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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Correlations between frailty and cardiopulmonary exercise testing markers in older adults suffering from specific cardiovascular diseases

Indy Bringmans
Janny Van Thienen

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

PROMOTOR :

Prof. dr. Dominique HANSEN

BEGELEIDER :

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This research paper forms a part of our master's thesis in our degree of Physiotherapy and Rehabilitation Sciences at Hasselt University. This investigation took place from October 2020 until May 2021 at Hasselt University and at the Jessa Hospital in Hasselt, Belgium. Throughout the development of this thesis, we have received a lot of support. Therefore, it isonly right for us to use this section to give our thanks to a few people.

Firstly, we want to thank our promotor, Prof. dr. Dominique Hansen, for helping us choose our research question and for guiding us through his research area of cardiorespiratory rehabilitation. We also want to thank our mentor, Dra. Nastasia Marinus, for filling us in about her doctoralstudy, where this thesis is a part of, and for always providing us with adequate feedback. Sheoffered us a helping hand throughout the whole process, from data collection in the Jessa Hospital to academic writing. Her dedication and support have helped us a lot and we want to wish her the best of luck for the remaining part of her doctoral study.

We want to thank the institutions that helped make this investigation possible. Thank you to Hasselt University for supplying us with enough information and materials to turn this study period into a learning period and for helping us take care of the administration that came with this investigation. We also want to thank the Jessa Hospital in Hasselt and their staff forgiving us access to their rehabilitation center and for providing us with the right instrumentsto complete the tests. The staff of the rehabilitation center Rego were always happy to help us with our questions, which was a large help during the data collection of this study.

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Research context

The elderly population is globally increasing, with almost 8.5% of the global population being65 years or older. Furthermore, this number is on the rise with an estimated increase to 16.7% in 2050 (He, Goodkind, Kowal, 2015). The extending life expectancy causes a greater number of older people with functional disabilities, which stresses the health care costs and highlights the importance of treating these multimorbidity's for the global health care system (Tamura et al., 2018; Bock et al., 2016). One of the most challenging health problemsin the geriatric medicine is the Frailty Syndrome (FS) (Dou et al., 2019).

FS is a state of decreased physiological reserve, combined with an elevated vulnerability to stressors that often leads to a higher risk of unfavourable health outcomes in the elderly population (Lee, Lee, & Jang, 2020; Pilotto et al., 2020). Multiple factors contribute to the development of this syndrome, including age-associated loss of lean body mass, low physical activity and a reduction in nutritional intake (Afilalo et al., 2014). Cardiovascular diseases (CVD) and several non-cardiovascular chronic diseases such as type 2-diabetes and Chronic Obstructive Pulmonary Disease (COPD) have been associated with the development of FS (Goldwater & Pinney, 2015). Recent literature indicated that psychosocial factors such as depression, loneliness and cognitive impairments contribute to the development of FS too (Morley et al., 2013).

Frailty often impairs the exercise capacity, which is one of the most powerful factors in predicting the life expectancy (Piepoli, Corrà, & Agostoni, 2017). Exercise capacity is usually measured by the maximal rate of oxygen consumption (VO_2-peak). Hence, one of the causes of exercise intolerance is the presence of factors that limit the transport or utilization of oxygen (O_2) (Houstis et al., 2018). Furthermore, poor exercise capacity predicts adverse outcomes in persons with or without CVD (Piepoli, Corrà, & Agostoni, 2017).

Cardiopulmonary exercise testing (CPET) is a non-invasive functional assessment that provides data about the functioning of the cardiovascular, respiratory, muscular and metabolic systems during exercise (Herdy et al., 2016). This assessment tool helps the clinician to differentiate pulmonary from cardiac disorders and to find the causes of fatigue and dyspnea in specific

pulmonary and cardiovascular disease populations. CPET is considered to be the golden standard in objectively assessing the exercise capacity inpersons with CVD (Guazzi et al., 2016).

The following study will be situated in the cardio-respiratory (CRI) research cluster of the REVAL Rehabilitation Research Centre in Diepenbeek, Belgium. It is a part of the doctoral study of Dra. Nastasia Marinus (NM) about the FS in the elderly population with cardiovascular diseases. The first part of this doctoral study investigated the prevalence ofthe FS within the population of heart failure (HF) patients and patients undergoing percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). The study indicated that FS often occurs within the population of people suffering from HF orundergoing CABG. In the second part of the study, where this thesis forms a part of, the researchers investigated the impact of aerobic training on people suffering from HF or undergoing CABG or Minimally Invasive Aortic Valve Replacement (mini-AVR) procedures.

The research design of this study was determined by professor Dominique Hansen (DH) andNM. The students JV and IB worked out the procedure together with DH and NM. The recruitment of participants took place in the Jessa Hospital in Hasselt, Belgium and was conducted by NM. The data-acquisition was conducted by NM and master students of Hasselt University.

The data processing and academic writing was conducted by the students JV and IB, working simultaneously on parts of the research and intensively discussing the relevant content. NM offered the students support where needed in this process.

In this study, the researchers examined correlations between the CPET markers and the markers of frailty in the elderly (65+) population suffering from HF or undergoing CABG or Mini-AVR procedures. Important markers of the CPET were, among others, maximal oxygenuptake (VO_2-peak), maximal Wattage (W-peak) and maximum heart rate (HR-peak). The frailty markers were determined based on the phenotype of Fried and the Vigorito criteria.

Abstract

Background

Frailty is a very prevalent comorbidity in the heart failure (HF) and coronary artery bypass grafting (CABG) population. It is associated with negative outcomes like greater disability, higher mortality rate and exercise intolerance. Cardiopulmonary exercise testing (CPET) was already used to assess exercise capacity, but it has recently been confirmed that it is also useful to detect frailty in the elderly HF population. More data about the correlation between frailty and CPET markers in the elderly HF and CABG population is still lacking.

Objectives

To investigate the correlation between frailty and CPET markers and to examine differences in CPET markers between fragile and non-fragile patients with HF or undergoing CABG.

Methods

Eighteen patients (HF n=7, CABG n=11), mean age 72.4±5.7 years old, who received ambulatory cardiac rehabilitation were examined for frailty at baseline, using the phenotype of Fried and the Vigorito criteria. CPET testing on an electronic bicycle ergometer was used to determine the different CPET parameters. Statistical analysis was performed using ANOVA, multiple and simple linear regression.

Results

In the whole sample, the assessment tools of Fried and Vigorito were significantly related to the markers of the ventilatory thresholds (VT). In the CABG group, handgrip strength (HGS) was significantly related to all CPET markers, except for two. In the HF group, the Mini Nutritional Assessment (MNA) and medication use (MED) were significantly correlated to several CPET markers. All results were found between non-frailty and early stage frailty.

Conclusion

Significant correlations were found between MNA/MED and CPET markers in the HF group and between HGS and CPET markers in the CABG group, between non-frailty and early stage frailty. More research is needed to confirm these results.

Keywords

Frailty, cardiopulmonary exercise testing, heart disease, elderly

Introduction

The life expectancy of people born between the 40's and 60's of the previous century (the so-called 'baby-boom' generation) is globally increasing (McGinnis & Moore, 2006). Getting older is associated with the development of multiple comorbidities and a common syndromethat affects the elderly population, for example, is the FS.

The FS is a syndrome among older people caused by deteriorations across multiple physiological systems, contributing to decreased resistance to stressors and increased vulnerability to adverse events (Lee, Lee, & Yang, 2020). It often leads to a higher risk for falls, disabilities, hospitalizations, functional decline and mortality (Fried et al., 2001; Sanders et al., 2018). Worldwide, this syndrome reaches nearly 10% of the elderly population. (Lee, Lee, & Yang, 2020; Collard, Boter, Schoevers, & Oude Voshaar, 2012).

Different instruments are used to determine frailty. Recent research indicated that, withinthe population of cardiovascular diseases, the Fried phenotype seems to be the most used assessment tool for frailty (Fried et al., 2001; Marinus et al., 2021). This 'phenotype' can be identified by five physical characteristics: slow walking speed, low physical activity, exhaustion, weakness and unintentional weight loss. The frailty criteria by Vigorito aim to determine FS in a broader way and take psychosocial and cognitive components into account as well. This assessment tool has been recently developed and has not been validated yet (Vigorito & Abreu, 2020).

Research about the FS has recently gained interest in the area of cardiovascular pathologies.The FS is associated with the development of multiple comorbidities, a poorer quality of life (QoL) and a high mortality rate in hospitalized patients with coronary artery disease (CAD) (Qayyum et al., 2020). Recent research indicated that nearly half the HF population suffers from FS (Denfeld et al., 2017). Other studies have already built a consensus about the negative outcomes of FS in elderly patients with HF (Cacciatore et al., 2005; Gastelurrutia etal., 2014; McNallan et al., 2013). These negative outcomes are associated with greater disability, higher hospitality rates and increased risk of early death (Jha et al., 2015; Yang et al, 2018). A systematic review indicated that frail patients undergoing CABG and/or valveprocedures were associated with a higher odds

ratio (OR) (from 1.10 to 2.63) of mortality (Sepehri et al., 2014).

FS is related to exercise intolerance and a loss of lean body mass (Aguirre & Villareal, 2015). In cardiovascular and cardiopulmonary diseases, exercise intolerance is an important clinical feature from the very beginning (Guazzi, Bandera, Ozemek, Systrom, & Arena, 2017). Aboveall, exercise capacity is a strong predictor of mortality, life expectancy and disease-specific morbidity (Kodama, 2009; Billingsley et al., 2019; Piepoli, Corrà, & Agostoni, 2017).

