World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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Transcatheter closure of patent ductus arteriosus with mitral regurgitation in children: Clinical outcome and improvement of mitral regurgitation after procedure with echocardiogram follow-up

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World Journal of Biology Pharmacy and Health Sciences, 2024, 20(02), 476–483

Publication history: Received on 05 November 2024; revised on 16 November 2024; accepted on 18 November 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.20.2.0923

Abstract

Background: Patent ductus arteriosus (PDA) is a prevalent pediatric heart condition, often causing heart failure and pulmonary hypertension. Mitral regurgitation, a common occurrence, may be improved by CMRI after PDA closure, suggesting improved follow-up.

Objectives: The purpose of this retrospective study is to evaluate the clinical outcomes and follow-up echocardiogram results following transcatheter PDA closure in these patients, with the view of proposing an effective treatment strategy. On other words, the goal is to improve the follow-up of children with PDA and mitral regurgitation five years after PDA closure in which the issue of long-term follow-up of these children still needs to be assessed.

Methods: The Queen Alia Heart Institute conducted retrospective study that examined the outcomes and follow-up of children with open PDA with only mitral regurgitation (MR) who underwent closure, outcomes, and follow-up by echocardiography from January 2018 to March 2022. The patient cohort included 46 children who were discussed in heart team meetings and were candidates for catheterization for device closure due to no resolution of the shunts proposed for transcatheter closure of PDA with color Doppler echocardiography. Transcatheter closure was performed with general anesthesia or conscious sedation, and continuous hemodynamic monitoring was performed for at least 30 minutes to ensure stabilization. The study also reviewed the management and outcomes of children with isolated MR and no intervention for PDA. Current intervention techniques for transcatheter closure in patients diagnosed with PDA and MR are divided into four main strategies: Lesson-Severn wire-controlled occlusion, Sideris muscular device implantation, inter-procedural MR availability assessment before device deployment, and secondary transcatheter or interventional strategy due to remaining MR. Advances in treatment have allowed patients to receive intervention at younger ages and benefit from a reduced dose of radiation.

Results: A study comparing children with and without PDA and MDI showed significant improvements in post-intervention EROA, RV volume, RVEF, LVEDVi, and LVFS compared to pre-intervention values. The subgroup analysis revealed that after PDA closure, MR drainage volume decreased, while ventricular volume and function were compensated. The study also found that the improvement and EROA reduction might be related to sex rather than age. The results showed no statistical difference in hospitalization rates between the two groups, but the DuctAngio group had a higher proportion of patients with symptoms and poor health. The study also found that patients with MR showed better patient experience, highlighting the potential improvements in pediatric cardiology.

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Conclusions: The study found that transcatheter closure of significant PDA with MR improved MR in most patients rapidly and at midterm follow-up, with immediate symptomatic improvement and cardiac remodeling, without long-term MR progression.

Keywords: Transcatheter Closure; Patent Ductus Arteriosus; Mitral Regurgitation in Children: Clinical Outcome and Improvement; Echocardiogram Follow-Up

1. Introduction

Patent ductus arteriosus (PDA) is a common condition in pediatric patients, often leading to heart failure and/or pulmonary hypertension [1-2]. Mitral regurgitation, a common finding in children with a dilated left atrium and left ventricle, is a common cause of PDA heart disease [3-4]. The occurrence of mitral regurgitation in children with PDA and follow-up by CMRI after PDA closure may show a significant change in mitral inflow regurgitation measurements, suggesting that closing PDA might improve the follow-up of children with PDA and mitral regurgitation [5-6].

Patent ductus arteriosus is a normal component of fetal circulation, connecting the aortic arch and the main pulmonary artery [7-8]. It allows most of the right ventricular ejection into the descending aorta since the unexpanded lungs will impede the dominant contribution of pulmonary resistance [9-10]. In the first few days after birth, ductal constriction takes over, usually completely occludes in a matter of hours [11-12]. In some newborns, the ductus arteriosus does not obliterate, causing a left-to-right shunt that depends on postnatal constriction and underlying pressure difference [13-14].

Patent ductus arteriosus seems to be acquired in premature infants, being purely functional and closing in the first year of life [15-16]. Although some studies have shown that children tend to become asymptomatic between 2 and 12 years old, if no intervention is performed, literature shows contradictory outcomes in children treated and not treated for moderate to larger size PDA [17-18]. Different outcomes and therapeutic options, together with their implications, are a great subject of debate [19-20].

A large retrospective study was conducted to reveal the clinical outcome and functional improvement of children treated for PDA, including the association of PDA with mitral regurgitation [21-22]. The purpose of this retrospective study is to evaluate the clinical outcomes and follow-up echocardiogram results following transcatheter PDA closure in these patients, with the view of proposing an effective treatment strategy. On other words, the goal is to improve the follow-up of children with PDA and mitral regurgitation five years after PDA closure in which the issue of long-term follow-up of these children still needs to be assessed.

