Quality of life in Maltese adults with congenital heart disease: a second look – An APPROACH-IS substudy

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Highlights

Background
A first quality of life (QOL) study among Maltese adults with congenital heart disease (ACHD) in 2016 found no significant differences when compared to the general population. The aims of the present study were to (1) compare QOL between Maltese and other European ACHD patients and (2) investigate medical predictors (i.e. number of surgical/non-surgical interventions, heart failure, arrhythmias, pacemaker/implantable cardioverter-defibrillator, cardiac hospitalisation during preceding year, follow-up frequency, other medical conditions, mood/anxiety/psychiatric disorders) of QOL in Maltese patients.

Methods
Data collected during “Assessment of Patterns of Patient-Reported Outcomes in Adults with Congenital Heart disease–International Study” (APPROACH-IS) was used. QOL was measured using linear analog scale (LAS) and Satisfaction With Life Scale (SWLS). QOL in 109 Maltese and 1510 European participants was compared. Multivariable logistic regression was used to test the predictive value of medical factors on QOL in Maltese patients.

Results
There were no significant differences in QOL between the two cohorts (mean LAS Malta 80.51 (95% CI 77.96,83.07) vs. European 79.43 (95% CI 78.65,80.21) (p=0.776); mean SWLS Malta 26.00 (95% CI 24.94,27.06) vs. European 26.26 (95% CI 25.95,26.57) (p=0.288)) and no significant differences when cohorts were divided by gender and age. Only a mood/anxiety/other psychiatric disorder significantly predicted poorer QOL on both scales in Maltese patients (LAS (β=.389, p<0.001), SWLS (β=.352, p=0.001)).
INTRODUCTION

With the majority of patients born with congenital heart disease (CHD) nowadays surviving into adulthood [1,2], there has been increasing interest in the study of quality of life (QOL) in adults with congenital heart disease (ACHD) [3,4]. An initial QOL study in Maltese ACHD patients used vitality and mental health questionnaires from the 36-item short-form health survey (SF-36), which had previously been applied to the general Maltese population during the 2008 European Health Interview Survey [5]. This study found no significant differences in QOL between ACHD patients and age- and sex-matched general Maltese subjects, and identified hospitalisation within the previous twelve months as the only clinical factor out of the ones studied to bear a significant negative impact on QOL in the patient cohort [5].

The present study utilises data from the large multi-centre collaboration “Assessment of Patterns of Patient-Reported Outcomes in Adults with Congenital Heart disease – International Study” (APPROACH-IS) [6,7] in which Malta was a participating centre, in order to gain further insight into QOL among Maltese ACHD patients. The aims were: (a) to compare QOL in Maltese ACHD patients with ACHD patients in other participating European countries, and (b) to investigate the role of several medical factors as predictors of QOL among Maltese patients.

METHODS

Study protocol

APPROACH-IS is a cross-sectional study conducted in partnership with the International Society of Adult Congenital Heart Disease (ISACHD). Data was collected from 15 countries from 5 continents between April 2013 and March 2015 using self-reporting questionnaires administered in person or sent by mail to eligible ACHD patients. Inclusion criteria were: (a) diagnosis of CHD before the age of 10 years, (b) age 18 years or older at enrolment (c) ongoing follow-up in a CHD centre or included in a national/regional database and (d) being in possession of physical, cognitive and language capabilities to answer the self-reporting questionnaires. Full details of rationale, design and methods have been previously published [6]. In Malta, the English language version of the questionnaires was used due to lack of availability of questionnaires appropriately translated to the Maltese language. These were sent by surface mail to eligible patients extracted from the local ACHD database. Medical data was obtained through review of participants’ medical records. Written informed consent was obtained from each participant. Institutional review board approval was obtained from participating centres where required; in Malta, the study was given clearance by the University of Malta Research Ethics Committee and the Data Protection Officer at Mater Dei Hospital.

Variables and measurements

Based on thorough conceptual work [8], QOL was defined as “the degree of overall life satisfaction that is positively or negatively influenced by individuals’ perception of certain aspects of life important to them, including matters both related and unrelated to health” [9]. Following this definition, for the purposes of APPROACH-IS, QOL was assessed using the Linear Analog Scale (LAS) and the Satisfaction With Life Scale (SWLS), both of which have good psychometric properties when used with ACHD patients [10]. LAS consists of a vertically-oriented graded line with indicators from 0 to 100, with 0 representing the worst imaginable and 100 representing the best imaginable QOL [10]. SWLS consists of five statements each requiring a response of 1 (strongly disagree) to 7 (strongly agree), with total scores ranging from 5 to 35 [11]. An SWLS score of 20 is the neutral point on the scale [6]. CHD lesion severity was classified in accordance with the recommendations of Task Force 1 of the 32nd Bethesda Conference [12].

