Prevalence and modifiable risk factors of degenerative valvular heart disease among elderly population in southern China

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ABSTRACT

Objective   To investigate the prevalence and modifiable risk factors of degenerative valvular heart disease (DVHD) among elderly population in southern China.

Methods   A stratified multistage sampling method was used to recruit subjects. The contents of the survey included the questionnaire, laboratory examination, echocardiography, and other auxiliary examinations. The possible risk factors of DVHD were analyzed by logistic regression analysis.

Results   A total of 3 538 subjects ≥ 65 years of age were enrolled. One thousand three hundred and seven subjects (36.9%) were diagnosed with DVHD. Degenerative was the most common etiology of VHD. Prevalence of DVHD increased with advancing age. The prevalence of DVHD differed by living region (χ^2 = 45.594, P < 0.001), educational level (χ^2 = 50.557, P < 0.001), and occupation (χ^2 = 36.961, P < 0.001). Risk factors associated with DVHD included age (two-fold increased risk for each 10-year increase in age), elevated level C-reactive protein (OR = 1.346, 95% CI: 1.100–1.646), elevated level low density lipoprotein (OR = 1.243, 95% CI: 1.064–1.451), coronary artery disease (OR = 1.651, 95% CI: 1.085–2.513), smoking (OR = 1.341, 95% CI: 1.132–1.589), and hypertension (OR = 1.414, 95% CI: 1.221–1.638). Other significant risk factors included reduced or elevated level red blood cell (OR = 1.347, 95% CI: 1.031–1.761; OR = 1.599, 95% CI: 1.097–2.331; respectively), elevated level platelets (OR = 1.891, 95% CI: 1.118–3.198), elevated level uric acid (OR = 1.282, 95% CI: 1.112–1.479), and stroke (OR: 1.738, 95% CI = 1.085–2.513).

Conclusions   The survey characterized the baseline conditions of DVHD cohort of elderly population in Guangzhou city. The established and emerging risk factors for DVHD may represent challenges and opportunities for therapy.

Valvular heart disease (VHD) is a common condition that is strongly associated with heart dysfunction in elderly population.[1] In developed countries, the etiology of VHD has changed in parallel with socio-economic development and an increasing aging population. In the Euro Heart Survey, etiology of VHD was mostly degenerative, which is present in approximately 63% of patients.[2] In developing countries, rheumatic heart disease remains the primary cause of VHD.[3] A retrospective hospital-based survey in China suggested that rheumatic fever and degenerative valvular changes remained predominant etiologies in patients < 65 and ≥ 65 years of age, respectively.[4]

Guangzhou city, a modern city of China, includes 11 administrative regions, which can be roughly divided into urban region and rural region according to the level of economic development. At present in China, there is a lack of large-scale epidemiological survey. With socio-economic development and an increasing aging population, the etiology of VHD in Chinese population may have changed. Therefore, the study was conducted to collect epidemiological data and risk factors of DVHD in elderly population in Guangzhou city.

METHODS

Study Population

We conducted a community-based survey of elderly population with DVHD in southern China (The Guangzhou Valvular Heart Disease Study) from

July 2015 to August 2017. A 5-stage, stratified multistage random sampling method was used to recruit subjects. Initially, all the 11 districts (Yuexiu, Haizhu, Liwan, Tianhe, Huangpu, Baiyun, Panyu, Nansha, Huadu, Conghua, and Zengchen districts) in Guangzhou city were divided into urban group and rural group, from which one urban and one rural district were selected by simple random sampling method. This stage leaded to the selection of Yuexiu district (urban region) and Panyu district (rural region). Later, the second stage of sample selection consisted of streets or townships. This stage leaded to the selection of Xinzao town, Nancun town and Xiaoguwei street to conduct the survey in Panyu district while Dadong street and Baiyun street were chosen in Yuexiu district. The third stage of sample selection consisted of residential committees or village committees. This stage leaded to the selection of 7 residential committees in Dadong street and Baiyun street while 17 village committees in Xinzao town, Nancun town and Xiaoguwei street were chosen to conduct the survey. The fourth stage of sample selection consisted of households. This stage leaded to the selection of households from a listing of all households in a selected community. Finally, the fifth stage leaded to the selection of people within the selected households. Every subject who was eligible to fit the inclusive criteria in a household was all included for the study.

