Coarctation of the Aorta: A 10-year follow-up study of patients treated at the Department of Peadiatric Cardiology, Universitas Academic Hospital.

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DECLARATION

I, Nompi Nyindi, declare that the coursework Master's Degree mini-dissertation that I herewith submit in a publishable manuscript format for the Master's Degree qualification in Paediatrics at the University of the Free State is my independent work ,and that I have not previously submitted it for a qualification at another institution of higher education .

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Nompi Nyindi

25/11/2019

Date

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- The clinical technologists in the Department of Paediatric Cardiology for helping with the process of data collection.
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ABSTRACT

Background: Coarctation of the aorta accounts for 6-8% of all congenital cardiac lesions. It can be treated surgically or percutaneously depending on the age and weight at presentation and associated cardiac lesions.

Objectives: To describe the outcomes of management in patients with native coarctation of aorta with regard to re-intervention and mortality rate.

Methods: A retrospective, descriptive review of patients with native coarctation of aorta was done at Universitas Academic Hospital using an electronic database. Included were patients who presented from 01 Jan 2007 – 31 Dec 2016, from birth to 19yrs.

Results: The study comprised of 107 patients, median age of 33 days (1 – 4940) with a median weight of 3.9kg (1 – 53.5kg).Common associated cardiac lesions included PDA (n=61; 57%), bicuspid valves (n=41; 38.3%) and VSD (n=31; 29%). A total of 82 patients (75.7%) required an intervention in which 71(86.6%) had surgery with 12(14.6%) requiring a second intervention, while 11(13.6%) had percutaneous procedures with 7(63.6%) requiring a second intervention. Overall mortality was 17(15.9%), the cause of death in 14(82.4%) was cardiac related.

Conclusion: From the results of this review surgery remains the preferred treatment for coarctation of the aorta and are associated with a lower recoarctation rate compared to percutaneous interventions.

KEYWORDS

1. Coarctation
2. Aorta
3. Hypertension
4. Restenosis
5. End-to-end anastomosis
6. Stents
7. Angioplasty
8. Balloon-dilatation
9. Turner Syndrome
10. Cardiac failure

LIST OF ABBREVIATIONS AND DEFINITIONS

ABBREVIATIONS

ADH	Anti-Diuretic Hormone
BP	Blood pressure
CXR	Chest X-ray
CT	Computed Tomography
ECG	Electrocardiogram
MRI	Magnetic Resonance Imaging
RAAS	Renin- Angiotensin – Aldosterone System
PDA	Patent Ductus Arteriosus
VSD	Ventricular Septal Defect

DEFINITIONS

Native Coarctation of Aorta: Narrowing of the aorta that has never had any corrective procedure performed.

Percutaneous Procedure: Where a needle puncture through the skin into the vessel is used to access the heart (closed).

Surgical procedure: Where an incision is made on the chest to access the heart (open).

CHAPTER 1: ORIENTATION OF THE STUDY

INTRODUCTION AND LITERATURE REVIEW

Coarctation of the aorta is defined as a narrowing of an aortic segment which is commonly situated near the ligamentum arteriosum, adjacent to the left subclavian artery.[1] It accounts for 6 – 8 percent of all congenital cardiac conditions [2] and may present in association with other cardiac defects, such as bicuspid aortic valve, ventricular septal defect (VSD), patent ductus arteriosus (PDA). Clinical presentation varies widely depending on the age of the patient at presentation and the associated cardiac defects. Neonates with duct-dependent lesions may present early with circulatory collapse following closure of the ductus arteriosus that usually requires an urgent intervention.[3] Older children usually present with hypertension which may result in varying degrees of end organ damage if left untreated. Early referral is essential to improve outcomes. However, in South Africa this remains a big challenge due to poor referral systems and patients are often lost to follow-up. Antenatal screening and diagnosis may be difficult due to patency of the ductus arteriosus. Post-natal screening is not routinely done.[4]

Pathogenesis

The precise pathogenesis of the congenital coarctation is unknown; however, there are three main theories that are widely recognized. This includes:

- Migration or extension of the ductal tissue into the wall of the fetal thoracic aorta.[5]
- Diminished antegrade intrauterine blood flow causing underdevelopment of the fetal aortic arch.[5]
- There is also a genetic influence on the development of coarctation that is recognizable in 35% of individuals with Turners XO Syndrome.[2] This may be secondary to lymphedema.[6]

Sequelae of Coarctation of aorta

Left Ventricular Hypertrophy

PDA closure and coarctation of the aorta increases left ventricular afterload, these result in wall stress and left ventricular hypertrophy.

Hypertension

Hypertension develops due to humoral mechanism and/or mechanical obstruction:

- Humoral Mechanism :

As a result of the outflow obstruction there is poor renal perfusion which results in activation of renin-angiotensin-aldosterone system (RAAS) mechanism. Angiotensin II will result in efferent vasoconstriction and further release of aldosterone and antidiuretic hormone (ADH). These will in turn result in re-absorption of sodium with subsequent water retention increasing the preload, left ventricular end diastolic volume and systemic vascular resistance .[7]

- Mechanical Obstruction theory

This mechanism postulates that there is a higher blood pressure required to maintain blood flow through the narrowed aortic segment and collateral vessels .This mechanism applies to the high pressure created proximal to the coarctation by the stroke volume ejected into the limited aortic receptacle. [7]

Cardiac Failure

Mechanism of developing heart failure is mainly thought to be secondary to activation RAAS which will increase preload and afterload resulting in shifting of the Frank-Starling curve to the right. Aldosterone plays a significant role in remodeling of the myocardium and may lead to ventricular dysfunction in the long run.

The second mechanism is through activation of central sympathetic nervous system which will lead to increase in heart rate and peripheral vascular resistance. [8]

Cardiac output is dependent on stroke volume and heart rate. Neonates compensate for low cardiac output mainly by increasing the heart rate and may therefore present early with tachycardia.

Clinical Presentation

Clinical presentation of coarctation of the aorta depends on the age of the patient, severity of the coarctation and presence /absence of other significant cardiac lesions.

Neonatal Period

Neonates may be asymptomatic while the ductus arteriosus is still patent, however once it closes they may present with signs of cardiac failure or shock with severe metabolic acidosis. These patients may also have differential cyanosis which is marked by pink upper extremities with cyanotic lower extremities. It is therefore important to document the pre- and post-ductal saturations when examining these neonates. [3]

Early childhood

In this age group patients commonly present with a systolic ejection murmur that is best heard over the upper left sternal border and in the left interscapular area posteriorly. A systolic ejection click may be audible at the apex if there is an associated bicuspid aortic valve, or a continuous murmur may be heard throughout the chest if there is a well-developed arterial collateral system. They may also present with varying degrees of hypertension. [5]

Older Children and Adolescence

These patients may present with a history of intermittent lower limb claudication, this is defined as calf muscle pain induced by activity and relieved by rest. It is caused by reduced blood supply to the muscle due to proximal vessel obstruction. Clinically they

may have upper limb hypertension, it is therefore imperative to measure four limb blood pressures in these patients. [5]

Investigations:

Doppler BP:

Awake four limb Doppler blood pressure monitoring is an accurate and non-invasive method to determine the gradient. The size of the blood pressure cuff should have a bladder width that is approximately 40 percent of the circumference of the upper arm, measured halfway between the acromion and the olecranon. The length of the cuff bladder should encircle 80 -100 percent of the circumference of the upper arm halfway between the acromion and the olecranon.[9] To get reliable results the patient must be as calm as possible. A Doppler gradient above 20mmHg at rest or 25mmHg during exercise is significant and may be used as an indication for intervention. [2]

Chest X-ray (CXR)

- This may reveal a cardiomegaly with significantly increased pulmonary vascular markings secondary to pulmonary congestion.
- Left or biventricular hypertrophy.
- A '3 sign' which is produced by indentation of the aortic wall at the site of coarctation with pre- and post-stenotic dilatation. X-ray usually shows an aortic knuckle with 3 –shaped left sided contour.
- Notching of the posterior third of rib three to eight due to erosion by the large collateral arteries. This is usually more apparent between the ages of 4 and 12 years. [8]

Electrocardiogram (ECG)

- In neonates, ECG findings may reveal age-appropriate right ventricular hypertrophy.
- Later in life there may be left ventricular hypertrophy with signs of left ventricular strain or ischemia. [3] The ventricular strain pattern on the ECG is marked by ST depression with an inverted T-wave. [9]

Echocardiogram

- This is a readily available in most referral centres and non-invasive investigation of choice for initial diagnosis.
- The high quality two dimensional and Doppler echocardiogram will establish/confirm the diagnosis and severity of the coarctation. This will also assist in detecting other associated cardiac lesions and early complications like pulmonary hypertension.
- The Doppler will assist in determining the hemodynamic severity of the coarctation and establish the pressure gradient.[3] Doppler flow patterns across the abdominal aorta can be used as indirect evaluation of the severity of the coarctation .Typical coarctation Doppler flow patterns demonstrate a continuous diastolic component.

