Long-term outcome in adult patients after surgery for isolated pulmonary valve stenosis in childhood

A systematic review and meta-analysis

Britt C.E. Kramer, Wouter J. van Genuchten, Myrthe E. Menting

ª Medical student, Erasmus MC University Medical Center Rotterdam, the Netherlands;
ª Supervisor, Fellow researcher, MD, Erasmus MC University Medical Center Rotterdam, the Netherlands
Correspondence: B. Kramer, 367265bk@student.eur.nl

Abstract

Objective: Information about the long-term survival and complications in patients after surgical repair of pulmonary valve stenosis (PVS) is important for defining an appropriate follow-up. We aim to provide a complete overview of long-term morbidity and mortality after PVS surgery at a young age.

Methods: This systematic review compared studies with at least 15 years follow-up of patients who had surgery for isolated PVS at a young age. The primary outcome is long-term survival. The secondary outcomes are reinterventions, heart failure, arrhythmia, endocarditis and NYHA class.

Results: Eight studies were included in this systematic review. Six studies showed a survival rate between 92% and 96% after a mean follow-up varying between 20 and 34 years in a total of 936 patients. Seven studies reported reinterventions for pulmonary valve regurgitation or restenosis. Arrhythmias were reported in seven studies and were divided in supraventricular and ventricular arrhythmias. Reintervention numbers differed between 2.6 and 52.8%. Most arrhythmias were ventricular arrhythmias, which was 24.4% of the arrhythmias patients, 13.2% of the reported arrhythmias were supraventricular arrhythmias. Two out of 126 patients suffered from endocarditis. In a group of 522 patients 11 patients developed heart failure. The majority of patients were in NYHA class 1 (323 of 430 patients) at last follow-up.

Conclusions: Long-term clinical outcome in patients after surgical repair of PVS is good. However the incidence of reinterventions and arrhythmias is worth mentioning and therefore life-long follow-up with long intervals seems advisable.

Pulmonary valve stenosis, surgery, long-term outcome, survival, reintervention, arrhythmia, heart failure, endocarditis

Introduction

A congenital heart defect occurs in 0.8% of all live births in Europe (1). Pulmonary valve stenosis (PVS) is one of the common congenital heart defects with a prevalence of 10% in children with congenital heart defects (2).

Surgery has been the treatment option for children with an isolated PVS for over 50 years. The surgical approach of closed valvulotomy was first performed in 1948. This evolved from open valvulotomy with inflow occlusion to open valvulotomy using cardiopulmonary bypass (3). In the last decades balloon valvuloplasty has taken over.

Long-term clinical outcome of patients with surgical PVS repair is only infrequently documented. Many patients are discharged from routine follow-up. Information about long-term outcome is important to define an appropriate follow-up for adult patients with an isolated PVS who have been operated in childhood.

This article reviews literature about long-term outcome of surgery in children with isolated PVS. We aim to provide a clear and complete overview of survival and late complications, like reintervention, heart failure, arrhythmia and endocarditis. Also the functional class (NYHA-class) in this patient group is studied.

Methods

Search strategy

On the 13th of October 2014 a systematic literature search for relevant studies was conducted in Pubmed. We searched for pulmonal (valve) stenosis (Mesh or Tiab) in combination with one of the following terms: outcome, survival, reintervention, events, quality of life, heart failure, morbidity, arrhythmia or endocarditis (all tiab). We limited our search to humans and the English language. The exact search we performed was: ((“Pulmonary Valve Stenosis”[Mesh] OR (pulmonary stenosis[tia] OR pulmonary stenosis[tia] OR pulmonary valve stenos* OR pulmonary valvular stenos*)) AND (outcome[tia] OR survival[tia] OR (re intervention[tia] OR re interventionnal[tia] OR re interventions[tia]) OR events[tia] OR quality of...
In- and exclusion criteria

Articles had to have a long term follow-up of patients surgically treated for isolated PVS. To accomplish our search the following inclusion criteria were used:
- Patients had to be surgically treated for PVS
- Minimal mean follow-up duration of 15 years
- Patients had to be treated before 18 years of age.

