Original Article

Can the inevitable be prevented? – An analysis of loss to follow-up among grown-ups with congenital heart disease in Malta

Maryanne Caruana, Oscar Aquilina, Victor Grech

Abstract

Aims: To investigate the prevalence of loss to follow-up, factors predisposing to loss to follow-up and the outcome of recall into specialist care among grown-ups with congenital heart disease (GUCH) of moderate or severe complexity prior to the introduction of formal transition in Malta.

Methods: Medical documentation for all live patients with tetralogy of Fallot, aortic coarctation/interrupted aortic arch, partial and complete atrioventricular septal defect, Fontan-type circulation and transposition of the great arteries in our institutional database aged ≥16 years was analysed to determine follow-up status. Patients lost to follow-up were recalled through a postal appointment. Ordinal logistic regression was used to analyse the effect of gender, CHD complexity, consistency of paediatric cardiology follow-up during childhood, number of cardiac surgical/interventional procedures and use of long-term cardiac medications on loss to follow-up.

Results: Forty-one of 187 patients (21.9%) (27 males; 34 with moderate disease) had been lost to follow-up. Limited paediatric cardiology input (OR, 5.08; 95% CI, 1.77-14.63) (p=0.003), ≤1 surgical/interventional procedures (OR, 3.34; 95% CI, 1.09-10.26) (p=0.035) and no long-term cardiac medications (OR 7.34; 95% CI, 1.74-31.02) (p=0.007) were associated with higher risk of loss to follow-up. A positive response to recall was obtained from 33/41 (80.5%) patients. Significant cardiac morbidity was found in 5/33 (15.2%) patients upon reassessment.

Conclusions: Loss to specialist follow-up occurs even in health systems with little perceived barriers to medical care. Consistent specialist input during all stages and patient and family education through formal transition can help ensure a smoother transfer to GUCH care.

Keywords

Congenital Heart Defects; Lost to Follow-up; Transition to Adult Care

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Introduction

Major advances in cardiac surgery and transcatheter interventions have made it possible for most children born with congenital heart disease (CHD) to survive into adulthood.[1-3] However, complete cure is seldom achieved and lifelong specialist follow-up is required to allow early detection and timely management of significant recurrent or residual structural lesions and arrhythmias as these patients grow older.[4] Several lesion-specific guidelines containing indications on the nature and frequency of long-term follow-up for these patients have been published.[5-7] Lapses of care resulting from loss to follow-up represent a major set-back in this surveillance process and can have a negative impact on long-term outcomes.[8-9]

The incidence of CHD in Malta is 8/1000 live births, which is similar to that in other European

countries.[10] Transfer of care from paediatric to adult services across all specialties takes place at the age of 14-16 years. Virtually all congenital cardiac surgery on children and adults is carried out in overseas tertiary referral centres, in the United Kingdom, through a bilateral national health service agreement, while a number of structural cardiac interventions are carried out locally by visiting specialists. A structured paediatric cardiology service started operating in the main teaching hospital in the early 1990s. A Grown-Up Congenital Heart disease service was set up a few years later, while a formal transition process was instituted at the end of 2015. Up to the time of writing, there was no clinical nurse specialist cover for paediatric cardiology, transition or GUCH clinics.[11]

The aims of this study were (a) to determine the prevalence of loss to GUCH follow-up (b) to investigate potential factors predisposing to loss to follow-up and (c) to analyse the outcome of an exercise in recall into GUCH care in a cohort of Maltese adult patients with CHD of moderate or severe complexity in the period preceding the introduction of a formal transition process.

