Frailty in Oncology Patients: Assessment and Prognosis

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Orientador: Daniel Moreira Gonçalves

Gabriela Ehrenbrink

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Palavras-chave: FRAIL, CANCER, READMISSION, SURGERY, ONCOLOGY

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Resumo

Objetivo: Este estudo tem como objetivo: i) revisar a literatura e sintetizar as informações sobre a relação entre pacientes oncológicos frágeis e readmissão hospitalar após a cirurgia e ii) comparar a prevalência e concordância de diferentes instrumentos de fragilidade em pacientes oncológicos eleitos para tratamento cirúrgico.

Métodos: O primeiro objetivo foi alcançado através da realização de uma revisão sistemática e metanálise. O segundo objetivo foi alcançado através da realização de um estudo observacional transversal com pacientes oncológicos aguardando cirurgia, onde foram testados 5 instrumentos amplamente utilizados para avaliar a fragilidade (Fragilidade Fenotípica, VES-13, velocidade da marcha, 8 foot up-and-go e força de preensão manual).

Resultados: Com a metanálise, observamos uma relação positiva entre a presença de fragilidade e o risco de readmissão hospitalar após a cirurgia (RR = 1,58; IC95% 1,07-2,33; P = 0,02), embora com heterogeneidade significativa (p = 0,05, e I2 = 54%). Com o estudo transversal, nossos dados sugerem que a prevalência de fragilidade variou amplamente (8,2 a 37,3%), dependendo do instrumento de avaliação e sua concordância foi limitada.

Conclusão: A fragilidade é uma medida valiosa para a avaliação pré-operatória de pacientes submetidos à cirurgia, principalmente para predizer aqueles em risco de readmissão hospitalar. No entanto, o instrumento para avaliar a fragilidade deve ser selecionado com cuidado, pois diferentes instrumentos geralmente têm uma concordância ruim e, portanto, podem levar a uma previsão de risco incorreta.

Abstract

Objective: This study aims to: i) review the literature and summarize the information regarding the relation between frail oncologic patients and hospital readmission after surgery and ii) compare the prevalence and agreement of different frailty tools in oncologic patients elected for surgical treatment.

Methods: The first aim was accomplished by performing a systematic review and meta-analysis. The second aim was accomplished by perform an observational cross-sectional study with cancer patients waiting for surgery, where tested 5 instruments widely used to assess frailty (Phenotypic Frailty, VES-13, gait speed, 8 foot up-and-go and hand grip strength).

Results: with the meta-analysis, we observed a positive relation between the presence of frailty and risk of hospital readmission after surgery (RR=1.58, 95% CI 1.07-2.33; P = 0.02) though with significant heterogeneity (p=0.05, and I2 = 54%). With the cross-sectional study, our data suggest that prevalence of frailty varied widely (8.2 to 37.3%) depending on the assessment tool and their agreement was limited.

Conclusion: Frailty is a valuable measure for the preoperative assessment of patients submitted to surgery, particularly to predict those at risk of hospital readmission. However, the instrument to assess frailty should be carefully selected, as different instruments often have poor agreement and thus, might lead to wrong risk prediction.

KEYWORDS: FRAIL, CANCER, READMISSION, SURGERY, ONCOLOGY

Abbreviations and symbols

5m= 5m Gait Speed

BMI= Body Mass Index

CI= confidence interval

Fried= Phenotypic Frailty test

I^2= Heterogeneity

K=kappa coefficient

r = Pearson correlation

RR= Risk ratio

Ves-13= The Vulnerability Elders Survey

Introduction

Frailty can be defined as a state of vulnerability that leads to adverse health outcomes, being a multifaceted state of lowered physiological reserve, resulting in an increased vulnerability and decreased resistance and adaptive capacity [1]. As life expectancy grows, there is an exponential growth of ill and frail people in the population, consequently bringing costs to the society and the individual [2]. The concept of frailty has been studied and recognized as a very important determinant of health-related outcomes, especially in oncology, were frail patients have poor tolerance to anti-cancer treatments, high risk of complications to anti-cancer treatments and high risk of readmission and mortality [1, 3]. There are over 70 interventions and tools to measure frailty, though not all have been validated, differing from individual assessment tools to multi domain interventions [1]. This variety is major obstacle to clinicians, as it is difficult to choose one. Indeed, there is no standard instrument to assess frailty and all have its own advantages and disadvantages that need to be considered case-by-case according to the purpose and context of its use. In addition, it has been recognized that frailty prevalence varies within the same population depending on the instrument that was used. Thus, it is of uppermost importance to also assess the agreement between different instruments to help in the decision of which tool matches the needs of a clinical or researcher. For instance, if a more comprehensive (and thus time consuming) instrument has a good predictive value for a certain outcome (e.g. postoperative complications) and if a simple test (e.g. gait speed or handgrip strength) presents a good agreement, than we could opt by the faster on when time is a constrain [4]. By defining a gold standard frailty assessment, health professionals may predict adverse outcomes and define which patients may receive pre-habilitation care, to rise patient´s ability to go through the stress of surgery and decrease the occurrence of postoperative complications, shorten hospital stay, reduce unplanned readmission thus, reduce the burden of surgery [5]. In order to give some insights about some of these concerns, this study aims: 1) to review the literature and summarize the information regarding the relation between frail oncologic patients and hospital

readmission after surgery. To accomplish this, a systematic review and meta-analysis was done and this will be presented in the first part of our work; 2) to compare the prevalence of frailty according to different instruments and test their agreement. To accomplish this, we will perform an observational cross-sectional study with cancer patients waiting for surgery and will test them for frailty using 5 instruments widely used to assess frailty (Phenotypic Frailty, VES-13, gait speed, 8 foot up-and-go and hand grip strength). This will be presented on the last part of this work.

Study 1: Frailty and the Risk of Hospital Readmission After Cancer Surgery: Systematic Review and Meta-Analysis

ABSTRACT

Introduction: Surgery is often the only option for cancer treatment and cure, the number of patients requiring this type of surgery is expected to increase over the next few years. However, surgery may cause adverse outcomes, such morbidity and mortality, especially in frail patients. An unplanned readmission is common outcome, bringing risks and expenses, though can be prevented. Aim: This study aimed to identify the risk of post-surgery readmission for frail cancer patients through a meta-analysis and systematic review.

Methods: This review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). MEDLINE and LILACS electronic databases were searched between September 2018 and April 2019. In addition, the reference list of other publications was checked for any unidentified study. Newcastle – Ottawa Quality Assessment Scale (NOS) was utilized to assess the quality of studies and Data synthesis was performed according to recommendations in the Cochrane Handbook for Systematic Reviews of Interventions, using Review Manager 5.3 (software Cochrane Collaboration).

Results: Nine observational studies were included in the meta-analysis, being 22.3% of the total of patients frail that underwent surgery. An association was found of the higher risk of post-surgery readmission for frail patients, a positive association for frail patients and readmission was also found when analyzing colorectal cancer individually and a longer follow-up after surgery.

Conclusion: Patient readmission is an adverse outcome when it comes to surgery cancer patients, having frail patients a higher risk of readmission. Further studies need to be done to determine the reasons for patient readmission.

KEYWORDS: READMISSION, FRAIL, SURGERY, CANCER, ONCOLOGY

INTRODUCTION

Demographic projections for Europe in 2030 indicate that 25% of the population will be 65 or over, being cancer the first cause of mortality [6]. Because surgery is the only curative option for solid cancers, particularly in early stage disease, it is estimated that the number of cancer patients requiring surgical treatment will increase. However, surgery is not free of adverse events such as risk for morbidity and mortality, particularly in the most vulnerable patients [7]. Unplanned hospital readmissions also are a common, expensive and often preventable postoperative adverse event for patients submitted to surgical treatment [8]. Despite the efforts on identifying those patients at highest risk of readmission, current options fail to accurately predict which patients will not successfully transition back into their normal lives [9-11]

Frailty is defined as a clinical syndrome, which indicates an increased state of vulnerability, associated with a decline in physiologic reserve and function across multiple organ systems, resulting in adverse health outcomes, which could be increased or reverted by interventions [12]. Frail patients are at increased risk of chemotherapy intolerance, postoperative complications and mortality [13]. It has even been reported that frailty is a stronger predictor of postoperative outcomes compared with several classic surgical risk-assessment tools [14-16]. Importantly, a higher number of positive frailty characteristics was associated with higher hospital readmission rate, suggesting that frailty might be useful to predict unplanned readmission and thus, its negative consequence [3, 17, 18]. However, the evidence has not been systematized and thus, we conducted this meta-analysis and systematic review with the intent to explore the association between frailty and the risk of post-surgery hospital readmission in cancer patients.

METHODS

This review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [19].

Eligibility criteria

We included studies that recruited adult patients aged 18 or older, of both sexes and any ethnicity, diagnosed with cancer and scheduled to surgery for tumor resection with and without neoadjuvant therapy. In addition, studies had to stratify and compare participants by frailty status, assessed before any treatment, using one or more frailty instrument.

The primary outcome for this review was frailty prevalence and post-operative readmission to the hospital. There was no minimum length of follow-up for the studies that were eligible for inclusion in the review, but they had to report the timing and duration of the readmission.

Only published observational (retrospective and prospective) and experimental (non-randomized and randomized clinical trials) studies, reporting crude or sufficient raw data to allow calculation of the association between frailty and post-operative re-admission to hospital, published in English in the last 10 years were considered eligible for inclusion in the review. The following criteria were used to exclude papers from analysis: articles that did not specify the postoperative complications and the readmission period, review papers, conference abstract, studies in languages other than English, studies that did not characterize participants by frailty status and studies with more than ten years.

Information sources

We searched MEDLINE and LILACS electronic databases between September 2018 and April 2019. In addition, the reference list of other publications was checked for any unidentified study.

Search

The electronic search was performed using the terms “Frail/Frailty AND cancer/oncologic/oncology AND postoperative AND readmission”.

Study selection

The title and abstract of the selected studies were screened by one reviewer (GE) to determine eligibility in terms of intervention, participants, and design. If in doubt about whether a study was relevant, the full article was checked. The full-text versions of all relevant studies were retrieved. If a full text version could not be retrieved, then the study was excluded due to the lack of a detailed methodology and the possibility of a high risk of bias.

Data collection process

After applying the inclusion/exclusion criteria, the following information was retrieved from the selected articles: author, year, study design and location, participant population (sample size, age, gender), the inclusion and exclusion criteria, type of cancer, stage of cancer, type of treatment, type of surgery (elective or emergency), methods used to assess frailty and its prevalence, and readmission rates. All the information was organized into tables.

Data items

Only numerical values reported by the studies (e.g. percentages, counts, means) were used to calculate frailty prevalence and risk of post-surgery readmission.

We anticipated the use of different frailty instruments and different classifications of frailty (frail and non-frail; frail, pre-frail and robust; cumulative frailty). Thus, and in order to include the greatest number of articles in this review and/or to perform analysis by frailty status, we dichotomized (frail and non-frail) or trichotomized (frail, pre-frail and robust) frailty classification. Regarding dichotomization, “pre-frail” and “robust” patients were merged and considered “non-frail”; for studies using cumulative frailty (from 0 to 1), we considered “non-frail” those with a frailty index <0.2 and “frail” those ≥0.2 [20]. For trichotomization,

we considered “robust”, “pre-frail” and “frail” those with a frailty index ≤0.10, 0.10 to 0.21 and >0.21, respectively [21].

Risk of bias

We used the Newcastle – Ottawa Quality Assessment Scale (NOS) to assess the quality of studies [22] . It uses a rating system, with a maximum of nine stars rewarded to judge the best level quality, distributed by three multi-item domains: selection (4 possible stars), comparability (2 possible stars) and outcome (3 possible stars). At the end all the stars were summed, and the scoring was rated to Agency for Healthcare Research and Quality (AHRQ) standards (good, fair, and poor) as follows: Good quality if 3 or 4 stars in Selection domain AND 1 or 2 stars in Comparability domain AND 2 or 3 stars in Outcome domain; Fair quality if 2 stars in Selection domain AND 1 or 2 stars in Comparability domain AND 2 or 3 stars in Outcome domain; Poor quality if 0 or 1 star in Selection domain OR 0 stars in Comparability domain OR 0 or 1 stars in Outcome domain. The assessment of risk of bias was also used to inform for the sensitivity analysis, where only data retrieved from studies judged as “Good” quality were considered.

Summary of measures

Readmission was expressed as Risk Ratio (RR) with 95% confidence intervals (CI).

Synthesis of results

Data synthesis was performed according to recommendations in the Cochrane Handbook for Systematic Reviews of Interventions, using Review Manager 5.3 (software Cochrane Collaboration). We calculated pooled risk ratio (RR) and 95% confidence intervals (95% CI) using the Mantel – Haenszel method. The random-effects mode was used because we assume that the true effect size varies from one study to the next, and that the studies in our analysis

represent a random sample of effect sizes that could have been observed. Only unadjusted data was pooled.

Assessment of heterogeneity

Statistical heterogeneity was observed by visual inspection of forest plots, by using a standard Chi^2 value with a significance cut off level of $P < 0.10$, and by the I^2 statistic. An I^2 estimate greater than or equal to 50% with a significant value for Chi^2, was interpreted as evidence of statistical heterogeneity [23].

Assessment of reporting biases

Funnel plots were used to visually inspect for publication bias.

