



Identification of Frailty in Geriatric Oncologic Patients

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KEYWORDS: FRAILITY; GERIATRIC; CANCER; COMPARISON; TOOLS.

Abstract

Introduction: Frailty has been recognized in the oncologic field due its predictive capacity for poor postoperative outcomes in aged patients. Despite the large number of available instruments, there is currently no consensus of which one should be used as the gold standard. The aim of this study was to analyze the agreement between different tools commonly used to evaluate frailty, in older patients with head and neck cancer and digestive cancer.

Methods: Geriatrics patients with ≥ 65 years old and elected for surgery were enrolled at the IPO-Porto, after signed consent. The patients were evaluated with the following frailty tools: Fried phenotype (FP), Vulnerable Elders Survey (VES-13) and the physical tests 8-Foot Up and Go (8FUG), Handgrip Strength (HS) and 5-Meter Walk Test scores (5-mWT). Continuous data were expressed as mean and categorical data as % (n). T-test and Chi-square Test were used for continuous and nominal variables with normally distributed data, respectively. Spearman's correlation coefficient was calculated to assess the relationship between the frailty tools and the agreement was tested with Kappa coefficient.

Results: Sixty-three patients (73.7 ± 6.4 years; 67.7 ± 11.3 kg and 1.62 ± 0.1 meter; 73.0% men; 60.3% digestive cancer) were assessed. The prevalence of frailty ranged according to the tool: 68.3% (n=43) with 8FuG, 47.6% (n=30) with HS, 28.6% (n=18) with FP, 15.9% (n=10) with VES-13 and 14.3% (n=9) with 5mWT. The 5mWT had the greatest correlation with the other tools, ranging from 0.28 (for 8FUG) to 0.49 (for FP). The FP showed a moderate agreement with 5mWT ($K=0.417$; $p=0.0001$) and fair agreement with VES-13 ($K=0.372$; $p=0.002$) and HS ($K=0.371$; $p=0.0001$). Also, VES-13 presented fair agreement with the 5mWT ($K=0.357$; $p=0.001$).

Conclusion: According to our data, frailty prevalence is highly dependent on the tool and the agreement between them is limited. In the absence of a gold standard tool, care should be taken when using frailty status to support clinical decision.

Keywords: Frailty; Geriatric; Cancer; Comparison; Tools.

Resumo

Introdução: A fragilidade tem sido reconhecida no campo oncológico devido à sua capacidade preditiva de desfechos pós-operatórios em pacientes idosos. Apesar do grande número de instrumentos disponíveis, atualmente não há consenso sobre qual deles deve ser usado como padrão-ouro. O objetivo deste estudo foi analisar a concordância entre diferentes ferramentas comumente usadas para avaliar a fragilidade, em pacientes idosos com câncer de cabeça e pescoço e câncer digestivo.

Métodos: Pacientes idosos com idade ≥ 65 anos e eleitos para cirurgia foram incluídos no IPO-Porto, após consentimento assinado. Os pacientes foram avaliados com as seguintes ferramentas de fragilidade: Fenótipo de Fried (FP), Protocolo de Vulnerabilidade (VES-13) e os testes físicos 8-Foot Up and Go (8FUG), Força de Preensão Manual (HS) o Teste de Caminhada de 5 metros (5-mWT). Os dados contínuos foram expressos em média e os categóricos em % (n). O Teste-T e Qui-quadrado foram utilizados para variáveis contínuas e nominais com dados normalmente distribuídos, respectivamente. O coeficiente de correlação de Spearman foi calculado para avaliar a relação entre as ferramentas de fragilidade e a concordância com o coeficiente Kappa.

Resultados: Sessenta e três pacientes (73.7 ± 6.4 anos; 67.7 ± 11.3 kg e 1.62 ± 0.1 metro; 73.0% homens; 60.3% câncer digestivo) foram avaliados. A prevalência de fragilidade variou de acordo com a ferramenta: 68.3% (n=43) com 8FuG, 47.6% (n=30) com HS, 28.6% (n=8) com FP, 15.9% (n=10) com VES- 13 e 14.3% (n=9) com 5mWT. O 5mWT teve a maior correlação com as demais ferramentas, variando de 0.28 (para 8FUG) a 0.49 (para FP). O FP mostrou concordância moderada com 5mWT ($K=0.417$; $p=0.0001$) e concordância fraca com VES-13 ($K=0.372$; $p=0.002$) e HS ($K=0.371$; $p=0.0001$). Além disso, o VES-13 apresentou concordância fraca com o 5mWT ($K=0.357$; $p=0.001$).

Conclusão: De acordo com nossos dados, a prevalência de fragilidade é altamente dependente da ferramenta e o acordo entre eles é limitado. Na ausência de uma ferramenta padrão-ouro, deve-se tomar cuidado ao usar o status de fragilidade para apoiar a decisão clínica.

Palavras-chave: Fragilidade; Geriátrico; Câncer; Comparação; Ferramentas.

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Abbreviations List

IL-6 – Interleukin 6
CRP – C-reactive protein
TNF- α – Tumor Necrosis Factor- α
5-mWT – 5-meters Walk Test
CFS – Clinical Frailty Scale
CAF – Comprehensive Assessment of Frailty
EFS – Edmonton Frailty Scale
GFM – Gill Frailty Measure
GI – Green Index
HS – Handgrip Strength
FP – Fried Phenotype
CGA – Comprehensive Geriatric Assessment
FI – Frailty Index
VES-13 – Vulnerable Elders Survey
TUG – Time Up and Go
8-FUG – 8-Foot Up and Go
BMI – Body Mass Index
GFI – Gronigen Frailty Index
BFC – Balducci Frailty Criteria
TRST – Triage Risking Screening Tool
G8 – Geriatric 8
SAOP – Senior Adult Oncology Program
SIOG1 – Society of Geriatric Oncology 1
SOF – Study Osteoporotic Fracture
IPO – Instituto Português de Oncologia do Porto

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1 Introduction

Aging is a non-modifiable risk factor for the emergence of diseases, including some cancers, increasing the number of cases and victims worldwide (de Magalhaes, 2013). Besides being the second leading cause of death worldwide (United Nations, 2017), by 2030, there is a projection that 70.0% of all cancers will occur among individuals 65 years and older (White et al., 2014). Currently, among all types of cancer treatments, surgery is the one that presents the best results in relation to solid tumors, providing in many cases the cure (Morgan, Ward, & Barton, 2004). However, surgery is not free of adverse effects, such as postoperative complications, which increase the risk of mortality, morbidity, length of hospitalization, post-discharge special care and delays subsequent treatments (Ferraris, Bolanos, Martin, Mahan, & Saha, 2014; Merkow et al., 2013; Tevis & Kennedy, 2013; Vester-Andersen et al., 2014). This huge burden is even more dramatic in elderly cancer patients have the worst postoperative prognosis (De Angelis et al., 2014). Because of this scenario, medical and research professionals have been working to understand and identify the risk factors for these complications, including the development of risk prediction scales, with the intention of selecting patients for surgery. The concept of frailty gained great relevance on this field as it seems to better differentiate patients who should benefit or not from surgical intervention (Bongue et al., 2017). Although there is no consensus on the definition of frailty, there is agreement that this is a multidimensional syndrome in which there is a state of increased vulnerability to stresses, that is detrimental to health, but this state is dynamic and thus potentially reversible. So, its identification is of utmost importance in medical care (Morley et al., 2013). Indeed, the assessment of frailty has shown interesting results in risk stratification in elderly patients, and the classification of "frail" is associated with a significant increase in the risk of postoperative mortality and morbidity, as well as length of hospitalization, which compromises the patient's quality of life and entails high costs for the health system and high resource consumption (Handforth et al., 2015; Joseph et al., 2014; Makary et al., 2010). However, there are more than 70 tools for assessing

frailty, each with its own advantages and disadvantages, and there is no consensus on which is best for a specific purpose or condition (Buta et al., 2016). Moreover, it can be noted that the prevalence of frailty in a given population sample varies depending on the tool that was used (Vermeiren et al., 2016; Walston et al., 2017) which poses a challenge in the comparison of studies or to on its use in clinical practice to support decisions. Additionally, the predictive accuracy for postoperative adverse events of most frailty tools has not yet been tested and/or compared (Bongue et al., 2017). Therefore, before one can advocate for the clinical utility of any particular tool, it is necessary to answer these questions.