Subjects were enrolled if they met all of the following inclusion criteria: (1) residents who had Guangzhou household register and had lived in selected communities for at least 6 months by the day they participated in the survey; (2) ≥ 65 years of age. Subjects were excluded if they had any of the following exclusion criteria: (1) residents who had mental or cognitive disorders, disturbance of understanding, deaf-mutters, mobility difficulties; (2) residents with malignant tumors who need to be treated; and (3) temporary residents who lived in Guangzhou for less than 6 months.

Transthoracic Echocardiography Protocol

All subjects underwent echocardiography, which was performed using a Vivid-i-Cardiovascular-Ultrasound-System (GE Healthcare, Horten, Norway). Cardiac structure and function were visualized along the standard parasternal long-axis, short-axis, suprasternal, subcostal, and apical four-chamber views.[5] Cardiac dimensions were measured by according to the recommendations of the American Society of Echocardiography.[6] The position and number of valvular leaflet, valvular thickness, echo, calcification and blood flow of each valve orifice were detailed recorded. All echocardiograms were judged and confirmed by two ultrasound specialists with > 10 years of experience to ensure quality. Poor echocardiograms were excluded.

Degeneration is characterized by increased echogenicity, thickness, and stiffness of the valvular leaflet, with no commissural fusion.[5] Degenerative mitral valve calcification is defined as increased valvular thickness, stiffness, and echogenicity on the fibrous base of the mitral valve. Degenerative aortic valve sclerosis is defined as increased valvular thickness, stiffness, and echogenicity without restriction of leaflet motion. Degenerative aortic valve stenosis was defined as thickened leaflets with increased anterograde jet velocity of aortic valve orifice.[7] Severe valvular heart disease was defined as follows:[8,9] (1) severe aortic valve stenosis with anterograde transvalvular blood flow velocity ≥ 4 m/s or mean; (2) tansvalvular pressure gradient ≥ 40 mmHg; (3) Severe mitral stenosis with a valve orifice area ≤ 1.5 cm^2; (4) severe mitral regurgitation with a grade ≥ 3/4; and (5) severe aortic regurgitation with a grade ≥ 3/4.

Questionnaire, Physical, Laboratory and Other Auxiliary Examinations

A structured and interviewer-administered questionnaire was used to survey each participant, including personal information (name, gender, date of birth, residential address, educational level, and occupation [classification intensity of physical work is classified on the basis of the National standard of the people's Republic of China [GB3869-83], and the Clinical Modification code [GB3869-1997]), living and eating habits (cigarette smoking, alcohol consumption, dietary preferences, sleep habits, and physical exercise), medical history (hypertension, diabetes, dyslipidemia, hyperuricaemia [HUA], chronic kidney disease [CKD], coronary artery disease [CAD], congestive heart failure, and cerebrovascular disease), and physical examination (body mass index [BMI], average systolic and diastolic blood pressure, waist and hip circumference, height, and weight).

Laboratory examination included serum biochemistry determinations and assessment of levels of fasting plasma lipids. Other auxiliary examinations included standard 12-lead electrocardiogram and single lead 24 h-holter electrocardiogram. Definition of suspicious risk factors as follow:[10] hypertension was defined as a blood pressure > 140/90 mmHg or a history of hypertension and the use of antihypertensive medications. Diabetes was defined as a level of fasting blood glucose ≥ 7.0 mmol/L or taking antidiabetic medications. Dyslipidemia was defined as presence of TC level ≥ 6.22 mmol/L (240 mg/dL), TG ≥ 1.70 mmol/L (150 mg/dL), LDL-C ≥ 4.14 mmol/L (160 mg/dL), HDL-C < 1.04 mmol/L (40 mg/dL), or taking medications to treat dyslipedemia. HUA was defined as serum uric acid level > 420 μmol/L in male gender and > 360 μmol/L in female gender. CKD was defined as serum creatinine level ≥ 2 mg/dL. BMI was defined as weight divided by height squared (kg/m^2). CAD was deemed to be present based on the following: a history of angina pectoris or; myocardial infarction; positive stress test results; angiographic evidence of CAD; coronary intervention; coronary artery bypass surgery; or the presence of significant Q waves on a surface electrocardiogram. Abdominal obesity was defined as waist circumference > 88 cm for female and 102 cm for male. Overall obesity was defined as BMI ≥ 30 kg/m^2.

