Master project in Medicine

The Mid-term results of surgical therapy on coarctation of the aorta

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1. General overview

1.1 “Quid” of the coarctation of the aorta?

Coarctation of the aorta (CoA) was first described in the middle of the 18th century(1). This pathology implies a restricted aortic diameter somewhere from the aortic arch to the abdominal part of the vessel, though the aortic isthmus (where the ductus arteriosus links to the aorta) is typically more touched(2,3). It goes from severe hypoplasia to mild restriction(4), and can also involve the aortic arch in some patients(5).

CoA stands for 5 to 8% of all congenital heart defects depending on the source(2,4–6) and seems to occur in one out of 2500 live births, knowing that the rate may be higher in stillborn. It appears to affect boys twice or three times more than girls(2,4).

Aortic coarctation is also known to be sometimes associated with other more or less complex cardiac defects(7). The most common ones are a bicuspid aortic valve (from 40 to 50 per cent depending on the authors(2,3)), mitral valve problems(8) and cardiac wall defects. Apart from cardiac issues themselves, the majority of anomalies that can be found in conjunction with CoA are related to great vessels and cerebrovascularization. In the majority of deaths related to CoA complications, “heart failure, aortic rupture, bacterial endocarditis and ischemic haemorrhage”(2) are involved.

A precise aetiology has not been established yet. Some hypotheses allude to genetic predispositions. Although most cases are isolated(9), familial clusters have been reported, as well as frequent (10-35%(9,10)) concomitance with Turner syndrome. It has been shown that an early overexpression of VEGF induces a gridlock mutation in the zebrafish, this leading to a pseudo-CoA. But, a disorder in VEGF regulation should not be the actual trigger, as in CoA the lower body vascularization suffers no problem in terms of anatomy(4). Investigations have been led, focused on disturbed blood flow patterns causing local vessels defects. It is not that rare to find associated malformations, which can be widely spread throughout the arterial tree, so that localised issues cannot explain the whole. But, as mentioned, the aortic coarctation is frequently associated with a bicuspid aortic valve. There is a clear link between these two pathologies. Ductal tissue remains exactly between the left pulmonary artery and the descending aorta, when flows through the left side and the right side of the heart are equilibrated. With an imbalance, there is a displacement of the ductal cells on one of those two vessels, as it would be pushed by an increased flow. The opening area over bicuspid aortic valve is reduced compared to that of a tricuspid aortic valve. This means that more
flow will go through the right ventricle than to the left ventricle and this excess of flow will push the ductal cells towards the descending aorta. After birth, the contraction of the ductal cells (in the aortic wall) creates the coarctation of the aorta. Likewise, in Fallot tetralogy, for instance, where the flow on the right side is reduced, the ductal cells are, then, pushed on the left pulmonary artery, which also frequently shows a narrowing similar to the narrowing of an aortic coarctation. The tissue structure in the vessel section above the CoA is made of increased collagen fibres and reduced smooth muscle tissue(4), this broadens both the intimal and medial layers(9). Each aspect contributes to increasing stiffness of the aorta and high ejection pressure.

In utero, it is hard to confirm an actual CoA or fully exclude it, although some signs have been described. For instance, the imbalance between ventricles size (the afterload being increased, it raises the left ventricle pressure, leading to an altered right to left shunt and a greater right ventricle) may help(4). Besides, the image finding of a slightly longer vessel between the left common carotid and the left subclavian artery could refer to a potential CoA(5). The main impediment to proper foetal diagnosis lies in the interference of the ductus arteriosus(4), because it covers the gradient and hides the narrowing(9). Further improvements in imaging may bring significant advantages, as diagnosis before birth not only magnifies life expectancy but also reduces the overall morbidity(2).

