical ethics committee in the Netherlands. However, in the Isala Hospital, an independent quality check, regarding the informed consent procedure, data management, privacy aspects, and legal aspects (Isala: 20230119), has been carried out to ensure compliance with legislation and regulations.

Written informed consent was sought from all participants before the interviews. The tapes and original transcripts are stored at the Isala hospital's secure internal storage. Only the interviewer has access to this source data and the key. Based on The Netherlands Code of Conduct for Scientific Practice, all data will be stored for ten years (Association of university of The Netherlands, 2012). According to Dutch privacy law, all transcripts are coded so personal data cannot be traced (Autoriteit Persoonsgegevens, n.d.). To ensure anonymity, we will refer to nurses, geriatricians, and other physicians without further specification.

Rigour

Central to a qualitative research design is trustworthiness. Several strategies were used to promote credibility, transferability, dependability, and confirmability (Lincoln and Guba, 1985; Nowell et al., 2017; Holloway and Galvin, 2017; Korstjens and Moser, 2018). The observational memos of the researcher increased the credibility of the results. It encouraged the researcher to reflect on the potential influence on the interpretation of the data. Four researchers from the research team conducted data analysis and interpretation, which contributed to the credibility and dependability of the study. By providing a complete description of the study population and its demographics, along with quotes from the participants to validate the findings, transferability and confirmability were enhanced (Lincoln and Guba, 1985; Nowell et al., 2017; Korstjens and Moser, 2018). M.W. realized that, as a researcher, she could influence the results. Therefore, multiple strategies were used to improve trustworthiness: M.W. discussed her role before each interview, observations were written down, and four researchers were involved in the thematic analysis process.

RESULTS

A total of 19 HCPs were approached. One HCP was unwilling to participate because she thought she had nothing to contribute with regard to frailty. Another HCP was on sabbatical at the time of data collection. Seventeen individuals from four different disciplines agreed to participate and were interviewed. Table 1 presents the characteristics of the participating HCPs. The participants' ages ranged from 29 to 63 years. Fifteen interviews took place face-to-face at the hospital and two were telephone interviews, of which one was a video call.

Table 1 - Characteristics of healthcare professionals (N=17)

Gender	
Female	12
Male	5
Age in years, mean (SD)*	46.3 (11.0)
Work experience; median number of years, (IQR)	14.0 (8.0-23.0)
Function	
Nurse	5
Nurse practitioner	3
Physician	9
Internal medicine / geriatrician	5
Internal medicine / oncologist	1
Surgeon	2
Gastroenterologist	1

*SD: standard deviation; IQR: interquartile range.

The nurses and geriatricians had experience with the use and content of the G8. The other physicians were only familiar with the process of frailty screening. All geriatricians had experience with the content of the CGA; all other participants had experience with the process and collaboration with each other.

Through analysis, two main themes were identified: 1) the perceived value of the G8 measurement for frailty screening and 2) the perceived value of the CGA. Underlying this, however, was a discussion about the complexity of frailty. Furthermore, we found that collaboration between HCPs and combining HCPs' perspectives are essential for the overall effectiveness of frailty assessment.

Complexity of frailty

When interacting with patients, HCPs try to form an impression of the patient's health status, functioning, and level of frailty based on their clinical judgement and the information they gather from various sources, such as medical records and discussions with the patient and their family. The HCPs commented that they could describe a frail person and the determinants of frailty. However, deciding whether an individual patient is frail and should, therefore, receive a different treatment from the standard appears to be more difficult since there are always different factors that determine whether someone is frail or not. A nurse stated: *'I also consider someone frail if they are struggling with low health literacy and have no network to rely on.'* (Nurse, I-6) In addition, the occurrence of complications is not always predictable. As a result, physicians may question the desirability of tailoring treatment based on the level of frailty. A physician commented: *'Just this week I operated on a very frail man who went home after two days. You think, yeah, I just don't get it sometimes.'* (Physician, I-7)

Theme 1: Perceived value of the G8 measurement for frailty screening

HCPs engaged in both positive and negative discussions regarding the supplementary benefits of screening with G8. Some overarching topics were discussed per theme: moment, content, and outcome.

Certain nurses and geriatricians expressed support for the timing of the screening, particularly its occurrence prior to treatment decision-making and the early engagement of nurses with patients along the care pathway. According to the nationally implemented pathway (IKNL, 2017), patients and their families receive the CRC diagnosis a few minutes before engaging with the nurse and undergoing a frailty assessment with the G8. This probably affects the degree of attention and carefulness spent answering the G8 questions. Much may depend on the state of mind immediately after hearing this bad news. One nurse commented: *'People can be quite emotional immediately after the diagnosis.'* (Nurse, I-2) Many nurses experienced the added value of seeing the patient and their family early in the process but wondered whether it would be preferable to be in contact even earlier, to be more familiar with the patient and their family when the final diagnosis is made. The only option is to see all patients who come in for a colonoscopy, but this is not considered efficient.

The content of the G8 has been the subject of debate, as have the reasons for the lack of added value. Clinical judgement when seeing the patient is more valuable in assessing frailty than the results of the G8. A physician commented:

'You don't just make decisions based on scores, you use your clinical view that you have slowly developed over the years.' (Physician, I-7)

In addition, the cognitive domain does not seem to be addressed adequately and objectively, so patients may say they do not have cognitive problems when they do. A geriatrician stated: *'The G8 is very disappointing because you ask people for their own opinion and they say, "But my memory is still good.'* (Geriatrician I-5) Nurses also noted that they would like their observations of mild complaints of forgetfulness to be included in the G8. Geriatricians and nurses also questioned whether the G8 assessment is too general, with the cognitive and social domains not being explored sufficiently. Suggestions have been made to use other screening tools such as the GFI, VMS, or the 6-item cognitive impairment test (6-CIT) (Katzman et al., 1983), or to add additional questions.

However, nurses saw more in having a professional in-depth conversation with the patient and their family instead of using a standardized instrument to judge the patient. One of the nurses said: *'The leaflet helps you to ask some preliminary questions but doesn't help you to see the person behind the patient. You need much more of a conversation for that.'* (Nurse, I-12)

Nurses and geriatricians using the G8 scores found that patients are labelled as frail too quickly, despite the fact that, due to the aforementioned generality of the G8, minimal cognitive problems are not detected. As a result, the G8 score frequently does not align with the level of frailty perceived by HCPs.

'The G8 is a short list that quickly leads to a positive score and I wonder if that is the goal. It might be better to do a more comprehensive screening, where it is important to look at the patient's context and not just the score.' (Geriatrician, I-8) Nurses and geriatricians experienced that referral to a geriatrician was often unnecessary if the G8 suggested frailty. One nurse described her experience with the G8 as: *'I would like to have a better screening tool, one where you can be sure you are not sending people to a geriatrician unnecessarily.'* (Nurse, I-12)

Theme 2: Perceived value of the comprehensive geriatric assessment

The value of CGA elicited varied responses from HCPs, encompassing both positive and negative feedback on its moment and outcome. While the discussion about the value of the G8 focused more on the instrument's content, the discussion about the value of CGA focused more on the process around it and for which patients it would add value.

HCPs voiced reservations regarding the additional benefit of the CGA when treatment decisions have already been made. Geriatricians indicated that their

recommendations had minimal influence on treatment decisions. A geriatrician shared:

'We only see them when the decision to operate has already been made. Whereas sometimes, because of someone's frailty, a different treatment, for example not having surgery or something else, is a better option, but yes, you don't have a choice in that anymore.' (Geriatrician, I-5).

Consequently, geriatricians often provide standardized, preventive guidance alongside their assessments.

The added value of a CGA becomes manifest for HCPs when uncertainty surrounds a patient's frailty, cognitive status, or optimal treatment modality, or when inconsistencies arise between clinical judgement and outcomes derived from the G8. The added value of a CGA was further acknowledged in cases of complexity (e.g. where there are problems in different domains or where HCPs have a different perception of patients' functioning and health) and in older people presenting with suspected cognitive impairments. A nurse stated: *'The geriatrician can take a good look at the elderly person and wonder: "Is this proposed treatment wise?" '* (Nurse, I-11)

The geriatricians confirmed that they were able to compose a complete picture of the patient. One of the geriatricians commented: *'I'm better at weighing up whether there's a certain life expectancy. I can't predict when someone will die either, but I think I have a more complete picture of the patient than the surgeon.'* (Geriatrician, I-14)

Bridging different perspectives

HCPs agreed that the way professionals look at patients depends on the specialism they work in. Nurses mentioned focusing on the social aspects, whereas surgeons can better assess surgical risk in order to provide an oncological advice. Geriatricians can better estimate life expectancy, besides functional and cognitive decline after surgery. A physician stated *'Geriatricians are trained to assess cognition. We are making mistakes there.'* (Physician, I-7)

In particular, improving collaboration between HCPs might help to understand each other's expertise and possibilities and, consequently, utilize each other's value. One of the nurses mentioned: *'The role of the geriatrician is not entirely clear and it would be important to share information from both disciplines.'* (Nurse, I-9)

The importance of collaboration between the surgical specialism and geriatricians was recognized by all HCPs. A physician commented: *'In the care for*

hospitalized elderly patients, all help is desirable to improve outcomes and reduce costs.' (Physician, I-17) However, if collaboration involves an extra appointment, nurses feel it is too much of a burden for the patient. Others saw the role of the geriatrician as a case manager who could have a good discussion about the patient's wishes and limitations, provide a risk assessment of complications and life expectancy, and also give advice on the proposed treatment.

Simultaneously, HCPs persist in struggling with accurately identifying the most frail patients for an additional assessment by geriatricians, a challenge provoked by the growing elderly population and an impending shortage of staff to perform this assessment.

DISCUSSION

Our study findings offer an insight into HCPs' perspectives on the value and practice of standardized frailty assessment of older patients with CRC. HCPs discussed the added value of screening with G8 and the referral for a CGA and commented on the moment, content, and outcome. When discussing the value of the CGA, the HCPs tended to discuss which patients it would benefit rather than its content. In addition, the complexity of frailty and collaboration between HCPs was considered. The integration of perspectives proved important to the overall added value of frailty assessment.

Geriatric-8 (G8) measurement

HCPs were in agreement that using the G8 does not add value and commented on the content, the moment, and the outcome that often did not match their clinical judgement of a patient's frailty. The perceived absence of added value is in line with our previous study that explored the prognostic value of the G8 and adverse outcomes within 30 days of surgery (Winters et al., 2024). The G8 showed no predictive value for those outcomes. Additionally, HCPs found that patients are too quickly labelled by the G8 as frail, leading to a perception that referrals for all such individuals are deemed futile. In line with this, a previous study highlighted the importance of nurses' clinical judgment and professional observations rather than simply relying on an overall score from a frailty assessment tool (Warnier et al., 2021). Consequently, HCPs in our study emphasized that, in their opinion, the pre-screening procedure in hospitals should be changed.

It is known that a perfect tool to detect frailty does not exist (Carpenter and Mooijaart, 2020). However, some HCPs preferred a different screening tool

(e.g. GFI) or combinations with extra questions (e.g. VMS and 6-CIT). Nurses and geriatricians missed specific questions about the cognitive functioning of the patients and mentioned that, in their opinion, a previously used frailty screening instrument (GFI) was better and identified fewer patients as being frail. At the same time, some nurses mentioned that the G8 provides guidance on working in a standardized manner and not forgetting important questions.

Timing and planning were also mentioned as factors influencing the perceived value of the G8. In Isala, the G8 was completed directly after the CRC diagnosis was communicated. This moment is not ideal for conducting an assessment. Frailty should not be regarded as an absolute measure but should always be judged in relation to the degree of stress on the patient (Goede, 2023). However, nurses preferred to familiarise themselves with the patients as soon as possible and early in the care process, so that they can better identify any frailty in different domains and better advocate the patient's wishes and boundaries. The interviewer found small differences between nurses' and nurse practitioners' experiences and perceptions of their role in frailty assessment. However, this was not explored further because it was outside the scope of this study and because responses were combined to ensure anonymity.

Comprehensive geriatric assessment (CGA)

HCPs also shared their views on the significance and implementation of the CGA in older patients with CRC, emphasizing that the added value becomes evident in cases where uncertainties arise regarding frailty, cognitive function, or the optimal treatment approach.

HCPs perceived that the power of geriatricians lies in engaging in meaningful conversations, conducting comprehensive risk assessments, exploring treatment options and their consequences, and providing informed guidance on treatment decisions. A geriatric assessment reveals insights beyond those attainable through standard consultations, aiding in identifying patient’s frailty and adverse outcomes such as mortality and functional decline (Hernandez Torres and Hsu, 2017). This also applies to oncology treatment regimens (Hamaker et al., 2022).

Currently, CGAs conducted by geriatricians occur after the decision for surgery has already been made, leading to a perception of them being redundant. Consequently, geriatricians often provide standardized, preventive advices. In the future, nurses could offer this standard guidance, provided they know when it can be applied. Guidance on this, must be included in a protocol.

In light of this, HCPs have proposed restarting interdisciplinary collaboration in the care pathway of CRC patients, recognizing the growing elderly population and scarcity of geriatric care specialists. This aligns with the notion that assessing frailty requires a comprehensive approach fostered by interdisciplinary collaboration (Coker et al., 2019), so that the perspectives of the nurse, the geriatrician (if required), different physicians, and the patient are included in the decision-making process.