Written Informed Consent and Ethics Approval

The written informed consent was obtained from all participants. This study was approved by the Guangzhou Medical Ethics Committee of the Chinese Medical Association (No. GDREC2015306H) and was conducted in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical Methods

Statistical analysis of all collected data was performed using SPSS (version 20.0; SPSS, Inc., Chicago, IL, USA). First of all, the research variables were described and characterized to exhibit the general profile of the sample. Then the results were analyzed by descriptive and related-statistics analysis. Categorical data were presented as number (percentage). Continuous data were presented as mean ± SD. Statistical tests were Pearson's Chi-square test and Fisher's exact test were used to compare categorical variables. Trends across uric acid level, red blood cell (RBC) count, hemoglobin (Hb) count, and platelet (PLT) count were assessed by the Mann-Whitney U test. Initially, univariable logistic regression analysis was used to assess DVHD-associated risk factors. Later, a P value ≤ 0.1 was used for entry into the multivariable logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to assess the associations. A two-sided $P < 0.05$ was considered to be statistically significant.

RESULTS

Baseline Characteristics

As shown in Table 1, of the 3 538 subjects aged 72 ± 5.8 years, 61.9% were female gender, and 48.2% were from urban region. Of these, 36.9% subjects were diagnosed with DVHD by echocardiography; in addition, 3.3% subjects had AF, 50.5% had hypertension, 7.7% had CAD, and 15.1% had diabetes mellitus. Moderate or severe aortic regurgitation was the most frequent (n = 528, 14.9%) followed by moderate or severe tricuspid regurgitation (n = 464, 13.1%), moderate or severe mitral regurgitation (n = 275, 7.8%), and aortic stenosis (n = 31, 0.9%). As shown in Table 2, excluding rheumatic and other causes of valvular disease, further comparison of valvular abnormalities between DVHD and non-DVHD, DVHD had significantly greater prevalence of moderate-severe aortic regurgitation, moderate- severe mitral regurgitation, and aortic stenosis ($P < 0.001$).

DVHD Prevalence Differed by Demography, Serum Biochemistry, and Medical History

As shown in Table 3, prevalence of DVHD increased with advancing age ($P < 0.001$), and up to 53.0% among those ≥ 75 years of age. DVHD prevalence were shown to be higher in rural region than urban region ($P < 0.001$). Compared to low educational level, subjects with higher educational level had higher DVHD prevalence ($P < 0.001$). Additionally, subjects served as heavy manual laborer had the highest DVHD prevalence ($P < 0.001$). Relative to never smoking, present smoking was associated with higher prevalence of DVHD ($P < 0.01$).

Among the routine serum biochemical variables we examined, subjects with elevated levels of CRP

and uric acid tend to have higher prevalence ($P < 0.01$). For medical history, there are significant differences for subjects whether have history of hypertension, CAD, stroke, heart failure, and AF ($P < 0.05$).

Table 1   Baseline characteristics.

Variables	Value
Age, yrs	72 ± 5.8
Female gender	2190 (61.9%)
Urban region	1705(48.2%)
Marital status	
Married	2564 (72.5%)
Divorced	22 (0.6%)
Separated	11 (0.3%)
Widowed	890 (25.2%)
Single	51 (1.4%)
Education	
Primary school or less	2113 (59.7%)
Middle school	1062 (30.0%)
College or more	363 (10.3%)
Occupation	
Light manual laborer	1064 (30.0%)
Medium manual laborer	1265 (35.8%)
Heavy manual laborer	1209 (34.2%)
Smoking	822 (23.2%)
Drinking	592 (16.7%)
Measures of adiposity	
Height, cm	156.3 ± 8.5
Weight, kg	58.6 ± 10.5
Body mass index, kg/m^2	24.0 ± 3.7
Obesity	188 (5.3%)
Waist, cm	86.7 ± 9.9
Abdominal obesity	1799 (50.8%)
Glucose metabolism	
Fasting blood glucose, mmol/L	5.8 ± 1.6
Diabetes mellitus	534 (15.1%)
Blood pressure	
Systolic blood pressure, mmHg	139.7 ± 20.4
Diastolic blood pressure, mmHg	80.5 ± 11.4
Hypertension	1788 (50.5%)
Lipids	
Triglyceride, mmol/L	1.7 ± 1.2
Triglyceride ≥1.70 mmol/L	1193 (33.7%)
Total cholesterol, mmol/L	5.5 ± 1.1
Total cholesterol ≥ 6.22 mmol/L	852 (24.1%)