Subgroup analysis

Subgroup analysis was conducted, according to the following: frailty status (robust vs. pre-frail vs. frail), cancer type (gynecologic vs. digestive), time of readmission (<30 and > 30 days), sample size (>100 and <100), type of treatment and type of study (prospective and retrospective).

Sensitivity analysis

Sensitivity analysis was performed by omitting every single study and re-calculating the RR.

RESULTS

Study Selection

A PRISMA diagram summarizing flow of studies through the review is presented (**Figure 1**). After the initial literature search, we identified 1073 articles and abstracts through database searching, and 16 additional articles from references of other reviews. After screening, only 74 articles remained to be assessed for eligibility and 48 papers were discarded because they were not related with the topic. After applying the inclusion and exclusion criteria on the remaining 26 articles, only 9 were eligible for qualitative and quantitative evaluation. Reasons for exclusion are listed in **Table 1**.

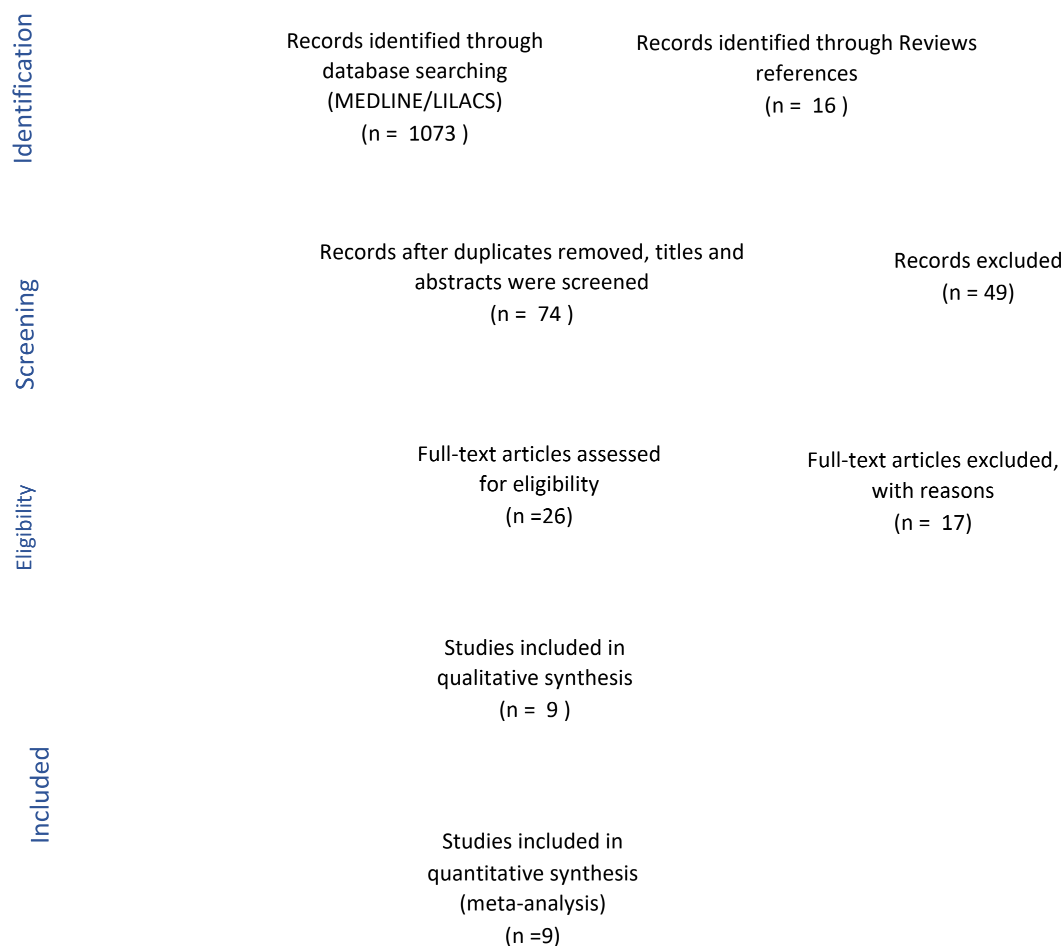


Figure 1: PRISMA Flow Diagram.

Table 1: Reasons for exclusion

Studies	Exclusion
Erekson, Yip [24]	Did not specify readmission rate
Tan, Kawamura [25]	Did not specify readmission rate
Finlayson, Zhao [26]	Frailty tool not mentioned, frailty not an outcome of the study
Choi, Yoon [27]	Did not specify readmission rate
George, Burke [28]	Did not specify readmission rate as independent outcome
Kenig, Mastalerz [29]	Did not specify readmission rate
Pujara, Mansfield [30]	Did not specify readmission rate in frail patients
Dale, Hemmerich [31]	Did not provide a final frailty score
[32]	Did not specify readmission rate in frail patients
Neuman, Weiss [33]	Frailty was not assessed
Fagard, Casaer [34]	Did not specify readmission rate in frail patients
Chen, Zhang [35]	Did not specify readmission rate in frail patients
Abt, Xie [36]	Did not specify readmission rate in frail patients
Hewitt, Moug [37]	No cancer mentioned
Badgwell, Stanley [38]	Did not provide a final frailty score
Ommundsen, Wyller [39]	Only had frail patients
Choe, Joh [17]	Results for Frail and pre-frail patients were presented together

Study characteristics

The study characteristics are summarized on **Table 2**. Of the 4655 patients enrolled in the 9 studies (6 prospective [3, 40-44]) and 3 retrospective [20, 21,

45]), 73.6% (n=3354) were male and 26.4% (n=1229) were female, with an average of 70.1 years old. Six studies were performed in the USA [3, 20, 21, 40, 44, 45], 1 in Norway [41], 1 in Japan [43] and 1 in Netherlands [42]. Frailty was defined using different frailty instruments, including the SOF Frailty index [17], the modified Frailty index [20, 21], sarcopenia [42, 43], Frailty index [3, 44] and Fried criteria [40]. Five articles addressed gastrointestinal cancer (3 studies for colorectal cancer [3, 42, 44], 1 for gastric cancer [17] and 1 for esophageal [43]), 2 studies addressed gynecologic cancer (not specified [40] and endometrial cancer [45]), 1 study addressed bladder cancer [20] and 1 head and neck cancer [21]. None of the surgeries reported were emergency surgeries, and most of the studies were either only major surgeries or major surgery was the most common. However three studies reported minimally invasive surgery, one occurred in 19% of patients [40], one on 4% of the patients [45] and the other on 29% of the patients [41].

Table 2: Study Characteristics.

Ref	Year	Country	Study Design	Sample	Age (mean)	Gender	Type of Cancer	Stage of cancer	Type of treatment	Time of Postoperative readmission
Courtney-Brooks, Tellawi [40]	2012	USA	Prospective	37	73	All Woman	Gynecologic	NA	Surgery	30-day readmission
Chappidi, Kates [20]	2016	USA	Retrospective	2679	69.65	F: 513 M:2166	Bladder cancer	NA	Surgery	30-day readmission
Kristjansson, Nesbakken [41]	2010	Norway	Prospective	178	79.6	M: 76 F: 102	Colorectal	Stage0: 8 Stage1-2: 100 Stage3-4: 57 Unclassified: 4	Surgery	30-day readmission
Kuroki, Mangano [45]	2015	USA	Retrospective	122	65.9	All Woman	Endometrial Cancer	Stage 1-2: 88 Stage 3-4: 34	Surgery, Radiation, Chemotherapy	90-day readmission
Robinson, Wu [3]	2011	USA	Prospective	60	75	M: 58 F: 2	Colorectal	Non-frail = Benign: 9 Stage 1-2: 12 Stage 3-4: 3 Prefrail = Benign:3 Stage 1-2: 5	Surgery	30-day readmission

								Stage 3-4: 5 Frail = Benign:7 Stage 1-2: 12 Stage 3-4: 4		
Robinson, Wu [44]	2013	USA	Prospective	72	74	NA	Colorectal	NA	Surgery	30-day readmission
Abt, Richmon [21]	2016	USA	Retrospective	1193	63.4	M: 807 F:386	Head and Neack	NA	Surgery	30-day readmission
Lodewick, van Nijnatten [42]	2014	Netherla nds	Prospective	171	64	M: 104 F: 67	Colorectal	NA	Surgery, chemother apy, tumor ablation, preoperati ve portal vein embolizati on	21 months (median, 1-90) readmission
Makiura, Ono [43]	2017	Japan	Prospective	98	67	M: 83 F: 15	Esophageal	Total= stage0: 1 stage1-2:57 Stage3-4: 40 Sarcopenia = stage0: 1 Stage1-2:16 Stage3-4:14 No Sarcopenia= Stage0: 0 Stage 1-2:41 stage3-4:26	Surgery, Neoadjuv ant chemother apy	90-day readmission

Table 2: *Continuation*

Ref	Frailty Tool	Thresholds used to define frailty status	Frailty Prevalence		Postoperative readmisson		
			n	%	n	%	Adjustment
Courtney-Brooks, Tellawi [40]	Fried	Not Frail: 0–1 Intermediately frail: 2–3 Frail: 4–5	Non- Frail: 21 Prefrail: 10 Frail: 6	Non-Frail: 28.7% Prefrail: 13.6% Frail:8.2%	Non-frail: 1 Prefrail: 0 Frail: 1	Non-Frail:4.7% Prefrail:0% Frail:16.6%	NA
Chappidi, Kates [20]	Modified Frailty Index	mFI >= 2 = Frail; mFI < 2 Non-frail	Non-Frail 2019 Frail: 660	Non-Frail: 75.3% Frail:24.7%	Non-Frail: 401 Frail: 137	Non-Frail: 19.8% Frail: 20.75%	NA
Kristjansson, Nesbakken [41]	CGA	NA	Non-frail = 21 Prefrail = 81 Frail = 76	Non-Frail:11.7% Prefrail:45.5% Frail:42.8%	Non-frail/Prefrail: 7 Frail: 13	Non-frail/Prefrail : 6.8% Frail: 17.1%	A separate logistic regression analysis looking at the predictive effect of frailty for severe complications for the subgroup colon cancer resulted in an odds ratio of 3.71, with a 95% confidence interval of 1.74–7.88. For the subgroup

							rectal cancer, the odds ratio was 2.0 with a 95% confidence interval of 0.61–6.56.
Kuroki, Mangano [45]	Sarcopenia	Muscle mass below the median (\4.33 cm2) on preoperative CT scan	Non-Frail:61 Frail: 61	Non-Frail: 50% Frail:50%	Non-Frail: 4 Frail: 3	Non-Frail:6.5% Frail:4.9%	Adjusted multivariable model (HR, 1.57; 95 % CI, 0.73–3.42; HRadj, 1.98; 95 % CI, 0.81–4.86, respectively).
Robinson, Wu [3]	Frailty Index	Non-frail: 0-1 abnormal Characteristic; Pre-frail: 2-3 abnormal characteristic; Frail: 4-7 abnormal characteristics	Non-Frail: 24 Pre-Frail: 13 Frail: 23	Non-Frail:40% Pre-Frail: 21.6% Frail: 38.3%	Non-Frail:1 Pre-Frail: 2 Frail: 7	Non-Frail:4.1% Pre-Frail: 15.3% Frail: 30.43%	ROC curves were performed, the area under the curve was compared with the null hypothesis in which the area is .5. The area equals .702 (95% CI, .576 to .828; P 5.004).
Robinson, Wu [44]	Frailty Index	Non-frail: 0-1 abnormal Characteristic; Pre-frail: 2-3 abnormal characteristic; Frail: 4-7 abnormal characteristics	Nonfrail: 33 Prefrail: 15 Frail: 24	Non-Frail:45.8% Pre-Frail: 20.8% Frail: 33.3%	Non-frail: 2 Prefrail: 3 Frail: 7	Non-Frail:6% Pre-Frail: 20% Frail: 29.1%	NA
Abt, Richmon [21]	Modified Frailty Index	Non-Frail mFI<=0.1 Prefrail: mFI0.1-0.21 Frail mFI>0.21	Non-Frail: 922 Prefrail: 206 Frail: 65	Non-Frail:77.2% Pre-Frail: 17.2% Frail: 5.4%	Non-Frail: 47 Prefrail: 12 Frail: 2	Non-Frail:5% Pre-Frail: 5.8% Frail: 3%	Independent variables included for adjustment during multivariable analysis were age, sex, body mass index (BMI), smoking status, American Society of Anesthesiologists' classification,wound classification, currentwound infection, diabetes mellitus status, corticosteroid use for a chronic condition, operative time, history of previous operation within 30 days of surgery, operation year, and the consumption of more than 2 alcoholic drinks per day within the past 2 weeks.
Lodewick, van Nijnatten [42]	Sarcopenia	Sarcopenia was defined as an L3 MI <41 cm2/m2 in women, <43 cm2/m2 in men with a BMI <25, and <53 cm2/m2 in men with a BMI >25	Non-Frail: 91 Frail: 80	Non-Frail: 53.2% Frail: 46.7%	Non-Frail: 10 Frail: 13	Non-Frail: 10.9% Frail: 16.2%	NA
Makiura, Ono [43]	Sarcopenia	Low muscle mass was defined as \7.0 kg/m2 for males and \5.7 kg/m2 for females. Low muscle strength was defined as a grip strength of \26 kg for males and \18 kg for females. Low physical performance was defined as a gait speed of\0.8 m/s.	Non-Frail: 67 Frail: 31	Non-Frail: 68.3% Frail: 31.6%	Non-Frail: 11 Frail: 12	Non-Frail: 16.4% Frail: 38.7%	Sarcopenia was a significant predictor of OS after adjustment for age, sex, and pathological stage (hazard ratio 2.35, 95% CI 1.21–4.54; p = 0.01).