The eight medical factors that were investigated for their role as predictors of QOL among Maltese patients were: (i) number of surgical or non-surgical interventions up to date of enrolment, (ii) congestive heart failure (CHF), (iii) arrhythmias, (iv) need for pacemaker or implantable cardioverter-defibrillator (ICD) implantation, (v) in-patient hospitalisation for cardiac reasons during preceding year, (vi) frequency of cardiac specialist follow-up, (vii) other medical (non-cardiac) conditions and (viii) documented mood, anxiety or other psychiatric disorders.

Statistical methods

To address the first study aim, a comparison of QOL as assessed by LAS and SWLS was performed between Maltese patients (“Maltese cohort”) and patients from all other participating European countries (“European cohort”); this was followed by a sub-analysis based on gender and age category. Younger age category was defined as age ≤ 30 years and older age category as age > 30 years. The 30-years age cut-off was chosen arbitrarily as one that generated a fair numerical split in the Maltese cohort. Categorical variables were analysed using Chi-square test, while in the case of smaller sample sizes, Fisher's
Exact test was applied. All numerical variables showed a non-normal distribution on Shapiro-Wilk testing, thus non-parametric tests (i.e. Mann-Whitney U and Kruskal-Wallis tests) were applied for their analyses.

To address the second study aim, multivariable linear regression analysis was used to test whether the eight chosen medical factors significantly predicted QOL among Maltese ACHD patients. In view of the small number of patients in the Maltese cohort, patients were grouped into two categories for each of the eight medical variables in order to avoid further reducing the sample sizes. For this purpose, frequency of cardiac surgery / interventional procedure was categorised as “up to 1” or “more than 1” procedure and specialist ACHD follow-up was categorised as “at least every 2 years” or “less often than every 2 years”. All analyses were performed using SPSS 21 (IBM® SPSS® 21, SPSS Inc., Chicago IL, USA). Statistical significance was defined as p<0.05 and all tests were two-sided.

RESULTS

Participant characteristics

In Malta, 119 of the 378 eligible ACHD patients agreed to participate in the study, of whom 109 completed LAS and SWLS questionnaires and were included in current analyses (“Maltese cohort”). Of the 1616 ACHD responders from the other 7 participating European countries, LAS and SWLS questionnaires were completed by 1510 participants (“European cohort”): (Leuven, Belgium n= 268; Lyon, France n= 89; Milan, Italy n= 59; Oslo, Norway n= 169; Sweden (Gothenburg, Stockholm, Umea) n= 448; Bern, Switzerland n= 232; the Netherlands (ConCor registry) n= 245). Table 1 summarises the participant characteristics for the two study cohorts. Maltese patients were significantly younger (median age 27 years vs. 34 years; p<0.001) while sex distribution was not significantly different between the two cohorts. Differences in distribution of CHD lesion complexity between the 2 cohorts did not reach statistical significance. Moderate lesion complexity was the commonest in both cohorts (51.4% in Maltese cohort; 47.2% in European cohort), although there was a larger proportion of patients with lesions of great complexity in the European cohort (21.1%) when compared to the Maltese cohort (11.9%).

Comparison of QOL between Maltese and European cohorts

There was no significant difference in QOL on either scale between Maltese and European participants. Mean QOL on the LAS was 80.51 (95% CI 77.96, 83.07) (median 80.00) for Maltese patients compared to 79.43 (95% CI 78.65, 80.21) (median 80.00) for patients in the European cohort (p=0.776). Mean QOL on the SWLS was 76.97 (95% CI 76.12, 77.83) (median 77.00) for Maltese patients compared to 77.49 (95% CI 76.62, 78.36) (median 77.00) for European patients (p=0.288). Comparisons based on gender and age category also demonstrated no significant differences in QOL on either scale (Table 2).