Based on this rationale, the purpose of this study is to test the agreement of 5 frailty tools (Fried Phenotype, Vulnerable Elders Survey, 8-Foot Up and Go, 5-Meters Walk Test and Handgrip Strength) in cancer patients. To accomplish this, we will first present the background around aging, cancer, frailty in the surgical setting and prehabilitation. This will be followed by a cross-sectional study with oncologic geriatric patients with head-neck and digestive cancer.

2 Background

2.1 Aging and Cancer Burden

Due to the demographic transition, the population age pyramid has experienced a global transformation, with more and more people reaching more advanced ages. As the elderly population grows 3.0% each year, it is estimated that by 2050 there will be approximately 2.1 billion elderly people in the world, with individuals aged 60 or over representing at least 25% of the population in all regions of the world, except in Africa (United Nations, 2017). It was estimated that the worldwide number of people with 60 years or more in 2017 was 962 million and it is expected that by 2050 there will be around 425 million people with 80 or more (United Nations, 2017). Europe was the first region where this transformation started during the nineteenth and twentieth centuries. Nowadays, Europe has one of the oldest populations in the world, with 25 % of their individuals with more than 60 or above (United Nations, 2017). In Portugal, the ageing index shows a rise from 27.5% in 1961 to 157.4% in 2018, with the 3th highest value between the European countries (FFMS, 2019). Increased longevity is in part explained by the overall improvements in terms of disease prevention and treatment (United Nations, 2017).

Aging is considered one the most important non-modifiable risk factors for the development of chronic diseases, such as cardiovascular, neurodegenerative, metabolic diseases and some types of cancer (Blagosklonny, 2013). Specifically cancer, it is thought to be the second leading cause of death in the population, estimated to have caused more than 9.5 million deaths worldwide in 2018 as shown in **Figure 1** (WHO, 2018a). Portugal had almost 29.000 deaths because of cancer in 2018, with a risk of dying of 10.6% before the 75 years (WHO, 2018b). Cancer is characterized by the unbridled development and spread of cells that can occur in practically any part of the body, surrounding the tissue and able to metastasize to the remaining parts (WHO, 2019b). Although cancer can occur at all ages, epidemiological data support a higher prevalence in the elderly population, with 56.0% of cancer diagnoses and

71.0% of cancer mortality occurring over 65 years old (de Magalhaes, 2013; Ghignone et al., 2016).

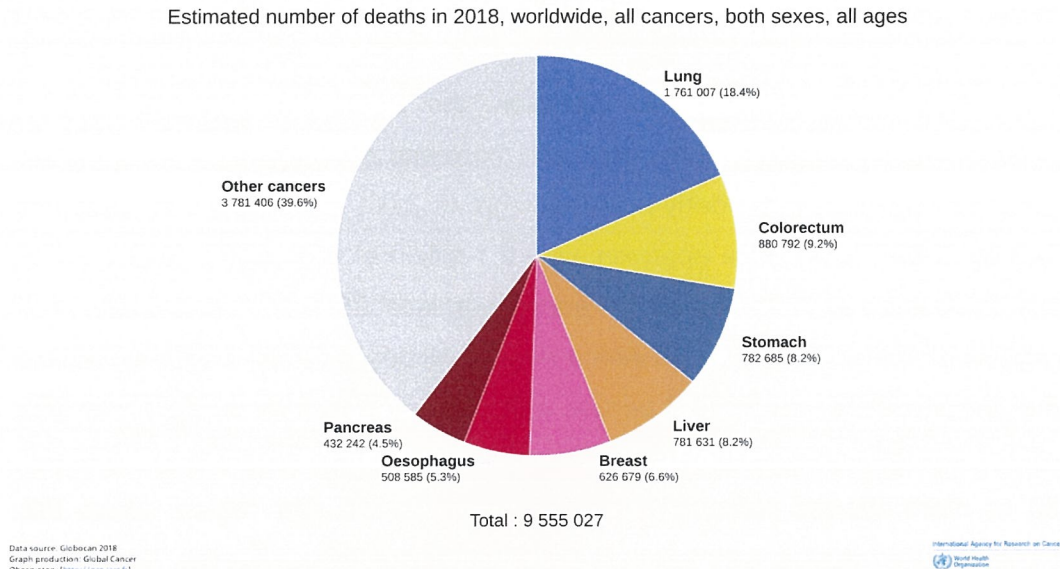


Figure 1: Estimated number of deaths according to the type of cancer in 2018, both sexes, all ages. Source and authorization: GLOBOCAN 2018.

While the relationship between aging and cancer has been highlighted in several studies, there is no consensus on the mechanisms underlying its increased susceptibility in the elderly (Iseghohi & Oimage, 2016). What is known is that, during the life, the human body accumulates molecular and cellular damages that together with the dysfunction of the cellular repair mechanisms, support the development of cancer (Iseghohi & Oimage, 2016).

2.2 The Impact of Surgical Treatment on the Prognosis of Old Oncological Patients

Currently, there are different therapeutic options that are used for the treatment of cancer such as surgery, radiotherapy, immunotherapy, chemotherapy and hormone therapy. They can either be used alone or in combination, according to several aspects, including the type and stage of cancer (Sudhakar, 2009). Among all treatments, surgical resection (complete tumor removal) is considered the most effective option for the treatment of solid tumors,

and may result in cure (Morgan et al., 2004). Even with all the advancements, surgery is not free of risks, from which the post-surgical complications stand out. Post-surgical complications arise from the primary disease, from the surgery itself or from factors that are not related (Doherty, 2010), and may exert a negative overload on the individual, health system and society, through increased morbidity, mortality, hospitalization time and the need for specialized care at the time of hospital discharge (Ferraris et al., 2014; Tevis & Kennedy, 2013; Vester-Andersen et al., 2014). At the same time, the occurrence of complications may lead to delayed initiation of other treatments, such as chemotherapy or radiotherapy, which may limit the chances of survival and cure (Merkow et al., 2013).

2.3 Importance of the Determination of Surgical Risk in the Reduction of Complications

Due to the awareness of the impact that surgical procedures may have on the prognosis of the cancer patient, there was an effort by the medical and scientific community to identify the risk factors that contribute to the occurrence of these complications, as well as an attempt to develop predictive scales to optimize the eligibility of patients who will experience surgical treatment. One of the most valued and used risk factors in the scales of surgical risk prediction is chronological age. In fact, the post-surgical prognosis of older patients is, in general terms, less favorable (De Angelis et al., 2014) and this perception makes professionals to change their attitude about treatment in these patients, opting for less radical treatments and often offering an underestimated intervention to the patient (MacMillan, 2012). For example, according to a study conducted in the United Kingdom, while 81.0% of the oncologists would prescribe chemotherapy to 68-year-old high-risk breast cancer patients, only 43.0% would prescribe it to the a patient with similar prognosis but aged 73 years (Ring, 2010). The same happened with surgery, with breast cancer patients over 70 years receiving less frequent surgical treatment than those under 70 years of age (NCIN, 2010).

However, chronological age has important limitations when defining the health condition of the patient, since two persons of the same age can have different tolerance to the same aggressor stimulus (Audisio & van Leeuwen, 2015; MacMillan, 2012; participants et al., 2008; Quoix et al., 2011). This fact is justified by the heterogeneity in the physiological reserve that characterizes each individual, a feature that is more reliable to estimate prognosis than the chronological age (Joseph et al., 2014; Makary et al., 2010). So, chronological age is not adequate to determine the biological condition of the patient and consequently is not rigorous to aid decision making on the eligibility of the elderly oncologic patient for a treatment (Saif, Makrilia, Zalonis, Merikas, & Syrigos, 2010; Sundermann et al., 2011). On the other hand, biological age seems to be more representative of the body's ability to respond to a stress, such as that imposed by surgery, which can be measured by tools based on the concept of frailty (Fried et al., 2005).