Prevalence of frailty and readmission

Irrespective of the frailty assessment method, the average prevalence of frailty was 22.3% (range 5.4%–50%). Postoperative readmission was reported at 30-days in 6 studies [3, 20, 21, 40, 41, 44], 90-days in 2 studies [43, 45], and 21 months in 1 study [42]. Overall, prevalence of postoperative hospital readmission was 19% (range 5.4%–23.4%) in frail patients and 13.9% (range 4.1%–19.8%) in non-frail patients (**Table 2**).

Risk of bias and applicability

The overall quality of the studies had a good mean score of 7.7, out of these three studies were qualified as poor and the other 6 as good, with scores of a total from 6-9. The results are shown in **Table 3**.

Quality assessment Criteria	Kristjansson S., et al. 2010	Chappidi et al. 2016	Robinson T, et al 2011	Robinson T, et al 2013	Brooks et al. 2012	Kuroki et al. 2015	Lodewick et al. 2014	Makiura 2017	Abt 2016
Selection									
• Representatives of exposed cohort?	*	*	*	*	*	*	*	*	*
• Selection of the non-exposed cohort?	*	*	*	*	*	*	*	*	*
• Ascertainment of exposure?	*	*	*	*	*	*	*	*	*
• Demonstration that outcome of interest was not present at start of study?	*	*	*	*	*	*	*	*	*
Comparability									
• Study controls for age/sex?								*	*
• Study controls for at least 3 additional risk factors?	*		*			*	*	*	*
Outcome									
• Assessment of outcome?	*	*	*	*	*	*	*	*	*

• Was follow-up long enough for outcome to occur?	*	*	*	*	*	*	*	*	*
• Adequacy of follow-up of cohorts?	*			*	*	*	*	*	*
Overall Quality Score (max = 9)	8	6	8	7	7	8	8	9	9
Quality	Good	Poor	Good	Poor	Poor	Good	Good	Good	Good

Table 3. Risk of bias.

Primary outcome

Pooled prevalence of frailty and pre-frailty frailty and the risk of readmission

We explored the association between frailty and postoperative risk of readmission in cancer patients. Only 2 [41, 43] of the 9 studies showed a significant risk difference of postoperative hospital readmission between frail and non-frail patients (**Figure 2**). The pooled data showed that the risk of postoperative hospital readmission in the frail group was higher than the non-frail group (RR=1.58, 95% CI 1.07-2.33; P = 0.02) though with significant heterogeneity (p=0.05, and I^2 = 54%).

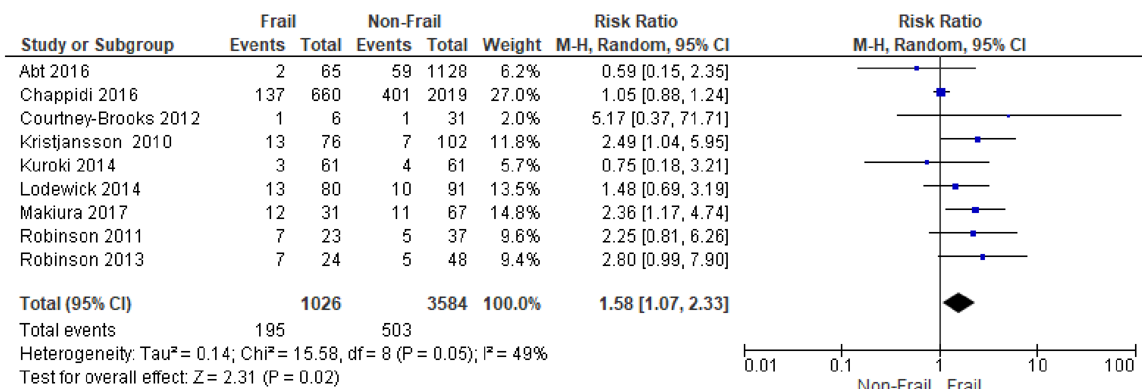


Figure 2: Forest plot for the association between frailty and the risk of readmission.

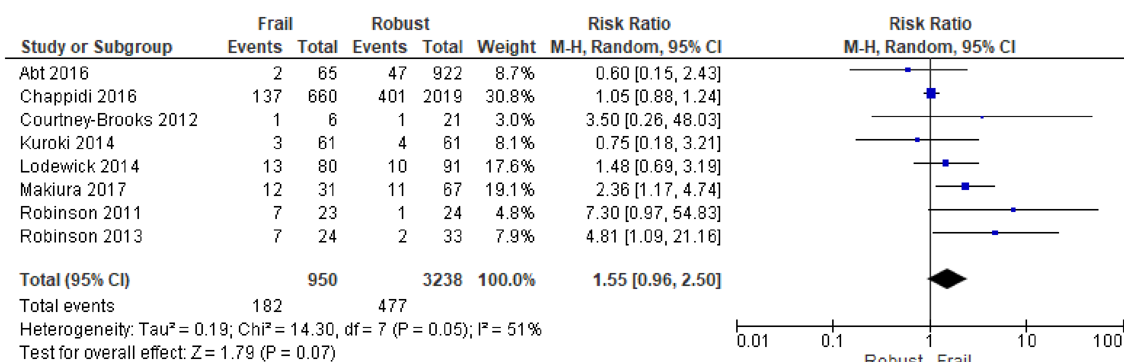
Subgroup analysis

As depicted in **Figure 2**, we found highly heterogeneous results regarding the association between frailty and postoperative readmission. Therefore, the following subgroup analysis were performed to explore the sources of this heterogeneity: by frailty status, follow-up period, frailty definition, type of cancer, and sample size (<100 vs >100).

Frailty status and risk of readmission

Figure 3 shows the subanalysis of the readmission risk by frailty status. For this analysis we divided the "non-frail" group in "robust" and "pre-frail" groups as explained in the methodological section. Comparison between frail and robust patients was possible to perform in 8 papers; between frail and pre-frail patients in 4 papers; and between pre-frail and robust patients in 4 papers. Frail patients were at greater risk of readmission than robust patients in 2 papers. Pooled analysis revealed a cumulative RR of 1.72 in frail patients (95% CI 1.02-2.89; P=0.04; I^2=56%). No significant risk was found between pre-frail and frail patients (RR 1.31; 95% CI 0.62-2.77; P=0.48; I^2=0%) or between pre-frail and robust patients (RR 1.35; 95% CI 0.78-2.34; P=0.29; I^2=0%).

A



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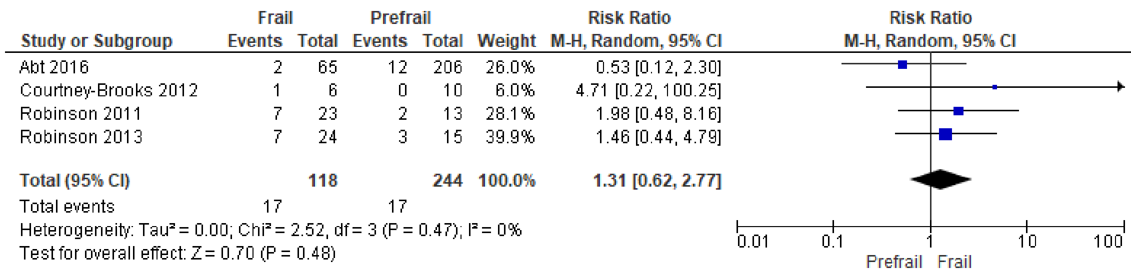

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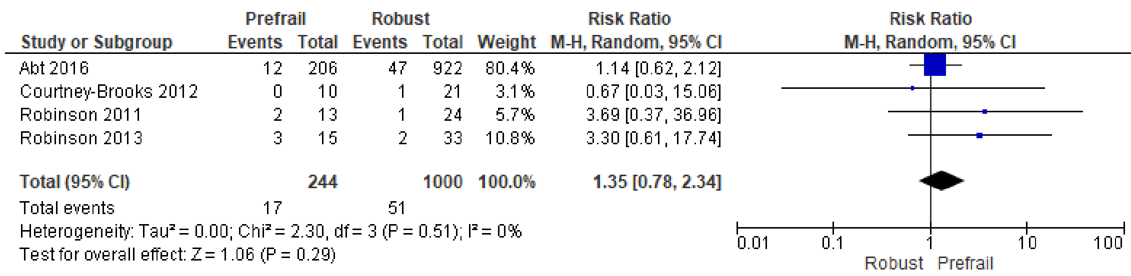


Figure 3. Forest plot for subanalysis of the risk of readmission by frailty severity: a) frail vs. robust; b) frail vs. pre-frail; c) pre-frail vs. robust.

Frailty and risk of readmission by follow-up period

Subgroup analysis was conducted according to time point of readmission after surgery (**Figure 4**). Five studies reported readmission data up to 30 days pos-surgery and 4 studies above 30 days. Pooled analyses showed that there was no-significant risk ratio between the frail and non-frail patients for 30-days readmission (RR 1.28; 95% CI 0.81-2.02; p = 0.29; I^2 = 39%). However, for readmission above 30 days (90 days to 7.5 years), there was a significant risk for frail in comparison to non-frail patients (RR 1.97; 95% CI 1.27-3.06; P = 0.003; I^2 = 11%).

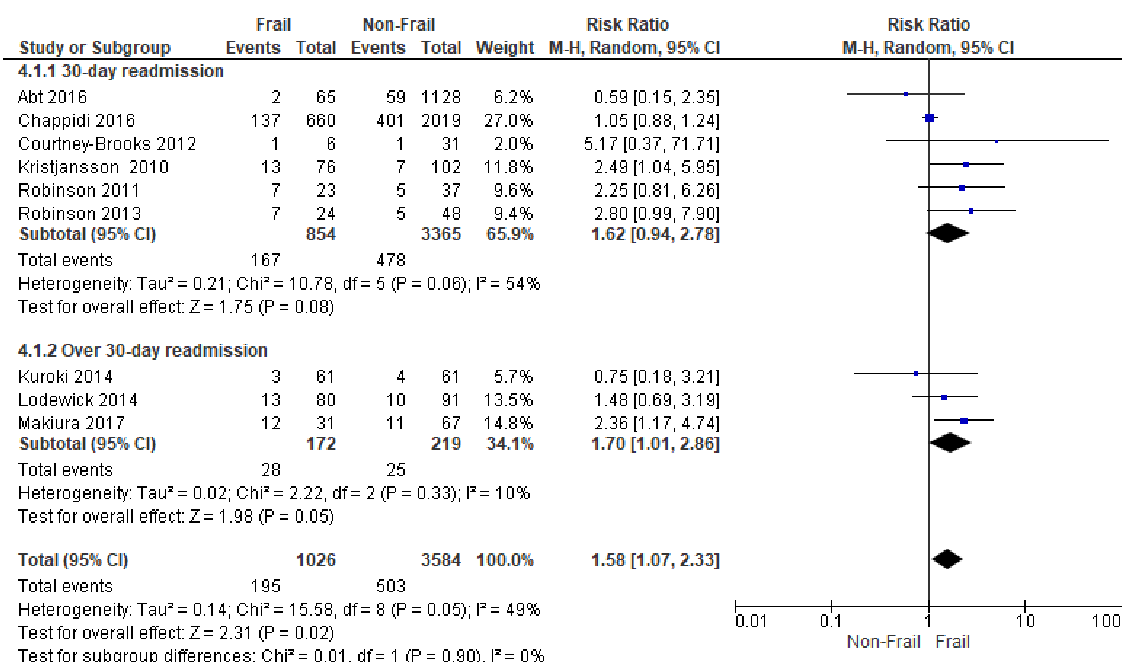


Figure 4: Forest plot for subanalysis of the risk of readmission by follow-up period.

Frailty definition and risk of readmission

Three different frailty tools formed sub analyses, the modified frailty index, sarcopenia and the frailty index. Comparing the two studies that utilized the modified frailty index, there was no show of significant risk difference between frail and non-frail patients (RR 1.04; 95% CI 0.87, 1.23; p = 0.69; I^2 = 0%). With

sarcopenia there was no significant difference in three of the studies, the general analysis between the three studies did not show a significant risk for readmission for patients that were considered frail, though the values were very close to a significant risk (RR 1.70; 95% CI 1.01, 2.86; p = 0.05; I^2 = 10%). The frailty index showed a significant risk difference between patients classified as frail and non-frail and their readmission (RR 2.51; 95% CI 1.21, 5.19; p = 0.01; I^2 = 0%). The general analysis between frailty tools showed no significant risk difference for patient readmission (RR 1.44; 95% CI 0.96, 2.14; p = 0.08: I^2=47%), as shown on **Figure 5**.