At birth, untreated CoA may be a cause of imminent death, though some patients reach adulthood without being diagnosed, for the severity of the narrowing may be little and the symptoms mild to absent(2,6). With the closure of the ductus arteriosus, the neonate experiences drastic circulatory changes. Symptoms at this age depend on the severity of the stenosis, as no or little collaterals exist to counterbalance(10). Pulse oximetry contributes to detect a marked difference in oxygen saturation of the upper versus lower limbs. In doubt, Ultrasonography must be performed in order to ensure the presumed diagnosis.(10)

Delayed diagnosis is mainly due to non critical narrowing or to sophisticated collateral web(4). Thus, symptoms may be absent. But CoA can also happen to be dire, causing severe heart failure potentially associated with cyanosis, subarachnoid haemorrhage or cerebral aneurysm(3). These threats are amplified by the closure of the ductus arteriosus. If missed, CoA leads to upper body hypertension, which is much of the major issues(3,4,11) as discussed later. The benefit of early suspicion cannot be more underlined, for it has been well demonstrated that hypertension is one of the main factors regarding survival rate and associated morbidity(3).

1.2 Long term issues of aortic coarctation

As mentioned before, CoA is an incurable pathology that brings many challenges. Hypertension is one of the greatest and most predictive aspects considering morbidity and survival, for it leads to “structural and functional damage” and potential major cardiovascular events(3,6). The exact cause is not so well understood but many hypotheses have been discussed. Here are listed the three main postulations. One involves a possible sympathetic system disorder with weaker responses to stimuli(3,4). Besides, aortic tissue above CoA expresses receptors (The lower body remains untouched.) that are more lenient to high pressure(3,4,6). A second implies vascular structure problems (component and shape) with reduced compliance(3,4,6) and another asks about an over-stimulated Renin-Angiotensin-Aldosterone System (RAAS) due to an insufficient renal perfusion(4).

As repeated, Hypertension is of bad prognosis(2). The overall cut-off for a re-intervention is a pressure gradient above 20 mmHg(4). In this case the treatment of choice is balloon catheterization(24). Beta-blockers should be used with additional anti-inflammatory medicine in case of tension above 140/90 in adults and tensions above the 95th percentile regarding age and sex in children(3).

Patients should be seen “every 1 to 3 years”(10). Routine follow-up has to include blood pressure check, heart murmurs determination as well as pulses palpation. An ECG is required in order to evaluate left ventricle hypertrophy. The regular use of a Holter device is mandatory since hypertension may only occur during exercise or daily life activities and not at rest(3,6), this being possibly linked to preoperative hypertension(10). Regarding heart anatomy evaluation and CoA recurrence, the tool of choice is ultrasonography Doppler(3,16). Meanwhile, MRI is known to be “cost-effective” as specific controls of cerebrovascular structures are to be done to detect aneurysms(4). In case of “turbulent flow endocarditis prophylaxis is recommended(10)”. 

The collateral web
1.3 Corrections through time and knowledge

CoA is a “life-long disease”(4). As knowledge improved, many surgical and interventional repairs came out but none leads to an absolute curing(6,12). All techniques aim at pressure gradient release. Severe hypertension causing cardiovascular diseases is a real threat for patient’s life. It has been described that patients with CoA have a relative shorter life expectancy with 90% of patients living no more than 58 years with a mean at 31 years. Repairing improves the survival with a new average of 38 years(2–6,13). The right approach depends on patient’s age and on associated lesions. Nevertheless, surgery remains the gold standard thanks to its “excellent”(14) results according to morbidity and mortality and should be performed as soon as the CoA is discovered(7).

Since 1944, the field of CoA treatment has become vaster and vaster. Step by step, different surgical techniques and less invasive approaches have been performed. Three main options have been developed throughout the years: surgery, balloon angioplasty and stenting. The first great achievement in terms of CoA treatment is Crafoord’s successful operation in October 1944(2,15,16). Nobody at that time was ready to accept the responsibility for clamping the aorta. But one operation made the difference. As a haemorrhage occurred while dealing with the ductus arteriosus of a patient, from necessity the aorta had to be clamped. It lasted 27 minutes until the cross clamp was finally removed(14,17). Hence, it was discovered that not damaging the spine, even if blocking the aortic flow, was something possible. (Indeed, a less than 30-minute procedure is of low risk regarding spine infarction(17)). Thus, a six-hour CoA repair was performed on a boy of eleven years old(15,18). The technique involves closure of the ductus arteriosus, excision of stenosis and direct bond of the two ends. Until spring 1945 two more operations took place and were successful in terms of performance and postoperative issues. Nowadays, resection and end-to-end anastomosis remain the treatment of choice regarding anatomy, recurrences and vascular consequences(14). In the 80’s, a variation named “extended resection” was published. It includes an inferior oblique incision going up to the left common carotid level(19) and allows to treat a concomitant arch hypoplasia(5). Extended end-to-end reconstruction or XETE is one of the most used approaches in native CoA of children(14), thanks to its very satisfying score in terms of outcome(20–22). If the operation takes place before the closing of the ductus arteriosus or while it can still be kept open by prostaglandin E1, there is no need of a cardiopulmonary bypass. Besides the infant’s pulmonary hypertension helps blood flow to perfuse the lower body via the ductus arteriosus(5).