Magnetic Resonance Imaging (MRI) / Computed Tomography (CT) Angiography:

- This mode of investigation remains the gold standard when evaluating the coarctations and the anatomy of the aortic arch.
- CT angiogram can be used for 3D reconstruction and revelation of important spatial orientation with information of associated structures.
- This modality will clearly define the location and severity of the coarctation and collateral vessels .[3]

- The advantage of MRI is that it is radiation free while with CT patients may be exposed to high cumulative doses of radiation and exposure to contrast.
- The disadvantage is that it may be difficult in younger children and infants

Cardiac Catheterization:

- Cardiac catheterization confirms the diagnosis when the echocardiogram findings are not completely clear.
- Left ventricle end diastolic and systolic pressure gradient are also measured, whereby below 20mmHg is regarded as mild coarctation. The low pressure gradients may be secondary to left ventricular dysfunction, PDA or anaesthetic effect.
- It is also used for therapeutic purposes like balloon angioplasty or stent implantation in the native or recurrent coarctation. [8]
- This modality also exposes patients to radiation, but may prevent open heart surgery if the percutaneous procedures to correct the coarctation are undertaken.

Treatment options: This includes medical and surgical or percutaneous treatment.

Medical

- Medical treatment includes a temporary bridge until definitive treatment can be performed.
- Prostaglandin E1 in duct dependent /critical coarctation used in neonates: This will help to keep ductus arteriosus open to allow oxygenated blood to the body temporarily. [6]
- Treatment of cardiac failure: Diuretics are used to reduce the fluid overload.
- Treatment of Hypertension: β-blockers remain treatment of choice for hypertension.

Surgical Procedures

- Resection with end-to-end anastomosis: In this case the coarctated area is completely resected and the remaining ends of the vessel are sutured together. This is a best option in neonates as it completely removes the ductal material and no prosthesis is used.
- Subclavian flap aortoplasty: The left subclavian artery is used as a roof over the previous coarctated area. The disadvantage in this procedure is the possible loss of left arm pulse.
- Patch aortoplasty: A prosthetic patch is used as a roof of the previous coarctated area. This is a good choice of repair in children > 2yrs but less than 16yrs.The disadvantage in this case is high risk for development of aortic aneurysm and restenosis.
- Bypass graft repair: Graft material is used to bypass the coarctated area. Extra anatomical grafts usually add a Gore-Tex tube/graft to bypass the coarctated area. Therefore, the graft will be attached to the arch of the aorta, bypasses the stenosis then attach to the descending aorta. [10]

Percutaneous Interventions

- Balloon Angioplasty: A catheter is inserted through the femoral artery and the tip is passed up to the coarctated area. A balloon around the area of the tip is inflated to dilate the narrowed area.
- Aortic Stent implantation: In this case a stent is inserted at the narrowed area. This technique is suitable for patients with long segment coarctation, or recurrent

coarctation or where there is hypoplasia of the isthmus or aortic arch.[10] Types of stents include Cheatham Platinum (CP) covered and bare metal stents, Formula stents (Cook), Coronary stents and V12 Advanta covered stents. These stents vary in size and strength and stent choice are dependent on patient anatomy and age.

Described outcomes in other settings:

Published studies shows a good prognosis after successful and uncomplicated repair of the coarctation of the aorta. However, there are numerous complications associated with repair of coarctation, which will invariably affect the long term prognosis.

A study done in Iran in 2011 comparing outcome of repair following surgery vs. balloon angioplasty in infants <1 year, revealed no difference in the effectiveness of the methods but a significant lower risk of recoarctation in the surgery group at 17% as opposed to the balloon angioplasty group at 20%,(p-value 0.047). [11]

When comparing surgical procedures, (resection with end-to-end anastomosis vs. subclavian flap aortoplasty vs. patch graft aortoplasty) , a retrospective review in children under 14 years treated at Rajee Heart Centre (Iran) revealed the lowest rate of re-coarctation with subclavian flap aortoplasty (3.2%) and highest rate with patch graft aortoplasty(12.7%).[12]

However, an American study which was published in 2015 from the paediatric department at the Duke University Medical Centre, showed that the subclavian aortoplasty was not the preferred surgical procedure because of compromising the subclavian artery. The latter was associated with a subclavian steal phenomenon, with retrograde flow from the vertebral artery, reduced muscle bulk and length in the left upper limb as well as claudication with exercise. The preferred technique for surgical repair appeared to be the extended end-to-end anastomosis especially in small children as it carried a low mortality , as well as only 4 -11% rate of restenosis . [12] Regarding balloon angioplasty, there was a high risk of restenosis, up to 53% in native coarctation compared with a 20% rate with endovascular stent placement. The latter, however revealed a higher rate of aortic wall complications i.e. aneurysm, intimal tear and dissection at 3.9% vs. 1 -2% with balloon angioplasty. [13]

A 10 year retrospective study was done in 2018 at the Bristol Royal Hospital for Children of neonates below 2kg. The aim was to outline if the low birth weight and prematurity was a high risk for morbidity and mortality post-surgical repair for coarctation of the aorta. The results showed no deaths and low incidence of recurrence. Therefore waiting for growth in patients below 2kg was not justified. [14]

Regarding mortality, studies reveal low mortality rate guided by early appropriate intervention. In a study published in 2016 from Iran, revealed an overall 2.8% mortality rate in infants (< 1year) who underwent resection with end-to-end and/or subclavian flap aortoplasty. Survival rate was 98.2% and 96% respectively for the two procedures. [15]

A long-term follow-up study was done at Texas Children's Hospital to analyze the outcomes of surgical repair through left thoracotomy in children < 18yrs. This revealed a perioperative mortality rate of 1% (all neonates) with the re-intervention rate of 14% at median follow-up at 6yrs (7days – 19years). Factors that contribute to mortality and morbidity were associated cardiac lesions, arch hypoplasia and genetic abnormalities. [16]

The following are the most common complications post percutaneous /surgical interventions:

- Residual coarctation
- Restenosis
- Aortic dissection
- Aortic aneurysm
- Rebound hypertension (Post coarctectomy syndrome)
- Intracranial hemorrhage
- Stent displacement with vessel disruption
- Infective Endocarditis

As mentioned earlier, these complications may occur with either of the treatment options though to varying extents. It is therefore imperative to choose a treatment option based on the age of the patient, the size of the narrowing and take into consideration the presence of other cardiac defects.

Follow –up remains key in these patients as it will help to monitor and manage possible complications.

GAPS IN THIS RESEARCH

Unfortunately there are no studies documenting the outcomes of management of coarctation of aorta in South Africa. As a result, our research results will be compared to international standards even though we function in a resource limited setting. More local studies on this subject will definitely be beneficial.

RESEARCH QUESTION (S)

Primary :

Are the methods being practiced to manage patients with coarctation of aorta at Universitas Academic Hospital optimal or do we need to change our current practice?

Secondary :

- Are our outcomes comparable to international standards?
- How do we compare outcomes in the low resource setting to high resource setting?

AIMS AND OBJECTIVES

AIM:

The aim of this study was to evaluate the outcomes of management in patients with native coarctation of the aorta aged from birth to 19 years, treated at the department of Cardiology at Universitas Academic Hospital over a 10 year period.

OBJECTIVES:

The main objective of this study was to describe the outcomes in patients with coarctation of the aorta over the period. These included:

Complications:

- Here we evaluated the procedure related complications .This could be during the procedure, shortly after or later during the follow-ups.
- Complications of the cardiac lesion itself will also be described.

Rate of re-intervention:

- This outlines the number of patients that required more than one intervention. This indicates the rate of recoarctation after the first procedure.
- We also described the difference in re-intervention rate between the patients who had surgery and those who had percutaneous procedures.

Mortality rate:

- Here we describes the number of patient who died by the end of the study period.
- Cause of death was also described, either cardiac or non-cardiac.

STUDY METHODS

Study Setting

This study was undertaken in the Department of Paediatric Cardiology at Universitas Academic Hospital in Bloemfontein, South Africa.

Study Design

The study was a descriptive, cross-sectional study. A retrospective review of a cardiology database was done of patients who presented with native coarctation of the aorta, who were managed and followed up within the 10 year period.

