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Frailty Syndrome: visceral adipose tissue and frailty in patients with symptomatic severe aortic stenosis

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Síndrome da Fragilidade: tecido adiposo visceral e fragilidade em doentes com estenose aórtica severa

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Resumo

Introdução: A síndrome da fragilidade é comum na esteno aórtica (EA), atingindo de 30 a 50% dos pacientes com EA grave. Essa síndrome tem sido associada à inflamação, à resistência à insulina, à resposta deficiente à glicose e à baixa percentagem de massa magra, características normalmente presentes na obesidade central. O ângulo de fase (AF) é um parâmetro derivado da análise de impedância bioelétrica (BIA), e seu valor reflete a integridade da membrana celular, sendo afetado pela inflamação e pelo estado nutricional. Pouco se sabe sobre a contribuição da distribuição de adiposidade na fragilidade, e sobre as influências de fragilidade e da obesidade visceral no valor do PA.

Objetivos: Avaliar a existência de associações entre fragilidade, depósitos de gordura visceral e AF em pacientes com EA grave.

Métodos: Em uma coorte de pacientes com EA grave referidos para cirurgia de substituição da válvula aórtica, a presença de fragilidade foi avaliada através da escala de Fried *et al*. Os valores do AF e da composição corporal dos pacientes foram obtidos a partir da avaliação de BIA [composição corporal dada em % de massa gorda (%MG) e % de massa magra (%MM)]. Utilizou-se tomografia computadorizada para a quantificação das gorduras: tecido adiposo epicárdico (TAE) e mediastínico (TAM), e gorduras abdominal total (GAT), visceral (GAV) e subcutânea (GAS). As medidas de adiposidade foram indexadas para a área de superfície corporal. Foram criados dois grupos: frágeis e não-frágeis, estando incluídos no último grupo os pacientes classificados como não frágeis e pré-frágeis. Outras medidas antropométricas avaliadas foram: índice de massa corporal (IMC), circunferências da cintura (CC) e do quadril (CQ) e relação CC/CQ.

Resultados: Cinquenta e cinco pacientes foram incluídos no estudo (73±9 anos, IMC = 29±5 kg/m², 57% do sexo masculino). A prevalência de fragilidade foi de 47%. Ajustando para idade e sexo, a fragilidade foi significativamente associada com o volume indexado de TAE (p = 0,042) e AF (p = 0,03), mas não com IMC, %FM e %FFM, CC, GAT, GAV ou GAS. Num modelo também ajustado para idade e sexo, o AF apresentou correlação inversa com a relação CC/CQ (p=0,02), %FM (p=0,02) e com o volume indexado de TAE (p=0,03), mas não com o IMC, % FFM, TAM indexado e áreas de GAV, GAS e GAT.

Conclusões: Em pacientes com EA grave, TAE é um preditor independente de fragilidade, o que não se verifica com o IMC ou com outros depósitos de gordura. Além disso, a fragilidade e o TAE parecem estar associados com redução da integridade da membrana celular, a qual foi avaliada através do AF.

Palavras-chave: fragilidade, tecido adiposo visceral, tecido adiposo epicárdico, ângulo de fase, estenose aórtica.

Abstract

Background: Frailty syndrome is common in aortic stenosis (AS), reaching 30-50% in the severe form of the disease. Frailty has been linked to increased inflammation, insulin resistance, impaired response to glucose exposure and low percentage of fat free mass, characteristics usually present in central obesity. Phase angle (PA) is a value derived from bioelectrical impedance analysis (BIA) that reflects cell membrane integrity and function, being affected by inflammation and nutritional status. Few studies are available on the relative contribution of adiposity distribution on frailty, and about the influences of frailty and visceral obesity in PA value.

Aims: To evaluate associations among frailty, visceral fat depots and PA in patients with symptomatic severe AS.

Methods: In a cohort of patients with severe AS referred to aortic valve replacement (AVR), we used Fried *et al*. scale to evaluate frailty syndrome, and BIA to obtain PA and body composition [given in % fat mass (%FM) and % fat free mass (%FFM)]. Multidetector computed tomography was performed to quantify the following adipose tissues: epicardial (EAT), mediastinal (MAT) and total (TAF), visceral (VAF) and subcutaneous abdominal fat (SAF). We created two groups: frail and non-frail, the latter group including patients classified as intermediate or robust. Other anthropometric measurements were performed: body mass index (BMI), waist (WC) and hip circumferences (HC), WC/HP ratio.

Results: We included fifty-five patients (73±9 years, BMI=29±5 kg/m², 57% males). The prevalence of frailty was 47%. Adjusting for age and gender, frailty was associated with indexed EAT volume (p=0.042) and PA (p=0.03), but not with BMI, %FFM and %FM, WC, TAF, VAF or SAF. In an age and gender adjusted model, PA was inversely correlated with WC/HC ratio (p=0.02), %FM (p=0.02) and indexed EAT volume (p=0.03), but not with BMI, WC, %FFM, indexed MAT, VAF, SAF and TAF areas.

Conclusions: In patients with severe AS referred to AVR, EAT is an independent predictor of frailty, but not BMI or other fat depots. Moreover, frailty and EAT appear to be associated with impaired cell membrane integrity and function assessed by BIA derived PA.

Keywords: frailty, visceral adipose tissue, epicardial adipose tissue, phase angle, aortic stenosis.

Summary

Lista de Abreviaturas

AC: arm circumference

APMuscle: adductor pollicis muscle

AS: aortic stenosis

ASE: American Society of Echocardiography

AVA: aortic valve area

AVAi: aortic valve area index

AVR: aortic valve replacement

BIA: Bioelectrical impedance analysis

BMI: body mass index

BSA: body superficies area

BSF: biceps skinfold

CAD: coronary artery disease

CC: calf circumference

EAT: epicardial adipose tissue

EATVi: indexed epicardial adipose tissue volume;

FFM: fat free mass

FM: fat mass

FTSF: front thigh skinfold

HC: hip circumference

HDL: low high-density lipoprotein

hsCTNT: high-sensitive Cardiac T troponin

ICSI: iliac crest skinfold

LAVI: left atrium volume index

LDL: small low-density lipoprotein

LV: left ventricular

LVF: left ventricular function

LVEDVi: left ventricular end diastolic volume index

LVEF: left ventricular ejection fraction

LVMi: left ventricular mass index

MAT: mediastinal adipose tissue

MATVi: indexed mediastinal adipose tissue volume

MDCT: multidetector computed tomography

NT-Pro-BNP: NT-pro-brain natriuretic peptide

PA: phase angle

RAVI: right atrium volume index

R: resistance

SAF: subcutaneous abdominal fat

SAFVi: indexed subcutaneous abdominal fat volume

SCSF: subscapular skinfold

SD: standard deviation

SPSS: Statistical Package for the Social Sciences

TAF: total abdominal fat

TAFVi: indexed total abdominal fat volume

TAPSE: tricuspid annular plane systolic excursion

TSF: triceps skinfold

VAF: visceral abdominal fat

VAFi: indexed visceral abdominal fat

WC: waist circumference

WC/HC: waist circumference/hip circumference ratio

Xc: reactance

Lista de Tabelas e Figuras

1. Introduction

Frailty is a geriatric syndrome characterized by accelerated decline in physiological reserves and failure of homeostatic mechanisms[1]. Consequently, there is a decreased responsiveness capacity of many physiological systems and increased vulnerability to stressful events[2-4]. This phenotype is associated with higher risks of adverse outcomes related to health in older people, such as increased mortality, morbidity, number of falls and hospitalizations, and reduced activities of daily living[2, 5].

Frailty prevalence has increased in western world given population aging, ranging from 7 to 12% in older adults (aged ≥ 65 years) in the United States[2], and 17% in Europe[6]. Although frailty syndrome can occur independently of a medical condition, its prevalence clearly increases in subjects with cardiovascular disease. In patients with aortic stenosis (AS), the prevalence of frailty reaches 30-50% when the severe form of the disease is present[7, 8].

1.1. Frailty pathophysiology

The pathophysiology of frailty has been imprecise and variously descripted. However, it is generally accepted that, in frailty, the gradual decline in physiological reserve associated with ageing is accelerated and the homeostatic mechanisms start failing early[1]. Beyond ageing, this syndrome arises as consequence of sedentary lifestyle, nutritional disorders, comorbidities and diseases.

A cumulative decline occurs in different physiologic systems, especially the skeletal muscle system[2], endocrine system (cortisol, estrogen, testosterone)[9, 10], immunological system (inflammation)[11] and neurologic system[12].

This imbalance in organic central systems gives rise a chronic inflammatory process, and frailty has significant association with elevated interleukin 6, white blood cell and reactive C-protein levels[13, 14]. The increase in proinflammatory cytokines is associated with lower muscle strength, lower

physical performance and higher risk of disability in older persons[15], characteristics commonly used in models to measure frailty. Hence, the degree of inflammatory load appears to be parallel to the degree of frailty.

1.2. Frailty phenotype and obesity

Models of frailty try to measure deficiencies in domains of functioning (physical, nutritive, cognitive, and sensory)[16] or deficit accumulation related to diseases, symptoms, conditions and disability[17].

In a landmark study, Fried *et al*.[2] defined the most well-known and widely used phenotype model of frailty, which is based on five variables: unintentional weight loss; self-reported exhaustion; low energy expenditure; slow gait speed and weak grip strength. The presence of three or more criteria characterizes frailty.

