Quality of life and health status of hospitalized adults with congenital heart disease in Vietnam: a cross-sectional study

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Abstract

Background: Little is known about the quality of life (QOL) and health status of adults with congenital heart disease (CHD) in developing countries. Therefore, this study aimed to describe the QOL and health status of hospitalized adults with CHD in Vietnam and investigate the association between QOL and their biological-social characteristics.

Methods: A cross-sectional study was conducted with 109 adults with CHD, hospitalized in the Vietnam National Heart Institute, between June and December 2019. Validated instruments to assess QOL and health status describing patient-reported outcomes were used, including the EuroQOL-5 Dimensions-5 Level, Satisfaction with Life Scale, and Hospital Anxiety and Depression Scale.

Results: The mean scores on the EuroQOL-descriptive system (EQ-DS) and EuroQOL visual analogue scale (EQ-VAS) were 0.792 (SD = 0.122, 95% confidence interval [CI] 0.769–0.815) and 66.3 (SD = 12.5, 95% CI 63.9–68.7), respectively. A total of 9.2% (n = 9) patients experienced life dissatisfaction. The prevalence of anxiety and depression were 18.7% (n = 20) and 11% (n = 12), respectively. Scores of QOL in patients aged > 30 years were lower than in those aged ≤ 30 years. Stratified multivariate logistic regression revealed that poor QOL related to being unemployed/unstable employment (OR 4.43, 95% CI 1.71–11.47, p = 0.002), life dissatisfaction associated with unmarried status (OR 4.63, 95% CI 1.2–17.86, p = 0.026), anxiety regarding unemployment/unstable employment (OR 3.88, 95% CI 1.27–11.84, p = 0.017) and complex CHD/PAH (OR 4.84, 95% CI 1.33–17.54, p = 0.016), and depression regarding unemployment/unstable employment (OR 4.63, 95% CI 1.22–17.59, p = 0.003).

Conclusions: Reduced QOL and elevated psychological problems were common experiences among hospitalized adults with CHD in Vietnam. Biological-social characteristics such as unmarried status, unemployment/unstable employment, and complex CHD/PAH related to poor QOL, life dissatisfaction, anxiety, and depression.

Keywords: Quality of life, Health status, Adults with congenital heart disease, Hospitalized, Vietnam

Background

Congenital heart disease (CHD) is a common cardiac structural abnormality that affects one in 100 live births, globally. Many countries have made efforts towards improving the diagnostic quality and treatment of CHD, which has resulted in many children with CHD surviving well into adulthood [1–3]. However, several adults with CHD continually face physical and psychosocial...
difficulties and experience declined quality of life (QOL) [4–7]. Therefore, QOL has become an important endpoint in the quality assessment of medical care in many countries. A recent study recognized the association between increased social activities and better QOL [8]. Thereby, current guidelines on adults with CHD addressed the comprehensive care provided by allied health professionals to improve physical-mental health and QOL [9]. In this context, knowledge of QOL and health status in adults with CHD is an emerging domain and deserves investigation. However, in the long term, many studies on QOL related to CHD have focused on children, adolescents, or their parents, despite the existence of a large gap in the knowledge regarding QOL and health status in adults with CHD, especially in developing countries [4, 10–15].

The discrepancy between the QOL status of adults with CHD in developed countries and developing countries is concerning. Previous studies conducted in developed countries showed high QOL in adults with CHD [4, 16, 17]. In contrast, in developing countries, the QOL of adults with CHD seems poorer than that of the healthier counterparts [15]. Notably, a high QOL is the result of good physical health, good psychological state, and positive social relationships. These items depend on medical intervention, healthcare systems, financial conditions of the concerned individual, the national economic conditions, and the sociocultural characteristics that differ between countries; for example, these characteristics may differ between Asian and European countries, low/middle-income and high-income countries, developing and developed countries. Recently, an international study found that the effect of country-specific characteristics of QOL score of adults with CHD differs by 10.5 points between countries with the highest and lowest QOL [10, 18]. From the abovementioned studies, we can conclude that researching QOL in adults with CHD in developing countries is essential. This would be the base for implementing important health and social policies to improve the QOL of adults with CHD in developing countries.

Vietnam is a densely populated, dynamic country in Southeast Asia, with a population of 97 million; it can be classified as a low-/middle-income country. Apart from economic development, the Vietnamese government has also focused on improving the healthcare system. In fact, a previous study has highlighted the screening programmes, diagnostic approaches, and treatment for patients with CHD throughout the country [19]. Owing to these programmes, many children have received timely interventions and have survived into adulthood. However, management with care is lacking for adults with CHD in Vietnam, including programmes for improving their QOL. In this context, the characteristics of Vietnamese patients may be generalised to adults with CHD in developing countries. Specifically, these characteristics include low level of education, unmarried status, unemployment, and unrepaired defects. However, we lack information about the assessed QOL in adults with CHD and its relationship with different sociodemographic characteristics in these countries. Therefore, the present study aimed to describe the QOL and health status of hospitalized adults with CHD in Vietnam and investigate the association between the QOL and the biological and social characteristics of these patients.

Methods
Study design
We performed a cross-sectional study at the Vietnam National Heart Institute, Bach Mai Hospital (Hanoi, Vietnam)—the largest hospital for adults with CHD in North Vietnam and the national referral cardiovascular hospital—between June and December 2019. Owing to the lack of availability of specialized outpatient services for adults with CHD, we recruited inpatients who were admitted for cardiac imaging, intervention, or surgery for CHD.

All patients included in this study provided informed consent. The protocol of the current study and ethics approval for the human subject study was obtained from the Science Boards and Ethics Committee of the Department of Cardiology, Hanoi Medical University (no: 6655/QD-DHYHN). The experiment protocol involving human subjects was adopted in accordance with the Declaration of Helsinki.

Inclusion criteria
The inclusion criteria were (1) individuals with structural CHD confirmed by cardiac imaging and (2) aged ≥16 years. When physicians or cardiologists had patients with CHD, they would transfer these patients to our hospital to confirm defects wherein the adults with CHD were hospitalized for defects to be confirmed by specialists using cardiac imaging techniques. Transthoracic echocardiography was performed by experts on patients with CHD at the Vietnam National Heart Institute at admission. If structural CHD by transthoracic echocardiography was doubted, we confirmed structural CHD by transoesophageal echocardiography, cardiac computed tomography, and/or cardiac magnetic resonance imaging. After that, the specialist would explain the findings and provide treatment plans for each patient (intervention or surgery or only internal medicine).

In the study, we defined the age for reaching legal adulthood as 16 years, according to the current Law on Children of Vietnam (http://vbpl.vn/TW/Pages/vbpqentoanvan.aspx?ItemID=11044). We also defined youth as
the age cohort of 16–30 years, according to the current Youth Law of Vietnam (http://vanban.chinhphu.vn/portal/page/portal/chinhphu/hethongvanban?class_id=1&page=1&mode=detail&document_id=200445).

Exclusion criteria
Exclusion criteria for participants were the following: (1) known cardiac diseases other than CHD, (2) other known chronic diseases that require ongoing medical attention or limit activities of daily living, (3) having received post-operative care, (4) having acute medical conditions, (5) known neuropathy disorders and syndromes affecting cognitive abilities, and (6) emotional fragilities such as dissociative and conversion disorders (Codes F44 according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision) identified by reviewing the participants’ medical records and during inpatient treatment. Notably, in case of a patient who was doubted to be emotionally fragile, a psychiatrist was consulted for final diagnosis.

Sample size
The sample size was calculated using the following formula for cross-sectional studies: $N = \frac{Z^2 \times 1/2 \times P \times (1 - P)}{d^2}$, where $N$ is the sample size, $Z$ the statistic corresponding to the confidence level, $P$ the expected prevalence, and $d$ precision. However, we chose $P$ from a recent international study with a prevalence rate of reduced QOL in adults with CHD of 29.7% [10] and a recent study in Germany with a prevalence rate of psychological problems in adults with CHD of 58.7% [20]. With a confidence interval (CI) of 95%, and a precision of 0.1, the sample size was calculated to be 94. To account for missing data, we added 15% to the sample size. Therefore, the final sample size was 108.

Additional file 1 shows the flow diagram of the selection strategy of adults with CHD, which provides information on the number of patients recruited and those determined ineligible for participation. From 290 adults with CHD, we excluded 181 for various reasons. Finally, we enrolled 109 adults with CHD in this study.

Outcome measures
The patients completed a survey that included items of biological and social characteristics such as age, gender, marital status, employment status, educational level, CHD type, and CHD treatment. Subsequently, the following validated instruments describing patient-reported outcomes were completed to assess QOL and health status: EuroQOL-5 dimensions-5 level (EQ-5D-5L), Satisfaction with Life Scale (SWLS), and Hospital Anxiety and Depression Scale (HADS). Additionally, face-to-face interviews were conducted by one well-trained nurse. This nurse answered and clarified the questions and doubts of patients during the survey. She also ensured that patients completed the survey independently.

Primary outcomes measures were self-reported QOL, which was evaluated using EQ-5D-5L and SWLS, and self-reported psychosocial functioning that was evaluated by HADS. Secondary outcomes measures were socioeconomic status and the relationship between socioeconomic status and QOL and health status in adults with CHD.