Variables	Continued Value
LDL-C, mmol/L	3.7 ± 1.0
LDL-C ≥ 4.14 mmol/L	1047 (29.6%)
HDL-C, mmol/L	1.5 ± 0.4
HDL-C < 1.04 mmol/L	371 (10.5%)
Dyslipidemia	917 (25.9%)
Inflammation	
hs-CRP, mg/L	1.6 (0.6−3.5%)
hs-CRP > 3 mg/L	920 (26.0%)
Uric acid	
Uric acid, mmol/L	0.4 ± 0.1
Hyperuricemia	1635 (46.2%)
Renal insufficiency	
Creatinine, μmol/L	83.9 ± 29.1
Estimated glomerular filtration rate, mL/min per 1.73 m^2	70.4 ± 16.9
Chronic kidney disease	49 (1.4%)
Valvular heart disease	
Non-valvular heart disease	2151 (60.8%)
Degenerative valvular heart disease	1307 (36.9%)
Rheumatic valvular heart disease	11 (0.3%)
Others	69 (2.0%)
Atrial fibrillation	115 (3.3%)
Coronary artery disease	201 (5.7%)
Stroke	138 (3.9%)
TIA	113 (3.2%)
Heart failure	280 (7.9%)
Echocardiographic variables	
Left ventricular ejection fraction	69.2 (5.2%)
Left ventricular end-diastolic dimension, mm	45.7 ± 4.6
Left ventricular end-systolic dimension, mm	27.5 ± 3.8
Left ventricular posterior wall thickness, mm	9.4 ± 1.1
Ventricular septal thickness, mm	10.1 ± 1.2
Left atrial dimension, mm	33.9 ± 4.9
Moderate or severe mitral regurgitation	275 (7.8%)
Moderate or severe tricuspid regurgitation	464 (13.1%)
Moderate or severe aortic regurgitation	528 (14.9%)
Aortic stenosis	31 (0.9%)

Data are expressed as mean ± SD, *n* (%) or median (IQR). CRP: C-reactive protein; HDL-C: high-density lipoprotein cholesterol; IQR: interquartile range; LDL-C: low-density lipoprotein cholesterol; TIA: transient ischemic attacks.

Table 2　Comparison of valvular abnormalities between DVHD and non-DVHD.

Characteristic	Overall	Non-DVHD	DVHD	P-value
Moderate-severe aortic regurgitation	528	214 (9.9%)	297 (22.7%)	< 0.001
Moderate-severe mitral regurgitation	275	132 (6.1%)	131 (10.0%)	< 0.001
Aortic stenosis	31	0	31 (2.4%)	< 0.001

Data are presented as n or n (%). DVHD: degenerative valvular heart disease.

Table 3　Prevalence of DVHD based on the selected variables.

Variables	Groups	Frequency	Prevalence (%)	P
Demographic				
Age, yrs				< 0.001
	65–74	748	30.1	
	75–84	480	51.6	
	≥ 85	79	64.2	
Gender				> 0.05
	Male	524	39.1	
	Female	783	36.6	
Region				< 0.001
	Rural	769	42.0	
	Urban	538	31.6	
Educational level				< 0.001
	Primary school or less	877	41.5	
	Middle school	319	30.0	
	College or more	111	30.6	
Occupation				< 0.001
	Light manual laborer	288	32.6	
	Medium manual laborer	365	33.7	
	Heavy manual laborer	451	43.9	
Cigarette smoking				< 0.01
	No	963	35.5	
	Yes	344	41.8	
Alcohol consumption				> 0.05
	No	1103	37.4	
	Yes	204	34.5	
Body mass index, kg/m^2				> 0.05
	< 18.5	68	36.0	
	18.5–25	727	36.5	
	25–30	428	39.3	
	≥ 30	84	44.7	
Serum biochemical				
Red blood cell				> 0.05
	Normal	1094	37.6	
	Reduced	121	47.3	
	Elevated	90	30.9	
Hemoglobin				> 0.05
	Normal	1239	37.8	
	Reduced	23	33.8	
	Elevated	42	39.3	