2.4 The Role of Frailty in the Determination of Surgical Risk

The concept of frailty is already considered one of the most important topics when it comes to health care (Ethun et al., 2017). Frailty is a multidimensional state in which there is an increase in vulnerability to stress stimulus. This situation occurs due to the decline in the physiological reserve of the individual, leading to a reduction in resilience and the ability to tolerate and respond appropriately to stress, such as infection or surgery. As a consequence, frailty increases the risk of harmful effects on health (Ethun et al., 2017; Robinson et al., 2015; Rodriguez-Manas et al., 2013). Even without agreement on the definition of frailty or on which tool is most appropriate for its assessment, there is a global consensus that frailty is a medical syndrome, is associated with a high vulnerability that negatively affects health but is a manageable situation (Morley et al., 2013). Although not exclusive to the elderly population, frailty is more prevalent at more advanced ages, with an estimated prevalence of 10.0% in individuals aged 65 and over (Collard, Boter, Schoevers, & Oude Voshaar, 2012; Hubbard, O'Mahony, Savva, Calver, & Woodhouse, 2009). This proportion is

even higher in cancer patients, with a prevalence of more than 50% (Hubbard et al., 2009). The fragile patient, in contrast to the non-fragile, has an increased risk of perioperative complications (ex: respiratory insufficiency, sepsis, wound infection) (Hewitt et al., 2015) and to be readmitted in 30 days, while at the same time there is a lower probability of being discharged to home or to maintain its functional independence (Fagard et al., 2016; Hewitt et al., 2015; McIsaac, Bryson, & van Walraven, 2016; Oakland, Nadler, Cresswell, Jackson, & Coughlin, 2016).

2.5 Frailty Pathophysiology

Even with all the interest around frailty, its pathophysiology remains undetermined (Gordon, Hubbard, 2018). Frailty is associated with the occurrence of multisystem impairments, including the musculoskeletal and endocrine systems (Chen; Mao; Leng, 2014). In several cross-sectional studies with older adults, frailty status was associated with the presence of inflammatory biomarkers, especially with Interleukin 6 (IL-6) and C-reactive protein (CRP) (Soysal et al., 2016). Interleukin 6 (IL-6), a pro-inflammatory cytokine, was shown to be increased in frail patients in comparison with robust patients (Leng; Yang; Walston, 2004; Leng et al., 2007; Walston et al., 2008; Hubbard et al., 2009; Collerton et al., 2012). Also, this biomarker has been associated with sarcopenia, anemia and insulin resistance, suggesting its negative impact in physiologic systems (Pal; Katheria; Hurria, 2010; Partridge et al., 2012). C-reactive protein (CRP) and tumor necrosis factor- α (TNF- α), also pro-inflammatory molecules, were shown to be present in high levels in frail patients (Walston et al., 2002; Hubbard et al., 2009; Collerton et al., 2012). Importantly, there is evidence of increased association between these inflammatory markers and a rise in the risks of poor health outcomes (Amrock; Deiner, 2014; Vigorito et al., 2016). A study in Norway with patients aged 70 or over going through colon or rectal tumors surgery, found high levels of IL-6 and CRP in patients considered frail according to both frailty phenotype and deficit accumulation definition (Ronning et al, 2018). TNF- α was increased only in frail patients as determined by the deficit

accumulation tool. Also, the IL-6 was shown to be an independent predictor of postoperative complications (Ronning et al., 2018). Another study that used different frailty measures in patients with 75 years or over, showed an increased level of these biomarkers in frail patients in association to the non-frail, in all the measures (Hubbard et al., 2009). Besides that, albumin levels were decreased in the frailest subjects (Hubbard et al., 2009).

Since weakness and slowed motor performance are components of frailty (Chen; Mao; Leng, 2014), impairments of the musculoskeletal system will influence physical frailty (Landi et al., 2015). Sarcopenia is characterized for the loss of muscles mass and strength, being common with the increase of age (Brown et al., 2010). The causes are due the age-related changes in sex-steroid levels, α -motor neurons, type 1 muscle fiber, muscular atrophy, physical inactivity, malnutrition growth hormone production (Chen; Mao; Leng, 2014). The contribution of the endocrine system is around the sex steroids and the insulin like growth factor - 1 that have an influence in skeletal muscle metabolism (Chen; Mao; Leng, 2014). These hormones were found in lower levels in frail older patients in contrast with the non-frail (Leng et al., 2004; Puts et al. 2005; Leng et al., 2009), leading to a reduction in muscle mass and strength.

2.6 Frailty Measurement

The assessment of frailty has been shown to be extremely useful in stratifying the risk of older patients, and through that, to contribute to reduce the rate of complications, mortality, hospitalization and costs by allowing clinical decision making in the selection of patients with the profile more favorable for surgical treatment (Brennan, Barlotta, & Simhan, 2018; Fagard et al., 2016; Handforth et al., 2015; Ingraham et al., 2010). There are two main models of frailty, the first concept based on physical frailty (Phenotypic Frailty model) and the second on the multidimensional concept of frailty (Frailty Index). The phenotypic frailty is one of the most widely used instruments in the frailty literature. It was developed by FRIED et al., 1991 and tested in the Cardiovascular Health Study (CHS) (FRIED et al., 1991; FRIED et al. 2001). The

model is based on the idea that aging results in age-related biological changes that are manifested through clinical signs and symptoms such as weight loss and lack of energy, which can be objectively assessed (Ethun et al., 2017). The phenotypic model evaluates five parameters: weakness, slow walk speed, low level of physical activity, shrinking and exhaustion. Patients with three or more criteria are considered frail, while the patient with one or two criteria is considered pre-frail. This measure proved to be an independent predictor of falls, disability, hospitalization and premature death (Fried et al., 2001). In turn, the idea of deficit accumulation initially proposed by Mitnitski, Mogilner, and Rockwood (2001) considers a concept of broader frailty, reflecting an accumulation of deficits in various dimensions of the individual, such as medical, social or functional deficits. Also, according to the Frailty Index, patients identified as frail are at increased risk of mortality and longer hospitalization (Armstrong, Mitnitski, Launer, White, & Rockwood, 2015; Kulminski et al., 2008).

2.7 Frailty Tools

Currently, according to a review from Buta et al. (2016), there are more than 70 different tools which can vary in the intention of the use, like risk-stratify for health outcomes, supporting in clinical decisions, predicting prognosis or even facilitating interventions targeting. The tools can follow the concept of phenotypic model and others the deficit accumulation model, through single-item or multi-dimensional tools. A systematic review found that the major components used for detecting frailty were physical function, mobility, cognition, weight loss and physical activity, respectively; death and disability were found as the major outcomes predicted by the tools (Sternberg, Wershof Schwartz, Karunanathan, Bergman, & Mark Clarfield, 2011). Some of the tools are represented in **Table 1**.

Table 1: Some of the most common frailty tools and its domains.

Frailty Assessment tool	Domains
5-Meters Walk Test	Gait speed measurement of the time it takes for the patient to walk a 5-meter distance
Clinical Frailty Scale (Rockwood et al., 2005)	Activities of Daily Living Instrumental Activities of Daily Living Physical signs Current illness
Comprehensive Assessment of Frailty (Sündermann et al., 2011)	Weakness Self-reported exhaustion Slowness of gait speed Low activity Physical performance Blood analysis Respiratory function
Edmonton Frailty Scale (Rolfson et al., 2006)	Cognition General health status Functional independence Social support Medication use Nutrition Mood Continence Functional performance
Gill Frailty Measure (Gill et al., 2002)	Disability
Green Index (Green et al., 2015)	Malnutrition Slowness Weakness IADL
Handgrip Strength	Muscle strength measurement of the dominant hand with a dynamometer
Phenotypic Frailty (Fried et al., 2001)	Shrinking Weakness Exhaustion Slow gait speed Low activity

(continuation of Table 1)