The inclusion of weight loss in frailty criteria is congruent with the conceptualization of frailty as a wasting disorder, with sarcopenia as the major feature. However, obesity in older people is associated with greater risk of impaired physical function, which is closely intertwined with frailty. In addition, obesity, in particular the visceral obesity, induces a chronic proinflammatory state[18, 19], which has been also associated with frailty, as previously described.

Beyond chronic inflammation[20], studies associate frailty syndrome with insulin resistance[21] (especially in the presence of increased abdominal fat[22]), deregulated response to glucose exposure[23] and low percentage of fat free mass (FFM)[24]. Although adipose tissue has been associated with frailty, it is not yet clearly established whether the different adipose compartments (visceral abdominal fat, subcutaneous abdominal fat, epicardial adipose tissue, myocellular and intermuscular adipose tissue) contribute in the same way to the presence of frailty. Moreover, despite the well-established knowledge about the negative changes in health associated with altered body fat distribution, there remains a lack of knowledge on interrelationships among these fat compartments and frailty in elderly populations.

1.3. Frailty and phase angle as cellular damage biomarker

The Fried *et al.* phenotype model of frailty includes both objective and subjective factors, but not a biomarker of frailty. Presently there is not enough data to separate the degrees of frailty (non-frail, pre-frail, frail) in different settings of elderly persons. Beyond the diagnosis of frailty, the identification of biomarkers is of great interest mainly for the follow-up of this syndrome course and also to monitor possible therapeutic interventions.

Bioelectrical impedance analysis (BIA) is a technique based in the bioelectrical properties of tissues and measures the cell membrane resistance to an electrical current passing through the body: the capacitative resistance (called reactance, Xc), and the resistive resistance (simply called resistance, R). Capacitance arises from cell membranes and R from extra and intracellular fluid, and the combination of both is called impedance[25].

The relationship between Xc and R reflects different electrical properties of tissues that change in different ways by disease, nutritional and hydration status[25]. The phase angle (PA), which is one measure of this relationship, is the angle between impedance vector and the R vector, and it is calculated in degrees by the formula: arc tangent (Xc/R)*180/π[26]. PA's values reflect cell membrane integrity and function by a direct correlation: the higher the PA's value, the greater the amount of intact cell membranes and body cell mass[26].

This BIA derived parameter varies with gender and body mass index (BMI), tending to decline with age[27]. Nutritional status[28, 29], disease, inflammation, infection or prolonged physical inactivity can result in disturbed electrical properties of tissues that directly affect the PA[30]. Many studies also underline the utility of PA as a marker of impaired clinical outcome and mortality in populations with chronic disease[31-33], and its correlation with membrane function enables earlier insight into disturbances of health and responses to pharmacological and other clinical interventions compared to the other levels of testing[30].

Therefore, we hypothesized that visceral obesity might be involved in the pathophysiology of global inflammatory process and cellular senescence present in frailty syndrome, and that PA might be used as a marker of this

potential link between visceral obesity and frailty. First, we determined if and how the body fat distribution was associated with the presence of frailty in patients with severe aortic stenosis who were referred to multidectector computed tomography (MDCT) before aortic valve replacement (AVR). Second, we assessed the association of PA with frailty and with each fat compartment. In the long term, we expect to evaluate the influence of visceral fat in frailty classification and PA's value changes after AVR.

2. Objectives

In a cohort of patients with severe symptomatic AS and preserved ejection fraction referred to MDCT before AVR, our main aims are to explore the association of visceral adiposity and frailty and to assess if preoperative PA determination could contribute to a better evaluation of frailty in this patient population. Our specific aims are:

Specific aim 1: To study the association of frailty with epicardial adipose tissue (EAT), mediastinal adipose tissue (MAT) and abdominal fat [total (TAF); visceral (VAF) and subcutaneous (SAF)] in patients with severe AS. In a cross-sectional design, we determined, using a multivariable logistic regression model including age, gender and body surface area, the independent association of frailty, according to Fried *et al*.[(2)] classification, with the preoperative amount of EAT, MAT, VAF and SAF quantified by MDCT.

Specific aim 2: To determine if BIA derived phase angle independently correlates with frailty in patients with severe AS. In a cross-sectional design, we evaluated the age and gender adjusted association of frailty with the PA values using a multivariable logistic regression model.

Specific aim 3: To evaluate if visceral obesity is associated with impaired cell membrane integrity assessed by BIA derived PA. In a cross-sectional design, we determined, using a multivariable linear regression model including age, gender and body surface area, the adjusted correlation of PA and the preoperative amount of EAT, MAT and VAF.

3. Methods

3.1. Study design and population

In order to determine the association of frailty syndrome with visceral obesity in patients with symptomatic severe AS referred to AVR, we conducted an observational cross-sectional, single center study at the Centro Hospitalar Vila Nova de Gaia e Espinho-EPE.

Patients were eligible if they were over 18 years of age, presented with symptoms on exertion, aortic valve area ≤0.8 cm^2 and if they had the ability to read and provide a written informed consent.

Exclusion criteria were: (1) moderate to severe aortic valve regurgitation, (2) moderate to severe mitral valve disease, (3) bicuspid aortic valve, (4) left ventricular (LV) dilatation [according to American Society of Echocardiography (ASE) guidelines [34]: LV end-diastolic volume index >75 mL/m^2, to women and men], (5) LV ejection fraction depression (according to ASE guidelines: LV ejection fraction <55%, to men and women), (6) paroxysmal or permanent atrial fibrillation, (7) permanent pacemaker, (8) previous cardiac surgery, (9) previous infectious endocarditis, (10) chronic renal failure stage 3 to 5, and (11) moderate to severe chronic pulmonary disease.

At the preoperative period, patients were evaluated using a validated frailty scale, clinical interview, nutritional assessment including anthropometric and bioimpedance analyses, echocardiogram, multidetector computed tomography (MDCT) and laboratory blood tests.

The institutional and national ethics committee of biomedical research approved the present study. We informed the patients about the purpose of the study and each enrolled patient signed an informed consent.

The study activities description is accessible in *Table 1*.

3.2. Frailty Scale

We used Fried *et al*.'s Frailty Scale [2] to classify the patients into three groups: participants meeting 3 or more criteria were classified as **frail**; those meeting 1 or 2 as **intermediate**; and those meeting none as **robust**. This

scale is based on six parameters: (1) unintentional weight loss; (2) exhaustion; (3) adductor pollicis muscle thickness, which was measured with a precision of 0.2 mm, using a calliper (John Bull, British Indicators Ltd, England); (4) hand grip strength, measured to the nearest 0.5 kg, using a mechanical dynamometer Smedlay (Smedlay, TTM, Tokyo, Japan); (5) walking speed, measured in seconds using a digital stopwatch; and (6) level of energy expenditure related to physical activity, measured by the Minnesota Leisure Time Activity Questionnaire[35].

During grip strength measurement, patients were positioned according to the American Society of Hand Therapists' recommendations[36], and instructed to apply as much pressure as they could handle. The measurement was performed in the dominant hand and the final value was the average of three measurements.

3.3. Nutritional assessment

The nutritional evaluation consisted in (1) anthropometric measurements and (2) bioelectrical impedance analysis. The nutritional assessment full form is available in Annex A.

3.3.1. Anthropometry

Anthropometric measurements were performed according to the reference manual ISAK (2011)[37]. All participants should be barefoot and wearing light clothing during the valuation. Weight was measured using an electronic digital scale, with weighing accuracy of 0.1 kg (model 764: Seca gmbh & co, Germany), and height was measured with a precision of 1 mm (model 764, Seca gmbh & co., Germany). The body mass index (BMI) was calculated by dividing body weight (kg) by height² (m), and was classified according to the World Health Organization[38]. For elderly, we used the Nutritional Screening Intervention's (NSI) cutoff points[39]: BMI < 22 (malnutrition); BMI > 22 and < 27 (normal weight); BMI > 27 (obese)

Body circumferences were measured with a tape measure, with a precision of 1 mm, obtaining the values of arm circumference (AC), waist circumference (WC), hip circumference (HC) and calf circumference (CC).

Skinfolds were measured with an accuracy of 0.2 mm, with the assistance of a calliper (John Bull, British Indicators Ltd, England), obtaining the triceps skinfold (TSF), biceps (BSF), subscapular (SCSF), iliac crest (ICSI) and front thigh skinfold (FTSF).

3.3.2. Bioelectrical impedance analysis (BIA)

The values of resistance (R) and reactance (Xc) were measured at 800 uA and 50 kHz with an impedance analyzer BIA 101 (Physiological Data Analyzer System, Akerne, Florence, Italy), with the subject lying in supine position and the electrodes fixed on the right hand and right foot, as described in the protocol of Lucaski *et al*. [40]. For measuring the BIA was required a minimum 4h of fasting and 24h of caffeine abstinence, and participants should withdraw any jewelry and metallic objects. The phase angle (PA) was calculated in degrees using the formula: PA = arc tangent (Xc/R)*180/π. The body composition was measured by Kyle *et al*.'s BIA formula[41] and given in percentage of fat free mass (FFM) and percentage of fat mass (%FM).

3.4. Adipose tissue quantification

In order to evaluate the adipose tissue distribution, the patients underwent a MDCT scan using a 64-slice computed tomography scanner (Somaton Sensation 64, Siemens Medical Solutions, Forchheim, Germany). The exam included three different acquirements: the first one for abdominal fat quantification, the second one for coronary artery calcification quantification (Calcium Score) and the third one for epicardial adipose tissue (EAT) and mediastinal adipose tissue (MAT) quantification. All adiposity measures were indexed for the body surface area.