Strengths and limitations

One of the strengths of this study lies in the inclusion of HCPs from diverse backgrounds and with diverse training, thereby enhancing the variability among participants. Furthermore, our study investigated the viewpoints of HCPs engaged in frailty assessment, encompassing the practical application of the G8 and the CGA, an aspect that has not been previously investigated. The prevailing practice predominantly involves comparing G8 outcomes with those derived from alternative frailty screening tools or patient-related outcomes, rather than investigating the clinical relevance of the G8. The findings from this study add value to the outcomes gleaned from quantitative studies, where the prognostic value of G8 is investigated.

However, this study has some limitations. First, two participants preferred a telephone interview, of which one was a video call. The disadvantage of conducting interviews without visual contact with participants is the potential lack of deeper interaction (Holloway and Galvin, 2017). Nevertheless, opting for this approach proved suitable for participants with busy schedules and gave them the opportunity to participate and share their opinion. For a homogeneous group, 10–20 participants typically achieves data saturation (Boddy, 2016). Although we had a heterogeneous group, we did achieve data saturation during the interviews. Our purpose was to provide in-depth explanations of and meanings of the HCPs, rather than generalizing findings. However, it is instructive and provides guidance for improving practice for other globally comparable hospitals working with the current vulnerability assessment. One final consideration is that the interviews did not encompass patients and their families. While this inclusion may be feasible at a later stage, the decision was taken to confine this qualitative study to healthcare professionals.

Implications for practice, policy, and research

This study adds to the existing knowledge of the perceived value of frailty assessment and screening with G8 in the care for patients with CRC in our

hospital. According to the majority of respondents, the G8 offers minimal to negligible value to the HCPs. Frailty assessments hold the potential to augment the comprehension of patients' preferences, risks, and capabilities, particularly when approached from diverse perspectives. Achieving this necessitates interdisciplinary collaboration. While a CGA proves beneficial for certain patients, it remains a challenge to determine for whom it is of value. In fact, we found that the current G8 questionnaire is inadequate, that frailty is defined differently, and that we need to consider the limited capacity of geriatricians.

The growing elderly population underscores the need for an effective resolution, such as improving the moment and content of the frailty screening, new agreements on the implications of frailty labelling, and, thus, collaboration between the different HCPs, which could potentially mean a greater role for nurses in the frailty assessment process, but knowledge about older people should also be improved.

Knowledge of older people is important in order to be able to assess the domains of frailty correctly and to make hospital care safer for frail older adults. Recent literature confirmed that knowledge of older adults among nurses and medical trainees is low (Dent et al., 2019 & Derks et al., 2021). In our view, starting with increasing the knowledge of professionals from other disciplines will improve care for this group. Another option is to involve geriatric nurses in non-geriatric specialties, to ensure appropriate assessment of frailty, and especially cognition on admission. The real impact of this will need to be studied. Moreover, the translation of research findings into practice is often lacking, resulting in a lack of knowledge on effective intervention strategies for vulnerability and on strategies for managing vulnerability in clinical practice (Guttman et al., 2022). The level of frailty is already known in primary care (the General Practitioner or home care). In principle, everyone in the Netherlands has a GP, who will refer you to a medical specialist, if necessary. In general, the primary care physician knows the patient quite well. He or she could assess frailty better than when a judgment is passed on the degree of frailty during an acute situation. It is therefore important to share this information between hospitals and primary care. Fourthly, developments in the current Dutch healthcare system to improve shared decision making could also help to improve this process. Shared decision making involves discussing and considering the available information, including treatment options and consequences, and then considering how this fits with the patient's preferences for health status and outcomes (Bomhof-Roordink et al., 2019). Follow-up studies could further explore patients' experiences and needs in the current decision-making process.

CONCLUSION

This study explores HCPs' perspectives on the value and practice of standardized frailty assessment of older patients with CRC. From the perspective of the participating HCPs, the G8 is not an appropriate screening instrument.

In their opinion, a CGA will add value for a specific, albeit elusive, subset of patients, such as those with uncertainty about frailty or impaired cognitive function, or in case of doubt about the optimal treatment approach. In addition, a CGA will add value, particularly if it is carried out before a treatment decision is made and is seamlessly integrated into an efficient, cost-effective

REFERENCES

Association of university of The Netherlands, 2012. 'The Netherlands Code of Conduct for Scientific Practice. Principles of good scientific teaching and research'. https://www.universiteitenvannederland.nl/files/documenten/Domeinen/Onderzoek/The_Netherlands_Code_of_Conduct_for_Scientific_Practice_2012.pdf (Accessed: August 2023)

Autoriteit Persoonsgegevens, n.d. Algemene verordening gegevensbescherming (AVG) https://autoriteitpersoonsgegevens.nl/nl/onderwerpen/algemene-informatie-avg/mag-u-persoonsgegevens-verwerken (Accessed: August 2023)

Bellera, C.A., Rainfray, M., Mathoulin-Pélissier, S., Mertens, C., Delva, F., Fonck, M., Soubeyran, P.L., 2012. 'Screening older cancer patients: first evaluation of the G-8 geriatric screening tool'. *Ann Oncol.* 23(8):2166-2172. DOI: 10.1093/annonc/mdr587.

Boddy, C. R., 2016. 'Sample Size for Qualitative Research'. *Qualitative Market Research: An International Journal,* 19, 426-432. https://doi.org/10.1108/QMR-06-2016-0053

Bomhof-Roordink, H., Gärtner, F.R., Stiggelbout, A.M., Pieterse, A.H., 2019. 'Key components of shared decision making models: a systematic review'. *BMJ Open.* 17;9(12):e031763. doi: 10.1136/bmjopen-2019-031763

Braun, V., Clarke, V., 2006. 'Using thematic analysis in psychology'. *Qualitative Research in Psychology, 3*(2), 77–101. https://doi.org/10.1191/1478088706qp063oa

Carpenter, C.R., Mooijaart, S.P., 2020. 'Geriatric Screeners 2.0: Time for a Paradigm Shift in Emergency Department Vulnerability Research'. *J Am Geriatr Soc*. 68(7):1402-1405. doi: 10.1111/jgs.16502.

Coker, J.F., Martin, M.E., Simpson, R.M., Lafortune, L., 2019. 'Frailty: an in-depth qualitative study exploring the views of community care staff'. *BMC Geriatr* **19**, 47. https://doi.org/10.1186/s12877-019-1069-3

Creswell, J.W., Creswell, J.D., 2017. '*Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*'. 4th Edition, Sage, Newbury Park.

Dent, D., Martin, F.C., Bergman, H., Woo, J., Romero-Ortuno, R., Walston, J.D., 2019. 'Management of frailty: opportunities, challenges, and future directions'. *The Lancet*. Volume 394, Issue 10206, 1376 – 1386. https://doi.org/10.1016/S0140-6736(19)31785-4

Derks, C.T.A.J., Hutten - van den Elsen, M.M.G.M., Hakvoort, L.J., Mersbergen, M.P.J., RENurse Consortium, Schuurmans, M.J., Dikken, J., 2021. 'Hospital nurses' knowledge regarding older patients: a multicenter study'. *BMC Nurs.* 4;20(1):135. https://doi.org/10.1186/s12912-021-00604-4

Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W.J., Burke, G., McBurnie, M.A., 2001. 'Frailty in older adults: evidence for a phenotype'. *J Gerontol A Biol Sci Med Sci.* 56(3):M146–57. DOI: 10.1093/gerona/56.3.m146

Goede, V., 2023. 'Frailty and Cancer: Current Perspectives on Assessment and Monitoring'. *Clin Interv Aging.* 28;18:505-521. doi: 10.2147/CIA.S365494.

Gobbens, R.J. Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M,. 2010a. 'Toward a conceptual definition of frail community dwelling older people', *Nurs Outlook*. 58(2):76–86. DOI: 10.1016/j.outlook.2009.09.005

Gobbens, R.J., van Assen, M.A., Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M., 2010b. 'The Tilburg frailty indicator: psychometric properties'. *J Am Med Dir Assoc*. 11(5):344–55. DOI: 10.1016/j.jamda.2009.11.003

Guttman, M.P., Haas, B., Kim, M., Mador, B., Nathens, A.B., Ahmed, N., Wheeler, S., Gotlib Conn, L., 2022. 'Innovative curriculum is needed to address residents' attitudes toward older adults: the case of geriatric trauma'. *BMC Med Educ*. 22(1):130. https://doi.org/10.1186/s12909-022-03196-y

Hamaker, M., Lund, C., te Molder, M., Soubeyran, P, Wildiers, H., van Huis, L, Rostoft, S., 2022. 'Geriatric assessment in the management of older patients with cancer – A systematic review (update)'. *Journal of Geriatric Oncology.* Volume 13, Issue 6,Pages 761-777, ISSN 1879-4068, https://doi.org/10.1016/j.jgo.2022.04.008.

Hernandez Torres, C., Hsu, T., 2017. 'Comprehensive Geriatric Assessment in the Older Adult with Cancer: A Review'. *Eur Urol Focus*. 3(4-5):330-339. doi: 10.1016/j.euf.2017.10.010.

Holloway, I., Galvin, K., 2017. '*Qualitative Research in nursing and healthcare (4th ed.)*'. Oxford: Wiley Blackwell.

IGJ, 2020. '17 kwetsbare groepen'. https://magazines.igj.nl/hetresultaattelt/2020/01/17-kwetsbare-groepen (Accessed: June 2023)

IGJ, 2019. 'Basisset Medisch Specialistische Zorg 2020'. https://www.igj.nl/publicaties/indicatorensets/2019/09/03/basisset-medisch-specialistische-zorg-2020 (Accessed: June 2023)

IKNL, 2022. 'Incidentie dikke darmkanker en endeldarmkanker'. Available at: https://www.iknl.nl/ (Accessed: 02 June 2023)

IKNL, 2017. Format transmuraal zorgpad colorectaal carcinoom, versie 5.0. https://iknl.nl/getmedia/9e2f168c-33a7-4cbb-a95c-c8a7f795f1fa/zorgpad-colorectaalcarcinoom.pdf (Accessed: June 2023)

Katzman, R., Brown, T., Fuld, P, Peck, A, Schechter, R., Schimmel, H., 1983. 'Validation of a short Orientation-Memory-Concentration Test of cognitive impairment'. *American Journal of Psychiatry*, 140(6), 734–739. doi: 10.1176/ajp.140.6.734

Korstjens, I., Moser, A., 2018. 'Series: Practical guidance to qualitative research. Part 4: Trustworthiness and publishing', *European Journal of General Practice*, 24:1, 120-124, DOI: 10.1080/13814788.2017.1375092

Kristjansson, S.R., Nesbakken, A., Jordhøy, M.S., Skovlund, E., Audisio, R.A., Johannessen, H.O., Bakka, A., Wyller, T.B., 2010. 'Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: A prospective observational cohort study', *Critical Reviews in Oncology/Hematology*. 76(3), 208–217. DOI: 10.1016/j.critrevonc.2009.11.002

Lincoln, Y.S., Guba, E.G., 1985 'N*aturalistic Inquiry*'. Beverly Hills, CA: Sage Publications, inc.

Liu, X., Le, M.K., Lim, A.Y.C., Koh, E.J., Nguyen, T.N., Malik, N.A., Lien, C.T.C., Lee, J.E., Au, L.S.Y., Low, J.A.Y.H., Wee, S.L., 2022. 'Perspectives on frailty screening, management and its implementation among acute care providers in Singapore: a qualitative study'. *BMC Geriatr* 22, 58 https://doi.org/10.1186/s12877-021-02686-w

Morley, J.E., Malmstrom, T., Miller, D., 2012. 'A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans'. *J Nutr Health Aging*.16(7):601–8. DOI: 10.1007/s12603-012-0084-2

Nowell, L.S., Norris, J., White, D., Moules, N., 2017. 'Thematic Analysis: Striving to Meet the Trustworthiness Criteria'. *International Journal of Qualitative Methods. 16*(1). https://doi.org/10.1177/1609406917733847

Peters, L.L., Boter, H., Buskens, E., Slaets, J.P., 2012. 'Measurement properties of the Groningen frailty Indicator in home-dwelling and institutionalized elderly people'. *J Am Med Dir Assoc.* 13(6):546–51. https://doi.org/10.1016/j.jamda.2012.04.007

Rikli, R., Jones, J., 1999. 'Development and validation of a functional fitness test for community-residing older adults'. *J Aging Phys Act*. 7(2):129–61. DOI: 10.1093/geront/gns071

Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D.B., McDowell, I., Mitnitski, A., 2005. 'A global clinical measure of fitness and frailty in elderly people'. *CMAJ.* 173(5):489–95. DOI: 10.1503/cmaj.050051

Rolfson, D.B., Majumdar, S.R., Tsuyuki, R.T., Tahir, A., Rockwood, K., 2006. 'Validity and reliability of the Edmonton Frail Scale'. *Age Ageing.* 35(5):526–9. DOI: 10.1093/ageing/afl041

Slaets, J.P.J., 2006. 'Vulnerability in the Elderly: Frailty'. *Medical Clinics of North America.* Volume 90, Issue 4, Pages 593-601. DOI: 10.1016/j.mcna.2006.05.008

Tong, A., Sainsbury, P., Craig, J., 2007. 'Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups'. *Int J Qual Health Care*. 19(6):349-57. DOI: 10.1093/intqhc/mzm042.