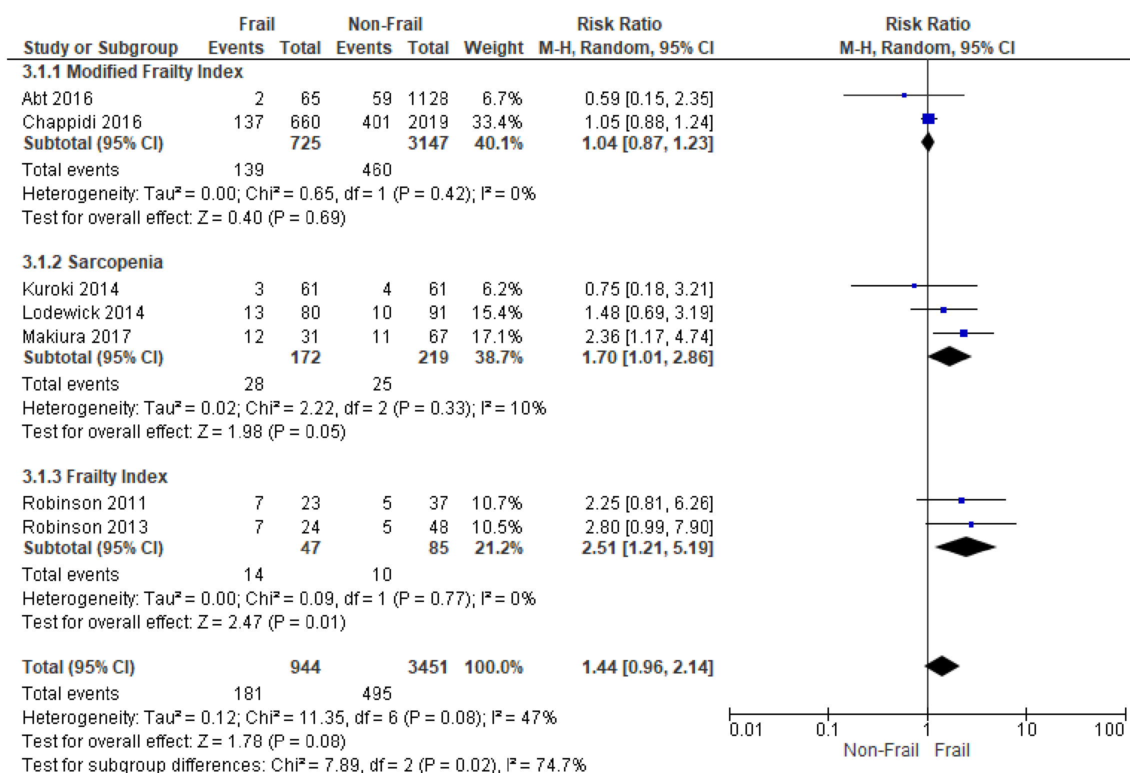


Figure 5: Forest plot by subanalysis of the risk of readmission by type of frailty tool.

Frailty and risk of readmission by type of cancer

The type of cancer that predominated between the different studies was digestive cancers (colorectal cancer and esophageal) and gynecologic cancer. The colorectal cancer sub-analysis showed a significant risk for frail patients for readmission (RR 2.16; 95% CI 1.48, 3.16; $p < 0.0001$; $I^2 = 0\%$), the gynecologic cancer did not show significant risk (RR 0.85; 95% CI 0.24, 3.06; $p = 0.80$; $I^2 = 0\%$) (**Figure 6**).

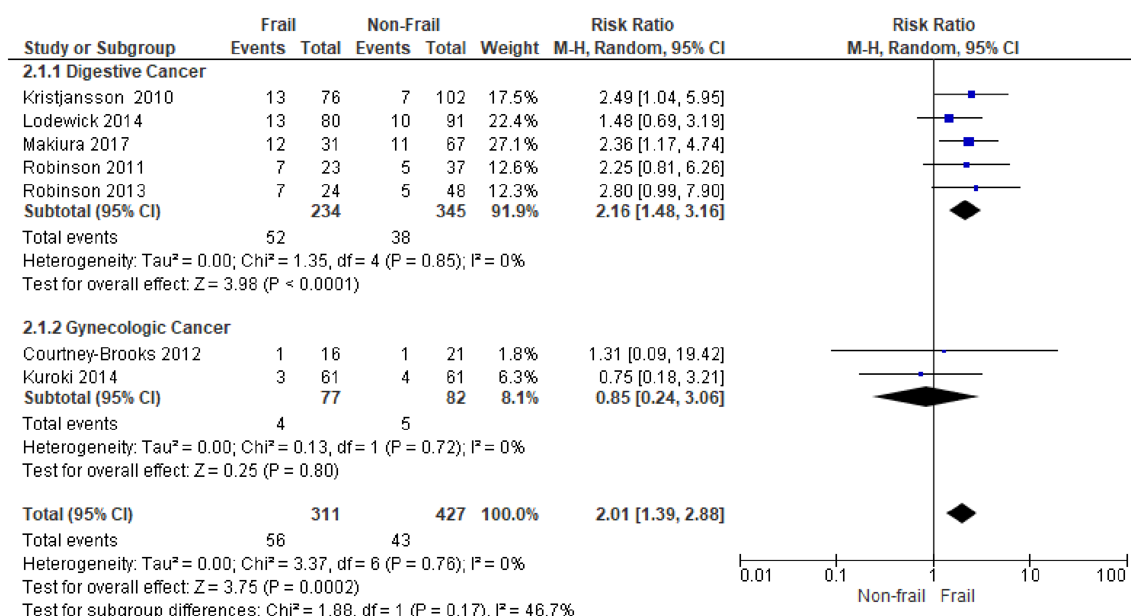


Figure 6: Forest plot by subanalysis of the risk of readmission by type of cancer.

Frailty and risk of readmission by sample size

Five studies presented a sample size over 100 patients, these did not show a significant increased risk for frail patients of hospital readmission (RR 1.18; 95% CI 0.83, 1.67; p=0.36; $I^2 = 25\%$). The studies with a smaller sample group, under 100 patients showed a significant risk for frail patients of hospital readmission with a low heterogeneity between the studies (RR 2.49; 95% CI 1.52, 4.09; p=0.0003; $I^2 = 0\%$) (**Figure 7**).

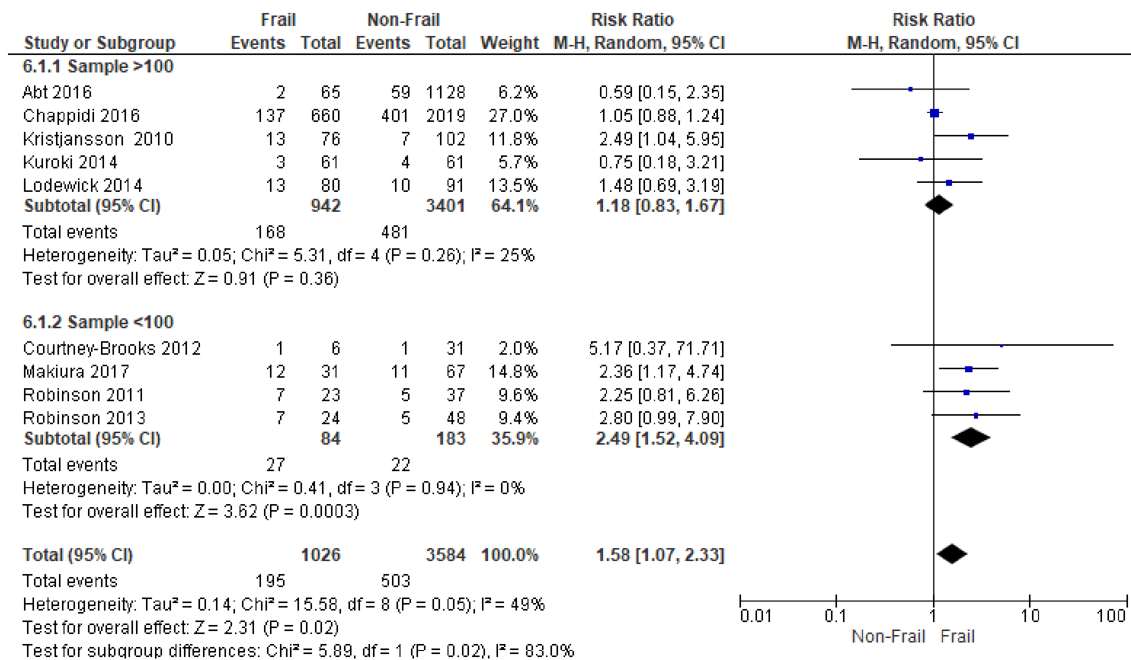


Figure 7: Forest plot by subanalysis of the risk of readmission by sample size of study.

Frailty and risk of readmission by type of treatment

Treatment type showed a significant higher risk of readmission for frail patients when comparing the two group analysis (RR 1.58; 95% CI 1.07, 2.33; p=0.02; I^2 = 49%), six studies reported on surgery as the only treatment plan but did not show a significant risk difference (RR 1.62; 95% CI 0.94, 2.78; p=0.08; I^2 = 54%) and the other three reported on surgery and other therapies, such as chemotherapy, radiotherapy, tumor ablation and preoperative portal vein embolization, also not resulting in a significant higher risk for frail patients (RR 1.70; 95% CI 1.01, 2.33; p=0.05; I^2 = 10%) (**Figure 8**).

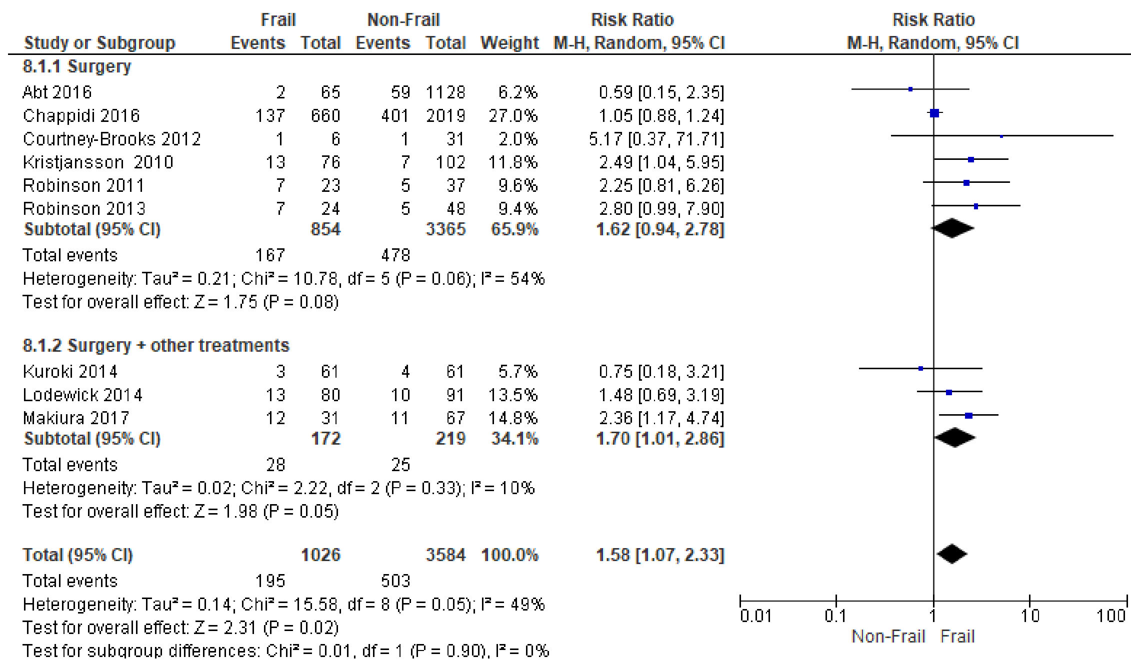


Figure 8: Forest plot by subanalysis of the risk of readmission by type of treatment.

Prospective and Retrospective studies and Frailty readmission

Of the nine studies, 6 were prospective studies and showed a high significant risk difference for readmission for frail patients (RR 2.20; 95% CI 1.51, 3.20; p<0.0001; I^2 = 0%). The other 3 studies did not have a significant risk difference for readmission (RR 1.03; 95% CI 0.87, 1.22; p= 0.72; I^2 = 0%), the overall analysis between both groups also showed a significant risk for frail patients and hospital readmission (**Figure 9**).

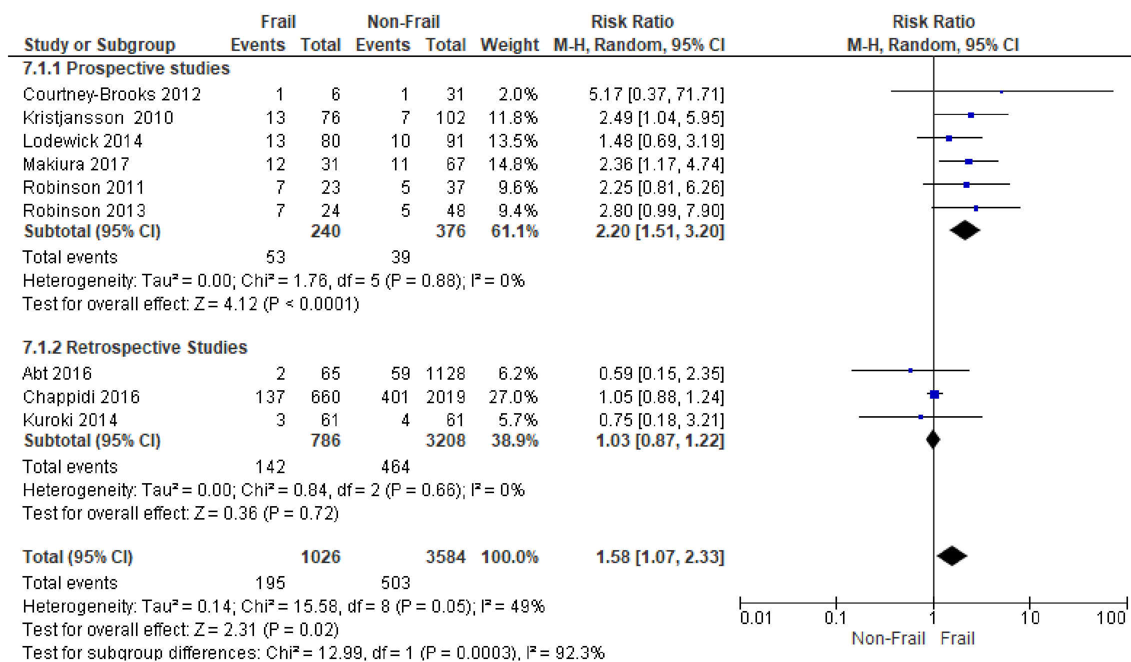


Figure 9: Forest plot by subanalysis of the risk of readmission by type of study design.

