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Perioperative outcome following late correction of tetralogy of Fallot in a humanitarian project

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ABSTRACT

Objective: To report our experience and results of late surgical correction of patients with tetralogy of Fallot (TOF) in the context of a humanitarian collaboration program.

Material & Patients: Retrospective analysis of the perioperative course of all patients undergoing correction of TOF after x years of age at the University Hospital Bern or the University Children's Hospital Rabat between November 2011 to November 2016.

Results: 25 children (mean age: 70.8 months, range: 23-163; 44% female) underwent total correction of TOF. Two patients were initially palliated with a shunt with subsequent correction after 108 and 24 months. Preoperative oxygen saturation was 84±12%; mean hemoglobin was 147±31g/l. Preoperative mean RV/PA gradient was 84±32mmHg with a Nakata index of 163.6±70.5mm2/m2. Large aorto-pulmonary collateral vessels (MAPCAs) were observed in n=8 (32%), and n=6 (26%) underwent transcatheter closure just before surgical correction. Presence of coronary abnormality in 28% of the cases (n=7). 96 % underwent a valve-sparing correction. Early mortality was 0%; perioperative morbidities were 0%, stroke 0%, postoperative pacing 0% and no patient required an extracorporeal membrane oxygenation. Mean duration of mechanical ventilation was 28.7±19.6h (range: 7-76).
Last follow-up was 1 month due to the setting of program. Last echocardiography demonstrated a mean RV/PA gradient of 34.6±14.8mmHg; LVEF >60% in all cases, with no RV dysfunction. Postoperative saturation was 98% (range: 95-100%). A residual pulmonary stenosis was light in n=7, moderate in n=10 patients. Concerning the residual subvalvular pulmonary stenosis: moderate in n= 3. Finally, the supravalvular pulmonary stenosis was light in n= 1, moderate in n=6 without any severe PV insufficiency. 1 patient underwent reoperation for patch dehiscence, 1 patient underwent reoperation for recurrent pulmonary stenosis. Length of stay was 11.7±4.5 days (4.8±2.4 days in ICU).
For 11 children, we have a 6-month follow-up exam which showed good results without any need of reoperation or reintervention.

Conclusions: Late correction of TOF can be safely performed in older children with good early postoperative results and low morbidity comparable to reported results for "timely" correction in infants. A valve-sparing correction might be possible in majority of those patients. Follow-up study for the evaluation of the development of right ventricular and pulmonary valve dysfunction is needed and under way…

Abbreviations:

CHD—congenital heart disease
TOF—tetralogy of fallot
RV— right ventricle
RVOT— right ventricle outflow tract
PV—pulmonal valve
TAP— transannular patch repair
ICU — intensive care unit
CBT — Cardiopulmonary bypass time
PS— pulmonal stenosis

Background

Tetralogy of Fallot is one of the most frequent cardiac malformations with a percentage of about 5-7% of the spectrum and is also the most frequent cause of cyanotic congenital heart disease (1)(2). This abnormality consists of a ventricular septal defect (VSD), an overriding aorta and stenosis of the right ventricular outflow tract or at the level of the right pulmonary valve/artery with a subsequent hypertrophy of the right ventricle.