Van Damme, J., Neiterman, E., Oremus, M., Lemmon, K., Stolee, P., 2020. 'Perspectives of older adults, caregivers, and healthcare providers on frailty screening: a qualitative study'. *BMC Geriatr* 20, 65. DOI: 10.1186/s12877-020-1459-6

VMS, 2009. 'Praktijkgids kwetsbare ouderen'. https://www.vmszorg.nl/wp-content/uploads/2017/07/web_2009.0104_praktijkgids_kwetsbare_ouderen.pdf (Accessed: July 2023)

Warnier, R.M.J., van Rossum, E., van Kuijk, S.M.J., Mulder, W.J., Schols, J.M.G.A., Kempen, G.I.J.M., 2017. 'The Maastricht Frailty Screening Tool for Hospitalised Patients (MFSTHP) to Identify Non-Frail Patients'. *International journal of clinical practice*. 71(9). DOI: 10.1111/ijcp.13003

Warnier, R.M.J., van Rossum, E., Du Moulin, M.F.M.T., van Lottum, M., Schols, J.M.G.A., Kempen, G.I.J.M., 2021. 'The opinions and experiences of nurses on frailty screening among older hospitalized patients. An exploratory study'. *BMC Geriatr* 21, 624. DOI: 10.1186/s12877-021-02586-z

Warps, A.K., Tollenaar, R.A.E.M., Tanis, P.J., Dekker, J.W.T., Dutch ColoRectal Audit, 2022. 'Postoperative complications after colorectal cancer surgery and the association with long-term survival', *European Journal of Surgical Oncology*. Volume 48, Issue 4, Pages 873-882, ISSN 0748-7983. DOI: 10.1016/j.ejso.2021.10.035

Winters, A.M., Bakker, J., Ten Hoor, J., Bilo, H.J.G., Roodbol, P.F., Edens, M.A., Finnema, E.J., 2024. 'Prognostic value of Geriatric-8 for adverse outcomes within 30 days of surgery in older adults with colorectal cancer: A retrospective cohort study'. *Eur J Oncol Nurs.* 16;70:102591. DOI: 10.1016/j.ejon.2024.102591.

World Medical Association, 2013. 'World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects'. *JAMA*. 27;310(20):2191-4. doi: 10.1001/jama.2013.281053.

Appendix 1: The Geriatric-8 measurement (Bellera et al., 2012)

Items	Possible answers	Score
Food intake in the last 3 months	0: severe decrease in food intake 1: moderate decrease in food intake 2: no decrease in food intake	…
Weight loss during the last 3 months	0: weight loss >3 kg 1: does not know 2: weight loss between 1 and 3 kg 3: no weight loss	…
Mobility	0: bed or chair bound 1: able to get out of bed/chair but does not go out 2: goes out	…
Neuropsychological problems	0: severe dementia or depression 1: mild dementia or depression 2: no psychological problems	…
Body Mass Index (BMI)	0: BMI < 19 1: BMI 19 to < 21 2: BMI 21 to < 23 3: BMI 23 and > 23	…
Takes more than 3 medications per day	0: Yes 1: No	…
Self-rated health status (compared to other people of the same age)	0: not as good 0.5: does not know 1: as good 2: better	…
Age (in years)	0: > 85 1: 80–85 2: < 80	…
Total score (0–17) [Cut-off $\leq$ 14 indicating impairment]		

Appendix 2: Interview Guide

Demographic data:

Gender	Male/Female
Age in years	
Job title	Nurse, nurse practitioner, oncologist, surgeon, gastroenterologist, geriatrician
Work experience in years	

Interview questions:

When it comes to the frailty assessment process for patients with CRC, what is the first thing that comes to your mind?

Tell me about your last frailty screening/assessment. (*only for nurses and geriatricians*)

What factors do you think determine frailty?

What would your ideal frailty assessment look like?

What first steps could you take to improve the frailty assessment process?

Any optional questions:

How is the frailty assessment process conducted?

Is this always the case and why or why not?

What parts of this process would you like to keep?

Can you tell me something about the role of frailty in this process?

When do you see the added value of this process?

Appendix 3: Generated codes

	Number of responses	Number of interviewees
1. Screening with G8		
Nurses		
Added value of G8 according to nurses and nurse practitioners	8	5
No added value of G8 according to nurses and nurse practitioners	33	8
Moment of the G8 screening	8	6
Content of the G8 screening	23	7
Outcome of the G8 screening	10	8
Geriatricians		
Added value of G8 according to geriatricians	5	1
No added value of G8 according to geriatricians	13	4
Moment of the G8 screening	5	1
Content of the G8 screening	7	4
Outcome of the G8 screening	6	4
Other physicians		
Added value of G8 according to other physicians	0	0
No added value of G8 according to other physicians	5	3
Moment of the G8 screening	0	0
Content of the G8 screening	0	0
Outcome of the G8 screening	5	3
2. Comprehensive geriatric assessment (CGA)		
Nurses		
Added value of CGA according to nurses and nurse practitioners	19	8
No added value of CGA according to nurses and nurse practitioners	16	6
Moment of the assessment	8	3
Content of the assessment	20	8
Category of patients	11	5
Geriatricians		
Added value of CGA according to geriatricians	17	5
No added value of CGA according to geriatricians	7	5
Moment of the assessment	3	3
Content of the assessment	14	5
Category of patients	5	2
Other physicians		
Added value of CGA according to other physicians	10	4
No added value of CGA according to other physicians	3	2

	Number of responses	Number of interviewees
Moment of the assessment	-	-
Content of the assessment	8	4
Category of patients	3	2

CHAPTER 7

DISCUSSION

This thesis explores the clinical relevance of frailty assessment in the care of older hospitalized patients. It also examines the frailty-assessment experiences of healthcare professionals (HCPs) working in the outpatient clinic of a Dutch hospital in terms of the perceived value they assign to such assessment in their daily practice. The investigation further addresses the predictive value of several screening tools that have been developed to assess the presence and level of frailty. Together, these studies provide insight into the added value of frailty assessment for HCPs and that of frailty-screening tools for patient-centred care. The primary emphasis of patient-centred care is that all individual patients are unique, with their own views and health preferences (1). Frailty-screening tools are widely available, and they are frequently used across diverse settings and patient populations. To ensure clinical relevance and effective application in patient-centred care, however, several factors are crucial: tool selection, follow-up after screening, and thoughtful implementation. To this end, the present thesis highlights the critical need to integrate frailty screening into an interprofessional process, in which teamwork and shared decision-making (SDM) play essential roles, and in which frailty-screening tool serve as indicators for the potential application of comprehensive geriatric assessment (CGA). The SDM model describes how HCPs and their patients can make shared decisions about the diagnostics and treatments that best meet the needs and wishes of the patient, with both the patient and the HCP as active participants (2,3).

This general discussion begins with a summary of the main findings, followed by a discussion and interpretation of these findings, along with the strengths and limitations of the research. After addressing the implications of the findings and corresponding recommendations, the conclusions are presented.

7.1 MAIN FINDINGS

Following a summary and analysis of the most important points, the findings of the separate studies are described according to the integral conceptual model of frailty (4). This model aligns with the definition of frailty applied in this thesis: ‘a dynamic condition affecting an individual who is experiencing losses in one or more domains of human functioning (physical, psychological, and/or social) caused by a range of variables and which increases the risk of adverse outcomes’ (5).

7.1.1. What are the challenges in evaluating frailty and predicting life expectancy in hospital practice? (Chapter 2)

A literature review focusing on systematic reviews and meta-analyses of frailty-screening tools yielded two relevant sources (6,7). In all, these sources included and compared 39 tools. No single tool emerged as the best for the acute setting of hospitalized older adults. Similar conclusions can be drawn for the assessment of predicting life expectancy. We identified four reviews providing evidence on tools for predicting shorter life expectancy (8-11). None of these tools was sufficiently accurate for use in acute settings, and external validity was often not examined. The comparison of results is further complicated by the variety of screening tools (12).

As clearly reflected in this literature review, frailty is a complex concept that is difficult to capture in a screening tool. At the same time, however, HCPs often depend on screening tools as diagnostic aids. This is particularly the case in urgent situations (e.g. acute admissions), in which time constraints limit opportunities for thorough patient assessments. The application of screening tools should be exercised with caution in such situations.

7.1.2. What is the predictive value of the Groningen Frailty Indicator (GFI) and the Dutch Patient Safety Program (VMS) frailty-screening tool for clinical outcomes in patients who have undergone hip-fracture surgery? (Chapter 3)

In a prospective observational cohort study of patients over 70 years of age who have undergone hip-fracture surgery (N = 280), we found that the VMS frailty score – based on three domains (GFI) (Table 1) – and the Groningen Frailty Indicator (Table 2) (13) significantly predicted overall survival, with hazard ratios (HR) of 3.5 and 2.3, respectively. This VMS frailty score was also associated with 30-day mortality, as were delirium during admissions, polypharmacy, and cardiovascular disease. Given that the conclusions are based on data from 2014/2015, we decided to update our view of the literature. According to a recent systematic literature review (14), VMS frailty scores are still being used as a frailty screening tool, albeit in different ways across different patient populations. The review showed that frailty, as measured by the VMS, is associated with adverse outcomes, but conflicting evidence has been found with regard to readmission, complications, functional decline, and mortality. Another recent literature review (15) examining the predictive value of frailty in patients with hip fractures establishes that, in this patient population, frailty is associated with greater risk of mortality (OR = 3.48, 95% CI: 2.50–4.85). Based on these findings, we concluded that the results of our

study are still applicable with regard to the predictive value of the GFI and the VMS frailty score, as no new studies have proven otherwise. Furthermore, frailty screening in patients with hip fractures remains relevant for scientific research purposes, as new developments are underway to offer conservative treatments with nerve blocks for frail patients (16).

In practice, the use of frailty-screening tools can help nurses to select appropriate interventions (e.g. to prevent falls or delirium). In addition, the GFI and VMS frailty-screening tools are utilized to differentiate between patients who are frail and those who are not, with the broader objective is to identifying patients who may be frail or at high risk of developing adverse outcomes. The results of these measurements are intended to support decision-making by HCPs. Given that these tools can be used only to make a preliminary selection, it is essential to raise awareness concerning such improper expectations. To support decision-making in patients with hip fractures, we recommend incorporating a CGA or a similar holistic assessment into the interprofessional process. This would ensure a comprehensive understanding of individual patients, in addition to allowing them to participate actively in decision-making, without the heavy influence of frailty-screening tools applied in advance. In this ideal approach, various disciplines and specializations collaborate closely to generate a complete overview of individual patients, including their views and preferences.

Table 1: VMS frailty-screening tool based on three domains

Question 1:	Do you have memory problems/have you ever been confused during a previous hospital stay or illness?
Question 2:	Have you fallen in the last six months?
Question 3:	Have you had help with activities of daily living in the last 24 hours?

Table 2: Groningen Frailty Indicator (17)

Items	Yes	No	Sometimes
Are you able to carry out these tasks single-handedly and without any help? (The use of help resources such as a walking stick, walking frame or wheelchair is considered to be independent.)			
1. Grocery shopping	0	1	
2. Walking around outside (around the house or to the neighbours)	0	1	
3. Dressing and undressing	0	1	
4. Going to the toilet	0	1	
5. Do you experience problems in daily life due to poor vision?	1	0	
6. Do you experience problems in daily life due to being hard of hearing?	1	0	
7. During the last 6 months have you lost a lot of weight unwillingly? (3 kg in 1 month or 6 kg in 2 months)	1	0	
8. Do you take 4 or more different types of medicine?	1	0	
9. Do you have any complaints about your memory?	1	0	1
10. Do you sometimes experience emptiness around yourself?	1	0	1
11. Do you sometimes miss people around yourself?	1	0	1
12. Do you sometimes feel abandoned?	1	0	1
13. Have you recently felt downhearted or sad?	1	0	1
14. Have you recently felt nervous or anxious?	1	0	1
15. What mark do you give yourself for physical fitness? (Scale 0 to 10) [0–6 = 1 7–10 = 0]	1	0	
score GFI Total	...		

7.1.3. What is the relationship between orthostatic hypotension and muscle strength with regard to the time to successful rehabilitation in older patients with hip fractures? (Chapter 4)

Of the 116 elderly patients with hip fractures in a prospective observational cohort study, 103 (89%) were successfully rehabilitated, having regained their pre-surgery level of function and returned to their previous living situations. Measuring muscle strength is a relevant method for gathering objective information about a patient's condition before interventions (e.g. surgical procedures), and it is performed as part of a CGA (18). Poor muscle strength is commonly observed in elderly patients, and it is associated with physical frailty (19). Orthostatic hypotension (OH) is a well-known condition that contributes to accumulating deficits, increasing the risk of frailty (20).

The prevalence of OH in the study sample was 34% (95% confidence interval [CI] 25–43%), and the median handgrip strength of the dominant arm was 20

kilograms (interquartile range [IQR] 15–26). There was no statistically significant relationship between OH and time to successful rehabilitation (hazard ratio [HR] 1.05; 95% CI 0.67–1.66). There was also no statistically significant relationship between handgrip strength and successful rehabilitation (HR 1.03; 95% CI 0.99–1.06). Given the wide CI, it can be neither concluded nor ruled out that handgrip strength had predictive value.