CPET testing evaluates the gas exchange during exercise and provides an accurate description of the body's O_2-transport and utilization during exercise (Santoro et al., 2019). CPET is a useful tool to provide data about functional and exercise capacity and outcome prediction in many cardiopulmonary diseases, which enables the clinician to learn about the prognosis in, for example, the HF and CABG population (Corrà et al., 2014; Guazzi, Arena, Halle, Piepoli, Myers, Lavie, 2016; Myers, 2005; Kawashima et al., 2019; Corrà et al., 2017; Balady et al., 2010; Arena, Guazzi, Cahalin, & Myers, 2014).

CPET is also useful for detecting frailty in the elderly stable HF population (Kawashima et al., 2009). More data about CPET in the frail cardiovascular patients still lack in the existing literature. Even though CPET provides more information about sarcopenia, fatigue, exercise intolerance and exercise capacity, which are important characteristics of the phenotype of Fried, the association of the CPET markers and markers of frailty has not been investigated in the cardiovascular research population in the previous literature (Guazzi, Bandera, Ozemek, Systrom, & Arena, 2017; Albouaini, Egred, Alahmar, & Wright, 2007; Myers, Arena, Cahalin, Labate, & Guazzi, 2015; Malhotra, Bakken, D'Elia, & Lewis, 2016).

In this research paper, we aim (1) to investigate the correlation between frailty and CPETmarkers and (2) to examine differences in CPET markers between fragile and non-fragile patients suffering from HF or undergoing CABG surgery or Mini-AVR.

Methods

1. Participants

1.1 Recruitment

The researchers of this study collaborated with the medical staff of the Jessa Hospital, Campus Virga Jesse in Hasselt, Belgium to recruit the patients from October 2020 until May 2021. The lead investigator NM checked which patients met the inclusion criteria and were therefore eligible to participate in the study. Subsequently, the aims and procedures of this study were thoroughly discussed with the patient or his/her legal representative and written informed consent was obtained. The study protocol was approved by the Ethics Committee of the Jessa Hospital Hasselt (20.85-REVA20.07) on October 13, 2020.

1.2 Selection

Patients were included in this study if they met the following criteria: 1) Age of 65 years or older at the start of the study, 2) Admitted to the Jessa Hospital Hasselt for cardiac rehabilitation (CR) after a cardiac event or diagnosis, 3) Being diagnosed with HF or had CABG or mini-AVR surgery. Patients were excluded in case of a persistent unstable medicalstate (e.g. angina, conduction disturbances, arrythmia, acute heart failure or any clinical condition requiring intervention).

1.3 Baseline characteristics

The baseline characteristics of all included participants were assembled through careful inspection of the electronic patient files on the day of the testing. These characteristics included age, gender, height, bodyweight, Body Mass Index (BMI) and use of walking aids. Inaddition, the use of medication of the participants was also taken into account. The goals of this baseline analysis were to gain a better understanding of the sample and to examine possible baseline differences at the start of the study.

2. Study design

An observational, cross-sectional study design was used to investigate correlations between frailty scores, based on the Fried Phenotype and the criteria of Vigorito, and relevant CPET markers. These correlations were examined in the entire sample of included cardiac patientsand

in the subgroups of HF, CABG and mini-AVR specifically.

3. Procedure

2.1 Frailty assessment

2.1.1. Phenotype of Fried

Fried et al used five criteria in their assessment tool: 1) Unintentional weight loss: participants were asked if they lost more than 4.5kg in the past year, involuntary, so not dueto diet or sports, 2) Exhaustion: measured by two questions of the Centre for Epidemiologic Studies (CES-D) Depression scale, 3) Walking speed: measured by the 4.6 meter walking test,
4) Level of physical activity: measured using the Katz-index, which is an assessment tool that scores the degree of independence of a person in the daily life on six different domains, 5) HGS: measured with the JAMAR handheld dynamometer. When one or two criteria were fulfilled, the participant was considered as being pre-fail. When at least three criteria were met, frailty was confirmed. This combination of criteria has been shown to have construct and predictive validity (Fried et al., 2001; Weiss, Hoenig, Varadhan, Simonsick, & Fried, 2009). A more detailed explanation of this assessment tool can be found in Table 1 in the Appendix.

2.1.2. Vigorito's Frailty assessment tool

The frailty assessment tool of Vigorito consisted of eight measurement tools: 1) The Mini Nutritional Assessment Tool (MNA), used to measure the nutritional status of the participant, 2) The Katz index, as mentioned earlier, 3) Gait speed, measured by the 4.6 meter walking test, 4) The Timed Up and Go Test (TUG), to measure balance, functional mobility and strength of the lower limbs, 5) Mini-mental state examination (MMSE), used tomeasurethe cognitive status of the participant, 6) The Geriatric Depression Scale (GDS), usedto detect possible depressive or negative emotions, 7) HGS, as mentioned earlier. Using the results of the preceding tools, the patients became divided into three categories, ranging from not frail (score 0) to severe frail (score 3). More information about this assessment toolcan be found in Table 2 in the Appendix.

2.2 Cardiopulmonary Exercise Testing (CPET)

Cardiopulmonary Exercise Testing was completed on an electronic bicycle ergometer (eBike;GE Medical Systems, Milwaukee, WI, USA), managed by Cardiosoft electrocardiography software

(Cardiosoft 6.6; GE Medical Systems, Freiburg, Germany). The testing procedure consisted of a 30-second resting period sitting upright on the cycle ergometer, followed by two minutes of unloaded warming-up cycling (60-70 revolutions/min (rpm)) and an incremental cycling test (60-70 rpm) until exhaustion. Six fixed protocol combinations were determined (expressed as initial workload (Watt)/workload increase/min): 10/5, 20/10, 30/15, 40/20, 50/25 and 60/30 from which 20/10, 30/15 and 40/20 were mostly applied in this study. This protocol was chosen for the purpose of finishing within 6-12 min. The test was terminated when the cycle frequency dropped below 60 rpm.

Resting heart rate (HR_rest) and peak heart rate (HR_peak) were determined using a 12-lead electrocardiogram (ECG) device (KISS Multilead; GE Medical Systems Freiburg, Germany).
Maximal oxygen uptake (VO_2_peak and VO_2_peak/kg) and peak respiratory gas exchange ratio (RER_peak) were measured using a mass spectrometer and volume turbine system (Jaeger MasterScreen CPX Metabolic Cart; CareFusion Germany GmbH, Hoechberg, Germany). The first ventilatory (aerobic) threshold was determined by the V-slope method and then double-checked by the EqO_2-curve (when EqO_2 started to rise). The second ventilatory (anaerobic) threshold was determined by the VE/VCO_2-slope and then double- checked by the $EqCO_2$-curve (when $EqCO_2$ started to rise). These thresholds were determined on the level of power (W), heart rate (beats per minute (bpm)) and VO_2-peak. This procedure was carried out by two blinded researchers.

2.3 Outcome measures

The primary outcome measures of this study were the 1) Peak power output (W-peak), 2) Peak heart rate (HR-peak), 3) Peak oxygen consumption (VO_2-peak), 4) Peak oxygen consumption per kilo bodyweight (BW) (VO_2-peak/kg), 5) Peak respiratory exchange ratio (RER-peak), 6) First ventilatory threshold determined on the level of VO_2-peak (VT1-VO_2 (ml/min)), heart rate (VT1-HR) and wattage (VT1-W), 7) Second ventilatory threshold determined on the level of VO_2max (VT2-VO_2 (ml/min)), heart rate (VT2-HR) and power (VT2-W), all these markers were obtained by a CPET testing, performed in the Jessa hospital in Hasselt.

The other primary outcome measures were the criteria of the test batteries of Fried and Vigorito: 8) MNA, 9) Katz Index of Independence in Activities of Daily Living (ADL), 10) Gait speed , 11)

TUG, 12) MMSE, 13) GDS, 14) number of medications (MED), 15) HGS (HGS of thedominant hand (HGS-D) and HGS of the non-dominant hand (HGS-nD)), 16) Weight loss, 17) Exhaustion and 18) Physical activity.

2.4 Statistical analysis

Statistical analyses were performed using SAS JMP® Pro 15.2 (SAS Institute Inc.). The outcome measures are presented as mean ± standard error (SD). P-values were consideredstatistically significant if they were <0.05.

To analyze the frailty assessment tools in their entirety, both the raw and classification scores of the Fried and Vigorito testings were used (Raw scores (classification); Fried: 0= notfrail (0),1-2= pre-frail (1), ≥3= frail (2); Vigorito: 0-6: not frail (0), 7-12: minor frail (1), moderate frail 13-18 (2), severe frail: 19-24 (3)) to investigate the correlation with the CPET-markers (W- peak, HR-peak, VO_2-peak, VO_2-peak/kg, RER-peak, HR-rest, VT1-VO_2, VT1-HR,VT1-W, VT2- VO_2, VT2-HR, VT2-W).

Two-way ANOVA was used to compare the frailty categories with the CPET-markers. Using Shapiro-Wilk Tests in case of a normal distribution or Kruskal-Wallis Test in case of a non- normal distribution among the variables, while homoscedasticity was evaluated using the Brown-Forsythe Test.

Simple linear regression was used to compare the raw scores of the frailty assessment toolswith the CPET markers.

The correlation between the individual frailty markers of the assessment tools of Vigorito and Fried (HGS-D, HGS-nD, MMSE, GDS-15, MNA, exhaustion (1: I felt that everything I did was an effort, 2: I could not get going), weight loss (lost more than 4.5 kg in the past year), TUG (sec), walking time (4.6m walking test), gait speed (m/s), KATZ scale (1: bathing (1-4), 2: dressing (1-4), 3: transferring (1-4), 4: toileting (1-4), 5: continence (1-4), 6: feeding (1-4), 7: total score) and number of medications) and the important CPET markers was examined using a multivariate regression model. Normality of the residuals was assessed using Shapiro-Wilk Tests, while homoscedasticity was evaluated by the residual versus predicted values plot for both the simple linear regression and the multivariate regression model.