Studies were excluded when other heart defects were present, e.g. Tetralogy of Fallot or transposition of the great arteries, except for small atrial septum defect (ASD) or patent foramen ovale.

Study selection

The titles and abstracts of the articles were screened by one of the researchers. The full-text articles were analysed by two researchers (BK and WvG) separately.

Outcome

As a primary outcome we analysed long-term survival. Secondary outcomes were: reinterventions, heart failure, arrhythmia, endocarditis and NYHA-class at last follow-up. NYHA-class is a functional classification for patients with heart failure. Parameters that are used are symptoms, limitations of physical activity and status of rest.

Data analysis

We only included articles when data on follow-up duration were provided or could be extracted from the articles. Percentages were calculated if they were not given and if the data was suitable. Continuous variables were described as mean ± standard deviation (SD) or median with range.

Results

Overview of the articles

Our search in Pubmed resulted in 631 articles. After applying the inclusion and exclusion criteria to title and abstract 593 articles were excluded. Thirty-eight articles were fully read and all were included (2, 4, 6-11). Reference checking did not produce extra relevant articles. A flowchart including the reasons for excluding is presented in Figure 1.

The study characteristics of the eight articles included are presented in Table 1. The eight studies were all cohort studies. Each study included between 12 and 331 patients and all surgeries were performed between 1951 and 2009. All studies had a mean long-term follow-up of at least 19 years and at most a mean follow-up of 45 years. The studies were published between 1988 and 2013. Five studies mentioned the age of patients at operation (2, 4, 6, 7, 9). This was between 3 and 13.6 years of age. Three studies reported the age at follow-up, Roos et al. (4) had a median age of 32 at follow-up and Vogel et al. (7) of 21 years. Moller et al (10) mentioned that the mean age at follow-up was 50.5 years.

Primary outcome

Four studies with a mean follow-up of 22 to 34 years showed a survival between 94.6% and 96.0% (2, 4, 9, 11). Each of these studies included between 53 and 331 patients who had been operated from 1958 to 2009. The studies of Kopecky et al. (6) and Morris et al. (8) showed a survival of 92 and 93% after a mean follow-up of 20 to 24 years. These studies were published in 1988 and 1991 and both included a little over 190 patients who were operated between 1956 and 1989. Vogel et al. (7) included 12 patients operated between 1967 and 1973. After a mean follow-up of 19 years a survival of 100% was found. Moller et al. (10) described an overall survival of 84% after a mean follow-up of 45 years in a group of 73 patients operated between 1952 and 1961.

Reintervention

Seven of the eight studies included reported the number of reinterventions. Earing et al. (9) reported 28 reintervention in a patient group of 53 (52.8%) subjects, whereas Kopecky et al. (6) reported 5 reinterventions in his cohort of 193 patients (2.6%). The other studies showed a reintervention rate somewhere between these two studies (2, 4, 7, 10, 11). Morris et al. (8) did not mention the number of reinterventions in his patients. The most
Three studies reported the implantation of pacemakers. In total, 28/53 (52.8%) of patients had NYHA class 1, 28/53 (54.3%) had NYHA class 2, 23/53 (43.4%) had NYHA class 3, and 1/53 (1.9%) had NYHA class 4. The survival rate was 100% in the study of Kopecky et al., 96.2% in the study of Moller et al., and 95.6% in the study of Roos-Hesselink et al. The mean follow-up was 10 ± 3 years in the study of Morris et al., 19 ± 3 years in the study of Hayes et al., and 22 (16-29) years in the study of Vogel et al.