3.4.1. Abdominal fat assessment

An abdominal single slice acquisition was performed between L4 and L5 to assess abdominal fat area as described by Borkan *et al*. [42]. Radiographic factors were 120 kV and 216 mAs with 5 mm thickness resulting in an estimated radiation exposure of 0.06 mSv. One blinded expert used the obtained slice to measure abdominal fat distribution according to the Yoshizumi *et al*.'s[43] method: the adipose tissue was identified in the areas with attenuation values

ranging from −150 to −50 Hounsfield Units[44]; the total abdominal fat (TAF) area was the sum of adipose tissue presented in the examined abdominal slice; a cursor pointer was used to trace the visceral abdominal fat (VAF) area by delineating the abdominal wall muscular layer. The subcutaneous fat area (SAF) was obtained by subtracting VAF from TAF.

3.4.2. Epicardial adipose tissue (EAT) quantification

A blinded experienced radiographer quantified EAT volume using a cursor pointer to trace manually the pericardial contour, using 1-mm-thick reconstructed axial slices. Pericardium contour was traced for every 10 mm starting from the lower visible level of pulmonary artery bifurcation until the top level of the pulmonary valve for every 20 mm from there until the first slice, where the diaphragm becomes visible, and for every 10 mm from this point until the last slice, where pericardium is still visible. The pericardium contour is extrapolated by the software (Syngo Volume, Siemens Medical Solutions) for the non-traced slices and rechecked by the operator. Within these limits, we identified EAT using the adipose tissue attenuation references already described. We excluded mediastinal adipose tissue and pericardial adipose fat (a fat depot outside the visceral pericardium and on the external surface of the parietal pericardium) from analysis.

3.4.3. Mediastinal adipose tissue (MAT) measurement

Mediastinal adipose tissue was measured by the difference between total thoracic fat volume, defined as any adipose tissue located within the thorax from the level of the right pulmonary artery to the diaphragm and from the chest wall to the descending aorta, and EAT.

3.5. Cardiac structure and function evaluation.

All participants were submitted to detailed echocardiographic assessment, by a single sonographer, using an ultrasound system (iE33, Philips Medical Systems, Best, The Netherlands) equipped with a S5-1 transducer. Images were digitally stored for posterior offline analysis. Cardiac chambers dimensions, volumes and left ventricular mass were measured according to current recommendation[45]. All values were indexed to body surface area. The doppler echocardiographic indices of AS severity included peak aortic jet

velocity, peak and mean transvalvular pressure gradients obtained with the use of the modified Bernoulli equation, and the aortic valve area (AVA) calculated by the standard continuity equation[46].

3.6. Clinical evaluation

All participants were submitted to clinical interview and review of medical registries to collect data on cardiovascular risk factors, previous medical history, medication use, psychosocial and demographic factors and physical daily activities.

Hypertension was defined as blood pressure above 140/90 mmHg or anti-hypertensive drug treatment[47].

Diabetes was defined as fasting blood glucose ≥ 126 mg/dL or anti-diabetic drug usage[48] and dyslipidemia as total cholesterol > 190 mg/dL or currently taking lipid-lowering drugs[49].

3.7. Statistical analysis

Studied patients were divided into two groups: frail and non-frail patients, with the latter including both robust and intermediate (pre-frail) patients. To eliminate the potential body surface area (BSA) confounder effect, we used for analysis the measures of fat depots indexed to BSA. Continuous variables were described using the mean and standard deviation (SD) if normally distributed or median and interquartile range when non-normally distributed. Student's t-test was used for the comparisons between continuous variables if normally distributed, and Mann-Whitney U when in cases of non-normally distributed variables. Categorical variables were described using relative frequencies, and compared between frail and non-frail patients using the Chi-square test.

Multivariate logistic regression analysis was used to determine the independent association between frailty and indexed EAT volume and indexed MAT, VAF, SAF and TAF areas. The association of PA and the indexed fat measures were determined using a multivariable linear regression model.

To eliminate confounding variables we adjusted the regression models for 1) all variables statistically significant on the univariate model; and

for 2) age and gender. Individual models were created to study the association of frailty and PA with each one of the fat depots. The MAT, VAF and SAF independent association of frailty and PA with EAT was also assessed. The statistical evaluation was performed using SPSS, version 21.0 (SPSS, Inc., Chicago, IL) and statistical significance was considered when $p < 0.05$.

The sample size was calculated based on data from a previous study including HIV-older patients[50] that showed a higher waist circumference in frail patients when compared with no frail patients (42±6 versus 37±5 cm). We estimated that at least 46 patients (ratio 1:1, n frail=n non-frail=23) are required to detect a 12% increase in waist circumference frail patients, with a type II error of 20% and a significance level of 5%. We used Stata 13® (StataCorp LP, College Station, Texas, USA) to perform the analysis.

Table 1 - Study activities description.

Activity	Variable description	Type	Variable type	Method
Body fat distribution assessment	• EAT volume • Mediastinal fat area • Total, subcutaneous and visceral abdominal fat area	Independent	Continuous	MDCT
	• Total and percentage of body fat mass and body free fat mass	Independent	Continuous	Bioimpedance analysis
	• BMI • Body circumferences: ArmC, CalfC, WC, HC • WC/HC ratio • Body skinfolds: TSF, BSF, SCSF, ICSF, FTSF • APMuscle	Independent	Continuous	Nutritional evaluation
Frailty	Frailty diagnosis	Dependent	Binary	Fried *et al.* (2001)'s scale
PA	Cells membrane integrity and function	Independent	Continuous	BIA
Cardiac structure and function		Independent	Continuous	Echocardiogram

APMuscle: adductor Pollicis Muscle; ArmC: arm circumference; BMI: body mass index; BSF: biceps skinfold; CalfC: calf circumference; FTSF: front thigh skinfold; HipC: hip circumference; ICSF: iliac crest skinfold; SCSF: subscapular skinfold; TSF: triceps skinfold; WaistC: waist circumference; WC/HC: waist circumference/hip circumference ratio.

4. Results

4.1. Population characteristics

Fifty-five patients (mean age of 73±9 years; 57% males) were included, with mean BMI of 29±5 kg/m^2 (52% of obese) mean %FFM of 65.2±6.6% and mean %FM of 34.8±6.6%.

Mean indexed EAT volume was 72 ± 38 mL/m^2, and mean indexed VAF area was 97±38 cm^2. Detailed sample characteristics are shown in *Tables 2 and 3.*

The three visceral fat depots were correlated (Pearson's correlation coefficient: 0.53 for EAT vs. MAT, 0.54 for EAT vs. VAF, and 0.55 for MAT vs. VAF; p< 0.001 for all). The visceral fat depots were not correlated with SAF (*Figure 1*).

***Figure 1* - Correlation of visceral fat depots.**

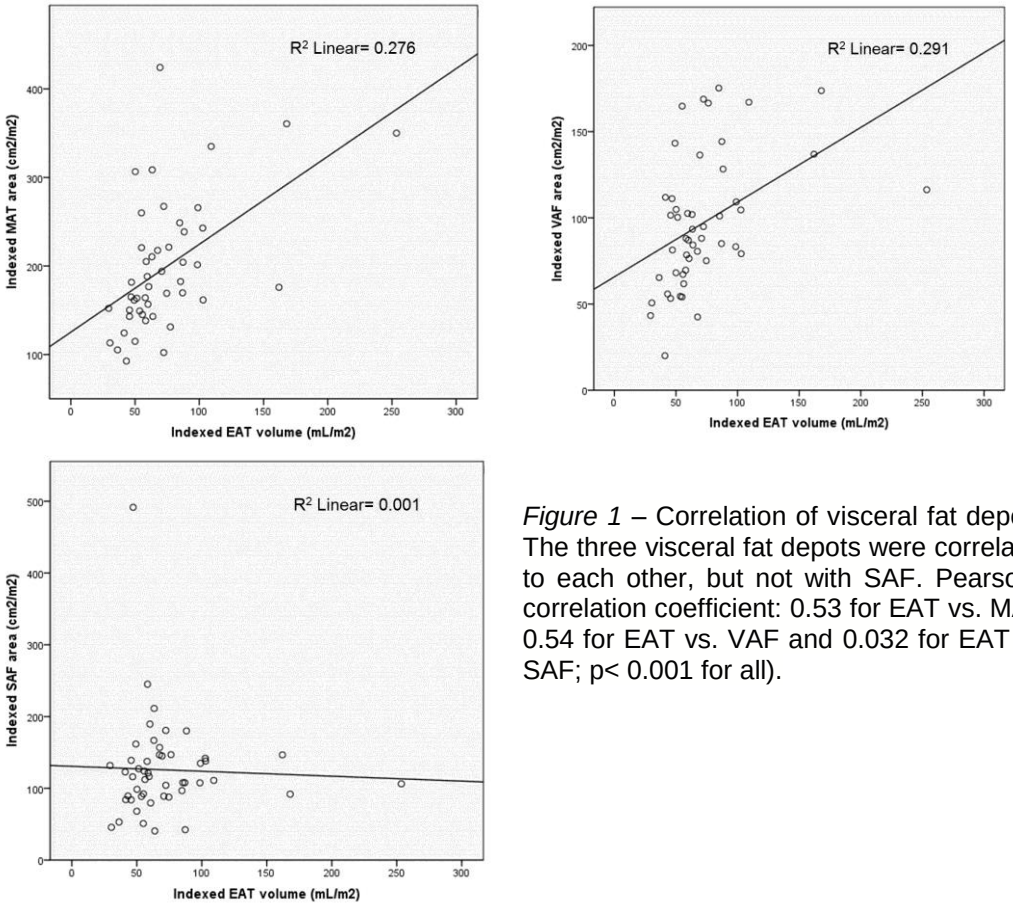

Figure 1 – Correlation of visceral fat depots. The three visceral fat depots were correlated to each other, but not with SAF. Pearson's correlation coefficient: 0.53 for EAT vs. MAT, 0.54 for EAT vs. VAF and 0.032 for EAT vs. SAF; p< 0.001 for all).