Within this last part of the analysis, no distinction was made between the assessment toolsof Fried and Vigorito, since some markers occurred in both tests (e.g. HGS and KATZ index).When evaluating HGS, both the dominant and non-dominant hand were included in the analysis. The analysis was performed for the entire sample, as well as divided into subgroups according to the CVD (HF, CABG or mini-AVR).

Results

1. Baseline characteristics

1.1. Follow-up

At the start of the study, 32 patients met the inclusion criteria and were then assessed for frailty markers. This sample consisted of 23 male and 9 female participants, with a current cardiac diagnosis of CABG (n=17), HF (n=12) or mini-AVR (n=3). A total of 14 patients were lost to follow-up during the course of this study. Six patients did not undergo CPET testing, whereas one patient died of COVID-19 before CPET testing was completed. Seven other patients were excluded from the analysis because their CPET data were incomplete and therefore could not be taken into account. Data about the measurements of their VT1 and VT2 were missing, so the decision was made to completely eliminate them from the analysesto keep the power of the study equal for all the outcome measures. The remaining sample consisted of 18 male and no female participants. The three mini-AVR patients were all lost tofollow-up, but the HF (n=7) and CABG (n=11) populations were still adequately represented in the final sample. Hence, the results of this study can only be relevant for males with a diagnosis of HF or CABG. For more information and the flowchart, see figure 1 in the Appendix.

1.2. Baseline characteristics

1.2.1. Participant characteristics

Baseline characteristics were very similar across both groups. Mean age in the HF group was 75.4±7.9 years old, whereas people in the CABG group were slightly younger with a mean age of 70.4±2.8 years old. Patients in the HF group also suffered from more cardiac events in the past (mean 3.6±6.1) than patients in the CABG group (mean 2.0±2.7), but neither of these differences reached statistical significance. Other baseline parameters were comparable for both groups, which can be found in table 3 in the Appendix.

1.2.2. Frailty assessment and CPET markers at baseline

Baseline test results also showed a very homogeneous group of participants, with only onetest resulting in a statistically significant difference between groups. The HF group used significantly more time (mean time 8.2±1.3 seconds) to complete the TUG test than the CABG group (mean time 6.9±1.2 seconds) (p=0.04). By contrast, gait speed (m/s) and walkingtime (4.6m walking

test) at baseline were similar in both groups. There were no significant differences found for the other baseline tests. Baseline test results of the CPET markers also revealed no significant differences between the HF and CABG groups. More information can be found in table 4, 5, 6 and 7 in the Appendix.

1.2.3. Total frailty score at baseline

The test results were analysed according to the phenotype of Fried. In the HF group, this means that no patients were classified as 'frail'. Three patients were considered as 'not frail'at baseline, while the remaining four patients in this group were considered to be 'pre-frail'.Similar results were obtained in the CABG group, where six patients were classified as 'not frail' and five patients as 'pre-frail'. This was in contrast with the Vigorito scale of frailty.

According to Vigorito, 17 out of the 18 patients in this sample were 'not frail'. There was only one patient (in the CABG group) with a slightly higher score who fell in the category of 'minor frail'. There were no patients in this sample diagnosed with 'moderate' or 'severe' frailty according to Vigorito. This information can also be found in table 7 in the Appendix.

2. Correlations between the frailty total scores of the assessment tools of Fried and Vigorito and the CPET markers

2.1. Correlations between the total score of the Fried assessment and CPET markers

In the total sample, the power when the first ventilatory threshold was reached (VT1-W) (p=0.03) (R^2=0.27) and the power when the second ventilatory threshold was reached (VT2- W) (p=0.004) (R^2=0.23) were significantly correlated with the categories of the assessment tool of Fried (Table 8) . The VO_2-peak during the first ventilatory threshold (VT1-VO_2 (ml/min)) (p=0.02) (R^2=0.29) and the VO_2-peak during the second ventilatory threshold (VT2-VO_2 (ml/min)) (p=0.03) (R^2=0.25) were significantly correlated with the raw scores of the assessment tool of Fried. In the HF and CABG populations separately, no significant correlations were found between the CPET scores and the assessment tool of Fried.

2.2. Correlations between the total score of the Vigorito assessment and CPET markers

The raw scores of the Vigorito assessment tool indicated a significant correlation with VT1- VO_2 (ml/min) (p=0.03) (R^2=0.27) and VT2-VO_2 (ml/min) (p=0.047) (R^2=0.22) for the total sample. The separate categories indicated no significant correlations within the total sample.In the CABG

population, no significant correlations were found for both the categories and the raw scores with any CPET markers. Within the HF population, a significant correlation was found between the Vigorito categories and VO_2-peak (p=0.02) (R^2=0.67), VT1-VO_2 (ml/min) (p=0.02) (R^2=0.70) and VT2-VO_2 (ml/min) (p=0.02) (R^2=0.71). The raw scores of Vigorito indicated no significant correlations with the CPET markers within the HF population.

3. Correlations between the individual frailty markers and the CPET markers

3.1. W-peak

In the total sample, W-peak was found to be significantly correlated with the HGS-D (p=0.004) (R^2=0.41) and HGS-nD (p=0.01) (R^2=0.38). More specifically, in the CABG population, W-peak was also significantly correlated with HGS-D (p=0.004) (R^2=0.62) and HGD-nD (p=0.0004) (R^2=0.76). No significant correlations were found in the HF population.

3.2. HR-peak

Within the total sample, HGS-D (p=0.03) (R^2=0.25) and weight loss (p=0.02) (R^2=0.28) were significantly correlated with HR-peak. More specifically, in the CABG population, HGS-D (p=0.01) (R^2=0.51) and HGS-nD (p=0.0004) (R^2=0.54) were significantly correlated with HR-peak. In the HF sample, HR-peak was significantly correlated with MED (p=0.047) (R^2=0.58).

3.3. VO_2-peak

In the total sample, HGS-D (p=0.001) (R^2=0.49) and HGS-nD (p=0.01) (R^2=0.37) were significantly correlated with VO_2-peak. More specifically, in the CABG population, HGS-D (p=0.01) (R^2=0.58) and HGS-nD (p=0.01) (R^2=0.56) were also significantly correlated with theVO_2-peak. In the HF population, no significant correlations were found.

3.4. VO_2-peak/kg

In the total sample, HGS-D (p=0.046) (R^2=0.23) correlated significantly with the VO_2-peak/kg. More specifically, in the CABG population, HGS-D (p=0.045) (R^2=0.37) and HGS-nD (p=0.02) (R^2=0.49) were significantly correlated with the VO_2-peak/kg. No significant correlations with VO_2-peak/kg were found in the HF population.

3.5. RER-peak

In the total sample, walking time (p=0.03) (R^2=0.28) and gait speed (p=0.02) (R^2=0.31) were

significantly correlated with RER-peak. No significant correlations were found in the CABG andHF population with RER-peak.

3.6. HR-rest

In the total sample, weight loss (p=0.001) (R^2=0.48) was significantly related to HR-rest. More specifically, in the CABG sample, weight loss (p=0.04) (R^2=0.39) was also significantly correlated with HR-rest. In the HF population, HR-rest was also significantly correlated with weight loss (p=0.02) (R^2=0.68) and with the MNA (p=0.01) (R^2=0.76).

3.7. VT1-VO_2 (ml/min)

In the total sample, HGS-D (p=0.002) (R^2=0.46) and HGS-nD (p=0.004) (R^2=0.41) were significantly correlated with VT1-VO_2 (ml/min). More specifically, in the CABG population, HGS-D (p=0.01) (R^2=0.58) and HGS-nD (p=0.0003) (R^2=0.78) were also significantly correlatedwith the VT1-VO_2 (ml/min). No significant correlations with VT1-VO_2 (ml/min) were found in the HF population.

3.8. VT1-HR

In the total sample, weight loss (p=0.01) (R^2=0.37) correlated significantly with VT1-HR. More specifically, in the CABG sample, HGS-nD (p=0.04) (R^2=0.39) correlated significantly with VT1-HR. In the HF sample, the MNA (p=0.004) (R^2=0.83) correlated significantly with VT1-HR.

3.9. VT1-W

In the total sample, HGS-D (p=0.02) (R^2=0.31), HGS-nD (p=0.02) (R^2=0.38), the total classification of Fried (p=0.03) (R^2=0.27) and the GDS (p=0.03) (R^2=0.27) were significantly correlated with VT1-W. More specifically, in the CABG sample, HGS-D (p=0.03) (R^2=0.44) andHGS-nD (p=0.0005) (R^2=0.75) correlated significantly with VT1-W. No significant correlationswere found in the HF sample.

3.10. VT2-VO_2 (ml/min)

In the total sample, HGS-D (p=0.001) (R^2=0.48), HGS-nD (p=0.01) (R^2=0.37), the raw scores of Fried (p=0.03) (R^2=0.25) and the raw scores of Vigorito (p=0.047) (R^2=0.22) were significantly correlated with VT2-VO_2 (ml/min). More specifically, in the CABG population, HGS-D (p=0.004) (R^2=0.63) and HGS-nD (p=0.002) (R^2=0.68) were significantly correlated with the VT2-VO_2 (ml/min). In the HF sample, the classification of Vigorito (p=0.02) (R^2=0.71) correlated significantly with VT2-VO_2 (ml/min).

3.11. VT2-HR

In the total sample, HGS-D (p=0.02) (R^2=0.31), HGS-nD (p=0.049) (R^2=0.47), weight loss (p=0.02) (R^2=0.24) and MED (p=0.03) (R^2=0.25) were significantly correlated with VT2-HR. More specifically, in the CABG population, HGS-D (p=0.01) (R^2=0.52) and HGS-nD (p=0.01) (R^2=0.60) were also significantly correlated with VT2-HR. In the HF sample, the MNA (p=0.004) (R^2=0.83) and MED (p=0.01) (R^2=0.73) were significantly correlated with VT2-HR.