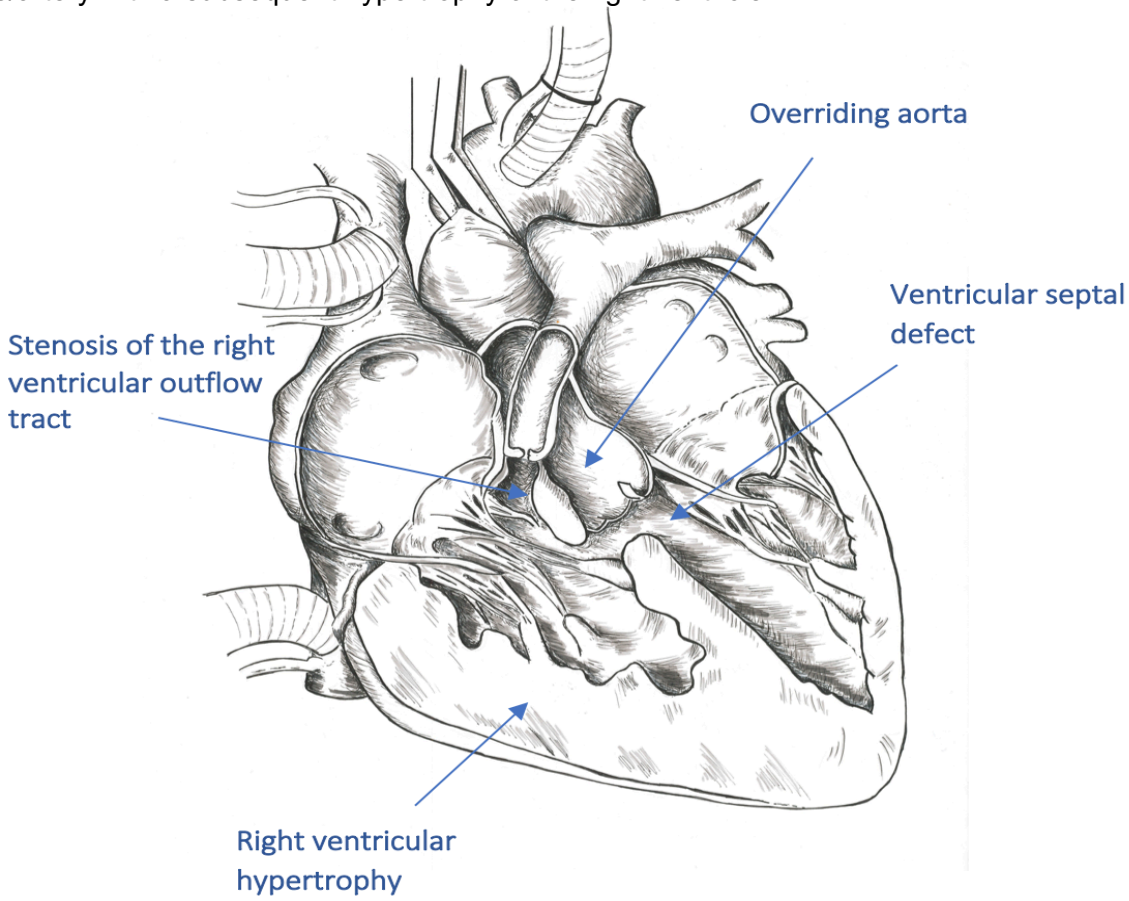


Figure 1 Anatomy of TOF

Other associated anomalies are a right-aortic arch, which is present in approximately 25% of cases, and an atrial septal defect (ASD) in about 5% of cases (3).
In addition, abnormalities of the coronary artery have been reported in 5% of patients affected by a TOF (4). Frequently, the left anterior coronary vessel arises from the right coronary artery and crosses the RVOT (4). This abnormality must be noticed and documented in order to avoid any intraoperative coronary injury when a total correction and intervention on the RVOT is planned.

The variability of this malformation is very large; one can observe only a muscular obstruction of the infundibulum in contrast to stenosis at the valvular or supravalvular level with or without a hypoplasty of the pulmonary valve or pulmonary artery and braches. This variability has important implications for the clinical conditions of the child leading to the possibility of earlier or later corrective surgery. One of the major problems caused by the

degree of the right outflow tract (RVOT) obstruction is the presence of cyanosis. The cyanosis usually develops by the age of 3-4 months (3), but the symptoms depend on the severity of the RVOT obstruction. The stenosis of the RVOT forces the blood through the ventricular septal defect, causing a right-to-left shunt into the left ventricle (LV). The larger the shunt volume the more severe is cyanosis and the subsequent rise of the haematocrit value is observed. In so-called “Pink tetralogy”, the RVOT- obstruction is of a lesser amount allowing even a left-to right shunt over the VSD with a consequent absence of cyanosis.