In 1966, Waldhausen described a new way for CoA repair, the “subclavian artery flap”(18), commonly call “SFA” (subclavian flap aortoplasty). The approach consists in lateral cutting of the proximal segment of the left subclavian artery up to the vertebral artery. Then, isolation and ligature of both arteries are needed to avoid subclavian steal syndrome(8). Giving up the subclavian artery is made possible by the collaterals network that supplies. The left subclavian artery may also be reconnected to the left common carotid(21). The proximal thoracic aorta should be similarly transversally incised to match the subclavian flap. Both the left subclavian artery “patch” and the open aorta are to be sewed together.

Other surgical techniques that require graft or prosthetic patch are also used(2).

In the early 80’s, balloon catheterization was first introduced and published by Lock in 1983(2) as a cure for CoA(2,4). The little invasiveness and the short-term efficiency of the approach contributed to its spreading. But at a certain point, the rate of recurrence of CoA and aneurysms became too important and in terms of “risk-benefit”(14), it was acknowledged not to be sufficient, at least for a first intervention in infants and children. However, the technique is still used in certain circumstances as a “bridge to surgery in critically ill infants”, for it is said that “less favourable outcome is to be found in sicker pre-operated patients”(4). It is commonly employ in relapses as well(21).

Since 1990 a new technique emerged in the area of interventional catheterization(2,14). Stenting was a success in improving the balloon approach. It matches the shape of the vessel and prevents it from

![Extended resection: The descending aorta is brought as much as possible underneath the distal aortic arch to enlarge it.](image)
collapsing. It led to refined intervention with larger final artery diameter(23). Thus, it is often used as a treatment of choice regarding teenagers and adults native CoA(2,4). It is also a good alternative in case of restenosis, in grown-up patient, as it reduces recurrences and aneurysms occurrences(2,4,14).

According to all those approaches, the essential role of follow-up must be emphasised, each techniques pairing with specific and generalised issues.

1.4 Focus of ours: The minimal invasive approach(14)

What follows is a descriptive and detailed focus on the muscle-sparing extrapleural approach of CoA. The technique allows a cut of no more than 5 to 6 cm in the back of the patient. It spares the latissimus dorsi and the intercostal muscles, prevents the lungs from per operative injury and collateral overgrowth(17).

One of the first goals lies in releasing the fifth rib. Therefore, an incision of 5 to 6 cm is performed between the medial border of the scapula and thoracic vertebrae. It opens in the triangle gap fenced between the latissimus dorsi, the trapezius and the scapula. In order to increase mobilization, the subcutaneous tissue has to be separated from the tissue above. The latissimus dorsi is to be spared in detaching it from the spine for 6 to 7 cm. The serratus anterior can be avoided, as the intervention is posterior. A right-angle retractor is then used to see the fourth intercostal space better.

The next step consists in peeling the periosteum of the upper side of the fifth rib, thus saving the intercostal muscle. Once facing the parietal pleura, it is softly removed from “the thoracic wall, the descending aorta and the aortic arch” without any incision required. “Four 6-0 stay stitches at regular intervals on the extrapleural tissue just medial to the descending aorta or the left subclavian artery” permit to clear the left lung from the visual field without damaging it or its vessels.