4.2. Association of frailty with body fat distribution

The prevalence of frailty was 47% (26 patients).

To investigate the association of frailty and measures of global and visceral adiposity, we used a multivariable logistic regression model including age and gender. In this model, frailty was not associated with BMI, %FFM and %FM. We also did not find a significant association with measures of visceral abdominal fat (i.e. WC, indexed VAF area and indexed TAF) and with mediastinal fat, but there was a significant association between frailty and indexed EAT volume (p=0.042).

Adjusting for age and gender, the odds of frailty increased 4.1-fold (95 % confidence interval of 1.03 to 16.4) per additional 100 cm^3/m^2 of EAT.

Frailty remained independently associated with EAT after further adjustment for SAF (p=0.045), but was attenuated after the inclusion of VAF in the model (p=0.056).

The age and gender adjusted associations of frailty and body fat distribution parameters are shown in *Table 4*.

4.3. Association of frailty with phase angle

Frail patients had a significantly lower PA than non-frail patients (3.9±0.7 vs. 4.5±1.2, p=0.02) and in a univariate logistic regression analysis, the odds of frailty duplicated when the PA decreased 1 degree (*Figure 2*).

Adjusting for gender, patients with narrow PA (lowest quartile, PA<3.4º) had 5.9-fold higher odds of frailty (95 % confidence interval of 1.2 to 30.7) when compared with the highest quartile (PA ≥ 4.8º). However, when adjusting for age and gender this association declined (p=0.08).

Since age was correlated with PA (Pearson's correlation coefficient: -0.54, p<0.001) (*Figure 2*), and it is a known intermediate variable in the pathophysiological process of frailty, the inclusion of this independent variable

Table 2 - Comparison of clinical, laboratorial and echocardiographic characteristics between frail and non-frail groups.

	All (n=55)	Frailty Classification		p value
		Frail (n=26)	Non-frail (n=29)	
Age, years	72.8±9.4	74.1±9.3	71.0±9.2	0.212
Male sex, n (%)	35 (57.4)	14 (53.8)	21 (60.0)	0.283
Hypertension, n (%)	45 (81.8)	20 (76.9)	25 (86.2)	0.373
Diabetes, n (%)	16 (29.1)	6 (23.1)	10 (34.1)	0.352
Dyslipidemia, n (%)	43 (78.2)	19 (73.1)	24 (82.8)	0.385
Laboratory evaluation				
hsCTNT, ng/dL*	0.01(0.02)	0.012 (0.01)	0.013 (0.03)	0.880
NT-Pro-BNP, pg/mL*	308.0 (748.0)	317.0 (704.0)	206.0 (383.5)	0.058
Reactive C-Protein, mg/dL*	0.19 (0.38)	0.22 (0.49)	0.11 (0.26)	0.082
Total cholesterol, mg/dL*	162.5 (59.5)	147.0 (62.5)	170.0 (49.5)	0.101
Tryglicerides, mg/dL*	101.5 (55.5)	123.0 (62.0)	95.0 (98.5)	0.170
LDL cholesterol, mg/dL*	87 (57.8)	82.0 (62.0)	91.0 (53.0)	0.170
HDL cholesterol, mg/dL	53.3 (15.2)	47.7 (14.0)	59.4 (15.3)	0.020
Calcium Score*	249.3 (1082.7)	254.7 (1488.3)	272.0 (922.1)	0.934
Glucose, mg/dL*	107.0 (35.0)	107.0 (35.0)	97.0 (96.5)	0.486
Insulin, uU/mL*	11.0 (14.2)	9.2 (17.2)	17.0 (14.6)	0.297
Echocardiografic evaluation				
AVAi, cm^2/m^2	0.4±0.09	0.4±0.07	0.4±0.10	0.828
LAVI, mL/m^2	49,1±12.8	48.9±9.7	49.3±15.2	0.941
RAVI, mL/m^2	24.2±9.5	26.2±12.7	23.3±4.9	0.255
LVMi, g/m^2	130±24	129±28	131±22	0.325
LVEDVi, mL/m^2	55.92±17.4	57.9±15.5	54.1±19.0	0.477
LVEF, %	63.9±6.2	64.1±7.1	63.7±5.5	0.818
TAPSE, mm	22.7±5.2	23.4±3.9	22.3±6.0	0.564

Results are presented as means ± SD.
p values shown compare frail and non-frail groups.
* median (IQR)
AVAi: aortic valve area index
HDL: high-density Lipoprotein Cholesterol
hsCTNT: high-sensitive Cardiac T troponin
LAVI: left atrium volume index
LDL: low-density Lipoprotein Cholesterol
LVEDVi: left ventricular end diastolic volume index
LVMi: left ventricular mass index
LVEF: left ventricular ejection fraction
NT-Pro-BNP: NT-Pro-brain Natriuretic Peptide
RAVI: right atrium volume index
TAPSE: tricuspid annular plane systolic excursion

Table 3 - Comparison of nutritional evaluation and body fat distribution characteristics between frail and non-frail groups.

	All (n=55)	Frailty Classification		p value
		Frail (n=26)	Non-frail (n=29)	
Anthropometric evaluation				
BMI, Kg/m²	29.4±4.7	29,3±5.0	29.3±4.2	0.976
ArmC, cm	32.7±2.9	32.2±3.2	33.1±2.6	0,303
WaistC, cm	100.9±13.2	101.5±12.1	99.6±13.0	0.577
HipC, cm	103.4±8.1	103.0±9.9	103.3±5.6	0.862
CalfC, cm	36.7±3.2	36.4±3.9	36.9±2.5	0.566
WC/HC	0.97±0.09	0.99±0.08	0.96±0.09	0.317
TSF, mm	18.4±7.6	19.5±7.1	17.5±8.1	0.370
BSF, mm	10.0±4.6	11.1±4.3	9.1±4,7	0.128
SCSF, mm	19.7±7.2	20.7±8.1	18.7±6.2	0.328
ICSF, mm	21.8±7.0	20.1±7.8	23.4±5.6	0.099
FTSF, mm	20.7±10.9	22.1±11.3	19.3±10.6	0.405
APMuscle, mm	20.2±4.4	19.6±4.3	20.8±4.5	0.330
Bioelectrical impedance analysis evaluation				
Resistance, ohms	473.3±76.6	472.3±72.6	474.2±81.2	0.926
Reactance, ohms	35.0±11.0	32.2±8.4	37.5±12.5	0.068
Phase angle, degrees	4.2±1.1	3.9±0.7	4.5±1,2	0.021
Fat free mass, Kg	48.9±11.1	47.0±11.0	50.3±11.1	0.286
Fat free mass, %	65.2±6.6	64.3±7.1	66.0±6.2	0.352
Fat mass, Kg	26.0±7.2	26.2±7.8	25.8±6.8	0.834
Fat mass, %	34.8±6.6	35.7±7.1	34.0±6.2	0.352
Multidetector computed tomography evaluation				
EATVi, mL/m²*	72.1 (38.0)	83.5 (50.6)	63.1 (21.1)	0.093
MATVi, mL/m²	198.0±73.4	203.3±86.3	193.3±61.3	0.644
TAFVi, cm³/m²	213.0±61.1	222.5±61.5	205.3±60.7	0.334
VAFVi, cm³/m²	97.0±38.2	98.5±38.6	95.7±38.5	0.801
SAFVi, cm³/m²	125.7±68.3	124.0±51.0	127.1±80.7	0.874

Results are presented as means ± SD.
p values shown compare frail and non-frail groups.
* median (IQR).
APMuscle: adductor Pollicis Muscle; ArmC: arm circumference; BMI: body mass index; BSF: biceps skinfold; CalfC: calf circumference; FTSF: front thigh skinfold; HipC: hip circumference; ICSF: iliac crest skinfold; SCSF: subscapular skinfold; TSF: triceps skinfold; WaistC: waist circumference; WC/HC: waist circumference/hip circumference.
EATVi: indexed epicardial adipose tissue volume;
MATVi: indexed mediastinal adipose tissue volume
SAFVi: indexed subcutaneous abdominal fat volume
TAFVi: indexed total abdominal fat volume
VAFi: indexed visceral abdominal fat

