Impact of gender and age on 6-Minute Walking Test performance of patients with coronary heart disease compared to healthy elders*

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Abstract— The performance of 6-minute walking test (6MWT) of patients with coronary heart disease (CHD) was significantly related to patients' cardiopulmonary functions. The 6MWT may provide prognostic information for patients. However, the impact of gender and age on the 6MWT performance and related cardiopulmonary parameters of patients with CHD compared to the healthy group has not be fully investigated and discussed. In this study, a total of 118 subjects, including 70 CHD patients and 48 healthy elders, were enrolled. The subjects performed the 6MWT while fourteen cardiopulmonary parameters were measured during the task and the walking distance was recorded at the end. Factors of gender, age, and disease on the 6MWT performance were analyzed using multivariate analysis of variance and the parameters between the patients and healthy people in age- and gender-specific subgroups were compared by Pearson's correlation coefficient. Results showed that age (60-65 and ≥65 years) and gender significantly influenced the 6MWT performance of subjects. Featured parameters were observed in older subgroups (≥65 years) between the patients and healthy people while patients aged 60-65 had similar 6MWT performance with the healthy control group. It would be potential to distinguish patients with CHD from healthy elders based on the 6MWT where factors of age and gender should be considered.

Keywords— 6-minute walking test; walking distance; coronary heart disease; cardiopulmonary function

I. INTRODUCTION

Coronary heart disease (CHD) is an inflammatory atherosclerotic disease[1], manifested as stable angina pectoris, unstable angina pectoris, myocardial infarction or sudden cardiac death[2]. As the cardiopulmonary function is affected, patients with CHD are usually unable to perform activities and exercise as healthy elders, which leads to a significant reduction in their locomotion capacity[3].

Studies have shown that there is a significant correlation between the performance of the 6-minute walking test (6MWT) and the cardiopulmonary parameters of patients. C. Zugck et al.[4] found that the walking performance during 6MWT was significantly related to the peak oxygen uptake in congestive heart failure patients with dilated cardiomyopathy, indicating that measurement from 6MWT may provide prognostic information. Both walking speed and 6MWT distance were independent predictors of all-cause mortality with no significant difference in prognostic capability[5].

Mathieu Gayda et al.[6] demonstrated that cardiopulmonary parameters measured during 6MWT for elderly patients with CHD have good repeatability and can be used to evaluate the effects of therapeutic interventions, such as cardiac rehabilitation. A study from [7] showed that patients with better exercise capacity (6MWT distance > 300 m) had a higher survival rate after coronary artery bypass graft surgery.

The 6MWT can not only provide prognostic information for patients with CHD, but also be widely used to assess the exercise function of patients[8] as an effective, safe and reliable test. Thatiana C.A. Peixoto et al.[13] evaluated the effect of early cardiac rehabilitation on health-related quality of life (HRQL) and functional ability in patients with acute myocardial infarction (AMI) in which 6MWT distance was used as an indicator of functional ability. B. Pavy et al. [14] utilized the 6MWT protocol to evaluate the functional capability of patients with CHD while comparing cardiac rehabilitation outcomes of patients with little or no exercise to those with exercise.

Researchers focus on not only the prognostics but also the diagnosis and early screening of patients with CHD. Salvioni E et al.[15] developed an age-adjusted model using gender-calculated ventilation. The model was proved to have good predictive power for 2-year survival in patients with heart failure and enable to identify heart failure patients at high risk. The significant difference in cardiopulmonary function between patients with CHD and healthy elders has been found in [16], which might be related to the decreased cardiac output and ejection fraction, the disharmony of myocardial contraction and diastole. Before the 6MWT, the factors, including sex, age, cigarette smoking, diabetes and systolic blood pressure, have been proved to be related to disease progression of patients with CHD[17]. However, the impact of gender and age on the 6MWT performance and related cardiopulmonary parameters of patients with CHD compared to healthy elders has not been investigated in current studies.