Sensitivity analysis and publication bias

When selected articles were individually removed and the effect size recalculated, the sensitivity analysis illustrated that there was significant change of the results (**Table 4).**

Table 4: Sensitive analysis

Author	Risk Ratio	Heterogenity	p
Abt 2016	1.70 [1.13, 2.55]	54%	0.01
Chappidi 2016	1.90 [1.34, 2.70]	0%	0.0004
Courtney-Brooks 2012	1.54 [1.04, 2.28]	51%	0.03
Kristjansson 2010	**1.48 [0.99, 2.20]**	**45%**	**0.05**
Kuroki 2014	1.67 [1.10, 2.53]	54%	0.02
Lodewick 2014	1.62 [1.03, 2.55]	54%	0.04
Makiura 2017	**1.45 [0.98, 2.16]**	**39%**	**0.06**
Robinson 2011	1.53 [1.01, 2.30]	50%	0.04
Robinson 2013	**1.48 [1.00, 2.19]**	**45%**	**0.05**

Publication bias was assessed by visual inspection of the funnel plot (**Figure 10**), which we considered low.

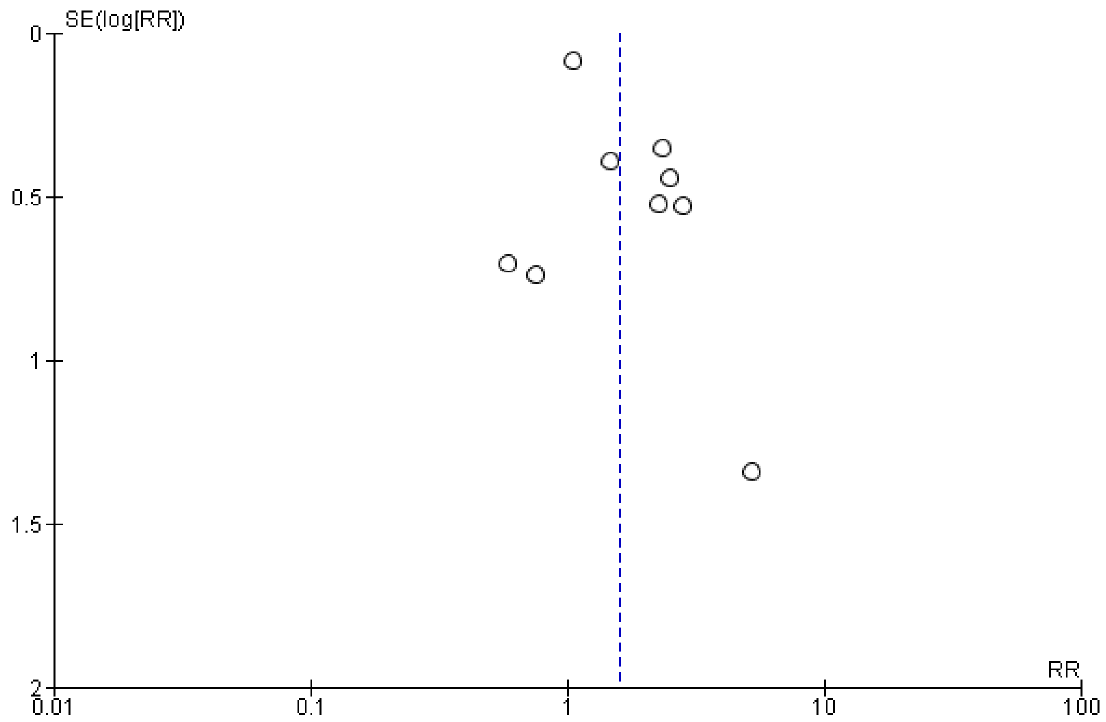


Figure 10: Funnel Plot for publication bias

DISCUSSION

We conducted this meta-analysis and systematic review with the intent to explore the association between frailty and the risk of post-surgery hospital readmission in cancer patients. Our data points that frailty is associated with greater risk of readmission and subanalysis suggest that this is influenced by the type of assessment tool, type of cancer, study design and sample size.

Summary of evidence

Several studies support that that frailty is a stronger predictor of postoperative outcomes compared with several classic surgical risk-assessment tools [14-16]. Recently, it was also suggested that frailty might be also useful to predict unplanned readmission and [3, 17, 18]. Readmissions are associated with lower survival and can result in the delay in receipt, or cancellation, of adjuvant treatment, thus altering the progression of the disease [46]. Thus, an effort to study the risk factors for readmissions is mandatory, as well as to identify and intervene on preventable causes. Frailty seems to be a risk factor for future readmission after surgery, as supported by one meta-analysis in adult population after elective major abdominal surgery [47]. However, that indication was based on a secondary analysis and not all patients submitted to surgical procedures were performed for cancer [47]. In our review of 9 observational studies, including 4655 patients, frailty was present in 22.3% (raged from 5.4% to 50%) of all cancer patients undergoing surgery, which is in accordance with the numbers of previous reports for this clinical population [13]. We found an association with increased risk of readmission after surgery for patients classified as frail. As far as we are aware, this is the first meta-analysis specifically addressing this question in cancer patients. Patient readmissions can be caused by multiple causes. A recent analysis of the US Nationwide Readmissions showed that the most common cause of a readmission after complex cancer surgery was infection (26.5%) followed by other GI complications (17.2%), respiratory conditions (9.5%), and dehydration/acute renal failure/electrolyte imbalances [46]. Other causes of readmission were reported in the literature regarding the post-surgery period,

however without specification if they were the reasons for readmission after hospital discharge. It included respiratory complications, cardiovascular complications, neurologic complications, renal complications, reoperation, blood transfusion, bowl reconstruction, thromboembolism, wound infection, sepsis, gastro-intestinal complications and hematological complications [20, 42, 44, 45].

We found significant heterogeneity and thus performed several subanalysis. The association between frailty and risk of readmission was lost when we pooled the data by severity of frailty, 30-day follow-up period and type of treatment. This surprising result can be explained, at least in part by the fact that frail patients have more complications and stay longer in the hospital to manage them [48]; and frail patients are at higher risk of short and long-term death [48, 49], which means that the total number of frail patients in risk of readmission is probably lower than the non-frail. When the same was performed for the type of frailty test, only frailty as defined by the Frailty Index had increased risk of readmission. This should not be interpreted as if Frailty Index is a good predictor of the risk of readmission because the 2 studies [3, 44] supporting that effect are from the same group and thus can be biased. Moreover, when stratification of data was performed by type of cancer, we observed that frail patients submitted to surgery because of digestive cancer (but not gynecologic) were at high risk. Future studies should address if these differences are due to cancer-specific issues (e.g. cachexia) or surgery-specific (e.g. caused by malabsorption of nutrients and dehydration) which are more prevalent in digestive cancers [50]. The greater risk of readmission in frail patients is also supported by prospective studies (which were mainly low-sample size) but not by retrospective studies. This can be explained by the fact that retrospective studies usually obtain their data through historical records and relevant information might be missing (leading to poor classification) or was introduced by different persons (leading to more subjectivity).

Limitations

There are few studies addressing the association of frailty and patient readmission after cancer surgery. In addition, the ones that exist only poorly reported the reasons for readmission.

CONCLUSIONS

Frailty was associated with a higher risk of readmission after cancer surgery. Special attention should be paid to patients with high risk factors, such as frail patients, during the postoperative follow-up and recovery periods.

Study 2: The Comparison of Prevalence and Agreement Between Different Frailty Assessment tools in Oncologic Patients

ABSTRACT:

Objectives: The aim of this study was to compare the prevalence and agreement between 5 widely used frailty instruments in patients with cancer undergoing surgery.

Methods: Patients with gastrointestinal cancer and head and neck cancer were recruited at the IPO-Porto. Frailty was assessed with the Vulnerability Elders Survey-13 (VES-13), Phenotypic Frailty (FP), 8 Foot up-and-go (8FuG), 5 m gait speed and the handgrip test to assess frailty. We compared the prevalence of frailty and the concordance between the different tests.

Results: We were able to recruit 166 patients, 53.3% of patients had gastrointestinal cancer and 46.7% head and neck cancer. Patients' mean age was 61.8±11.50 years old, and 77% (n=128) were male, mean weight was 69.1 ±15.84 kg and 5.3% were underweight, 35.5% were classified as pre-obese and 18.1% as obese. Frailty prevalence was 37.3%, 25.9%, 20.49.4% 8.2% as assessed by hand grip, VES-13, FP, 5m gait speed and 8 foot up and go, respectively. A small-moderate correlation and concordance was found between the instruments.

Conclusions: Different frailty instruments lead to different estimates of frailty and present little concordance even within the same population.

Keywords: FRAILTY, ONCOLOGIC PATIENTS, PREVALENCE, AGREEMENT

INTRODUCTION

For the majority of cancer types, the incidence and mortality by cancer increase as we age, with a tendency of leveling off in the very old ages [51, 52]. With the increase in life expectancy that our society is experiencing nowadays, it is anticipated that the overall incidence of cancer will continue to rise and will impose a significant burden [53]. According to the current projections, the number of older adults above the age of 65 years will double by 2050, leading to a nearly 50% increase in the annual cancer incidence [7]. Because surgery is the only curative option for solid cancers, particularly in early stage disease, it is also evident that the number of cancer patients requiring surgical treatment will increase. In 2015, from the 15.2 million individuals diagnosed with cancer worldwide, 80% required surgery, and this number is predicted to rise to 45 million by 2030 [7]. Despite the advances in surgical procedures and perioperative management, surgery is not free of risk for morbidity and mortality, particularly in the geriatric patient [7]. This often results in geriatric patients being refused surgery, as they are believed to be have poor tolerance to surgical stress and thus, to be at increased risk of postoperative morbidity and mortality [54]. However, it is becoming clear that older adults are very heterogeneous and the risk of adverse postoperative outcomes is not adequately described by chronological age, comorbidities, or the type of surgical procedure alone [55], which is traditionally used to assess the patient's "fitness" for surgery [1].

Frailty is increasingly recognized as a valuable measure for the preoperative assessment of patients submitted to surgery in different settings such as vascular [56], cardiac [57] orthopedic [58] and cancer [13]. This syndrome is characterized by a decline in the reserve of multiple physiological systems, decreasing tolerance to stresses such as disease or surgery, typically linked with advanced age, nevertheless younger patients can also be classified as frail [1]. More than 50% of geriatric cancer patients have pre-frailty or frailty and are at increased risk of chemotherapy intolerance, postoperative complications and mortality [13]. Of note, it has been demonstrated that frailty is a stronger predictor of postoperative outcomes compared with several classic surgical risk-assessment tools [14-16]. After determining the frailty status, the

clinician can provide a tailored intervention to optimize the patient before surgery, for instance through prehabilitation programs [59] and thus increase tolerance to surgical stress and reduce the occurrence of adverse outcomes [60-62].

Despite the negative consequences of frailty are well-established, clinicians will find tremendous difficulties when choosing an instruments as a gold standard measure of frailty does not exist and a wide range of frailty instruments are used [63]. Moreover, there are no consensus on which frailty assessment instrument is appropriate to a specific purpose (e.g. risk of morbidity and mortality), context (e.g. community, primary or secondary care, critical care) [64]. Importantly, there is scarcity of studies comparing the agreement between frailty instruments, which is fundamental to compare data from different studies and to facilitate the choice for future research or use in the clinical setting. This is very important as it has been shown that different instruments provide different frailty prevalence (and thus risk profile estimation) when tested in the same population [65, 66]. Thus, the purpose of this work was to compare the prevalence and agreement between 5 widely used frailty instruments in patients with cancer undergoing surgery: the Vulnerability Elders Survey-13 (VES-13), Phenotypic Frailty (FP), 8 Foot up-and-go (8FuG), 5 m gait speed and the handgrip test.

METHODS

Study design

This is an observational cross-sectional study.

Setting and participants

Participants were recruited at the Portuguese Oncology Institute of Porto (IPO-Porto), every Monday, in the Gastrointestinal and the Head and Neck wing, between December 2018 and June 2019. Data was collected in all the patients fulfilling our inclusion criteria that agreed to be a part of the study.

Inclusion criteria for patients was to be over 18 years old, to be diagnosed with cancer that required a surgery procedure and to be able to answer the questioners in Portuguese or English. Any patients not meeting the inclusion criteria were excluded from the study.

This work has been approved by the ethical committee of the IPO-Porto (Comissão de Ética Para a Saúde do Instituto Português de Oncologia do Porto Francisco Gentil, E.P.E. (Doc. CES-IPOP 03)), institution where it was developed and all the subjects gave their informed consent (Appendix I) and received an information sheet briefly explaining the study (Appendix II).