3.12. VT2-W

In the total sample, HGS-D (p=0.01) (R^2=0.40), HGS-nD (p=0.049) (R^2=0.40) and the classification of Fried (p=0.004) (R^2=0.23) were significantly correlated with VT2-W. More specifically, in the CABG sample, HGS-D (p=0.01) (R^2=0.55) and HGS-nD (p=0.0004) (R^2=0.76)correlated significantly with VT2-W. No significant correlations with VT2-W were found in the HF sample.

Discussion

1. General findings

Both Fried and Vigorito found significant correlations with the VT1-W and VT2-W, which indicated significant differences between non-frail and pre-frail (Fried) and between non- frail and minor frail (Vigorito) participants for the previous markers in the total sample. VO_2-peak, VT1-VO_2 and VT2-VO_2 were significantly correlated to the Vigorito categories in the HF population, which indicates that a higher score on the Vigorito assessment was related to lower VO_2-peak values and achieving earlier ventilatory thresholds during exercise, which indicates worse prognostic outcomes.

Our results clearly demonstrated that HGS was the most common parameter of frailty to be correlated with the markers of CPET within the entire sample and within the CABG population. All the CPET markers were significantly correlated with HGS, except for RER- peak and HR-rest. The correlation between weight loss and HR-rest was the only frailty marker aside from HGS that seemed to be significantly correlated to a CPET marker in the CABG population. All the other CPET markers, except HR-rest, were significantly correlated toHGS-D and HGS-nD. This indicated that only HGS showed significant differences between theCPET markers of non-frail and pre-frail (Fried) and between non-frail and minor frail (Vigorito) participants. From this point of view, HGS and weight loss seemed to be the most important markers in determining frailty in the CABG population. Caution must be taken when interpreting these results due to the small sample size and the absence of 'higher frailty' levels/scores in both the assessment tools.

In the HF population, different frailty markers seemed to be significantly linked to some CPET markers. In general, MED was significantly correlated to VT2-HR and HR-peak, MNA was significantly correlated to HR-rest, VT1-HR and VT2-HR and weight loss was significantly correlated to HR-rest. These results indicated correlations between HR during rest and during exercise and weight management. In this sample, the MNA seemed to be more sensitive to discover malnutrition because it took different aspects of malnutrition into consideration instead of just weight loss. Both the MNA (Vigorito) and weight loss (Fried) discovered malnutrition in five patients, but they only agreed on two of those patients. Thishighlighted the difference

between the two chosen measurements, which was confirmed inthe current sample.

2. Clinical relevance

Earlier research indicated the link between power (Watt) and the time of the ventilatory thresholds in the healthy population (Wasserman, 1984). In the elderly CVD population, evidence about this was rare (Suzuki et al., 2004; Kunz, Serra, Borges, Serra, & Silva, 2012). This was an interesting finding, because using power output, in addition to VO_2-peak and HR,to define the ventilatory thresholds, seemed to be relevant to predict the exercise capacity in the elderly (HF and CABG) population.

In the HF population, the Vigorito classification score correlated significantly with VO_2-peak VT1-VO_2 and VT2-VO_2. VO_2-peak forms an important survival predictor within the HF population: a VO_2-peak lower than 14 ml/kg per minute indicated a significantly lower 1-yearsurvival (Francis, Goldsmith, & Cohn, 1982; Francis, Goldsmith, Ziesche, & Cohn, 1982; Smith et al., 1993; Paolillo & Agostoni, 2017). The VO_2-peak and VT1 are important parameters in indicating the exercise tolerance (Tomono, Adachi, Oshima, & Kurabayashi, 2016; Koike et al., 2000; Corrà, Mezzani, Bosimini, & Giannuzzi, 2004; Mancini et al., 1991). As mentioned earlier, FS is typically related to exercise intolerance (Kawashima et al., 2019). Even though the VT2 does not form an important marker for prognosis, it is the only marker that determines the critical power and forms, together with VT1, an import indicator for exercise prescription (Carvalho & Mezzani, 2011; Coplan, Gleim, & Nicholas, 1986; Mezzani et al., 2009, 2010). Based on these findings, the Vigorito assessment tool seemed more representative to identify minor frailty and its functional impact on important markers of prognosis and survival in the HF population.

HGS is an import marker to measure prognosis in the elderly. It forms a good predictor of muscular fitness and overall body strength, but also of functional capacity and the FS (Rantanen et al., 1999). Recent research indicated the link between low HGS and arterial stiffness, which forms an independent risk factor in developing the coronary artery disease(CAD) (König et al., 2021; Bonarjee, 2018). In the CAD population, HGS is an important predictor of mortality and cardiovascular events (Larcher, 2020). CR has shown to improve muscular strength and functional capacity in the CAD population (Yamamoto, Hotta, Ota, Mori, & Matsunaga, 2016;

Marzolini, Oh, & Brooks, 2011). Note must be made, that there were no studies yet that found improvements in the HGS itself, even though functional parameters and general strength increased due to CR in the CAD population (Mandic et al.,2013; Mroszczyk-McDonald, Savage, & Ades, 2007). For CR after the CABG-procedure, research indicated favourable results on muscle strength and exercise tolerance/functionalcapacity in this population (Nishitani et al., 2013; Ghroubi et al., 2013; Borges et al., 2016). Caution must be taken, because two studies had low power and the study of Borges et al. (2016) was conducted during the hospital stay (Ghroubi et al., 2013; Borges et al., 2016). However, these results highlighted the importance of CR and strength training to improvefunctional capacity and strength in the CAD and CABG populations in the short term. Evidence about long term CR to improve HGS, muscle strength or functional capacity lackedwithin in the existing literature of the CABG population.

Interestingly, no CPET marker was significantly correlated to HGS in the HF population, in contrast to the CABG and the total sample. Earlier research about the correlation betweenHGS and exercise markers is limited in the elderly HF population (Weng, Lin, Tarng, & Lin, 2021; Izawa, 2012, 2009). Future research within this population with a higher power is required to clarify these results.

In the HF population, a significant correlation was found between the MED and the VT2-HR and HR-peak. This seemed reasonable, because the use of Beta-blockers (85.7% in this studysample) is related to adverse effects on the exercise capacity and functional outcomes, which eventually increases the risk of developing the FS (Meyer, Rambod, & LeWinter, 2018; Nambiar & Meyer, 2018; Epstein, Robinson, Kahler, & Braunwald, 1965). Earlier research indicated a HR lowering effect of ACE-inhibitors in the middle-aged hypertensive population and a short-term HR lowering effect of the ACE-inhibitor enalapril in dogs with naturally acquired HF (Pierdomenico, Bucci, Lapenna, Cuccurullo, & Mezzetti, 2002; Sisson, 1995). Unfortunately, research about the effects of ACE-inhibitors on the HR in the HF population lacked in the existing literature. Previous research indicated the effect of statins on heart rate variability inthe HF population (Pierdomenico, Bucci, Lapenna, Cuccurullo, & Mezzetti, 2002; Horwich & Middlekauff, 2008). Some research also indicated that FS may affect the pharmacokinetics of metoclopramide and the clearance of renal drugs. When looking at these results, it seemed as though the HR lowering effect of beta-blockers, ACE-inhibitors and statins was a reasonable pathway to explain the

correlation between the frailty marker 'medication use' and different CPET markers related to HR, but research about the exact effects of CVD medication in the HF population has not been established yet in the existing literature (Wynne et al., 1993; Johnston et al., 2014).

Malnutrition often appears in the elderly HF population and has an impact on the adverse outcomes, the development of sarcopenia and the eventual development of FS, so these factors are important to take into account (Rahman et al., 2015; Sze, 2017; Yin, Lu, Qian, Xu,& Zhou, 2019). Research even indicated that up to 50% of the HF population suffers from malnutrition (Grossniklaus, O'Brien, Clark, & Dunbar, 2008). This process of malnutrition is often more complex to solve in HF patients, due to the co-development of cardiac cachexia in 8-42% in the HF cases (Christensen et al., 2012). Individualized nutritional interventions have been shown to be effective in the malnourished elderly HF patients in previous literature (Bonilla-Palomas et al., 2016; Colín Ramírez et al., 2004). Recent research indicated significant improvements in functional and nutritional status due to a switch from ACE- inhibitor/angiosine II receptor blocker therapy to sacubitril/valsartan in the elderly HF population with preserved ejection fraction (HFrEF) (Dereli, Bayramoglu, & Kaya, 2020). A limitation of this study is that only male subjects were eventually included due to loss to follow-up of the female sample, because elderly woman in general have greater odds of malnutrition, compared to men (Evans, 1995). This evidence highlighted the link between nutrition and exercise capacity parameters like HR-rest and VT.

It was difficult to compare results regarding MNA (Vigorito) and weight loss (Fried) in the HF population, because the weight loss was unvoluntary and not due to conscious diet. However, The MNA seemed to be a more objective tool to indicate malnutrition. The weight loss marker was measured by the question 'did you lose 4.5kg in the past year?', which madeit more sensitive to recall bias and which did not tell any information about the cause of the weight loss. Even though both markers have the same purpose to detect malnutrition, sarcopenia or cardiac cachexia, the MNA seemed a better choice to determine these problems (Saitoh et al., 2016; Vellas et al., 1999; Liguori et al., 2018). Because Fried did nottake into account the medicine usage and the MNA questionnaire, the assessment tool of Vigorito seemed to be a better choice to distinct non-frail patients from minor frail or pre- frail patients in relation to the important CPET markers in the HF population. Important to consider is that the Vigorito assessment tool has not been validated yet, as mentioned earlier (Vigorito & Abreu, 2020).

3. Strengths

This is the first study to investigate the different correlations between CPET markers and frailty. Since exercise capacity is crucial in determining the prognosis of elderly patients, especially in those with cardiovascular pathologies (which was mentioned earlier) (Aguirre &Villareal, 2015), this constitutes a new promising pathway for future research. This article highlights the importance of frailty and the associated exercise intolerance in choosing adequate treatment options for patients with specific cardiovascular diseases.