Vietnamese translation scales for QOL and health status
The EQ-5D-5L is a questionnaire to assess health-related QOL and that includes EQ-descriptive system (EQ-DS) and EQ visual analogue scale (EQ-VAS); (Additional file 2, https://euroqol.org/eq-5d-instruments/sample-demo/). Here, we referred to the previous Vietnamese translation EQ-5D-5L version, which was developed by considering the health preferences of the general adult population of Vietnam and validated elsewhere [21]. The EQ-DS defines health based on five dimensions: Mobility, Self-Care, Usual Activities, Pain/Discomfort, and Anxiety/Depression. Responses are rated on a five-point Likert scale (no problems, slight problems, moderate problems, severe problems, and extreme problems). The value set for the EQ-DS was redesigned for the Vietnamese population on a scale ranging from 0 (worst imaginable QOL) to 1 (best imaginable QOL), while on the EQ-VAS, respondents rated the overall health on the day of the interview with scores ranging from 0 to 100, representing the worst and the best imaginable health state, respectively. Notably, poor QOL was defined as an EQ-VAS score of less than 65 [22].

The SWLS was a five-item instrument to measure general cognitive fundaments of life satisfaction. Each item is rated from one (strongly disagree) to seven (strongly agree) for a total score of 5–35 (Additional file 3, http://labs.psychology.illinois.edu/~ediener/SWLS.html). A score of 20 represents a neutral point on the scale, while scores of 31–35, 26–30, 21–25, 15–19, 10–14, and 5–9 indicate that the respondent is extremely satisfied, satisfied, slightly satisfied, slightly dissatisfied, dissatisfied, and extremely dissatisfied with life, respectively [23]. In our study, we referred to the available Vietnamese translation version of the SWLS (https://eddiener.com/scales/7).

The HADS comprises 14 items (graded as 0–3), which include seven items each for symptoms of anxiety (HADS-Anxiety subscale, HADS-A) and depression (HADS-Depression subscale, HADS-D); (Additional file 4, https://www.svri.org/sites/default/files/attachments/2016-01-13/HADS.pdf). The total scores for depression and anxiety range between 0 and 21. We considered a score of 8–10 to represent borderline abnormality and
A total of 109 adults with CHD were enrolled in this study. The patients were predominantly women (n = 76, 69.7%). The participants’ overall mean age was 37.8 years (SD = 12.7, 95% CI 35.4–40.2); the mean age of men and women was 33.7 years (SD = 13.4, 95% CI 29.0–38.5) and 39.6 years (SD = 12.0, 95% CI 36.9–42.3), respectively. Most patients (n = 70, 64.2%) were older than 30 years. The characteristics of patients are summarized in Table 1. In addition, many patients had an education level of less than high school (n = 49, 45%), were unmarried (never married, widowed, divorced or separated; n = 30, 27.5%), were unemployed or had unstable employment (n = 27, 24.8%), and had complex CHD or pulmonary artery hypertension (PAH; n = 16, 14.7%). Notably, most patients had unrepaired CHD (n = 81, 74.3%) or repaired palliation (n = 5, 4.6%).

Characteristics of quality of life
The overall mean for EQ-D5 and EQ-VAS was 0.792 (SD = 0.122, 95% CI 0.769–0.815) and 66.3 (SD = 12.5, 95% CI 63.9–68.7), respectively. The overall mean EQ-DS was significantly higher than EQ-VAS (p < 0.001, Student t-test). A significant number of adults with CHD had poor QOL, defined as EQ-VAS < 65 (n = 45, 41.3%). Table 2 summarises in detail the distribution of the EQ-5D-5L scale. Additionally, the most common problems measured by EQ-DS were pain/discomfort (n = 95, 87.2%), anxiety/depression (n = 83, 76.1%), mobility problems (n = 46, 42.2%), and problems with usual activities (n = 41, 37.6%), whereas the least reported complaint regarded self-care (n = 11, 10.1%).

Characteristics of health status
The overall mean SWLS score was 25.2 ± 4.3 (95% CI 24.3–25.9). Specifically, 3.7% (n = 4) of patients reported being dissatisfied, 5.5% (n = 6) slightly dissatisfied, 2.8% (n = 3) neutral, 42.2% (n = 46) slightly satisfied, 36.7% (n = 40) satisfied, and 9.2% (n = 10) extremely satisfied. Regarding the HADS, the overall mean score for anxiety was 6.9 (SD = 4.4, 95% CI 6.1–7.8) and 5.9 (SD = 3.8, 95% CI 5.2–6.6) for depression. The anxiety component revealed that 18.7% (n = 20) of patients had experienced significant anxiety. Meanwhile, 11% (n = 12) of patients displayed significant symptoms of depression.

Association between quality of life, health status, and biological-social characteristics in adults with congenital heart disease
As shown in Table 3, EQ-DS differs between subgroups. For EQ-DS, patients aged > 30 years had a lower score than those aged ≤ 30 years (0.764 [SD = 0.125], 95% CI 0.734–0.794 vs 0.841 [SD = 0.097], 95% CI 0.81–0.873, p = 0.001 overall; 0.766 [SD = 0.111], 95% CI 0.704–0.827 vs 0.853 [SD = 0.086], 95% CI 0.81–0.896, p = 0.016 in men; 0.764 [SD = 0.13], 95% CI 0.729–0.799 vs 0.831...
Table 1  Demographic characteristics of adults with congenital heart disease

| Characteristics                                      | N (%)       |
|------------------------------------------------------|-------------|
| Gender                                               |             |
| Men                                                  | 33 (30.3)   |
| Women                                                | 76 (69.7)   |
| Age groups                                           |             |
| 16–30                                                | 39 (35.8)   |
| 31–40                                                | 31 (28.4)   |
| 41–50                                                | 18 (16.5)   |
| 51–60                                                | 14 (12.8)   |
| 61+                                                  | 7 (6.4)     |
| Marital status                                       |             |
| Never married                                        | 23 (21.1)   |
| Married/cohabiting                                   | 79 (72.5)   |
| Window or divorce or separate                        | 7 (6.4)     |
| Educational level                                    |             |
| Secondary school and less                            | 49 (45.0)   |
| High school                                          | 19 (17.4)   |
| Undergraduate and postgraduate                       | 37 (33.9)   |
| Missing data                                         | 4 (3.7)     |
| Occupation                                           |             |
| Farmer                                               | 30 (27.5)   |
| Blue-collar                                          | 22 (20.2)   |
| White-collar                                         | 30 (27.5)   |
| Student                                              | 6 (5.5)     |
| Others                                               | 21 (19.3)   |
| Employment status                                    |             |
| Stable                                               | 59 (54.1)   |
| Homemaker or retired                                 | 14 (12.8)   |
| Unstable                                             | 21 (19.3)   |
| Unemployed                                           | 6 (5.5)     |
| Student or other works                               | 6 (5.5)     |
| Missing data                                         | 3 (2.8)     |
| Type of congenital heart disease                     |             |
| Isolated atrial septal defect                        | 53 (48.6)   |
| Isolated ventricular septal defect                   | 29 (26.6)   |
| Isolated patent ductus arteriosus                    | 19 (17.4)   |
| Combined ventricular septal defect and patent ductus arteriosus  | 1 (0.9)   |
| Combined atrial septal defect and pulmonary stenosis | 1 (0.9)     |
| Combined ventricular septal defect and pulmonary stenosis | 2 (1.8) |
| Tetralogy of Fallot                                  | 3 (2.8)     |
| Pulmonary atresia with ventricular septal defect     | 1 (0.9)     |
| Congenital heart disease status                      |             |
| Simple                                               | 93 (85.3)   |
| Complex or pulmonary artery hypertenstion            | 16 (14.7)   |
| Treatment for congenital heart disease               |             |
| Interventional/surgical correction                  | 23 (21.1)   |
| Interventional/surgical palliation                   | 5 (4.6)     |
| Unrepaired                                           | 81 (74.3)   |

[SD=0.106], 95% CI 0.782–0.879, $p=0.039$ in women; using the Student t-test; respectively), patients who had an education level lower than high school had a lower score than those with an education level of high school or higher (0.754 [SD=0.13], 95% CI 0.716–0.791 vs 0.827 [SD=0.104], 95% CI 0.8–0.855, $p=0.002$ overall; 0.746 [SD=0.132], 95% CI 0.652–0.841 vs 0.863 [SD=0.061], 95% CI 0.835–0.891, $p=0.002$ in men; using Student t-test; respectively), patients with an unemployed status/unstable employment had a lower score than those with an employed status (0.754 [SD=0.136], 95% CI 0.7–0.808 vs 0.807 [SD=0.114], 95% CI 0.782–0.833, $p=0.049$ overall; 0.737 [SD=0.151], 95% CI 0.598–0.877 vs 0.848 [SD=0.071], 95% CI 0.817–0.878, $p=0.01$ in men; using the Student t-test; respectively). Moreover, EQ-DS in employed women was lower than in employed men (0.79 [SD=0.125], 95% CI 0.756–0.823 vs 0.848 [SD=0.071], 95% CI 0.817–0.878, $p=0.037$; using Student t-test; respectively).

