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

Shang-Fei HE¹,², Jun-Rong JIANG¹,², Fang-Zhou LIU², Hong-Tao LIAO², Yu-Mei XUE², Mu-Rui ZHENG³, Huo-Xing LI², Hai DENG²,⁴✉, Shu-Lin WU²,⁴✉

1. South China University of Technology School of Medicine, Guangzhou, China; 2. Department of Cardiology, Guangdong Provincial People’s Hospital, Guangzhou, China; 3. Guangzhou Center for Disease Control and Prevention, Guangzhou, China; 4. Qinghai Province Cardio Cerebrovascular Disease Specialist Hospital, Xining, China

✉ Correspondence to: doctordh2020@163.com; wushulincn@126.com

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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 ($\chi^2 = 45.594$, $P < 0.001$), educational level ($\chi^2 = 50.557$, $P < 0.001$), and occupation ($\chi^2 = 36.961$, $P < 0.001$). 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 led 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 led 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 led 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. Cardiac dimensions were measured by according to the recommendations of the American Society of Echocardiography. 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. 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. Severe valvular heart disease was defined as follows: (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 cm²; (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:

- **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 dyslipidemia.
- **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/m²).
- **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/m².

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 3538 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/m²     | 24.0 ± 3.7             |
| Obesity                    | 188 (5.3%)             |
| Waist, cm                  | 86.7 ± 9.9             |
| Abdominal obesity          | 1795 (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                  | 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 m² | 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/m²     |                             |           |                | > 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           |         |
| Variables       | Groups     | Frequency | Prevalence (%) | \( P \) |
|-----------------|------------|-----------|----------------|--------|
| **Platelet**    | Normal     | 1145      | 37.2           | > 0.05 |
|                 | Reduced    | 29        | 29.3           |        |
|                 | Elevated   | 131       | 47.5           |        |
| **CRP, mg/L**   | Elevated   | 216       | 46.0           | < 0.001|
|                 | Not-elevated | 1091     | 36.5           |        |
| **Total cholesterol, mmol/L** | Elevated | 764 | 37.9 | > 0.05 |
|                 | Not-elevated | 543 | 37.7 |        |
| **HDL-C, mmol/L** | Reduced | 168 | 40.5 | > 0.05 |
|                 | Not-reduced | 1139 | 37.4 |        |
| **LDL-C, mmol/L** | Elevated | 409 | 40.1 | > 0.05 |
|                 | Not-elevated | 898 | 36.8 |        |
| **Triglyceride, mmol/L** | Elevated | 219 | 37.7 | > 0.05 |
|                 | Not-elevated | 1088 | 37.8 |        |
| **Uric acid, mmol/L** | Normal | 580 | 34.9 | < 0.01 |
|                 | Reduced    | 5         | 50.0           |        |
|                 | Elevated   | 722       | 40.4           |        |
| **Blood glucose, mmol/L** | Elevated | 317 | 39.4 | > 0.05 |
|                 | Not-elevated | 990 | 37.3 |        |
| **Medical history** | Atrial fibrillation | No | 1247 | 47.8 | < 0.01 |
|                 | No         | 1247      | 47.8           |        |
|                 | Yes        | 60        | 52.2           |        |
| **Hypertension** | No         | 519       | 32.4           | < 0.001|
|                 | Yes        | 788       | 42.4           |        |
| **Diabetes**    | No         | 1092      | 37.3           | > 0.05 |
|                 | Yes        | 215       | 40.7           |        |
| **Dyslipidemia** | No         | 987       | 38.6           | > 0.05 |
|                 | Yes        | 320       | 35.6           |        |
| **Chronic kidney disease** | No | 1288 | 37.8 | > 0.05 |
|                 | Yes        | 19        | 38.8           |        |
| **Stroke**      | No         | 1235      | 37.2           | < 0.001|
|                 | Yes        | 72        | 53.7           |        |
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 = 1.97; 95% CI: 1.18–3.198), 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. In another survey in Turkey that included 1300 patients hospitalized in 42 centers in 2009, rheumatic VHD accounted for 46% of subjects. 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, and slightly lower than the previous study in hospital in southern China, as reported by
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 chose those subjects ≥ 65 years of age. DVHD causes stenosis or insufficiency of single or multiple heart valves, resulting in limited blood flow or regurgitation. 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

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.11 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 chose 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, 1307 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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Hai Deng and Shulin Wu conceived the study. Shangfei He and Junrong Jiang collected data, drafted the manuscript, and completed the survey. Fangzhou Liu, Yumei Xue, and Hongtao Liao analysed data and interpreted results. Murui Zheng and Huoxing Li collected data and completed the survey.