Arrhythmia and pacemaker implantation

Six studies reported patients with arrhythmias in their follow-up (2, 6, 8-11). Morris et al. reported one death caused by an arrhythmia (8). Supraventricular arrhythmias like atrial fibrillation or atrial flutter were reported in 27 of 205 (13.2%) patients who underwent an electrocardiogram (ECG) or 24-hour ECG monitoring (2, 9, 10). Ventricular arrhythmias such as premature ventricular contractions or ventricular tachycardia were reported in 85 of 347 patients (2, 9, 11). Roos-Hesselink et al. did not find any patients with supraventricular or ventricular arrhythmia in 1990 or 2001 on 24-hour ECG monitoring. Vogel et al. (7) did not report any case of arrhythmia. Kopecky et al. (4) reported two permanent pacemaker implantations for tachycardia-bradycardia syndrome which we count in our secondary outcome for pacemaker and arrhythmia. Three studies reported the implantation of pacemakers. In total, pacemaker implantations were reported in 8 of 334 patients (4, 6, 9).

Endocarditis

Three studies mentioned endocarditis. Earing et al. (9) reported three studies mentioned endocarditis, so did Möller et al. (10). Roos-Hesselink et al. (4) reported that there were no cases of endocarditis in the patient group.

NYHA class

Three studies reported the number of patients per NYHA class (4, 9-11). Of a total of 430 patients, 323 were in NYHA class 1 (75.1%), 50 in NYHA class 2 (11.6%), 48 in NYHA class 3 (11.1%), and 9 in NYHA class 4 (2.1%). Roos-Hesselink reported NYHA classes in percentages: 67% had NYHA class 1, 30% had NYHA class 2 and 3% had NYHA class 3. No patients had NYHA class 4 in the studies of Earing et al. Roos-Hesselink et al. and Möller et al. (4, 9, 10). Eleven of the 12 patients in Vogel et al. (7) were in NYHA class 1. One patient in Vogel et al. had a cerebral-vascular accident and has left hemiplegia. All patients in Kopecky et al. (6) considered themselves to be asymptomatic at the time of last follow-up, but no NYHA classes were reported. Voet et al. and Morris et al. did not report NYHA classes either (2, 8).

Discussion

Our study suggests that the long-term outcome of patients with pulmonary valve stenosis who underwent surgery at a young age is excellent. Seven of the eight studies show a survival rate of over 90% at least 20 years after initial surgery. Vogel et al. showed an excellent survival rate of 100%, however. This number should be interpreted with caution as this concerns only 12 patients, which makes this group less representative for the whole study. The study with the lowest survival is Möller et al. with 84% after 45 years. This study had a mean follow-up of 45 years, the patients had a mean age of 50.5 years at the time of the last follow-up. The lower survival rate could be caused by higher age and some late complications such as heart failure after surgery.

Table 1 - study characteristics with primary outcome and secondary outcome

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Year published</th>
<th>Surgical era</th>
<th>Mean age at operation (years)</th>
<th>Mean follow-up (years)</th>
<th>Median follow-up (range)</th>
<th>Survival (n)</th>
<th>Reintervention (n)</th>
<th>Heart failure (n)</th>
<th>Arrhythmia (n)</th>
<th>Pacemaker (n)</th>
<th>Endocarditis (n)</th>
<th>NYHA Class (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. L. Kopecky et al, 1991 [9]</td>
<td>192</td>
<td>1991</td>
<td>1958-1991</td>
<td>22 (16-29)</td>
<td>9/331</td>
<td>(5.1%)</td>
<td>1/12</td>
<td>(8.3%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 = 228 (71%)</td>
</tr>
<tr>
<td>C. J. Hayes et al, 1993 [11]</td>
<td>331</td>
<td>1993</td>
<td>1958-1969</td>
<td>22 (16-29)</td>
<td>9/331</td>
<td>(5.1%)</td>
<td>1/12</td>
<td>(8.3%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 = 228 (71%)</td>
</tr>
<tr>
<td>C. N. Moller et al, 2012 [2]</td>
<td>79</td>
<td>2012</td>
<td>1960-2009</td>
<td>23 (0-45)</td>
<td>16/79</td>
<td>(5.1%)</td>
<td>1/12</td>
<td>(8.3%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 = 228 (71%)</td>
</tr>
</tbody>
</table>

* The hyphen-minus means that the number was not mentioned in the article. ** Events are presented as number of events / total number of patients and in percentages.
longer follow-up. Year of surgery could be another explanation. The patients in this cohort were operated the earliest of all studies (1952-1963). Surgical techniques and perioperative care have improved since the start of open-heart surgery in the early 50’s. This is why it is important to do more studies with 40-50 year follow-up in this group of patients.