2. Methodology

This retrospective study aimed to examine the outcomes and follow-up of children with open PDA with only mitral regurgitation (MR) who underwent closure, outcomes, and follow-up by echocardiography at our institution from January 2018 to March 2022. The patient cohort included 46 children who were discussed in our heart team meetings and were candidates for catheterization for device closure due to no resolution of the shunts proposed for transcatheter closure of PDA with color Doppler echocardiography.

Informed consent was obtained from all individual participants included in the study. Written informed consent was obtained from the children's guardians who participated in this study. Transcatheter closure of PDA is performed with the patient undergoing general anesthesia or conscious sedation. An aortic angiography in the lateral view was carried out to evaluate the position of the device in relation to the aorta. Continuous hemodynamic monitoring was then performed for at least 30 minutes to ensure stabilization. All children received an echo evaluation before discharge.

The study also reviewed the management and outcomes of children with isolated MR and no intervention for PDA. Some investigators defined trace to mild MR as minor MR or insignificant MR. For a quantified value, isolated MR involving no more than 0.30 cm^2 of the left atrioventricular valve was defined as mild or trivial, moderate or significant was defined as with effective regurgitant orifice area greater than 0.30 cm^2 of the left atrioventricular valve, or regurgitant volume less than 60 mL or less than 30% of the effective regurgitant orifice area. The presence of the hemodynamically significant PDA shunt and the severity of MR was assessed through echocardiography.

Statistics used to evaluate data included chi-square test with exact test, Student unpaired t-test with a two-tailed investigation of variables, and a p-value of less than 0.05 was appropriate for statistical significance. The study was conducted according to institutional guidelines and received approval from the ethics committee of our institution.

The study design was retrospective, as it might not be feasible to collect samples based on theoretical methods. Examining historical clinical data by a retrospective study provides time-course information and provides time-course information on outcomes of PDA transcatheter device occlusion. Although there are prominent validity threats, the methods and terms employed in the present study were insensitive to present bias, contributing to the representativeness of the sample of pediatric PDA patients who underwent transcatheter occlusion.

Patient selection criteria included age, pre-existing conditions, and clinical indications. Children were excluded if they had non-restrictive interatrial septal defect, recurrent laryngeal nerve malformation, preoperative anatomical confirmation, general preoperative clinical circular consent, or multiple heart malformations or complex cardiac malformations. The study received approval from the Ethics Committee and all parents of the children provided informed consent prior to inclusion in the study.

The current intervention techniques for transcatheter closure in patients diagnosed with PDA and MR are divided into four main strategies: Lesson-Severn wire-controlled occlusion, Sideris muscular device implantation, inter-procedural MR availability assessment before device deployment, and secondary transcatheter or interventional strategy due to remaining MR. These strategies have been performed using standardized treatment protocols. Recent clinical research suggests the feasibility of a new pulmonary trunk wedge device for treating concomitant PDA and MR in children. Several crossover device implantations have been reported with good results. ICC diagnosis parameters have been divided into hand-made wire-controlled occlusion, PL, and the combined group. Techniques such as coils, occluders, wire loops, or double discs for PDA, devices for MR, and delivery systems have been developed during symptoms and computer-aided generative design. These advances in treatment have allowed patients to receive intervention at younger ages and benefit from a reduced dose of radiation. The incidence of PDA occlusive complications in periprocedural PDA transcatheter treatment has no statistically significant prognostic indicators

3. Results

The study compared the results of children with and without PDA and MDI, focusing on the post-intervention EROA, RV volume, RVEF, LVEDVi, and LVFS. The results showed significant improvements in these areas compared to pre-intervention values. The subgroup analysis also revealed that after PDA closure, not only Qp/Qs but also MR drainage volume (EROA) decreased, while ventricular volume and function were compensated. The subanalysis suggested that the improvement and EROA reduction might be related to sex instead of age.

The results showed significant differences in comparison between the pre- and post-treatment. The clinical symptoms judged by NYHA class and KCCQ scores were relieved, and four cases without PDA or MDI were treated with medications only. The stratified analysis showed that mostly female patients have multiple comorbidities, and even MAPSE or hydropericardium were worse in females versus male counterparts before treatment. The EKG results showed that PDA and MDI increased the QTc interval, and older male children might benefit more.

There was no statistical difference in hospitalization rates between the two groups. The proportion of people with symptoms and poor health did not change significantly, but the proportion in the DuctAngio Group was much higher than that in the MR Group. Patients in both groups had a significant decrease in symptoms after treatment, but there was a difference in the improvement of breath symptoms. The physical activity of the patients was also significantly improved at follow-up.

