ORIGINAL ARTICLE

Prevalence of Frailty in Patients Undergoing Cardiac Valve Surgery: Comparison of Frailty Tools

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Abstract

Background: There is no consensus among tools for assessing frailty.

Objective: To evaluate the prevalence of frailty according to different tools in patients referred for elective valve cardiac surgery.

Methods: This is a cross-sectional study. All patients were ≥ 18 years of age, clinically stable. The following patients were excluded: those unable to perform the tests because of physical, cognitive, or neurological limitations; those requiring non elective/emergency procedures or hemodynamic instability. During the preoperative cardiology visit, frailty was assessed by the Short Physical Performance Battery (SPPB), the Frailty Deficit Index (FDI), handgrip strength, and gait speed 3m. For the entire analysis, the statistical significance was set at 5%.

Results: Our cohort consisted of 258 subjects. From the total cohort, 201 were ≤ 70 years of age (77.9%), the predominant etiology according to rheumatic disease (50.7% *vs* 8.8%; p=0.000) with double mitral lesion (24.9% *vs* 0%; p=0.000). Frailty was present in 32.9% according SPPB, 29.1% with reduced muscular strength. and 8.9% with FDI. Handgrip strength was weaker in elderly patients (26.7 *vs* 23.6; p=0.051) and gait speed was lower in the younger group, in which 36% were considered frail (36% *vs* 14%; p=0.002). Variables associated with frailty were age ≥ 70 years, female gender, aortic stenosis, and regurgitation.

Conclusion: Frailty in adult patients who will have elective heart valve surgery is present even in the younger groups, although the older group with comorbidities are more frail. Frailty was more clearly shown by the SPPB than by the FDI and handgrip tests.

Keywords: Heart Valve Diseases/surgery; Cardiac Surgery; Frailty; Frail Elderly.

Introduction

Associated with an increased life expectancy worldwide is a growing prevalence of valvular heart disease (VHD).[1] The number of cardiovascular procedures in older adults has also increased in recent years and, heart valve disease accounts for a high number of hospitalizations requiring surgery in Brazil.[2] The impact of frailty on cardiovascular disease is striking; it relates to adverse outcomes following surgery, including postoperative morbidity and mortality.[3, 4]

Frailty is defined as a biological syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiological systems, and causing vulnerability to adverse outcomes.[5] Although not routinely estimated in the preoperative setting, prevalence of frailty in community-dwelling older adults can vary in the literature from 10% to nearly 60% depending on comorbidity burden, population, and measurement tool.[6] Even younger patients undergoing cardiac surgery may have a high degree of frailty, and frailty in younger patients (40-64 years) is also related to worse outcomes.[7]

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The rheumatic etiology is the main cause of VHD in Latin America, different from most developed countries, where degenerative etiology is more prevalent.[2] Moreover, patients with rheumatic heart disease have a greater risk of disease progression and often need reoperation 10 or 20 years after the first procedure. Even though the prevalence of rheumatic heart disease worldwide remains alarmingly high, the impact of frailty assessment in this population in unknown.[8]

Heart valve surgery is an inherently relevant iatrogenic stressor for frailty and surgical intervention is the cornerstone of treatment for symptomatic disease – the only definitive approach able to change mortality.[2] Preoperative frailty evaluation would result in better risk assessment for cardiac surgery and could identify patients at a higher risk for adverse clinical outcomes, mortality, and prolonged institutional care.[9]

Operative risk for cardiac surgery is usually measured by the European System of Cardiac Operative Risk Evaluation (EuroSCORE)[10, 11] or the Society of Thoracic Surgeons (STS) score.[12, 13] However, none of these scores have incorporated frailty. Patients who are frail may need rehabilitation because of a decline in functional status after an intervention, with significant loss in quality of life and independence. Higher frailty scores lead to longer mechanical ventilation, prolonged ICU and hospital length of stay, and a higher risk for complications, such as stroke and in-hospital death. The incorporation of frailty into operative risk scores may improve classification with STS and EuroSCORE.[6, 14, 15]

Recent data report that not only do frail patients have higher complications, but there is also an association between pre-frailty and adverse postoperative outcomes following cardiovascular surgery. Rodrigues et al. reported higher rates of stroke and in-hospital deaths in a Brazilian center even in pre-frail subjects.[16]

The clinician often evaluates frailty by the 'eye-ball test, and despite the fact that' – these patients usually have sarcopenia and adverse outcomes,[17] this approach is subjective, unreliable, and prone to bias.[18,19] Objective measurement for frailty is recommended, but many tools are available for assessing frailty, and there is no consensus among them.[4]

The aim of this study was to evaluate the prevalence of frailty according to different tools in patients with VHD referred for elective cardiac surgery in a tertiary reference university hospital.