Study Sample

The inclusion criteria in this study were as follows:

- Patients aged 0 up to 19yrs who presented at the department of cardiology between 01 January 2007 and 31 December 2016.
- These patients must have presented with native coarctation of the aorta.

The exclusion criteria were:

- Patients above 19 years of age.
- Associated inoperable cardiac lesions.
- Patients with incomplete data. These were the patients whose gradients and interventions were not recorded.
- Patients presenting for the first time with re-coarctation of the aorta.

Prior to the collection of data, the study sample was estimated to be at 150 patients.

MEASUREMENTS

Patient information was sourced from an existing database called "File Maker Pro" at the department of Pediatric Cardiology. This system has been designed to safely secure clinical information for all patients that are seen in cardiology. It includes admission and follow-up notes of clinical, echocardiogram and procedural findings.

Each patient was provided with a number which was used for identification purposes in case information needed to be rechecked. A data collection sheet was designed with all necessary variables for this study.

The variables were as follows:

- Age and weight at presentation
- Echocardiogram findings before and after surgery
- Date of the first procedure
- Type of procedure (surgical or percutaneous)
- Date of subsequent procedures where applicable
- Complications
- Death (if cardiac or non-cardiac)
- Date of death
- Date of last consultation.

Data of the patients included in the study was used from the first date of presentation up to the last consultation date within the study period.

METHODOLOGICAL AND MEASUREMENT ERRORS

- Patients that were lost to follow-up may contribute to an inappropriately low rate of some of the long term complications since their complications were not counted.
- Patients were followed-up for different periods of time which resulted in a shorter period to evaluate the last group of patients.

ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Health Sciences Research Ethics Committee of the Faculty of Health Sciences, University of the Free State, as well as the Free State Department of Health. The allocated study number is **UFS-HSD2017/1545/2808.**
To ensure confidentiality, the names of the patients that fulfilled inclusion criteria were not captured in the data collection sheet. No information that could identify the patient was transferred to the research study records. Since this was a retrospective study that was conducted using available data which was collected by the researcher, consent/assent was therefore not necessary.

BUDGET

Expenses included stationery, paper and cartridges for printing data collection sheet. These expenses were paid for by the researcher.

PILOT STUDY

Once an approval was obtained from the Health Sciences Research Ethics Committee (HSREC) and the Department of Health Free State, a pilot study was conducted using information of the first 5 patients seen at the beginning of the 10 year period. At the end of the pilot study, there was a meeting with the biostatistician in which a spreadsheet was designed for effective data capturing. As no changes to the data collection process were necessary after the pilot study was done, the patients included in the pilot study were included in the main study.

DATA ANALYSIS

Descriptive statistics namely mean and standard deviations or medians and percentiles were calculated for continuous data. Frequencies and percentages were calculated for categorical data .The analysis was done by the Department of Biostatistics at the University of the Free State.

IMPLEMENTATION OF THE FINDINGS

The results of the study have been made available to the head of the department of Pediatric Cardiology and will also be presented to the department of cardiothoracic surgery. Depending on the outcome of the study recommendations will be made to improve the outcome of the repairs of coarctations of the aorta at Universitas Academic Hospital.

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CHAPTER 2

PUBLISHABLE MANUSCRIPT

Format as for SA Heart Journal.

(See attached instructions for authors)

Coarctation of Aorta: A 10 year follow up study of patients treated at the Department of Paediatric Cardiology, Universitas Academic Hospital.

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ABSTRACT

Background: Coarctation of aorta accounts for 6-8% of all congenital cardiac lesions. It can be treated surgically or percutaneously depending on the age and weight at presentation and associated cardiac lesions.

Objectives: To describe the outcomes of management in patients with native coarctation of aorta with regard to re-intervention and mortality rate.

Methods: A retrospective, descriptive review of patients with native coarctation of aorta was done at Universitas Academic Hospital using an electronic database. Included were patients who presented from 01 Jan 2007 – 31 Dec 2016, from birth to 19yrs.

Results: The study comprised of 107 patients, median age of 33 days (1 – 4940) with a median weight of 3.9kg (1 – 53.5kg). Common associated cardiac lesions included PDA (n=61; 57%), bicuspid aortic valves (n=41; 38.3%) and VSD (n=31;29%). A total of 82 patients (80.3%) required an intervention of which 71(86.6%) had surgery with 12(14.6%) requiring a second intervention, while 11(13.6%) had percutaneous procedures with 7(63.6%) requiring a second intervention. Overall mortality was 17(15.9%), the cause of death in 14(82.4%) was cardiac related.

Conclusion: Surgery is currently the preferred treatment for coarctation of the aorta and carries a lower recoarctation rate compared to percutaneous interventions.

INTRODUCTION

Coarctation of the aorta is a congenital cardiac lesion in which there is a narrowing of the aortic segment. It is usually located near the ligamentum arteriosum, adjacent to the left subclavian artery.[1] It accounts for 6 – 8 percent of all congenital cardiac conditions

and may present in association with other cardiac defects. The most common lesions are bicuspid aortic valve, ventricular septal defect (VSD) and patent ductus arteriosus (PDA).[2] Clinical presentation varies widely depending on the age of the patient and the degree of the coarctation. Neonates with duct-dependent or critical coarctation may present early with circulatory collapse following closure of the ductus arteriosus while older children usually present with hypertension of varying degrees.[3] Early detection and referral improves the outcome, but in South Africa this remains a big challenge due to poor referral systems and patients lost to follow-up. Antenatal screening and diagnosis can be difficult while post-natal screening is not done routinely.[4]

The precise pathogenesis of congenital coarctation is unknown; however, there are three main theories that are widely recognized. These include: migration or extension of ductal tissue into the wall of the fetal thoracic aorta, diminished antegrade intrauterine blood flow causing underdevelopment of the fetal aortic arch and genetic influences. There is a recognizable pattern in patients with Turner syndrome [5], where up to 35% of individuals can be affected, and may be secondary to lymphedema.[6]

Diagnosing coarctation of the aorta includes four limb Doppler blood pressure monitoring which is an accurate, non-invasive method of determining the gradient. Echocardiography is the investigation of choice for early diagnosis and is readily available. CT angiogram with 3D reconstruction remains the gold standard when evaluating coarctations and the anatomy of the aortic arch.[3] Catheterization is invasive but provides a definitive diagnosis and opportunity for interventional procedures.[7]

The treatment of coarctation of aorta includes both medical and surgical modalities. Medical treatment is temporary until the definite surgery or intervention can be undertaken. Neonates who present with duct dependent/critical coarctation will require prostaglandin E1; this will keep the ductus arteriosus patent allowing distal blood flow. Diuretics are used in patients with cardiac failure and beta-blockers for hypertensive patients. Interventions can either be surgical or percutaneous depending on the age, weight and clinical presentation.[8] Possible complications include restenosis, aortic dissection, aortic aneurysm, rebound hypertension, stent displacement with vessel disruption and infective endocarditis.

What is known regarding outcomes?

Studies show a good prognosis after successful and uncomplicated repair of the coarctation of the aorta. However, there are various complications including recoarctation, chylothorax and laryngeal nerve injury are associated with repair of coarctation of the aorta, which may affect the long-term prognosis.

A study done in Iran in 2011 comparing the outcome of repair following surgery vs. balloon angioplasty in infants <1 year, revealed no difference in the effectiveness of the methods but there was significant lower risk of recoarctation in the surgery group at 17% as opposed to the balloon angioplasty group at 20%(p-value=0.0470).[9]

When comparing the surgical procedures, (resection with end-to-end anastomosis vs. subclavian flap aortoplasty vs. patch graft aortoplasty), a retrospective review in children <14 years who were treated at Rajee Heart Centre(Iran) showed that the lowest rate of re-coarctation was after the subclavian flap aortoplasty (3.2%) and highest rate after patch graft aortoplasty (12.7%).[10]

A 10-year retrospective study was done in 2018 at the Bristol Royal Hospital for Children in neonates below 2kg. The aim of the study was to establish whether the low birth weight and prematurity were a high risk for morbidity and mortality post repair for coarctation of the aorta. Results revealed zero deaths and low incidence of recurrence. Waiting for growth in patients below 2kg was therefore not justified.[11]

Overall, studies reveal low mortality rate guided by early appropriate intervention. In an Iranian study published in 2016, mortality rate was 2.8% in infants under 1 year who underwent resection with end-to-end and/or subclavian flap aortoplasty. Survival rates were 98.2% and 96% respectively.[12]

Follow–up remains imperative in monitoring progression, assessing for possible complications and planning future treatment if indicated.