**Secondary outcomes**

Seven studies reported a considerable number of reinterventions. One study showed an reintervention rate of 52.8% in after 33 years, this is more than half of the patients, whereas the lowest reintervention rate was 2.6% in a study with a 24 years follow-up. This could possibly be explained by different definitions of reinterventions. The reason for reintervention is mostly pulmonary valve replacement for regurgitation and sometimes pulmonary valve re-stenosis.

Only eleven heart failure patients were described in all articles. However five articles did not mention it. It is possible that the follow-up rate is too short to do a make prediction of heart failure numbers. The incidence of heart failure will increase with longer duration of follow-up and can be caused by compensatory mechanism based on right ventricular dilatation or by other factors such as aging with cell destruction and apoptosis (4).

We have found a great difference in numbers of arrhythmia between studies. Kopecky et al. showed a low rate of arrhythmia 1.0%. A high number of arrhythmia was found in the study of Earing et al. with 37.7%. An explanation for the higher number of arrhythmia in some studies is probably the method of investigation: some studies incorporated 24-hour ECG monitoring while others did not.

Only eight pacemaker implantations were reported in 334 patients (2.4%), therefore the need to implant a pacemaker after PVS surgery seems rare. Two cases of endocarditis were reported in all studies (9, 10). This suggests that endocarditis is also a rare complication.

Discussion exists about the clinical condition at longterm follow-up. Some studies report a limitation in some form of their physical condition. This was shown by the NYHA classes in the articles of Hayes et al. Earing et al and Roos-Hesselink et al. On the other hand, other articles showed no physical limitations (6, 7, 10).

Morris et al. did not report much about secondary outcomes except for arrhythmia. However, they have described the survival, our primary outcome, very well. The fact that this article reported many different congenital heart defects could be a reason for missing secondary outcomes. Meantime Earing showed higher numbers of complications. The higher number of the secondary outcome in this article may be caused by longer follow-up. However, this number of complications is much higher than that from Moller et al. which had a longer follow-up. The explanation is probably the different definition of reintervention and arrhythmia.

**Limitations**

This systematic review has a few limitations. Firstly, we did not do a statistical analysis of the raw data of all patients. Furthermore not all patients had at least 15 years follow-up. For example, in Voet et al. (published in 2012) the last patient was operated in 2009 and thus had a follow-up of only 3 years. Nevertheless, studies were included if the mean (or median) follow-up was over 15 years conform one of our inclusion criteria.

Our review showed the importance of extensive follow-up including an interview, physical examination, electrocardiogram and echocardiogram. In this way a complete image of the patients will be acquired and thereby arrhythmias and pulmonary valve problems may be detected in time. Except for these complications there were no other common complications found which need specific attention.

Nowadays surgery of PVS is not always the first choice of treatment because of the use of balloon valvuloplasty. According to Peterson et al. (12) surgical treatment produces lower long-term complications and lower number of reinterventions. Despite these results, balloon valvuloplasty could well be the preferred therapy for PVS, because the intervention is less invasive, less expensive and requires a shorter hospital stay. We think more research is needed to determine which patients with PVS are best treated with balloon valvuloplasty or with surgery.

**Conclusion**

Patients with PVS who undergo surgery at a young age have good long-term survival, but because of the incidence of reintervention and arrhythmia life-long follow-up with long intervals is advisable.

**References**