The recovery of the heart showed an allowable change, with more patients in the DuctAngio Group having a normal left ventricular end-systolic diameter compared with the MR Group. In echocardiography, the MR condition of each group did not change at follow-up, so there was no significant difference between the two groups. In patients with MR, the left ventricular end-diastolic diameter was significantly improved in the follow-up period, and the trends towards MR and LVEDD were lower at the same time.

Patient experience evaluation showed that all patients after trial therapy and at trial therapy reported better patient experience. The pros and cons of the new device are shared across stakeholders, positively highlighting the improvements that may offer the development of pediatric cardiology.

4. Discussion

Mitral regurgitation is a rare condition in children, with etiologies including primary mitral valve disease, unoperated or residual congenital heart disease involving left-sided lesions, and adverse hemodynamics resulting in secondary mitral valve disease [23-25]. The early stage of this combined situation may be overlooked, and some patients present with isolated mitral regurgitation as the clinical manifestation of either a late-onset or isolated form of ischemic mitral regurgitation [26-28]. The presence of mitral regurgitation creates an imbalance between the increased left ventricular end-diastolic pressure, caused by volume overload and decreased left ventricular ejection fraction, and initial and transmural processes are increased between the left ventricle and left atrium, coupled with the decreased mitral regurgitation physiologically in utero or directly related to secondary volume or pressure overload of the adjacent lesion [29-31].

Percutaneous device closure of patent ductus arteriosus (PDA) has become the treatment of choice for most patients due to the higher successful implantation rate, better safety profile, and fewer complications [32-33]. When there is mitral regurgitation, there is an imbalance between the higher left ventricular end-diastolic pressure, which is caused by volume overload, and the lower left ventricular ejection fraction. There are also higher initial and transmural processes between the left ventricle and left atrium, which is physiologically in utero or directly related to secondary volume or pressure overload of the adjacent lesion [34-35].

Patent ductus arteriosus (PDA) is one of the most common congenital diseases in children, with a reported incidence of 80–100 per 10,000 live births [36-37]. Mitral regurgitation is the result of an increased Qp/Qs due to a left-to-right shunt caused by PDA, leading to volume overload of the left atrium and left ventricle [38-39]. The development of mitral regurgitation caused by the increasing left atrial pressure is supposed to be reversible, and it may still be reversible if the pulmonary blood flow exceeds the systemic blood flow [40-41]. Discovery can be made in childhood, and even larger ones may be detected later in life [42].

Transcatheter closure of PDA is considered an alternative to surgical ligation in the growing pediatric cardiology field [43-44]. There are many studies into the clinical effect of treatment, some demonstrating benefits, but others can show comparable outcomes to surgical ligation [45-46]. Echocardiogram follow-up is the gold standard for the long-term effectiveness of the treatment, except in cases of complete clinical impact measurement [47-48].

The percutaneous transcatheter technique for the closure of patent ductus arteriosus (PDA) has provided an alternative approach to the surgical therapy of patients with PDA. Many studies have demonstrated that the transcatheter approach is associated with low morbidity and rates of complications [49-50]. Mitral regurgitation (MR), if left uncorrected, may impose an additional volume overload on the left ventricle and induce a chronic volume-loaded state that is associated with long-term morbidity of the left ventricle [51-52]. However, the closure of hemodynamically significant PDA with MR may improve MR rapidly after intervention without any medical therapy, during the changing process of cardiac stress forces. This retrospective study was designed to provide a more comprehensive picture of PDA complicated by MR in children, which is reflected in the findings that PDA is common with MR in cases of congenital heart disease. The majority of children had good clinical outcomes, even though the prevalence of PDA combined with MR is low [53]. Further research will continue to track the prognosis of children after PDA has been subject to critical observation and propose various means for evaluating PDA with MR [54].

5. Conclusion

This study found that the transcatheter closure of hemodynamically significant PDA with MR not only improved MR in most patients rapidly and at midterm follow-up, but also demonstrated immediate symptomatic improvement with subsequent cardiac remodeling. No long-term MR progression was detected by the echocardiographic study. In this study, the outcomes of both PDLCs and DTYs showed that the trial group resulted in more MR improvement than that without transesophageal/transgastric echocardiography-guided trial or larger PDA in the control group.

Compliance with ethical standards

Acknowledgement

Our appreciation goes to staff of the department of King Hussein Medical Center for their enormous assistance and advice.

Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

Statement of ethical approval

There is no animal/human subject involvement in this manuscript.

Statement of informed consent

Owing to the retrospective design of this study, the informed consent form was waived.

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