**CONFLICTS OF INTERESTS**

None

**REFERENCES**

[1] Liu F, Xue Y, Liao H, et al. Five-year epidemiological survey of valvular heart disease: changes in morbidity, etiological spectrum and management in a cardiovascular center of Southern China. J Thorac Dis 2014; 6: 1724–1730.

[2] Jung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on valvular heart disease. Eur Heart J 2003; 24: 1231–1243.

[3] Marijon E, Ou P, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med 2007; 357: 470–476.

[4] Hu P, Liu XB, Liang J, et al. A hospital-based survey of patients with severe valvular heart disease in China. Int J Cardiol 2017; 231: 244–247.

[5] Stewart BF, Siscovick D, Lind BK, et al. Clinical factors associated with calcific aortic valve disease. Cardiovascular Health Study. J Am Coll Cardiol 1997; 29: 630–634.

[6] Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015; 16: 233–270.

[7] Wasilewski J, Mirotka K, Wilczek K, et al. Calcific aortic valve damage as a risk factor for cardiovascular events. Pol J Radiol 2012; 77: 30–34.

[8] Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 63: e57–e185.

[9] Nishimura RA, Otto CM, Bonow RO, 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: 2440–2492.

[10] Marmelo FC, Mateus SM, Pereira AJ. Association of
aortic valve sclerosis with previous coronary artery disease and risk factors. Arq Bras Cardiol 2014; 103: 398–402.

[11] Sliwa K, Carrington M, Mayosi BM, et al. Incidence and characteristics of newly diagnosed rheumatic heart disease in urban African adults: insights from the heart of Soweto study. Eur Heart J 2010; 31: 719–727.

[12] Demirbağ R, Sade LE, Aydın M, et al. The Turkish registry of heart valve disease. Turk Kardiyol Dern Ars 2013; 41: 1–10.

[13] Iung B, Vahanian A. Epidemiology of acquired valvular heart disease. Can J Cardiol 2014; 30: 962–970.

[14] Pasca I, Dang P, Tyagi G, Pai RG. Survival in patients with degenerative mitral stenosis: results from a large retrospective cohort study. J Am Soc Echocardiogr 2016; 29: 461–469.

[15] Chen HY, Engert JC, Thanassoulis G. Risk factors for valvular calcification. Cur Opin Endocrinol Diabetes Obes 2019; 26: 96–102.

[16] Lindroos M, Kupari M, Valvanne J, et al. Factors associated with calcific aortic valve degeneration in the elderly. Eur Heart J 1994; 15: 865–870.

[17] Aronow WS, Schwartz KS, Koenigsberg M. Correlation of serum lipids, calcium, and phosphorus, diabetes mellitus and history of systemic hypertension with presence or absence of calcified or thickened aortic cusps or root in elderly patients. Am J Cardiol 1987; 59: 998–999.

[18] Hsu SY, Hsieh IC, Chang SH, et al. Aortic valve sclerosis is an echocardiographic indicator of significant coronary disease in patients undergoing diagnostic coronary angiography. Int J Clin Pract 2005; 59: 72–77.

[19] Bouchareb R, Boulanger MC, Tastet L, et al. Activated platelets promote an osteogenic programme and the progression of calcific aortic valve stenosis. Eur Heart J 2019; 40: 1362–1373.

[20] Uchida S, Kumagai T, Chang WX, et al. Time to target uric acid to retard chronic kidney disease progression. Contrib Nephrol 2018; 192: 56–68.

[21] Fox CS, Larson MG, Vasan RS, et al. Cross-sectional association of kidney function with valvular and annular calcification: the Framingham heart study. J Am Soc Nephrol 2006; 17: 521–527.

[22] Mehta T, Nuccio E, McFann K, et al. Association of uric acid with vascular stiffness in the framingham heart study. Am J Hypertens 2015; 28: 877–883.

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