***Figure 2* - Association of phase angle with frailty and age.**

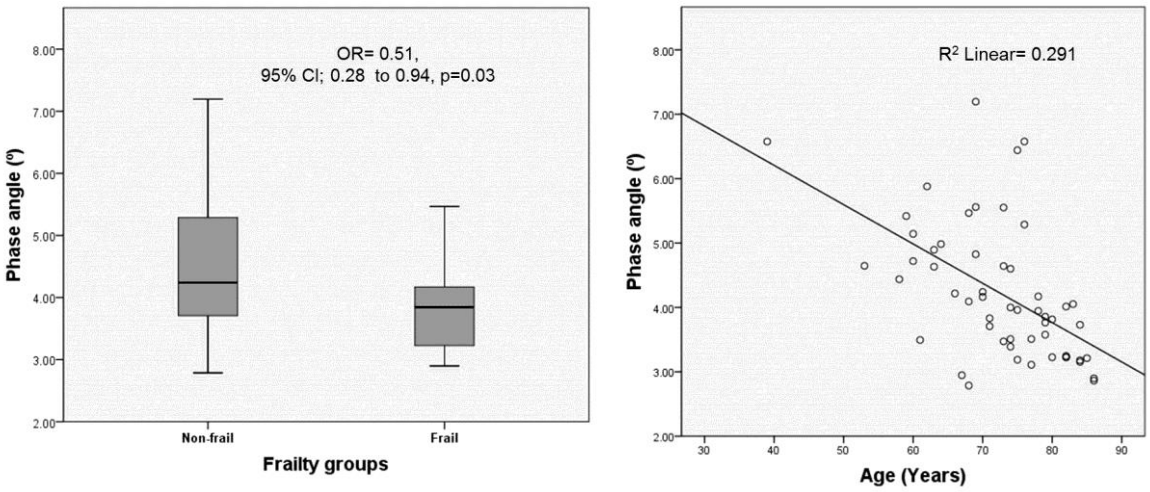

Figure 2 – Association of phase angle with frailty and age. Frailty was inversely associated with PA, frail patients had a significantly lower mean PA than non-frail patients (p=0.03); for each degree of increase of PA, the odds of frailty are reduced by half. (Left) Age and PA was inversely correlated (r=-0.54, p<0.001). (Right)

Table 4 - Age and gender adjusted association of frailty syndrome and body fat distribution parameters.

	Frailty Syndrome		
	OR	**CI, 95%**	**p value**
BMI	1.006	0.890 to 1.137	0.918
Waist circumference	1.021	0.972 to 1.073	0.412
WC/HC ratio	400.4	0.114 to 141412	0.150
% Fat free mass	0.981	0.877 to 1.097	0.738
% Fat mass	1.019	0.912 to 1.140	0.738
EATVi	1.014	1.000 to 1.028	0.045
MATAi	1.000	0.997 to 1.009	0.281
VAFAi	1.005	0.994 to 1.016	0.397
SAFAi	1.000	0.995 to 1.005	1.000
TAFAi	1.000	0.999 to1.015	0.106
EATVi*MATAi	1.014	0.999 to 1.029	0.063
EATVi*VAFAi	1.014	1.000 to 1.029	0.056
EATAi*SAFAi	1.014	1.001 to 1.028	0.042

p values shown compare frail and non-frail groups.
BMI: body mass index
WC/HC ratio: waist circumference/hip circumference ratio
EATVi: indexed epicardial adipose tissue volume;
MATVi: indexed mediastinal adipose tissue volume
SAFVi: indexed subcutaneous abdominal fat volume
TAFVi: indexed total abdominal fat volume
VAFi: indexed visceral abdominal fat

in the model did not enable us to find a significant association between PA and frailty. To surpass this statistical problem, we decided to perform a stepwise backward conditional multivariable logistic regression analysis including age, gender and PA. Using this method, the variable age was the first term removed from the equation (p=0.996), followed by gender (p=0.518).PA was the only independent variable that remained in the model (p=0.03).

The cell membrane reactance (32.2±8.4 vs 37.5±12.5 ohms, p=0.068) tended to be inversely associated with frailty but not the cell membrane resistance.

The crude and adjusted association of phase angle quartiles and frailty are shown in *Table 5*.

Table 5 - Crude and adjusted association of phase angle quartiles and frailty.

	Crude		Adjusted for gender		Adjusted for gender and age	
	OR, 95% CI	**P value**	**OR, 95% CI**	**P value**	**OR, 95% CI**	**P value**
1st quartile	6.2, 1.2 to 32.2	0.028	5.9, 1.2 to 30.7	0.036	5.7, to 0.8 to 39.9	0.078
2nd quartile	2.1, 0.4 to 10.5	0.348	2.1, 0.4 to 10.5	0.350	2.1, 0.6 to 12.0	0.408
3rd quartile	1.9, 0.4 to 9.0	0.433	1.8, 0.4to 8.9	0.449	1.8, 0.4to 9.0	0.461

PA Quartiles in degrees: 1st [2.79; 3.4[; 2nd [3.4; 4.0[; 3rd [4.0; 4.8[; 4th [4.8; 7.19].
p value for the comparison between PA quartiles using the 4th quartile as the reference category

4.4. Association of phase angle and body fat distribution

After observing a significant association of frailty with EAT and of frailty with PA, we studied the correlations of PA with body fat distribution parameters.

In an adjusted age and gender linear regression model, PA was inversely correlated with WC/HC ratio (r= -0.61, p=0.02), %FM (r= -0.60, p=0.02) and indexed EAT volume (r= -0.59, p=0.03), but not with BMI, WC, %FFM, indexed MAT, VAF, SAF and TAF areas.

Adjusting for age, gender, and VAF there was still a significant association between PA and indexed EAT volume, with a PA decrease of 8% per additional 10 mL/m^2 of EAT (p=0.041).

The associations of PA and body fat distribution parameters are shown in *Table 6*.

Table 6 - Age and gender adjusted association of phase angle and body fat distribution parameters.

	Phase angle		
	Beta	**CI, 95%**	**p value**
BMI	-0.018	-0.073 to 0.037	0.506
Waist Circumference	-0.018	-0.040 to 0.003	0.093
WC/HC ratio	-4.04	-7.390 to -0.680	0.019
% Fat free mass	-0.004	-0.048 to 0.041	0.866
% Fat mass	-0.040	-0.074 to -0.007	0.019
EATVi	-0.008	-0.015 to -0.001	0.026
MATAi	-0.003	-0.007 to 0.001	0.107
VAFAi	-0.003	-0.011 to 0.005	0.508
SAFAi	-0.001	-0.006 to 0.003	0.497
TAFAi	-0.002	-0.007 to 0.003	0.463
EATVi*MATAi	-0.007	-0.015 to 0.009	0.086
EATVi*VAFAi	-0.008	-0.016 to 0.000	0.041
EATAi*SAFAi	-0.008	-0.015 to -0.001	0.031

p values shown compare frail and non-frail groups.
BMI: body mass index
WC/HC ratio: waist circumference/hip circumference ratio
EATVi: indexed epicardial adipose tissue volume;
MATVi: indexed mediastinal adipose tissue volume
SAFVi: indexed subcutaneous abdominal fat volume
TAFVi: indexed total abdominal fat volume
VAFi: indexed visceral abdominal fat

5. Discussion

In this observational, cross sectional study including patients with symptomatic severe AS referred to MDCT before AVR, we demonstrated that (1) EAT was an independent predictor of frailty, but not BMI, WC or VAF; (2) Narrow PA was associated with frailty independently of age and gender, and (3) EAT, contrarily of VAF, appeared to be associated with impaired cell membrane integrity and function assessed by BIA derived PA.

5.1 Frailty was independently associated with EAT, but not with abdominal visceral fat or global adiposity

Currently, it remains to be elucidated how overweight or obesity correlates with frailty. In our study, BMI was not an independent predictor of frailty in patients with severe AS. Blaum *et al*.[51] associated the excess of weight assessed by BMI with the pre-frailty phenotype, and the obesity with both pre-frailty and frailty, suggesting a positive association between body fat and frailty. Hubbard *et al*.[52] found an interesting U-shaped association between BMI and frailty. These authors determined the association of BMI categories with the frailty index (FI), which is a proportion (i.e. range from 0 to 1) of the summed individual's deficit divided by the total number of deficits considered (in this case, 58). FI scores were lowest in those with BMI ranging from 20 to 29.9 kg/m^2 (normal weight and overweight participants) and higher in those underweight and obese (BMI<20 kg/m^2 and BMI>30 kg/m^2, respectively). The limitations of BMI are well recognized[53, 54]. The sensitivity of the most used cutoff value for obesity (BMI>30 kg/m²) for identifying excessive adiposity is low, missing about half of persons with excess body fat, who have BMI values <30 kg/m²[55]. Moreover, BMI does not distinguish if the body fat accumulation occurs in the subcutaneous or visceral compartment. To fill this gap, WC has been used as an estimative of VAF and WC/HC ratio as a relationship between visceral and subcutaneous adipose tissue[56, 57]. Visceral fat has stronger endocrine activity and inflammatory characteristics than subcutaneous adipose tissue[58], having a major role in the pathophysiology of the metabolic syndrome[59].

Our sample size was powered to detect WC differences between frail and non-frail patients based on data from Shah *et al.*[50]. In this work including HIV-patients with mean age of 58±5 years old, the authors showed a significantly higher WC in frail patients when compared with those non-frail. Contrarily, in our cohort of 55 patients with severe AS, WC was not associated with frailty, as well as the intra-abdominal visceral adipose tissue. The lipodystrophy present in HIV-patients could explain this divergent result. However, this finding is congruent with our observation that intra-abdominal visceral adipose tissue determined by MDCT was not associated with frailty as

well. Indeed, in our study only increased EAT was significantly associated with frailty, independently of age, gender and body superficies area.

EAT is the visceral fat located between the myocardium and the visceral pericardium, and it has the same embryological origin of the abdominal visceral adipose tissue[60].