A dangerous and life-threatening situation might occur due to so-called “Tet-spells”, which present acute hypoxic spells of infant with TOF. The physiopathology behind these crises is a spasm of the ventricular infundibulum, which increases the obstruction of the RVOT with a following intensification of the right-to-left shunt. After crying/feeding or agitation, the child will suddenly develop a bluish pale skin, and lips caused by a rapid drop of oxygenation. The profound hypoxemia and hemodynamic instability can be lethal and might even happen in cases without severe prior cyanosis.

Figure 2 Tet Spell

A natural spontaneous corrective reaction can be observed by the so-called “Squatting” maneuver in TOF children. Squatting is a compensatory mechanism in response to hypoxemia by which the child is increasing the venous return from the higher oxygenated blood from the splanchnique circulation, and increase the peripheral resistances what is going to decrease the right-to-left shunt. By decreasing this shunt, he allows more blood to cross the lungs, and thus increases the content of oxygen of the blood.
Approximately 70% of patients with TOF require surgical intervention in early childhood because of hypoxic spells or persistent hypoxemia. (4).

Figure 3 Typical squatting postures in two children with Fallot’s tetralogy

Technique for Surgical Correction of TOF

The surgical strategy for correction of TOF has progressed considerably over the last decades. TOF was first treated surgically with a palliative concept by creating a systemic–to-pulmonary shunt. The concept was realized and established by the surgeon Alfred Blalock (1899-1964) and the pediatrician Helen Taussig (1898- 1986) in Baltimore in 1944. It consists of a palliative shunt by connecting the subclavian artery with an end-to side anastomosis to one of the corresponding side branches of the pulmonary artery. The access was through a thoracotomy and could be performed without need for a heart-lung-machine. Aim of the operation is the improved perfusion of the lungs with a subsequent improvement of oxygenation and reduction of the cyanosis. This palliative technique became known as the "Blalock-Taussig shunt" and presents an established part of surgical armamentarium for the treatment of cyanotic congenital cardiac malformations.

During the last decades, a significant modification has made by avoiding the ligation of the subclavian artery with direct end-to side anastomosis to the pulmonary artery and instead

implanting a Goretex tube graft (for the majority of patients with a diameter between 3 to 3.5 mm) as a systemic to pulmonary artery shunt, the so-called “modified BT-shunt”.

A first total correction of TOF, which means a intracardiac intervention by VSD-closure and correction of the RVOT/PV stenosis was performed by C. Walton Lillehei at the University of Minnesota in 1954.

Figure 4 C. Walton Lillehei

The biggest problem of this pioneering period was the lack of a functioning heart-lung machine, particularly the lack of a functioning oxygenator.
Consequently, surgeons were limited to perform corrections of rather simple congenital cardiac defects, such as ASDs, by applying the idea of hypothermic circulatory arrest without heart lung machine (“off pump”). The patient was anesthetized and the body temperature lowered until the heart started to fibrillate. By lowering the body core temperature, the oxygen consumption was lowered allowing intracardiac interventions on a fibrillating heart for the duration of a few minutes without causing severe brain and end-organ damage.

A significant improvement and strategy to overcome the short-comings of “off pump” hypothermic circulatory arrest and bypassing the lack of a functioning oxygenator, presented Walton Lillehei by persued his idea of “cross circulation”, meaning that the blood-compatible parent was utilized as a “human heart-lung machine”. This concept allowed Lillehei the first “complete” repair of a TOF malformation.(5) (6)