Sarcopenia	Morphometric measurement through density, volume or lean muscle area
The Comprehensive Geriatric Assessment (Wildiers et al., 2012)	Functional status Comorbidity Cognition Mental health Social functioning Social support Nutrition
The FRAIL Scale (Abellan et. al, 2008)	Fatigue Resistance Ambulation Illness Loss of weight
The Frailty Index (Mitnitski et al., 2001, 2004; Rockwood et al., 2006, 2007; Rockwood and Mitnitski, 2007)	Medical Social Functional
The Vulnerable Elders Survey-13 (Saliba et al., 2001)	Age Health Functional capacity Physical performance
Time Up and Go	Mobility measurement of the time it takes for the patient to rise from a chair, walk 10 feet, turn around and return to being seated

To date, there is no consensus on the superiority of one tool over another. In addition, it becomes evident that the different frailty tools present a divergence in the identification of groups that are frail, which limits their use in supporting clinical decision-making. A research in United Kingdom with old people (75-86 years old; 60.0% male) obtained differences in the identification of frail patients, with a percentage of 48.0% for FP, 34.0% for FRAIL and 32.0% for sarcopenia (European Working Group in Sarcopenia) (Ibrahim, Howson, Culliford, Sayer, & Roberts, 2019). In Germany, a study with old people (73±6.0 and 63.0% female) with the aim of validate the Gronigen Frailty Index (GFI), PRISMA-7 and FRAIL to German population presented prevalence of 23.0% for GFI and FI, 10.0% for

FRAIL and 4.0% for FP (Braun, Gruneberg, & Thiel, 2018). Patients with solid abdominal tumor going to surgery (75 ± 6.6 years, 76.0% female and 42.2% colon cancer) in Poland had numbers of 85.0% for G8, 75.5% for Balducci (BFC), 65.0% for aCGA, 49.0% for GFI, 47.0% for TRST and 40.0% for both FP and CFS for frailty prevalence (Kenig, Zychiewicz, Olszewska, & Richter, 2015). Again with polish surgical patients with 74 (63-90) years and 52.8% female, the prevalence was of 59.4% for CGA and 45.3% for VES-13 (Kenig, Richter, Zychiewicz, & Olszewska, 2014). In a study in Italy, geriatrics (80.52 ± 6.68 years and 52.2% male) with colorectal cancer undergoing to surgery showed a prevalence of frailty of 23.9% for TUG, 43.5% for VES-13 and 52.2% for GFI, with TUG and VES-13 scores being associated with long-term mortality and disability (Ugolini et al., 2015). Again in Italy, with early stage solid tumors patients (medium of 77 years, 80.0% female, 65.0% breast cancer), also showed different prevalence between the tools, with 25.0% for both BFC and VES-13 and 17.0% for FP; the study suggest that VES-13 is a good predictor of death or functional decline (Biganzoli et al., 2017). Another study in the same country with patients with solid cancer (79 ± 5.87 years, 54.0% female and 49.0% colorectal cancer) showed 94.0% to Senior Adult Oncology Program (SAOP2), 89.0% for G8 and 62.0% for CGA, suggesting that both G8 and SAOP2 showing a good screening capacity (Russo et al., 2018). In France, a study with an elderly sample (77.7 years 51.9% female) revealed difference in the frailty measured, with 15.0% for FP, 30.9% for GFI, 50.7% for aCGA and 52.2% for VES-13, suggesting the need for a more predictive tool (Bongue et al., 2017). An oncologic French elderly sample (80.3 ± 5.7 years, 52.4% male and 19.1% colorectal cancer) who were assessed by frailty, showed 72.2% BFC, 37.9% Society of Geriatric Oncology 1 (SIOG1) and 67.4% for SIOG2, suggesting that all of them have a good prognostic (Ferrat et al., 2017). In Spain a comparison with FP, VES-13 and CGA, both FP and VES-13 had a frailty prevalence of 34.5% of the oncologic old sample and 87.9% for CGA (Melina-Garrido et al., 2011). Belgium patients with 77 (66-97) years, 54.0% male and 29.0% urological cancer 78.0% for G8, 64.0% for CGA and 47.0% for GFI (Baitar et al., 2013). Also, in Belgium, patients with cancer who were under treatment or not (77 ± 4.0 years, 60.0% male and 32.0%

prostate cancer) presented prevalence of frailty of 68.0% for CGA, 49.0% for VES-13 and 31.0% for GFI (Kellen et al., 2010). Canada did a study in older people with cancer (74 (70-92) years and 71.4% male 57.1% gastrointestinal cancer) presented a frailty prevalence of 78.6% for CGA, 63.0% for G8, 35.7% for VES-13, 32.1% for modified FP (Yokom, Alibhai, Sattar, Krzyzanowska, & Puts, 2018). A study in United States of America compared Study of Osteoporotic Fracture (SOF) and FP in cardiac surgical patients (75.0% male 74.1±6.5 years) that showed different prevalence, with 9.0% and 28.0%, respectively, suggesting that SOF is a better identifier of frailty (Henry et al., 2019). In Mexico, aged people with 69.8±7.6 years and 54.6% female presented a variance of 24.9% for FP and 27.5% for FI in their frailty prevalence (Garcia-Pena, Avila-Funes, Dent, Gutierrez-Robledo, & Perez-Zepeda, 2016). Diseased patients with low-middle income (79.6±8.4 years and 63.5% female) in Brazil participated in a comparison of FP, SOF and FRAIL tools, showing a prevalence of 51.0% for FP, 38.0% for SOF and 37.0% for FRAIL, with all being a good predictor for adverse outcomes (S. M. Lin et al., 2018). In healthy Japanese older adults (69.4±4.5 and 56.8% female), the difference in the prevalence of frailty was 13.5% for FI and 1.5% FP (Arakawa Martins et al., 2019). China also did a study comparing frailty tools in the elderly population (that showed prevalence of 47.9% for FP, 14.0% for FRAIL 1.6% for Hubbard (Woo, Leung, & Morley, 2012).

Thus, it is evident that more than creating new tools, it seems urgent to compare the performance of existing tools in order to understand which is more accurate in the prediction of postoperative complications (or other specific outcomes) to be used in clinical practice to select patients for surgery or for optimization before surgery, as with prehabilitation programs (Armstrong et al., 2015; Huisingh-Scheetz & Walston, 2017; Kulminski et al., 2008; Rockwood et al., 2005).

2.8 The Role of Prehabilitation

Prehabilitation is an intervention designed to be implemented before surgery, with the aim of improving the patient's tolerance to treatment and reduce

postoperative complications perioperative period (Carli & Zavorsky, 2005). The prehabilitation program is a preparation that occurs inside of the rehabilitation process, between the cancer diagnosis and pretreatment, that aims to improve the health status of the patient, trying to prevent or reduce the effects of the treatment of all kinds (Silver & Baima, 2013). It is an opportunity to prepare the patient in a nutritional, psychological and physical way through patient-tailored interventions (MacMillan, 2018).

This process has the purpose to improve cardiorespiratory, nutritional and neuro-cognitive condition; reduce postoperative complications and length of stay; improve recovery; educate the patient about bad habits like smoking and drinking, consequently, improving patient's quality of life (MacMillan, 2018). Evidences around physical exercise in the prehabilitation are emerging in the literature, considering that the exercise approach in the oncologic population is safe and feasible (Loughney, West, Kemp, Grocott, & Jack, 2016). **Table 2** summarizes the main findings from systematic reviews or/and meta-analysis of exercise interventions:

Table 2: The impact of prehabilitation with exercise training in oncologic patients.

Author	Evidences
Crandall et al., 2014	Exercise improve cardiopulmonary exercise capacity, muscle strength and reduce fatigue, postoperative complications and length of stay in patients with non-small cell lung cancer.
Kreuts et al., 2019	Physical and mind-body exercise improve subjective sleep problems.
Moran et al., 2016	Aerobic, resistance and/or respiratory exercises decrease of postoperative complications after intra-abdominal surgeries.
Nadler et al., 2019	Exercise is associated with clinically meaningful improvements in quality of life, function, and 6-MWT in some patients with metastatic cancer.
Nakano et al., 2018	Aerobic and resistance exercises improve fatigue, pain, insomnia and might have reduced dyspnea in cancer patients.