Given that the conclusions are based on data from 2014/2015, we updated our view of the literature accordingly. Between 2020 and 2023, a similar retrospective study was conducted amongst patients aged 65 years and older (N = 253) who had undergone hip-fracture surgery. This study investigated the potential predictive value of OH and handgrip strength for successful rehabilitation. The results reveal predictive value for HGS and successful rehabilitation (21). This confirms suspicions that, as a measure of physical frailty, handgrip strength can provide insight into the expected rehabilitation trajectory of older patients with hip fractures.

7.1.4. To what extent is the Geriatric-8 measurement a discerning instrument for predicting 30-day adverse outcomes for older patients (aged ≥70 years) undergoing surgery for colorectal cancer? (Chapter 5)

A retrospective cohort study was conducted to determine the value of the Geriatric-8 (G8) measurement (Table 3) (22) in predicting 30-day adverse outcomes for older patients (aged ≥70 years) undergoing surgery for colorectal cancer (CRC). Univariate and multivariable data analyses from 200 patients revealed no statistically significant predictive value. At the same time, however, the odds of adverse outcomes were greater for those 80 years of age or older (sign.), as well as for those responding positively to the VMS screening question about cognitive decline and previous delirium. Based on these outcomes, we conclude that implementing an objective cognitive assessment could significantly strengthen the frailty-screening process in older patients with CRC.

Table 3: The Geriatric-8 measurement (22)

Items	Possible answers	Score
Food intake in the last 3 months	0: severe decrease in food intake 1: moderate decrease in food intake 2: no decrease in food intake	…
Weight loss during the last 3 months	0: weight loss >3 kg 1: does not know 2: weight loss between 1 and 3 kg 3: no weight loss	…
Mobility	0: bed or chair bound 1: able to get out of bed/chair but does not go out 2: goes out	…
Neuropsychological problems	0: severe dementia or depression 1: mild dementia or depression 2: no psychological problems	…
Body Mass Index (BMI)	0: BMI < 19 1: BMI 19 to < 21 2: BMI 21 to < 23 3: BMI 23 and > 23	…
Takes more than 3 medications per day	0: Yes 1: No	…
Self-rated health status (compared to other people of the same age)	0: not as good 0.5: does not know 1: as good 2: better	…
Age (in years)	0: > 85 1: 80–85 2: < 80	…
Total score (0–17) [Cut-off ≤ 14 indicating impairment]		

7.1.5. To what extent do healthcare professionals working in outpatient clinics perceive the value of standardized frailty assessment in older adults with colorectal cancer? (Chapter 6)

A qualitative study was conducted based on semi-structured interviews exploring the perspectives of 17 healthcare professionals (HCPs) with regard to frailty assessments in older adults with CRC. Frailty assessment consists of screening with the G8 measurement, followed by a CGA in cases of identified frailty. The perceived value is strongly influenced by the complexity of frailty and the collaboration amongst HCPs, whose perspectives converge to generate a comprehensive understanding of the patient.

In evaluating the perceived value of the G8 measurement, key concerns include the limited assessment of cognition, the absence of items on social functioning, and its application at undesirable moments. Regarding the CGA,

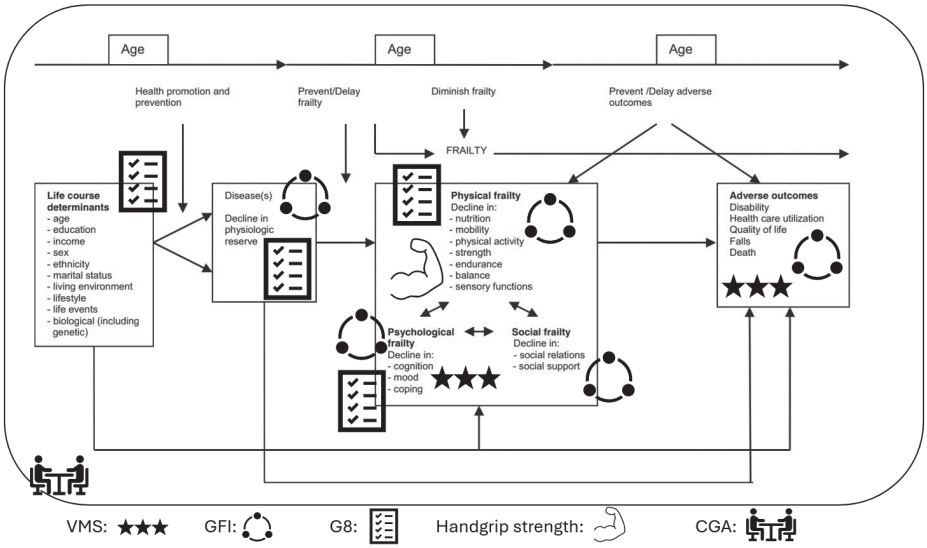
key concerns include timing and the role that its outcomes play or should play in the decision-making process. In the perspectives of HCPs, it was clear that CGAs were not always conducted for patients who required it, and they often took place after treatment decisions had already been made. Furthermore, the conclusions did not always align with the expectations of the referring specialism, possibly due to unclear expectations and possibilities across the various specialisms. As a result, the predominant experience of the HCAs with regard to the current perceived value of the G8 measurement and the CGA was that they were limited. On the other hand, they strongly believed that collaborating with experts in geriatrics could significantly enhance the ability to identify the most suitable treatment for and improve the outcomes of frail older adults. We consequently conclude that, in addition to the content of the frailty screening, procedural factors (e.g. time management, decision-making, and mutual coordination) have a substantial influence on the perceived value of frailty assessment.

7.2 GENERAL DISCUSSION

7.2.1 DISCUSSION OF MAIN FINDINGS

This thesis explores the clinical relevance of frailty assessment in caring for older patients within the Dutch population in the hospital setting. The VMS frailty-screening instrument, the G8 measurement, the GFI, handgrip strength, and the CGA were central to the studies conducted as part of the current thesis. In this order, the screening tools and assessment are further examined by comparing their content to the integral conceptual model of frailty (4). The components of the screening tools and assessment within the model are illustrated below (Figure 1).

Figure 1: The components of the screening tools and assessment within the integral conceptual model of frailty (4)



Frailty screening (specifically, the application of the VMS, G8, and GFI)

The VMS frailty-screening tool (Table 1) includes items about disability, falls, and cognitive functioning, as well as delirium, which – according to the model – can be regarded as an assessment of psychological frailty and an evaluation of adverse outcomes in the past. The tools do not examine life-course determinants, diseases, physical frailty, or social frailty. A history of falls or delirium increases the likelihood that such adverse outcomes will recur. This score thus serves as a prompt for nurses to initiate preventive measures during hospitalization. A previous fall, delirium, and dependence on others for activities of daily living (ADL) are characteristics of geriatric syndromes. These conditions are more prevalent in individuals who are frail, as compared to those who are not, and they are associated with adverse outcomes (23). The ability of the VMS to screen for frailty is limited, however, and it may overlook factors contributing to the frailty of an individual.

The G8 measurement (Table 3) incorporates items related to physical frailty, including food intake, weight loss, BMI, and mobility. Age is one of the life-course determinants of the integral conceptual model of frailty (4), and it is also addressed in the G8 measurement. Although items about polypharmacy and the patient's health self-assessment cannot be immediately placed in the

model, polypharmacy may indicate the presence of disease. Furthermore, a patient's health self-assessment may offer insights into their overall health status. The item regarding the presence of neuropsychological problems can be placed under 'disease(s)' or 'psychological frailty'.

Notably, social frailty is not assessed in the G8 measurement, and the item about neuropsychological problems is limited. It is known that patients with cognitive impairment often overestimate their abilities (24), making it unlikely for them to select the option of severe/mild dementia or depression. This could explain the observation of nurses that G8 outcomes often do not correspond to their clinical judgment (Chapter 6). This could also be related to the fact that the G8 is a pre-screening instrument, and not a diagnostic instrument.

Despite the limitations of available tools, insight into the cognitive functioning of hospitalized elderly patients is essential. Through multivariate analysis, we determined that memory problems or a history of delirium – one of the VMS screening items – offers significant predictive value for complications occurring within 30 days post-surgery in older adults with CRC (Chapter 5), and cognitive dysfunction is common in hospitalized older patients (25). In a recent flash-mob study, 347 of 757 patients exhibited cognitive dysfunction. These patients had been enrolled in a multicentre, cross-sectional observational study in 13 university and general hospitals in the Netherlands (25).

Geriatric nurses and nurse practitioners of the outpatient clinic preferred using the GFI (Table 2) instead of the G8 measurement (Table 3) (Chapter 6). In terms of the integral conceptual model of frailty, the GFI notably addresses the three different domains of frailty. It also includes items about a patient's level of dependency before admission and situations that could be fit into the model as adverse outcomes. In addition, self-rated physical fitness may offer insight into overall health status. Although the life-course determinant is not addressed in the GFI, it is known that lifestyle components (e.g. maintaining a healthy weight, staying active, avoiding smoking, and moderating alcohol intake) may reduce the long-term risk of frailty (26). This information is crucial to the customization of both preventive interventions and treatments. Assessments that rely solely on the GFI would thus overlook these important life-course determinants.

Handgrip strength and frailty

Our findings suggest that incorporating physical measurements into a comprehensive assessment may help predict relevant patient-centred outcomes (27). Medical records contain information on physical tests, including laboratory results and various measures (e.g. handgrip strength and blood

pressure). These outcomes are important to obtaining a complete picture of the patient. Handgrip strength – or, more specifically, the decrease of such strength – is regarded as being associated with the degree of physical frailty (4). Given that muscle strength influences recovery (28), the assessment of frailty through muscle strength measurements may provide a reasonable estimation of recovery, in addition to predicting the time to successful rehabilitation in patients with hip fractures (Chapter 4) (21).

Comprehensive geriatric assessment (CGA)

As expected, the CGA encompasses all key components of the conceptual frailty model and more, including the existential dimension, which considers the patient's future perspective, coping mechanisms, and quality of life, as well as how a treatment might or might not contribute to these aspects. Although it might not seem feasible to administer the CGA to all hospitalized elderly patients, due to the extensiveness of the instrument, its implementation could ultimately allow more customization in treatments and improvements in patient-centred outcomes. Time investments at the beginning could yield greater time savings in the long run. In support of this perspective, a recent dissertation highlights patient involvement and experiences in understanding frailty, emphasizing the importance of individual differences that HCPs should recognize (29).

Despite the value of this instrument, it is not always effectively applied in practice. The CGA guidelines advise that treatment decisions for older adults should be made only after completing and correctly interpreting the results of the CGA (18). As demonstrated in Chapter 6, although the CGA has proven its added value in the care of older hospitalized patients with CRC, the final assessment of frailty and the recommendations of geriatricians had little or no impact on the treatment decisions in our study sample. It is nevertheless important to find a solution that takes into account the timing of assessment, interdisciplinary coordination, and strong patient involvement.

7.2.2 STRENGTHS AND LIMITATIONS

The studies included in this thesis are subject to a number of strengths and limitations, which are addressed in this section. The main strength of the studies has to do with the application of different methodological approaches that rely primarily on structurally available and real-world data (i.e. data collected outside the laboratory or conventional randomized controlled trials) (30). The use of real-world data has provided valuable insights into clinical

practice. In addition, the findings are grounded in the demands of clinical practice, thereby enhancing the potential that they can be translated into practical applications.

Another strength of the current research is its focus on evaluating patient-centred care within a healthcare context in which an ageing population and staff shortages pose daily challenges. The thesis offers a novel perspective on frailty and the associated screening process, as approached from a nursing standpoint and supported by multiple studies. These insights could contribute to the realization of more patient-centred and efficient hospital care for older adults.

The primary limitations of our studies lie in their observational design and small sample sizes. Due to the observational design, it was not possible to establish any causal relationships, instead allowing only the description of associations. Furthermore, the small sample sizes of the studies, which were conducted in a single-centre population of older patients (aged ≥70 years) with hip fractures or CRC, significantly reduced the generalizability of the findings.

It is also important to acknowledge the limitations of screening instruments and their associated outcomes. Given the retrospective nature of the study examining complications within 30 days after surgery for CRC, we were confronted with missing data in our dataset. Despite combining hospital data with information from a national database to collect the most comprehensive data possible, there may still be potential for bias, particularly with regard to the recording of complications, including in the case of delirium, for which underreporting is a known issue (31). Another limitation concerns the inconsistent use of screening instruments in practice, including variations in the timing or manner of their application. Such variations could affect the outcomes and reliability of the screening tools. In addition, the period covered by the follow-up data may have been too short for patients with CRC. Whereas other studies report follow-up periods of three to five years (32), our study concluded after just one year. Addressing these limitations, however, would have required additional resources to recruit a larger sample of participants and different settings. Moreover, these studies did not assess quality of life or other functional measures, which are frequently overlooked in similar research, but that may be more relevant to patients than the outcomes examined (33).

Although the interviews with HCPs provided valuable insights into their experiences with frailty assessment in clinical practice, and although they offered guidance for improving the process, the evaluation of patient experiences could have added a crucial dimension, thereby making the

research truly comprehensive. We still do not have a thorough understanding of patient experiences with the frailty-assessment process, and we must rely only on assumptions made by HCPs.

7.2.3. Implications for practice

In addition to challenges related to content, the added value of frailty assessment in the hospital setting is affected by process-related factors. Both aspects are reflected in the implications for practice and the recommendations.