In this study, we collected cardiovascular parameters and walking distance for 70 patients with CHD and 48 healthy elders during the 6MWT experiment. Section II described details of the experiment protocol and statistical methods. The correlation between the cardiovascular parameters and walking performance were investigated while the impact of gender and age on 6MWT performance of patients with CHD compared to the healthy control group was analyzed and

discussed. The results were detailed in Section III and conclusion was given in Section IV.

II. METHODS

A. Participants

This study included 118 patients with CHD and healthy subjects. A total of 118 subjects were enrolled, including 70 patients with CHD (age: 67.89 ± 4.65 (SD) years) and 48 healthy subjects (age: 65.65 ± 3.80 (SD) years), who were admitted to Tianjin University Tianjin Chest Hospital between December 2019 and August 2020. Inclusion criteria for CHD patients included: (1) age above 60 years old; (2) suffer from CHD or have had operations related to CHD; (3) enable to walk independently without the aid of auxiliary tools; (4) have no neurological disorders or other serious comorbidities that may affect the patient's motor and cognitive functions. Healthy elders are required to be over 60 years of age and have none known diseases that may affect the heart, lung or motor functions. The experiment was approved by the institutional Ethics Committee of Tianjin University Tianjin Chest Hospital and all participants gave their written informed prior to their trials.

B. Data Collection

Patient's age, height, weight, medical history and other basic information is provided by patients. During the test, the participant was required to wear the PhysioFlow device (Manatec Biomedical, U.S.) during the 6MWT. The walking test consists of a 6-minute round trip along a 25-meter corridor. During this period, the researcher did not provide any external encouragement. After 6 minutes, the subjects were prompted to stop walking, and the total distance of 6-minute walking was recorded (6MWD). The distance is measured in meters. The researchers did not know the subjects' cardiopulmonary parameters or CHD conditions. The experiment would be stopped immediately if any signs and symptoms of significant distress (such as angina, severe dyspnea, skeletal muscle pain) occurred. All people had no obvious gait disorder, and only one participant was interrupted due to the lack of motor ability to complete the whole experiment. All other participants successfully completed 6MWT without any concurrent symptoms.

During the 6MWT, the device measured and recorded 14 cardiopulmonary parameters in real time, including: stroke volume (SV), stroke volume index (SVi), heart rate (HR), cardiac output (CO), cardiac index (CI), systolic arterial blood pressure (SABP), diastolic arterial blood pressure (DABP), mean arterial blood pressure (MABP), contractility index (CTI), ventricular ejection time (VET), early diastolic filling ratio (EDFR), left cardiac work index (LCWi), systemic vascular resistance index (SVRi) and systemic vascular resistance (SVR). The subject information, such as age, height, weight, medical history and etc., were also collected.

C. Statistical Analysis

The resting cardiopulmonary parameters were compared between patients and healthy control (HC) groups using the t-test. The maximum values of relative cardiopulmonary parameters during the 6MWT were calculated for assessing the cardiopulmonary function of subjects. The factor effects of age, gender, disease and BMI on the 6MWD and maximum relative cardiopulmonary parameters were analyzed by multivariate analysis of variance (MANOVA). The correlation between the cardiovascular cardiopulmonary parameters and 6MWD was investigated using Pearson's correlation coefficient (PCC) method while the values of maximum relative cardiopulmonary parameters and 6MWD between different subgroups were compared using the t-test.

All data analysis was completed with the use of IBM SPSS Statistics 22. A P value <0.05 was considered significant.