Methods

(a) Study cohort and prevalence of loss to GUCH follow-up

Five specific congenital cardiac lesions of moderate or severe complexity – (i) tetralogy of Fallot (TOF), (ii) aortic coarctation and interrupted aortic arch (CoA/IAA), (iii) partial and complete atrioventricular septal defects (AVSD), (iv) univentricular physiology with Fontan-type palliation (UVH-Fontan), (v) transposition of the great arteries (TGA) with arterial or atrial switch repair - were chosen arbitrarily for inclusion in this study, based on the well-established notion that all these lesions warrant regular long-term specialist follow-up.[5-7] A query for each of these lesions as the primary diagnosis was run in our institutional congenital cardiac database (MAPCAD)[3,12] at the end of 2013, among Maltese subjects born before end December 1997 (and thus aged 16 years or over by time of data extraction). Following this initial query, only live subjects whose complete medical documentation could be traced were subsequently included. Non-Maltese nationals that might have entered the congenital cardiac system upon relocating to the islands were purposefully excluded to avoid the potential bias introduced by differences in access to medical care. The study protocol was approved by the University of Malta Research Ethics Committee and conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Clinical details and follow-up records were obtained from hospital paper notes and digital appointment systems in use at our institution. Loss to GUCH follow-up was defined as lack of written or digital documentation attesting to ongoing clinical encounters within the GUCH service as of the age of 16 years.

(b) Investigation of potential factors predisposing to loss to GUCH follow-up

The potential impact of five factors – (a) patient gender (b) CHD complexity (c) paediatric cardiology follow-up during childhood (d) number of cardiac surgical/interventional procedures (e) use of long-term cardiac medications – on loss to GUCH follow-up were investigated. CHD complexity was classified in line with the recommendations of Task Force 1 of the 32nd Bethesda Conference.[4] The term "paediatric cardiology follow-up during childhood" referred to significant input by a local or visiting paediatric cardiologist in the management of CHD up to the age of transfer to adult care, and was classified as 'limited' or 'regular'. "Surgical/interventional procedures" refers to any open surgical procedure or transcatheter intervention undertaken to repair or relieve the original congenital defect and any important residual or recurrent lesions related to it but excluded diagnostic cardiac catheter studies. This term also included electrophysiological procedures and the implantation of a permanent pacemaker or implantable cardioverter-defibrillator for the management of significant arrhythmias. "Long-term cardiac medications" refers to any medications being used for the management of ventricular systolic and/or diastolic dysfunction, antiarrhythmic drugs, antiplatelet and anticoagulant agents and antihypertensive medications.

(c) Analysis of exercise of recall into GUCH care

All subjects that had been lost to follow-up were recalled to GUCH clinic through a postal appointment as per our institution's outpatient policy, with a second appointment given in case of a negative initial response. The responses to recall and cardiac morbidity at time of reassessment were

obtained from the hospital digital patient management systems and medical notes. The term "reassessment" refers to the GUCH clinic visit and subsequent imaging, functional testing and arrhythmia assessment triggered by the cardiologist. "Significant cardiac morbidity" at time of reassessment refers to a significant structural lesion, impairment of functional status or arrhythmias requiring a prompt surgical, percutaneous or electrophysiological intervention or change in medical management.

(d) Statistical methods

Descriptive statistics included proportions for categorical variables and mean ± 1 standard deviation for continuous variables. Ordinal logistic regression was used to generate odds ratios (OR) for loss to GUCH follow-up based on patient gender (male vs. female), moderate vs. severe lesion complexity, limited vs. regular paediatric cardiology follow-up, ≤1 vs. >1 surgical/interventional procedure and no vs. on long-term cardiac medications. All analyses were performed using SPSS 21 (IBM® SPSS® 21, SPSS Inc., Chicago IL, USA). Statistical significance was defined as $p<0.05$.

Results

(a) Study cohort characteristics and prevalence of loss to follow-up

The initial database query returned 211 subjects with one of the above congenital cardiac lesions aged ≥16 years. Twenty-four subjects could not be traced or had died before the time of data extraction and were excluded. The study cohort consisted of 187 patients as follows: TOF = 70, CoA/IAA = 56, AVSD = 34, UVH-Fontan = 13, TGA = 14 (Figure 1). The main characteristics of these patients are summarised in Table 1. Forty-one of 187 patients (21.9%) (27 males; 34 moderate CHD) had been lost to GUCH follow-up: TOF = 10/70 (14.3%), CoA/IAA = 22/56 (39.3%), AVSD = 4/34 (11.8%), UVH-Fontan palliation = 1/13 (7.7%), TGA = 4/14 (26.7%).