As demonstrated in Section 7.2, all frailty-screening tools fail to capture certain aspects of frailty as depicted in the integral conceptual model of frailty (4). The assessment of life-course determinants, psychological frailty, and social frailty within the instruments applied in this research was often limited, which possibly could explain why the clinical judgments did not always align with the outcomes of the screening instruments (Chapter 6), or why frailty-screening tools do not always predict adverse outcomes (Chapter 4 & 6). Consequently, uncertainty remains with regard to the ability of such tools to distinguish between patients who are frail and those who are not, and whether they would or would not benefit from a CGA. This is because some factors (e.g. life-course determinants, psychological aspects, and social frailty,) are not covered by a questionnaire but could nevertheless contribute to frailty. Furthermore, whether patients are or are not frail says nothing about their preferences and boundaries, the knowledge of which is necessary in order to determine an appropriate treatment. We therefore wonder whether such differentiation might contribute to the realization of more personalized patient-centred care.

Even though, in practice, frailty-screening tools are often used as diagnostic instruments, despite their limitations, they can be applied to identify increased risks of adverse outcomes and guide interventions to mitigate frailty or minimize risks. These interventions include preventing falls and delirium, improving strength, enhancing nutritional status, and initiating rooming-in during hospitalization. One condition is that there is proper follow-up to the frailty assessment. This ensures that such assessment will serve a meaningful purpose rather than becoming a mere box-ticking exercise – as is sometimes experienced in practice (Chapter 6) – meeting the required standards but failing to be integrated into an interprofessional pathway. The integration of diverse perspectives into this pathway could ensure that patients are informed and advised more effectively about potential treatment decisions (Chapter 6). For example, the incorporation of a CGA into an oncology-focused treatment

team has been shown to enhance patient outcomes (34). In addition, it might be beneficial to all older patients, both with and without cancer.

The CGA, which is applied after an unfavourable score on a frailty-screening tool, encompasses all aspects of the frailty model, in addition to evaluating the existential dimension (18). In hospital practice, however, the perceived value of frailty assessment is significantly affected by procedural factors, including the choice of the screening tool that determines whether a CGA will be conducted, the timing of its execution, and how the outcomes are applied in the decision-making process (Chapter 5 & 6).

Given the time investment required for a CGA, it would not seem efficient to offer one to every older adult upon hospital admission. Nevertheless, a comprehensive geriatric assessment should ideally take place as early as possible in the process, in order to ensure a thorough understanding of the patient before it is necessary to take treatment decisions. The early application of CGA for all older adults would ultimately result in more customized treatments and improved patient-centred outcomes. Dedicating more time at the beginning could maximize efficiency and time savings in the long term. This approach thus clearly requires further investigation.

7.2.4. RECOMMENDATIONS

As highlighted by this research, there is considerable uncertainty regarding the clinical relevance of frailty screening for hospitalized older adults. A more comprehensive approach – based on patient-centred care and shared decision-making – is being considered for all older adults, without a major focus on frailty.

Policy

It is essential to recognize that frailty is often not seen as the primary focus when considering treatment options in healthcare. The current healthcare-payment system provides reimbursement based on a patient's assigned diagnosis and the volume of care delivered, rather than on meaningful, patient-centred outcomes (e.g. as emphasized in value-based healthcare) (35). A gap thus remains, and there is room for improvement in the reimbursement system. Such improvement is necessary, given the ageing population.

Education

As the proportion of older adults continues to grow – they now represent the largest group of hospitalized patients (36) – it is becoming increasingly important to integrate knowledge and expertise in geriatric care into the education and training of all healthcare professionals working with this population. All HCPs, including doctors, nurses, and physiotherapists, should have knowledge of and experience in geriatric care, and this should be regarded as a fundamental skill rather than a specialization for a small number of HCPs. Experts in geriatrics will obviously continue to be essential for complex geriatric issues.

Practice

Given our concerns regarding the use of frailty screening, and despite the uncertainty about their feasibility, if screening tools are to remain in clinical practice, careful attention to the following recommendations will be essential. First, professionals must be involved in selecting the frailty-screening tool to be applied, thereby ensuring that it will evaluate all domains of frailty and provide a thorough assessment of cognitive functioning. Furthermore, the tool should be multidimensional, adequately developed, and validated for the specific patient category and setting, such that it aligns with the original screening goals for that group of patients (37). In addition, HCPs should take responsibility for adequately addressing the results of frailty-screening tools while recognizing that their purpose is not diagnostic. The outcome of a screening tool should therefore not be regarded as a definitive indicator for treatment decisions. Instead, a holistic assessment is required in order to develop a nuanced understanding of individual patients, which can serve as the basis for informed and collaborative decision-making. Furthermore, discussions between HCPs and patients about frailty and its consequences are crucial to ensuring that the values, wishes, and boundaries of patients are understood in advance (29).

9.4 CONCLUSIONS

Consistent with existing literature (14,38), our findings indicate that none of the screening tools (VMS frailty-screening tool, G8 measurement, GFI, and handgrip strength) we examined proved universally optimal for assessing frailty in elderly patients admitted to a hospital or outpatient clinic. This is due

primarily to the complexity of the concept of frailty itself (Chapter 2, Chapter 6) (39), as well as to the process-related factors that significantly influence the added value of frailty assessment in clinical practice.

Compared to the integral conceptual model of frailty (4), we conclude that frailty-screening tools often limit the assessment of life-course determinants, psychological aspects, and social frailty, thereby resulting in a lack of insight into lifestyle, cognitive functioning, and social support. The selection of a screening tool, the timing of its administration, and the follow-up after screening – including its integration into the decision-making process – are process-related factors that are just as crucial as the content itself.

The increasing number of older adults and the large number of hospitalized older patients highlights the necessity of finding a solution for the imperfect current approach to assessing frailty. A solution that enhances patient-centred care through an interprofessional approach, in which geriatric knowledge is regarded as a fundamental competency, could strengthen collaboration among HCPs, deepen patient engagement, and enhance relevant patient-centred outcomes.

REFERENCES

1. Barry MJ, Edgman-Levitan S. Shared decision making: Pinnacle of patient-centered care. N Engl J Med. 2012; 366(9):780–1. doi:10.1056/NEJMp1109283
2. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: A model for clinical practice. J Gen Intern Med. 2012; 27(10):1361–7. doi:10.1007/s11606-012-2077-6
3. Bomhof-Roordink H, Gärtner FR, Stiggelbout AM, Pieterse AH. Key components of shared decision making models: A systematic review. BMJ Open. 2019; (12):e031763. doi:10.1136/bmjopen-2019-031763
4. Gobbens RJ, Krans A, van Assen MA. Validation of an integral conceptual model of frailty in older residents of assisted living facilities. Arch Gerontol Geriatr. 2015; 61(3):400–10. doi:10.1016/j.archger.2015.06.001
5. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community-dwelling older people. Nurs Outlook. 2010; 58(2):76–86. doi:10.1016/j.outlook.2009.09.005
6. Apóstolo J, Cooke R, Bobrowicz-Campos E, Santana S, Marcucci M, Cano A, et al. Predicting risk and outcomes for frail older adults: An umbrella review of frailty screening tools. JBI Database System Rev Implement Rep. 2017; 15(4):1154–1208. doi:10.11124/JBISRIR-2016-003018
7. Gilardi F, Capanna A, Ferraro M, Scarcella P, Marazzi MC, Palombi L, et al. Frailty screening and assessment tools: A review of characteristics and use in Public Health. Ann Ig. 2018; 30(2):128–139. doi:10.7416/ai.2018.2204
8. Downar J, Goldman R, Pinto R, Englesakis M, Adhikari NK. The “surprise question” for predicting death in seriously ill patients: A systematic review and meta-analysis. CMAJ. 2017; 189(13):E484–E493. doi: 0.1503/cmaj.160775
9. Thomas R, Pieri A, Cain H. A systematic review of generic and breast cancer specific life expectancy models in the elderly. Eur J Surg Oncol. 2017; 43(10):1816–1827. doi: 10.1016/j.ejso.2017.06.014
10. Keuning BE, Kaufmann T, Wiersema R, Granholm A, Pettilä V, Hylander Møller M, et al. Mortality prediction models in the adult critically ill: A scoping review. Acta Anaesthesiol Scand. 2020; 64(4):424–442. doi: 10.1111/aas.13527
11. Pobar I, Job M, Holt T, Hargrave C, Hickey B. Prognostic tools for survival prediction in advanced cancer patients: A systematic review. J Med Imaging Radiat Oncol. 2021; 65(6):806–816. doi: 10.1111/1754-9485.13185
12. Carpenter CR, Mooijaart SP. Geriatric Screeners 2.0: Time for a paradigm shift in emergency department vulnerability research. J Am Geriatr Soc. 2020; 68(7):1402–1405. doi:10.1111/jgs.16502
13. Steverink N, Slaets J, Schuurmans H, Van Lis M. Measuring frailty: Developing and testing of the Groningen frailty indicator (GFI). Gerontologist 2001; 41:236–237.
14. Oud FMM, Meulman MD, Merten H, Wagner C, van Munster BC. Value of the Safety Management System (VMS) frailty instrument as a frailty screener in care for older hospital patients: A systematic review. Eur Geriatr Med. 2024; 15(3):609–620. doi:10.1007/s41999-024-00957-4

15. Yan B, Sun W, Wang W, Wu J, Wang G, Dou Q. Prognostic significance of frailty in older patients with hip fracture: A systematic review and meta-analysis. Int Orthop. 2022; 46(12):2939–2952. doi:10.1007/s00264-022-05605-9

16. Loggers SAI, Willems HC, Van Balen R, Gosens T, Polinder S, Ponsen KJ, et al. Evaluation of quality of life after nonoperative or operative management of proximal femoral fractures in frail institutionalized patients: The FRAIL-HIP Study. JAMA Surg. 2022 May 1; 157(5):424–434. doi:10.1001/jamasurg.2022.0089

17. Drubbel I, Bleijenberg N, Kranenburg G, Eijkemans RJ, Schuurmans MJ, de Wit NJ, et al. Identifying frailty: Do the Frailty Index and Groningen Frailty Indicator cover different clinical perspectives? A cross-sectional study. BMC Fam Pract. 2013; 21; 14(64). Available from: https://bmcprimcare.biomedcentral.com/articles/10.1186/1471-2296-14-64 doi:10.1186/1471-2296-14-64

18. Kennisinstituut Federatie Medisch specialisten. [Federation of Institutes of Expertise for Medical Specialists] 2021. Comprehensive geriatric assessment (CGA). [Accessed: April 2024] Available from: https://richtlijnendatabase.nl/richtlijn/comprehensive_geriatric_assessment_cga/startpagina_-_comprehensive_geriatric_assessment_cga.html

19. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, at el. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001; 56(3):M146–56. doi:10.1093/gerona/56.3.m146

20. Shaw BH, Borrel D, Sabbaghan K, Kum C, Yang Y, Robinovitch SN, et al. Relationships between orthostatic hypotension, frailty, falling and mortality in elderly care home residents. BMC Geriatr. 2019; 9(1):80. Available from: https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-019-1082-6 doi:10.1186/s12877-019-1082-6

21. Hilali AEK, Shacham D, Frenkel R, Abu-Ajaj A, Zikrin E, Freud T, et al. Successful rehabilitation after surgical repair of hip fracture has been associated with handgrip strength but not with orthostatic hypotension in patients 65 yrs of age and above. Am J Phys Med Rehabil. 2025; 104(5):407–414. doi:10.1097/PHM.0000000000002618.

22. Bellera CA, Rainfray M, Mathoulin-Pélissier S, Mertens C, Delva F, Fonck M, et al. Screening older cancer patients: First evaluation of the G-8 geriatric screening tool. Ann Oncol. 2012; 23(8):2166–2172. doi:10.1093/annonc/mdr587

23. Oud, F. Towards tailored screening for frailty and geriatric syndromes in older hospital patients: A special focus on the VMS frailty instrument. Thesis fully internal (DIV). Groningen: University of Groningen; 2025. doi:10.33612/diss.116660655

24. Kok AAL, Henstra MJ, van der Velde N, Rhebergen D, van Schoor NM. Psychosocial and health-related factors associated with discordance between 13-year trajectories of self-reported functional limitations and performance-based physical functioning in old age. J Aging Health. 2020; 32(9):1084–1097. doi:10.1177/0898264319884404

25. Visser FCW, van Eersel MEA, Hempenius L, Verwey NA, Band C, van der Bol JM, et al. Recognition of cognitive dysfunction in hospitalised older patients: A flash mob study. BMC Geriatr. 2024; 24(1):66. doi:10.1186/s12877-023-04588-5

26. Barrera A, Rezende LFM, Sabag A, Keating CJ, Rey-Lopez JP. Understanding the causes of frailty using a life-course perspective: A systematic review. Healthcare (Basel). 2023; 12(1):22. doi:10.3390/healthcare12010022

27. Peters XD, Russell MM. Patient centered outcomes after surgery in the older adult. Curr Geri Rep. 2024; 13:78–85. doi:10.1007/s13670-024-00411-0.

28. Di Monaco M, Castiglioni C, De Toma E, Gardin L, Giordano S, Tappero R. Handgrip strength is an independent predictor of functional outcome in hip-fracture women: A prospective study with 6-month follow-up. Medicine (Baltimore). 2015; 94(6):e542. doi:10.1097/MD.0000000000000542.

29. Golbach, R. (2025). Through their eyes: Older people's perspectives on and experiences of frailty. Thesis fully internal (DIV). Groningen: University of Groningen. Available from: https://research.rug.nl/en/publications/through-their-eyes-older-peoples-perspectives-on-and-experiences- doi: 10.33612/diss.1227091992.