(continuation of Table 2)

Padilha et al., 2017	Resistance exercise increase muscle strength, maintain lean body mass and reduce body fat in cancer patients undergoing neoadjuvant and adjuvant therapy.
Piriaux et al., 2018	Combined aerobic and resistance exercises improve physical fitness and quality of life and decrease length of stay and postoperative pulmonary complications.
Rodriguez-Larrad et al., 2014	Moderate to intense aerobic exercises improve functional condition and reduce postoperative morbidity in patients with lung cancer resection.
Zeng et al., 2019	Exercise during or post chemotherapy are beneficial in physical fitness and depression in cancer patients.

Even with all the benefits of the exercise training programs in the oncologic patients before surgery, it still remains to be shown if the time frame from cancer to diagnosis to surgery (2-6 weeks) is enough to modulate de frailty status (e.g. frail individual can become pre-frail) and if it will translate into better outcomes in this high-risk population.

3 Objectives and Hypothesis

The occurrence of complications in the postoperative period will have a marked impact on the prognosis of cancer patients but will also represent a huge social and economic burden. Frailty assessment in the preoperative period is now widely recognized for its potential in risk prediction of adverse events and to assists in the selection of patients for cancer surgery (or to optimization programs before proceeding to surgery). Yet, there are no standardized tools for that purpose. Also, in literature, there is a lack of studies comparing VES-13, FP and or single-item frailty tools, like physical tests, which are all widely used.

3.1 General Objective

Compare the agreement of Fried Phenotype, Vulnerable Elders Survey, 8-Foot Up and Go, 5-Meters Walk Test and Handgrip Strength in identifying frailty in oncologic geriatric patients with head-neck and digestive cancer.

3.2 Specifics Objectives

- a) Evaluate and compare the prevalence of frailty as determined by Fried Phenotype, Vulnerable Elders Survey, 8-Foot Up and Go, 5-Meters Walk Test and Handgrip Strength in oncologic geriatric patients with head-neck and digestive cancer.
- b) Evaluate the correlation between Fried Phenotype, Vulnerable Elders Survey, 8-Foot Up and Go, 5-Meters Walk Test and Handgrip Strength to determine frailty in oncologic geriatric patients with head-neck and digestive cancer.
- c) Evaluate the degree of agreement between Fried Phenotype, Vulnerable Elders Survey, 8-Foot Up and Go, 5-Meters Walk Test and Handgrip Strength to determine frailty in oncologic geriatric patients with head-neck and digestive cancer.

3.3 Hypothesis

- The prevalence of frailty varies in the same population depending on the use of Fried Phenotype, Vulnerable Elders Survey, 8-Foot Up and Go, 5-Meters Walk Test and Handgrip Strength;
- Fried Phenotype present the best correlation and agreement with all other instruments.

4 Methods

4.1 Study Design

This research was an observational (cohort) and prospective study approved by Instituto Português de Oncologia do Porto Francisco Gentil (IPO-Porto) ethics committee (process number 193/016).

4.2 Participants

Ambulatory patients were enrolled between September 2018 and June 2019. For eligibility criteria, the subjects could be man or woman, aged 65 or more and have been diagnosed with head-neck or digestive cancer and elected for surgery. Patients in wheelchair or that are not lucid to answer the research were excluded. The participants were recruited by convenience, since we only recruited patients attending at IPO-Porto, on Monday morning. After reading a document explaining the study (**Attachment 1**), the elderlies who agreed to participate in it signed the Free Informed Consent, according to Declaration of Helsinki (**Attachment 2**). The consent ensured the confidentiality and anonymity of the participant, who also were informed previously of the procedure and tests that would be performed, including the aim of the study. All the processes were performed after the patient's medical appointment at IPO-Porto. The file with all the five tools is in the **Attachment 3**.

4.3 Sample Characterization

Sociodemographic data as age, gender, education level and marital status were collected through specific questions. Anthropometric data were collected through a portable stadiometer for height (Seca 213) and a digital scale (Tanita Inner Scan BC 532) for weigh. The body mass index (BMI) was calculated using the weight (kg) divided by the square of the height in meters (kg/m^2), categorizing the subjects through WHO (2019a) classification for Europeans.

4.4 Frailty Assessment Tool

The Fried Phenotype is a frailty assessment tool based on the concrete measurement of physical aspects of the patient, requiring physical tests, which may require more time than other tools. However, the tool is widely used in the oncological field, mainly because it is faster than the scales of the multidimensional frailty model. For the measurement of the physical frailty, the individual was assessed by measuring weight loss, handgrip strength, exhaustion, reduced walking speed and low physical activity, as summarized in the **Table 3** (Fried et al., 2001).

Table 3: Domains evaluated of frailty phenotype according to Fried criteria (Fried et al., 2001).

Domain	Tool	Score for Frailty
Shrinking	Weight loss unintentional in the last year.	Weight loss unintentional of $\geq 5\%$ of the body weight in the last year.
Weakness	The result was the best value of two attempts of the Handgrip Strength Test.	Men: BMI ≤ 24: ≤ 29 Kg BMI 24.1-26: ≤ 30 Kg BMI 26.1-28: ≤ 30 Kg BMI > 28: ≤ 32 Kg Women: BMI ≤ 23: ≤ 17 Kg BMI 23.1-26: ≤ 17.3 Kg BMI 26.1-29: ≤ 18 Kg BMI > 29: ≤ 21 Kg
Exhaustion	Questions 7 and 20 of the Center for Epidemiologic Studies of Depression (CES-D) validated for Portuguese population for Loureiro (2009).	Answer 3 or more days for both questions.

(continuation of Table 3)

Low walk speed	Walk test of 5.0 meters. 2.0 meters were added at the beginning and at the end (total of 9.0 meters) that were discounted for the moment of acceleration and deceleration. The result was an average of three attempts.	Men: Height ≤ 173 cm: ≥ 7 seconds Height > 173 cm: ≥ 6 seconds
		Women: Height ≤ 159 cm: ≥ 7 seconds Height > 159 cm: ≥ 6 seconds
Low physical activity	Short form of International Physical Activity Questionnaire (IPAQ) validated for Portuguese population (Craig et al., 2003).	Men: <383 kcal/week
		Women: <270 kcal/week

BMI: Body Mass Index.

Each item has its own instrument, and so its own score. When a deterioration in the evaluated item is evidenced, a score of 1 was attributed and when it is not evident, nothing was added. Given that Fried criteria has five domains, the final score ranged from 0 to 5. The non-scoring was considered as non-frail, from 1 to 2 items was considered as pre-frail, while values equal to or greater than 3 identified the elderly as frail.

4.5 Frailty Screening Tool

The Vulnerable Elders Survey (VES-13) is a screening tool created for Saliba et al. (2001) and validated for the Portuguese population by Carneiro, Sousa, Azevedo, and Saliba (2015). Based on the patient's self-assessment, this tool can generate overestimated data of the actual situation (Ethun et al., 2017), but because it is a questionnaire, it makes its use very practical and fast for the hospital setting. The VES-13 consists of thirteen questions (**Table 4**), distributed through 4 domains: age, health, physical limitations and disabilities.

Table 4: Domains evaluated of VES-13 created for Saliba et al. (2001).

Domains		Score for Frailty
Age	<75 year	0
	75 to 84 year	1
	≥85 years	3
Self-rated Health	In general, comparing with other people your age, would you say that your health is:	
	Good, very good or excellent	0
	Poor or fair	1
Physical limitation	How difficulty, on average, do you have with the following physical activities:	
	a. Stooping, crouching or kneeling?	Number of answers with "a lot of difficulty" or "unable to do": 0 items - 0 1 item - 1 ≥ 2 items - 2
	b. Lifting or carrying objects as heavy as 10 pounds?	
	c. Reaching or extending arms above shoulder level?	
	d. Writing or handling and grasping small objects?	
	e. Walking a quarter of mile?	
	f. Heavy housework such as scrubbing floors or washing windows?	
Disability	Because of your health or physical condition, do you have any difficulty:	
	a. Shopping for personal items?	Number of answers with "yes": 0 items - 0 ≥ 1 item - 4
	b. Managing money?	
	c. Walking across the room?	
	d. Doing light housework?	
	e. Bathing or showering?	