Methods

This is a cross-sectional study. The present investigation was conducted from March to November 2018, with a convenience sample of 383 patients with symptomatic valve heart disease, who were referred for either elective transcatheter valve therapy or cardiac surgery at our institution. All patients were ≥18 years of age and clinically stable. The following patients were excluded: those unable to perform the tests because of physical, cognitive, or neurological limitations; patients unwilling to perform the tests; patients experiencing symptoms at rest (chest pain, dyspnea); and those requiring non-elective/emergency procedures or presenting hemodynamic instability defined as systolic blood pressure <60 or >150mmHg and heart beats <50 or >130 beats per minute.

Data with baseline characteristics were assessed by reviewing electronic records that included comorbidities, symptoms (e.g. NYHA class assessed by the New York Heart Association functional classification), cardiovascular risk factors, prior cardiovascular events and procedures, medication, height, weight, and ejection fraction.

Age cutoff

The optimal age cutoff to define elderly patients undergoing cardiac surgery is unknown, usually ranging from 65 to 80 years of age. Although the use of 75 years as a cutoff was proposed recently[20] for patients undergoing cardiac surgery, since it marks a steeper increase in mortality, we chose to use the definition of 70 years of age because: 1) our population is different from this cohort regarding multiple aspects of aging (Brazil x USA/Canada); 2) the 70 year cutoff was previously used in other groups;[21,22] 3) we had a representative proportion of patients over 70 years (22%) but not over 75 years (10%).

Frailty assessment

During the preoperative cardiology visit, physical performance (Short Physical Performance Battery [SPPB]), Frailty Deficit Index (FDI), and handgrip strength (dynamometer hydraulic Saehan®) were assessed by a single trained physiotherapist. SPPB is an established tool to assess one's physical performance of the lower limbs and consists of three

timed tasks: standing balance (semi-tandem and tandem), 3-meter gait-speed, and 5-chair sit-to-stand tests. Every task can be given a score between 0 and 4. The score range from 0 to 3 means disability, from 4 to 6 means poor performance, from 7 to 9 moderate performance, and from 10 to 12 good performance. Frailty was considered when SPPB was ≤8, as previously reported in patients undergoing cardiac valvar surgery.[6]

The FDI ranges from 0 to 32 points, and the final score is calculated from the sum of points divided by the number of variables. According to the existing literature, frail patients were defined as those with an FDI index of greater than or equal to 0.25.[23]

Muscular strength was measured using a dominant hand handgrip. The patients were seated with their shoulders adducted, their elbows flexed to 90°, and their forearms in a neutral position. The frailty criteria were based on the highest measure of three tests of grip strength, adjusted for gender and body mass index (BMI).[5]

The Gait Speed was extracted from the SPPB test and calculated with a 3m distance, with the best time out of two assessments. Patients could use their usual walking assistance device. In this study, 0.83m/s was defined as the cutoff for frailty.[24]

Ethical aspects

This study was approved by the Ethics Committee on Human Research of the Hospital das Clínicas at the College of Medicine, University of São Paulo (CAAE 08882019.4.0000.0068). Patients were informed about the purpose of the research, and evaluation procedures and written consents were obtained from all patients. Possible questions were clarified and the patients were informed that they could withdraw from the research whenever they wanted.

Statistical analysis

Statistical analysis was performed using the SPSS software (version 17.0; SPSS Inc.). Continuous data are presented in median and interquartile intervals, and categorical data are expressed in percentages. The Kolmogorov-Smirnov test was used to determine the normality of data distribution; The Mann-Whitney tests were used to assess the differences in data between groups with continuous data as appropriate. The X^2 test was used for categorical data. Spearman's Correlation was conducted to study the association between the tools used to assess frailty, considering the degree of association as weak, r=0.30 to 0.50; moderate, r= 0.50 to 0.70; and strong, r>0.7.[25] For all analyses, statistical significance was set at $p < 0.05$.