Measurements

Information regarding demographics (age, gender, education level, marital status), anthropometry [weight, height, body mass index (BMI)], and cancer type were collected (Apendix III). The weight was measured using a digital scale (Tanita Inner Scan BC 532), patients were asked to stand on the scale without shoes and coats, with help when necessary to get on the scale. Height was measured using a stadiometer (Seca 213), patients were placed with their backs to the stadiometer looking forward and the measures were checked twice, a third time if there was a difference between the two previous measurements. Body mass index was calculated using the weight and the height with the formula BMI

= kg/m^2, being kg the weight of the patient in kilograms and m^2 patient height in meters squared.

Frailty was assessed by different tools, including FP, VES-13, 8FuG, 5 m gait speed and the handgrip test. These tests have been previously validated in cancer patients [1], and have shown to predict risk of adverse health outcomes, post-operative complications and mortality outcomes [1, 63, 67, 68].

Frailty assessment

The Vulnerability Elders Survey-13

The vulnerability Elders Surgey-13, or VES-13, is a questionnaire divided into four categories to evaluate age, health auto-perception, physical impairment and disabilities. The questions involve the ability to perform specific activities including, crouching/kneeling, carrying heavy objects (approximately 5kgs), extending arms over shoulder level, precision to handle small objects, resistance to walk 500m, heavy housework chores and difficulties to perform daily tasks due to health concerns. Answers were scored 1 point due to impairments and a sum of the points resulting into a score ≥3 classified patients as "frail" [69]. This questionnaire was already validated for identification of frailty in our population [70] and was shown to predict risk of mortality, medical care institutionalization and disability [71].

8 Foot Up-and-go

This is a feasible test that has been used for oncologic and non-oncological patients [72]. The test consists of patients being timed, in seconds, from the moment they stand from a chair, walk 2.44m and return to the chair to sit back down. The patient is categorized as "frail" if spending ≥15s to perform the test, "pre-frail" if 11-14s and "robust" if ≤10s [72]. For the purpose of this study, "pre-frail" and "robust" were grouped to form the "non-frail" to allow comparison with other tests that only allow dichotomization of frailty.

Phenotypic Frailty

The phenotypic frailty assessment considers 5 domains (shrinking, weakness, exhaustion, gait speed and physical activity), evaluated as follows:

- **Shrinking:** unintentional weight loss of ≥ 4.5 Kg in prior year OR unintentional weight loss of at least 5% of previous year's body weight [73];
- **Weakness:** grip strength was assessed with a dynamometer (Takei 5401 Digital Dynamometer), adjusted for gender and body mass index; Each patient performed 3 measures, and the average of them was considered the patients final score, to be adjusted according to gender and body mass index (BMI). Thus, frailty should be considered for this criterion if [73]:
  - Men: BMI ≤ 24 and ≤29 Kg; BMI 24.1–26 and ≤30 Kg; BMI 26.1–28 and ≤30 Kg; BMI > 28 and ≤32 Kg
  - Woman: BMI ≤ 23 and ≤17 Kg; BMI 23.1–26 and ≤17.3 Kg; BMI 26.1–29 e ≤18 Kg; BMI > 29 and ≤21 Kg

- **Poor endurance and energy**: as indicated by self-report of exhaustion. Self-reported exhaustion, identified by two questions from the Centers for Epidemiologic Studies Depression (CESD) scale. Subjects were asked: How often in the last week did you feel like everything you did was an effort? How often in the last week did you feel like you cannot get going? Answers include: 0= rarely or none of the time (≤1 day), 1= some or a little of the time (1–2 days), 2= a moderate amount of the time (3–4 days), or 3= most of the time. Subjects answering “2” or “3” to either of these questions are categorized as frail by the exhaustion criterion [73];
- **Slowness:** Gait speed was assessed by measuring the time the patient took to complete a 5m course. Score was as follows [73]: Men Height ≤ 173 cm and time ≥ 7.14 s = 1; Men Height > 173 cm and time ≥ 6.57 s = 1; Woman Height ≤ 159 cm and time ≥ 7.14 s = 1; Woman > 159 cm and time ≥ 6.57 s = 1;

- **Low physical activity level:** A weighted score of kilocalories expended per week. Physical activity levels were obtained with the International Physical Activity Questionnaire short form (IPAQ-SF) [74]. Total energy expenditure (Kcal/week) was calculated as follows: time spent on each physical activity category (in hours) x corresponding MET value x weight (kg). Male subjects with total energy expenditure (kcal/week) ≤383 are classified as “frail”. Female subjects with total energy expenditure (kcal/week) ≤270 are classified as “frail” [73].

Frailty classification is performed according to the overall summation of deficits presented in the 5 domain as follows: “robust” if “0”, “pre-frail” if “1-2” and “frail” if “≥3” deficit [73]. The phenotypic frailty assessment has been validated and used in oncological setting, being a predictor of mortality and postoperative complications [75, 76].

Gait speed

Gait speed was assessed as part of the PF assessment (described above), but is also used as a single test to assess frailty [1] and was shown to be a good predictor of morbidity and mortality in older patients undergoing cardiac surgery [77].

Handgrip Test

Handgrip test was assessed as part of the PF assessment (described above), but is also used as a single test to assess frailty [1, 78, 79].

Statistical Methods

Statistical analysis was performed using the IBM SPSS 25 software (SPSS, USA). Normal data distribution was examined by the Kolmogorov-Smirnov test. Categorical data are reported as absolute values and percentages,

and continuous data as mean±standard deviation. Between gender comparisons were performed by independent t-test and chi-square test as appropriated. Pearson's correlation was used to analyze the relationship between frailty tools and Kappa Cohen for concordance analysis. Agreement was interpreted as poor, slight, fair, moderate or substantial, if Kappa value was 0.0, 0.20, 0.40, 0.60, 0.80 or 1.0, respectively [80]. Statistical significance was established for $p<0.05$.

RESULTS

Participants

We were able to recruit a total of 166 patients, 88 from gastrointestinal aisle and 77 from the head and neck aisle. The demographic characteristics are presented in **Table 1**. Patients' mean age was 61.8±11.50 years old, and 77% (n=128) were male. Overall, mean weight was 69.1 ±15.84 kg and, according to BMI, 5.3% were underweight, 35.5% were classified as pre-obese and 18.1% as obese.

Table 1: General characterization of the sample.

		Total (n=166)	**Men (n=128)**	**Women (n=38)**	**p**
Age (Years)		61.8 ±11.50	61.9 ±10.76	61.3 ±13.85	0.794
Weight (Kg)		69.3 ±15.27	69.1 ±15.84	69.9 ±13.37	0.803
Height (m)		1.64 ±0.07	1.66 ±0.06	1.56 ±0.06	**0.000**
BMI	<18,5	9 (5.4)	9 (100)	0 (0)	
	18.5 – 24.9	68 (41)	57 (83.8)	11 (16.2)	**0.001**
	25 - 30	59 (35.5)	47 (79.7)	12 (20.3)	
	>30	30 (18.1)	15 (50)	15 (50)	
Place_assessment, n (%)	Gastrointestinal	88 (53.3)	62 (70.5)	26 (29.5)	0.340
	Head and Neck	77 (46.7)	65 (84.4)	12 (15.6)	
Marietal_status, n (%)	Single	11 (6.7)	9 (81.8)	2 (18.2)	0.653
	Married	117 (71.3)	90 (76.9)	27 (23.1)	
	Divorced	17 (10.4)	14 (82.3)	3 (17.7)	
	Widow	17 (10.4)	11 (64.7)	6 (35.3)	
	Other	2 (1.2)	2 (100)	0 (0)	
Education, n (%)	Basic 1o	86 (52.1)	66 (76.7)	20 (23.3)	**0.020**
	Basic 2o	31 (18.8)	27 (87)	4 (13)	
	Basic 3o	14 (8.5)	11(78.5)	3 (21.5)	
	Secondary	16 (9.7)	13 (81.2)	3 (18.8)	
	No education	9 (5.5)	8 (88.8)	1 (11.2)	
	Higher Degree	9(5.5)	3 (33.3)	6 (66.7)	

M= metres; BMI= Body mass índex

Prevalence of individual frailty markers by frailty test

Table 2 shows the distribution of positive frailty markers on each domain of each instrument. Based on Fried's criteria, patients on the frail category had frequent weakness (37.3%), physical activity (42.8%), shrinking (36.7%), gait speed (9.4%) and exhaustion (22.9%). According to VES-13, frail patients mainly reported poor health auto-perception (45.8%) and physical impairment (35.5%). Age had the lowest prevalence of frailty (1.8%) and disabilities presented the second lowest (14.5%). The domain that had the least patient frailty was gait speed, 38.7% of frail patients on the Fried classification presented a low score for gait speed, the highest was weakness were 93.5% of frail patients had a low score on the weakness domain.

Table 2: Distribution of positive frailty markers.

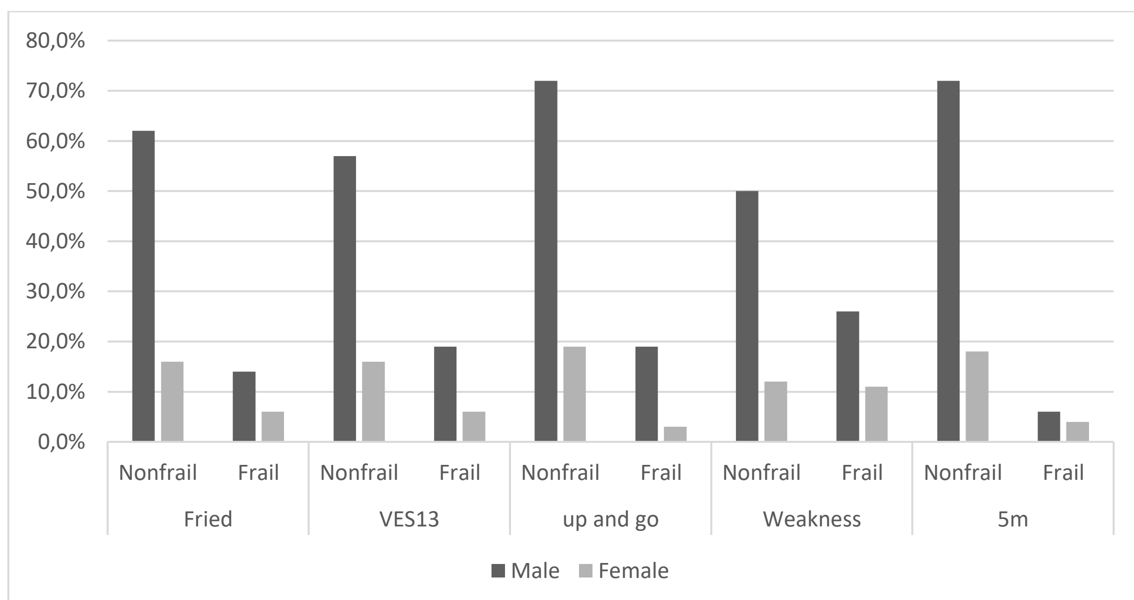
		Total (n,%)	Frail (n, %)	Non-frail (n,%)
Fried	Shrinking	61 (36.7)	25 (73.5)	36 (27.3)
	Weakness	53 (37.3)	29 (93.5)	24 (21.6)
	Exhaustion	38 (22.9)	21 (61.8)	17 (12.9)
	Gait speed	15 (9.4)	12 (38.7)	3 (2.3)
	Physical Activity	71 (42.8)	29 (85.3)	42 (31.8)
VES13	Age	3 (1.8)	2 (4.7)	41(95.3)
	Health auto-perception	76 (45.8)	35 (81.4)	8 (18.6)
	Physical Impairment	59 (35.5)	38 (88.4)	5 (11.6)
	Disabilities	24 (14.5)	24 (55.8)	19 (44.2)
8 Foot Up and go		13 (8.2)		

Ves-13=The Vulnerability Elders Survey; 5m= 5m Gait speed; Fried= Phenotypic Frailty test

Prevalence of frailty by frailty test

Figure 1 shows the prevalence of frail and non-frail patients by gender, according to each frailty definition. As it is possible to observe, the prevalence of frailty differed between each instrument, with frailty as defined by the handgrip presenting the highest prevalence (37.3% of patients), followed by VES-13 (25.9%), FP (20.4%), 5m gait speed (9.4%) and 8 foot up and go (8.2%). Frailty prevalence was men had a higher result than in woman, 14.5% of frail patients were men on Fried, while woman prevalence was 6%, on VES-13 19.3% of frail patients were men and 6.6% woman, Up and go 19% were man and only 3.8% were woman. The highest prevalence was on the Handgrip test, with 26.1% of frail patients were man and 11.3% woman and the lowest prevalence was on the 5m Gait speed, only 5.7% of patients were man and 3.8% woman were classified as frail, with a total of 9.5% of patients classified as frail.

Figure 1: Prevalence of frailty among different tools.



VES-13=The Vulnerability Elders Survey; 5m= 5m Gait speed; Fried= Phenotypic Frailty test; Weakness= Handgrip Test

Table 3: General patient's characteristics by frailty tool.