(b) Factors predisposing to loss to GUCH follow-up

Ordinal logistic regression analysis identified the following factors to be associated with a significantly higher risk of loss to GUCH follow-up: limited paediatric cardiology follow-up (OR, 5.08; 95% CI, 1.77-14.63), ≤1 surgical/interventional procedure (OR, 3.34; 95% CI, 1.09-10.26) and no long-term cardiac medications (OR 7.34; 95% CI, 1.74-31.02). Patient gender and lesion complexity (moderate compared to severe complexity) had no statistically significant impact on loss to follow-up (Table 2).

(c) Analysis of recall into GUCH care

The mean age at time of recall for the 41 patients that were lost to GUCH follow-up was 34.73 ± 13.88 years. A positive response was obtained from 33/41 (80.5%) patients (21 males; moderate CHD = 28/34, severe CHD = 5/7). Significant cardiac morbidity was found in 5/33 (15.2%) patients upon reassessment in the GUCH service (Figure 2). Two patients with previous transannular patch TOF repair needed surgical pulmonary valve replacement (PVR) for severe pulmonary regurgitation (PR) and one patient with TOF and previous palliative open pulmonary valvotomy was offered balloon pulmonary valvuloplasty for severe recurrent valvular pulmonary stenosis (PS). One patient with unrepaired partial AVSD and severe left atrioventricular valve (LAVV) regurgitation underwent surgical defect closure and LAVV repair and one patient with Eisenmenger AVSD required optimisation of pulmonary vasodilator treatment.

***Table 1**: Characteristics of the 187 patients included in the study*

Characteristic	No. of patients (n (%))
Male gender	107 (57.2)
Moderate complexity	145 (77.5)
≤1 surgical/interventional procedure	111 (59.4)
No cardiac medications	103 (65.2)
Limited paediatric cardiology follow-up	60 (32.1)

Figure 1: Generation of study cohort. The term "missing" refers to subjects logged in the institutional congenital cardiac database (MAPCAD) that either died before the end of 2013 (time of data extraction) or who could not be traced on the institutional data information system. (AVSD = atrioventricular septal defect; CoA = coarctation of the aorta; IAA = interrupted aortic arch; TGA = transposition of great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart)