Results

During the study, 383 patients were screened for the preoperative visit, of which 125 were excluded mainly due to incomplete data. Our sample, therefore, consisted of 258 subjects (Figure 1). The median age was 59 (48.7-68) years of age, and 57.8% were female patients .

Table 1 shows the baseline characteristics between the groups <70 and ≥70 years of age. From the total cohort, 201 (77.9%) were <70, and the predominant etiology was rheumatic heart disease, with double mitral lesion as the main etiology of heart valve disease. This group also showed a significant prevalence of previous stroke and pulmonary hypertension.

Aortic stenosis was more prevalent in the older group, with more than half of the subjects presenting this condition. A higher number of comorbidities were related to older age, such as diabetes, hypertension, dyslipidemia, anemia, and coronary artery disease. Musculoskeletal limitations were present in both groups but with no statistical difference (21.5% vs. 31.6, p=0.115); the level of physical activity was similar between the groups (9.0% vs.8.8, p=0.966).

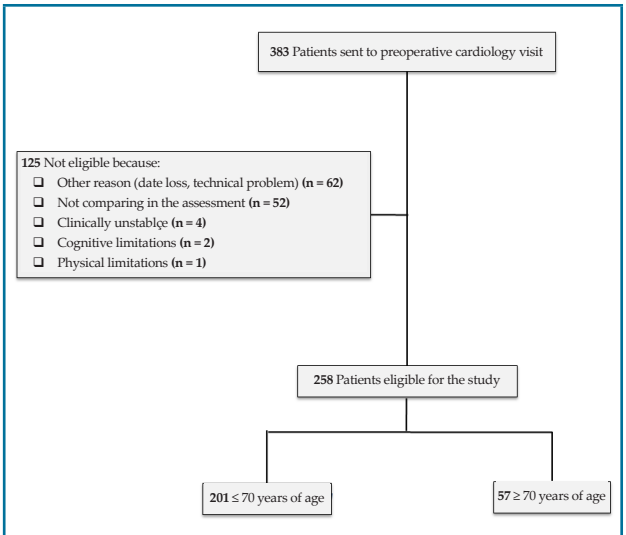

Figure 1 – Flow diagram.

Table 1 – Clinical features of patients evaluated for frailty in the preoperative period for elective heart valve replacement surgery; Heart Institute, March to November, 2018

	< 70 years of age (n=201)	≥ 70years of age (n=57)	Total (n=258)	p-value
Age (years)	54(46-61.5)	74(71.5-79)	59(48.75-68)	**<0.001**
Female, sex (%)	62.2	42.1	57.8	0.007
BMI (kg/m²)	27.1(22.8-30.4)	26.4(24.6-30.6)	26.5(23.4-30.4)	0.319
Valvular Lesion (%)				
Mitral stenosis	9.0	1.8	7.4	0.006
Mitral Regurgitation	22.9	14.0	20.9	0.147
MS/MR	24.9	0.0	19.4	**<0.001**
Aortic stenosis	20.9	56.1	28.7	**<0.001**
Aortic regurgitation	11.9	14.0	12.0	0.944
AS/AR	10.4	56.1	28.7	**<0.001**
Comorbid Conditions (%)				
NYHA functional class	3 (2-3)	2 (2-3)	3(2-3)	0.129
Prior Cardiac Surgery	43.3	31.6	40.7	0.112
Active smoking	8.0	3.5	7.0	0.244
Myocardial infarction	6.5	8.8	7.0	0.966
Diabetes	14.4	40.4	20.2	**<0.001**
PAD	5.0	5.3	5.0	0.930
Stroke	14.9	3.5	12.4	**0.021**
Hemiplegia	5.0	0.0	3.9	0.086
COPD	6.5	1.8	5.4	0.166
Renal impairment	4.0	7.0	4.7	**0.036**
Rheumatic disease	50.7	8.8	41.5	**<0.001**
Hypertension	56.7	87.7	63.6	**<0.001**
Dyslipidemia	28.4	50.9	33.3	**0.001**
Heart failure	35.8	8.6	36.4	0.701
LVEF	62(56-66)	63(55-66)	62(25-75)	0.895
Depression	6.0	1.8	5.0	0.309
Anemia	9.0	21.1	11.6	**0.012**
Pulmonary hypertension	47.7	28.1	43.0	**0.010**
Atrial fibrillation	40.5	28.1	37.7	0.088
CAD	13.9	29.8	17.4	**0.005**