Unfortunately, there are no studies in South Africa or neighboring countries on this subject, which calls for further research to describe local pathology and outcomes.

AIMS AND OBJECTIVES

AIM:

The aim of this study was to evaluate the outcomes of management of patients with native coarctation of the aorta aged from birth to 19 years, treated at the department of Pediatric Cardiology at Universitas Academic Hospital from 1 January 2007 – 31 December 2016.

OBJECTIVES:

The main objective of this study was to describe the outcomes in patients with coarctation of the aorta. These include:

Complications:

Here we evaluated the procedure related complications. This could be during the procedure, shortly after or later during the follow-ups. Complications of the cardiac lesions were also listed.

Rate of re-intervention:

This outlines the number of patients that required more than one intervention. This indicated the rate of re-coarctation after the first procedure.

Mortality rate:

The number of patients that had died by the end of the study period was evaluated. The cause of death was also described as cardiac or non-cardiac.

METHODOLOGY

Study design and population

The study was undertaken in the Department of Paediatric Cardiology at Universitas Academic Hospital in Bloemfontein, South Africa. This is a descriptive, cross-sectional study in which a retrospective review of cardiology database was done on patients who presented with native coarctation of the aorta. These patients were managed and followed up over a 10-year period. Included in the study were patients aged 0 – 19yrs who presented at the Department of Cardiology from 01 January 2007 – 31 December 2016. Exclusion criteria consisted of patients above 19 years of age, associated

inoperable cardiac lesions, patients with incomplete data (patients whose gradients and interventions were not recorded) and those who presented for the first time with re-coarctation of aorta.

Ethical approval was obtained from the Health Sciences Research Ethics Committee of the Faculty of Health Sciences, University of the Free State, as well as the Free State Department of Health. To ensure confidentiality, no information that could identify the patient was made available. Since this was a retrospective study that was conducted using available data which was collected by the researcher, consent/assent was therefore not necessary.

Data capturing and analysis

Patient information was sourced from an existing database called "File Maker Pro". This system has been designed to safely secure clinical information for all patients that are seen in the department of Pediatric Cardiology. It includes admission and follow-up notes of clinical, echocardiogram and procedural findings. Each patient was provided with a number which was used for identification purposes in case information needed to be rechecked. A data collection sheet was designed with all necessary variables for this study. The variables included age, weight and gender at presentation, echocardiographic findings before and after surgery, date of the first procedure, type of procedure (surgical or percutaneous), date of subsequent procedures where applicable, complications, death (cardiac or non-cardiac), date of death and date of last consultation. Each patient was followed from the first date of presentation to the last date consultation within the study period.

Means and standard deviations or medians and percentiles were calculated for continuous data. Frequencies and percentages were calculated for categorical data. The analysis was done by the Department of Biostatistics at the University of the Free State.

RESULTS

<u>Patient demographics:</u>

There was a total of 135 patients who presented with coarctation of aorta in the 10-year period of which 107 met the inclusion criteria. Exclusions included associated in-operable complex cardiac lesions (19 patients) and age >19years (9 patients). The study population consisted of 48(45%) males and 59(55%) females. The study sample comprised mainly of neonates and the recoarctation rate amongst this group was 20.5 %(n=8) The median age was 33 days (1day – 4940 days) and median weight of 3.9kg (1kg – 53.5kg). Only two patients in this study were diagnosed antenatally.

AGE		WEIGHT	
<1 month	48(44.8%)	< 3kg	24(22.4%)
1month – 1 year	36(33.6%)	3 – 10kg	53(49.5%)
>1 – 5 years	14(13%)	>10 – 20kg	13(12.1%)
>5 – 10years	7(6.5%)	20 - 40kg	3(2.8%)
>10years	2(1.9%)	>40kg	1(0.9%)
		Unknown	13(12.1%)

Table (i): Weight/Age category

Associated Cardiac Lesions:

Associated cardiac lesions were found in 98(91.6%) patients. The most common associated lesions are shown in the bar graph (figure 1).

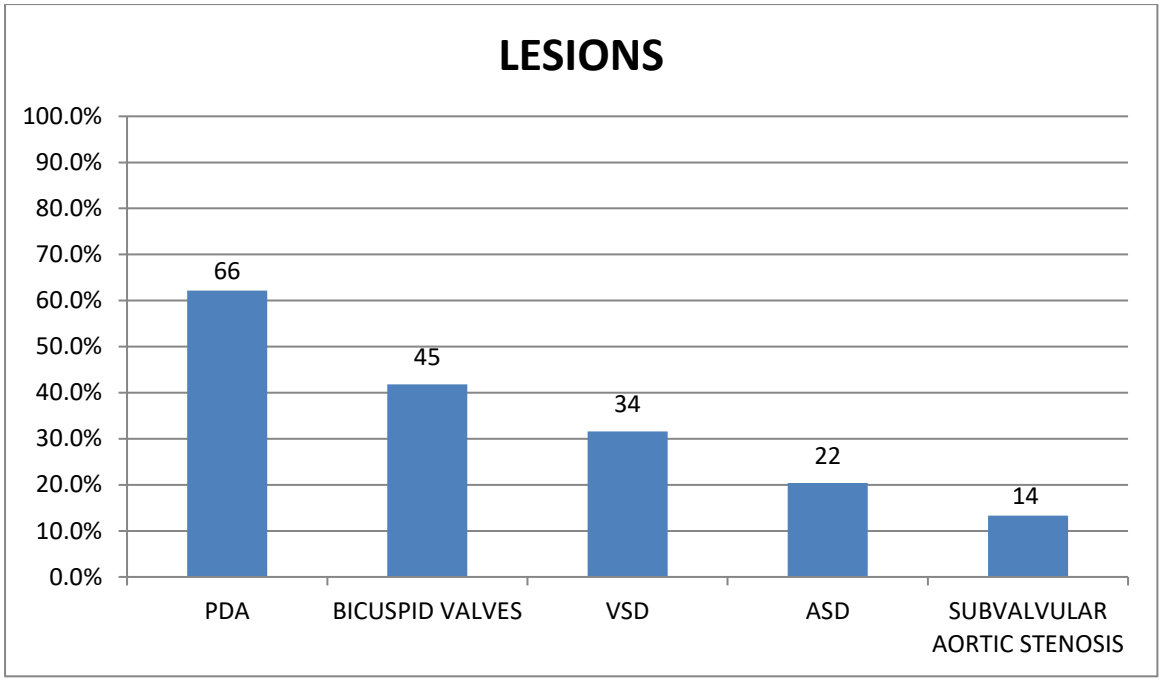

Figure 1: Associated cardiac lesions

Of all the patients that were included in the study, only 1(0.9%) patient had confirmed Turner syndrome.

INTERVENTIONS

Of the total patients that were included in the study, 82(76.6%) had interventions performed while the rest presented with mild coarctation. The interventions were surgical correction (resection with end-to-end anastomosis /patch grafting/ subclavian aortoplasty) or percutaneous (stent or balloon angioplasty). Stents used included: coronary stents, Formula^{R}, V12 Advanta^{R} or Cheatham Platinum^{R} (CP) (covered or bare-metal) stents. The selection of the stent depended on the age and weight of the patient.

First intervention procedures were divided into surgery 71(86.6%), stents 9(11.0%) and balloon angioplasty 2(2.4 %). Amongst the patients who had surgery, 39(54.9%) were neonates and 34(87.2%) of them were operated within 30 (2-30) days of presentation. End-to-end anastomosis was the preferred surgical intervention in 34 (87.2%) of the neonatal patients. The mean gradient reduction was 21 mmHg (39mmHg – 89mmHg).

In the surgical group as first intervention, 12(16.9%) and 6(66.6%) in the stent group required a second intervention respectively. In 16(84%) patients the second

reintervention (surgical of percutaneous) was performed within the first year postoperative with mean period at 4months (range 1m – 9m). These interventions included surgery 4(21.1%), stent 6(31.6%) and balloon angioplasty 9(47.4%), with a mean gradient reduction of 16mmHg(16mmHg – 48mmHg).

Seven(7.5%) of the patients required a third and 3(2.3%) a fourth intervention. Only 1 patient underwent five interventions.

OUTCOMES:

Complications

Outlined below are the complications that were noted during follow up.

Cardiac Failure	42
Re-coarctation	24
Pulmonary Hypertension	15
Hypertension	7
Pericardial Effusion	6
Dysrhythmia	4
Aortic Aneurysm	2
Coronary fistula	1
Stent displacement	1
Femoral vein avulsion	1
Thromboembolic event	1
Aneurysm of the sinus of valsava	1

Table (ii): Complications

The complications mentioned above includes primary complications due to the coarctation of the aorta itself and secondary complications related to the procedures performed. Some patients experienced more than one complication all of which were managed accordingly. Medical treatment included diuretics, angiotensin-converting-enzyme inhibitors and Beta-blockers.