Table 3 also shows that EQ-VAS in patients who were aged ≥30 years was lower than in those aged ≤30 years (64.3 [SD=13.1], 95% CI: 61.2–67.4 vs 69.9 [SD=10.8], 95% CI: 66.4–73.4, $p=0.024$ overall; 60.7 [SD=12.1], 95% CI: 53.6–67.8 vs 72.2 [SD=10.2], 95% CI: 67.0–77.1, $p=0.008$ in men; using Student t-test; respectively), EQ-VAS in patients with an employed status/unstable employment was lower than in those with an educational level of high school or higher (63.2 [SD=11.9], 95% CI: 59.7–66.6 vs 69.5 [SD=12.0], 95% CI: 66.3–72.7, $p=0.008$ overall; 61.0 [SD=13.7], 95% CI: 51.2–70.8 vs 71.9 [SD=9.1], 95% CI: 67.6–76.1, $p=0.015$ in men; using the Student t-test; respectively), EQ-VAS in patients with an unemployed status/unstable employment was lower than in those with an employed status (61.3 [SD=10.0], 95% CI: 57.4–65.2 vs 68.4 [SD=12.5], 95% CI: 65.6–71.2, $p=0.009$ overall; 58.6 [SD=13.5], 95% CI: 46.1–71.1 vs 71.1 [SD=9.6], 95% CI: 67.1–75.2, $p=0.009$ in men; using Student t-test; respectively), EQ-VAS in patients with complex CHD/PAH was lower than in those with simple CHD (60.0 [SD=14.1], 95% CI: 52.5–67.5 vs 67.4 [SD=12.0], 95% CI: 64.9–69.9, $p=0.029$ overall; 56.0 [SD=11.4], 95% CI: 41.8–70.2 vs 68.8 [SD=12.0], 95% CI: 64.2–73.5, $p=0.034$ in men; using the Student t-test; respectively). Moreover, EQ-DS in unmarried women was 58.5 (SD=16.9, 95% CI: 48.3–68.7), which was lower than that in married women (67.6; SD=11.0, 95% CI: 64.8–70.4), with $p=0.016$, using the Student t-test.

Table 4 compares SWLS, HADS-A, and HADS-D among subgroups. Specifically, the mean of SWLS of patients with an unemployed status/unstable employment was lower than that of patients with an employed status. Based on the HADS classification, mean of
HADS-A and HADS-D in patients aged > 30 years, had educational level at high school and above, had an unemployed status/unstable employment, and had complex CHD/PAH were lower than those in patients aged ≤ 30 years, had an educational level of high school and above, had an employed status, and had simple CHD, respectively. These differences were statistically significant (p = 0.001, p = 0.001, p = 0.007, p = 0.032 for HADS-A; p = 0.002, p = 0.001, p = 0.004, p = 0.028 for HADS-D; respectively).

Figure 1 shows the prevalence of poor QOL, defined as EQ-VAS < 65, by subgroup. The prevalence of poor QOL in patients who were aged > 30 years was higher than those aged ≤ 30 years (50%, n = 35 vs 25.6%, n = 10, p = 0.013; using the Chi-square test; respectively). The prevalence of poor QOL in patients with an unemployed status/unstable employment was higher than in those with an employed status (29.6%, n = 8 vs 5.1%, n = 4, p = 0.002; using Chi-square test; respectively). The prevalence of depression of patients aged > 30 years is higher than that of patients aged ≤ 30 years (17.1%, n = 12 vs 0%, n = 0, p = 0.004; using Fisher’s exact test; respectively). The prevalence of depression in patients with an educational level of high school and above was higher than in those with an educational level of high school and above (22.4%, n = 11 vs 1.8%, n = 1, p = 0.001; using Fisher’s exact test; respectively).

The results of the stratified logistic regressions predicting poor QOL and health status are summarized in Table 5. Multivariable logistic regression showed that poor QOL, defined as EQ-VAS < 65, was associated with

Table 2 Profiles of EQ-5D-5L in adults with congenital heart disease

| Scales | Score range | 0–0.1 | 0.11–0.2 | 0.21–0.3 | 0.31–0.4 | 0.41–0.5 | 0.51–0.6 | 0.61–0.7 | 0.71–0.8 | 0.81–0.9 | 0.91–1 |
|--------|-------------|-------|----------|----------|----------|----------|----------|----------|----------|----------|--------|
| EuroQOL-Descriptive System | N | 0 | 0 | 0 | 0 | 4 | 3 | 16 | 31 | 30 | 25 |
| | % | 0 | 0 | 0 | 0 | 3.7 | 2.8 | 14.7 | 28.4 | 27.5 | 22.9 |
| EuroQOL Visual Analogue Scale | N | 0 | 1 | 0 | 4 | 13 | 27 | 36 | 25 | 2 | 1 |
| | % | 0 | 0.9 | 0 | 3.7 | 11.9 | 24.8 | 33 | 22.9 | 1.8 | 0.9 |

| Domains of EuroQOL-Descriptive System | Levels | Extreme problems | Severe problems | Moderate problems | Slight problems | No problems |
|--------------------------------------|--------|------------------|-----------------|-------------------|-----------------|-------------|
| Mobility | N | 0 | 0 | 6 | 40 | 63 |
| | % | 0 | 0 | 5.5 | 36.7 | 57.8 |
| Self-care | N | 0 | 0 | 0 | 11 | 98 |
| | % | 0 | 0 | 0 | 10.1 | 89.9 |
| Usual activities | N | 0 | 0 | 4 | 37 | 68 |
| | % | 0 | 0 | 3.7 | 33.9 | 62.4 |
| Pain/discomfort | N | 0 | 1 | 17 | 77 | 14 |
| | % | 0 | 0.9 | 15.6 | 70.6 | 12.8 |
| Anxiety/depression | N | 1 | 5 | 16 | 61 | 26 |
| | % | 0.9 | 4.6 | 14.7 | 56 | 23.9 |
| Groups                                      | Total       | Men                  | Women                  | p value* | Cohen's d* |
|---------------------------------------------|-------------|----------------------|------------------------|----------|------------|
|                                             | Mean (SD)  | 95%CI                | p value | Mean (SD)  | 95%CI | p value | Mean (SD)  | 95%CI | p value | Cohen's d |
| EuroQOL-Descriptive System (EQ-DS)          |             |                      |         |             |       |       |             |       |       |           |
| Total                                       | 0.792 (0.121) | 0.769–0.815 | – | 0.777–0.851 | – | – | 0.782 (0.127) | 0.753–0.811 | – | – | 0.22 | 0.274 |
| Age groups                                  |             |                      |         |             |       |       |             |       |       |           |
| 16–30                                        | 0.841 (0.097) | 0.81–0.873 | 0.001 | 0.688 | 0.853 (0.086) | 0.81–0.896 | 0.016 | 0.901 | 0.831 (0.106) | 0.782–0.879 | 0.039 | 0.565 | 0.472 | 0.228 |
| 31+                                          | 0.764 (0.125) | 0.734–0.794 | 0.766 (0.111) | 0.704–0.827 | 0.764 (0.13) | 0.729–0.799 | 0.964 | 0.017 |
| Marital status                              |             |                      |         |             |       |       |             |       |       |           |
| Married                                      | 0.795 (0.108) | 0.771–0.819 | 0.659 | 0.091 | 0.795 (0.106) | 0.739–0.851 | 0.339 | 0.338 | 0.795 (0.11) | 0.767–0.823 | 0.056 | 0.49 | 0.999 | 0 |
| Unmarried                                    | 0.783 (0.152) | 0.727–0.804 | 0.831 (0.107) | 0.776–0.886 | 0.721 (0.183) | 0.611–0.832 | 0.049 | 0.734 |
| Educational level                           |             |                      |         |             |       |       |             |       |       |           |
| High school+                                 | 0.827 (0.104) | 0.8–0.855 | 0.002 | 0.535 | 0.863 (0.061) | 0.835–0.891 | 0.002 | 1.138 | 0.808 (0.118) | 0.768–0.848 | 0.074 | 0.417 | 0.057 | 0.586 |
| High school–                                 | 0.754 (0.13) | 0.716–0.791 | 0.746 (0.132) | 0.652–0.841 | 0.756 (0.131) | 0.713–0.798 | 0.842 | 0.076 |
| Employment status                           |             |                      |         |             |       |       |             |       |       |           |
| Employed                                    | 0.807 (0.114) | 0.782–0.833 | 0.049 | 0.422 | 0.848 (0.071) | 0.817–0.878 | 0.01 | 0.941 | 0.79 (0.125) | 0.756–0.823 | 0.372 | 0.232 | 0.037 | 0.571 |
| Unemployed/had unstable employment          | 0.754 (0.136) | 0.7–0.808 | 0.737 (0.151) | 0.598–0.877 | 0.76 (0.134) | 0.697–0.823 | 0.718 | 0.161 |
| CHD type                                    |             |                      |         |             |       |       |             |       |       |           |
| Simple                                      | 0.8 (0.119) | 0.776–0.825 | 0.008 | 0.459 | 0.829 (0.097) | 0.791–0.866 | 0.053 | 0.872 | 0.788 (0.126) | 0.757–0.819 | 0.349 | 0.299 | 0.131 | 0.365 |
| Complex PAH                                 | 0.743 (0.129) | 0.674–0.812 | 0.729 (0.13) | 0.568–0.89 | 0.749 (0.135) | 0.659–0.84 | 0.786 | 0.151 |
| CHD treatment                               |             |                      |         |             |       |       |             |       |       |           |
| Repaired                                    | 0.796 (0.117) | 0.771–0.821 | 0.501 | 0.149 | 0.819 (0.093) | 0.783–0.855 | 0.5 | 0.257 | 0.785 (0.126) | 0.752–0.818 | 0.772 | 0.077 | 0.206 | 0.307 |
| Unrepaired/palliative                       | 0.777 (0.138) | 0.717–0.836 | 0.783 (0.175) | 0.567–1.0 | 0.775 (0.133) | 0.709–0.841 | 0.905 | 0.051 |
Table 3 (continued)