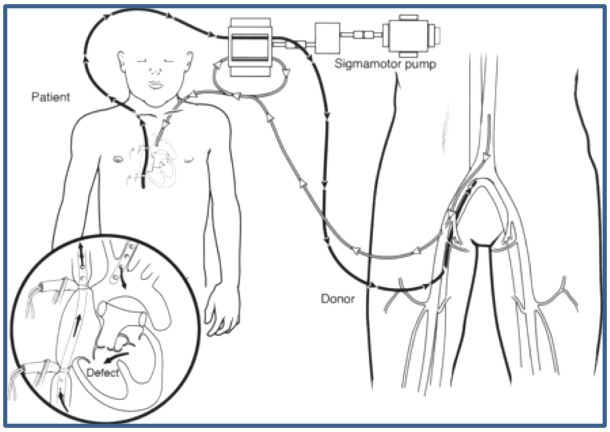


Figure 5 Diagram of the cross-circulation technique used by C. Walton Lillehei in 1954-1955

The first complete repair using a heart-lung machine with a functioning oxygenator was performed by John Kirklin at the Mayo Clinic in 1955, who also reported the first transannular patch repair in 1959.
However, it was early reported that correction of TOF in infancy was associated with a huge mortality due to the incapacity of the current extracorporeal-circulation to manage low weight patient at this time. The correction with a “two-stage” strategy, consisting of an initial palliation by a BT-shunt, followed by a years-later total correction with a bigger child was pursued and proven to significantly decrease the high mortality rate.

Nowadays, the treatment of TOF aims towards early correction during infancy and the majority of paediatrics cardiac centres attempts a total correction at the age of 6 to 9 months. Mortality is very low with 1.3% according to the recent analysis of the Society of Thoracic Surgeon’s congenital database (6). Regarding palliation with BT shunt, most major centres proclaiming that is not at all necessary in absence of relative contraindications, such as

multiples VSD-associated atrioventricular septal defect, important coronary abnormalities, very small branch or extreme tubular pulmonary artery hypoplasia (4).

Early repair of TOF has many advantages: it reduce time of hypoxemia and its negative sequela, such as development of cyanotic nephropathy, preserve the myocardial function, allows to normalize more quickly the pulmonary flow that stimulates the angiogenesis - the pulmonary vascular bed development and lung growth. In addition, chronic hypoxia, especially during the first year of life results in important cognitive and developmental delays. In addition, due to the usual unrestrictive ventricular septal defect, the right ventricle is chronically exposed to a systemic pressure resulting in right ventricle hypertrophy with subsequent fibrosis, right ventricle dysfunction and ventricular arrhythmias. Finally, an early repair decreases the psychosocial impact of the disease for the child and its family. (2) (7) (8) (9) (10) (11)

The relevant concern remains in regard to the intervention and management of the stenotic/hypoplastic pulmonary valve. In general it is agreed on that the pulmonary valve should be preserved when possible (6)(12)(13)(14). One of the concerns presents the problematic situation associated with the replacement of a valve in paediatric and young patients.
Current valve prostheses don't allow for a growth potential resulting in repetitive reinterventions. Available biological prostheses, such a xeno- or homografts come along with a significant risk of an accelerated degeneration. Mechanical prosthesis demonstrating the drawbacks of a bad hemodynamic performance in smaller sizes, a mandatory chronic anticoagulation therapy and the risk of endocarditis. Furthermore oversizing of the prosthesis in order to avoid early reintervention due to an "prosthesis outgrowth" is not an adequate strategy in young children is also predisposing to early SVD (15)(16)(17)(12).

Traditionally, obstruction at the level of the pulmonary valve was approached by either commissurotomy, in the setting of a well-developed pulmonary valvular annulus with only a stenotic mostly bicuspid valve or in the setting of a hypoplastic annulus by placement of a generous transannular patch. Even if the transannular patch (TAP) repair has dramatically reduced death in TOF, over the last decades it has been well realized that pulmonary valve (PV) incompetence following TAP repair of TOF results in an increase of morbidity and mortality in the long-term (12).