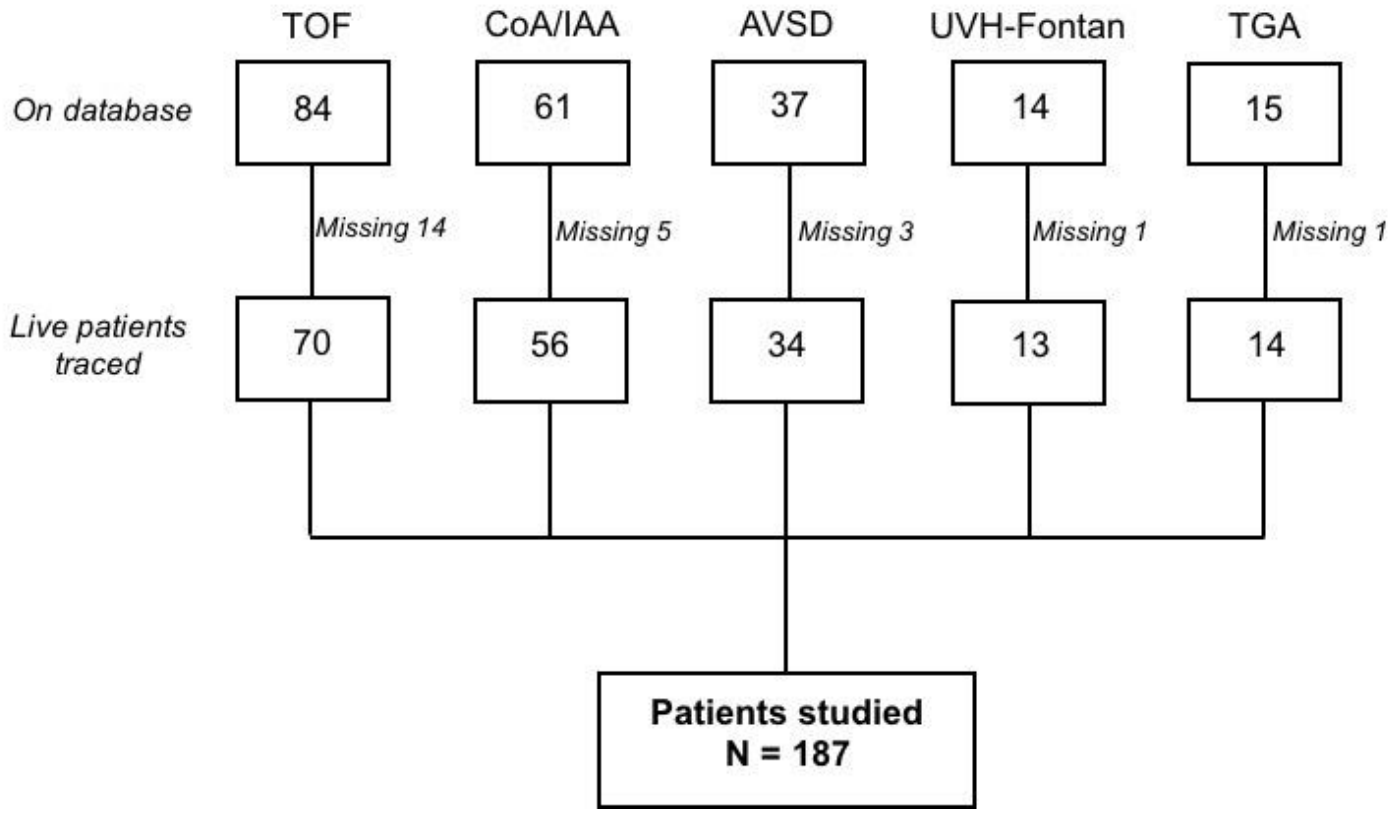
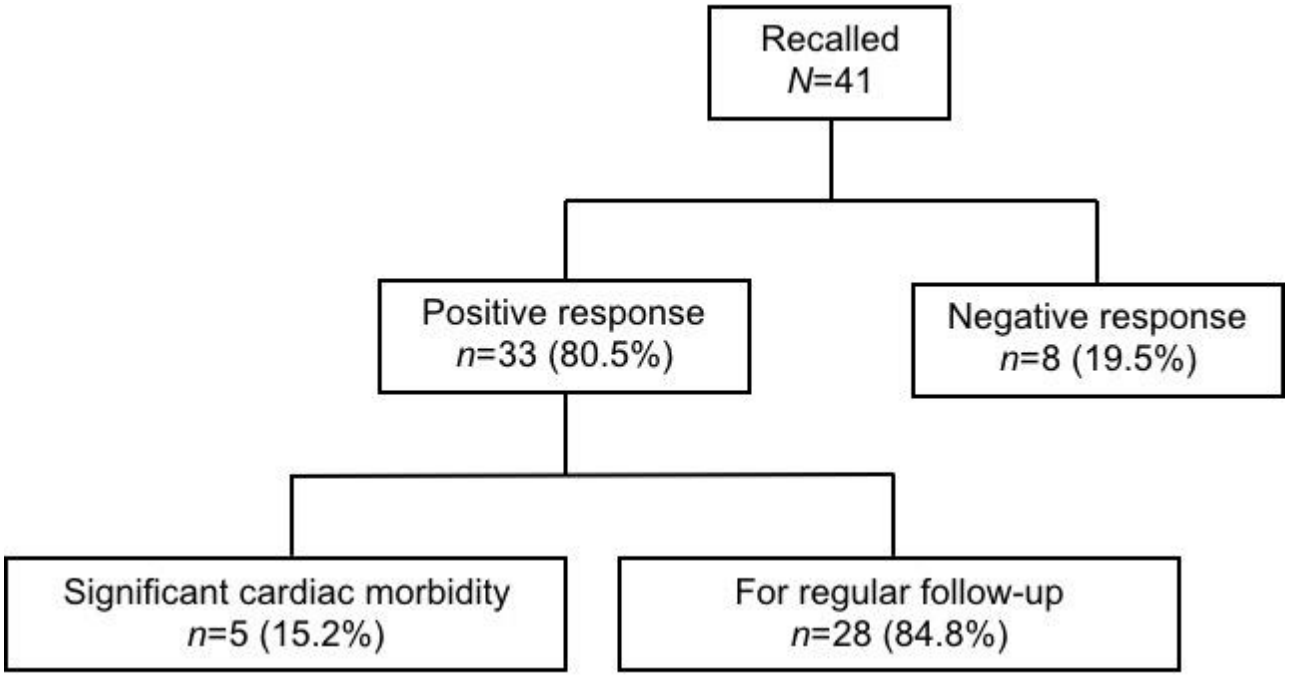