Continued

Variables	Groups	Frequency	Prevalence (%)	P
Platelet				> 0.05
	Normal	1 145	37.2	
	Reduced	29	29.3	
	Elevated	131	47.5	
CRP, mg/L				< 0.001
	Elevated	216	46.0	
	Not-elevated	1 091	36.5	
Total cholesterol, mmol/L				> 0.05
	Elevated	764	37.9	
	Not-elevated	543	37.7	
HDL-C, mmol/L				> 0.05
	Reduced	168	40.5	
	Not-reduced	1 139	37.4	
LDL-C, mmol/L				> 0.05
	Elevated	409	40.1	
	Not-elevated	898	36.8	
Triglyceride, mmol/L				> 0.05
	Elevated	219	37.7	
	Not-elevated	1 088	37.8	
Uric acid, mmol/L				< 0.01
	Normal	580	34.9	
	Reduced	5	50.0	
	Elevated	722	40.4	
Blood glucose, mmol/L				> 0.05
	Elevated	317	39.4	
	Not-elevated	990	37.3	
Medical history				
Atrial fibrillation				< 0.01
	No	1 247	47.8	
	Yes	60	52.2	
Hypertension				< 0.001
	No	519	32.4	
	Yes	788	42.4	
Diabetes				> 0.05
	No	1 092	37.3	
	Yes	215	40.7	
Dyslipidemia				> 0.05
	No	987	38.6	
	Yes	320	35.6	
Chronic kidney disease				> 0.05
	No	1 288	37.8	
	Yes	19	38.8	
Stroke				< 0.001
	No	1 235	37.2	
	Yes	72	53.7	

Continued

Variables	Groups	Frequency	Prevalence (%)	P
TIA				> 0.05
	No	1256	37.5	
	Yes	51	46.4	
Coronary artery disease				< 0.05
	No	1213	37.2	
	Yes	94	47.2	
Heart failure				< 0.05
	No	1186	37.3	
	Yes	121	43.5	

CRP: C-reactive protein; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TIA: transient ischemic attacks.

Analysis of DVHD Risk and Prevalence

As shown in Table 4, multivariate logistic regression analyses were used to evaluated the risk factors for DVHD. Based on multivariate logistic regression analysis, age (two-fold increased risk for each 10-year increase in age), living region (OR = 1.801; 95% CI: 1.557−2.082), intensity of physical work (OR = 1.672; 95% CI: 1.385−2.018 and OR = 1.718; 95% CI: 1.414−2.087, respectively), cigarette smoking (OR = 1.341; 95% CI: 1.132−1.589), hypertension (OR = 1.414; 95% CI: 1.221−1.638), stroke (OR = 1.738; 95% CI: 1.085−2.513), CAD (OR = 1.651; 95% CI: 1.085−2.513), reduced or elevated level RBC (OR = 1.347; 95% CI: 1.031−1.761 and OR = 1.599; 95% CI: 1.097−2.331, respectively), elevated level platelets (OR = 1.891; 95% CI: 1.118−3.198), elevated level CRP (OR = 1.346; 95% CI: 1.100−1.646), elevated level LDL-C (OR = 1.243; 95% CI: 1.064−1.451), and elevated level uric acid (OR = 1.282; 95% CI: 1.112−1.479), while the risk of subjects with higher educational level significantly reduce (OR = 0.792; 95% CI: 0.644−0.975 and OR = 0.772; 95% CI: 0.563−0.876, respectively).

DISCUSSION

There were three main findings from the present survey. First, the prevalence of DVHD in the elderly population in Guangzhou was 36.9%. Second, the prevalence of DVHD increased with advancing age, especially when the age was ≥ 75 years of age. Third, the prevalence of DVHD differed based on demography, serum biochemistry, and medical history, which were also shown to be independent risk factors for DVHD.

DVHD Prevalence

In developing countries, etiology of VHD was mostly rheumatic. The prevalence of rheumatic VHD ranged from 46%−72% according to previous reports depending on the enrolled cohorts, or survey method. A survey of South African center, the prevalence of rheumatic VHD was reported at 72% of subjects.[11] In another survey in Turkey that included 1300 patients hospitalized in 42 centers in 2009, rheumatic VHD accounted for 46% of subjects.[12] In developed countries, since the 1950s, the predominance of VHD has a significant shifted from a rheumatic towards a degenerative etiology. Due to the superior social and economic status and favorable living environment found in Guangzhou compared to the rest of China, our survey was conducted to collect epidemiological data in Guangzhou. In the present study, we conducted Guangzhou City in which urban region and rural region were involved. All subjects underwent echocardiography for VHD screening. Degenerative was the most common etiology of VHD. Prevalence of DVHD increased with advancing age. Compared to 65−74 years of age, the prevalence of DVHD in age of 75−84 and ≥ 85 increased 2- and 3-fold, respectively. Because a stratified multistage sampling method was used to recruit subjects. DVHD prevalence and characteristic should be considered representative. In subjects ≥ 75 years of age, DVHD was present in 53.0% in our survey, which was slightly lower than the global average,[13] and slightly lower than the previous study in hospital in southern China, as reported by