30. Lipworth W. Real-world data to generate evidence about healthcare interventions: The application of an ethics framework for big data in health and research. Asian Bioeth Rev. 2019; 11(3):289–298. doi:10.1007/s41649-019-00095-1

31. Hshieh TT, Inouye SK, Oh ES. Delirium in the elderly. Clin Geriatr Med. 2020; 36(2):183–199. doi:10.1016/j.cger.2019.11.001

32. Martinez-Tapia C, Paillaud E, Liuu E, Tournigand C, Ibrahim R, Fossey-Diaz V, et al. Prognostic value of the G8 and modified-G8 screening tools for multidimensional health problems in older patients with cancer. Eur J Cancer. 2017; 83:211–219. doi:10.1016/j.ejca.2017.06.027

33. Denkinger M, Knol W, Cherubini A, Simonds A, Lionis C, Lacombe D, et al. Inclusion of functional measures and frailty in the development and evaluation of medicines for older adults. Lancet Health policy. 2023; [Accessed: February 2025] Available from: https://dspace.library.uu.nl/bitstream/handle/1874/450503/1-s2.0-S2666756823002088-main.pdf?sequence=1 doi:10.1016/S2666-7568(23)00208-8

34. Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: An update on SIOG recommendations. Ann Oncol, 2015; 26(2):288–300. doi: 10.1093/annonc/mdu210

35. Porter ME, Michael Porter EOT, Teisberg EO. Redefining health care: Creating value-based competition on results. Harvard Business School Press; 2006.

36. Vektis.1 op de 11 65-plussers heeft een ongeplande ziekenhuisopname [1 in 11 people 65 years and older has an unplanned hospital admission]. 2022 August. [Accessed march 2022] Available from: https://www.vektis.nl/intelligence/publicaties/1-op-de-11-65-plussers-heeft-een-ongeplande-ziekenhuisopname

37. Terwee CB, Bot SDM, de Boer MR, van der Windt DAWM, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol. 2007; 60(1):34–42. doi: 10.1016/j.jclinepi.2006.03.012.

38. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: A review. Eur J Intern Med. 2016; 31:3–10. doi:10.1016/j.ejim.2016.03.007.

Summary

OLDER ADULTS AND FRAILTY

According to projections, population ageing in the Netherlands will reach its peak in 2040, with one of every four inhabitants being 65 years of age or older. An estimated 22% of all people in this age group are frail (1). As we age, changes take place in physical and cognitive functioning, although the pace at which and the extent to which this occurs varies from one person to another. Various factors influence ageing, including environmental factors, genetic predisposition, and lifestyle, as well as social and psychological factors (2). Together, these factors determine the level of fitness, and thus also of frailty. In this thesis, frailty is defined as follows: *'a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, social), which is caused by the influence of a range of variables and which increases the risk of adverse outcomes'.* (3)

ASSESSMENT OF FRAILTY

When frail elderly patients are admitted to the hospital, they are at greater risk of adverse outcomes, such as complications, delirium, falls, prolonged admissions, and being unable to return home, either permanently or temporarily (4). It is assumed that the identification of frailty prior to hospital admission could contribute to reduce further deterioration by initiating timely interventions and adjustments to the treatment plan (5). It is therefore essential to have reliable tools capable of accurately identifying frailty, in alignment with the screening criteria established by Wilson and Jungner in 1968 (6). Some of these criteria include: the reliability of the screening, the availability of diagnosis and treatment, and clear agreements on who is responsible for follow-up (6). The Groningen Frailty Indicator (GFI), the 'Veiligheidsmanagementsysteem' (VMS) screening questions, and the Geriatric-8 (G8) are three of many frailty-measurement tools that are used in Dutch hospitals. The gold standard for establishing frailty is the Comprehensive Geriatric Assessment (CGA) (7), which is carried out by an expert in geriatrics, and it is usually performed after a screening that indicates a risk of frailty.

RESULTS

This thesis investigates the clinical relevance of frailty assessment. The studies were conducted among elderly patients who had been admitted due to a hip fracture or were scheduled to be admitted for surgery related to colorectal

cancer (CRC). The experiences of nurses, nurse practitioners, and doctors involved in the care for patients with CRC, were also explored in relation to frailty assessment.

The first study (**Chapter 2**) outlines a global overview of meta-analyses and systematic reviews of tools that can identify a greater risk of frailty and shorter life expectancy in older adults who have been hospitalised in acute situations. The objective was to identify the best tool for predicting frailty and shorter life expectancy. Despite the existence of many different tools, there is no consensus on which tool should be used at what point. Given the limitations of each tool, the results of this review did not allow the identification of any single best tool for acutely hospitalised patients. The researchers conclude that customised care could be strengthened by placing more emphasis on individual characteristics and risks, with the analysis of frailty and estimated life expectancy as part of the process, complemented by information on the characteristics and preferences of individual patients.

To evaluate whether the frailty-measurement tools used in the hospital (GFI and VMS) can also predict adverse outcomes, a prospective observational cohort study was conducted (**Chapter 3**). To this end, we selected all patients 70 years of age or older with hip fracture who had undergone surgery at a general hospital between November 2014 and November 2015. In all, 280 patients were included, with a median follow-up of 25 months. This study examined differences and similarities between the two screening methods, as well as their relationship to overall survival and mortality after 30 days. Both tools (VMS and GFI) showed a significant difference in overall survival between frail and non-frail patients with hip fracture, and they were thus able to differentiate on survival as a measure of adverse outcomes in the patient population studied.

Muscle strength (measured as handgrip strength) can be seen as a measure of physical frailty. **Chapter 4** describes a prospective, observational cohort study, in which we examined the relationship between muscle strength and time to successful rehabilitation in elderly patients with hip fracture who had been admitted to a general hospital. The primary outcome was time to successful rehabilitation, defined as discharge to the patient's own home. Handgrip strength was measured with a hand dynamometer. The total sample consisted of 116 patients 70 years of age and older with hip fracture. During a median follow-up period of 36 days (interquartile range, 9–57 days), 103 patients (89%) achieved successful rehabilitation. No statistically significant relationships were

found between handgrip strength and successful rehabilitation (hazard ratio = 1.03; 95% confidence interval, 0.99–1.06).

Chapter 5 details a retrospective cohort study examining whether the G8 measurement predicts outcomes in patients 70 years of age and older undergoing surgery for CRC. The objective was to determine whether the G8 measurement (or other variables from the medical record) could be applied to predict adverse outcomes within 30 days of surgery in elderly patients with CRC. The primary finding was 'adverse outcomes', a composite measure of surgical and non-surgical complications, re-admission, and mortality. The study included 200 patients, with 36.5% having experienced adverse outcomes in the first 30 days after surgery. The G8 scores showed no prognostic value for adverse outcomes, complications, or mortality within 30 days of surgery in elderly patients with CRC at the hospital studied. Factors associated with a higher risk of adverse outcomes were male gender and the VMS item concerning cognitive decline and previous delirium. Alternative options for predicting adverse outcomes within 30 days of surgery must be sought and investigated.

Chapter 6 describes a qualitative study that explored how healthcare professionals perceive the value and application of standardised frailty assessment in elderly patients with CRC. Between February and July 2023, 17 healthcare professionals who were involved in the care of elderly patients with CRC in the outpatient department of a general hospital in the Netherlands were asked to participate in the study. These healthcare professionals were nurses, nurse practitioners, and doctors with a variety of specialities, including oncology, surgery, gastro-enterology, and geriatrics. The frailty assessment consists of an initial frailty screening using the G8 measurement, followed by a CGA for the further evaluation of any frailty detected during screening. The complexity of the concept of frailty and the level of coordination between healthcare providers were found to have a major impact on the perceived clinical relevance of the frailty assessment. There appeared to be a discrepancy between the judgements of healthcare professionals and the outcomes of the screening tool in patients. In addition, outcomes proved difficult to predict, and they did not always contribute to reaching a treatment decision. Furthermore, two main themes emerged from the interviews: 1) the perceived value of the G8 measurement for frailty screening and 2) the perceived value of the CGA. The timing, content, and outcome of the G8 and CGA were discussed. The G8 was deemed an unsuitable screening tool for this patient population, partly due to the lack of objective cognitive screening and low specificity. The CGA was seen as valuable if integrated into an efficient, multidisciplinary pathway

aimed at shared decision-making with the patient. Healthcare professionals suggested that the CGA was certainly of value for patients with suspected cognitive decline, or in cases of uncertainty concerning the degree of frailty or doubts about the most appropriate treatment.

Chapter 7 discusses the results of the conducted studies, analysing and interpreting them within the framework of existing literature. Based on this, an overall conclusion is drawn, and recommendations are provided. Although frailty screening tools have limitations and certain conditions must be met, they can be meaningfully applied in clinical practice. At the same time, it remains uncertain whether each instrument is appropriate for every patient and clinical condition. Moreover, whether patients are or are not frail says nothing about their preferences and boundaries, even though knowledge of these aspects is essential to the determination of appropriate treatment. As a result, we question whether such differentiation can indeed help to promote more personalised, patient-centred care. We therefore suggest performing a CGA for all elderly patients as early in the process as possible, as this will ultimately lead to more customised care and thus to better patient-centred outcomes. This CGA does not aim to establish the presence and degree of frailty with absolute certainty. Rather, its outcomes contribute to building a more complete picture of the individual, on whom a clinical impression must be formed.

For this to happen, however, this CGA must be integrated into an inter-professional process, in which collaboration and shared decision-making (SDM) play an essential role. Investing more time at the beginning of the process could optimise efficiency and time utilisation in the long run.

REFERENCES

1. Centraal Bureau voor de Statistiek (CBS) [Statistics Netherlands]. Bevolking. Bevolkingsomvang [Population. Population size]. November 2024 [Accessed March 2025]. Available from: https://www.vzinfo.nl/bevolking/bevolkingsomvang
2. World Health Organization (WHO). *Ageing and health*. October 2024 [Accessed March 2025]. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
3. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community-dwelling older people. Nurs Outlook. 2010;58(2):76-86. doi: 0.1016/j.outlook.2009.09.005.
4. Age UK Group and/or its National Partners. *Common conditions and frailty*. 2024 [Accessed March 2025]. Available from: https://www.ageuk.org.uk/our-impact/policy-research/frailty-in-older-people/common-conditions-frailty/
5. Praktijkgids kwetsbare ouderen. Dutch Patient Safety Programme. [Accessed: July 2024]. Available from: https://nvz-ziekenhuizen.nl/sites/default/files/2025-03/web_2009.0104_praktijkgids_kwetsbare_ouderen.pdf
6. Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: World Health Organization; 1968.
7. Nederlandse Vereniging voor Klinische Geriatrie. Comprehensive geriatric assessment (CGA): Identificatie kwetsbare ouderen. Richtlijnendatabase. 2021 [Accessed October 2025]. Available from: https://richtlijnendatabase.nl/richtlijn/comprehensive_geriatric_assessment_cga/identificatie_kwetsbare_ouderen_bij_cga.html

Nederlandse samenvatting

OUDEREN EN KWETSBAARHEID

Volgens prognoses bereikt de vergrijzing in Nederland in 2040 zijn hoogtepunt, waarbij één op de vier inwoners 65 jaar of ouder is. Naar schatting is 22% van de 65-plussers kwetsbaar (1). Naarmate we ouder worden, treden er veranderingen op in het fysieke en cognitieve functioneren, al verschilt het tempo en de mate waarin dit gebeurt sterk per persoon. Verschillende factoren beïnvloeden veroudering, zoals omgevingsfactoren, genetische aanleg, leefstijl, maar ook sociale en psychologische factoren (2). Gezamenlijk bepalen deze factoren de mate van fitheid en dus ook van kwetsbaarheid. Kwetsbaarheid wordt in dit proefschrift gedefinieerd als: *"een dynamische toestand waarbij een individu verlies ervaart in een of meer domeinen van het menselijk functioneren (fysiek, psychologisch en/of sociaal), veroorzaakt door een verscheidenheid aan factoren en gepaard gaand met een verhoogd risico op negatieve uitkomsten."* (3)

BEOORDELING VAN KWETSBAARHEID

Wanneer kwetsbare oudere patiënten worden opgenomen in het ziekenhuis hebben zij een hogere kans hebben op ongunstige uitkomsten, zoals complicaties, delier, vallen, lange ligduur en niet, of tijdelijk niet meer thuis kunnen wonen (4). Er wordt aangenomen dat wanneer kwetsbaarheid wordt geïdentificeerd voorafgaand aan een ziekenhuisopname, dit zou kunnen bijdragen aan het minderen van de mate van kwetsbaarheid, door middel van vroegtijdig inzetten van interventies en aanpassing van het behandelplan (5). Het is daarom van belang om over geschikte instrumenten te beschikken die kwetsbaarheid accuraat kunnen vaststellen, met inachtneming van de in 1968 geformuleerde criteria voor verantwoorde screening volgens Wilson en Jungner. Enkele van deze criteria zijn: de betrouwbaarheid van de screening, de beschikbaarheid van een diagnose en behandeling, en duidelijke afspraken over wie verantwoordelijk is voor de opvolging (6). De Groningen Frailty Indicator (GFI), Veiligheidsmanagementsysteem (VMS)-screeningsvragen en de Geriatric-8 (G8), zijn drie van vele kwetsbaarheidsscreeningsinstrumenten die worden ingezet in Nederlandse ziekenhuizen. De gouden standaard om kwetsbaarheid vast te stellen is een Comprehensive Geriatric Assessment (CGA) (7), die uitgevoerd moet worden door een expert op gebied van ouderengeneeskunde. Deze vindt plaats nadat een screening het risico op kwetsbaarheid signaleert.