The result of the VES-13 is based on the sum of the score (ranging from 0 to 10) of the 4 evaluated domains. The elderly who score up to 2 points was classified as non-frail and 3 or more points the elderly was classified as frail.

4.6 Frailty Physical Tests and Single-Item Tools

4.6.1 8-Foot Up and Go

The 8-Foot Up and Go is a physical test used as a single-item scale for frailty that required the patient to rise from a chair position, walk 8 foot previously marked on the floor, turn around and walk back to the chair position (Rose, 2002). The instruction consisted of making the performance as fast as possible, but carefully. It was not allowed that the patients used its hands to help with the chair. The timing started when the instructor gave a verbal order “go” and ended when the patient returned to the starting position. The score for frail was based on Chang et al. (2014) showed in the **Table 5**.

4.6.2 5-Meters Walk Test

For this physical single-item scale, the subjected was instructed to walk in 5 meters previously marked on the floor at a normal pace. The timing started when the instructor said “go” and finished when the patient reached the 5-meter point. It has become very useful for allow the patient to have a good performance without producing cardiopulmonary symptoms (Afilalo et al., 2014). The score was according to Fried et al. (2001) and is explained in the **Table 5**.

4.6.3 Handgrip Strength

The Handgrip Strength is a physical test measured in two attempts with a handgrip Takei 5401 Digital Dynamometer, with a rest between the attempts around 10 seconds. If these two values were distinct, a third attempt was made. The patient was instructed to seat and put the dominant forearm in the chair’s arm, with the elbow in a 90-degree position and asked to hold the dynamometer as strong as possible. The cutoff used was based on the scale created for Fried et al. (2001) represented in **Table 5**.

Table 5: Scores for frailty used according to the physical tests.

Physical Test	Score for Frailty
8-Foot Up and Go	> 8.13 seconds
5-meters Walk Test	Men:
	Height ≤ 173 cm: ≥ 7.14 seconds
	Height > 173 cm: ≥ 6.57 seconds
	Women:
Handgrip Strength	Height ≤ 159 cm: ≥ 7.14 seconds
	Height > 159 cm: ≥ 6.57 seconds
	Men:
	BMI ≤ 24: ≤ 29 Kg
	BMI 24.1-26: ≤ 30 Kg
	BMI 26.1-28: ≤ 30 Kg
	BMI > 28: ≤ 32 Kg
	Women:
	BMI ≤ 23: ≤ 17 Kg
	BMI 23.1-26: ≤ 17.3 Kg
	BMI 26.1-29: ≤ 18 Kg
	BMI > 29: ≤ 21 Kg

BMI: Body Mass Index.

4.5 Data Analysis

The data was tabulated in a spreadsheet of Microsoft Office Excel software, version 16.2, and analyzed using SPSS software (version 25). The baseline characteristics of frail and non-frail patients were compared through descriptive statistics. For quantitative data, categorical variables were presented in absolute values and percentages, while continuous variables were presented as mean (and standard deviation) or median (and interquartile range), depending on the distribution. The differences between the groups were evaluated using the following tests, according to their suitability: t-student test and Chi-square test. The correlation between the quantitative variables was evaluated using Spearman's correlation coefficient, while the agreement between them was assessed using Kappa coefficient (Landis; Koch et al., 1977). The differences were considered statistically significant when the value of $p < 0.05$.

5 Results

5.1 Sample Characterization

A total of 63 subjects with cancer was studied. **Table 6** shows the sociodemographic profile of the sample. The majority of the subjects were male (74.6%) with an average age of 73.7 ($\pm$ 6.4) years old, had digestive cancer (60.3%), married (74.6%) and has the 4^o year of basic education (66.7%). No differences were found by gender.

Table 6: Sociodemographic data of the geriatric oncologic sample.

Variables	Male (n=47)	Female (n=16)	Total (n=63)
Age	73.5 $\pm$ 6.5	74.3 $\pm$ 6.3	73.7 $\pm$ 6.4
Type of cancer			
Digestive	57.4 (27)	68.8 (11)	60.3 (38)
Head-neck	42.6 (20)	31.2 (5)	39.7 (25)
Marital Status			
Single	2.1 (1)	-	1.6 (1)
Married	78.7 (37)	62.5 (10)	74.6 (47)
Divorced	-	12.5 (2)	3.2 (2)
Widower	17.0 (8)	25.0 (4)	19.0 (12)
Other	-	-	-
Education Level			
Illiterate	6.4 (3)	18.8 (3)	9.5 (6)
1 ^o to 4 ^o year	72.3 (34)	50.1 (8)	66.7 (42)
5 ^o to 6 ^o year	4.3 (2)	6.3 (1)	4.8 (3)
7 ^o to 9 ^o year	6.4 (3)	12.5 (2)	7.9 (5)
10 ^o to 12 ^o year	4.2 (2)	6.3 (1)	4.8 (3)
College	2.1 (1)	6.3 (1)	3.2 (2)

Values are median (interquartile range: 25th to 75th percentiles) or % (n).

Anthropometric data is represented in **Table 7**. The average body weight in this sample was 66.7 kg, with an average height of 162 cm. The average BMI was 26.0 kg/m² and most of the sample was considered in the stage of pre-obesity 84.3% (n=28). In the female sample, the same number was found for pre-obese and obese 37.5% (n=6).

Table 7: Anthropometric data of the geriatric oncologic sample.

Variables	Male (n=47)	Female (n=16)	Total (n=63)
Body Weight (kg)	68.2±12.0	66.3±9.2	66.7±11.3
Height (cm)	164±7	154±6	162±8
BMI (kg/m²)			
Underweight	2.1 (1)	-	2.1 (1)
Normal weight	40.4 (19)	25.0 (4)	65.4 (23)
Pre-obesity	46.8 (22)	37.5 (6)	84.3 (28)
Obesity	10.6 (5)	37.5 (6)	48.1 (11)

Values are median (interquartile range: 25th to 75th percentiles) or % (n).

5.2 Prevalence of Frailty

Table 8 shows the prevalence of frailty by each domain, for each tool. The domains that mostly contributed for frailty according to FP definition were “Low physical activity” (50.8%), “weakness” (47.6%) and “shrinking” (36.5%). According to VES-13, “self-rated health” (50.8%) and “physical impairment” (18.8%) were the domains that mostly contributed to classify a patient as frail.

Table 8: The prevalence of frailty by each domain.

Tool	Non-frail	Frail	Missing data
5-mWT	81.0%	14.3%	4.8%
HS	39.7%	47.6%	12.7%
8FUG	30.2%	68.3%	1.6%
FP			
Low Physical Activity	49.2%	50.8%	
Exhaustion	85.7%	14.3%	
Shrinking	60.3%	36.5%	3.2%
Low Walk Speed	81.0%	14.3%	4.8%
Weakness	39.7%	47.6%	12.7%

(continuation of Table 8)

VES-13

Age - Q1	61.9%	38.1%	
Self-rated Health - Q2	49.2%	50.8%	
Physical Impairment (Q3-Q8)			
	73.0%	27.0%	
	76.2%	22.2%	1.6%
	82.6%	17.4%	
	95.2%	4.8%	
	84.1%	15.9%	
	74.6%	25.4%	
Disabilities (Q9-Q13)			
	88.9%	11.1%	
	90.5%	7.9%	1.6%
	95.2%	4.8%	
	88.9%	9.5%	1.6%
	93.7%	6.3%	

Values are median (interquartile range: 25th to 75th percentiles). Q: question. FP: Fried Phenotype. VES-13: Vulnerable Elders Survey. 5-mWT: 5-meters Walk Test. 8FUG: 8 Foot Up and Go. HS: Handgrip Strength.

The categorization of frailty varied in all the five different tools. The prevalence of frail patients was 14.3% (n=9) in 5-mWT, 15.9% (n=10) in VES-13, 28.6% (n=18) in FP, 47.6% (n=30) in HS and 68.3% (n=43) in 8FUG, as shown in **Figure 3**.