		Fried			Ves-13			Up and go			Handgrip			5m		
		Nonfrail	**Frail**	**p**	**Nonfrail**	**Frail**	**p**	**Nonfrail**	**Frail**	**p**	**Nonfrail**	**Frail**	**p**	**Nonfrail**	**Frail**	p
Total (n,%)		132 (79.5)	34 (20.5)		123 (74.1)	43 (25.9)		145 (91.8)	13 (8.2)		89 (62.7)	53 (37.3)		144 (90.6)	15 (9.4)	
Age (Years)		60.5 ±11.2	67.2 ± 11	**0.002**	59.7 ±10.6	67.7±11.9	**0.000**	60.2±10.5	78.4 ±7.6	**0.000**	59 ± 11.2	66.7 ± 11	**0.000**	60.6 ± 10.9	73.5±11.9	**0.000**
Weight (kg)		70.5 ±15.4	64.9 ±14.3	0.062	70.9 ±16.3	64.7±10.4	**0.005**	69.4±15.6	72.5±12.7	0.489	72.2±15.9	65 ±12.6	**0.006**	69.6 ± 15.5	67.1 ±13.4	0.559
Height (m)		1.65 ± 0.07	1.61 ± 0.08	**0.010**	1.65 ± 0.07	1.61 ±0.07	**0.010**	1.64 ±0.07	1.60 ±0.10	**0.042**	1.65 ±0.07	1.60 ±0.07	**0.000**	1.64 ±0.07	1.59 ±0.08	**0.006**
BMI (n,%)	**<18,5**	6 (3.6)	3 (1.8)		7 (4.2)	2 (1.2)		8 (5.1)	0 (0)		3 (2.1)	2 (1.4)		8 (5)	0 (0)	
	18,5 - 24,9	54 (32.5)	14 (8.4)		49 (29.5)	19 (11.4)		63 (39.9)	2 (1.3)		35 (24.6)	24 (16.9)		61 (38.4)	6 (3.8)	
	25 – 30	48 (28.9)	11 (6.6)	0.792	42 (25.3)	17 (10.2)	0.614	47 (29.7)	8 (5.1)	**0.011**	35 (24.6)	17 (12)	0.852	49 (30.8)	7 (4.4)	0.650
	>30	24 (14.5)	6 (3.6)		25 (15.1)	5 (3)		27 (17.1)	3 (1.9)		16 (11.3)	10 (7)		26 (16.4)	2 (1.3)	
Place of Assessment (n,%)	**Digestives**	70 (79.5)	18 (20.5)		67 (76.1)	21 (23.9)		75 (87.2)	11 (12.8)		45 (59.2)	31 (40.7)		75 (88.2)	10 (11.7)	
	Head and Neck	61 (79.2)	16 (20.8)	0.959	55 (71.4)	22 (28.6)	0.492	69 (97.1)	2 (2.9)	**0.024**	43 (66.1)	22 (33.9)	0.396	68 (93.1)	5 (6.9)	0.293
Marietal status (n,%)	**Single**	9 (5.5)	2 (1.2)		9 (5.5)	2 (1.2)		11 (7)	0 (0)		8 (5.7)	2 (1.4)		11 (7)	0 (0)	
	Married	96 (58.5)	21 (12.8)		93 (56.7)	24 (14.6)		109 (69.4)	6 (3.8)		70 (50)	33 (23.6)		108 (68.8)	6 (3.8)	
	Divorced	15 (9.1)	2 (1.2)		12 (7.3)	5 (3)		14 (8.9)	0 (0)		6 (4.3)	6 (4.3)		13 (8.3)	2 (1.3)	
	Widow	9 (5.5)	8 (4.9)	0.054	7 (4.3)	10 (6.1)	**0.014**	8 (5.1)	7 (4.5)	**0.000**	4 (2.9)	10 (7.1)	**0.017**	9 (5.7)	6 (3.8)	**0.000**
	Other	2 (1.2)	0 (0)		1 (0.6)	1 (0.6)		2 (1.3)	0 (0)		0 (0)	1 (0.7)		2 (1.3)	0 (0)	
Education (n,%)	**Basic 1o**	65 (39.4)	21 (12.7)		57 (34.5)	29 (17.6)		74 (47.1)	8 (5.1		42 (29.8)	31 (22)		72 (45.6)	9 (5.7)	
	Basic 2o	26 (15.8)	5 (3)		26 (15.8)	5 (3)		29 (18.5)	1 (0.6)		22 (15.6)	7 (5)		30 (19)	1 (0.6)	
	Basic 3o	10 (6.1)	4 (2.4)		14 (8.5)	0 (0)		13 (8.3)	0 (0)		5 (3.5)	7 (5)		13 (8.2)	0 (0)	
	Secondary	14 (8.5)	2 (1.2)		12 (7.3)	4 (2.4)		15 (9.6)	0 (0)		9 (6.4)	3 (2.1)	0.177	14 (8.9)	1 (0.6)	**0.005**
	No education	7 (4.2)	2 (1.2)	0.456	5 (3)	4 (2.4)	**0.015**	5 (3.2)	3 (1.9)	**0.013**	5 (3.5)	3 (2.1)		5 (3.2)	4 (2.5)	
	Higher Degree	9 (5.5)	0 (0)		9 (5.5)	0 (0)		9 (5.7)	0 (0)		6 (4.3)	1 (0.7)		9 (5.7)	0 (0)	

Ves-13= The Vulnerability Elders Survey; 5m= 5m Gait speed; Fried= Phenotypic Frailty test; BMI= Body mass index

Characterization of the sample by frailty level

Table 3 shows the general characteristics of the sample by frailty level, as assessed by each instrument. On the handgrip test 29 patients weren't able to do the test, either due to problems with the handgrip dynamometer or to physical difficulty. 12 patients weren't able to complete the 5m test and 13 the up and go test due to mobility difficulty, and 5 patients didn't complete the Fried or VES-13 test. The total of frail patients varied from 13 (8.2%), on the Up and go, to 53 (37.3%) on the Handgrip test. Lowest BMI scores for frail patients were found on Fried, with only 3 (1.8%) frail patients presented a low BMI, while the highest BMI results, classifying patients as obese, was found on the handgrip test, were 10 (7%) of patients were frail. The highest number of frail patients for both cancer types were classified as frail on the handgrip test, 31 (40.7%) of digestive patients were classified as frail and 22 (33.9%) of head and neck cancer patients were classified as frail.

Relationship between different frailty tools

The bivariate correlation between frailty tools was analyzed with the Pearson correlation (**Table 4)**. No test had a strong positive correlation, but all had a significant correlation, the strongest correlations were between Fried and the Handgrip test and the 5m and the Up and go, both with r = 0.673.

Table 4: Bivariate correlation between frailty instruments.

	Fried		**VES- 13**		**Up and go**		**Handgrip**	
	r	p	r	p	r	p	r	p
VES-13	0.292	**0.000**						
Up and go	0.318	**0.000**	0.441	**0.000**				
Handgrip	0.673	**0.000**	0.176	**0.036**	0.363	**0.000**		
5m	0.421	**0.000**	0.374	**0.000**	0.673	**0.000**	0.384	**0.000**

r = Pearson correlation; Ves-13 The Vulnerability Elders Survey; 5m= 5m Gait speed; Fried= Phenotypic Frailty test

The Kappa Cohen was used to measure the agreement between the different frailty tools, as shown in **Table 5**. All tests had a significant result, Fried had a moderate agreement with the handgrip test and with the 5m, indicating a moderate similarity between patient frail classification. All the other analyses presented a weak agreement between, showing a low similarity between the results, suggesting that different patients were classified as frail when using different instruments.

Table 5: Agreement between frailty instruments.

	Fried		**VES- 13**		**Up and go**		**Handgrip**	
	K	p	K	p	K	p	K	p
VES-13	0.209	**0.007**						
Up and go	0.142	**0.000**	0.153	**0.000**				
Handgrip	0.573	**0.000**	0.165	0.360	0.090	**0.001**		
5m	0.452	**0.000**	0.324	**0.000**	0.350	**0.000**	0.281	**0.000**

K=kappa coefficient; Ves-13= The Vulnerability Elders Survey; 5m= 5m Gait speed; Fried= Phenotypic Frailty test

DISCUSSION

The purpose of this work was to compare the prevalence and agreement between 5 widely used frailty instruments in patients with cancer undergoing surgery: the Vulnerability Elders Survey-13 (VES-13), Phenotypic Frailty (FP), 8 Foot up-and-go (8FuG), 5 m gait speed and the handgrip test. Our data suggest that prevalence of frailty varied widely between these instruments, and their agreement was limited.

Despite the advances in surgical procedures and perioperative management, surgery is not free of risk for morbidity and mortality, particularly in the geriatric patient [1, 3, 7]. frailty is a stronger predictor of postoperative outcomes compared with several classic surgical risk-assessment tools [14-16]. Despite that, as a gold standard measure of frailty does not exist, there are several instruments available and each instrument has its upside and downsides features, which might be an obstacle in terms of deciding which should be used for what. The data from our study shows that the choice of the instrument is not straightforward, as frailty prevalence ranged from 8.2 to 37.3% depending on the assessment tool. This notion is in accordance with the results from other authors who showed similar findings with these and other instruments [65, 66]. [4, 71]. This is a concern that needs to be taken into account when basing clinical decisions on frailty assessment, as it may lead to inaccurate risk profile estimation.

In addition, we showed that VES-13, FP, 8FuG, 5 m gait speed and the handgrip test had poor correlation and agreement. This limited agreement has also been confirmed by other studies comparing different frailty tools but some showed positive results. For instance, the Balducci frailty criteria, Fried and VES-13 had poor concordance also with oncologic patients [81] while low-moderate agreement was reported in relation to FP, the Frailty Index and with the 5m Gait speed in geriatric patients in primary care [4]. However a moderate-strong correlation and a close agreement was between Fried, the Deficit Index, the Edmonton frailty, the clinical frailty scale, the Derby frailty index and the acute frailty network frailty criteria, in patients with chronic heart failure, indicating that

though each assessment method consists of different components, they can result into a common outcome [82]. The difference between these and the previous studies could be due to the assessment tools analyzed, sample size, different clinical populations. Thus, more than adding new frailty scales to the existing one, it will be important to test agreement of the existing ones, understand the factors underlying such discrepancies. Importantly, it is mandatory to compare their diagnostic accuracy for specific adverse outcomes, which need to be the point of reference when defining the standard instrument.

Limitations, strengths, and future perspectives

This is a single-center study conducted in IPO-Porto with a limited sample size for each cancer type, an external validation from other populations with a different health care system could be useful to improve the analyses. Data was collected exclusively on Mondays, limiting the extrapolation of our data to other patients with same cancer type treated in IPO-Porto. Also, only a small percentage of participants were female. Due to time constrains of finishing this work, we were unable to collect information regarding risk factors, comorbidities, location of cancer and its severity, which has to be collected by hand on physical files. Despite these limitations, this is to our knowledge the first study to compare FP, Ves-13, Up and go, 5m Gait speed and Handgrip test, in the same population of cancer patients for head and neck and gastrointestinal cancer. Further studies are needed to compare the frailty classification with other tools, perform patient follow-up to record different adverse outcomes and check which tools had better prediction agreement for that specific outcome. If accuracy and agreement can be found between a single-item test and complex / time-consuming tool, it will eventually be an optimal option for hospital implementation.

CONCLUSION

Our results suggest that Fried, VES-13, 5m gait speed, Up and go and Handgrip categorize different patients as frail or non-frail. This finding emphasizes the need for consensus on the definition of frailty, requiring further work to optimize the choice of frailty tool.

Conclusion

Cancer patients have a decrease in physiological reserve, making frailty an important factor to determine the increased risk of adverse outcomes.

The results of our systematic review and meta-analysis suggest that:

1) Frail cancer patients submitted to surgery are at higher risk of unplanned readmission;
2) This association is also made for readmission with a longer follow-up period and cancer type.
3) No association was found for frailty and risk of readmission with severity of frailty, 30 day follow-up period and type of treatment.

The results of our cross-sectional study suggest that:

1) Frailty prevalence ranges widely according to the frailty instrument within the same population;
2) There was a poor agreement between the different frailty tools, indicating that different methods select different patients as frail, highlighting that care should me made when taking decisions based on a specific instrument.

Further studies need to be done to define a gold standard tool, which will probably be case and context-specific.

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Appendices

Appendix I. Patient Consent form

Consentimento Informado

Considerando a "Declaração de Helsínquia", da Associação Médica Mundial
(Helsínquia 1964; Tóquio 1975; Veneza 1983; Hong Kong 1989; Somerset West 1996; Edimburgo 2000; Washington 2002, Tóquio 2004 e Seoul, 2008)

Designação do estudo / projeto de investigação (em português)

"Estudo dos mecanismos moleculares subjacentes ao acastanhamento do tecido adiposo branco induzido pelo cancro e do impacto do estilo de vida"

Eu, abaixo-assinado (nome completo do doente adulto ou do voluntário são) ____________________

____

Recebi o texto de *Informação ao Participante* relativo ao procedimento que concordei em efetuar. Compreendi a explicação que me foi fornecida pelo investigador que assina este documento. Foi-me ainda dada oportunidade de fazer as perguntas que julguei necessárias, e de todas obtive resposta satisfatória.
Tomei conhecimento de que, de acordo com as recomendações da Declaração de Helsínquia, a informação ou explicação que me foi prestada versou os objetivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto. Além disso, foi-me afirmado que tenho o direito de anular a todo o tempo a minha participação no estudo, sem que isso possa ter como efeito qualquer prejuízo na assistência que me é prestada.

Por isso, consinto que me seja aplicado o método, o tratamento ou o inquérito proposto pelo investigador.