| Groups                          | Total Mean (SD) | 95%CI  | p value | Cohen's d | Men Mean (SD) | 95%CI  | p value | Cohen's d | Women Mean (SD) | 95%CI  | p value | Cohen's d |
|--------------------------------|-----------------|--------|---------|-----------|---------------|--------|---------|-----------|-----------------|--------|---------|-----------|
| EuroQOL Visual Analogue Scale (EQ-VAS) |                 |        |         |           |               |        |         |           |                 |        |         |           |
| Total                          | 66.3 (12.5)     | 63.9–68.7 | -       | -         | 66.9 (12.6)   | 62.4–71.4 | -       | -         | 66.1 (12.6)   | 63.2–68.9 | -       | 0.754 0.016 |
| (n = 109)                      | (n = 33)        | (n = 76) |         |           | (n = 18)      | (n = 21)  |         |           | (n = 21)       | (n = 55) |         |           |
| Age groups                     |                 |        |         |           |               |        |         |           |                 |        |         |           |
| 16–30                          | 69.9 (10.8)     | 66.4–73.4 | 0.024   | 0.466     | 72.1 (10.2)   | 67.0–77.1 | 0.008   | 0.985     | 68.1 (11.2)   | 63.0–73.2 | 0.385 0.23  |
| (n = 39)                       | (n = 18)        | (n = 21) |         |           | (n = 15)      | (n = 21)  |         |           | (n = 21)       | (n = 55) |         |           |
| 31+                            | 64.3 (13.1)     | 61.2–67.4 | 60.7 (12.8) | 53.6–67.8 | 65.3 (13.1) | 61.7–68.8 | 0.259   | 0.355     |                 |         |         |           |
| (n = 70)                       | (n = 15)        | (n = 15) |         |           | (n = 15)      | (n = 55) |         |           |                 |         |         |           |
| Marital status                 |                 |        |         |           |               |        |         |           |                 |        |         |           |
| Married                        | 67.0 (11.2)     | 64.4–695 | 0.376   | 0.177     | 64.4 (12.1)   | 57.9–70.8 | 0.276   | 0.382     | 67.6 (11.0)   | 64.8–704 | 0.016 0.638 |
| (n = 79)                       | (n = 16)        | (n = 17) |         |           | (n = 16)      | (n = 36)  |         |           | (n = 63)       | (n = 13) |         |           |
| Unmarried                      | 64.6 (15.5)     | 58.8–704 |         |           | 69.2 (13.0)   | 62.5–75.9 | 58.5 (16.9) | 48.3–687 | 0.058 0.71 |
| (n = 30)                       | (n = 17)        | (n = 17) |         |           | (n = 17)      | (n = 13)  |         |           | (n = 13)       | (n = 71) |         |           |
| Educational level              |                 |        |         |           |               |        |         |           |                 |        |         |           |
| High school+                   | 69.5 (12.0)     | 66.3–727 | 0.008   | 0.527     | 71.9 (9.1)    | 67.6–76.1 | 0.015   | 0.937     | 68.2 (13.3)   | 63.7–72.7 | 0.124 0.361 |
| (n = 56)                       | (n = 20)        | (n = 36) |         |           | (n = 20)      | (n = 36)  |         |           | (n = 36)       | (n = 36) |         |           |
| High school−                   | 63.2 (11.9)     | 59.7–66.6 | 61.0 (13.7) | 51.2–70.8 | 63.7 (11.6)   | 60.0–67.5 | 0.526   | 0.213     |                 |         |         |           |
| (n = 49)                       | (n = 10)        | (n = 39) |         |           | (n = 10)      | (n = 39) |         |           |                 |         |         |           |
| Employment status              |                 |        |         |           |               |        |         |           |                 |        |         |           |
| Employed                       | 68.4 (12.5)     | 65.6–71.2 | 0.009   | 0.627     | 71.1 (9.6)    | 67.1–75.2 | 0.009   | 1.067     | 67.2 (13.5)   | 63.5–70.8 | 0.134 0.431 |
| (n = 79)                       | (n = 24)        | (n = 55) |         |           | (n = 24)      | (n = 55)  |         |           | (n = 55)       | (n = 39) |         |           |
| Unemployed/had unstable employ- | 61.3 (10.0)     | 57.4–65.2 | 58.6 (13.5) | 46.1–71.0 | 62.3 (8.7)    | 58.2–66.3 | 0.411   | 0.326     |                 |         |         |           |
| ment                           | (n = 27)        | (n = 7) |         |           | (n = 7)       | (n = 20) |         |           |                 |         |         |           |
| CHD type                       |                 |        |         |           |               |        |         |           |                 |        |         |           |
| Simple                         | 67.4 (12.0)     | 64.9–69.9 | 0.029   | 0.565     | 68.8 (12.0)   | 64.2–73.5 | 0.034   | 1.094     | 66.8 (12.0)   | 63.8–69.8 | 0.23 0.362 |
| (n = 93)                       | (n = 28)        | (n = 65) |         |           | (n = 28)      | (n = 65)  |         |           | (n = 65)       | (n = 65) |         |           |
| Complex/PAH                    | 60.0 (14.1)     | 52.5–67.5 | 56.0 (11.4) | 41.8–70.2 | 61.8 (15.4)   | 51.5–72.2 | 0.465   | 0.428     |                 |         |         |           |
| (n = 16)                       | (n = 5)         | (n = 11) |         |           | (n = 5)       | (n = 11)  |         |           |                 |         |         |           |
### Table 3 (continued)

| Groups                  | Total       | 95% CI       | p value | Cohen’s d | Men          | 95% CI       | p value | Cohen’s d | Women        | 95% CI       | p value | Cohen’s d |
|-------------------------|-------------|--------------|---------|-----------|--------------|--------------|---------|-----------|--------------|--------------|---------|-----------|
|                         | Mean (SD)   |              |         |           | Mean (SD)    |              |         |           | Mean (SD)    |              |         |           |
|                         |             | p value      | Cohen’s d |           |             | p value      | Cohen’s d |           | p value      | Cohen’s d   |         |           |
| CHD treatment           |             |              |         |           |             |              |         |           |             |             |         |           |
| Repaired                | 669 (12.6)  | 64.2–69.6    | 0.352   | 0.225     | 67.4 (11.8)  | 62.8–72.0    | 0.588   | 0.222     | 666 (13.1)  | 63.2–70.1   | 0.47    | 0.199     | 0.797 | 0.064     |
|                         | (n = 86)    |              |         |           | (n = 28)     |              |         |           | (n = 58)     |              |         |           |
| Unrepaired/palliative  | 641 (12.3)  | 58.8–69.5    |         |           | 64.0 (18.2)  | 41.4–86.6    |         |           | 642 (10.9)  | 58.8–69.6   |         | 0.979     | 0.013 |
|                         | (n = 23)    |              |         |           | (n = 5)      |              |         |           | (n = 18)     |              |         |           |

CHD, Congenital heart disease; PAH, Pulmonary artery hypertension; SD, Standard Deviation; CI, Confidence Interval; Employed status included stable employment, homemaker, retired, student or other works; * Compared between men and women; Cohen’s d is the appropriate effect size measure; Using independent samples t-test.
### Table 4  SWLS, HADS-A and HADS-D by subgroups in adults with congenital heart disease