BMI: body mass index; MS/MR: mitral stenosis and mitral regurgitation; AS/AR: aortic stenosis and aortic regurgitation; NYHA: New York heart association; PAD: peripheral artery disease; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; CAD: coronary artery disease. Used Mann-Whitney test and X^2 test, statistical significance was p<0.05.

Frailty prevalence differed significantly with age and the assessment tool used (Figure 2). Frailty was present in 32.9%, according to SPPB; in 29.1%, according to reduced muscle strength; and in only 8.9% when FDI was applied. No patient used a walking assistance device.

Table 2 shows the groups divided according to age. Handgrip strength was lower in elderly patients, classifying almost half of them as frail. When SPPB was used, 43.9% were considered frail in the oldest group, with moderate performance. Gait speed was lower in the young group, and 36% were considered frail with the SPPB assessment instrument. Only when the FDI was applied, no statistical difference was observed between the groups regarding the degree of frailty.

Frail patients were compared with non-frail patients, according to SPPB. Frail patients were mainly ≥ 70 years

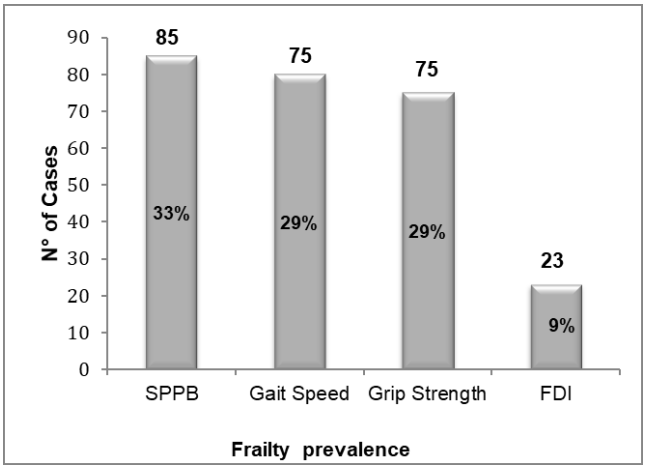

Figure 2 – Prevalence of frailty in the total sample analysis.

Table 2 – Frailty assessment according to age

Frailty Assessment	< 70 years of age (n =201)	≥ 70years of age (n =57)	p-value
SPPB			
Score	0(8-11)	9(7-10)	0.008
(% Frail)	29.9	43.9	0.047
Grip strength			
(Kgf)	26.7(20.8-34.6)	23.6(16.9-33.9)	0.051
(% Frail)	22.9	50.9	**<0.001**
Gait Speed			
(m/s)	1.0(0.75-1.00)	1.0(0.87-1.25)	**0.004**
(% Frail)	36	14	**0.002**
FDI			
Score	0.12(0.07-0.18)	0.12(0.10-0.16)	0.417
(% Frail)	9.0	8.8	0.966

SPPB: Short Physical Performance Battery; Kgf: kilograms force; FDI: Frailty Deficit Index. Used Mann-Whitney test and X2 test, statistical significance was p<0.05.

of age, female, and had aortic stenosis and regurgitation as the main lesion. They also presented a worse NYHA class, and more than half had a previous cardiac surgery. These patients had lower physical activity (2.3% vs. 12.1%, p=0,010) and other comorbidities were more prevalent, such as anemia, atrial fibrillation, musculoskeletal disorders (35.3% vs.18%, p=0.002) and hemiplegia (Table 3).

SPPB score showed a significant and strong correlation with gait speed, which was statistically significant, but a weak association with strength and FDI (Table 4).