Assinatura do doente ou voluntário são:____ *Data:___/___/201_*

Nome do Investigador responsável: Lúcio Lara Santos

Assinatura do Investigador:____ *Data:___/___/201_*

Anulação do Consentimento Informado

Declaro que recebi a *Informação ao Participante* relativo ao estudo / projeto de investigação em questão, que me foi proposto pelo investigador que assina este documento e **pretendo anular** o consentimento dado na data ____/____/201___.

Assinatura do doente ou voluntário são:____ Data:___/___/201_

Assinatura do Investigador responsável:_____________________________________ Data:___/___/201_

Nota: Fornecimento obrigatório de cópia ao participante

Comissão de Ética Para a Saúde do Instituto Português de Oncologia do Porto Francisco Gentil, E.P.E. (Doc. CES-IPOP 03)

Appendix II. Patient Information

FOLHA DE INFORMAÇÃO AO PARTICIPANTE

Qual o propósito deste estudo?

A fragilidade é uma condição caracterizada por diminuição da reserva fisiológica do organismo, que predispõe o indivíduo a um maior risco de complicações e mortalidade pós-cirúrgica. A identificação do instrumento de diagnóstico de fragilidade com maior capacidade discriminativa do prognóstico irá auxiliar a tomada de decisão sobre o tratamento cirúrgico e permitirá identificar os indivíduos frágeis que mais beneficiarão de programas de reabilitação/preparação pré-cirúrgica. Assim, o presente estudo tem como objetivo melhorar a determinação do risco cirúrgico, através da avaliação do nível de fragilidade e aptidão física. O estudo foi apresentado e aprovado pelo CES-IPO Porto (projeto n.º 193/016).

O que acontece se aceitar participar no estudo?

Os indivíduos que aceitarem participar no estudo serão submetidos a um conjunto de avaliações (testes físicos e preenchimento de questionários) que visam recolher informação sobre aspetos relacionados com a condição física, psicológica e nutricional. Para além disso, poderá ser realizada uma simples colheita de sangue venoso, sendo que o eventual desconforto poderá ser minimizado pelo facto de ser efectuada por pessoal de enfermagem treinado e experiente nesse procedimento. Finalmente, será fornecido e colocado um pequeno aparelho de uso diário, durante uma semana, com o objetivo de avaliar o movimento corporal.

Quanto tempo demoram as avaliações? Tem custos associados?

A realização da totalidade das avaliações não deverá ultrapassar os 30 minutos e será feita somente numa sessão, sem necessidade de consultas extra, exames complementares ou deslocações. A realização das avaliações é completamente gratuita, não havendo qualquer custo adicional.

Como será utilizada a informação recolhida?

A informação recolhida será posteriormente analisada para avaliar o nível de fragilidade ou robustez de cada participante. A performance obtida nas avaliações será

1

combinada com os dados da sua recuperação pós-cirúrgica, permitindo assim identificar as variáveis mais discriminativas do prognóstico pós-cirúrgico. Todos os dados recolhidos são anónimos e confidenciais e serão trabalhados estatisticamente a nível colectivo e nunca individual.

A participação no estudo implica algum risco?

Os riscos de participação neste estudo são mínimos, já que os procedimentos são simples e com supervisão e monitorização adequada por profissionais qualificados.

O que acontece se optar por não participar no estudo?

A participação neste estudo é totalmente voluntária. Assim sendo, poderá optar por não participar, sem qualquer penalização nos cuidados médicos que lhe são prestados e nos seus direitos legais, e sem qualquer obrigação de justificação.

De seguida, ser-lhe-á apresentado o Consentimento Informado, documento que indica que aceita participar no estudo, devendo ser assinado por ambas as partes e que ficará na posse do investigador.

Se aceitar participar neste estudo, por favor, assine este documento e guarde-o para si. Para qualquer questão ou se quiser tomar conhecimento dos resultados globais do estudo, deverá contactar o investigador através dos seguintes contactos:

- llarasantos@gmail.com
- +351 225 084 000

Appedix III. Questionnaires and Patient characteristics

DADOS SOCIODEMOGRÁFICOS

NOME: ______________________________ ID: ______________

DATA:____________________IDADE:__________ SEXO: ( ) FEMININO ( ) MASCULINO

ESTADO CIVIL: ( ) Solteiro ( ) Casado ( ) Divorciado ( ) Viúvo ( )

Outro:_____________

NÍVEL DE ESCOLARIDADE: ________________________________

DADOS DA COMPOSIÇÃO CORPORAL

ESTATURA (cm): _____________ PERCENTAGEM ÁGUA (%): ____________

PESO (Kg): __________________ MG (%):__________

PERDEU PESO NO ULTIMO ANO? ( ) S ( ) N Se sim, quantos quilos? ______________

TESTES FUNCIONAIS				
TESTES	1ª AVAL.	2ª AVAL.	3ª AVAL.	MÉDIA
SENTAR E LEVANTAR 30 segundos máx. de repetições		X	X	X
SENTAR E ALCANÇAR Alcançar a ponta do pé e sustentar por 2 seg. Caso não alcance o valor será negativo. Membro dominante				
FLEXÃO DE ANTEBRAÇO Mão dominante. Máximo de repetições 30s. Virar a mão durante execução.		X	X	X
LEVANTAR DA CADEIRA, CAMINHAR E VOLTAR A SENTAR 2,44 metros; Anotar tempo total do percurso.		X	X	X
FORÇA DE PREENSÃO MANUAL Mão dominante. 3x caso os 2 primeiros valores sejam diferentes.				
ALCANÇAR ATRÁS DAS COSTAS Alcançar mão atras das costas. Caso não alcance os valores serão negativos.				
VELOCIDADE DA MARCHA 5 METROS		X	X	X
STEP- 2MIN				

Levou acelerómetro? Sim (___) **ID do AC: _______________;**
Não (____)

Contacto: _________________________
Morada:
____
____

1

PROTOCOLO DE IDENTIFICAÇÃO DA VULNERABILIDADE (VES-13)

IDADE

1 – Qual é a sua idade? ___________

AUTOPERCEÇÃO DA SAÚDE

2 – Comparando com outras pessoas da sua idade, como é a sua saúde?

( ) Ruim
( ) Regular
( ) Boa
( ) Muito boa
( ) Excelente

LIMITAÇÕES FÍSICAS

3 – Que dificuldade tem para curvar-se, agachar-se ou ajoelhar-se?

( ) Nenhuma dificuldade
( ) Pouca dificuldade
( ) Alguma dificuldade
( ) Muita dificuldade
( ) Não consegue fazer

4 – Que dificuldade tem para levantar ou carregar objetos com peso de cerca 5kg?

( ) Nenhuma dificuldade
( ) Pouca dificuldade
( ) Alguma dificuldade
( ) Muita dificuldade
( ) Não consegue fazer

5 – Que dificuldade tem para levantar os braços ou chegar a objetos acima do nível do ombro?

( ) Nenhuma dificuldade
( ) Pouca dificuldade
( ) Alguma dificuldade
( ) Muita dificuldade
( ) Não consegue fazer

6 – Que dificuldade tem para escrever, manusear ou agarrar objetos pequenos?

( ) Nenhuma dificuldade
( ) Pouca dificuldade
( ) Alguma dificuldade
( ) Muita dificuldade
( ) Não consegue fazer

7 – Que dificuldade tem para caminhar 400 metros?

( ) Nenhuma dificuldade
( ) Pouca dificuldade
( ) Alguma dificuldade
( ) Muita dificuldade
( ) Não consegue fazer

8 – Que dificuldade tem para realizar tarefas domésticas pesadas, como esfregar o chão, lavar janelas ou carregar lenha?

( ) Nenhuma dificuldade
( ) Pouca dificuldade
( ) Alguma dificuldade
( ) Muita dificuldade
( ) Não consegue fazer

INCAPACIDADES

9 – Por causa da sua saúde ou condição física tem alguma dificuldade para comprar itens de uso pessoal (como produtos de higiene ou medicamentos)?

( ) SIM. Precisa de ajuda para fazer compras? ( ) SIM ( ) NÃO
( ) NÃO
( ) NÃO FAZ. Por motivos de saúde? ( ) SIM ( ) NÃO

10 – Por causa da sua saúde ou condição física tem alguma dificuldade para lidar com dinheiro (como controlar os gastos ou pagar contas)?

( ) SIM. Precisa de ajuda para lidar com o dinheiro? ( ) SIM ( ) NÃO
( ) NÃO.
( ) NÃO FAZ. Por motivos de saúde? ( ) SIM ( ) NÃO

11 – Por causa da sua saúde ou condição física tem alguma dificuldade para caminhar dentro de casa?

( ) SIM. Precisa de ajuda para caminhar (além da bengala ou andarilho)? ( ) SIM ( ) NÃO
( ) NÃO.
( ) NÃO FAZ. Por motivos de saúde? ( ) SIM ( ) NÃO

12 – Por causa da sua saúde ou condição física tem alguma dificuldade para fazer trabalho doméstico leve (como lavar a louça, arrumar a casa ou limpeza leve)?

( ) SIM. Precisa de ajuda com as tarefas domésticas leves? ( ) SIM ( ) NÃO
( ) NÃO.
( ) NÃO FAZ. Por motivos de saúde? ( ) SIM ( ) NÃO

13 – Por causa da sua saúde ou condição física tem alguma dificuldade para tomar banho?

( ) SIM. Precisa de ajuda para tomar banho? ( ) SIM ( ) NÃO
( ) NÃO.
( ) NÃO FAZ. Por motivos de saúde? ( ) SIM ( ) NÃO

AVALIAÇÃO DO NIVEL DE ATIVIDADE FÍSICA (IPAQ-VERSÃO CURTA)

Para responder as perguntas pense somente nas atividades que você realiza **por pelo menos 10 minutos contínuos** de cada vez.

Este questionário inclui questões sobre a atividade física que realiza habitualmente para se deslocar de um lado para o outro, no trabalho, nas atividades domésticas (femininas ou masculinas), na jardinagem e nas atividades que efetua no seu tempo livre para entretimento, exercício ou desporto. As questões referem-se à atividade física que realiza numa semana normal, e não em dias excecionais, como por exemplo, no dia em que fez a mudança da casa ou em dias de férias.

Ao responder às seguintes questões considere o seguinte:

Atividades físicas VIGOROSAS são aquelas que precisam de um GRANDE esforço físico e tornam a respiração MUITO mais intensa que o normal;
Atividades físicas MODERADAS são aquelas que requerem ALGUM esforço físico e que tornam a respiração um POUCO mais intensa que o normal.

Para responder as perguntas considere apenas as atividades que realiza durante pelo menos **10 minutos seguidos**.

1a Na última semana, quantos **dias** efetuou atividade física **vigorosa** como levantar ou transportar objetos pesados, cavar, fazer ginástica, correr nadar, jogar futebol ou andar de bicicleta a uma velocidade acelerada?

Dias _____ por SEMANA
( ) Nenhum (passe à questão 2a)

1b Quanto **tempo** no total despendeu num desses dias a realizar atividade física **vigorosa**?

Horas: ______ Minutos: _____

2a. Durante a última semana, quantos **dias** efetuou atividades físicas **moderadas** como levantar e/ou transportar objetos leves, andar de bicicleta a uma velocidade moderada, atividades domesticas (ex.: limpar, aspirar), cuidar do jardim, fazer trabalhos de carpintaria, jogar ténis de mesa? Não inclua andar/caminhar.

Dias _____ por SEMANA
( ) Nenhum (passe à questão 3a)

2b. Quanto **tempo** no total despendeu num desses dias a realizar atividade física **moderada**?

Horas: ______ Minutos: _____

3a Durante a última semana, quantos dias **andou/caminhou** durante pelo menos 10 minutos seguidos? Inclua caminhadas para o trabalho e para a casa, para se deslocar de um lado para o outro e qualquer outar caminhada que possa fazer somente para recreação, lazer ou desporto.

Dias _____ por SEMANA
( ) Nenhum (passe à questão 4a)

3b Quanto **tempo** no total despendeu num desses dias a andar/caminhar?

Horas: ______ Minutos: _____

Estas últimas questões referem-se ao tempo que permanece sentado diariamente, no percurso para o trabalho, no trabalho, na escola ou faculdade, em casa e durante os tempos livres. Isto inclui o tempo sentado à mesa ou secretária, sentado a ler, sentado enquanto descansa, sentado enquanto visita um amigo, ou sentado/deitado a ver TV. Não inclua o tempo gasto sentando durante o transporte.

4a. Quanto **tempo,** no total, passou sentado(a) durante um dos dias de semana (segunda-feira a sexta-feira)?

______horas ____minutos

4b. Quanto **tempo,** no total, passou sentado(a) durante um dos dias do fim-de-semana (sábado ou domingo)?

______horas ____minutos

CENTER FOR EPIDEMIOLOGIC STUDIES DEPRESSION SCALE (CES-D), NIMH

Durante a semana passada:

Sentiu que tudo o que fazia era esforço?
( ) Nunca ou muito raramente (menos de 1 dia)
( ) Ocasionalmente (1 ou 2 dias)
( ) Com alguma frequência (3 ou 4 dias)
( ) Com muita frequência ou sempre /5 ou 7 dias)

Sentiu falta de energia?
( ) Nunca ou muito raramente (menos de 1 dia)
( ) Ocasionalmente (1 ou 2 dias)
( ) Com alguma frequência (3 ou 4 dias)
( ) Com muita frequência ou sempre /5 ou 7 dias)

DISTRESS: _____________

Muito obrigado pela colaboração!