| Groups | Total | Men |
|--------|-------|-----|
|        | Median | IQR | U  | Z   | p value | Cohen’s d | Median | IQR | U  | Z   | p value | Cohen’s d |
| Satisfaction with Life Scale (SWLS) |       |     |    |     |         |          |       |     |    |     |         |          |
| Total  | 25.0   | 5.0 | –  | –   | –       | –        | 26.0   | 4.5 | –  | –   | –       | –        |
| Age groups |       |     |    |     |         |          |       |     |    |     |         |          |
| 16–30  | 26.0   | 4.0 | 12.265 | –0.88 | 0.379 | 0.168 | 26.5   | 5.25 | 12.45 | –0.384 | 0.708 | 0.132 |
| 31+    | 25.0   | 5.0 | –  | –   | –       | –        | 26.0   | 4.0 | –  | –   | –       | –        |
| Marital status |       |     |    |     |         |          |       |     |    |     |         |          |
| Married | 25.0   | 5.0 | 9.115 | –1.865 | 0.062 | 0.361 | 26.5   | 4.0 | 9.6 | –1.457 | 0.157 | 0.518 |
| Unmarried | 25.0   | 6.25 | –  | –   | –       | –        | 26.0   | 6.5 | –  | –   | –       | –        |
| Educational level |       |     |    |     |         |          |       |     |    |     |         |          |
| High school+ | 26.0   | 4.75 | 11.085 | –1.7 | 0.089 | 0.335 | 26.5   | 4.0 | 7.9 | –0.935 | 0.373 | 0.342 |
| High school− | 25.0   | 5.0 | –  | –   | –       | –        | 25.5   | 8.25 | –  | –   | –       | –        |
| Employment status |       |     |    |     |         |          |       |     |    |     |         |          |
| Employed | 26.0   | 5.0 | 7.795 | –2.09 | 0.037 | 0.413 | 27.0   | 4.0 | 5.3 | –1.457 | 0.153 | 0.536 |
| Unemployed/had unstable employment | 24.0   | 7.0 | –  | –   | –       | –        | 25.0   | 11.0 | –  | –   | –       | –        |
| CHD type |       |     |    |     |         |          |       |     |    |     |         |          |
| Simple | 25.0   | 5.0 | 6.320 | –0.964 | 0.335 | 0.184 | 26.5   | 4.75 | 5.8 | –0.609 | 0.575 | 0.211 |
| Complex/PAH | 25.0   | 4.75 | –  | –   | –       | –        | 25.0   | 4.5 | –  | –   | –       | –        |
| CHD treatment |       |     |    |     |         |          |       |     |    |     |         |          |
| Repaired | 26.0   | 5.0 | 9.330 | –0.418 | 0.676 | 0.08 | 26.0   | 2.0 | 5.9 | –0.533 | 0.069 | 0.184 |
| Unrepaired/palliative | 25.0   | 5.0 | –  | –   | –       | –        | 26.5   | 5.5 | –  | –   | –       | –        |
| Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) |       |     |    |     |         |          |       |     |    |     |         |          |
| Total  | 6.0    | 7.0 | –  | –   | –       | –        | 4.0    | 5.0 | –  | –   | –       | –        |
| Groups                          | Total | Men |
|--------------------------------|-------|-----|
|                                | Median| IQR| U  | Z      | p value | Cohen's d |
|                                |       |    |    |       |         |           |
|                                | Median| IQR| U  | Z      | p value | Cohen's d |
|                                |       |    |    |       |         |           |
| **Age groups**                 |       |    |    |       |         |           |
| 16–30                          | 3.5   | 6.25| 8.245|−3.179| 0.001  | 0.643     |
| (n=38)                         |       |    |    |       |         |           |
| 31+                            | 7.0   | 0.0 | 5.0 |       |         |           |
| (n=69)                         |       |    |    |       |         |           |
| **Marital status**             |       |    |    |       |         |           |
| Married                        | 6.5   | 6.0| 10.645|−0.468| 0.64   | 0.09      |
| (n=78)                         |       |    |    |       |         |           |
| Unmarried                      | 4.0   | 0.0| 10.0|       |         |           |
| (n=29)                         |       |    |    |       |         |           |
| **Educational level**          |       |    |    |       |         |           |
| High school+                   | 5.0   | 0.0| 5.0| 4.75 | 0.001  | 0.717     |
| (n=50)                         |       |    |    |       |         |           |
| High school−                   | 9.0   | 0.0| 7.0|       |         |           |
| (n=47)                         |       |    |    |       |         |           |
| **Employment status**          |       |    |    |       |         |           |
| Employed                       | 6.0   | 0.0| 6.550|−2.706| 0.007  | 0.548     |
| (n=78)                         |       |    |    |       |         |           |
| Unemployed/had unstable employment| 9.5  | 7.5 | 0.0  | 0.0  |        |           |
| (n=26)                         |       |    |    |       |         |           |
| **CHD type**                   |       |    |    |       |         |           |
| Simple                         | 6.0   | 0.0| 6.75| 4.515|−2.148  | 0.032     |
| (n=92)                         |       |    |    |       |         |           |
| Complex/PAH                    | 10.0  | 7.0| 0.0  | 0.0  |        |           |
| (n=15)                         |       |    |    |       |         |           |
| **CHD treatment**              |       |    |    |       |         |           |
| Repaired                       | 6.0   | 8.25| 8.765|−0.453| 0.651  | 0.087     |
| (n=22)                         |       |    |    |       |         |           |
| Unrepaired/palliative          | 7.0   | 0.0| 7.0 |       |         |           |
| (n=85)                         |       |    |    |       |         |           |
| Hospital Anxiety and Depression Scale-Depression subscale (HADS-D) |       |    |    |       |         |           |
| Total                          | 5.0   | 5.0| 0.0  | 0.0  |        |           |
| (n=109)                        |       |    |    |       |         |           |
| Groups                  | Total                | Median | IQR  | U     | Z     | p value | Cohen's d | Men                | Median | IQR  | U     | Z     | p value | Cohen's d |
|------------------------|----------------------|--------|------|-------|-------|---------|-----------|---------------------|--------|------|-------|-------|---------|-----------|
|                        |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| Age groups             |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| 16–30                  | 40 (n=39)            | 4.0    | 4.0  | 878.0 | −3.096| 0.002   | 0.617     | 2.5 (n=18)         | 3.5    | 690  | −2.407| 0.016 | 0.913   |
| 31+                    | 60 (n=70)            | 5.25   | 5.0  |       |       |         |           |                     |        |      |       |       |         |           |
| Marital status         |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| Married                | 50 (n=79)            | 5.0    | 5.0  | 1144.0| −0.28 | 0.78    | 0.053     | 5.0 (n=16)         | 4.75   | 1190 | −0.618| 0.557 | 0.214   |
| Unmarried              | 40 (n=30)            | 8.0    | 0.0  |       |       |         |           |                     |        |      |       |       |         |           |
| Educational level      |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| High school+           | 40 (n=56)            | 3.0    | 4.0  | 846.5 | −3.395| 0.001   | 0.698     | 3.0 (n=20)         | 2.0    | 410  | −2.622| 0.008 | 1.076   |
| High school−           | 70 (n=49)            | 6.0    | 0.0  |       |       |         |           |                     |        |      |       |       |         |           |
| Employment status      |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| Employed               | 40 (n=79)            | 4.0    | 4.0  | 673.0 | −2.87 | 0.004   | 0.577     | 3.0 (n=24)         | 3.75   | 430  | −1.955| 0.054 | 0.742   |
| Unemployed/had unstable employment | 80 (n=27) | 8.0 | 8.0  |       |       |         |           |                     | 8.0    | 11.0 |       |       |         |           |
| CHD type               |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| Simple                 | 40 (n=93)            | 5.0    | 5.0  | 489.5 | −2.191| 0.028   | 0.427     | 3.0 (n=28)         | 5.0    | 36.5 | −1.696| 0.093 | 0.612   |
| Complex/PAH            | 70 (n=16)            | 6.0    | 6.0  |       |       |         |           |                     | 6.0    | 9.5  |       |       |         |           |
| CHD treatment          |                      |        |      |       |       |         |           |                     |        |      |       |       |         |           |
| Repaired               | 60 (n=23)            | 7.0    | 7.0  | 796.5 | −1.438| 0.151   | 0.276     | 3.0 (n=5)          | 7.0    | 56.5 | 0.494 | 0.509 | 0.238   |
| Unrepaired/palliative  | 50 (n=86)            | 5.0    | 5.0  |       |       |         |           |                     | 4.0    | 5.0  |       |       |         |           |
Table 4 (continued)

| Groups                        | Women U* | Z* | p value | Cohen’s d* |
|-------------------------------|----------|----|---------|------------|
|                               | Median   | IQR | U      | Z      |     |
| Satisfaction with Life Scale (SWLS) |          |     |        |        |    |
| Total (n = 76)                | 25.0     | 4.75 | –      | –      | –   |
| Age groups                    |          |     | –      | –      | –   |
| 16–30 (n = 21)                | 26.0     | 3.5  | 481.5  | –1.12  | 0.263 | 0.258 |
| 31+ (n = 55)                  | 25.0     | 5.0  | –      | –      | –   |
| Marital status                |          |     | –      | –      | –   |
| Married (n = 63)              | 25.0     | 5.0  | 276.5  | –1.843 | 0.065 | 0.431 |
| Unmarried (n = 13)            | 24.0     | 6.5  | –      | –      | –   |
| Educational level             |          |     | –      | –      | –   |
| High school+ (n = 36)         | 26.0     | 5.0  | 595.0  | –1.14  | 0.254 | 0.264 |
| High school− (n = 39)         | 24.0     | 4.0  | –      | –      | –   |
| Employment status             |          |     | –      | –      | –   |
| Employed (n = 55)             | 25.0     | 5.0  | 438.0  | –1.348 | 0.178 | 0.314 |
| Unemployed/had unstable employ (n = 20) | 24.0 | 6.25 | –      | –      | –   |
| CHD type                      |          |     | –      | –      | –   |
| Simple (n = 65)               | 25.0     | 5.0  | 302.5  | –0.816 | 0.415 | 0.187 |
| Complex/PAH (n = 11)          | 24.0     | 5.0  | –      | –      | –   |
| CHD treatment                 |          |     | –      | –      | –   |
| Repaired (n = 18)             | 25.5     | 6.0  | 466.0  | –0.687 | 0.492 | 0.157 |
| Unrepaired/palliative (n = 58) | 25.0 | 4.0  | –      | –      | –   |