Mortality:

Overall mortality was 17(15.9%) and the cause of death in 14(82.3%) patients was cardiac related. The median period of death was within 14 days (range of 24hours – 9months) from the intervention. The most common cause of early death was arrhythmias while late deaths were associated with pulmonary oedema secondary to cardiac failure. Findings show that 10(58.8%) of the patients who demised had surgery performed and the most common associated cardiac lesions were bicuspid aortic valve valves (5; 35.7%), VSD (4; 28.5%) and ASD (4; 28.5). The cause of non-cardiac death in children who had undergone surgery was septicemia.

Follow-up:

Patients were followed up for median time interval of 607 days (1 – 3511 days) after the first procedure. Median pressure gradient over the coarctation on the last consultation was 21mmHg (0 – 58mmHg). A total of 13(12.1%) patients were lost to follow-up, 11 of whom were lost within the first 6 months post-procedure.

DISCUSSION

Coarctation of the aorta is an important congenital cardiac lesion with possible high morbidity and mortality if left untreated. Early diagnosis offers the opportunity to plan and provide best age-appropriate treatment.

Surgery is the treatment of choice in our center, but we are moving towards a mixed strategy which includes surgical and percutaneous interventions on a patient specific basis. The majority of patients in this series had a surgical intervention, but this may change in the future with the development of more percutaneous options. The risk of developing complications remains regardless of chosen therapy and patients should be monitored for aortic aneurysms, recoarctation and hypertension.

The study sample comprised mainly of neonates and the recoarctation rate amongst this group was 20.5 %(n=8) which was higher than expected in comparison to an

American study which described 4-11%.[13] This may be attributed to low weight at presentation and critically ill neonates treated with stent implantation as bridge to surgery.

Percutaneous treatment of coarctation has greatly improved and reduced the perioperative burden, but possible complications and risk of stent fracture and migration has to be considered. In our center we are performing less balloon dilatations due to the risk of aneurysm formation, and covered stents should always be available if this is considered. Even though reliable long-term data is not available regarding the effectiveness of stent implantation, it has become our choice in patients with ventricular dysfunction and other serious comorbidities. Stent implantation commits a patient to future interventions and one should accept a higher rate of reintervention.

The increased mortality may be multifactorial and includes patients presenting late with poor ventricular function and pulmonary hypertension.

As indicated above, 12.1% of the patients were lost to follow-up which is of concern and needs to be addressed. This might be due to issues related to transportation since this institution caters for two provinces (Free State & Northern Cape) and a neighboring country (Lesotho). Follow up remains a problem in our setting and should include a multidisciplinary team that range from the primary physician monitoring the blood pressure and distal pulses to the cardiologist and surgeon treating complications. Patient and parent education continue to be important and follow-up needs to be clearly communicated and individualized. Irrespective of the treatment modality this should be lifelong as no treatment is curative.

Association with Turner Syndrome in this study appeared to be low compared to a 2015 study done at Utah that revealed 12.6% association.[14] Neurological deficits are described but did not occur in our experience.

STUDY LIMITATIONS

The follow up of the participants varied (followed up over different periods) and the patients that were lost to follow-up may have created inappropriate impression of the complication rate.

CONCLUSION

In this study surgery carries a lower re-intervention rate compared to percutaneous interventions although not statistically shown. This is also to be expected as stent implantation commits the patient to reintervention. Follow-up remains important as all patients have the long-term risk for developing complications. Future studies may be indicated to determine the complexity of the increased mortality rate compared to international standards and the possible influence of the interventional area.

RECOMMENDATIONS

An efficient antenatal screening program is important as it may establish early diagnosis and development of a patient specific management plan

The poor follow-up rate is of concern and factors responsible needs to be studied. Regular outreach clinics may play a role in improving follow-up rates.

Conflict of interest

None.

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WORD COUNT:

Abstract: 193

Article: 3081

APPENDIX A: ETHICS APPROVAL

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA

UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

23-Aug-2018

Dear **Dr Nompi Nyindi**

Ethics Clearance: **Coarctation of Aorta : A 10 year follow-up study of patients treated at the Department of Cardiology , Universitas Hospital .**

Principal Investigator: **Dr Nompi Nyindi**

Department: **Paediatrics and Child Health Department (Bloemfontein Campus)**

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2017/1545/2808**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
T: +27 (0)51 401 7795/7794 | E: ethicsfhs@ufs.ac.za
IRB 00006240; REC 230408-011; IORG0005187; FWA00012784
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APPENDIX B: DOH APPROVAL

health
Department of Health
FREE STATE PROVINCE

12 July 2018

Ms. N Nyindi
Dep. Of Paediatrics and Child Health
UFS

Dear Ms. N Nyindi

Subject: Coarctation of Aorta: A 10 year follow-up study of patients treated at the Department of Cardiology, Universitas Hospital.

- Please ensure that you read the whole document, Permission is hereby granted for the above – mentioned research on the following conditions:
- Serious Adverse events to be reported to the Free State department of health and/ or termination of the study
- Ascertain that your data collection exercise neither interferes with the day to day running of Universitas Hospital nor the performance of duties by the respondents or health care workers.
- Confidentiality of information will be ensured and please do not obtain information regarding the identity of the participants.
- **Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).**
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of The University of the Free State and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of The University of the Free State and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to** sebeelats@fshealth.gov.za or lithekom@fshealth.gov.za **before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- Please discuss your study with the institution manager/CEOs on commencement for logistical arrangements
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- You are encouraged to present your study findings/results at the Free State Provincial health research day
- Future research will only be granted permission if correct procedures are followed see http://nhrd.hst.org.za

Trust you find the above in order.
Kind Regards

Dr D Motau
HEAD: HEALTH
Date: 19/07/2018

Head : Health
PO Box 227, Bloemfotein, 9300
4th Floor, Executive Suite, Bophelo House, cnr Maitland and, Harvey Road, Bloemfotein
Tel: (051) 408 1646 Fax: (051) 408 1556 e-mail:khusemj@fshealth.gov.za@fshealth.gov.za/chikobvup@fshealth.gov.za

APPENDIX C: APPROVED PROTOCOL

Coarctation of Aorta: A 10 year follow up study of patients treated at the Department of Paediatric Cardiology, Universitas Academic Hospital.

NOMPI

PROTOCOL TITLE

Coarctation of Aorta: A 10 year follow-up study of patients treated at the Department of Cardiology, Universitas Hospital.

REGISTRAR NAME: Dr NM Nyindi

STUDY LEADER: Dr D Buys

DEPARTMENT: Department of Paediatric and Child Health

School of Medicine

Faculty of Health Sciences

University of the Free State, Bloemfontein

DATE OF SUBMISSION: 23 Nov 2017

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LIST OF ABBREVIATIONS AND DEFINITIONS

2.1 ABBREVIATIONS

ADH	Anti-diuretic hormone
BP	Blood pressure
CXR	Chest X-ray
CT	Computed Tomography
ECG	Electrocardiogram
MRI	Magnetic Resonance Imaging
RAAS	Renin- Angiotensin - Aldosterone

2.2 DEFINITIONS

Native Coarctation of Aorta: Narrowing of the aorta that had never a procedure performed.

Percutaneous Procedure: Where a needle puncture through the skin is used to access the heart (closed)

Surgical procedure: Where an incision is made on the chest to access the heart (open)

INTRODUCTION AND LITERATURE REVIEW

Coarctation of the Aorta is defined as a narrowed aortic segment, located most commonly near the ligamentum arteriosum adjacent to the left subclavian artery. (1) It accounts for 6 – 8 percent of all congenital cardiac conditions (2) and may present in

association with other cardiac defects, such as bicuspid aortic valve, ventricular septal defect, patent ductus arteriosus etc. There's a wide spectrum of patients with this condition, those presenting during neonatal period, early childhood and later in life. Neonates with duct-dependent or 'critical coarctation' may present with heart failure, acidosis and shock following closure of the ductus arteriosus. These patients will require resuscitation and urgent intervention to prevent death(3) .In childhood and adolescence , coarctation usually present with hypertension which may result in end organ damage if left untreated .The earlier the referral the better the outcome , however in our country patients present late due to poor referral systems . Antenatal screening also don't always pick up the lesions, post-natal screening not done routinely and some of those that are diagnosed are lost to follow-up.