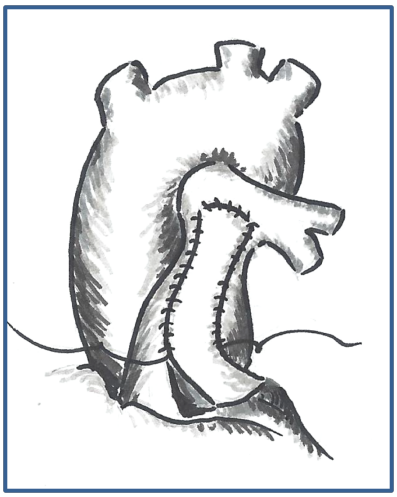


Figure 6 Transannular patch plasty

Consequently, the strategy turned towards more aggressive replacement of hypoplastic stenotic pulmonary valves by using either aortic/pulmonary homograft valves or more recently by using xenograft valve prosthesis or conduits, such as xenograft valve prosthesis with tube grafts or complete xenograft conduits such as the bovine jugular vein graft (Contegra). However, it was realized that this approach results in more frequent reinterventions due to the valve degeneration and subsequent a negative impact on long-term RV function (12)(13).

Consequently, the current strategy turned towards a **valve sparring approach** trying to achieve a potential "ideal constellation" of creating a light residual stenosis of a hypoplastic pulmonary valve with a light insufficiency following valvular commissurotomy with preservation of the pulmonary annulus and enlargement of the hypoplastic pulmonary artery

and, if needed, of the RVOT by a patchplasty. Several groups advocate that even if the effect of these strategies on the long-term function of the right ventricle and pulmonary valve, and on the need for eventual reoperation, remain unknown so far, a strategy that preserves the pulmonary annulus will maximize the preservation of the valve function in the long-term (6)(13)(12).

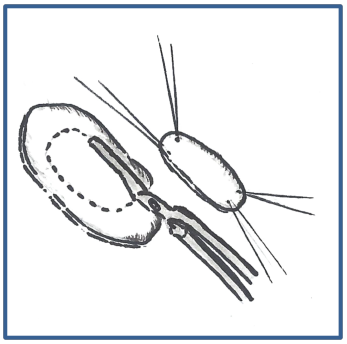


Figure 7 Subvalvular patchplasty

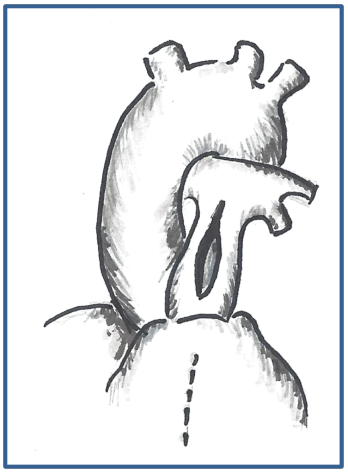


Figure 8 Opening the main pulmonary artery with a infravalvular RVOT incision

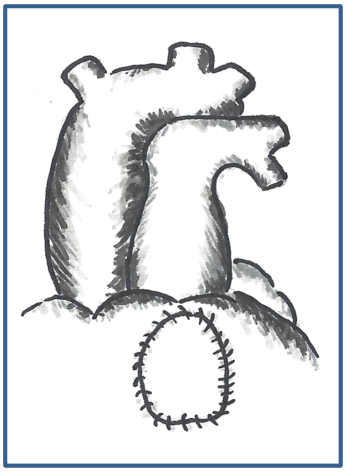


Figure 9 Tailoring of a Xenopericard patch

In contrast to all those efforts on the improvement of the long-term outcome of the correction and management of TOF, in so-called " third world countries" less than 50% of the population has access to health care and many children suffering of TOF have not a chance of corrective surgery (18). Many of those children are diagnosed very late of heart disease due to limited availability of specialized medical centres, the lack of infrastructures and cultural background. Furthermore, in regions with a low socioeconomic status, majority of the people have no health insurance, particularly children. As a result, any therapy, diagnosis and above all intervention is beyond the reach of the average patient in these countries. Furthermore, even in the existence of medical centres performing a mostly very limited number of corrective surgeries in children affected by a TOF, those interventions are performed rarely timely during infancy. Frequently, the patients and their families have to wait for years. The waste majority of children die cruelly "un-corrected" due to a progressively developing cyanosis and cardiac insufficiency over the course of several years.