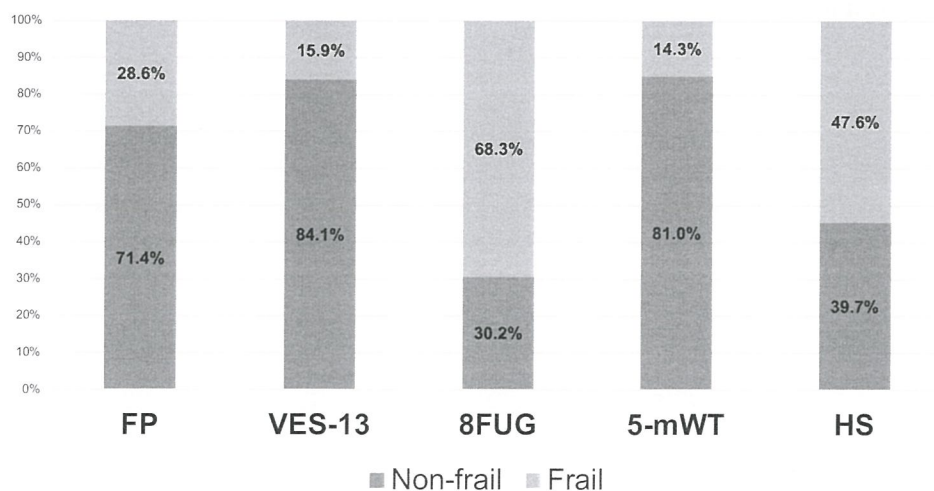


Figure 3: Frailty categorization according to Fried Phenotype, Vulnerable Elders Survey, 8 Foot Up and Go, 5-meters Walk Test and Handgrip Strength.

5.3 Relationship Between the Tools

The correlation between the frailty tools showed that 5-mWT had the strongest correlation with the others, all statistically significant: 0.49 with FP, 0.46 with VES-13, 0.33 with HS and 0.28 with 8FUG. It was also possible to find significant correlations between VES-13 and FP (0.40), VES-13 and HS (0.37) and HS and FP (0.31) (**Table 9**).

Table 9: Correlation coefficient between the frailty tools.

	HS	5-mWT	8-FUG	VES-13
FP	0.31*	0.49**	0.14	0.40**
VES-13	0.37**	0.46**	0.17	
8FUG	0.18	0.28*		
5-mWT	0.33**			

* Significant correlation 0.05. ** Significant correlation 0.01.

FP: Fried Phenotype. VES-13: Vulnerable Elders Survey. 5-mWT: 5-meters Walk Test. 8FUG: 8 Foot Up and Go. HS: Handgrip Strength.

The agreement between the tools showed the FP had a moderate agreement with 5-mWT tool ($K=0.417$; $p=0.0001$) and a fair with VES-13 ($K=0.372$; $p=0.002$) and HS ($K=0.371$; $p=0.0001$). VES-13 presented a fair agreement with the 5mWT ($K=0.357$; $p=0.001$). The others agreement was considered minor.

Table 10: Agreement coefficient between the frailty tools.

Tool	VES-13		5-mWT		8FUG		HS	
FP	NF	F	NF	F	NF	F	NF	F
NF	66.7 (42)	4.8 (3)	66.7 (42)	3.2 (2)	23.8 (15)	47.6 (30)	38.1 (24)	22.2 (14)
F	17.5 (11)	11.1 (7)	14.3 (9)	11.1 (7)	6.3 (4)	20.6 (13)	1.6 (1)	25.4 (16)
	K=0.372 p=0.002		K=0.417 p= 0.0001		K=0.058 p=0.514		K=0.371 p=0.0001	
VES-13								
NF			74.6 (47)	6.3 (4)	28.6 (18)	1.6 (1)	39.7 (25)	0 (0)
F			7.9 (5)	6.3 (4)	54.0 (34)	14.3 (9)	36.5 (23)	11.1 (7)
			K=0.357 p=0.001		K=0.104 p=0.115		K=0.167 p=0.022	
5-mWT								
NF					28.6 (18)	1.6 (1)	38.1 (24)	34.9 (22)
F					52.4 (33)	12.7 (8)	1.6 (1)	11.1 (7)
					K=0.131 p=0.037		K=0.213 p=0.003	
8FUG								
NF							17.5 (11)	7.9 (5)
F							22.2 (14)	38.1 (24)
							K=0.197 p=0.045	

Values are median (interquartile range: 25th to 75th percentiles) or % (n). NF: Non-frail. F: Frail. FP: Fried Phenotype. VES-13: Vulnerable Elders Survey. 5-mWT: 5-meters Walk Test. 8FUG: 8 Foot Up and Go. HS: Handgrip Strength.

6 Discussion

This study compared the agreement of five different tools in geriatric patients with head-neck and digestive cancer. Our data suggests that frailty is very common in geriatric oncologic patients, but with its prevalence varies depending on the tool.

Over the last years, a considerable amount of frailty assessment instruments have been developed and supported the association between frailty and adverse health outcomes in older adults submitted to surgery, including cancer (H. S. Lin, Watts, Peel, & Hubbard, 2016; Panayi et al., 2019). Like in the present study, it has also become evident that the prevalence of frailty could present significant variations depending on the instrument in use, even within the same population. In a non-cancer setting in France, 1224 aged community-dwelling, a prevalence of 15.0% for FP and 52.2% for VES-13 was found, pointing for this divergence (Bongue et al., 2017). Forty-six elderly with colorectal cancer (80.52 ± 6.68 years and 52.2% man) were evaluated for Ugolini et al. (2015) presented a prevalence of frailty of 23.9% for TUG and 43.5% for VES-13, although TUG has a route of 3 meters and 8FUG has 2.4 meters of it, the tests are similar. Yokom et al. (2018) did a research in oncologic older patients with 74 (70-92) years (71.4% man and 57.1% with gastrointestinal cancer) in Canada that showed a prevalence of 35.7% for VES-13 and 32.1% for FP. However, the FP was a modified version of the original. These conflicts can be explained since there is no consensus of the concept around frailty and the measurement of frailty, as well. In part, this is explained by the fact that a great part of the studies in the area were dedicated to the development of new scales of fragility and not so much to the evaluation of the external validity of the existing scales, or even to the comparison of their performance in terms of stratification of risk. In addition, the enormous diversity of frailty scales, although validated for the surgical population, eventually creates confusion when choosing one over another. Consequently, there is a disagreement about which domains are important to be measured in a frailty setting (Rodriguez-Manas et al., 2013).

The relationship between the tools revealed the FP and 5-mWT had the highest correlation and agreement (moderate). The 5-mWT also had significant correlations with the other tools. In concerning of the agreement, FP had fair agreement with the other tools, except 8FUG. A study in Italy among 185 patients with 77 (70-91) years with early-stage solid tumors (80.0% woman with 65.0% breast cancer) from Biganzoli et al. (2017) compared the performance between three tools, including 2 of the ones used in our study (VES-13 and FP). The frailty prevalence was 25.0% for VES-13 and 17.0% for FP, with a coefficient of agreement of 0.55, indicating a moderate value. However, the sample was majority woman with breast cancer, different from the sample in this study. The highest relationship between 5-mWT and FP that was found in this study is explained by the fact that 5-mWT is one of the tests of Fried Phenotype domains, scoring for the low walk speed. The agreement between FP and VES-13, even though it was fair, may be explained due the fact that both tools focus on functional disabilities (Biganzoli et al., 2017).

There is no one perfect tool for measure frailty (Dent, Kowal, & Hoogendijk, 2016). Fried is widely known and used worldwide, however, it takes some time to evaluate it. VES-13 is an easy and quick way to evaluate frailty, but the data can be overestimated sometimes, considering that is based on a self-report approach. The single-item measure, like physical tests although is a very fast way to evaluate the frailty is just focus on the functional status and for a frail person its performance can be dangerous. In general, all the frailty tools used in this study belong to a physical frailty approach, not including nutritional or psychological aspects, for example, which can be a disadvantage.

6.1 Limitations

The present study has some limitations that should be exposed. This study is a single center, with a restricted sample, being needed a validation from other populations with different conditions. Although all evaluators were trained, the assessments were conducted by five different evaluators, being possible divergences around data collection. Clinical data was not provided in this study,

so it was not possible to make adjustments for stage of cancer or comorbidities, for example.