Table 4 Analysis of risk factors of DVHD in multivariate logistic regression model.

Variables	Group	Multivariate logistic regression	
		OR (95% CI)	*P*-value
Age, yrs	65–74	Reference	
	75–84	2.393 (2.035–2.814)	0.000
	≥ 85	4.018 (2.713–5.951)	0.000
Residential region	Urban	Reference	
	Rural	1.801 (1.557–2.082)	0.000
Educational level	Primary school or less	Reference	
	Middle school	0.792 (0.644-0.975)	0.028
	College or more	0.772 (0.563-0.876)	0.000
Occupation	Light manual laborer	Reference	
	Medium manual laborer	1.672 (1.385–2.018)	0.000
	Heavy manual laborer	1.718 (1.414–2.087)	0.000
Cigarette smoking	No	Reference	
	Yes	1.341 (1.132–1.589)	0.001
Red blood cell	Normal	Reference	
	Reduced	1.347 (1.031–1.761)	0.029
	Elevated	1.599 (1.097–2.331)	0.015
Platelet	Normal	Reference	
	Reduced	1.397 (0.890-2.191)	0.146
	Elevated	1.891 (1.118–3.198)	0.018
CRP, mg/L	Not-elevated	Reference	
	Elevated	1.346 (1.100-1.646)	0.004
LDL-C, mmol/L	Not-elevated	Reference	
	Elevated	1.243 (1.064–1.451)	0.006
Uric acid, mmol/L	Normal	Reference	
	Reduced	1.807 (0.516–6.323)	0.355
	Elevated	1.282 (1.112–1.479)	0.001
Hypertension	No	Reference	
	Yes	1.414 (1.221–1.638)	0.000
Stroke	No	Reference	
	Yes	1.738 (1.085–2.513)	0.016
Coronary artery disease	No	Reference	
	Yes	1.651 (1.085–2.513)	0.008

CRP: C-reactive protein; DVHD: degenerative valvular heart disease; LDL-C: Low-density lipoprotein cholesterol.

Liu, *et al*.[1] In agreement with previous reports, DVHD was the most common VHD. Nevertheless, the DVHD prevalence in present study was neither extremely low nor high, which differed from previous findings. Because the cohorts in our study were from community; additionally, we only chosed those subjects ≥ 65 years of age. DVHD causes stenosis or insufficiency of single or multiple heart valves, resulting in limited blood flow or regurgitation.[4] In present study, DVHD had significantly greater prevalence of moderate-severe aortic regurgitation, moderate-severe mitral regurgitation, and aortic stenosis, which was consistent with the results of the Pasca study.[14]

DVHD Prevalence and Relative Risk Factors

Age, smoking, and hypertension were not unexpected predictors, having been noted in previous studies. Chen, *et al*.[15] described hypertension, age, smoking, and gender were independent predictors

of valvular calcification. Opposing results reported by the Helsinki Aging Study[16] showed that smoking was not a risk factor respect to the prevalence of DVHD. In our present study, 1 307 subjects were diagnosed with DVHD. Of these, 41.8% subjects had smoking, which was much higher when compared with the prevalence of approximately 30% found in the study by the Helsinki Aging Study.[16]

Aronow, et al.[17] described an association between hypercholesterolemia and aortic valve calcification. Opposing results reported by Hsu, et al.[18] showed that there was no association between hypercholesterolemia and aortic valve calcification. In our present study, the prevalence of hypercholesterolemia registered in current study was 37.9%, which was similar to the results found in the study by Aronow and colleagues,[17] but much lower when compared with the prevalence of 65% found in the study by Hsu and colleagues.[18] This variable did not present statistical significance. The absence of significance in hypercholesterolemia was a surprise, since the presence of cholesterol is an important factor in the process of valvular degeneration. We speculate that the difference can be attributed to the low number of diagnoses established in the cohort.