The methodology and statistical analysis of this research paper are reported in a very transparent and detailed manner so that future research can focus on examining the sametopic in larger samples and possibly different (cardiovascular) populations. This will make iteasier for other researchers to compare their study results to the results of this article, so that there will be more conclusive evidence surrounding this topic in the future.

Another strength of this study is that it found strong correlations between HGS and almost all CPET markers (particularly W-peak, HR-peak, VO2-peak, VO2-peak/kg, VT1-VO2, VT1-W, VT2-VO2, VT2-HR and VT2-W) in the CABG group and between MNA/MED and most heart rate related CPET markers (particularly HR-rest, VT1-HR and VT2-HR with MNA; HR-peak andVT2-HR with MED) in the HF group. These results confirm the relevance of frailty in specific cardiovascular pathologies and highlight the importance of multidisciplinary CR to improve functional capacity and avoid the development of adverse outcomes.

Two different frailty assessment tools were used to determine frailty in this article. Both the phenotype of Fried and the Vigorito criteria have multiple categories to define frailty insteadof binary labelling a patient as frail or not frail. This means that patients who are pre-frail or who are at risk for frailty are also discovered and can be treated accordingly. This is beneficial because it helps in tackling frailty and the associated exercise intolerance as soon as possible and in assigning the patients to the right treatment options. Moreover, most patients in this study sample were, in fact, pre frail or minor frail, which means that these patients would not have been discovered if there were only two categories (frail or not frail).Another strength is that, in

this study, frailty characteristics were measured in a very standardized and reproducible way to minimize the risk of detection bias and measurement errors.

4. Limitations

Despite promising results, this study still contained a few limitations. According to Fried, nine patients in this sample were categorized as 'not frail' and the other nine patients were categorized as 'pre-frail', with zero patients who were diagnosed as 'frail'. The analysis usingthe Vigorito criteria showed similar results with seventeen patients 'not frail', one patient 'minor frail' and zero patients 'moderate frail' or 'severe frail'. This was an underestimation of the prevalence of frailty in the general population of HF and CABG patients. Recent research investigated the prevalence of frailty in different populations and showed that, in the HF population, 46-49% of patients suffered from 'pre-frailty' and 12-24% suffered from 'frailty' (O'Caoimh et al., 2020). An important remark about this study, however, was that it was a meta-analysis of 240 different articles about frailty. Since consensus is still lacking about the instruments that measure frailty, it is unclear which instruments were used in these 240 studies. This made it difficult to compare with the current study, where the phenotype of Fried and Vigorito criteria were used to define frailty. In the CABG population,a study indicated that the prevalence of frailty increased with age. This article stated that 21.7% of people aged 65-74,25.6% of people aged 75-84 and 31.5% of people aged 85 or older were considered to be frail (Tran, Tu, Dupuis, Bader Eddeen, & Sun, 2018). The prevalence of frailty was thus underestimated in the current sample, with a high risk of selection bias. This made it difficult to make verified statements about the correlations between frailty and CPET markers, because frailty was not adequately represented in this study.

Other studies also indicated that frailty was more prevalent in women than in men (O'Caoimh et al., 2020; Davis et al., 2021). Although both women and men were originally included, the final sample of this study consisted of eighteen men and zero women. The lackof women could be a possible argument as to why frailty scores were low in this sample.

Analogous to women, patients with a mini-AVR were also originally included in this study.

Because of a loss to follow-up of three mini-AVR patients, the final sample ended up with eleven CABG, seven HF and zero mini-AVR patients. Hence, the results were only relevant forthe CABG and HF population and not for the mini-AVR population.

There is still a lack of consensus regarding the FS in the existing literature. As mentioned earlier, different articles investigate frailty with different instruments (Afilalo et al., 2012; Denfeld et al., 2017; Dent, Kowal, & Hoogendijk, 2016). A study of Afilalo et al. (2012), for example, used the following four different scales to define frailty: (1) the Cardiovascular Health Study (CHS) frailty scale with five items (gait speed, HGS, inactivity, exhaustion and weight loss), which equals the phenotype of Fried, (2) the expanded CHS frailty scale with seven items (cognitive impairment, depressed mood and the five previous criteria of the CHSfrailty scale), (3) the MacArthur Study of Successful Aging (MMSA) frailty scale with four items (gait speed, HGS, inactivity and cognitive impairment), (4) gait speed alone. Another article by Dent et al. (2016) revealed fourteen different measuring tools to define frailty. The large variability between the measuring instruments and their components madeit difficult to compare the results of this study to the results in the rest of the literature. So this is not specifically a limitation of this study, but a limitation to compare the current study to the existing literature about frailty.

Another large limitation of this study was the small sample size. The final sample contained eighteen participants in total, with eleven CABG and seven HF patients. This made it difficult to make solid conclusions about correlations between frailty and CPET markers and to exclude the possible contribution of coincidences, because the small sample might have overestimated possible correlations (Hackshaw, 2008). The small sample size also impairedthe statistical power of this study (Deziel, 2018).

Two separate markers (VT1-VO_2 and VT1-HR) were not normally distributed across the sample. Using ANOVA and multiple linear regression, corrections were made for two of thethree analyses with the Kruskall-Wallis test. However, it was not possible to make corrections in the third analysis using simple linear regression. This did not have a large impact on the results, but it made the subsequent evidence less strong.

A possible limitation in the use of both the Fried and Vigorito assessment tool in this study was

the use of the KATZ index to measure physical activity. The KATZ index was not able to detect any significant differences between the patients. Correlations between the KATZ components and the CPET markers could not be calculated because all patients had the exact same score (score 1) for every component, with the exception of one patient, who hada score of 2 on the item 'bathing'. One of the limitations of this instrument was that it only evaluated the very basic activities of daily living without taking into consideration the more advanced activities (Katz, Down, Cash, & Grotz, 1970). A possible explanation for the lack of significant differences is that the participants in the current sample were all ambulatory HF or CABG patients who only visited the hospital to perform the CR and who all lived independently at home. Their scores on the KATZ index were relatively low because they might have been more likely to be able to do the items independently than people with the same age who lived in a retirement home. Hence, there was a risk of selection bias because elderly HF or CABG patients who lived in a retirement home were less likely to come to the hospital for rehabilitation.

Besides selection bias, there was also a risk of interview bias with tests like the GDS. Respondents might have answered differently if they could have written down their own answers without having to tell them to an investigator. A risk of reporting bias also existed, because the researchers who performed the data collection and analysis were not blinded tothe identity and group of the participants. Lastly, there was a risk of measurement error because the Vigorito criteria for frailty have not yet been validated. However, this was a minor risk because the different tests (MNA, KATZ, 4.6m walking test,TUG, MMSE, GDS, MED, HGS) have been validated in the elderly population (Arik et al., 2015; Vellas et al., 1999; Nightingale, Mitchell, & Butterfield, 2018; Foroughan, Jafari, Peimaneh, Farahani, &Rahgozar, 2008; Pocinho, Farate, Dias, Lee, & Yesavage, 2009; Lee et al., 2020).

5. Future research

Further research is needed to investigate samples who adequately represent the targeted research population. Especially studies that include women and men equally and where the prevalence of frailty is representative for the entire population. Articles that include 'moderate' and 'severe' frailty as well as 'minor' and 'non' frailty might be able to detect more meaningful correlations between frailty and the CPET markers. Ideally, future studieswill focus on collecting

a larger sample size to increase the statistical power. In addition, itwould also be interesting to investigate this topic in the mini-AVR and other cardiac populations.

Conclusion

In the HF population, significant correlations were found between MNA, MED and most HR-related CPET parameters. There were also significant correlations between the VO_2-peak parameters and Vigorito classification scores in this population. In the CABG and total population, HGS was significantly correlated to nearly all the CPET parameters. No correlations were found in the CABG population between CPET markers and the assessmenttools. All these results were found between non-frailty and early stage frailty. More research is needed to confirm these results.

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Appendix

Table 1

Frailty Assessment Tool of Fried

Frailty markers		
Weight loss	The researcher asks the question: "Have you lost more than 4.5 kg (10 pounds) in the past year unintentionally (i.e., not due to dieting or exercise)? If yes, then the criterium for weight loss was met. Note: weight loss due to diuretics is taken into account as unintentional as well	
Exhaustion	Measured by two statements of the CES-D Depression Scale, the researcher asked how many times the participant felt this way in the last week: 1)I felt that everything I did was an effort; 2) I could not get going. The participant could reply with: 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 (3-4days)3: most of the time The answers "2" or "3" to both of these questions are categorized as frail by the criterium of exhaustion	
Physical activity (/6)	The Katz Index of Independence in Activities of Daily Living (Katz-scale) is an assessment tool to measure the degree of independence in the elderly population. The total score is determined by 6 separate parts: "bathing", "dressing", "transferring", "toileting" and "feeding". The scores vary from 1 (completely independent) to 4 (completely dependent). The participant was considered frail as he lost independence in one or morepartsof the scale.	
Walking time (sec)	Investigated by measuring the time the participant needs to walk a distance of 4.6 meter (15 feed). The cut-off values for frailty were determined by stratification of gender andheight of the participant.	
	Men	
	Height ≤173 cm (68 in)	≥7 seconds
	Height ≥173 cm (68 in)	≥6 seconds
	Women	
	Height ≤159 cm (63 in)	≥7 seconds
	Height ≥159 cm (63 in)	≥6 seconds
HGS (kg)	Investigated by the JAMAR handheld dynamometer. The participant was given 3 trials to squeeze as hard as they could with their dominant and non-dominant hand. The grip strength (kg) cut-off values for frailty were determined by stratificationof gender and BMI quartiles.	
	Men	
	BMI≤24	≤29 kg
	BMI 24.1-26	≤30 kg