Surprisingly, the data and literature on late correction of TOF patients is very limited. There are many concerns and insecurity regarding the perioperative outcome of late intervention in those patients. However, this information might be of importance to programs which are confronted with elderly children suffering from TOF, such as humanitarian programs in so-called industrialized countries or programs in "second or third world" countries with a congenital cardiac service.

Aim of the study

The aim of this study is to report on the perioperative results and outcome of late corrective surgery of children with TOF.

Patients and Methods

All patients undergoing corrective surgery of TOF beyond the age of one year at the University Hospital Bern, starting November 2012 until November 2016 were included in this study. Patient medical records were retrospectively reviewed and evaluated for the peri-operative course ("in-hospital").

Operative procedure

All patients were operated through median sternotomy, using cardiopulmonary bypass and mild/ moderate hypothermia. In certain case, hypothermia had to be decreased down to 28° degrees due to significant backflow from collateral pulmonary vessels. In case of presence of a modified BT shunt, shunt takedown was performed at the time of the total correction. The closure of the VSD was either performed by using a transatrial approach, or by closing it through RVOT incision in case of a RVOT enlargement by patchplasty. Regarding the management of the PV: a valve-sparring approach was preferred with commissurotomy and shaping of the leaflets. Thus, the drawbacks of related to RVPA conduits, such as multiple reinterventions and an elevated risk of endocarditis could be avoided. A transvalvular gradient from the RV to the PA was always measured directly invasive following weaning from cardiopulmonary bypass. Routinely, transesophageal echocardiography (TEE) was performed for evaluation of the corrective surgery and assessment of the transvalvular gradient. Applied patch material consisted of xenopericard.

All patients received a prophylactic antibiotic treatment

Postoperative Management

Postoperative management followed standard treatment. Patients were discharged from hospital to a specialised pediatric care center ("La maison Massongex") of the NGO Terre des hommes from where the children finally returned back to their country of origin.

Results

Patient characteristics

Preoperative patients characteristics are shown in **Table 1, Charts 1-2.**

There were 25 children (44% female) with their country of origin from (24% Iraq; 24% Morocco; 12% Senegal; 12% Benin; 8% Mauritania, 8% Tunisia, 8% Togo; 4% Nigeria) who underwent total correction of TOF. The mean age was 70.8±42 months (range: 23-163). The median weight was 17.7±10.2 kg with a BMI of 14.6 kg/m^2. Preoperative oxygen saturation was 84±12.2%; mean hemoglobin was 147±31g/l (range: 105 – 210).

Preoperative echocardiography demonstrated a mean left ventricle ejection fraction of > 60% in all children, with no signs of RV dysfunction. Assessment of the **pulmonary valve** showed a PV insufficiency of a mild degree in 13%, and moderate in 4% of the children. There was no severe preoperative PV insufficiency studied. **Subvalvular pulmonary stenosis (PS)** was found to be severe in 88% of the cases. While a **valvular PS** was found to be mild in 12%, moderate in 4% and severe in 42% of the children. A mild **supravalvular PS** was

identified in 25% of the cases, moderate in 4%, while 38% of the patients demonstrated a severe supra-valvular PS.
Preoperative mean RV to PA gradient was 84±32 mmHg**, PV diameter** was 11.6 mm (range: 8-18) with a mean z-score of -1.9 ± 1.5. The mean diameter of the left pulmonary arteria (LPA) was 8.7±2.4 mm with a z-score of –0.05 ± 1.27; the mean diameter of the right pulmonary artery (RPA) was 8.1±2.8 mm with a z-score of -1.32 ± 1.41. **The calculated Nakata index** was 163.6±70.5 mm^2/m^2.