If any arch hypoplasia coexists, it is first taken care of. Pericardial or pulmonary artery tissue patches are used to improve the arch section(17). Once it is corrected, a standard extended end-to-end resection can be performed. Firstly, it implies the releasing of the aortic arch and the associated vessels, typically down to the seventh intercostal space. “One or two pairs of intercostal arteries are ligated or clipped and divided”. After testing the effectiveness of brain retro-perfusion by determining the right radial pulse(5), one Cooley-clamp is placed between the truncus brachiocephalicus and the left common carotid artery. Hand-held clips are placed on the left common carotid artery and the left subclavian artery, so that the operative field is not overcrowded with instruments. A “straight vascular clamp” is placed on T4 level of the descending aorta. Once the patent ductus arteriosus sutured and cut, the CoA is removed and the inferior side of the aortic arch is transversally incised, up to the take off of the left common carotid artery. The distal aortic arch end and the proximal descending aorta end are sewed together with a “running suture of 7-0 or 8-0 polydioxanone.” The elasticity of the vessels is optimal, as most patients are treated within 1 or 3 days of life(17). All clamps are, then, removed. Parietal pleura is freed. In the extra-pleural space remain a “periostial analgesia delivery catheter and a low-vacuum drain”. A “continuous absorbable suture” was used to attach the periosteum to the rib. The operation ends in suturing the latissimus dorsi back to its aponeurosis and in a “two-layer absorbable suture” of the skin.
2. Objectives

The main purpose of minimal invasive approach is to treat coarctation of the aorta in order to prevent or at least to reduce the incidence of hypertension and therefore to alleviate a chronic cardiac pressure overload. Indirectly, this correction will impact on the quality of life and life expectancy. The reduce invasiveness of our approach should achieve these goals while providing a benefit on the shoulder and spine stature and mobility. We aimed to compare the mid-term results of this approach with other standard techniques to make sure that the circulatory load was favourably controlled.

3. Methodology

An observational retrospective study was carried out on a cohort of 40 consecutive patients with no selection. One operator operated all of them with a “minimal invasive approach” from June 2002 to October 2004. The purpose was to focus on mid-term (more than 4 years) outcomes of three endpoints. Firstly, the rate of CoA recurrence was evaluated and was defined by a pressure gradient of more than 20mmHg at rest or by the need of an endovascular or surgical re-intervention. Secondly, the incidence of hypertension was established, following OMS criteria (25) of minimal blood pressure of 140/90 mmHg. Its severity level was stratified, based on the number of different medications and on an analysis of the dosage. Lastly, scarring issues were assessed, considering shoulder static disorders and mobility problems. We reclaimed the last chest radiographs in order to determine if variations occurred at the surgical site. In the intercostal space, rib fusion or excessive width was considered scarring failures.

Information was obtained via questionnaires filled by the referring cardiologists, as well as their sending the last ultrasound reports and cardiovascular check-up. The questionnaire was created simple in order to be user-friendly and to maximise the rate of answers.

Statistical analyses were based on events occurrence according to time, using the Kaplan-Meier method and Chi-square testing, with a theoretical frequency of 5% at 4 years and a p-value below 0.05 considered significant.

Follow-up was achieved in most cases (n=22, 55%) and we were able to obtain the last ultrasound and full check-up reports (dated 2010-2014) except from three patients, about whom we only got raw values. We also received one detailed orthopaedic report. Regarding each outcome individually, we are lacking hypertension data about two patients. We do not know about spine stability of three patients. Information about 5 patients is missing regarding shoulder stability. The average follow-up (n=22) is of 10,5 years with a standard deviation of 1,3. The median is of 10,6 with a range going from 7,6 to 12,3 years.

This article follows a previous study (14) carried on the exact same cohort (n=40). Here are repeated some pieces of information about pre-operative status and per-operative parameters. It involves 21 males and 19 females, the majority of who was operated before the first month of life. The medial age is 8 and half days with a range of 1 to 447 days. Regarding the weight, the median is 3250 grams with the lightest kid weighing 980 grams and the heaviest one 16 kilograms.