Medical factors as predictors of QOL in the Maltese ACHD cohort

The medical factors investigated among the 109 patients in the Maltese cohort are summarised in Table 3. Regression analysis indicated that the medical predictor model explained 17.0% of the variance in LAS score (R²=.233, F(8,98)=3.718, p=0.001) and 9.4% of the variance in SWLS score (R²=.163, F(8,98)=2.379, p=0.022). The only factor to significantly predict QOL using either score was the presence of a mood, anxiety or other psychiatric disorder (LAS (β = -0.389, p<0.001), SWLS (β = -0.352, p=0.001)). More frequent specialist ACHD follow-up, defined as follow-up at least every 2 years, was significantly predictive of better QOL as measured by LAS (β = .210, p=0.028).

DISCUSSION

Several factors in the day-to-day life of adults with congenital heart disease, including symptoms, frequent hospital appointments and need for repeat surgeries and structural cardiac interventions, can be expected to have a negative impact on QOL. Findings of QOL research in CHD have been inconsistent, in good part due to differences in methodological approaches among studies [3]. Furthermore, it is becoming increasingly clear that medical factors might not be as important in contributing to QOL when compared to certain psychosocial factors [13,14].

In a previous study, Maltese ACHD patients showed no significant differences in QOL when compared to the general Maltese population, as assessed using vitality and mental health elements from the SF-36 questionnaire [5]. In the present study, Maltese ACHD patients also reported good QOL as measured by LAS and SWLS and this was not significantly different from that of patients from other European countries. Indeed, Maltese participants had the fourth best QOL overall among all participating countries in the main APPROACH-IS study [7]. As per the second study aim, the presence of mood, anxiety or other psychiatric disorders was revealed to be the only medical factor to predict a poorer QOL as assessed by either scale among Maltese ACHD patients. It has been shown that ACHD patients are at increased risk of mood and anxiety disorders and that these conditions tend to be under-treated in this patient population [15]. This finding underlines the importance of close collaboration with clinical psychologists to ensure timely diagnosis and management of such psychiatric disorders, as well as the introduction of means to routinely screen for psychological difficulties from an early stage [16,17]. Interestingly, and contrary to expectation, more

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### Table 1. Baseline characteristics of participants in the two study cohorts

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Maltese cohort (N=109)</th>
<th>European cohort (N=1510)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender (n (%))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>50 (45.9)</td>
<td>765 (50.7)</td>
<td>0.372</td>
</tr>
<tr>
<td>Females</td>
<td>59 (54.1)</td>
<td>745 (49.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Median age, years</strong></td>
<td>27 (IQR: 22-34)</td>
<td>34 (IQR: 26-45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Lesion complexity (n (%))</strong></td>
<td></td>
<td></td>
<td>0.068</td>
</tr>
<tr>
<td>Simple</td>
<td>40 (36.7)</td>
<td>479 (31.7)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>56 (51.4)</td>
<td>712 (47.2)</td>
<td></td>
</tr>
<tr>
<td>Great</td>
<td>13 (11.9)</td>
<td>319 (21.1)</td>
<td></td>
</tr>
</tbody>
</table>

IQR = interquartile range
frequent ACHD specialist follow-up was found to be a significant predictor of better QOL as assessed by LAS, though it had no significant predictive value on SWLS. One explanation for this finding could be the establishment of a better rapport between ACHD specialist and patient because of more frequent clinical encounters, which could in turn lead to the earlier detection of issues that warrant psychological input. All other chosen predictors had very small numbers recorded and this could have affected the result of multivariable logistic regression analysis. The presence of a mood, anxiety or other psychiatric disorder was the only significant predictor of QOL on both scales. More regular follow-up was predictive of better QOL as assessed by LAS.

Table 2. Comparison of quality of life (QOL) on the Linear Analog Scale (LAS) and Satisfaction With Life Scale (SWLS) between ACHD patients in the Maltese and European cohorts, divided by gender and by age group

<table>
<thead>
<tr>
<th>QOL</th>
<th>Male participants</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maltese (n=50)</td>
<td>European (n=765)</td>
</tr>
<tr>
<td>LAS</td>
<td>80.36 (95% CI 76.82, 83.90) (80.00)</td>
<td>80.29 (95% CI 79.22, 81.36) (80.00)</td>
</tr>
<tr>
<td>SWLS</td>
<td>25.88 (95% CI 24.35,27.41) (27.00)</td>
<td>26.16 (95% CI 25.73,26.60) (29.00)</td>
</tr>
</tbody>
</table>