	BMI 26.1-28	≤30 kg
	BMI > 28	≤32 kg
	Women	
	BMI≤23	≤17kg
	BMI 23.1-26	≤17.3kg
	BMI 26.1-29	≤18kg
	BMI≥29	≤21kg
Total scoring		
0	Not frail	
1-2	Pre-frail	
≥3	frail	

i.e. id est, HGShandgrip strength

Table 2

Frailty Assessment Tool of Vigorito

Frailty markers	
MNA (/30)	The nutritional status of the patient was investigated by the Mini Nutritional Assessment (MNA) questionnaire. This tool is validated in the elderly populationand is used to identify malnutrition or the risk of developing malnutrition. The questionnaire is composed of 6 parts. If the participants scores ≤11, 12 more research questions will be asked.
	Not frail — Score ≥ 25
	Minor frailty — Score 21-24
	Moderate frailty — Score 17-20
	Severe frailty — Score < 17
KATZ-index (/6)	See earlier
	Not frail — 5-6 activities independently
	Minor frailty — 3-4 activities independently
	Moderate frailty — 1-2 activities independently
	Severe frailty — 0 activities independently
Gait speed (m/s)	Measured by calculating the average speed during the 4.6m walking test
	Not frail — > 0.80
	Minor frailty — 0.61-0.79
	Moderate frailty — 0.40-0.60
	Severe frailty — < 0.40
TUG (sec)	Measurement of the time that is needed to rise from a chair, walk 3 meters, turn around, walk back and sit down again
	Not frail — ≤ 10
	Minor frailty — 11-14
	Moderate frailty — 15-20
	Severe frailty — > 20
GDS (/15)	Self-reported screening instrument to measure depression in the elderly
	Not frail — < 3
	Minor frailty — 3-5
	Moderate frailty — 6-10
	Severe frailty — 11-15
MMSE (/30)	The cognitive status of the participant was measured by the Mini Mental State Examination (MMSE). This instrument evaluates the orientation in time and

	space, attention, memory, language and constructive values in the elderly population. The maximal score is 30 points. A higher score indicates better cognitive and mental functions.	
	Not frail	> 24
	Minor frailty	21-24
	Moderate frailty	16-21
	Severe frailty	11-15
Medication (#)	The number of medications the patient uses will be registered based on the information of the patient files of the hospital.	
	Not frail	1-4
	Minor frailty	5-8
	Moderate frailty	9-12
	Severe frailty	> 12
HGS (kg)	See earlier (male reference values in table below)	
	Not frail	≥ 30.6
	Minor frailty	25.7-30.5
	Moderate frailty	19.0-25.6
	Severe frailty	≤ 18.9
Total scoring		
0-6	No frailty	
7-12	Minor frailty	
13-18	Moderate frailty	
18-24	Severe frailty	

MNA mini nutritional assessment, TUG timed up and go test, GDS geriatric depression scale, MMSE mini mental state examination, # number, HGS handgrip strength

Figure 1

Flowchart

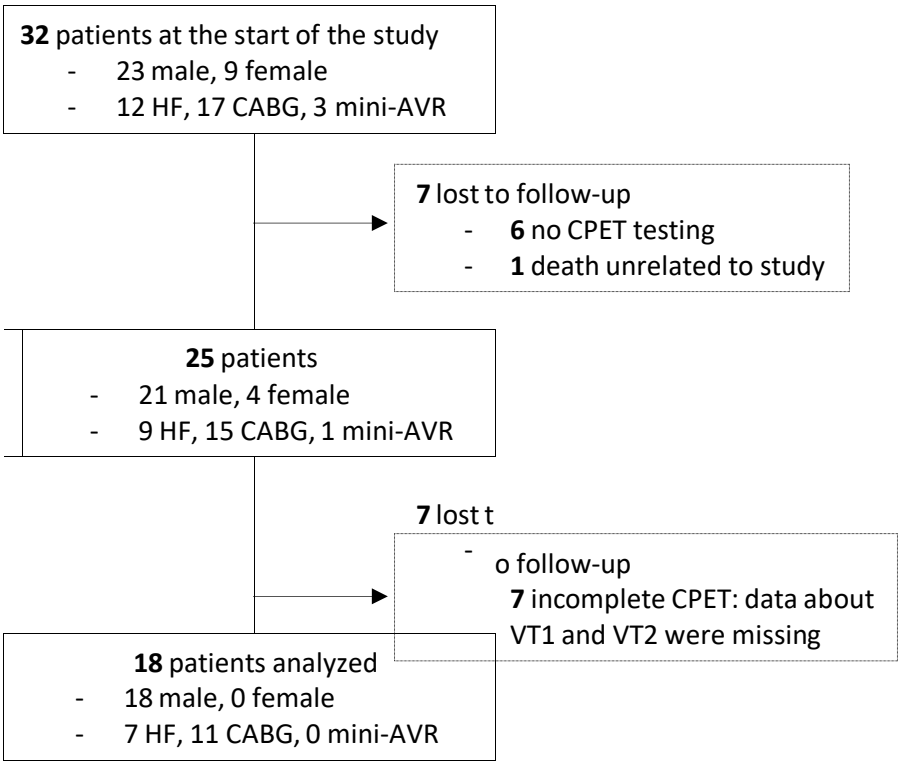

Table 3

Baseline Characteristics

			HF	CABG	Total
N (M/F)			7(7/0)	11(11/0)	18
Age (years)			75.4±7.9	70.4±2.8	72.4±5.7
Height (cm)			173.1±5.3	173.1±8.1	173.1±6.9
Weight (kg)			83.1±16.3	78.2±9.3	80.1±12.3
BMI (kg/m2)			27.6±4.4	26.1±2.8	26.7±3.5
Loophulpmiddel (n)			0	0	0
Cardiac events in the past (n)			3.6±6.1	2.0±2.7	2.6±4.3
	STEMI		0	0	0
	NON-STEMI		1	1	2
	Cardiomyopathy		2	1	3
	Atrial fibrillation		3	0	3
	Pacemaker		1	0	1
	Ablation		1	0	1
	CABG		1	0	1
	Endo-CABG		1	0	1
	PCI	**PTCA**	1	3	4
		(#BV)	3	3	6
		LAD	1	1	2
		CFX	1	2	3
		RAC	1	0	1
	Valvular disease		0	1	1
	HF	**HFpEF**	0	0	0
		HFrEF	2	2	4
		LVEF (%)	2(35±7.1)	2(40±7.1)	4(37.5±6.5)
	Others		2	3	5
Current diagnosis n(%)	**Cardiomyopathy**		5(71.4%)	0	5(27.8%)
	Endo-CABG		0	10(90.9%)	10(55.6%)
	Endo-ACAB		0	1(9.1%)	1(5.6%)
	Coronarography		1(14.3%)	0	1(5.6%)
	PCI	**PTCA**	1(14.3%)	1(9.1%)	2(11.1%)
		(#BV)	1(14.3%)	1(9.1%)	2(11.1%)
		LAD	1(14.3%)	0	1(5.6%)
		CFX	1(14.3%)	0	1(5.6%)
		RAC	0	1(9.1%)	1(5.6%)
	ICD		2(28.6%)	0	2(11.1%)
	HF	**HFpEF**	0	0	0
		HFrEF	7(100%)	1(9.1%)	8(44.4%)
		LVEF (%)	7(37.0±6.4)	1(40.0±0.0)	8(37.3±6.0)
	Others		4(57.1%)	3(27.3%)	7(38.9%)
Risk factors, n(%)	**Total # CVD risk factors**		2.0±0.6	2.1±0.7	2.1±0.6
	Hypertension		7(100%)	11(100%)	18(100%)
	Hypercholesterolemia		5(71.4%)	9(81.8%)	14(77.8%)
	Diabetes type I		0	0	0
	Diabetes Type II		0	2(18.2%)	2(11.1%)
	Obese		2(28.6%)	1(9.1%)	3(16.7%)
	Smoking		0	0	0

Medication, #(%)	**Betablocker**	6(85.7%)	6(54.5%)	12(66.7%)
	Ca_antagonist	0	7(63.6%)	7(38.9%)
	ACE_inhibitor	5(71.4%)	5(45.5%)	10(55.6%)
	Diuretica	5(71.4%)	7(63.6%)	12(66.7%)
	Antiarrhythmic	1(14.3%)	3(27.3%)	4(22.2%)
	Blood thinners	6(85.7%)	11(100%)	17(94.4%)
	Ezetimibe	0	1(9.1%)	1(5.6%)
	Statines	5(71.4%)	8(72.7%)	13(72.2%)
	Sacubitril/Valsartan complex	2(28.6%)	0	2(11.1%)
	Molsidomine	0	3(27.3%)	3(16.7%)
	Opioiden	0	2(18.2%)	2(11.1%)
	Analgetics	1(14.3%)	9(81.8%)	10(55.6%)
	Vitamins/ minerals/ food supplements	1(14.3%)	2(18.3%)	3(16.7%)
	Others	5(71.4%)	9(81.8%)	14(77.8%)
	# total CVD medication	5.1±1.6	5.5±1.6	5.4±1.6
	# total medication	6.7±2.9	7.5±2.1	7.4±2.3

HF heart failure, CABG coronary artery bypass grafting, BMI body mass index, STEMI ST-segment elevation myocardial infarction, non-STEMI non-ST segment elevation myocardial infarction, PCI percutaneous coronary intervention, PTCA percutaneous transluminal coronary angioplasty, #BV number of blood vessels, LAD left anterior descending artery, CFX circumflex artery, RAC right coronary artery, HFpEF heart failure with preserved ejection fraction, HFrEF heart failure with reduced ejection fraction, LVEF left ventricular ejection fraction, endo-ACAB endoscopic atraumatic coronary artery bypass, ICD implantable cardioverter-defibrillator, CVD cardiovascular diseases