U* = Mann-Whitney U, Z* = z-test, p value* = p-value of the test, Cohen’s d* = Cohen’s d effect size.
| Groups | Women | IQR | U   | Z   | p value | Cohen's d | U*   | Z*   | p value* | Cohen's d* |
|--------|-------|-----|-----|-----|---------|-----------|------|------|---------|------------|
|        |       |     |     |     |         |           |      |      |         |            |
| Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) | | | | | | | | | | |
| Total  | 70    | 60  | –   | –   | –       | –         | 74.55| –2.982 | 0.003    | 0.6        |
|        | (n = 76) | | | | | | | | | |
| Age groups | | | | | | | | | | |
| 16–30  | 6.0   | 7.5 | 440.0 | –1.603 | 0.109 | 0.373 | 11.30 | –1.944 | 0.006 | 0.657 |
|        | (n = 21) | | | | | | | | | |
| 31+    | 8.0   | 5.0 | –   | –   | –       | –         | 2.980 | –1.303 | 0.019 | 0.316 |
|        | (n = 55) | | | | | | | | | |
| Marital status | | | | | | | | | | |
| Married | 7.0   | 6.0 | 317.5 | –1.274 | 0.203 | 0.294 | 30.60 | –2.119 | 0.034 | 0.492 |
|        | (n = 63) | | | | | | | | | |
| Unmarried | 12.0  | 12.5 | –   | –   | –       | –         | 62.5  | –1.835 | 0.068 | 0.718 |
|        | (n = 13) | | | | | | | | | |
| Educational level | | | | | | | | | | |
| High school+ | 7.0   | 7.0 | 551.0 | –1.607 | 0.108 | 0.376 | 163.5 | –3.38  | 0.001 | 1.005 |
|        | (n = 36) | | | | | | | | | |
| High school− | 8.0   | 7.0 | –   | –   | –       | –         | 155.5 | –0.014 | 0.989 | 0.004 |
|        | (n = 39) | | | | | | | | | |
| Employment status | | | | | | | | | | |
| Employed | 7.0   | 7.0 | 421.5 | –1.545 | 0.122 | 0.361 | 340.0 | –3.221 | 0.001 | 0.779 |
|        | (n = 55) | | | | | | | | | |
| Unemployed/had unstable employment | 9.5   | 6.75 | –   | –   | –       | –         | 58.5  | –0.092 | 0.929 | 0.036 |
|        | (n = 20) | | | | | | | | | |
| CHD type | | | | | | | | | | |
| Simple | 7.0   | 6.5 | 242.0 | –1.711 | 0.087 | 0.399 | 540.5 | –2.905 | 0.004 | 0.632 |
|        | (n = 65) | | | | | | | | | |
| Complex/PAH | 10.0  | 6.0 | –   | –   | –       | –         | 21.0  | –0.131 | 0.949 | 0.067 |
|        | (n = 11) | | | | | | | | | |
| CHD treatment | | | | | | | | | | |
| Repaired | 6.0   | 7.5 | 520.0 | –0.025 | 0.98  | 0.006 | 22.5  | –1.159 | 0.262 | 0.505 |
|        | (n = 18) | | | | | | | | | |
| Unrepaired/palliative | 7.5   | 6.0 | –   | –   | –       | –         | 490.0 | –2.777 | 0.005 | 0.629 |
|        | (n = 58) | | | | | | | | | |
| Groups                                                                 | Women | Median | IQR | U   | Z    | p value | Cohen's d |
|-----------------------------------------------------------------------|-------|--------|-----|-----|------|---------|-----------|
| Hospital Anxiety and Depression Scale-Depression subscale (HADS-D)   |       |        |     |     |      |         |           |
| Total                                                                 |       | 5.0    | 5.0 | −   | −    | 91.40   | −2.255    | 0.024     | 0.555     |
| (n = 76)                                                              |       |        |     |     |      |         |           |           |           |
| Age groups                                                            |       |        |     |     |      |         |           |           |           |
| 16–30                                                                |       | 4.0    | 4.0 | 438.0 | −1.631 | 0.103 | 0.378      | 11.65     | −2.064    | 0.04     | 0.692     |
| (n = 76)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| 31+                                                                  |       | 6.0    | 6.0 | −   | −    | 3.775   | −0.503    | 0.615     |           |           |           |
| (n = 55)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Marital status                                                        |       |        |     |     |      |         |           |           |           |           |           |
| Married                                                               |       | 5.0    | 4.0 | 30.75 | −1.416 | 0.157 | 0.327      | 4.200     | −1.032    | 0.302    | 0.232     |
| (n = 63)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Unmarried                                                             |       | 10.0   | 10.5| −   | −    | 6.05    | −2.104    | 0.035     | 0.827     |           |           |
| (n = 13)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Educational level                                                     |       |        |     |     |      |         |           |           |           |           |           |
| High school+                                                          |       | 4.0    | 3.75| 5.19 | −1.948 | 0.051 | 0.459      | 18.80     | −2.975    | 0.003    | 0.855     |
| (n = 36)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| High school−                                                          |       | 7.0    | 6.0 | −   | −    | 19.15   | −0.087    | 0.932     | 0.025     |           |           |
| (n = 39)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Employment status                                                     |       |        |     |     |      |         |           |           |           |           |           |
| Employed                                                              |       | 4.0    | 5.0 | 378.0 | −2.074 | 0.038 | 0.49       | 4.115     | −2.674    | 0.007    | 0.624     |
| (n = 55)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Unemployed/ had unstable employment                                   |       | 8.0    | 7.5 | −   | −    | 6.55    | −0.251    | 0.808     | 0.096     |           |           |
| (n = 20)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| CHD type                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Simple                                                                |       | 5.0    | 5.5 | 26.0 | −1.441 | 0.15   | 0.333      | 6.305     | −2.355    | 0.019    | 0.5       |
| (n = 65)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Complex/PAH                                                           |       | 8.0    | 6.0 | −   | −    | 2.60    | −0.172    | 0.913     | 0.085     |           |           |
| (n = 11)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| CHD treatment                                                         |       |        |     |     |      |         |           |           |           |           |           |
| Repaired                                                              |       | 6.5    | 6.0 | 433.0 | −1.094 | 0.274 | 0.251      | 3.15      | −1.015    | 0.325    | 0.429     |
| (n = 18)                                                              |       |        |     |     |      |         |           |           |           |           |           |
| Unrepaired/palliative                                                |       | 5.0    | 5.0 | −   | −    | 6.105   | −1.868    | 0.062     | 0.409     |           |           |
| (n = 58)                                                              |       |        |     |     |      |         |           |           |           |           |           |

CHD: Congenital heart disease; PAH: Pulmonary artery hypertension; IQR: Interquartile Range; Employed status included stable employment, homemaker, retired, student or other works; Using independent samples Mann–Whitney-U test; Cohen’s d is the appropriate effect size measure; *Compared between men and women
being unemployed/unstable employment (OR = 4.43, 95% CI 1.71–11.47, \( p = 0.002 \)). Life dissatisfaction was associated with being unmarried (OR = 4.63, 95% CI 1.2–17.86, \( p = 0.026 \)). Anxiety was associated with being unemployed/unstable employment (OR = 3.88, 95% CI 1.27–11.84, \( p = 0.017 \)) and having a complex CHD/PAH (OR = 4.84, 95% CI 1.33–17.54, \( p = 0.016 \)). Moreover, depression was associated with being unemployed/unstable employment (OR = 4.63, 95% CI 1.22–17.59, \( p = 0.025 \)).

Discussion

To the best of our knowledge, this study is the first to provide evidence regarding QOL and health status in adults with CHD in Vietnam, thus contributing to the essential knowledge on these matters in Vietnam. Hospitalized adults with CHD had reduced scores of QOL as measured using EQ-5D-5L. A significant number of hospitalized adults with CHD reported poor QOL, anxiety, and depression. Notably, we found that poor QOL and psychological problems were significantly related to biological and social characteristics including gender, age, marital status, education level, employment status, and CHD type in these patients.

Characteristic participants

In our study, 69.7% of adults with CHD were women. A recent study in Quebec indicated a higher prevalence of women among the patients with CHD (57%) [27]. Female predominance was observed in simple CHD such as atrial septal defect, ventricular septal defect, and patent ductus arteriosus. In particular, women constituted about 60–65% of patients with atrial septal defect [27, 28]. Similarly, 85.3% of the patients in our study had simple CHD and 48.6% an isolated atrial septal defect. A recent study in Vietnam reported that the prevalence of atrial septal defect among patients with CHD increased from children to adults (12.3% aged 0–9 years, 28.7% aged 10–19 years, 49.6% aged 20–39 years and 70.8% aged 40 years) [29].

We also noted that the rate of young patients, married/cohabiting patients, and patients with an education level of high school and above in our study was similar to that of the general population reported by the General Statistics Office of Vietnam in 2019 [http://tongdieutradanso.vn/trang-chu.html]: 35.8% vs 29.7%, 72.5% vs 69.2%, and 55% vs 36.6%, respectively.

Our patients presented a higher rate of unemployment than the general Vietnamese population (5.5% vs 2.04% in 2019, respectively; [https://data.worldbank.org/]). The high rate of unemployment in adults with CHD was also described in a recent study in Germany, amounting to 7.8% [30]. Furthermore, employment rate in our study also revealed a high rate of unstable employment (19.3%), suggesting a relationship between employment status and QOL and health status in adults with CHD.