RESULTATEN

In dit proefzicht hebben we de klinische relevantie van screening en assessment van kwetsbaarheid onderzocht. De onderzoeken vonden plaats bij oudere patiënten die in verband met een heupfractuur waren opgenomen of zouden worden opgenomen in verband met een operatie in het kader van colorectaal carcinoom (CRC). Hierbij werden ook de ervaringen met kwetsbaarheidsbeoordeling geëxploreerd, van de bij die zorg betrokken verpleegkundigen, verpleegkundig specialisten en artsen.

In de eerste studie (**Hoofdstuk 2**) wordt een globale weergave geschetst van meta-analyses en systematische reviews over instrumenten die een hoger risico op kwetsbaarheid en een kortere levensverwachting kunnen signaleren bij ouderen die acuut opgenomen zijn in het ziekenhuis. Hiermee beoogden we het beste instrument te vinden dat kwetsbaarheid en een kortere levensverwachting kon voorspellen. Er zijn veel verschillende instrumenten. Er is echter is geen consensus over welke instrument gebruikt zou moeten worden op welk moment. Gezien de beperkingen die elk instrument heeft, kon op basis van deze review geen beste instrument gekozen worden voor acuut opgenomen oudere patiënten. De onderzoekers concluderen dat zorg op maat kan worden versterkt door meer nadruk te leggen op individuele kenmerken en risico's, waarbij analyse van kwetsbaarheid en geschatte levensverwachting onderdeel kunnen zijn, aangevuld met patiëntkenmerken en voorkeuren van patiënten.

Om te beoordelen of de in het ziekenhuis gebruikte screeningsinstrumenten (GFI en VMS) voor kwetsbaarheid, daarmee ook ongunstige uitkomsten kunnen voorspellen, werd een prospectieve observationele cohortstudie verricht (**Hoofdstuk 3**). Hiervoor selecteerden we alle patiënten van 70 jaar of ouder met een heupfractuur die tussen november 2014 en november 2015 een operatie ondergingen in een algemeen ziekenhuis. In totaal werden 280 patiënten geïncludeerd, met een mediane follow-up van 25 maanden. In dit onderzoek werden verschillen en overeenkomsten tussen de twee screeningsmethoden onderzocht, maar ook de relatie met algehele overleving en sterfte na 30 dagen. Beide instrumenten (VMS en GFI) toonden een significant verschil in algehele overleving tussen kwetsbare en niet-kwetsbare patiënten met een heupfractuur en zouden dus kunnen differentiëren op overleving als maat voor ongunstige uitkomsten bij deze onderzochte patiëntenpopulatie.

Spierkracht, gemeten als handknijpkracht, kan worden gezien als een maat voor fysieke kwetsbaarheid. In **hoofdstuk 4** wordt een prospectieve, observationele cohortstudie beschreven, waarin we de relatie onderzoeken tussen spierkracht

versus tijd tot succesvolle revalidatie bij oudere patiënten met een heupfractuur die opgenomen waren in een algemeen ziekenhuis. Met als primaire uitkomst de tijd tot succesvolle revalidatie, gedefinieerd als ontslag naar eigen huis. Handknijpkracht werd gemeten met een handdynamometer. In totaal werden patiënten (N=116) van 70 jaar of ouder met een heupfractuur geïncludeerd. Tijdens een mediane follow-up periode van 36 dagen (interkwartielafstand, 9-57 dagen) werden 103 patiënten (89%) succesvol gerevalideerd. Er werden geen statistisch significante relaties gevonden tussen handknijpkracht en succesvolle revalidatie (Hazard Ratio=1.03; 95% Betrouwbaarheidsinterval, 0.99-1.06).

In **hoofdstuk 5** is een retrospectieve cohortstudie uitgevoerd naar de voorspellende waarde van de G8-vragenlijst, bij patiënten van 70 jaar en ouder die een operatie ondergingen in het kader van CRC. Het doel was te bepalen of de G8, of andere variabelen in het medische dossier, toepasbaar waren bij het voorspellen van ongunstige uitkomsten binnen 30 dagen na operatie bij oudere patiënten met CRC. De primaire uitkomst was ongunstige uitkomst(en), een samengestelde maat van chirurgische en niet-chirurgische complicaties, heropname en sterfte. De studie omvatte 200 patiënten, waarbij 36,5% ongunstige uitkomsten hadden in de eerste 30 dagen na de operatie. G8-scores bleken geen prognostische waarde te hebben voor ongunstige uitkomsten, complicaties en sterfte binnen 30 dagen na operatie bij oudere patiënten met CRC in het onderzochte ziekenhuis. Factoren met een hogere kans op ongunstige uitkomsten waren het mannelijk geslacht en de VMS vraag over cognitieve achteruitgang en eerder delier. Alternatieve opties voor het voorspellen van ongunstige uitkomsten binnen 30 dagen na de operatie zullen gezocht en onderzocht moeten worden.

In **hoofdstuk 6** wordt een kwalitatieve studie beschreven, waarin onderzocht is hoe zorgprofessionals de waarde en toepassing van gestandaardiseerde kwetsbaarheidsbeoordeling bij oudere patiënten met CRC ervaren. Tussen februari en juli 2023 zijn zorgprofessionals die betrokken waren bij de poliklinische zorg voor oudere patiënten met CRC, gevraagd deel te nemen aan het onderzoek (N=17). Het betrof verpleegkundigen, verpleegkundig specialisten en artsen, gespecialiseerd in diverse specialismen zoals oncologie, chirurgie, gastro-enterologie en ouderengeneeskunde. De kwetsbaarheidsbeoordeling bestaat uit een initiële kwetsbaarheidsscreening met behulp van de G8-meting, gevolgd door een uitgebreide CGA om de tijdens de screening gedetecteerde kwetsbaarheid verder te evalueren. De complexiteit van het concept kwetsbaarheid en de mate van afstemming tussen zorgverleners bleken van invloed op de ervaren klinische relevantie van de kwetsbaarheidsbeoordeling.

Er bleek een discrepantie te bestaan tussen het oordeel van zorgverleners en de uitkomst van het screeningsinstrument bij patiënten. Daarnaast bleken de uitkomsten moeilijk voorspelbaar en droegen ze niet altijd bij aan het nemen van een behandelbeslissing. Verder kwamen er twee hoofdthema's uit de interviews naar voren: 1) de meerwaarde van de G8-meting voor kwetsbaarheidsscreening en 2) de meerwaarde van een CGA. Het moment, de inhoud en de uitkomst van de G8 en CGA werden bediscussieerd. De G8 werd als ongeschikt screeningsinstrument gezien voor deze patiëntenpopulatie, mede door het ontbreken van objectieve cognitieve screening en een lage specificiteit. Een CGA werd als waardevol gezien mits geïntegreerd in een efficiënt, multidisciplinair traject, gericht op gezamenlijke besluitvorming met de patiënt. Zorgverleners suggereerden dat een CGA van waarde is bij patiënten met vermoedelijke cognitieve achteruitgang, wanneer er sprake was van onzekerheid over de mate van kwetsbaarheid, of bij twijfel over de meest geschikte behandeling.

In **hoofdstuk 7** worden de resultaten van de uitgevoerde studies besproken, waarbij ze worden geanalyseerd en geïnterpreteerd binnen het kader van bestaande literatuur. Op basis daarvan volgt een overall conclusie en worden aanbevelingen gedaan. Hoewel kwetsbaarheidsscreeningsinstrumenten beperkingen hebben en aan enkele randvoorwaarden moet worden voldaan, kunnen ze in de praktijk zinvol worden ingezet. Tegelijkertijd blijft het de vraag of elk instrument passend is voor iedere patiënt en aandoening. Bovendien zegt het al dan niet kwetsbaar zijn van patiënten niets over hun voorkeuren en grenzen, terwijl kennis daarvan essentieel is om een passende behandeling te kunnen bepalen. We adviseren daarom om zo vroeg mogelijk in het behandeltraject, bij alle oudere patiënten een CGA toe te passen, omdat dit uiteindelijk zal leiden tot meer zorg op maat en betere patiëntgerichte uitkomsten.

Deze CGA beoogt niet het zonder enige twijfel vaststellen van de aanwezigheid en mate van kwetsbaarheid. De uitkomsten van de CGA leveren een bijdrage aan het opbouwen van een completer beeld van het individu waarover een indruk moet worden gevormd. Noodzakelijk hiervoor is integratie van het CGA in een interprofessioneel proces, waarin gezamenlijke besluitvorming (SDM) een essentiële rol speelt. Meer tijd investeren aan het begin van het traject kan op de lange termijn de efficiëntie en tijdsbesteding optimaliseren.

BRONNEN

1. Centraal Bureau voor de Statistiek (CBS) Bevolking. Bevolkingsomvang. November 2024 [Geraadpleegd in maart 2025]. Beschikbaar via: https://www.vzinfo.nl/bevolking/bevolkingsomvang
2. World Health Organization (WHO). *Ageing and health*. October 2024 [Geraadpleegd in maart 2025]. Beschikbaar via: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
3. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community-dwelling older people. Nurs Outlook. 2010;58(2):76-86. doi: 0.1016/j.outlook.2009.09.005.
4. Age UK Group and/or its National Partners. *Common conditions and frailty*. 2024 [Geraadpleegd in maart 2025]. Beschikbaar via: https://www.ageuk.org.uk/our-impact/policy-research/frailty-in-older-people/common-conditions-frailty/
5. Praktijkgids kwetsbare ouderen. [Geraadpleegd in juli 2024]. Beschikbaar via: https://nvz-ziekenhuizen.nl/sites/default/files/2025-03/web_2009.0104_praktijkgids_kwetsbare_ouderen.pdf
6. Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: World Health Organization; 1968.
7. Nederlandse Vereniging voor Klinische Geriatrie. Comprehensive geriatric assessment (CGA): Identificatie kwetsbare ouderen. Richtlijnendatabase [Internet]. 2021 [Geraadpleegd in oktober 2025]. Beschikbaar via: https://richtlijnendatabase.nl/richtlijn/comprehensive_geriatric_assessment_cga/identificatie_kwetsbare_ouderen_bij_cga.html

LIST OF PUBLICATIONS

In this thesis:

Hartog LC, **Winters AM**, Roijen H, Kamper AM, Inia H, Kleefstra N, Bilo HJG, van Hateren KJJ. Association Between Orthostatic Hypotension and Handgrip Strength With Successful Rehabilitation in Elderly Hip Fracture Patients. *Arch Phys Med Rehabil.* 2017 Aug;98(8):1544-1550.e3. doi: 10.1016/j.apmr.2016.11.009. Epub 2016 Dec 16. PMID: 27993582.

Winters AM, Hartog LC, Roijen H, Brohet RM, Kamper AM. Relationship between clinical outcomes and Dutch frailty score among elderly patients who underwent surgery for hip fracture. *Clin Interv Aging.* 2018 Dec 5;13:2481-2486. doi: 10.2147/CIA.S181497. PMID: 30584288; PMCID: PMC6287424.

Winters AM, Bilo HJG, Roodbol PF and Finnema EJ. Frailty and Life Expectancy Assessments are Essential in Older Adults but Remain Challenging. *Gerontology And Geriatric Research*. 2022; 4(2):130

Winters AM, Bakker J, ten Hoor J, Bilo HJG, Roodbol PF, Edens MA, Finnema EJ. Prognostic value of Geriatric-8 for adverse outcomes within 30 days of surgery in older adults with colorectal cancer: a retrospective cohort study. *European Journal of oncology nursing.* 2024, Volume 70, 102591, ISSN 1462-3889, https://doi.org/10.1016/j.ejon.2024.102591

Winters M, Bakker J, Ardesch V, van der Zwaag S, Kamper A, Bilo H, Roodbol P, Finnema E. Perspectives of healthcare professionals on frailty assessment among older patients with colorectal cancer: A qualitative study. Eur J Oncol Nurs. 2025 Apr;75:102827. doi: 10.1016/j.ejon.2025.102827.

Other publications:

Winters AM, Lindberg M, Sol BG. Validation of a dutch self-efficacy scale for adherence to fluid allowance among patients on haemodialysis. *J Ren Care*. 2013 Mar;39(1):31-8. doi: 10.1111/j.1755-6686.2012.00325.x. Epub 2012 Dec 4. PMID: 23206251.

Van der Zwaag S., **Winters AM**, Voorhorst W, Kamper AM. Rooming-in. *tijdschr verpleegkd experts* 126, 48–51 (2016). https://doi.org/10.1007/s41184-016-0145-9

Ditzel FL, Hut SCA, van den Boogaard M, Boonstra M, Leijten FSS, Wils EJ, van Nesselrooij T, Kromkamp M, Rood PJT, Röder C, Bouvy PF, Coesmans M, Osse RJ, Pop-Purceleanu M, van Dellen E, Krulder JWM, Milisen K, Faaij R, Vondeling AM, Kamper AM, van Munster BC, de Jonghe A, **Winters AM**, van der Ploeg J, van der Zwaag S, Koek DHL, Drenth-van Maanen CAC, Beishuizen A, van

den Bos DM, Cahn W, Schuit E, Slooter AJC. DeltaScan for the Assessment of Acute Encephalopathy and Delirium in ICU and non-ICU Patients, a Prospective Cross-Sectional Multicenter Validation Study, The American *Journal of Geriatric Psychiatry,* 2023, ISSN 1064-7481, https://doi.org/10.1016/j.jagp.2023.12.005.