Pathogenesis

The precise pathogenesis of congenital coarctations is unknown; however, there are three main theories that are widely recognized:

a. Migration or extension of the ductal tissue into the wall of the fetal thoracic aorta. (4)
b. Reduced antegrade intrauterine blood flow causing underdevelopment of the fetal aortic arch. (4)
c. There is also a genetic influence on the development of coarctation that is recognizable in patients with Turners XO Syndrome, where about 35% are affected (2). This may be secondary to lymphedema.

Pathophysiology:

As a result of the coarctation, the left ventricle (LV) is placed under a significant afterload which results in wall stress and LV hypertrophy. This increase in afterload may be acute or gradual, in neonates with severe coarctation following closure of ductus arteriousus or in older children with less severe obstruction respectively. The latter

group tends to develop collateral vessels that partially bypass the aortic obstruction, hence more gradual increase in afterload (5).

Development of hypertension is postulated to be as a result of the following mechanisms:

- Humoral mechanism

As of the outflow obstruction there is poor renal perfusion which results in activation of Renin-Angiotensin-Aldosterone mechanism. Renin is produced from the juxtaglomerular cells of the afferent arteriole of the proximal tubules, which then result in the production of Angiotensin I from the liver with subsequent production of Angiotensin II using Angiotensin –Converting Enzyme from the lungs. Angiotensin II will result in efferent vasoconstriction and further release of aldosterone which will result in re-absorption of sodium with subsequent water retention, leading to an increase in blood pressure. Angiotensin II also results in the release of anti-diuretic hormone (ADH) also called vasopressin .This is produced from the supraoptic and paraventricular nuclei of the hypothalamus ,then transported to the posterior pituitary gland which will also result in vasoconstriction (V1 receptors) ,increasing systemic vascular resistance .Secondly ,vasopressin act on V1 –receptors in the collecting ducts of the kidneys resulting in re-absorption of free water ,increasing blood volume and therefore resulting in increasing blood pressure .(6)

- Mechanical Obstruction theory

This mechanism postulates that there is a higher blood pressure required to maintain blood flow through the narrowed aortic segment and collateral vessels .This mechanism applies to the high pressure created proximal to the coarctation by the stroke volume ejected into the limited aortic receptacle. This theory however does not explain the mechanism involved in increased peripheral resistance distal to the obstruction and the delay or failure of resolution of hypertension post the release of the obstruction. (6)

b) Cardiac Failure

Mechanism of developing heart failure is thought to be secondary to the RAAS mechanism and its effects as mentioned above.

Secondly through activation of central sympathetic nervous system which will lead to increase in heart rate and blood pressure. (5)

Diagnosis

Clinical presentation of coarctation of the aorta depends on the age of the patient and presence /absence of other significant cardiac lesions.

Neonatal Period (Birth to 28 days of life)

In neonates, they may be asymptomatic while the ductus arteriosus is still patent, however once the duct closes then will quickly decompensate.

On history parents may complain of difficulty feeding, sweating, dyspnea or lethargy.

On assessment these patients will be acutely ill, with signs of congestive cardiac failure (edema, tachypnea, tachycardia), may be in shock with metabolic acidosis. These patients may also have differential cyanosis (pink upper extremities with cyanotic lower extremities), this may not always be obvious to the eye, and hence it is important to document the preductal and postductal saturations. (3)

It is important to feel for femoral pulses as the delay (radio-femoral) or absence thereof is the hallmark sign of coarctation of the aorta. (2)

Early childhood (1 month – 5 years)

These patients may be referred for evaluation of a murmur. This is usually best heard as grade 2 -3/6 systolic ejection murmur over the upper left sternal border, at the base and in the left interscapular area posteriorly. A constant systolic ejection click may be heard at the apex, signaling the presence of a bicuspid valve or a continuous murmur may be heard throughout the chest anteriorly, posteriorly and laterally if there's well developed arterial collateral system. (4)

Older Children and Adolescence (> 5 – 19 years)

These patients may present with intermittent claudication (calf muscle pain induced by activity). Clinically will be found to have hypertension. It is therefore imperative to measure the blood pressure (BP) in all four limbs as this will help note any difference between upper and lower extremities 'BP. Higher BP in upper extremities compared to lower signifies the presence of coarctation of the aorta. (4)

Investigations

Chest X-ray (CXR)

- This may reveal a cardiomegaly with increased pulmonary vascular markings due to pulmonary congestion.
- Indentation of the aortic wall at the site of coarctation with pre and post coarctation dilatation which can produce a "3" sign.
- Notching of the posterior one-third of the third to eighth ribs due to erosion by the large collateral arteries. This is usually more apparent between the ages of 4 and 12 years. (5)

Electrocardiogram (ECG)

- In neonates, ECG findings may reveal age-appropriate Right Ventricular Hypertrophy
- However later in life may reveal Left Ventricular Hypertrophy with signs of left ventricular strain or ischemia (3)

Echocardiogram

- The high quality two dimensional and Doppler echo will establish/confirm the diagnosis and severity of the coarctation. This will also assist in detecting other cardiac lesions.
- The Doppler will assist in determining the hemodynamic severity of the coarctation and the establishing the pressure gradient. (3)

Magnetic Resonance Imaging (MRI) / Computed Tomography (CT) Angiography:

- This mode of investigation remains the gold standard when evaluating the coarctations and the anatomy of the aortic arch.

- This modality will clearly define the location and severity of the coarctation and collateral vessels. The pressure gradient across the coarctation can also be accurately measured.(3)

Cardiac Catheterization:

- This helps to confirm the diagnosis when Echo findings are not completely clear.
- Systolic Pressure gradient is also measured, whereby <20mmHg is regarded as mild coarctation and above which may be severe provided there's neither PDA nor other cardiac lesions or left ventricular dysfunction.
- It is also used for therapeutic purposes like balloon angioplasty or stent implantation in the native or recurrent coarctation. (5)

Treatment options:

Medical

- Prostaglandin E1 in duct dependent /critical coarctation: This will help to keep ductus arteriosus open to allow oxygenated blood to the body.
- Treatment of cardiac failure: Diuretics are used to reduce the fluid overload.

Treatment of Hypertension: B-blockers remain treatment of choice for hypertension.

Surgical

- Resection with end to end anastomosis: In this case the coarctated area is completely cut out then the remains ends of the vessel are sutured together. This is a best option for the neonates as it completely removes the ductal material and no prosthesis is used.
- Subclavian flap aortoplasty: Here the left subclavian artery is used as a roof over the previous coarctated area.
- Patch Aortoplasty: In this case a prosthetic patch is used as a roof of the previous coarctated area. This is a good choice of repair in children > 2yrs but less than 16yrs.
- Bypass graft repair: Here a graft is used to bypass the coarctated area. Therefore, the graft with be attached to the arch of the aorta then bypasses the stenosis then attach to the descending aorta. (7)

Percutaneous

- Balloon Angioplasty: A catheter is inserted through the femoral artery up into the coarctated area, whereby a balloon will be inflated to dilate the narrowed area.
- Aortic Stent implantation: In this case a stent is inserted at the narrowed area. This technique is best suited for patients with long segment coarctation, or recurrent coarctation or where it is associated with hypoplasia of the isthmus or aortic arch. (8)

Outcomes

Evidence shows a good prognosis post successful, uncomplicated repair of the coarctation of the aorta. However, there are a number of complications associated with repair of this lesion, which will affect the long term prognosis.

A study done in Iran in 2011 comparing outcome of repair following surgery vs. Balloon angioplasty in infants <1 year, revealed no difference in the effectiveness of the methods but significant lower risk of recoarctation with surgery group at 17% as opposed to the Balloon angioplasty group as 20%. (8)

However, when comparing the surgical procedures, (Resection with end-to-end anastomosis vs. Subclavian flap aortoplasty vs. patch graft aortoplasty) the study the revealed lowest rate of re-coarctation with subclavian flap aortoplasty and highest rate with patch graft aortoplasty. (9)

Regarding mortality, it appears to also be low in infants below 1 year where end-to-end anastomosis was done. (10)

The following are the most common complications post percutaneous /surgical interventions:

- Residual coarctation
- Restenosis
- Aortic dissection
- Aortic aneurism
- Rebound hypertension (Post coactectomy syndrome)
- Intracranial hemorrhage
- Stent displacement with vessel disruption
- Infective Endocarditis

As mentioned earlier, these complications may occur with either of the treatment options but not to same extents. It is therefore imperative to choose a treatment option based on the age of the patient, the size of the narrowing and take into consideration the presence of other cardiac defects.

Follow –up remains key in these patients as it will help to assess for these complications and management thereof if experienced.