III. RESULTS

A. Patients' Baseline Characteristics

The baseline characteristics of 70 patients and 46 healthy elders prior to the 6MWT were shown in Table TABLE I. . All data were expressed as mean value$\pm$standard deviation (SD). The age of the patient group was 67.89 ± 4.65 years old and the HC group had an age of 65.65 ± 3.80 years old. There was no significant difference in gender ratio between the two groups (male:female, patients: 47:23, HC: 31:17, p=0.884). The BMI parameter in the patient group was slightly higher than that in the HC group, but there was no significant difference (p=0.432). Compared to the HC, the patient group had a significantly higher HR and lower VET. Moreover, the HC

TABLE I.   BASELINE CHARACTERISTICS OF ALL SUBJECTS

	Patients (n=70)	*Healthy Elderly (n=48)*	*p-value*
Age	**67.89$\pm$4.65**	**65.65$\pm$3.80**	**0.007**
Sex, %, Male/Female	67.14/32.86	64.58/35.42	0.844
BMI (m/kg^2)	26.20$\pm$4.05	25.67$\pm$2.71	0.432
SV (ml)	78.26$\pm$20.16	79.90$\pm$20.45	0.668
SVi (ml/m^2)	43.00$\pm$10.55	43.42$\pm$10.63	0.834
HR (bpm)	**85.46$\pm$13.76**	**80.02$\pm$13.96**	**0.038**
CO (l/min)	6.60$\pm$1.67	6.25$\pm$1.46	0.236
CI (l/min/m^2)	3.63$\pm$0.90	3.40$\pm$0.79	0.154
SABP (mmHg)	137.94$\pm$18.76	140.96$\pm$17.09	0.376
DABP (mmHg)	76.26$\pm$10.66	78.17$\pm$10.52	0.338
MABP (mmHg)	102.34$\pm$12.69	104.90$\pm$12.26	0.279
CTI (ms)	122.04$\pm$62.88	141.73$\pm$64.15	0.101
VET	**314.28$\pm$83.84**	**346.45$\pm$82.97**	**0.042**
EDFR (%)	72.08$\pm$22.53	69.42$\pm$25.06	0.548
LCWi (kg.m/m^2)	4.91$\pm$1.69	4.70$\pm$1.50	0.488
SVRi (dyn.s/cm5.m^2)	2245.39$\pm$562.59	2424.40$\pm$618.11	0.106
SVR (dyn.s/cm5)	1234.41$\pm$302.25	1315.73$\pm$307.12	0.156
6MWD (m)	**264.51$\pm$103.17**	**342.40$\pm$80.31**	**<0.001**

BMI: body mass index; SV: stroke volume; SVi: stroke volume index; HR: heart rate; CO: cardiac output; CI: cardiac index; SABP: systolic arterial blood pressure; DABP: diastolic arterial blood pressure; MABP: mean arterial blood pressure; CTI: contractility index; VET: ventricular ejection time; EDFR: early diastolic filling ratio; LCWi: left cardiac work index; SVRi: systemic vascular resistance index; SVR: systemic vascular resistance; 6MWD: 6-minute walking distance.

group performed significant better in the 6MWT (6MWD, patients: 264.51±103.17m, HC: 342.40±80.31m, p<0.001). The result in TABLE I. demonstrated that the healthy elders had better cardiopulmonary functions and exercise performance than patients with CHD.

B. Factor effects for 6-Minute Walking Test and Cardiopulmonary Parameters

As the existing study[9] has showed that the 65 years old is an important boundary for patients with CHD, we divided subjects into two age groups, respectively 60-65 and above 65 years old. The MANOVA was used to investigate factor effect of age, BMI, gender and group on the 6MWT performance where the Levene's test was utilized to assess the homogeneity of variance (p=0.117, α=0.05). As shown in TABLE II. , the BMI did not have a significant influence on the 6MWT performance (p=0.166) while on the other hand, the age, gender and group were all significant factors (age: p=0.005, gender: p=0.001, group: p=0.005).

TABLE II.   RESULTS OF MULTIVARIATE ANALYSIS OF VARIANCE BETWEEN AGE, BMI, GENDER, GROUP AND 6MWT PERFORMANCE

		6MWD (m)	p-value
Age	60-65	341.74±87.12	**0.005**
	≥65	277.76±101.84	
Gender	Male	315.01±100.61	**0.001**
	Female	259.50±94.65	
BMI	<18.5	130.00	0.166
	18.5-23.9	308.74±88.90	
	24-27.9	299.03±104.65	
	28-31.9	290.50±104.04	
	≥32	187.50±95.46	
Group	Patient	264.51±103.17	**0.005**
	HC	342.40±80.12	

BMI: body mass index; 6MWD: 6-minute walking distance.