Increased visceral abdominal fat and EAT have been both associated with metabolic syndrome components[61, 62], coronary artery disease (CAD)[62, 63], left ventricular hypertrophy[64, 65] and diastolic dysfunction[66, 67]. As the visceral abdominal fat, EAT is a source of several inflammatory mediators in high-risk cardiac patients, being linked with high levels of TNF-alfa, monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6), interleukin-1 (IL-1) and plasminogen activator inhibitor-1 (PAF-1)[68, 69]. Although EAT is highly correlated and share similar biochemical properties and adipokines production with VAF[70-72], it has been speculated that EAT and VAF may play differential physiological and pathological roles given its different anatomical location and particular lipolysis and lipid mobilization features.

Under physiological conditions, earlier studies showed that the rate of free-fatty-acid synthesis, breakdown and release in response to catecholamines in EAT were markedly higher than in other visceral adipose depots. This high lipolysis observed in EAT suggests that EAT may have a special function of supplying cardiac muscle with free fatty acids[73]. Moreover, recent studies showed that EAT associates with coronary atherosclerotic burden[74, 75] and with worse diastolic function[67] independently of VAF. Interestingly, Mazurek *et al*.[68] found no correlation between inflammatory signals from EAT and plasma inflammatory biomarkers, with no attenuation of these signals by chronic treatment with conventional cardiovascular therapies, suggesting that the current drug treatment does not eliminate local inflammatory indicators in EAT.

These evidences suggest that EAT has a more relevant local than systemic effects. Its close proximity with the cardiac structures provides conditions for a direct crosstalk between EAT, the myocardium and the

endothelial cells through the release of proatherosclerotic, proinflammatory and profibrotic adipocytokines that can modulate, by paracrine and vasocrine mechanisms, the coronary arteries endothelial cells and the cardiomyocytes, as well as the cardiac stromal cells.

With ageing process, there is an expansion of the EAT, the number of myocytes decreases while the remaining individual myocytes hypertrophy, and there is an intracellular lipid accumulation[76]. In skeletal muscle, there is an increased fat muscle infiltration with an underling chronic inflammation, which leads to a decreased muscle quantity and quality. This phenomenon is called sarcopenia[77]. Ultimately, EAT is “the cardiac muscle fat”, with a paracrine inflammatory regulation, hence it is expected that the same sarcopenia process occurs in cardiac muscle. This new concept is currently called “cardiac sarcopenia”.

Therefore, the process linking EAT and frailty could follow the sequence: (1) a local compensatory mechanism: the EAT increases to feed the cardiac tissue during the catabolic state typically present in cardiac diseases; (2) increased EAT and the catabolic state itself enhance the release of inflammatory mediators to the myocardium; and (3) the lipid accumulation and the excess of inflammatory mediators could lead to cardiac sarcopenia, which could lead to frailty and restart the cycle.

5.2 PA as a marker of frailty and EAT-related inflammation

The role of PA as a marker of nutritional status, impaired clinical outcomes and mortality in populations with chronic disease is widely recognized[31-33]. However, the relation between PA and frailty is little explored. Wilhelm-Leen *et al*.[78] found a significant association between PA and frailty, which remained significant even when adjusted for age, sex, race-ethnicity and comorbidity in 4.667 community American older adults. In cardiac surgical patients, a low PA was associated with less muscle mass and strength and with prolonged intensive care unit and hospital stay length[79]. In this work we found that patients with a narrow PA (lowest quartile, PA<3.4º) had 5.9-fold higher odds of frailty (95 % confidence interval of 1.2 to 30.7) when compared with

patients in the highest quartile (PA ≥ 4.8º). This finding supports the idea that PA could be used as a biomarker to diagnose and to grade frailty in the preoperative risk assessment of patients with AS.

There is sparse data evaluating how different fat depots affect the overall cell membrane integrity and function. Our study showed that EAT was the only fat depot significantly associated with PA. Narrow PA was associated with higher indexed EAT volume even when adjusted for age, gender, VAF, %FFM and %FM.

As narrow PA correlates with high levels of inflammation markers[30, 80] and impaired cellular membrane[26], our results demonstrate that the amount of EAT is more closely linked to cellular health than VAF in patients with AS. Our findings corroborate Mazurek's *et al*. study[68], which demonstrated that proinflammatory properties of EAT were independent of BMI, diabetes or chronic therapy with statins or angiotensin converting enzyme inhibitors in patients with coronary artery disease.

To the best of our knowledge, only one study correlates PA with EAT, however the authors found opposite data[81]. In this study the authors compared the association of EAT and PA in patients with ischemic and non-ischemic cardiomyopathy with reduced ejection fraction (<35%) with heathy controls. The main findings were that EAT and PA were lower in patients with heart failure in comparison to healthy controls, irrespective of its etiology.

Doesch *et al.*[82] showed that the amount of EAT differs according to the left ventricular ejection fraction (LVEF) in patients with CAD. Patients with CAD and preserved LVEF had significantly more EAT than healthy controls and patients with reduced LVEF. Then, in patients at an early stage of the coronary disease, EAT is increased, but with disease progression there is a reduction of this fat depot. In line with this observation, since we restricted our sample to patients with preserved ejection fraction, our positive association between PA and frailty and negative association of PA and EAT suggests that this BIA derived value could be a marker of frailty and EAT-related decline of cellular function.

5.3 Limitations and strengths

The strengths of this study are:

1) We studied a homogenous cohort of patients with AS regarding its heart disease severity;
2) We quantified fat by MDCT and a detailed nutritional assessment was performed;
3) Frailty was determined using a validated scale for cardiovascular patients.

However, same limitations should be noted:

1) We did not include a control group;
2) The cross-sectional design prevent us from determining the long-term influences of frailty and PA in this population, especially in patients who undergo surgery and the cause-and-effect relationship between greater amount of EAT and frailty;
3) Also, our sample size may not have been large enough to pick up differences among groups in some variables, as well as the lack of a control group prevent us to identify differences between our sample and a healthy population;
4) In addition, although our patients are in the same level of impaired cardiac function, we do not know the previous influence of the cardiac disease in the development of a frailty state or in body composition;
5) Beyond the ejection fraction, we should have used more sensitive parameters to evaluate the cardiac function, for instance doppler echocardiography;
6) The localized MDCT used to access the abdominal obesity do not describe the total trunk fat, which could influence our results;
7) Finally, we did not obtain laboratorial analysis of all patients, preventing us from correlate EAT, PA and frailty with metabolic syndrome, insulin resistance and inflammatory markers in this population.

6. Conclusions

In patients with severe AS, there are ongoing efforts to better identify the patient with high perioperative risk of death since these patients should be

referred to transcatheter aortic valve implantation rather than surgical replacement. The current perioperative risk scores (i.e. EuroScore II[83] and STS score[84]) do not consider the frailty phenotype features. Recent guidelines on the management of valve disease from the American Society of Cardiology recommend the evaluation of frailty before surgery[85]. However, none of the frailty models is currently feasible for widespread clinical application.

This study highlights that increased indexed EAT as well as a low PA might be surrogate markers of frailty in patients with severe AS and preserved ejection fraction. Then, in these patients, the additional preoperative EAT and PA determination could contribute to a better diagnose and grade of frailty.

These results show that the subjective evaluation of frailty usually performed in clinical practice is not reliable, since it is typically based in BMI and central adiposity.

The intersection of body composition analysis and frailty is an important area of research with much to explore. Future research should focus on longitudinal data that demonstrate how preoperative PA and EAT predict clinical outcomes after surgery, including the frailty syndrome recovery. It remains to be demonstrated if and how EAT volume and PA change after surgery and what will be its prognostic implications.

7. References

1. Ferrucci L, Cavazzini C, Corsi A, Bartali B, Russo CR, Lauretani F, et al. Biomarkers of frailty in older persons. Journal of endocrinological investigation. 2002;25(10 Suppl):10-5.

2. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M146-56.

3. Ahmed N, Mandel R, Fain MJ. Frailty: an emerging geriatric syndrome. The American journal of medicine. 2007;120(9):748-53.

4. Hamerman D. Toward an understanding of frailty. Annals of internal medicine. 1999;130(11):945-50.

5. Woods NF, LaCroix AZ, Gray SL, Aragaki A, Cochrane BB, Brunner RL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. Journal of the American Geriatrics Society. 2005;53(8):1321-30.

6. Santos-Eggimann B, Cuenoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. The journals of gerontology Series A, Biological sciences and medical sciences. 2009;64(6):675-81.

7. Green P, Woglom AE, Genereux P, Daneault B, Paradis JM, Schnell S, et al. The impact of frailty status on survival after transcatheter aortic valve replacement in older adults with severe aortic stenosis: a single-center experience. JACC Cardiovascular interventions. 2012;5(9):974-81.

8. Ewe SH, Ajmone Marsan N, Pepi M, Delgado V, Tamborini G, Muratori M, et al. Impact of left ventricular systolic function on clinical and echocardiographic outcomes following transcatheter aortic valve implantation for severe aortic stenosis. American heart journal. 2010;160(6):1113-20.

9. Varadhan R, Walston J, Cappola AR, Carlson MC, Wand GS, Fried LP. Higher levels and blunted diurnal variation of cortisol in frail older women. The journals of gerontology Series A, Biological sciences and medical sciences. 2008;63(2):190-5.

10. Carcaillon L, Garcia-Garcia FJ, Tresguerres JA, Gutierrez Avila G, Kireev R, Rodriguez-Manas L. Higher levels of endogenous estradiol are associated with frailty in postmenopausal women from the toledo study for healthy aging. The Journal of clinical endocrinology and metabolism. 2012;97(8):2898-906.