Major aorto-pulmonary collateral arteries (MAPCAs) were observed in 8 cases (32%), and 6 patients (26%) underwent transcatheter closure preoperatively.

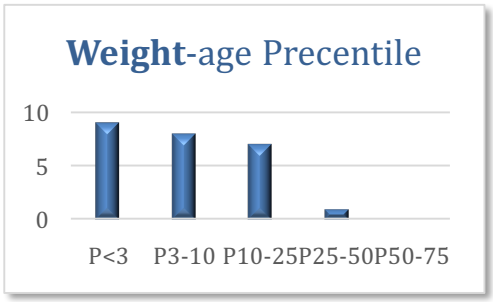
Presence of a coronary abnormality was observed in 28% (n=7) of the cases.

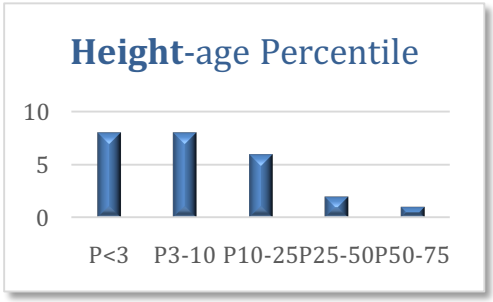
Two patients were initially palliated with a shunt with subsequent correction after 108 and 24 months. The percentage and evaluation of the preoperative RVOT gradient was made on 24 patients instead of 25 patients due to the existence of a BT shunt in one patient.

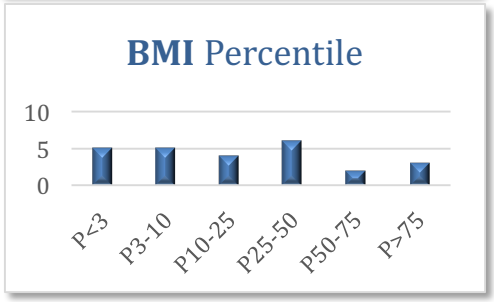
Table 1 : Patients characteristics

	Value		Range
Number of Patients	25		
Male (%)	56		
Age (month)	70.8	±42	23-163
Weight (kg)	17.7	±10.2	9.0-53.9
Height (cm)	107	±23	77-167
BMI (kg/m2)	14.6		10.9-19.3
CT index	0.6	±0.1	-
Preop. Sat (% O^2)	84	±12.2	55-99
Preop. hemoglobin (g/l)	146.8	±30.9	105-210
ASD (%)	60		
Aberrant coronary artery (%)	40	(n=7)	
RV/PA gradient (mmHg)	84.3	±31.6	40-180
PV diameter (mm)	11.6	±2.9	8-18
PV Z-score	-1.9	±1.6	
LPA diameter (mm)	8.7	±2.4	5-13
LPA Z-score	-0.05	±1.27	-2.49-2.37
RPA diameter (mm)	8.1	±2.8	4-14
RPA Z-score	-1.32	±1.41	-3.74-1.30
Nakata-index	163.6	±70.5	66-321
MAPCAS (n)	8	(32%)	
MAPCAS coiling	6	(26%)	