Table 4

Frailty Assessment Fried

		HF	CABG	Total
Weight loss	**Lost 4.5kg in past year (1=yes, 0= no)**	2	3	5
Exhaustion	**I felt that everything I did was an effort**	0.9±1.2	0.7±1.1	0.7±1.1
	I could not get going	0.6±1.1	0.7±1.3	0.7±1.2
	Total	4(57.1%)	5(45.5%)	9(50%)
Walking time (4.6m test) (sec)		3.61±0.70	3.79±0.96	3.72±0.85
Physical activity (KATZ-scale)		6.0±0.0	5.9±0.3	5.9±0.2
Handgrip strength (kg)	**Mean of dominant and non-dominant hand**	37.0±7.5	37.8±6.4	37.5±6.6
	Dominant hand	37.7±5.7	38.5±7.0	38.2±6.3
	Non-dominant hand	36.3±9.7	37.0±6.5	36.8±7.6
Total score		0.6±0.5	0.5±0.7	0.6±0.6

HFheart failure, CABG coronary artery bypass grafting

Table 5

Frailty assessment Vigorito

	HF	CABG	Total
MNA (/30)	25.6±1.6	25.0±2.6	25.3±2.3
Katz-index total (/6)	6.0±0.0	5.9±0.3	5.9±0.2
Gait speed (m/s)	1.3±0.2	1.3±0.3	1.3±0.3
TUG (sec)	8.2±1.3*	6.9±1.2*	7.4±1.4
MMSE (/30)	27.4±2.9	27.1±3.2	27.5±2.9
GDS (/15)	2.0±2.0	2.2±2.9	2.1±2.5
Medication (#)	6.7±2.9	7.5±2.1	7.4±2.3
Total score	2.3±0.8	2.5±2.3	2.4±1.8

HF heart failure, CABG coronary artery bypass grafting, MNA Mini nutritional assessment, TUG Timed up and go test, GDS Geriatric depression scale, # number

*P<0.05 *HF vs. CABG*

Table 6

CPET Markers

	HF	CABG	Total
W-peak (Watt)	115.9±17.6	116.5±44.5	116.3±35.7
HR-peak (bpm)	113.3±21.3	119.5±24.2	117.1±22.6
VO2-peak (ml/min)	1416.6±319.2	1448.7±384.1	1436.2±350.7
VO2-peak/kg (ml/min)	17.3±2.1	18.5±4.6	18.1±3.8
RER-peak	1.2±0.1	1.2±0.1	1.2±0.1
HR-rest (bpm)	70.7±21.3	77.3±15.2	74.7±17.5
VT1-VO_2 (ml/min)	905.1±186.9	918.2±294.3	913.1±251.6
VT1-HR (bpm)	90.0±24.9	93.1±16.8	91.9±19.7
VT1-W (Watt)	59.9±13.1	64.4±21.9	62.6±18.6
VT2-VO_2 (ml/min)	1245.3±353.5	1318.1±395.3	1289.8±370.6
VT2-HR (bpm)	105.3±19.2	112.7±22.4	109.8±21.0
VT2-W (Watt)	94.1±23.7	108.3±37.7	102.8±33.0

CPET cardiopulmonary exercise testing, HF heart failure, CABG coronary artery bypass grafting, W-peak peak wattage, HR-peak peak heart rate, bpm beats per minute, VO_2-peak peak oxygen uptake, VO_2-peak/kg peak oxygen uptake per kilogram bodyweight, RER-peak peak respiratory gas exchange ratio, HR-rest resting heart rate, VT1-VO_2 first ventilatory threshold measured by VO_2 (ml/min), VT1-HR first ventilatory threshold measured by heart rate, VT1-W first ventilatory threshold measured by power, VT2-VO_2 second ventilatory threshold measured by VO_2 (ml/min), VT2-HR second ventilatory threshold measured by HR, VT2-W second ventilatory threshold measured by power

Table 7

Frailty of Participants (raw scores)

Frailty score				HF	CABG	Total
Fried						
Classification	Not frail (0)			3(42.9%)	6(54.5%)	9(50%)
	Pre-frail (1-2)			4(57.1%)	5(45.5%)	9(50%)
	Frail (≥3)			0	0	0
Raw score		Weight loss	Lost 4.5kg in past year (1=yes, 0= no)	2	3	5
		Exhaustion	I felt that everything I did was an effort	0.9±1.2	0.7±1.1	0.7±1.1
			I could not get going	0.6±1.1	0.7±1.3	0.7±1.2
			Total	4(57.1%)	5(45.5%)	9(50%)
		Walking time (4.6m test) (sec)		3.61±0.70	3.79±0.96	3.72±0.85
		Physical activity (KATZ-scale)		6.0±0.0	5.9±0.3	5.9±0.2
		Handgrip strength (kg)	Dominant hand	37.7±5.7	38.5±7.0	38.2±6.3
			Non-dominant hand	36.3±9.7	37.0±6.5	36.8±7.6
		Total score		0.6±0.5	0.5±0.7	0.6±0.6
Vigorito						
Classification	Not frail (0-6)			7(100%)	10(90.9%)	17(94.4%)
	Minor frail (7-12)			0	1(9.1%)	1(5.6%)
	Moderate frail (13-18)			0	0	0
	Severe frail (19-24)			0	0	0
Raw score		MNA (/30)		25.6±1.6	25.0±2.6	25.3±2.3
		Katz-index	Bathing	6.0±0.0	5.9±0.3	5.9±0.2
			Dressing			
			Transferring			
			Toiletting			
			Continence			
			Feeding			
			Total (/6)			
		Gait speed (m/s)		1.3±0.2	1.3±0.3	1.3±0.3
		TUG (sec)		8.2±1.3*	6.9±1.2*	7.4±1.4
		MMSE (/30)		27.4±2.9	27.1±3.2	27.5±2.9
		GDS (/15)		2.0±2.0	2.2±2.9	2.1±2.5
		Medication (#)		6.7±2.9	7.5±2.1	7.4±2.3
		Total score		2.3±0.8	2.5±2.3	2.4±1.8

HF heart failure, CABG coronary artery bypass grafting, MNA mini nutritional assessment, TUG timed up and go test, GDS geriatricdepression scale, # number

Table 8

Significant Correlations between Frailty Marker/Assessment Tool and CPET Marker (p-value (R^2))

		W-peak	HR-peak	VO2-peak	VO2-peak/kg	RER-peak	HR-rest	VT1-VO_2	VT1-HR	VT1-W	VT2-VO_2	VT2-HR	VT2-W
TOTAL													
Fried	Classification	0.11	0.33	0.59	0.71	0.68	0.08	0.26	0.21	**0.03* (0.27)**	0.23	0.60	**0.004* (0.23)**
	Raw score	0.09	0.43	0.46	0.40	0.89	0.06	**0.02*(0.29)**	0.20	0.70	**0.03*(0.25)**	0.28	0.24
Vigorito	Classification	0.14	0.07	0.16	0.21	0.58	0.99	0.16	0.55	0.12	0.20	0.11	0.19
	Raw score	0.06	0.13	0.09	0.21	0.78	0.92	**0.03* (0.27)**	0.06	0.07	**0.047* (0.22)**	0.07	0.57
Weight loss		0.38	**0.02* (0.28)**	0.48	0.94	0.72	**0.001* (0.48)**	0.26	**0.01* (0.37)**	0.26	0.20	**0.04 (0.24)**	0.28
Exhaustion	I felt that everything I did was an effort	0.47	0.94	0.21	0.40	0.95	0.60	0.47	0.52	0.56	0.30	0.87	0.53
	I could not getgoing	0.90	0.64	0.62	0.78	0.11	0.37	0.95	0.68	0.84	0.73	0.64	0.80
Walking time (4.6m walk test) (sec)		0.52	0.45	0.86	0.33	**0.03*(0.28)**	0.96	0.73	0.53	0.38	0.80	0.83	0.89
Gait speed (4.6m walk test) (m/s)		0.36	0.41	0.59	0.23	**0.02*(0.31)**	0.96	0.61	0.62	0.34	0.99	0.89	0.77
KATZ-index	Bathing	0.37	0.93	0.46	0.16	0.58	0.32	0.71	0.72	0.29	0.47	0.89	0.28
	Dressing	.	.	.	.	.	.	.	.	.	.	.	.
	Transferring	.	.	.	.	.	.	.	.	.	.	.	.
	Toiletting	.	.	.	.	.	.	.	.	.	.	.	.
	Continence	.	.	.	.	.	.	.	.	.	.	.	.
	Feeding	.	.	.	.	.	.	.	.	.	.	.	.
	Total (/6)	0.37	0.93	0.46	0.16	0.58	0.32	0.71	0.72	0.29	0.47	0.89	0.28
Handgrip strength (kg)	Dominant hand	**0.005* (0.41)**	**0.03* (0.25)**	**0.001* (0.49)**	**0.046* (0.23)**	0.73	0.12	**0.002* (0.46)**	0.19	**0.02* (0.31)**	**0.002* (0.48)**	**0.02* (0.31)**	**0.01* (0.40)**
	Non-dominant hand	**0.01* (0.38)**	0.09	**0.01* (0.37)**	0.07	0.88	0.07	**0.004*(0.41)**	0.17	**0.01* (0.38)**	**0.01*(0.37)**	**0.049*(0.47)**	**0.005* (0.40)**
MNA (/30)		0.15	0.75	0.37	0.64	0.16	0.16	0.26	0.46	0.05	0.17	0.76	0.06
TUG (sec)		0.29	0.10	0.79	0.13	0.17	0.34	0.87	0.17	0.46	0.95	0.14	0.45
GDS (/15)		0.08	0.48	0.23	0.29	0.65	0.50	0.11	0.85	**0.03* (0.27)**	0.17	0.38	0.09
MMSE (/30)		0.60	0.18	0.61	0.98	0.55	0.31	0.59	0.27	0.37	0.68	0.11	0.53