Table 2: *Outcome of ordinal logistic regression analysis of the impact of five studied factors on likelihood of loss to ACHD follow-up*

Factor	OR	95% CI lower, upper	*p* value*
Male vs. female gender	2.12	0.80, 5.65	0.132
Moderate vs. great complexity	1.60	0.32, 8.03	0.569
Limited vs. regular paediatric cardiology follow-up	5.08	1.77, 14.63	**0.003**
≤1 vs. >1 cardiac surgery/intervention	3.34	1.09, 10.26	**0.035**
No vs. on long-term cardiac medication	7.34	1.74, 31.02	**0.007**

* Significant p values are shown in bold

Figure 2: *Outcomes of recall exercise for the 41 patients lost to GUCH follow-up. Thirty-three of the recalled subjects attended an appointment in GUCH clinic, and 5/33 needed management of significant cardiac morbidity.*



Discussion

Nowadays, loss to specialist follow-up is recognised as an important stumbling block to the effective management of GUCH patients worldwide.[8-9,13-18] Ours is the first study to investigate this phenomenon among adult patients with CHD of moderate and severe complexity in the Maltese population.

(a) Prevalence of loss to follow-up and associated factors

The prevalence of loss to follow-up in our study cohort was 21.9%. There are wide variations in loss to follow-up rates in the published literature and ours appears to be one of the lowest reported. In their 2009 study on 643 subjects with CHD of all complexities in Quebec, Canada, Mackie *et al* [14] found that 61% of CHD patients were not being seen by a cardiologist by the age of 22 years, while the 2013 multi-centre North American study by Gurvitz *et al* [19] reported that 42% of the 922 patients with CHD of all complexities aged ≥18 years and attending their GUCH centre visit admitted to at least one >3-year gap in cardiology care. From their single-centre experience in Leuven, Belgium, Moons *et al* [18] reported that 54% of all CHD patients were not under active clinical follow-up. Yeung *et al* found a >2-year lapse in cardiology care in 63% of 158 patients with moderate/severe CHD in a centre in Colorado, US, and Reid *et al* [13] reported a rate of failure to transfer to GUCH care of 53% among 360 patients with complex CHD in Toronto, Canada. Wray *et al* [20] carried out a similar exercise to ours concentrating on repaired TOF in one main tertiary centre in the United Kingdom (UK) and found a 24% loss to follow-up rate. De Bono *et al* [21] documented a nearly 50% rate of loss to follow-up among patients with repaired aortic coarctation referred to a UK regional GUCH centre. It is likely that the small geographical area of the Maltese islands, the universal access to medical care and the concentration of specialist care in one main centre together contribute significantly to the relatively low rate of loss to follow-up documented in our study. All the other studies referred to earlier were conducted in countries far larger than Malta, and often where GUCH care is provided in multiple centres possibly different to those delivering paediatric care. At the same time, the fact that over one fifth of patients with moderate or severe CHD in our study were lost to follow-up despite this combination of favourable circumstances highlights the relative ease with which these patients can "slip through the net" and underlines the importance of implementing a robust infrastructure to ensure their

safe transfer from paediatric to adult care.