Visser FCW, van Eersel MEA, Hempenius L, Verwey NA, Band C, van der Bol JM, Boudestein K, van Dijk SC, Gobbens R, van der Hooft CS, Kamper AM, Ruiter R, Sipers W, Spoelstra BNA, Stoffels J, Stolwijk-Woudstra DJ, van Stralen KJ, van Strien AM, Wijngaarden MA, **Winters AM**, Strijkert F, van Munster BC. Recognition of cognitive dysfunction in hospitalised older patients: a flash mob study. *BMC Geriatrics* (2024) 24:66 https://doi.org/10.1186/s12877-023-04588-5

CURRICULUM VITAE

Marian was born in Vollenhove on August 7, 1985, as the second of four children. After completing her pre-university education (VWO) at Emelwerda College in Emmeloord, she began her Bachelor of Nursing studies in 2003 at the Gereformeerde Hogeschool in Zwolle. From the outset, she arranged an agreement with Isala Hospital to follow the dual-track program starting in her third year, gaining practical experience in the pulmonary, oncology, and internal medicine nephrology departments.

In 2007, Marian obtained her Bachelor's degree in Nursing and secured a permanent position in the internal medicine nephrology department. A year later, she began the Pre-Master in Nursing Science at Utrecht University, which she pursued alongside her clinical work. She completed her Master's degree in 2011 with a thesis titled *Validation of a Dutch Self-Efficacy Scale for Adherence to Fluid Allowance Among Patients on Haemodialysis*, for which she was awarded the Johanna Diepeveen-Speekenbrink Prize.

Combining clinical work with research proved challenging, but Marian saw potential in the role of nurse practitioner in geriatric medicine. In 2012, she enrolled in the Master of Advanced Nursing Practice (MANP), completing a shortened version of the dual-track program and earning her degree in 2013.

From the start of her career as a nurse practitioner, Marian initiated research projects, some of which are now included in this thesis. In 2018, she became a PhD candidate at the Department of Health Psychology at the University Medical Center Groningen (UMCG), focusing on frailty assessment in hospitalized older patients. In 2019, Isala introduced a new position for academically trained nurses who wished to combine research with clinical practice—an ideal opportunity for Marian, who is committed to continuing her care for the elderly and offering appropriate support in any capacity or role, to pursue her doctoral degree.

Driven by the ambition to further develop her research skills to provide the best possible care for patients, she will be actively involved in research projects, educational programs, and healthcare improvement networks in the future.

DANKWOORD

Het schrijven van dit proefschrift was een bijzondere reis, met hoogte- en dieptepunten. Ik ben dankbaar voor iedereen die mij onderweg heeft gesteund, aangemoedigd en geïnspireerd. Aan het begin van die reis had ik nooit gedacht dat een proefschrift een tussentijdse bestemming zou zijn. Ik begon met nieuwsgierigheid naar het willen weten hoe het zit en met ambitie om de kwaliteit van zorg te verbeteren van de patiënten waar ik als verpleegkundige en later als verpleegkundig specialist (VS) voor zorgde. Door gesprekken met anderen verlegde ik grenzen in kennis en kunde en juist daarvan is dit het resultaat. Daarom gaat mijn dank gaat uit naar alle personen die hebben bijgedragen aan dit proefschrift en sommigen wil ik graag speciaal noemen.

Dr. A.M. Kamper. Beste Ad, zonder jou was dit traject überhaupt nooit begonnen. Je toonde je vertrouwen in mij als VS-ouderengeneeskunde en als onderzoeker. Je leerde mij de kneepjes van het vak door geregeld te zeggen: 'ga het maar doen', of 'zoek het eerst zelf uit', maar ook 'zweet op de juiste rug'. Je motiveerde mij hiermee, maar was er ook als ik er toch niet zelf uitkwam of een luisterend oor nodig had. Daar kon ik op vertrouwen. Je stimuleerde ook het doen van onderzoek en bracht mij in contact met Henk.

Prof. Dr. H.J.G. Bilo. Beste Henk, vanaf het eerste moment dat we elkaar spraken was ik onder de indruk van je kennis en analytische vermogen, dat je combineert met bescheidenheid en bereidwilligheid om anderen, inclusief mij te helpen. Je gaf me zelfvertrouwen, liet me leren en hielp mij het promotietraject te starten en af te ronden. Ondanks je tijdelijke afwezigheid door mooie uitjes naar het buitenland, vervelende gezondheidsproblemen, bleef je betrokken en voelde ik dat ook zo. Het is een voorrecht dat ik met jou als promotor, dit proefschrift heb kunnen afronden.

Prof. dr. P. Roodbol. Beste Petrie, het siert ook jou dat je als hoogleraar en later als emeritus-hoogleraar verplegingswetenschappen mij wilde begeleiden tijdens het promotietraject. Je meldde mij aan bij het UMCG en het was allemaal zo geregeld. Dat liet je mij ervaren, terwijl het voor mij in werkelijkheid een hele nieuwe, maar ook spannende wereld was. Je straalde rust en vertrouwen uit, maakte het niet moeilijker dan het was. Het is een eer om jou als grondlegster van ons mooie vak als VS in mijn promotieteam te hebben.

Prof. dr. E.J. Finnema. Beste Evelyn, je sloot als laatste aan in ons promotieteam, maar stond gelijk open voor de rol als promotor. Je verpleegkundige achtergrond, kennis en passie voor de kwetsbare mens sloten perfect aan bij mijn onderzoeken en zorgende voor voortgang en persoonlijke aandacht

gedurende het proces. Dank voor je aanstekelijke enthousiasme en ruimte die je in je bomvolle agenda, die je toch altijd wist vrij te maken.

Prof. dr. B.C. van Munster, Prof. dr. H. Vermeulen en Prof. dr. R.C. Oude Voshaar wil ik bedanken voor hun bereidwilligheid om zitting te nemen in de leescommissie en voor het goedkeuren van mijn proefschrift.

Zo fijn, Sanneke en Janita dat jullie mijn paranimfen willen zijn! Sanneke, als tweede VS ouderengeneeskunde hebben we veel samengewerkt en opgebouwd. Jij vulde mij mooi aan met je drive naar duidelijkheid en afspraken in de dagelijkse patiëntenzorg, maar ook je energie die nooit op leek te gaan. Met die positieve energie heb je mij ook geholpen om data te verzamelen en mee te schrijven aan studies. Janita, wij zijn als verpleegkundig onderzoekers tegelijkertijd begonnen. Gelijk was ik onder de indruk van jou kennis over regels, wetgeving en financiële afspraken. Dit is iets waar ik de kriebels van krijg. In samenwerken waren wij gedurende dit proces in vele opzichten een goede match. Dank voor jullie betrokkenheid, enthousiasme, motiverende gesprekken en hulp!

Via Henk heb ik ook Marion en Joep leren kennen. Enthousiaste experts op het gebied van onderzoek en de wegen binnen onderzoeksland, zowel in Isala als daarbuiten. Dank voor jullie adviezen en gezelligheid.

Laura en Jolanda, dank voor de samenwerking bij de STOK studie. Wat klinkt dat als langgeleden! Ik denk terug aan een mooie tijd, waarop we door onze samenwerking patiënten konden includeren voor onze eigen onderzoeken. Dit heeft mede geleidt tot 2 mooie hoofdstukken in dit proefschrift. Die samenwerking heeft mij doen inzien dat samen onderzoek doen niet alleen leuker is, maar ook gemakkelijker is. Bedankt!

Dr. M.A. Edens en Dr. R.M. Brohet. Beste Mireille en Richard. Hartelijk dank voor jullie statistische input. Ondanks dat ik veel analyses zelf heb uitgevoerd had ik dat nooit kunnen doen zonder jullie hulp en tips. De mails en feedback die ik vaak meerdere keren moest lezen of overdenken om ze volledig te begrijpen, hebben zeker bijgedragen aan wat het proefschrift nu is.

Alle co-auteurs van de hoofdstukken van dit proefschrift. Ik wil jullie allen bedanken voor jullie ingebrachte expertise, fijne samenwerking en waardevolle commentaren.

Team ouderengeneeskunde, wat ben ik trots op jullie en het feit dat we samen mogen zorgen voor een doelgroep die volop in ontwikkeling is. Speciaal genoemd mijn directe collega VS, jullie hebben het niet altijd makkelijk gehad, zeker niet toen ons rooster het eigenlijk niet toeliet, maar ik toch als

onderzoeker een contract kreeg. Dank voor jullie betrokkenheid en gezelligheid tijdens momentjes met koffie, ijs, taart, diners, teambuildingsactiviteiten en wandelingen. Graag wil ik ook de RVE interne bedanken, voor de mogelijkheid die mij geboden is om mijzelf te ontwikkelen. Mijn eerste leidinggevenden en RVE-managers van de ouderengeneeskunde hebben hier ook aan bijgedragen en mij altijd gesteund, daarom wil ik Marco, Jolande, Leonard en Coen hierbij speciaal noemen. Dian, jij ook bedankt voor de vele gezellige uurtjes, o.a. tijdens het maken van stroomdiagrammen en protocollen, die nog steeds de basis zijn voor de zorg voor de ouderen in Isala.

Collega verpleegkundig onderzoekers in Isala. Wat zijn jullie een betrokken en enthousiaste groep mensen. Jullie ambitie, vinden eigenlijk altijd alles leuk, hebben net als ik liefde voor onderzoek en het verpleegkundige vak. We hebben veel gemeen en toch werken we elk vanuit onze eigen specialismen. Ik kon met al mijn frustraties, mijlpalen, ideeën en zorgen bij jullie terecht. Dit kon tijdens een research bijeenkomst, één op één met een kopje cappuccino, tijdens een etentje of bij gevierde feestjes. Dank voor alles!

Beste collega zorgverleners die ik heb mogen interviewen voor mijn laatste hoofdstuk: het stuk wat naar mijn idee mijn proefschrift verbindt. Jullie tijd en perspectieven zijn een waardevolle inbreng geweest voor het artikel en mijn kijk op (screening van) kwetsbaarheid, waar we hopelijk in toekomst verder op kunnen bouwen.

Bij de afronding van mijn proefschrift is mijn netwerk steeds verder uitgebreid en terwijl ik dit schrijf hoop ik echt dat ik niemand vergeet te noemen! Allereerst wil ik graag de gepassioneerde collega's van het expertisecentrum OI noemen. Dank voor de mogelijkheden die jullie geven om in de zorg voor deze patiënten en ook in onderzoek van betekenis te kunnen zijn. Daarnaast is de samenwerking met verpleegkundig specialisten en paramedisch onderzoekers binnen Isala, maar ook de contacten met docenten en lectoren van onderwijsinstellingen een verrijking van mijn netwerk.

Studievriendinnen verplegingswetenschap. In 2008 kwamen we elkaar tegen in Utrecht en sindsdien spreken we elkaar helaas minimaal 1x per jaar. Ik geniet ervan deel uit te maken van dit clubje, omdat jullie net zo gelukkig werden van onderzoek combineren met het verpleegkundig vak. Toch een beetje gelijkgestemden, die ook weer enorm van elkaar verschillen. Eigenlijk altijd te weinig tijd om jullie te spreken! Spreken we binnenkort weer af?

Lieve vrienden, het is fijn te merken dat jullie er altijd voor ons zijn. Door dit promotietraject, hebben we elkaar soms minder gezien en gesproken dan

ik had gewild, maar op de momenten dat we elkaar zagen genoot ik er met volle teugen van en was het alsof het niet zolang geleden was. Ik denk dan aan onze koffiemomentjes, wandelingen, etentjes, bezoeken van concerten en sauna's, maar ook het krijgen van kaartjes en bloemen op het moment dat gezondheidsperikelen ervoor zorgden dat het niet zo ging als we hoopten.

Ook niet te vergeten, veel dank voor de liefde, steun en interesse van de (schoon)familie. We voelen ons altijd welkom bij jullie en onze jongens zijn dol op jullie! Is er hulp nodig om op te passen, te verhuizen, of wat dan ook, jullie zijn er met raad en daad.

Lieve Julian en Laurens. Jullie hebben geen idee wat ik hiermee heb bereikt en uitleggen is ook lastig, maar ik hoop een voorbeeld te zijn en dat het jullie later inspireert om kansen te pakken, maar niet ten koste van alles. Jullie zijn het meest waardevolle wat ik in mijn leven mocht krijgen en geniet daar volop van. Ik ben trots op jullie! Jongens, doe wat je leuk vindt en koester de mensen om je heen waar je op kan rekenen en waar je van houdt. Ik hou van jullie.

Lieve Marc, als ik jou niet had, was het realiseren van dit proefschrift zeker niet gelukt. Je stimuleerde me om te doen wat ik leuk vond. Je hebt me afgelopen jaren gesteund met je nuchterheid en oplossingsgerichtheid, maar ook het regelen van een vakantiebestemming, een goede computer en internetverbinding, volgetankte auto, verwarming, eigenlijk alle dingen die voor jou vanzelfsprekend zijn, maar voor mij een wereld van verschil maken. Schat, ik hou van je en wat hebben we het goed samen!

Marian