19th of June 2023

A comparison of morbidity between patients with pulmonary atresia with intact ventricular septum and uni- or biventricular circulation

19th of June 2023

Research Question

Do mortality, quality of life, comorbidity, cardiac function, and work capacity differ between patients with pulmonary atresia with intact ventricular septum (PA-IVS) who has univentricular and biventricular circulation?

Overview of the Area

PA-IVS is a rare congenital heart defect occurring in 4-5 live births per year in Sweden [1]. This malformation entails a duct-dependent circulation, which, if left untreated, leads to death. The closed pulmonary valve (atresia) can present in various ways, ranging from fused valve leaflets to a valve plane primarily composed of myocardial tissue. This variation affects the development of the right ventricle to different degrees during the fetal stage. In the most severe form, there is only an inflow portion that cannot function as a ventricle, and these patients undergo a surgical procedure to establish univentricular circulation. This operation involves using cardiopulmonary bypass, and the thymus is removed. In milder cases, patients can undergo different interventions to achieve one-and-a-half- or biventricular circulation. Coronary fistulas may also be present between the right ventricle and the coronary arteries. In the most severe cases, the coronary circulation is dependent on the right ventricle, and ligating the fistulas could risk myocardial ischemia.

We aim to investigate the well-being of patients born with PA-IVS in adulthood, focusing on comorbidity, quality of life, and physical capacity. We are interested in comparing patients within the group with uni- or biventricular circulation.

Method

The inclusion criterion is individuals born PA-IVS who are 15 years or older at the start of the study. The study population consists of all individuals with PA-IVS who have been registered in Swedcon (a national register for patients with congenital heart defects) or in the National Patient Register and Cause of Death Register since 1980 and meet other inclusion criteria, including age.

The selection of research subjects has been based on the purpose of the study, which is to conduct a long-term follow-up of a rare heart defect where treatment differs between patients depending on the morphology of the heart defect. We will divide the patients into two groups based on whether they have uni- or biventricular circulation. The basis for this division is that uni- and biventricular circulation provide very different conditions for meeting the increased cardiac output demands.

We aim to carry out a long-term register-based follow-up study regarding comorbidity in patients with PA-IVS. Additionally, we want to evaluate work capacity, cardiac health, and quality of life in the same patient group.

Patients with PA-IVS are identified through Swedcon (a national register for patients with congenital heart defects) and the National Patient Register, where information on comorbidity (mentioned below) is also requested. To ensure that the diagnosis is correct and that the included research subjects meet the inclusion criteria, validation will be conducted through a review of the research subjects' medical records. In the medical record review, we will also note the current NYHA class, cardiac function measured by echocardiography, and results from cardiac function assessments. The included individuals will be grouped based on whether they have uni- or biventricular circulation. The frequency of comorbidity (myocardial infarction, heart failure, arrhythmia, stroke, malignancy, autoimmune diseases, infections, atopy, certain liver diseases, and protein-losing enteropathy) will be compared between these two groups.

We also intend to send a Quality-of-Life questionnaire (PROMIS Scale v1.2-Global Health) to the included research subjects. We will also inquire with all research subjects about their participation in a series of examinations (ergo-spirometry to assess work capacity, echocardiogram, and blood sampling to assess cardiac function and cardiac health) at the cardiology clinic at Queen Silvia's Children's Hospital.

Diagnoses related to the immune system will be sought as the thymus is involved in immune system development, and its early excision can affect the well-being of patients later in life [2].

We will analyze the material using chi-square test and t-test.

Clinical Relevance

Congenital heart defects are one of the most common birth defects, occurring in approximately 1 in 100 children. PA-IVS is a rare heart defect, but increased knowledge about it can also contribute to improved management of children with other heart defects.

Increased knowledge about the connection between univentricular circulation and other illnesses may lead to changes in treatment strategies and thereby improve the prognosis regarding morbidity and mortality for this patient group. There is a knowledge gap, that we aim to address, regarding univentricular circulation with a working left ventricle due to the majority of the research being made focuses on the patient group with hypoplastic left heart syndrome.

References

1. Manhem, S., et al., *Survival With Respect to Morphology in Pulmonary Atresia and Intact Ventricular Septum in Sweden. World J Pediatr Congenit Heart Surg, 2021. 12(1): p. 27-34.*
2. *Gudmundsdottir, J., et al., Long-term clinical effects of early thymectomy: Associations with autoimmune diseases, cancer, infections, and atopic diseases. J Allergy Clin Immunol, 2018. 141(6): p. 2294-2297.e8.*