Studies have shown that platelets are activated in calcific aortic valve stenosis (CAVS) and promote the progression of the disease. The process relies on the activation of P2RY1-GPIIb/IIIa-LysoPA pathway, which drives an osteogenic program in valvular interstitial cells (VICs),[19] which explains an association between platelets and higher prevalence of DVHD in our study. Interestingly, our study also showed an association between red blood cell and higher prevalence of DVHD. This is the first report of a significant increase in the DVHD prevalence among the elderly residing in Guangzhou City. Although the proportion of red blood cell was small (approximately 30%) in the present study, the difference was statistically significant. How red blood cell affected the prevalence of DVHD has not been established.

Uric acid (UA) is the end product of purine metabolism in humans. Although the causal relationship between uric acid and DVHD remains unclear, many epidemiological studies suggest the existence of a significant association between high uric acid levels and increased risk of cardiovascular diseases as well as CKD.[20] In the Framingham Heart Study,[21] 284 subjects (9.3%) were diagnosed with valve/annular calcification; of these, 20% subjects had CKD, which had a 60% increased odds of mitral annular calcification (OR = 1.6; 95% CI: 1.03−2.5). Mehta and colleagues demonstrated that serum uric acid was independently associated with carotid-femoral pulse wave velocity (CF PWV) and carotid-radial pulse wave velocity (CR PWV) in a Framingham Heart Study.[22] This positive correlation between uric acid and CF PWV and CR PWV suggests that uric acid may play a role in increasing arterial stiffness. In our study, hyperuricemia was defined according to the criteria adopted by the National Health and Nutrition Examination Survey. Our data indicated that 40.4% of elderly are hyperuricemia in Guangzhou residents. Logistic regression was used to examine the odds of valvular calcification among subjects with hyperuricemia. After adjustment for age, participants with hyperuricemia had a approximately 30% increased odds of DVHD (OR = 1.282; 95% CI: 1.112−1.479). Further studies are needed to evaluate whether serum uric acid is an independent predictor of increased vascular stiffness in prospective analysis and to define populations in which lowering serum uric acid levels may reduce the cardiovascular burden.

DVHD was prevalent among the elderly. As we known, DVHD might be mainly relevant considering the socioeconomic development and improvements in quality of life, as well as an increasing aging population. Interestingly, we found a two-fold increased prevalence of DVHD in elderly who lived at rural region compared to elderly who lived at urban region. This finding could be due to the following reasons: (1) the gap between urban and rural region in Southern China has gradually narrowed; and the prevalence of DVHD is increasing progressively. (2) Echocardiography is one of the most effective methods for assessment of valvular structure and function. In the past, compared with urban areas, residents in rural areas were not screened; in present study, echocardiography screening was routinely performed, so more and more valvular diseases were detected, especially in rural areas. (3) The subjects who lived in rural region often with more risk factors, such as obesity, hypertension, and diabetes mellitus.

In addition, stroke appears to be a most common risk factor of DVHD in Guangzhou elderly. The prevalence of stroke with DVHD in our study was 53.7%, which is much higher than the rate found by Marmelo, *et al*.[10] in which the prevalence of stroke in individuals with aortic valve sclerosis was 8%. Although the difference in rate of stroke from both studies, stroke appears to be a common risk factor of degenerative VHD in both studies. We speculate that the influence of stroke in the development of DVHD may be explained by the fact that some same risk factors exist both in DVHD and stroke. However, further investigations are needed to clarify the relationship between stroke and DVHD development.

Study Limitations

The study had some limitations. First, this study are that it is a cross-sectional analysis and includes only subjects ≥ 65 years of age, which may bias the results against an even stronger relation between these risk factors and DVHD. Second, the number of cases of some risk factors for DVHD in present study is too small, resulting in weakening the effectiveness of logistic regression analysis prediction; therefore, long-term follow-up is necessary to determine the risk factors regarding the prevalence of DVHD.

Conclusion

Degenerative is the most common etiology of VHD in elderly population in southern China. The prevalence of DVHD differed by living region, educational level, and occupation. Emerging evidence indicates RBC, PLT, uric acid and stroke are likely contributors. More attention should be paid to DVHD in order to detect the disease earlier and improve the quality life of patients.

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CONFLICTS OF INTERESTS

None

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