Quality of life characteristics

Our findings demonstrated a high rate of poor QOL, as measured using EQ-5D-5L, in hospitalized adults with CHD in Vietnam. The participants of our study showed lower mean EQ-DS and EQ-VAS scores compared to healthy individuals from a general population study in Vietnam [31] (for EQ-DS, 0.792 [SD = 0.121] vs 0.91 [SD = 0.15], and for EQ-VAS, 66.3 [SD = 12.5] vs 87.4 [SD = 14.3], respectively). We noted that, in this study, most of the Vietnamese general population comprised women (61.5%), youths (aged < 35, 54.2%), and people living with their spouse/partner (65.5%) [31]. Similarly, of our patients, 69.7% were women, 35.8% were aged < 31, and 72.5% were married/cohabiting. Compared to our results, other studies had also reported a tendency of reduced EQ-DS and EQ-VAS scores among Vietnamese patients with chronic cardiovascular diseases [32, 33]. CHD is a chronic condition; if it is under-diagnosed or under-treated, it can result in reduced QOL and may even be life-threatening [4].

We highlighted reduced scores of QOL and health status in patients from Vietnam—a typical developing country—similar to the findings from previous studies in Iran [15]. Indeed, our participants with CHD had greater problems with pain/discomfort, anxiety/depression, mobility, and usual activities, similar to the results of a previous study [34]. Meanwhile, a previous systematic review and meta-analysis of 18 studies from developed countries found that QOL in young adults with CHD was comparable or better compared with the healthy controls [4]. This result may be explained by the differences in economic factors, educational status, cultural factors, and medical quality between developing and developed countries [10]. A report from APPROACH-IS on 15 countries observed that patient with CHD in countries with a lower power distance index and higher individualism tended to have a stronger sense of coherence. Further, a stronger sense of coherence positively contributed to QOL in adults with CHD [35]. Besides, high standards of living, which was expressed as high Gross Domestic Product per capita, high Human Development Index, and a good healthcare system, were common in developed countries but limited in developing countries. The APPROACH-IS report also noted that adults with CHD in countries with a higher standard of living had better physical and psychological health than those in countries with lower standards of living [36].
Life satisfaction
The prevalence of life dissatisfaction was low in adults with CHD in Vietnam (9.2%), with a high mean score of satisfaction of 25.2 points. This life satisfaction score appeared to be better than that recently reported in another developing country, Iran [15], but was similar to that of the 15 countries reported in APPROACH-IS [10]. Consistent with Vietnamese adults with other complex diseases such as spinal cord injury [37], our patients with CHD also presented trends of positive cognitive judgments about their life. Notably, positive thinking about life was common among the Vietnamese population, which ranked fifth out of 140 countries worldwide and second in the Asia Pacific region in the Happy Planet Index of 2019 (http://happyplanetindex.org/). Life satisfaction of one individual was influenced by specific country variables such as economic status, cultural factors, and social characteristics. Level of life satisfaction was more strongly associated with financial satisfaction in low- and middle-income countries than in high-income countries [38]. Likewise, life satisfaction of individuals in Asian countries was strongly affected by a society's national integration [39]. It explained the trending life
satisfaction in patients living in a country in Asia with a dynamic economy and culture such as Vietnam.

**Anxiety and depression of adults with congenital heart disease**

We noted the high prevalence of anxiety and depression in adults with CHD. In Vietnam, the prevalence of self-reported anxiety among adults with CHD is more than seven times higher than that of the general population (18.7% vs. 2.6%, respectively), while the prevalence of self-reported depression among adults with CHD is more than four times higher than that of the general population (11% vs 2.8%, respectively) [40]. The prevalence of anxiety and depression in our patients is similar to that in Vietnamese adults with cancer (18.7% vs 15.5%, respectively) [26]. Our findings were similar to that of a recent study, which reported that 30.7% of adults with CHD had mood disorders and 28% had anxiety disorders [20]. However, the exact prevalence of psychological disturbances, their geographical differences, and valid scales of evaluations are lacking. Based on the literature, adults with CHD constitute a high-risk group for developing emotional problems related to reduced exercise capacity, complications, and social barriers [5, 20, 41–44]. Therefore, screening for mental disorders in adults with CHD is important for early diagnosis and appropriate treatment because they require special medical attention and psychosocial interventions [45]. Notably, worrying causes patients to take positive or negative actions regarding the heart disease. At adequate levels, worrying is useful in promoting health-protective behaviours and adherence to treatment. However, high levels of stress can adversely affect health outcomes [46]. Furthermore, patients with high levels of anxiety have been reported to have fewer healthy coping strategies for stressful situations, an increased chance of adopting unhealthy behaviours, and non-adherence to treatment [47].

**Effect of biological and social characteristics to quality of life and health status**

Similar to the findings of previous studies, we observed that women with CHD tended to have reduced QOL scores and increased risks of psychological problems compared to men [7, 34, 43, 48]. Indeed, differences in QOL and psychological problems between women and men were also found in the general Vietnamese population [31, 49] and other countries [50, 51]. This may be related to women’s tendencies to being sensitive to the social environment and worrying about the vulnerability to diseases [52].

Our study found significantly lower scores of QOL as measured by EQ-DS and EQ-VAS in older adults compared to younger adults. Certain research found lower QOL in older adults compared to the younger adults with CHD but others noted increased or unchanged QOL in
older adults compared to younger adults [53]. A prior study found that older age plays a small role in predicting poor QOL, anxiety, and depression in adults with CHD [36]. In the current study, a logistic regression revealed that older age did not predict poor QOL and mental problems. Notably, we also found lower QOL scores in

![Symptoms of anxiety and depression by subgroups in adults with congenital heart disease. Anxiety was defined as HADS-A > 10. Depression was defined as HADS-D > 10. The prevalence of anxiety in patients with an unemployed status/unstable employment was higher than in those with an employed status (34.6%, n = 9 vs 14.1%, n = 11, p = 0.022; using Chi-square test, respectively). The prevalence of depression in patients with an unemployed status/unstable employment was higher than in those with an employed status (29.6%, n = 8 vs 5.1%, n = 4, p = 0.002; using the Fisher’s exact test, respectively). The prevalence of anxiety in patients who had complex CHD/PAH is higher than in those with simple CHD (40%, n = 6 vs 15.2%, n = 14, p = 0.022; using Chi-square test, respectively). The prevalence of depression of patients aged > 30 years is higher than that of patients aged ≤ 30 years (17.1%, n = 12 vs 0%, n = 0, p = 0.004; using Fisher’s exact test, respectively). The prevalence of depression in patients with an educational level of high school and below was higher than in those with an educational level of high school and above (22.4%, n = 11 vs 1.8%, n = 1, p = 0.001; using Fisher’s exact test, respectively). CHD: Congenital heart disease; HADS-A: Hospital Anxiety and Depression Scale-Anxiety subscale; HADS-D: Hospital Anxiety and Depression Scale-Depression subscale; PAH: Pulmonary artery hypertension]
Table 5  Univariable and multivariable predictors of poor quality of life and health status in adults with congenital heart disease on logistic regression

| Independent variables | Beta | Standard error | p value (Wald statistic) | OR (95%CI) |
|-----------------------|------|----------------|-------------------------|------------|
| **Univariable logistic regression** | | | | |
| **Poor quality of life** | | | | |
| Women | 0.295 | 0.43 | 0.492 | 1.34 (0.58; 3.12) |
| > 30 years old | 1.065 | 0.438 | 0.015 | 2.9 (1.23; 6.84) |
| Unmarried | 0.491 | 0.433 | 0.257 | 1.63 (0.7; 3.81) |
| Less than high school | 1.121 | 0.412 | 0.007 | 3.07 (1.37; 6.88) |
| Unemployed/ had unstable employment | 1.463 | 0.475 | 0.002 | 4.3 (1.7; 10.95) |
| Complex CHD or PAH | 1.016 | 0.559 | 0.069 | 2.76 (0.92; 8.26) |
| Unrepaired CHD or repaired palliation | 0.114 | 0.474 | 0.81 | 1.12 (0.44; 2.84) |
| **Life dissatisfaction** | | | | |
| Women | 0.014 | 0.724 | 0.984 | 1.01 (0.25; 4.19) |
| > 30 years old | −0.198 | 0.679 | 0.77 | 0.82 (0.22; 3.1) |
| Unmarried | 1.545 | 0.687 | 0.024 | 4.69 (1.22; 18.01) |
| Less than high school | 0.148 | 0.665 | 0.824 | 1.16 (0.32; 4.27) |
| Unemployed/ had unstable employment | 1.213 | 0.677 | 0.073 | 3.36 (0.89; 12.69) |
| Complex CHD or PAH | 19.087 | 10048.242 | 0.998 | – |
| Unrepaired CHD or repaired palliation | 19.175 | 8380.813 | 0.998 | – |
| **Anxiety** | | | | |
| Women | 1.504 | 0.779 | 0.054 | 4.5 (0.98; 20.73) |
| > 30 years old | 0.606 | 0.562 | 0.281 | 1.83 (0.61; 5.51) |
| Unmarried | 0.74 | 0.521 | 0.155 | 2.1 (0.76; 5.81) |
| Less than high school | 0.984 | 0.519 | 0.058 | 2.68 (0.97; 7.41) |
| Unemployed/ had unstable employment | 1.171 | 0.525 | 0.026 | 3.23 (1.15; 9.03) |
| Complex CHD or PAH | 1.312 | 0.602 | 0.029 | 3.71 (1.14; 12.08) |
| Unrepaired CHD or repaired palliation | 0.643 | 0.561 | 0.252 | 1.9 (0.63; 5.71) |
| **Depression** | | | | |
| Women | 0.854 | 0.805 | 0.289 | 2.35 (0.49; 11.37) |
| > 30 years old | 19.627 | 6436.026 | 0.998 | – |
| Unmarried | 1.112 | 0.623 | 0.074 | 3.04 (0.9; 10.32) |
| Less than high school | 2.768 | 1.066 | 0.009 | 15.92 (1.97; 128.52) |
| Unemployed/ had unstable employment | 2.066 | 0.664 | 0.002 | 7.9 (2.15; 29.01) |
| Complex CHD or PAH | 0.767 | 0.73 | 0.293 | 2.15 (0.52; 9.01) |
| Unrepaired CHD or repaired palliation | 0.719 | 0.664 | 0.279 | 2.05 (0.56; 7.54) |
| **Multivariable logistic regression** | | | | |
| **Poor quality of life** | | | | |
| Step 1 | | | | |
| Unemployed/ had unstable employment | 1.426 | 0.475 | 0.003 | 4.16 (1.64; 10.56) |
| Constant | -0.693 | 0.408 | 0.09 | – |
| Step 2 | | | | |
| Unemployed/ had unstable employment | 1.487 | 0.486 | 0.002 | 4.43 (1.71; 11.47) |
| Complex CHD or PAH | 1.138 | 0.587 | 0.053 | 3.12 (0.99; 9.87) |
| Constant | -1.695 | 0.676 | 0.012 | – |
| Life dissatisfaction | | | | |
| Step 1 | | | | |
| Unmarried | 1.533 | 0.689 | 0.026 | 4.63 (1.2; 17.86) |
| Constant | 1.344 | 0.458 | 0.003 | – |
| Anxiety defined | | | | |
| Step 1 | | | | |
older patients compared to young patients than the general Vietnamese populations [31].