As expected, a lower number of cardiac interventional or surgical procedures was associated with a higher risk of loss to adult specialist cardiology follow-up in our study population. Similar findings were documented by Mackie *et al* [14] and Reid *et al* [13], in whose studies a higher number of cardiac procedures was associated with a better chance to transfer to adult care. In another study by Mackie and colleagues [15], cardiac catheterisation in the preceding 5 years was also found to be associated with a lower likelihood of loss to follow-up. It is likely that a higher number of cardiac procedures, especially if undertaken in older years, acts as a "reminder" to patients and family of their cardiac condition. In addition to this, a higher number of cardiac procedures leads to more encounters with specialists that are more likely to reiterate the importance of long-term follow-up and ensure its implementation. We found that the lack of regular cardiac medications was also associated with a higher risk of loss to follow-up. To our knowledge, ours is the first study to investigate the association between cardiac medication use and loss to GUCH follow-up. It can be postulated that the need for daily medications acts as another "reminder" to patients of a chronic condition that warrants specialist follow-up. Furthermore, the need to have prescriptions written from time to time, ensures patients' contact with medical professionals who can in turn ensure that such follow-up is in place.

The other factor with a significant association with loss to follow-up in our study cohort was a limited paediatric cardiology follow-up when compared to a more consistent input. Findings in several other studies reinforce our observation. In analysing the timing of loss to follow-up in their population, Mackie *et al* demonstrated that the greatest loss to follow-up happened during childhood and prior to the time of transfer to adult care.[14] Others showed that clear documentation in medical notes about the need for follow-up in a GUCH centre and recommendations on follow-up timeframes correlated with more successful transfer to adult care.[13,15] A number of interview-based studies featured the impression of the congenital defect being treated or of not knowing about the need for follow-up [8,15,19-20] as leading patient-reported responses for gaps in cardiology care. With their better understanding of the sequelae of repaired and unrepaired CHD, it would be reasonable to expect paediatric cardiologists to better convey the idea of need for long-term follow-up both in their written treatment plans and in their communication with patient and family from an early stage, thus ensuring better transfer to adult care.

We found no association between lesion complexity (moderate vs. severe) and likelihood of loss to GUCH follow-up. This contrasts with the findings by Yeung *et al* [8], who also restricted their study to patients with lesions of moderate or severe complexity and found those with moderate disease to have a significantly higher likelihood of >2-year gaps in cardiology care. Other studies that included patients with CHD of all complexities [14,19], found those with mild disease to be at highest risk of loss to follow-up or to experience gaps in care. Males often show an increased prevalence of risk-taking behaviour, and some authors found male gender to be associated with loss to follow-up before adulthood.[14] Although a previous study among Maltese GUCH patients had confirmed more risk-taking behaviours in male patients with respect to some lifestyle habits [11], our current study failed to show a significant association between gender and loss to follow-up.

(b) Recall of GUCH patients lost to follow-up

To our knowledge, there are only two other nationwide exercises aimed at recalling GUCH patients lost to follow-up reported in the literature to date: a Danish television and newspaper campaign in 2005 [16] and a national media campaign organised by the CONCOR project group in the Netherlands in 2009.[22] The exercise carried out in the Netherlands helped identify 593 patients aged 20-40 years that had previously been lost to follow-up, 85% of whom had mild disease, 14% had moderate CHD and 1% had lesions of severe complexity.[22] Of the 147 responders to the Danish campaign seen in one main institution, 71% had simple lesions and 29% had moderate CHD.[16] Our recall exercise differed by using hospital appointment letters and by concentrating on only five specific congenital lesions of moderate or severe complexity.