Most of the time, coarctation was not the only diagnosis. Almost all of the operated children suffered from other congenital defects. Some of them are very redundant and others more exceptional. Here is a graph showing the incidence of the most relevant cardiac or non-cardiac pathologies. Included in “others” are transposition of great arteries (TGA), double outlet right ventricle (DORV), arteria lusoria, myocardial infarction, left ventricular outflow tract obstruction (LVOTO), small aortic annulus, mitral dysplasia, atrio-ventricular and aortic insufficiency, aortic and mitral stenosis, partial anomalous pulmonary venous connection of the right superior pulmonary vein, hypoplastic right ventricle, left superior vena cava (LSVC), diaphragmatic hernia, esophageal atresia and subependymal bleeding. Out of
40 patients, 27 were duct-dependent, which implies a patent ductus arteriosus with or without prostaglandin help or the ductus closure causing heart failure.

Three infants underwent balloon angioplasty on the aortic isthmus stenosis before surgery was performed. It allowed either to stabilize the heart function or to reach a stenotic aortic valve. All children went through an extended resection followed by an end-to-end anastomosis. Supplementary procedures such as flow watch implantation or pulmonary artery banding ($n=7$), subclavian flap plasty ($n=2$), left subclavian artery translocation ($n=6$) or right subclavian artery reimplantation ($n=1$) were needed in some cases.

Regarding timing, out of 36 patients, the average cross clamping time was of 21,3 minutes with a standard deviation of 7,08. The median was 20,5 minutes with a range going from 8 to 37 minutes. The overall procedure lasted 90 minutes (median), the quickest operation having been of 50 minutes and the longest having stretched out to 240 minutes.

No early post-operation complications were to be found except from one chylothorax which was properly treated with surgery.

### 4. Results

Four patients died but it was most probably not due to the coarctation repair. One of the patients was suffering from a Shone’s syndrome with a ventricular septal defect (VSD), associated with a right diaphragmatic hernia, a hypoplasia of the right lung and multiple other pathologies. The child died 2 days post-operation. It was probably due to a constellation of a cardiac parachute mitral valve, forward failure of the left ventricle, lung problems and a diaphragmatic hernia. The other early death was caused by an impaired left ventricular function, which involved an aortic insufficiency (secondary to balloon angioplasty) and an endocardiac fibroelastosis. The two other deaths occurred late. One child died seven months after surgery from sepsis (due to intestinal necrosis), acute respiratory disease syndrome and multi-organ failure. The fourth patient died two years after coarctation repair. It was not well documented but most likely unrelated neither to surgery nor to pulmonary hypertension. At last
follow-up in 2006, the child suffered from mild aortic, mitral and tricuspid valves insufficiency, pulmonary hypertension, Down syndrome and dorsal corpus callosum hypoplasia. As these four deaths seem not to be related to the surgery performed, as well as for ethical reasons and time issues, we decided not to take these cases into account in our analysis.

The graph above shows the results of two different groups. It gathers infants operated before one month (n=18) and those operated after one month of life (n=4). All of them were under the age of a year old at surgery. This cohort was too small to obtain significant results.

The overall (n=16) recurrence rate, at ten years, is of 25% (4/16). It involves three re-interventions with two surgical and one angioplastic approaches and one patient presenting a gradient of 21mmHg corrected. The two surgical procedures occurred at three and four years after the first intervention and the only angioplasty recorded was performed within the first year post-operation. No patient operated after 1 month presented any sign of recurrence.

Considering hypertension itself, the last reports show that all patients (n=20) are under 140/90mmHg and none of them has to take any antihypertensive drug.

Regarding scarring evolution, one patient is diagnosed with scoliosis, but it is not related to the surgery as notified in the orthopaedic report. No patient has any spine (n=18) or shoulder (n=17) stability problems. We could receive no chest radiography.

5. Discussion

An increased mortality rate is often found in the population of children presenting associated diagnoses(7,12,24). For the reasons explained above, we decided not to include the four deaths, but indeed, all of our patients combined different pathologies. As the fields of technology and knowledge are expending, neonates that would have been impossible to operate, a few years ahead, are now cared of. Thus, operated infants suffer from more severe comorbidities than in the past, which make them be at higher risks of complications(12,24).