Based on TABLE II. , we further divided the patient and HC groups into four subgroups respectively corresponding to their age and gender. The PCC analysis was used to analyze the differences in maximum relative cardiopulmonary parameters and 6MWD among the patients and healthy elders based on the age and gender specific subgroup. The results were shown in TABLE III. and TABLE IV. . There was no change in the value of MABP, so we excluded it in our correlation analysis. For male group aged 60-65 years, patients' DABP was significantly positively correlated with 6MWD while the CO was significantly positively correlated with 6MWD in healthy subjects. In the subgroup of males over 65 years, the HR, CI and LCWi was significantly positively correlated with the 6MWD in patients. In healthy individuals, the CI, CTI and LCWi was significantly positively correlated with the 6MWD while the CO was significantly negatively correlated with the 6MWD. The SABP and LCWI were significantly positively correlated with the 6MWD in female patients aged 60-65 years, but no significant correlation was observed in healthy females. In the group of female patients above 65, the SVi, CO and SVRi were significantly negatively correlated with the 6MWD, while the CTI had a significantly positively correlation with the 6MWD. For healthy females

over 65 years old, there were a significantly negative correlation between the SVi and 6MWD.

TABLE III.   RESULTS OF CORRELATION ANALYSIS BETWEEN CARDIOPULMONARY PARAMETERS AND 6MWD FOR MALE subgroups

R-value	60-65 male (n=22)		≥65 male (n=56)	
	Patients (n=10)	HC (n=12)	Patients (n=37)	HC (n=19)
SV	0.094	0.356	0.286	0.036
SVi	-0.167	0.187	-0.159	-0.392
HR	0.200	0.277	**0.388***	0.379
CO	0.151	**0.585***	0.006	**-0.526***
CI	0.167	0.316	**0.449****	**0.512***
SABP	0.310	-0.065	-0.061	0.262
DABP	**0.722***	-0.046	0.151	0.107
CTI	0.115	0.520	0.154	**0.512***
VET	0.044	-0.289	0.035	0.280
EDFR	-0.045	-0.247	0.048	0.383
LCWi	0.273	0.326	**0.431****	**0.513***
SVRi	-0.100	-0.028	0.095	0.045
SVR	-0.156	-0.034	0.054	0.051

**. The correlation was significant at a confidence level of 0.01 (two-tailed)

*. The correlation was significant at a confidence level of 0.05 (two-tailed)

HC: healthy control; SV: stroke volume; SVi: stroke volume index; HR: heart rate; CO: cardiac output; CI: cardiac index; SABP: systolic arterial blood pressure; DABP: diastolic arterial blood pressure; CTI: contractility index; VET: ventricular ejection time; EDFR: early diastolic filling ratio; LCWi: left cardiac work index; SVRi: systemic vascular resistance index; SVR: systemic vascular resistance.

TABLE IV.   RESULTS OF CORRELATION ANALYSIS BETWEEN CARDIOPULMONARY PARAMETERS AND 6MWD FOR FEMALE subgroups

R-value	60-65 female (n=12)		≥65 female (n=28)	
	Patients (n=6)	HC (n=6)	Patients (n=17)	HC (n=11)
SV	0.574	0.121	-0.080	0.042
SVi	0.501	0.391	**-0.633****	**-0.753****
HR	0.637	0.075	-0.049	0.468
CO	0.619	0.173	**-0.640****	-0.236
CI	0.785	0.034	0.083	0.376
SABP	**0.838***	-0.336	0.254	0.317
DABP	0.800	-0.324	0.294	-0.062
CTI	0.176	0.485	**0484***	0.364
VET	0.097	-0.679	0.213	-0.292
EDFR	0.194	-0.392	-0.431	0.569
LCWi	**0.826***	-0.017	0.138	0.303
SVRi	0.571	0.172	**-0.485***	-0.368
SVR	0.486	-0.001	-0.368	-0.350