11. Li H, Manwani B, Leng SX. Frailty, inflammation, and immunity. Aging and disease. 2011;2(6):466-73.

12. Walston J, Hadley EC, Ferrucci L, Guralnik JM, Newman AB, Studenski SA, et al. Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. Journal of the American Geriatrics Society. 2006;54(6):991-1001.

13. Leng SX, Xue QL, Tian J, Walston JD, Fried LP. Inflammation and frailty in older women. Journal of the American Geriatrics Society. 2007;55(6):864-71.

14. Hubbard RE, O'Mahony MS, Calver BL, Woodhouse KW. Nutrition, inflammation, and leptin levels in aging and frailty. Journal of the American Geriatrics Society. 2008;56(2):279-84.

15. Cesari M, Penninx BW, Pahor M, Lauretani F, Corsi AM, Rhys Williams G, et al. Inflammatory markers and physical performance in older persons: the InCHIANTI study. The journals of gerontology Series A, Biological sciences and medical sciences. 2004;59(3):242-8.

16. Strawbridge WJ, Shema SJ, Balfour JL, Higby HR, Kaplan GA. Antecedents of frailty over three decades in an older cohort. The journals of gerontology Series B, Psychological sciences and social sciences. 1998;53(1):S9-16.

17. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. The journals of gerontology Series A, Biological sciences and medical sciences. 2007;62(7):738-43.

18. Lemieux I, Pascot A, Prud'homme D, Almeras N, Bogaty P, Nadeau A, et al. Elevated C-reactive protein: another component of the atherothrombotic profile of abdominal obesity. Arteriosclerosis, thrombosis, and vascular biology. 2001;21(6):961-7.

19. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. Diabetes. 2007;56(4):1010-3.

20. Walston J, McBurnie MA, Newman A, Tracy RP, Kop WJ, Hirsch CH, et al. Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities: results from the Cardiovascular Health Study. Archives of internal medicine. 2002;162(20):2333-41.

21. Barzilay JI, Blaum C, Moore T, Xue QL, Hirsch CH, Walston JD, et al. Insulin resistance and inflammation as precursors of frailty: the Cardiovascular Health Study. Archives of internal medicine. 2007;167(7):635-41.

22. Goulet ED, Hassaine A, Dionne IJ, Gaudreau P, Khalil A, Fulop T, et al. Frailty in the elderly is associated with insulin resistance of glucose metabolism in the postabsorptive state only in the presence of increased abdominal fat. Experimental gerontology. 2009;44(11):740-4.

23. Kalyani RR, Varadhan R, Weiss CO, Fried LP, Cappola AR. Frailty status and altered glucose-insulin dynamics. The journals of gerontology Series A, Biological sciences and medical sciences. 2012;67(12):1300-6.

24. Villareal DT, Banks M, Siener C, Sinacore DR, Klein S. Physical frailty and body composition in obese elderly men and women. Obesity research. 2004;12(6):913-20.

25. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gomez JM, et al. Bioelectrical impedance analysis--part I: review of principles and methods. Clinical nutrition (Edinburgh, Scotland). 2004;23(5):1226-43.

26. Selberg O, Selberg D. Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis. European journal of applied physiology. 2002;86(6):509-16.

27. Bosy-Westphal A, Danielzik S, Dorhofer RP, Later W, Wiese S, Muller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. JPEN Journal of parenteral and enteral nutrition. 2006;30(4):309-16.

28. Slee A, Birc D, Stokoe D. Bioelectrical impedance vector analysis, phase-angle assessment and relationship with malnutrition risk in a cohort of frail older hospital patients in the United Kingdom. Nutrition. 2015;31(1):132-7.

29. Kyle UG, Genton L, Pichard C. Low phase angle determined by bioelectrical impedance analysis is associated with malnutrition and nutritional risk at hospital admission. Clinical nutrition (Edinburgh, Scotland). 2013;32(2):294-9.

30. Lukaski HCaS, M. G. Phase angle as a prognostic indicator in cancer. Procedings of the AAAI. 2011;1:37-41.

31. Gupta D, Lammersfeld CA, Burrows JL, Dahlk SL, Vashi PG, Grutsch JF, et al. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in advanced colorectal cancer. The American journal of clinical nutrition. 2004;80(6):1634-8.

32. Mushnick R, Fein PA, Mittman N, Goel N, Chattopadhyay J, Avram MM. Relationship of bioelectrical impedance parameters to nutrition and survival in peritoneal dialysis patients. Kidney international Supplement. 2003(87):S53-6.

33. Gupta D, Lis CG, Dahlk SL, Vashi PG, Grutsch JF, Lammersfeld CA. Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer. The British journal of nutrition. 2004;92(6):957-62.

34. Lang RM BM, Devereux RB, et al. Recommendations for chamber quantification. European journal of echocardiography: the journal of the Working Group on Echocardiography of the European Society of Cardiology. 2006;7:79-108.

35. Taylor HL, Jacobs DR, Jr., Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. Journal of chronic diseases. 1978;31(12):741-55.

36. Fess. E. Grip strength. In: Casanova J, editor. Clinical assessment recommendations. 2nd ed. Chicago: American Society of Hand Therapists1992. p. p. 41–5.

37. Stewart A, Marfell-Jones, M., Olds, T., and de Ridder, H. International standards for anthropometric assessment. ISAK: Lower Hutt, New Zealand.2011.

38. Fryar CD GQ, Ogden CL. Anthropometric reference data for children and adults: United States, 2007–2010. . National Center for Health Statistics Vital Health Stat. 2012;11(252).

39. Lipschitz DA. Screening for nutritional status in the elderly. Primary care. 1994;21(1):55-67.

40. Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. The American journal of clinical nutrition. 1985;41(4):810-7.

41. Kyle UG, Genton L, Karsegard L, Slosman DO, Pichard C. Single prediction equation for bioelectrical impedance analysis in adults aged 20--94 years. Nutrition. 2001;17(3):248-53.

42. Borkan GA, Gerzof SG, Robbins AH, Hults DE, Silbert CK, Silbert JE. Assessment of abdominal fat content by computed tomography. The American journal of clinical nutrition. 1982;36(1):172-7.

43. Yoshizumi T, Nakamura T, Yamane M, Islam AH, Menju M, Yamasaki K, et al. Abdominal fat: standardized technique for measurement at CT. Radiology. 1999;211(1):283-6.

44. Ashwell M, Cole TJ, Dixon AK. Obesity: new insight into the anthropometric classification of fat distribution shown by computed tomography. British medical journal (Clinical research ed). 1985;290(6483):1692-4.

45. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification. Eur J Echocardiogr. 2006;7(2):79-108.

46. Rosenhek R, Binder T, Porenta G, Lang I, Christ G, Schemper M, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. The New England journal of medicine. 2000;343(9):611-7.

47. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr., et al. Seventh report of the Joint National Committee on Prevention,

Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42(6):1206-52.

48. Standards of medical care in diabetes--2015: summary of revisions. Diabetes care. 2015;38 Suppl:S4.

49. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama. 2001;285(19):2486-97.

50. Shah K, Hilton TN, Myers L, Pinto JF, Luque AE, Hall WJ. A new frailty syndrome: central obesity and frailty in older adults with the human immunodeficiency virus. Journal of the American Geriatrics Society. 2012;60(3):545-9.

51. Blaum CS, Xue QL, Michelon E, Semba RD, Fried LP. The association between obesity and the frailty syndrome in older women: the Women's Health and Aging Studies. Journal of the American Geriatrics Society. 2005;53(6):927-34.

52. Hubbard RE, Lang IA, Llewellyn DJ, Rockwood K. Frailty, body mass index, and abdominal obesity in older people. The journals of gerontology Series A, Biological sciences and medical sciences. 2010;65(4):377-81.

53. Flegal KM, Shepherd JA, Looker AC, Graubard BI, Borrud LG, Ogden CL, et al. Comparisons of percentage body fat, body mass index, waist circumference, and waist-stature ratio in adults. The American journal of clinical nutrition. 2009;89(2):500-8.

54. Oreopoulos A, Ezekowitz JA, McAlister FA, Kalantar-Zadeh K, Fonarow GC, Norris CM, et al. Association between direct measures of body composition and prognostic factors in chronic heart failure. Mayo Clinic proceedings. 2010;85(7):609-17.

55. Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell ML, Korinek J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. International journal of obesity (2005). 2008;32(6):959-66.

56. Sampaio LR, Simoes EJ, Assis AM, Ramos LR. Validity and reliability of the sagittal abdominal diameter as a predictor of visceral abdominal fat. Arquivos brasileiros de endocrinologia e metabologia. 2007;51(6):980-6.

57. Illouz F, Roulier V, Rod A, Gallois Y, Pelle CP, Aube C, et al. Distribution of adipose tissue: quantification and relationship with hepatic steatosis and vascular profiles of type 2 diabetic patients with metabolic syndrome. Diabetes & metabolism. 2008;34(1):68-74.

58. Fain JN, Madan AK, Hiler ML, Cheema P, Bahouth SW. Comparison of the release of adipokines by adipose tissue, adipose tissue matrix, and adipocytes from visceral and subcutaneous abdominal adipose tissues of obese humans. Endocrinology. 2004;145(5):2273-82.

59. Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006;444(7121):881-7.

60. Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. Nature clinical practice Cardiovascular medicine. 2005;2(10):536-43.

61. Ormseth MJ, Lipson A, Alexopoulos N, Hartlage GR, Oeser AM, Bian A, et al. Association of epicardial adipose tissue with cardiometabolic risk and metabolic syndrome in patients with rheumatoid arthritis. Arthritis care & research. 2013;65(9):1410-5.