Discussion

In this study, despite the fact that the population predominantly consisted of younger adults, frailty was

Table 3 – Comparison between frail and non-frail patients by SPPB; March to November, 2018

	SPPB		
	NON-FRAIL (n= 173)	FRAIL (n= 85)	p-value
≥ 70 years (%)	18.5	29.4	0.047
Female, sex (%)	47	80	**<0.001**
BMI (kg/m²)	26.3(23.4-29.8)	27.4(23.4-31.9)	0.293
Valvular Lesion (%)			
Mitral stenosis	6.9	8.2	0.707
Mitral Regurgitation	23.7	15.3	0.119
MS/MR	17.3	23.5	0.237
Aortic stenosis	28.3	29.4	0.856
Aortic regurgitation	15.0	5.8	**0.034**
AS/AR	8.6	17,6	**0.035**
Comorbid Conditions (%)			
NYHA functional class	2(2-3)	3(2.5-3)	**<0.001**
Prior cardiac surgery	33.0	56.5	**<0.001**
Myocardial infarction	7.5	5.8	0.442
Diabetes	19.6	21.2	0.774
PAD	4.6	5.8	0.436
Stroke	9.8	17.6	0.073
Hemiplegia	1.7	8.2	**0.016**
COPD	5.8	4.7	0.486
Renal impairment	5.2	3.5	0.401
Rheumatic valve disease	38.7	47.0	0.202
Hypertension	60.7	69.4	0.171
Dyslipidemia	34.7	30.6	0.512
Heart failure	35.8	37.6	0.777
Depression	4.6	5.8	0.436
Anemia	8.7	17.6	**0.035**
Pulmonary hypertension	42.4	44.0	0.807
Atrial fribillation	32.4	48.8	**0.011**
CAD	17.9	16.5	0.773

BMI: body mass index; MS/MR: mitral stenosis and mitral regurgitation; AS/AR: aortic stenosis and aortic regurgitation; PAD: peripheral artery disease; COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease. Used Mann-Whitney test and X^2 test, statistical significance was p<0.05.

Table 4 – Spearman's correlation coefficients (r) between the frailty tools

	SPPB	
	r	p-value
Gait speed	-0.805	**<0.001**
Grip strength	0.447	**<0.001**
FDI	-0.417	**<0.001**

SPPB: Short Physical Performance Battery; FDI: Frailty Deficit Index. Spearman test.

present in almost one-third of the total population. In a geriatric population, this prevalence is even higher and frailty evaluation may help to better identify patients at risk for adverse outcomes. Although prior studies have shown that routine risk scores are applied to identify morbidities, they do not assess functional capacity.

A consensus on a validated frailty scoring system that is precise and objective has not yet been established in the literature. Our study applied four different strategies to perform a thorough patient assessment of frailty status, using physical performance, grip strength, gait speed, and deficit measurements. The prevalence of frailty varied considerably according to each tool.

The FDI identified less than 10% of frail subjects, with no significant difference between those over 70 and those under 70. This is probably underestimated according to the current literature, despite a great variation in the prevalence of comorbidities present in each population study. It is possible that FDI did not show a difference between frail and non-frail patients because the questions related to activities of daily living showed low scores and were similar across the sample. Our patients were stable and were referred for elective surgery, which may have contributed to a lower FDI score, although comorbidities were more prevalent in the older group.

The prevalence of frailty, by handgrip strength, however, was more than 2-fold more prevalent in the oldest group (22.9% vs. 50.9%, p =0.000). In this group, the standard deviation was bigger (SD=8.97vs. 0.7), which can be attributed to a large variation in the physical performance that we noted when the test was applied. Bottura et al.[26] evaluated the frailty of 100 individuals in the preoperative period before cardiac surgery, using Fried criteria, handgrip strength, and a gait speed of 5m. Results showed that 70% of the sample were pre-frail and 17% frail, and muscle strength was significantly lower in frail individuals (31±11 vs. 22±8; p=0.007).[26] It was hypothesized that FDI could underestimate the prevalence of frailty, whereas the measure of handgrip strength alone could overestimate it, especially among the elderly.