AIMS AND OBJECTIVES

Aim

To evaluate the outcome of management in patients with native coarctation of the aorta from 1 January 2007 – 31 December 2016, in the department of Cardiology at Universitas Hospital .Patients from birth – 19yrs.

Objectives

Survival rate

Of the total patients that will be included in the study ,we will look at the number of those that were alive by the end of the study period and those that had died.

For those that died we will establish the cause of death ,whether cardiac or non-cardiac.

Each patient will be followed from the first date of presentation to the last consultation date

The rate of re-intervention .

This will identify the number patients that required a repeat intervention/procedure

The number of the procedures performed per patient will also be taken into consideration

Procedure may be surgical or percutaneous .

Procedural Complications

This will identify the complications experienced during and/or after a procedure to the last day of follow-up.

3.2.3.1 All procedures done per patient will be taken into account.

4.Study Methods

4 .1 Study Setting

This study will be undertaken in the Department of Paediatric Cardiology at Universitas Academic Hospital in Bloemfontein, South Africa. Patients are usually diagnosed during neonatal period, infancy period, early and later in childhood. Depending on the age and general condition at first presentation, decision will be made whether to repair the lesion surgically or percutaneously . Treatment of choice for repair in neonates is surgical while in older children percutaneous interventions could suffice. Surgical repair includes: resection with end-to-end anastomosis, subclavian flap aortoplasty, patch aortoplasty and graft interposition while percutaneous repair includes balloon angioplasty and stent insertion.

4.2 Study Design

This will be a descriptive, cross-sectional study. A retrospective review of a cardiology database will be done on patients who presented with native coarctation of the aorta that were managed and followed up within a 10year period.

4.3 Study Sample

The sample will include every patient who was seen at the Department of Cardiology , with a native coarctation of the aorta , and had a procedure performed in attempt to correct the lesion. This is an estimated total of 150 patients.

4.3.1 Inclusion criteria

- Patient must have presented with native coarctation of aorta between 01 January 2007 and 31 December 2016

4.3.2 Exclusion Criteria:

- Patients presented before 01 January 2007 and/or after 31 December 2016
- Patients with associated inoperable lesions
- Patients with incomplete data
- Patients presenting for the first time at Universitas Hospital with re-coarctation will be excluded.

4.4 Measurement

Patient information will be sourced from an existing database called "File Maker Pro". This system has been designed to safely secure clinical information for all patients that are seen in the department of Pediatric Cardiology .This includes admission and follow-up notes of clinical ,echocardiogram and procedural findings.

It is available on specific computers in the Pediatric Cardiology Department with security codes to prevent free access into patient information.

Each patient will be provided with a number; this will be for identification purposes in case information needs to be rechecked. A data collection sheet will be designed with all necessary variables for this study.

The variables will be as follows:

- Age and weight at presentation
- Echocardiogram findings before and after surgery
- Date for first procedure
- Type of procedure (surgical or percutaneous)
- Date of subsequent procedures where applicable
- Complications
- Death (If Cardiac or Non-cardiac)
- Date of death
- Date of last consultation.

4.5 Methodology and Measurement Errors

4.7.1 Patients that are lost to follow-up may give inappropriate low impression of some of the long term complication rate since their complications will not counted.
4.7.2 Patients will unfortunately be followed over different periods of time giving minimal time to evaluate the last group of patients.

4.6 Pilot Study

Once an approval has been obtained from the Ethics committee and the Department of Health Free State, a pilot study will be conducted using information of 5 patients. This will help to examine the efficacy of the designed excel spreadsheet. If any problems are encountered and changes need to be made, the ethics committee will be informed. These patients will be included in the main study.

5. ANALYSIS

Descriptive statistics namely means and standard deviations or medians and percentiles will be calculated for continuous data. Frequencies and percentages will be calculated for categorical data .The analysis will be done by the Department of Biostatistics.

6. IMPLEMENTATION OF THE FINDINGS

The results of the study will be made available to the head of the department of Pediatric Cardiology and Cardiothoracic Surgery. Hopefully measures will be employed to improve the outcome of the repairs of coarctations of the aorta.

7. TIME SCHEDULE

June 2017: Planning, Literature Review + writing of Protocol

November 2017: Ethics Committee Approval

December- January 2017: Pilot Study and Data Collection

February2018: Data Analysis

March- May 2018: Writing up of the Results

8. BUDGET

An estimate of R 370.00 will be divided as follows:

Item	**Cost**
Paper	R 100
Printing	R 120
Other Stationery	R150
Total	R370.00

9. REGULATORY APPROVAL

The protocol will be submitted for approval by the Ethics Committee at the University of the Free State, Health Sciences. This will be done prior to data collection. Once approved then the Department of Health will be contacted for approval as well.

Also of importance will be patient Names which will be kept confidential. This study will be retrospective using records, thus no consent will be required.

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APPENDIX D: DATA COLLECTION SHEET

ENGLISH **DATA COLLECTION SHEET**

Patient No: _____ **Patient Code: _____**

SECTION 1: DEMOGRAPHIC INFORMATION

1	**Date of birth (DD/MM/YY)**	_____DD/MM/YY	
2	**What is your gender?**	(a) Male	1
		(b) Female	2

SECTION 2: PRESENTATION

3	**Age at presentation (months)**	(a) 0 - 1 month	1	□
		(b) > 1 - 60 months	2	□
		(c) > 60 - 228 months	3	□
4	**Weight at presentation (kg)**	_____ kg		□
5	**Date of presentation (DD/MM/YY)**	_____DD/MM/YY		□

SECTION 3: ECHO DATA

SECTION 3.1: ASSOCIATED LESIONS (OTHER THAN COARCTATION OF AORTA)

6	**Associated lesions, other than coarctation of aorta, present?**	Yes	1
		No	2
7	**If Yes, type of lesion?**	a.	
		b.	
		c.	
		d.	
		e.	

SECTION 3.2: ECHO DATA AND INTERVENTIONS FOR COARCTATION OF AORTA

GRADIENT VALUES AND SHORTENING FRACTION (PRE AND POST INTERVENTIONS)

Section 3.2.1

8	**Intervention?**	Yes	1
		No	2
9	**If Yes, type of intervention?**	(a) Surgery	1
		(b) Stent	2
		(c) Balloon dilatation	3
10	**Date of intervention (DD/MM/YY)**	_____DD/MM/YY	
11	**Gradient values:**	Pre mmHg	
		Post mmHg	
		Gradient reduction	
12	**Shortening fraction:**	Pre intervention	
		Post intervention	

Section 3.2.2

13	**Intervention 2?**	Yes	1

		No	2
14	**If Yes, type of intervention?**	(a) Surgery	1
		(b) Stent	2
		(c) Balloon dilatation	3
15	**Date of intervention (DD/MM/YY)**	_____DD/MM/YY	
16	**Gradient values:**	Pre mmHg	
		Post mmHg	
		Gradient reduction	
17	**Shortening fraction:**	Pre intervention	
		Post intervention	

Section 3.2.3

18	**Intervention 3?**	Yes	1
		No	2
19	**If Yes, type of intervention?**	(a) Surgery	1
		(b) Stent	2
		(c) Balloon dilatation	3
20	**Date of intervention (DD/MM/YY)**	_____DD/MM/YY	
21	**Gradient values:**	Pre mmHg	
		Post mmHg	
		Gradient reduction	
22	**Shortening fraction:**	Pre intervention	
		Post intervention	

Section 3.2.4

23	**Intervention 4?**	Yes	1
		No	2

24	**If Yes, type of intervention?**	(a) Surgery	1
		(b) Stent	2
		(c) Balloon dilatation	3
25	**Date of intervention (DD/MM/YY)**	_____DD/MM/YY	
26	**Gradient values:**	Pre mmHg	
		Post mmHg	
		Gradient reduction	
27	**Shortening fraction:**	Pre intervention	
		Post intervention	

Section 3.2.5

28	**Intervention 5?**	Yes	1
		No	2
29	**If Yes, type of intervention?**	(a) Surgery	1
		(b) Stent	2
		(c) Balloon dilatation	3
30	**Date of intervention (DD/MM/YY)**	_____DD/MM/YY	
31	**Gradient values:**	Pre mmHg	
		Post mmHg	
		Gradient reduction	
32	**Shortening fraction:**	Pre intervention	
		Post intervention	

SECTION 4: ASSOCIATED NON-CARDIAC CONDITIONS

1	
2	
3	

SECTION 5: MEDICAL TREATMENT

33	**Medical Treatment received**	Yes	**1**
		No	**2**
34	**If Yes: Medication used**	(a) Anti-failure	**1**
		(b) B-blocker	**2**
		(c) PGE	**3**
		(d) Anti-platelet	**4**

SECTION 6: FOLLOW-UP (date of follow up?)