Our patients' turnout to recall was encouraging at 80.5%. Response rates to recall reported in other studies with a known patient denominator were all lower: 40% response rate from repaired atrial and

ventricular septal defects recalled in Belgium by Gabriels *et al* [23], 47% return to clinical care among the patients with moderate/severe CHD contacted for telephone interview by Mackie *et al* [15] and 38% of patients with operated TOF accepting to be referred to a GUCH service after a telephone interview in the study by Wray *et al*.[20] Although, at first glance, patient response to our exercise was better, it is difficult to compare considering the differences in congenital pathologies and means of contacting patients employed by different author groups.

(c) Consequences of loss to follow-up

The main risk of loss to follow-up is that patients find themselves living with residual or new structural lesions, arrhythmias or ventricular dysfunction for a protracted period of time and only present late with symptoms of decompensation, when it is either too late to get an optimal outcome from intervention or possibly too late to even contemplate one. Indeed, cardiac symptoms [8,19] and arrhythmias [8] were among the commonest reported reasons for patients not under active follow-up to seek clinical assessment.

Among patients in our cohort that returned to specialist care after recall, significant cardiac morbidity was found in 15.2%, with these patients needing some form of prompt intervention after their reassessment. Following their nationwide campaign in the Netherlands, Vis *et al* [22] diagnosed previously unknown residual lesions in 16% of patients that accepted a new cardiology review and, of these, 6% were found to warrant prompt intervention. Among the patients returning to care after the Danish recall exercise, Iversen *et al* reported moderate/severe PR in 55.6% of TOF patients, moderate/severe atrioventricular valve regurgitation in 75% of AVSDs and significant recoarctation in 20% of patients with repaired CoA.[16] De Bono *et al* [21] found 55% of the patients with repaired CoA referred to their regional GUCH centre to require the introduction of new medications mainly for better management of arterial hypertension and 22% of patients needed referral for specialist investigation or invasive treatment following their initial assessment. Yeung *et al* [8] made a new diagnosis of haemodynamic significance in 60% of their patients returning to cardiology care and were able to demonstrate a significant association between lapse of medical care and need for urgent cardiovascular intervention. Considering the early timing of interventions in a proportion of patients returning to care in these different studies, it is reasonable to postulate that some, if not all, would have been put forward for such treatment even earlier had they not been lost to follow-up. Furthermore, as Wray *et al* argue in their study on repaired TOF patients lost to follow-up [20], loss to follow-up could also increase the risk of premature cardiac-related death by denying patients access to procedures that could improve long-term outcomes if performed in a timely fashion.

Limitations

A main limitation of our study is the small number of patients included, which is in itself a result of the small Maltese population. In our study, patients with mild CHD were purposefully excluded as we aimed to concentrate on patients with moderate/severe disease where a consensus on need for regular follow-up is well-established. Automatically, this precluded us from analysing loss to follow-up among patients with milder disease compared to those with more severe forms as done in other studies referred to earlier. The authors recognise that the use of an interview or questionnaire for patients returning to specialist care would have helped shed a different light on reasons behind loss to follow-up so as to avoid it recurring in the future. Incomplete note keeping made it difficult to determine the age at last visit prior to loss to follow-up for some of the patients and thus this aspect was omitted during analysis.

Conclusions

Patients with CHD remain prone to loss to specialist follow-up even in health systems with little perceived barriers to medical care like the one in place in Malta. Loss to follow-up can delay the management of significant new or residual structural lesions, arrhythmias or ventricular dysfunction, which in turn can have a negative impact on outcomes. Effective transfer from paediatric to adult care requires consistent specialist input from the early stages, coupled with age-appropriate patient and family education highlighting the rationale for and importance of, long-term follow-up, even in the absence of symptoms. Non-congenital cardiologists and physicians should be made equally aware of the

importance of follow-up for CHD patients and be provided with an easy referral route to GUCH services. A formal transition process should help consolidate the process of patient empowerment [18,24-25], while also identifying patients with social and financial issues that might be at higher risk of defaulting future appointments.[8]

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