**. The correlation was significant at a confidence level of 0.01 (two-tailed)

*. The correlation was significant at a confidence level of 0.05 (two)\]\-tailed)

HC: healthy control; SV: stroke volume; SVi: stroke volume index; HR: heart rate; CO: cardiac output; CI: cardiac index; SABP: systolic arterial blood pressure; DABP: diastolic arterial blood pressure; CTI: contractility index; VET: ventricular ejection time; EDFR: early diastolic filling ratio; LCWi: left cardiac work index; SVRi: systemic vascular resistance index; SVR: systemic vascular resistance.

Overall, various significant correlations between the cardiopulmonary parameters and 6MWD were observed in age- and gender-specific subgroups.

We further compared the maximum relative cardiopulmonary parameters and 6MWD between patients and healthy elders in 4 subgroups. According to the results of P-P diagram, the 6MWD and the logarithm of cardiopulmonary parameters conforms to normal distribution. As showed in TABLE V. , the SV, SVRi, SVR and 6MWD were significantly different between patients and healthy people for male groups over 65 years. In the subgroup of females aged 60-65 years old, only the HR had significant difference while the SV, CTI and 6MWD were significant different between groups of female subjects over 65 years. There were no significance for cardiopulmonary parameters as well as the 6MWD between the patient and HC groups of males aged 60-65 years.

TABLE V.   RESULTS OF T-TEST FOR COMPARING 6MWT PERFORMANCE BETWEEN PATIENTS AND HEALTHY ELDERS

p-value	60-65 male (n=22)	≥65 male (n=56)	60-65 female (n=12)	≥65 female (n=28)
log SV	0.196	**0.008**	0.340	**0.046**
log SVi	0.180	0.086	0.370	0.762
log HR	0.194	0.936	**0.006**	0.860
log CO	0.260	0.109	0.271	0.064
log CI	0.148	0.344	0.100	0.154
log SABP	0.796	0.682	0.645	0.072
log DABP	0.624	0.313	0.521	0.437
log CTI	0.409	0.042	0.194	**0.004**
log VET	0.722	0.120	0.833	0.709
log EDFR	0.670	0.148	0.992	0.858
log LCWi	0.147	0.221	0.241	0.129
log SVRi	0.081	**0.001**	0.552	0.355
log SVR	0.087	**0.002**	0.677	0.204
6MWD	0.638	**0.017**	0.055	**0.001**

SV: stroke volume; SVi: stroke volume index; HR: heart rate; CO: cardiac output; CI: cardiac index; SABP: systolic arterial blood pressure; DABP: diastolic arterial blood pressure; CTI: contractility index; VET: ventricular ejection time; EDFR: early diastolic filling ratio; LCWi: left cardiac work index; SVRi: systemic vascular resistance index; SVR: systemic vascular resistance.

IV. CONCLUSIONS

In this study, we investigated the impact of gender and age on the 6MWT performance and related cardiopulmonary parameters of patients with CHD compared to healthy elders. The results demonstrated that the age (60-65 and ≥65 years) and gender significantly influenced the 6MWT performance (6MWD) of subjects. For patients in age- and gender-subgroups, different maximum relative cardiopulmonary parameters were found significantly correlated with the 6MWD. The patients aged 60-65 years had a similar cardiopulmonary and 6MWT performance compared to that of HC group, despite of the HR in female subgroups (60-65 years). More featured parameters were observed in elder subgroups (≥65 years, male and female), such as the SV,6MWD, etc. Therefore, it would be potential to distinguish patients with CHD from healthy elders based on the 6MWT protocol where factors of age and gender should be considered.

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