Date of last consultation	_____DD/MM/YY
Age	_____ months
Gradient	_____ mmHg
Duration since 1st procedure	_____ months

SECTION 7: OUTCOMES

35	**Complications?**	Yes	1
		No	2
36	**If Yes, list complications:**	a.	
		b.	
		c.	
37	**Death**	Yes	1
		No	2
38	**If Yes, cause of death:**	Cardiac	1
		Non-cardiac	2
39	**Date of death (DD/MM/YY)**	_____DD/MM/YY	

APPENDIX E: AUTHOR GUIDLINES

Author Guidelines

Instructions for authors

SA Heart publishes peer reviewed articles dealing with cardiovascular disease, including original research, topical reviews, state-of-the-art papers and viewpoints. Regular features include an ECG quiz, image in cardiology and local guidelines. Case reports are considered for publication only if the case or cases are truly unique, incorporates a relevant review of the literature and makes a contribution to improved future patient management.

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Disclosures

Authors must declare all financial disclosures and conflicts of interest in the cover letter and on the title page of the manuscript.

Ethics

All studies must be in compliance with institutional and international regulations for human and animal studies such as the Helsinki declaration (2008) (http://www.wma.net/en/30publications/10policies/b3/17c.pdf) and the South African MRC ethics guidelines (http://www.sahealthinfo.org/ethics/index.htm). Human studies require ethics committee approval and informed consent which must be documented in your manuscript. Animal studies require ethics committee approval and must conform to international guidelines for animal research, as well as the South African National Standard for the care and use of animals for scientific purposes. Compliance with these requirements must be documented in your manuscript.

Content

1. Title page: It should contain the title of the manuscript, the names of all authors in the correct sequence, their academic status and affiliations. If there are more than 4 authors, the contribution of each must be substantiated in the cover sheet. The main author should include his/her name, address, phone, fax and email address.
2. Authors are solely responsible for the factual accuracy of their work.
3. Articles should be between 3 000 and 5 000 words in length.
4. A 200-word abstract should state the main conclusions and clinical relevance of the article.
5. All articles are to be in English.
6. Abbreviations and acronyms should be defined on first use and kept to a minimum.

7. Tables should carry Roman numeral, I, II etc., and figures Arabic numbers 1, 2 etc.

8. References should be numbered consecutively in the order that they are first mentioned in the text and listed at the end in numerical order of appearance. Identify references in the text by Arabic numerals in superscript after punctuation, e.g. …trial.

9. Articles are to be submitted directly via the journal. The text should be in MS Word. Pages should be numbered consecutively in the following order wherever possible: Title page, abstract, introduction, materials and methods, results, discussion, acknowledgements, tables and illustrations, references.

10. Where possible all figures, tables and photographs must also be submitted electronically. The illustrations, tables and graphs should not be imbedded in the text file, but should be provided as separate individual graphic files, and clearly identified. The figures should be saved as a 300 dpi jpeg file. Tables should be saved in a MS Word or PowerPoint document. If photographs are submitted, two sets of unmounted high quality black and white glossy prints should accompany the paper. Figures and photographs should be of high quality with all symbols, letters or numbers clear enough and large enough to remain legible after reduction to fit in a text column. Each figure and table must have a separate self-explanatory legend.

11. Remove all markings such as patient identification from images and radiographs before photographing.

The following format should be used for references:

Articles

Kaplan FS, August CS, Dalinka MK. Bone densitometry observation of osteoporosis in response to bone marrow transplantation. Clin Orthop 1993;294:73-8. (If there are more than six authors, list only the first three followed by et al.)

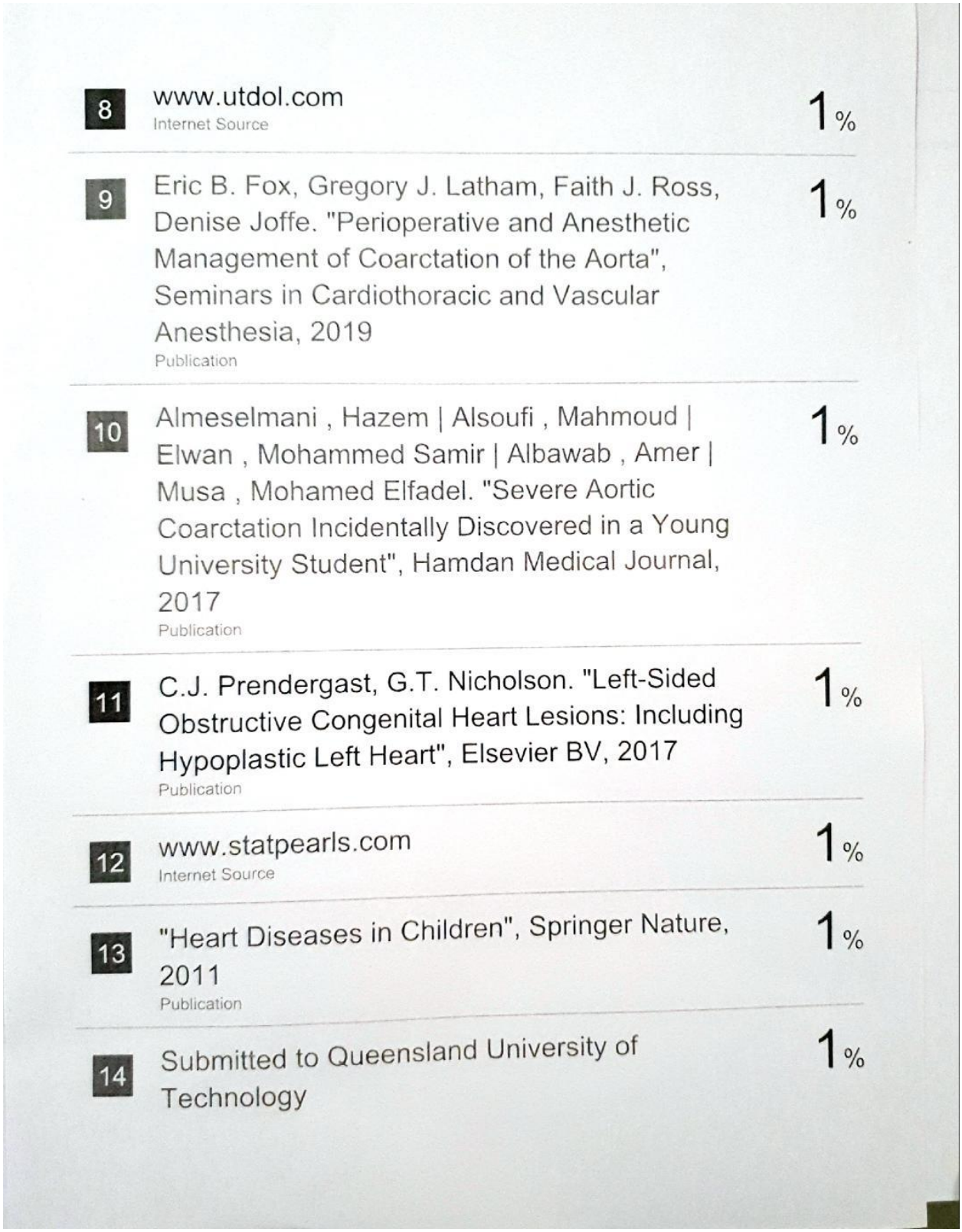
Chapter in a book

Young W. Neurophysiology of spinal cord injury. In: Errico TJ, Bauer RD, Waugh T (eds). Spinal Trauma. Philadelphia: JB Lippincott; 1991:377-94.

Online media

Norback JS, Lwellyn DC and Hardin JR (2001). Shoptalk 101. Integrating workplace communication into undergraduate engineering curricula [online]. Retrieved February 15, 2012: http://www.lionhrtpub.com/orms/orms-8-01/norback.html.

APPENDIX F : TURNITIN REPORT



8	www.utdol.com Internet Source	1%
9	Eric B. Fox, Gregory J. Latham, Faith J. Ross, Denise Joffe. "Perioperative and Anesthetic Management of Coarctation of the Aorta", Seminars in Cardiothoracic and Vascular Anesthesia, 2019 Publication	1%
10	Almeselmani , Hazem | Alsoufi , Mahmoud | Elwan , Mohammed Samir | Albawab , Amer | Musa , Mohamed Elfadel. "Severe Aortic Coarctation Incidentally Discovered in a Young University Student", Hamdan Medical Journal, 2017 Publication	1%
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