The FRAILTY-AVR STUDY[27] reported an overall prevalence of frailty that varied from 26% to 68%, with different tools, and SPPB achieved the highest prevalence. Their population was older (median 82 years) than the median from our study group.

In 2010, a study with a 46% prevalence of frailty, according to gait speed, had a 2 to 3-fold increased risk predictive ability beyond the STS-Predicted Risk of Mortality or Major Morbidity and the European System for Cardiac Operative Risk Evaluation (EuroSCORE)[28]. Recently, gait speed has been added to the STS tool.

Interestingly, gait speed was lower in the younger adults probably due to a higher prevalence of pulmonary hypertension which could account for this difference. The pulmonary hypertension in this population results from high left atrial pressure and changes in the pulmonary vasculature, and is considered a marker of disease severity in these patients.[29] Additionally, the prevalence of stroke with hemiplegia may justify the lower walking speed in this population. We believe that these different clinical profiles in younger patients are the result of different etiologies of the valvar disease: more rheumatic heart disease in patients <70 years and more degenerative disease in patients ≥70 years of age. Previous studies showed that rheumatic heart disease is the most common cause of atrial fibrillation in developing countries, affecting mainly young patients, especially women. The uncoordinated contractions of the heart muscle provide an irregular ejection of blood for the ventricle, which can create clots. Atrial fibrillation is

associated with significant morbidity, such as embolic events and stroke.[30,31] This association seems to be present in our sample with a significant number in the younger group.

These data may refine preoperative evaluations and guide future pre-rehabilitation targets that could diminish adverse outcomes of surgery. In 2000, a small randomized trial, conducted in a Canadian tertiary care hospital, randomized 249 patients who had been on a waiting list for elective CABG to receive exercise training, twice per week, education and reinforcement, and monthly nurse-initiated telephone calls. Patients who received the preoperative intervention spent one day less in the hospital overall (p = 0.002) and less time in the intensive care unit.[32]. More recently, another study showed a potential benefit of home pre-rehabilitation in frail patients in the 6 weeks before they underwent elective cardiac and valve surgery.[33] The PREQUEL STUDY (Trial Registration number: ChiCTR1800016098) is a randomized controlled trial in progress that will compare a pre-rehabilitation program with standard of care in frail and pre-frail patients undergoing elective coronary artery bypass graft, with or without valve repair or replacement, and define quality recovery as the primary outcome.

The poorer physical performance, strength, and frailty status of female subjects shown in our analysis are in accordance with results from previous studies.[28] Frailty is more prevalent in women, and there are several hypothesis for this finding: higher inflammatory cytokines, higher insulin resistance, as well as lower testosterone and estrogen levels resulting in a progressive decline in muscle mass and physical vulnerability.[34, 35]

Our study has several limitations: 1) The evaluation time consisted of only 10 months, which limited the sample size; furthermore, we lost 114 patients due to incomplete data; 2) The adopted instruments may not be sensitive enough to characterize the functional capacity of this group and predict final outcomes; 3) because not all of the patients have undergone cardiac surgery, we were not able to correlate frailty with mortality and worse outcomes after surgery; 4) we used a shorter walking distance to calculate gait speed.

Conclusion

Frailty is present in elective heart valve surgery even in young patients. The older group, women, those with comorbidities like pulmonary hypertension and previous stroke are likely to be frail. SPPB showed frailty better than did FDI and handgrip. These results can contribute to the implementation of therapeutic intervention, like exercise training in the pre-operative period for patients to reduce postoperative risks.

Author contributions

Conception and design of the research: Harada G, Andrade MC, Feltrim MI. Acquisition of data: Harada G, Andrade MC, Feltrim MI. Analysis and interpretation of the data: Harada G, Andrade MC, Brito JN, Tavares CM, Feltrim MI. Statistical analysis: Brito JN, Tavares CM. Writing of the manuscript: Harada G, Brito JN, Tavares CM, Tarasoutchi F, Pomenrantzeff PM, Bortolotto L, Feltrim MI. Critical revision of the manuscript for intellectual content: Tarasoutchi F, Pomenrantzeff PM, Bortolotto L, Feltrim MI.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital das *Clínicas da Faculdade de Medicina da Universidade de São Paulo* under the protocol number 08882019.4.0000.0068. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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