Multivariable logistic regression showed that the likelihood of depression in unmarried adults with CHD is greater compared to married adults with CHD and EQ-VAS in unmarried women was significantly lower compared to married women. With reference to previous studies, we noted that reduced QOL, anxiety, and depression were more common in unmarried than married individuals. This may be related to the disadvantages of the psychological distress and socioeconomic and psychosocial resources that appear frequently in unmarried compared to married individuals, especially in women [50, 54]. For example, married individuals often share financial expenses and receive sympathy from spouses, while unmarried individuals do not have such support.

In this study, educational level was associated with QOL and health status. Prevalence of poor QOL, anxiety, and depression in patients with less than a high school education was higher than patients with high school education and above. Although studies regarding educational level in adults with CHD in developing countries are limited, previous studies in developed countries have reported similar results between education level and QOL and mental disorders [7, 30, 48].

Our results also indicated that patients who had an unemployed status/unstable employment had a higher risk of having poor QOL, anxiety, and depression; this is consistent with the results of a previous study on adults with CHD [7]. Generally, unemployment or unstable employment negatively affect self-assessed health [55, 56]. We believe that the impact of unemployment or unstable employment on poor QOL results from declined financial consequences, reduced self-esteem, and barriers in social relationships. Therefore, patients with CHD should be provided with stable employment, which may help them cope with their illness, encourage them to overcome psychological barriers, and improve their social relationships and QOL.

Furthermore, we observed the negative effect of complex CHD/PAH on the QOL of patients with CHD. Previous studies have reported a negative association between regular physical activity and anxiety [57, 58]. Exercise and physical activity are useful to gain self-confidence. Exercise and physical activity are also good opportunities to meet or socialize with others and can help improve one’s mood and cope in a healthy way. However, exercise intolerance was common in patients with complex CHD or PAH [59].

The high rate of reduced QOL in our hospitalized adults with CHD was consistent with a recent study that showed the association between worse QOL and hospitalization in adults with CHD. Specifically, adults with CHD who had been hospitalized during the previous

| Independent variables | Beta (Step 1) | Standard error (Step 1) | p value (Wald statistic) (Step 1) | OR (95% CI) (Step 1) |
|-----------------------|--------------|-------------------------|----------------------------------|---------------------|
| Unemployed/ had unstable employment | 1.141 | 0.526 | 0.03 | 3.13 (1.12; 8.76) |
| Constant | 0.636 | 0.412 | 0.123 | – |
| **Step 2** | | | | |
| Unemployed/ had unstable employment | 1.29 | 0.552 | 0.02 | 3.63 (1.23; 10.72) |
| Complex CHD or PAH | 1.43 | 0.636 | 0.024 | 4.19 (1.2; 14.56) |
| Constant | −0.616 | 0.701 | 0.379 | – |
| **Step 3** | | | | |
| Women | 1.62 | 0.849 | 0.056 | 5.05 (0.96; 26.67) |
| Unemployed/ had unstable employment | 1.36 | 0.57 | 0.017 | 3.88 (1.27; 11.84) |
| Complex CHD or PAH | 1.58 | 0.657 | 0.016 | 4.84 (1.33; 17.54) |
| Constant | – | | | – |

CHD: Congenital heart disease; PAH: Pulmonary artery hypertension; OR: Odds Ratio; CI: Confidence Interval. Poor quality of life was defined as EQ-VAS < 65; Life dissatisfaction was defined as SWLS < 20; Anxiety was defined as HADS-A > 10; Depression was defined as HADS-D > 10.
12 months had significantly lower EQ-VAS and SWLS scores, and higher HADS-D scores than those who had not been hospitalized [60]. Notably, medical sources in developing countries are limited. For example, in our hospital—a national referral cardiovascular hospital—the number of specialists for adults with CHD was still not enough, especially in the outpatient clinic. This maybe because of inadequacies in diagnosis, treatment, and intervention and psychological problems in adults with CHD. In this context, we suggest a consistent approach such as a targeted screening programme for reduced QOL in hospitalized adults with CHD, which would be useful to understand QOL better. Then, we would have the information to adjust the appropriate health policies and screening programme for adults with CHD, including inpatients and outpatients, to improve their QOL.

To ensure the accuracy of patient self-reported information, a high number of inpatients with CHD were excluded in our study. We attempted to understand the reasons for the high number of inpatients who declined participation. Records during interviews of these patients noted that some patients could be classified as showing rejection of illness identity, consistent with adults with chronic disorders [61]. This suggested the need for a future study on illness identity in adults with CHD in Vietnam. Besides, we had given particular attention toward encouraging participants to fill up the questionnaire by themselves, which is useful in collecting the maximum number of accurate responses in patient self-reported outcome research.

Limitations
This study had few limitations. First, this was a cross-sectional study, which does not prove causality between reduced QOL, health status, and biological and social characteristics. Second, although this study was conducted at a reference hospital in Vietnam, using a single location may have caused a sampling bias, which may have affected the representativeness of the study. Third, our study focused on hospitalized patients, which may present a higher rate of reduced QOL compared to outpatients. Fourth, exclusion of a high number of inpatients with CHD could cause biases. Fifth, using patient self-reported data may cause certain biases, since responses could be exaggerated or under-reported. Finally, because some subgroups had small samples, our study had just enough participants to divide each biological and social characteristic into two subgroups and analyse the differences.

Conclusions
To the best of our knowledge, our study provides the first evidence on the high prevalence of poor QOL, anxiety, and depression in hospitalized adults with CHD in Vietnam. The findings highlight the relationship between poor QOL, life dissatisfaction, anxiety, depression, and biological-social characteristics including the female gender, older age, unmarried status, educational level lower than high school, unemployed status/unstable employment, and complex CHD/PAH. Therefore, we recommend that health-related QOL of hospitalized adults with CHD, especially for those presenting the abovementioned characteristics, should be screened and monitored.

Abbreviations
CHD: Congenital Heart Disease; CI: Confidence Intervals; EQ-SD-5L: EuroQOL-5 Dimensions-5 Level; EQ-DS: EuroQOL-Descriptive System; EQ-VAS: EuroQOL Visual Analogue Scale; HADS: Hospital Anxiety and Depression Scale; HADS-A: Hospital Anxiety and Depression Scale Anxiety subscale; HADS-D: Hospital Anxiety and Depression Scale Depression subscale; OR: Odds Ratios; PAH: Pulmonary Artery Hypertension; QOL: Quality of Life; SWLS: Satisfaction with Life Scale.

Supplementary Information
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Additional file 1. Flow diagram of the selection strategy of adults with congenital heart disease.
Additional file 2. English version of EuroQOL-5 dimensions-5 level.
Additional file 3. English version of Satisfaction with Life Scale.
Additional file 4. English version of Hospital Anxiety and Depression Scale.
Additional file 5. The modified Vietnamese translation versions for quality of life and health status.

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Authors’ contributions
THT and NTK conceived the study, designed the data collection tools, monitored the data collection, analysed the data, and drafted and revised the paper. MNTN, DLD, HTN, TTL, and HAL monitored data collection, analysed the data, and revised the draft of the study. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed in the current study will be made available by the corresponding author upon reasonable request.
Declarations

Ethics approval and consent to participate
The Council for Science and Ethics Committee for the human study, Department of Cardiology, Hanoi Medical University (no: 6655/QD-DHYHN) of Vietnam had approved this study. All participants and legally authorized representatives of minors below 18 years of age provided written informed consent after receiving clear explanation of the study objective and procedures. Participants were allowed to withdraw from the interview at any time. All personal information was kept confidential and only anonymous data were utilized for the study. All the experiment protocol for involving human data was in accordance with the Declaration of Helsinki.

Consent for publication
All participants provided their consent for publication.

Competing interests
The authors have no competing interests to declare.

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