Female participants

<table>
<thead>
<tr>
<th>Maltese (n=59)</th>
<th>European (n=745)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAS</td>
<td>80.64 (95% CI 76.91, 84.38) (80.00)</td>
</tr>
<tr>
<td>SWLS</td>
<td>26.10 (95% CI 24.60, 27.60) (28.00)</td>
</tr>
</tbody>
</table>

Younger age category participants (≤ 30 years of age)

<table>
<thead>
<tr>
<th>Maltese (n=65)</th>
<th>European (n=572)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAS</td>
<td>81.18 (95% CI 78.07, 84.29) (80.00)</td>
</tr>
<tr>
<td>SWLS</td>
<td>26.03 (95% CI 24.64, 27.42) (28.00)</td>
</tr>
</tbody>
</table>

Older age category participants (> 30 years of age)

<table>
<thead>
<tr>
<th>Maltese (n=64)</th>
<th>European (n=936)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAS</td>
<td>79.52 (95% CI 75.03, 84.02) (80.00)</td>
</tr>
<tr>
<td>SWLS</td>
<td>25.95 (95% CI 24.25, 27.66) (29.00)</td>
</tr>
</tbody>
</table>

QOL on both scales is expressed as mean (95% CI) followed by median

Table 3. Medical factors investigated as QOL predictors among Maltese ACHD patients (N=109)

<table>
<thead>
<tr>
<th>Medical factor</th>
<th>n (%)</th>
<th>LAS</th>
<th>SWLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 cardiac surgery / interventional procedure</td>
<td>82 (75.2)</td>
<td>.087</td>
<td>0.349</td>
</tr>
<tr>
<td>Documented congestive heart failure</td>
<td>3 (2.8)</td>
<td>.123</td>
<td>0.241</td>
</tr>
<tr>
<td>Documented arrhythmias</td>
<td>9 (8.3)</td>
<td>.101</td>
<td>0.441</td>
</tr>
<tr>
<td>Permanent pacemaker/ implantable cardioverter-defibrillator</td>
<td>3 (2.8)</td>
<td>-.115</td>
<td>0.317</td>
</tr>
<tr>
<td>In-patient cardiac admissions in previous year</td>
<td>6 (5.5)</td>
<td>-.015</td>
<td>0.892</td>
</tr>
<tr>
<td>Other medical conditions</td>
<td>51 (46.8)</td>
<td>-.130</td>
<td>0.154</td>
</tr>
<tr>
<td>Specialist ACHD follow-up at least every 2 years</td>
<td>54 (49.5)</td>
<td>0.210</td>
<td>0.028</td>
</tr>
<tr>
<td>Documented mood / anxiety / other psychiatric disorder</td>
<td>6 (5.5)</td>
<td>-.389</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The presence of a mood, anxiety or other psychiatric disorder was the only significant predictor of QOL on both scores. More regular follow-up was predictive of better QOL as assessed by LAS.

Overall, the eight medical factors studied explained only a small proportion of the variance in QOL among Maltese ACHD patients. This finding is in line with previously reported observations [7,13] reinforcing the notion that objective medical variables bear very little weight in determining QOL in ACHD patients. The main APPROACH-IS paper by Apers et al reported several social characteristics, including older age, job seeking, being unemployed and never having been married, as being linked with poorer QOL, even though these factors still explained only a small proportion of variability in QOL in the whole APPROACH-IS cohort [7].

Methodological limitations

The main limitation of this study is the small number of patients in the Maltese ACHD cohort, in itself an inevitable consequence of the small Maltese population. Despite efforts to collapse all eight medical variables into two categories, 5 of the 8 medical predictors had very small numbers recorded and this could have affected the result of multivariable logistic regression analysis. Maltese ACHD participants were significantly younger compared to those in the European cohort and this could have affected the outcome of QOL comparison analysis. This is particularly relevant in light of findings reported in the main APPROACH-IS paper where older age was one element linked with poorer QOL [7]. However, in the present study, comparison of QOL by age category failed to demonstrate a significant difference between the two cohorts.

CONCLUSIONS

Maltese ACHD patients have a very good QOL, which is on par with that of their European counterparts. Though thorough specialist long-term follow-up remains imperative to ensure good clinical outcomes, most medical factors appear not to bear as much weight in determining QOL as one might expect. The presence of mood, anxiety and other psychiatric disorders...
appears to play an important role in determining QOL in the Maltese patient population and, thus, more efforts should be made to facilitate access to clinical psychologists through clearer referral pathways to ensure earlier diagnosis and treatment of these disorders.

Declarations of interest

The authors declare no conflicts of interest.

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