7 Conclusion

Frailty is common in oncologic geriatric patients, independent of the frailty tool used, although the prevalence is highly dependent on it, limiting comparability between studies. Moreover, the agreement between FP, VES-13, 8FUG, 5-mWT and HS was limited. Future studies should validate not only the agreement but also compare the accuracy of these and other tools to predict specific prognostic outcomes in specific contexts.

8 References

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9 Attachment

9.1 Attachment 1 – Explication around the study for the participant.



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



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

9.2 Attachment 2 - Free Informed Consent, according to Declaration of Helsinki.

Consentimento Informado

*Considerando a "Declaração de Helsinquia", da Associação Médica Mundial
(Helsinquia 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)

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 Helsinquia, 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:

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)

9.3 Attachment 3 – File with all the frailty tools.



Data: ____/____/____

ID: _____

CARACTERÍSTICAS SOCIODEMOGRÁFICAS

1 – Qual é o seu nome?

2 – Qual a sua idade? _____ anos completos.

3 – Qual o seu sexo?

(01) Feminino

(02) Masculino

4 – Qual o seu estado civil?

(01) Solteiro

(02) Casado

(03) Divorciado

(04) Viúvo

(05) Outro: _____

5 – Qual o seu nível de escolaridade? _____

COMPOSIÇÃO CORPORAL

1 – Estatura (cm): _____

2 – Peso (kg): _____

TESTES FÍSICOS

8-Foot Up and Go: _____ segundos

Teste caminhada: _____ segundos

Força de preensão manual:

1ª Tentativa: _____ Kg

2ª Tentativa: _____ Kg

3ª Tentativa: _____ Kg

PROTOCOLO DE IDENTIFICAÇÃO DA VULNERABILIDADE (VES-13)

- IDADE

1 – Qual é a sua idade? _____

- AUTOPERCEPÇÃO DA SAÚDE

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

(01) Ruim	(02) Regular	(03) Boa
(04) Muito boa	(04) Excelente	

- LIMITAÇÕES FÍSICAS

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

(01) Nenhuma dificuldade	(02) Pouca dificuldade	(03) Alguma dificuldade
(04) Muita dificuldade	(05) Não consegue fazer	

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

(01) Nenhuma dificuldade	(02) Pouca dificuldade	(03) Alguma dificuldade
(04) Muita dificuldade	(05) Não consegue fazer	

5 – Que dificuldade tem para levantar os braços ou alcançar objetos acima dos ombros?

(01) Nenhuma dificuldade	(02) Pouca dificuldade	(03) Alguma dificuldade
(04) Muita dificuldade	(05) Não consegue fazer	

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

(01) Nenhuma dificuldade	(02) Pouca dificuldade	(03) Alguma dificuldade
(04) Muita dificuldade	(05) Não consegue fazer	

7 – Que dificuldade tem para caminhar 400 metros?

(01) Nenhuma dificuldade	(02) Pouca dificuldade	(03) Alguma dificuldade
(04) Muita dificuldade	(05) Não consegue fazer	

8 – Que dificuldade tem para realizar trabalho de casa pesado, como esfregar o chão, lavar janelas ou carregar lenha?

(01) Nenhuma dificuldade	(02) Pouca dificuldade	
(04) Muita dificuldade	(05) Não consegue fazer	(03) Alguma dificuldade

- INCAPACIDADES

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

() Sim. ➡ Você tem ajuda para fazer compras? () Sim () Não
() Não.
() Não faz. ➡ É por causa da sua saúde? () Sim () Não

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

() Sim. ➡ Você tem ajuda para lidar com o dinheiro? () Sim () Não
() Não.
() Não faz. ➡ É por causa da sua saúde? () Sim () Não

11 – Por causa da sua saúde tem dificuldade para caminhar dentro de casa?

() Sim. ➡ Você tem ajuda para caminhar? () Sim () Não
() Não.
() Não faz. ➡ É por causa da sua saúde? () Sim () Não

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

() Sim. ➡ Você tem ajuda com o trabalho doméstico? () Sim () Não
() Não.
() Não faz. ➡ É por causa da sua saúde? () Sim () Não

13 – Por causa da sua saúde você tem dificuldade para tomar banho?

() Sim. ➡ Você tem ajuda para tomar banho? () Sim () Não
() Não.
() Não faz. ➡ É por causa da sua saúde? () Sim () Não

FENÓTIPO DE FRAGILIDADE

(FRIED et al., 2001)

- PERDA DE PESO

1 – Perdeu peso de forma não intencional no último ano?

(01) Não

(02) Sim ➡ Quanto? _____

- EXAUSTÃO

Durante a semana passada:

1 – Sentiu que tudo o que fazia era um esforço?

(01) Nunca ou muito raramente (menos que 1 dia)

(02) Ocasionalmente (1 a 2 dias)

(03) Com alguma frequência (3 a 4 dias)

(04) Com muita frequência ou sempre (5 a 7 dias)

2 – Sentiu falta de energia?

(01) Nunca ou muito raramente (menos que 1 dia)

(02) Ocasionalmente (1 a 2 dias)

(03) Com alguma frequência (3 a 4 dias)

(04) Com muita frequência ou sempre (5 a 7 dias)

- FRAQUEZA

Força de Preensão Manual

1ª Tentativa: _____

2ª Tentativa: _____

3ª Tentativa: _____

- REDUÇÃO DA VELOCIDADE DE CAMINHADA

Teste de Caminhada de 5.0 Metros

Tentativa: _____

- BAIXA ATIVIDADE FÍSICA

Avaliação do Nível de Atividade Física – IPAQ (versão curta)

As questões que se apresentam, referem-se ao tempo que despende na atividade física numa semana. Este questionário inclui questões acerca de

atividades que faz no trabalho, para se deslocar de um lado para outro, atividades referentes à casa ou ao jardim e atividades que efetua no seu tempo livre para entretenimento, exercício ou desporto. As suas respostas são importantes. Por favor responda a todas as questões mesmo que não se considere uma pessoa ativa. Ao responder às seguintes questões considere o seguinte:

Atividade física vigorosa refere-se a atividades que requerem muito esforço físico e tornam a respiração muito mais intensa que o normal.

Atividade física moderada refere-se a atividades que requerem esforço físico moderado e torna a respiração um pouco mais intensa que o normal.

Ao responder às questões considere apenas as atividades físicas que realize durante pelo menos 10 minutos seguidos.

1a – Habitualmente, por semana, quantos dias faz atividades físicas vigorosas como levantar e/ou transportar objetos pesados, cavar, ginástica aeróbica ou andar de bicicleta a uma velocidade acelerada?

___ dias por semana ___ Nenhum (passe para a questão 2a)

1b – Quanto tempo costuma fazer atividade física vigorosa por dia?

___ horas ___ minutos

2a – Normalmente, por semana, quantos dias faz atividade física moderada como levantar e/ou transportar objetos leves, andar de bicicleta a uma velocidade moderada ou jogar ténis? (Não inclua o andar/caminhar).

___ dias por semana ___ Nenhum (passe para a questão 3a)

2b – Quanto tempo costuma fazer atividade física moderada por dia?

___ horas ___ minutos

3a – Habitualmente, por semana, quantos dias caminha durante pelo menos 10 minutos seguidos? Inclua caminhadas para o trabalho e para casa, para se deslocar de um lado para outro e qualquer outra caminhada que possa fazer somente para recreação, desporto ou lazer.

___ dias por semana ___ Nenhum (passe para a questão 4a)

3b – Quanto tempo costuma caminhar por dia?

____ horas ____ minutos

As últimas questões referem-se ao tempo que está sentado diariamente no trabalho, em casa, no percurso para o trabalho e durante os tempos livres. Estas questões incluem o tempo em que está sentado numa secretária, a visitar amigos, a ler ou sentado/deitado a ver televisão.

4a – Quanto tempo costuma estar sentado num dia de semana?

____ horas ____ minutos

4b – Quanto tempo costuma estar sentado num dia de fim-de-semana?

____ horas ____ minutos

Muito obrigado pela colaboração!