MED (#)		0.56	0.07	0.35	0.45	0.42	0.14	0.40	0.14	0.63	0.24	**0.03*(0.25)**	
		W-peak	HR-peak	VO2-peak	VO2-peak/kg	RER-peak	HR-rest	VT1-VO_2	VT1-HR	VT1-W	VT2-VO_2	VT2-HR	VT2-W
HEART FAILURE													
Fried	Classification	0.14	0.20	0.80	0.30	0.15	0.21	0.84	0.23	0.24	0.75	0.13	0.22
	Raw score	0.14	0.20	0.80	0.30	0.15	0.21	0.84	0.23	0.24	0.75	0.13	0.22
Vigorito	Classification	0.45	0.87	**0.02* (0.67)**	0.77	0.20	0.68	**0.02* (0.70)**	0.94	0.41	**0.02* (0.71)**	0.63	0.25
	Raw score	0.42	0.78	0.11	0.39	0.36	0.87	0.40	0.09	0.89	0.25	0.12	0.73
Weight loss		0.07	0.07	0.29	0.42	0.58	**0.02* (0.68)**	0.19	0.05	0.16	0.17	0.06	0.09
Exhaustion	I felt that everything I did was an effort	0.91	0.21	0.26	0.95	0.72	0.25	0.24	0.09	0.91	0.22	0.28	0.78
	I could not get going	0.68	0.91	0.07	0.79	0.48	0.56	0.08	0.86	0.61	0.07	0.79	0.44
Walking time (4.6m walk test) (sec)		0.78	0.95	0.46	0.74	0.13	0.99	0.34	0.90	0.82	0.36	0.73	0.99
Gait speed (4.6m walk test) (m/s)		0.62	0.91	0.62	0.68	0.13	0.99	0.48	0.92	0.66	0.50	0.70	0.82
KATZ-index	Bathing	.	.	.	.	.	.	.	.	.	.	.	.
	Dressing	.	.	.	.	.	.	.	.	.	.	.	.
	Transferring	.	.	.	.	.	.	.	.	.	.	.	.
	Toiletting	.	.	.	.	.	.	.	.	.	.	.	.
	Continence	.	.	.	.	.	.	.	.	.	.	.	.
	Feeding	.	.	.	.	.	.	.	.	.	.	.	.
	Total (/6)	.	.	.	.	.	.	.	.	.	.	.	.
Handgrip strength (kg)	Dominant hand	0.69	0.98	0.22	0.85	0.17	0.31	0.34	0.86	0.72	0.30	0.72	0.51
	Non-dominant hand	0.48	0.98	0.27	0.94	0.52	0.33	0.42	0.79	0.48	0.40	0.81	0.39
MNA (/30)		0.38	0.38	0.80	0.99	0.97	**0.01* (0.76)**	0.63	**0.004* (0.83)**	0.61	0.64	**0.004* (0.83)**	0.47
TUG (sec)		0.29	0.57	0.11	0.35	0.61	0.53	0.06	0.46	0.29	0.05	0.77	0.19
GDS (/15)		0.23	0.15	0.51	0.22	0.70	0.11	0.37	0.13	0.28	0.36	0.21	0.25
MMSE (/30)		0.42	0.66	0.98	0.09	0.11	0.23	0.92	0.48	0.45	0.80	0.55	0.46

MED (#)		0.65	**0.047* (0.58)**	0.81	0.39	0.79	0.05	0.94	0.08	0.94	0.89	**0.01* (0.73)**	0.85
		W-peak	HR-peak	VO2-peak	VO2-peak/kg	RER-peak	HR-rest	VT1-VO_2	VT1-HR	VT1-W	VT2-VO_2	VT2-HR	VT2-W
CORONARY ARTERY BYPASS GRAFTING													
Fried	Classification	0.39	0.74	0.68	0.94	0.19	0.22	0.28	0.67	0.09	0.27	0.79	0.16
	Raw score	0.56	0.91	0.78	0.41	0.24	0.41	0.22	0.90	0.58	0.52	0.95	0.30
Vigorito	Classification	0.14	0.07	0.19	0.26	0.60	0.88	0.22	0.44	0.16	0.20	0.09	0.19
	Raw score	0.56	0.30	0.58	0.69	0.15	0.66	0.62	0.70	0.35	0.58	0.33	0.50
Weight loss		0.9254	0.1738	0.9388	0.6931	0.4648	**0.0405* (0.39)**	0.6068	0.1223	0.6032	0.6214	0.2481	0.7168
Exhaustion	I felt that everything I did was an effort	0.45	0.34	0.48	0.47	0.44	0.93	0.71	0.66	0.37	0.60	0.26	0.44
	I could not get going	0.91	0.40	0.78	0.80	0.17	0.43	0.90	0.49	0.78	0.97	0.37	0.85
Walking time (4.6m walk test) (sec)		0.54	0.37	0.58	0.38	0.11	0.87	0.49	0. 45	0.42	0.80	0.63	0.83
Gait speed (4.6m walk test) (m/s)		0.46	0.35	0.42	0.31	0.09	0.99	0.46	0.57	0.99	0.73	0.72	0.82
KATZ-index	Bathing	0. 35	0.86	0.48	0.21	0.60	0.33	0.74	0.73	0.33	0.45	0.80	0.28
	Dressing	.	.	.	.	.	.	.	.	.	.	.	.
	Transferring	.	.	.	.	.	.	.	.	.	.	.	.
	Toiletting	.	.	.	.	.	.	.	.	.	.	.	.
	Continence	.	.	.	.	.	.	.	.	.	.	.	.
	Feeding	.	.	.	.	.	.	.	.	.	.	.	.
	Total (/6)	0. 35	0.86	0.48	0.21	0.60	0.33	0.74	0.73	0.33	0.45	0.80	0.28
Handgrip strength (kg)	Dominant hand	**0.004* (0.62)**	**0.01* (0.51)**	**0.01* (0.58)**	**0.045* (=0.37)**	0.82	0.30	**0.01* (0.58)**	0.10	**0.03 (0.44)**	**0.004* (0.63)**	**0.01* (0.52)**	**0.01* (0.55)**
	Non-dominant hand	**0.0004* (0.76)**	**0.01* (0.54)**	**0.01* (0.56)**	**0.02* (0.49)**	0.74	0.19	**0.0003* (0.78)**	**0.04* (0.39)**	**0.0005 (0.75)**	**0.002* (0.68)**	**0.01*(0.60)**	**0.0004* (0.76)**
MNA (/30)		0.22	0.53	0.42	0.61	0.19	0.78	0.37	0.58	0.08	0.21	0.20	0.09
TUG (sec)		0.17	0.16	0.21	0.07	0.21	0.82	0.56	0.28	0.25	0.37	0.20	0.27
GDS (/15)		0.20	0.14	0.37	0.50	0.78	0.76	0.23	0.34	0.08	0.33	0.11	0.21
MMSE (/30)		0.31	0.22	0.55	0.55	0.83	0.97	0.51	0.50	0.16	0.50	0.16	0.28
MED (#)		0.44	0.56	0.34	0.79	0.36	0.69	0.33	0.90	0.63	0.19	0.48	0.36

CPET cardiopulmonary exercise testing, R^2 correlation coefficient, W-peak peak power output, HR-peak peak heart rate, VO_2-peak peak oxygen uptake, VO_2-peak/kg peak oxygen uptake per kilogram bodyweight, RER-peak peak respiratory gas exchange ratio, HR-rest resting heart rate, VT1-VO_2 first ventilatory threshold determined on the level of VO_2, VT1-HR first ventilatorythreshold determined on the level of heart rate, VT1-W first ventilatory threshold determined on the level of power, VT2-VO_2 second ventilatory threshold determined on the level of VO_2, VT2-HR second ventilatory threshold determined on the level of heart rate, VT2-W second ventilatory threshold determined on the level of power, MNA mini nutritional assessment, TUG timed up and go test, GDS geriatric depression scale, MMSE mini mental state examination, MED (#) number of medications

** p-value <0.05 was defined as significantValues*

expressed as p-value (R^2)

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UHASSELT

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
04/05/2021	Bespreking methode + data-analyse	Promotor: Copromotor/Begeleider: Student(e): Student(e):
18/05/2021	Bespreking data-analyse	Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
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		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Indy Brinsmans x Jary Van Thienen **Datum:** 4/6/2021

Titel Masterproef: Correlaties tussen frailty and cardiopulmonary exercise testing markers in older adults suffering from specific cardiovascular diseases.

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	●	O	O	O	O	O
Methodologische uitwerking	●	O	O	O	O	O
Data acquisitie	O	O	O	O	O	●
Data management	O	O	O	O	O	●
Dataverwerking/Statistiek	O	O	O	O	●	O
Rapportage	O	O	O	O	●	O

2) Niet-bindend advies: Student(e) krijgt toelating/~~geen toelating~~ (schrappen wat niet past) om bovenvermelde ~~Wetenschappelijke stage~~/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze ~~wetenschappelijke stage~~/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) openbaar verdedigd worden.

4) Deze ~~wetenschappelijke stage~~/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
Indy 4/06/2021	04/06/2021	4/6/2021

Dominique HANSEN
aan Janny, Nastasia, mij

15:48 (1 uur geleden)

Dag Janny,

deze lijst is ok voor me.

mvg,

D

Prof. dr. Dominique Hansen

Full Professor, Rehabilitation and Exercise Physiology in Cardiometabolic Diseases
Vice Dean, Faculty of Rehabilitation Sciences
Head, Rehabilitation of Cardiorespiratory and Internal Diseases (CRI) research group
Vice-Chair, REVAL Research group
Chair, EAPC Secondary Prevention and Rehabilitation Section
Board member, European Association of Preventive Cardiology
Fellow of the European Society of Cardiology