62. Sam S, Haffner S, Davidson MH, D'Agostino RB, Sr., Feinstein S, Kondos G, et al. Relationship of abdominal visceral and subcutaneous adipose tissue with lipoprotein particle number and size in type 2 diabetes. Diabetes. 2008;57(8):2022-7.

63. Xu Y, Cheng X, Hong K, Huang C, Wan L. How to interpret epicardial adipose tissue as a cause of coronary artery disease: a meta-analysis. Coronary artery disease. 2012;23(4):227-33.

64. Erdogan T, Cetin M, Kocaman SA, Durakoglugil ME, Ergul E, Ugurlu Y, et al. Epicardial adipose tissue is independently associated with increased left ventricular mass in untreated hypertensive patients: an observational study. Anadolu kardiyoloji dergisi : AKD = the Anatolian journal of cardiology. 2013;13(4):320-7.

65. Capoulade R, Larose E, Mathieu P, Clavel MA, Dahou A, Arsenault M, et al. Visceral adiposity and left ventricular mass and function in patients with aortic stenosis: the PROGRESSA study. The Canadian journal of cardiology. 2014;30(9):1080-7.

66. Cetin M, Kocaman SA, Durakoglugil ME, Erdogan T, Ergul E, Dogan S, et al. Effect of epicardial adipose tissue on diastolic functions and left atrial dimension in untreated hypertensive patients with normal systolic function. Journal of cardiology. 2013;61(5):359-64.

67. Fontes-Carvalho R, Fontes-Oliveira M, Sampaio F, Mancio J, Bettencourt N, Teixeira M, et al. Influence of epicardial and visceral fat on left ventricular diastolic and systolic functions in patients after myocardial infarction. The American journal of cardiology. 2014;114(11):1663-9.

68. Mazurek T, Zhang L, Zalewski A, Mannion JD, Diehl JT, Arafat H, et al. Human epicardial adipose tissue is a source of inflammatory mediators. Circulation. 2003;108(20):2460-6.

69. Baker AR, Silva NF, Quinn DW, Harte AL, Pagano D, Bonser RS, et al. Human epicardial adipose tissue expresses a pathogenic profile of adipocytokines in patients with cardiovascular disease. Cardiovascular diabetology. 2006;5:1.

70. Iacobellis G, Assael F, Ribaudo MC, Zappaterreno A, Alessi G, Di Mario U, et al. Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. Obesity research. 2003;11(2):304-10.

71. Iacobellis G, Leonetti F, Di Mario U. Images in cardiology: Massive epicardial adipose tissue indicating severe visceral obesity. Clinical cardiology. 2003;26(5):237.

72. Iacobellis G, Ribaudo MC, Assael F, Vecci E, Tiberti C, Zappaterreno A, et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. The Journal of clinical endocrinology and metabolism. 2003;88(11):5163-8.

73. Marchington JM, Pond CM. Site-specific properties of pericardial and epicardial adipose tissue: the effects of insulin and high-fat feeding on lipogenesis and the incorporation of fatty acids in vitro. International journal of obesity. 1990;14(12):1013-22.

74. Bettencourt N, Toschke AM, Leite D, Rocha J, Carvalho M, Sampaio F, et al. Epicardial adipose tissue is an independent predictor of coronary atherosclerotic burden. International journal of cardiology. 2012;158(1):26-32.

75. Oikawa M, Owada T, Yamauchi H, Misaka T. Epicardial adipose tissue reflects the presence of coronary artery disease: comparison with abdominal visceral adipose tissue. 2015;2015:483982.

76. Lin J, Lopez EF, Jin Y, Van Remmen H, Bauch T, Han HC, et al. Age-related cardiac muscle sarcopenia: Combining experimental and mathematical modeling to identify mechanisms. Experimental gerontology. 2008;43(4):296-306.

77. Beyer I, Mets T, Bautmans I. Chronic low-grade inflammation and age-related sarcopenia. Current opinion in clinical nutrition and metabolic care. 2012;15(1):12-22.

78. Wilhelm-Leen ER, Hall YN, Horwitz RI, Chertow GM. Phase angle, frailty and mortality in older adults. Journal of general internal medicine. 2014;29(1):147-54.

79. Visser M, van Venrooij LM, Wanders DC, de Vos R, Wisselink W, van Leeuwen PA, et al. The bioelectrical impedance phase angle as an indicator of undernutrition and adverse clinical outcome in cardiac surgical patients. Clinical nutrition (Edinburgh, Scotland). 2012;31(6):981-6.

80. de Luis DA, Aller R, Romero E, Duenas A, Perez Castrillon JL. Relation of phase angle tertiles with blood adipocytokines levels, insulin resistance and cardiovascular risk factors in obese women patients. European review for medical and pharmacological sciences. 2010;14(6):521-6.

81. Doesch C, Suselbeck T, Leweling H, Fluechter S, Haghi D, Schoenberg SO, et al. Bioimpedance analysis parameters and epicardial adipose tissue assessed by cardiac magnetic resonance imaging in patients with heart failure. Obesity (Silver Spring, Md). 2010;18(12):2326-32.

82. Doesch C, Haghi D, Suselbeck T, Schoenberg SO, Borggrefe M, Papavassiliu T. Impact of functional, morphological and clinical parameters on epicardial adipose tissue in patients with coronary artery disease. Circulation journal : official journal of the Japanese Circulation Society. 2012;76(10):2426-34.

83. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2012;41(4):734-44; discussion 44-5.

84. O'Brien SM, Shahian DM, Filardo G, Ferraris VA, Haan CK, Rich JB, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2--isolated valve surgery. The Annals of thoracic surgery. 2009;88(1 Suppl):S23-42.

85. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(23):2440-92.

Annex A

***Epic*HEART**

Avaliação Nutricional

NÚMERO DO DOENTE [ID]

Dados Pessoais	
Data da avaliação:	
Data de Nascimento:	Sexo:
Escolaridade:	
Profissão:	
Uso de tabaco:	Qtde/dia:
Uso de álcool:	Qtde/dia:
Diabetes:	
Hipertensão:	
Hipercolesterolemia:	
Ativ. Física:	Frequência:
Uso de suplementos:	Duração:

Avaliação Nutricional	
Peso:	
Altura:	
IMC:	
Circunferências	
C. Braço: _____ C. Cintura: _____	C. Quadril: _____ C. Geminal: _____
Pregas Cutâneas:	
PC Tricipital: _____ PC Bicipital: _____ PC Subescapular: _____	PC Iliocristal: _____ PC Coxa Medial: _____ M. Adutor Polegar: _____
Bioimpedância:	
Resistência: _____ Reatância: _____ Ângulo de fase: _____	% Massa Gorda: _____ % Massa Magra: _____

Força de Preensão da Mão: _____/_____/_____

Escala de Fragilidade (Fried *et al*., 2001)

Perda de Peso:

Pergunta-se: “no último ano, você perdeu peso de forma não intencional, ou seja, sem fazer dieta ou atividade física com esse objetivo?” Em caso de resposta positiva, pergunta-se quantos quilos. São considerados frágeis aqueles que relatam perda superior a 4,5kg ou 5% do peso corporal.

Fadiga:

Baseado na escala de depressão do Center for Epidemiological Studies-Depression (CES-D), as duas sentenças seguintes são lidas:

1. Senti que eu fazia tudo com um esforço.
2. Eu não consegui continuar / tive que parar.

Então pergunta-se: “com que frequência você se sentiu assim na última semana?

0 = nunca ou raramente (<1 dia)

1 = pouco tempo (1–2 dias)

2 = um tempo razoável (3-4 dias)

3 = a maior parte do tempo.

Pacientes com respostas 2 ou 3 são caracterizados como frágeis no critério fadiga.

Velocidade da marcha:

O idoso deve percorrer em passo usual, no plano, uma distância de 4,6m.

Homens	**Ponto de Corte para Fragilidade**

Altura ≤ 173 cm	≥ 7 segundos
Altura > 173 cm	≥ 6 segundos
Mulheres	
Altura ≤ 159 cm	≥ 7 segundos
Altura > 159 cm	≥ 6 segundos

Força de preensão manual:

Medida com dinamômetro colocado na mão dominante de cada idoso, em três tentativas, respeitando um minuto de intervalo entre elas.

Homens	**Ponto de Corte para Fragilidade**
IMC ≤ 24 Kg/m²	≤ 29 Kg
IMC 24,1 – 26 Kg/m²	≤ 30 Kg
IMC 26,1 – 28 Kg/m²	≤ 30 Kg
IMC > 28 Kg/m²	≤ 32 Kg
Mulheres	
IMC ≤ 23 Kg/m²	≤ 17 Kg
IMC 23,1 – 26 Kg/m²	≤ 17,3 Kg
IMC 26,1 – 29 Kg/m²	≤ 18 Kg
IMC > 29 Kg/m²	≤ 21 Kg

Atividade Física

Pacientes com gasto energético ligado à atividade física <383 kcal/semana, para mulheres, e <270 kcal/semana, para homens, são considerados como frágeis no critério atividade física.

IAM = ∑ (I x M x F x T), onde IAM = gasto energético; I = intensidade de cada atividade física em METS; M = número de meses/ano em que a atividade foi realizada; F = número médio de vezes que foi realizada no mês; T = duração média da atividade em cada ocasião. Para obter o valor em kcal: I x 0,0175 x Peso (kg).

Classificação final:

0 componentes → sem fragilidade

1 ou 2 componentes → risco de fragilidade

3 ou mais componentes → fragilidade