In aortic coarctation, hypertension is one of the biggest threats. A surgical intervention can often not prevent long-term hypertension. Moreover, established hypertension is sometimes maintained despite proper repair(6). Hypertension occurs in up to 45% of operated patients, although early surgery (infancy) reduces the risk down to 10%. It is shown that the later the age of repair, the greater the hypertension will be(3). In terms of vessel structure, there seems to be benefit in early intervention too, as it slows the stiffening process(3). Baroreceptors function appears to be independent of surgery. It has been shown that even after anatomical repair, their physiology is impaired and consequently tolerates raised pressure(14). It is interesting to notice that in the majority of studies cited below, the chosen cut-off, considering hypertension, is much higher than OMS criteria. O’Sullivan et al.(11) reported, from a cohort of 119 patients operated in median at the age of 0,22 year (interquartile range (IQR) of 0,04 to 2,02 years) and followed-up in average 9,5 years (IQR 7,1 -12,8), that 28,5% had a mean “casual systolic blood pressure of more than 95th centile of the normal population”. They also showed that casual blood pressure had a specificity of 88% in “detecting an increased 24 hours pressure” with a sensitivity of 66%. Cohen et al.(12) described, from a group of patient (27/646) operated before 1 year old of nothing but CoA and seen at late follow-up, that 7% suffered from hypertension (defined 150/90mmHg). In our study, blood pressure was mainly measured at doctor’s offices and although, we opted for more challenging values, none of our patients is known to suffer from any hypertension or to need any drug.

In terms of recurrence, defined as the need of re-intervention and/or high gradient occurrence, our results are comparable with those of other groups. They corroborate and integrate the global trend(7,11,12,26,27) of early surgery leading to suitable blood pressure and gradient values at long-term follow-up. Cohen et al.(12) presented 26% of re-operation and concluded that “the increased need for reoperation for recurrent coarctation in this age group did not seem to negatively influence long-term outcome.” At four years, our technique provided a recurrence rate of 18,2% with all patients diagnosed with associated defects. Zehr et al.(24) showed, from a group (n=94) followed-up 3,0 ± 2,9 years and which involved 70% neonates operated before 30 days of life, 12% (11/94) of restenosis, that was defined as a gradient of 30mmHg or more. Out of 12 patients presenting recurrence, three went through a surgical procedure. Regarding the procedure, out of 52 patients who underwent end-to-end anastomosis, “restenosis occurred a mean of 6,5 ± 1,5 years postoperatively in 25%”. In our case, at three years, 9% (2/22) had restenosis and 13,6% (3/22), at four years post-operation. No patients suffered any recurrence
beyond four years. Früh et al.(26) studied a cohort (n=91) involving 48 patients aged less than 6 months which they followed during a median of 20.5 months (range going from 0 to 60). In this particular population, they determined a re-intervention rate of 16.6%. We may here mention that Kaushal et al.(22) obtained a re-intervention rate of 4%, 75% of which occurred during the first postoperative year. They studied a cohort of 201 patients. All patients went under end-to-end extended resection at a median age of 23 days and with a median weight of 4000 grams. The follow-up was 5.0± 4.3 years and only “patients with simple CoA repair or CoA repair with ventricular septal defect (VSD) closure (simultaneous or later)” were included. Our rate of re-interventions, at four years, is based on 40 consecutive patients with no selection. This may partly explain the difference.

Thanks to results comparable with what have been published on more invasive techniques, our study confirms our approach with reduce invasiveness. It shows that extended end-to-end resection provides good results in children with CoA, with all parameters remaining in good range and comparing favourably with published studies. We further studied the cosmetic results. Regarding scarring and mobility issues, based on practitioner evaluation, it seems that all children has been keeping excellent spine stability and shoulder mobility through growth.

6. Conclusion

In conclusion, the “minimal invasive” approach is a reliable technique. The vast majority of patients stay free of recurrence and our data match the standards. The good value of extended resection is upheld while performing a less invasive method, which offers stable long-term results and aesthetic progress.

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