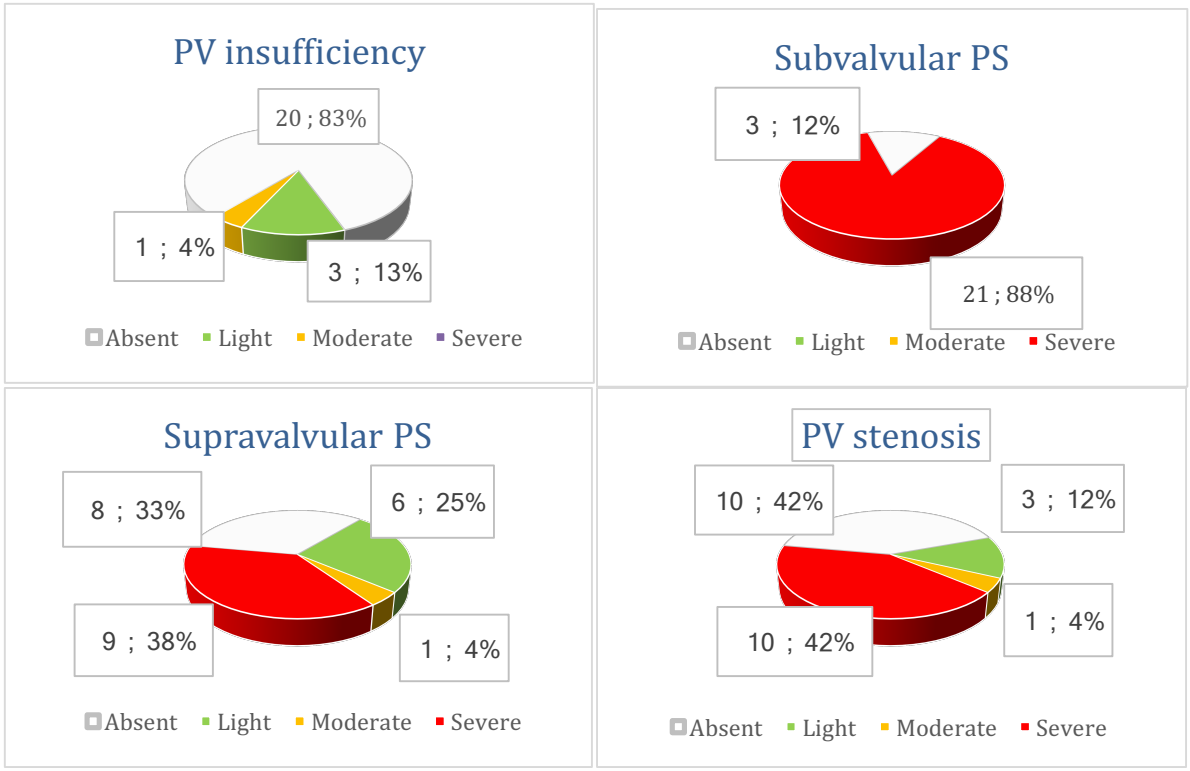
Charts 1







Charts 2



PV : pulmonal valve ; **PS** : pulmonal stenosis

Operative characteristics

Operative characteristics are summarized in **Table 2**

Mean total cardiopulmonary bypass time was 93±22 mins (range: 35-140) with total aortic cross-clamp time of 56±15 mins (range: 21- 93). The mean intraoperative temperature was 30.6±2.1°C, while it was necessary to lower the temperature on CPB below 28°C in 7 patients (28 %) due to the management of hemodynamic significant collateral vessels.
In 96 % of the patients a valve-sparing correction was performed. In one case a PV replacement by using a RVPA conduit (Contegra 20 mm) had to be performed due to endocarditis. A infraannular patch plasty was performed in 71%; a supravalvular patch plasty in 71%, while a transannular patch plasty was only performed in 4%. All patients underwent RVOT enlargement by extensive muscle resection. A surgical valvulotomy of the pulmonary valve was performed in 62%. A concomitant ASD was closed in 72%. In all cases the patch plasty were performed by using xenopericardium.

Table 2 : Echographic preoperative characteristics

	Value	Range
Cardiopulmonary bypass time (min)	93 ±22	35-140
Aortic cross-clamp time (min)	56 ±15	21-93
Temperature (degree)	30.6 ±2.1	25-32

PV replacement	4%
Valve sparring approach	96%
Subvalvular patch plasty	71%
Supravalvular patch plasty	71%
RVOT resection	100%
Transannular patch plasty	4%
Valvulotomy	63%
ASD closure	72%

Postoperative course

The postoperative data are summarized in **table 4, Charts 3.**

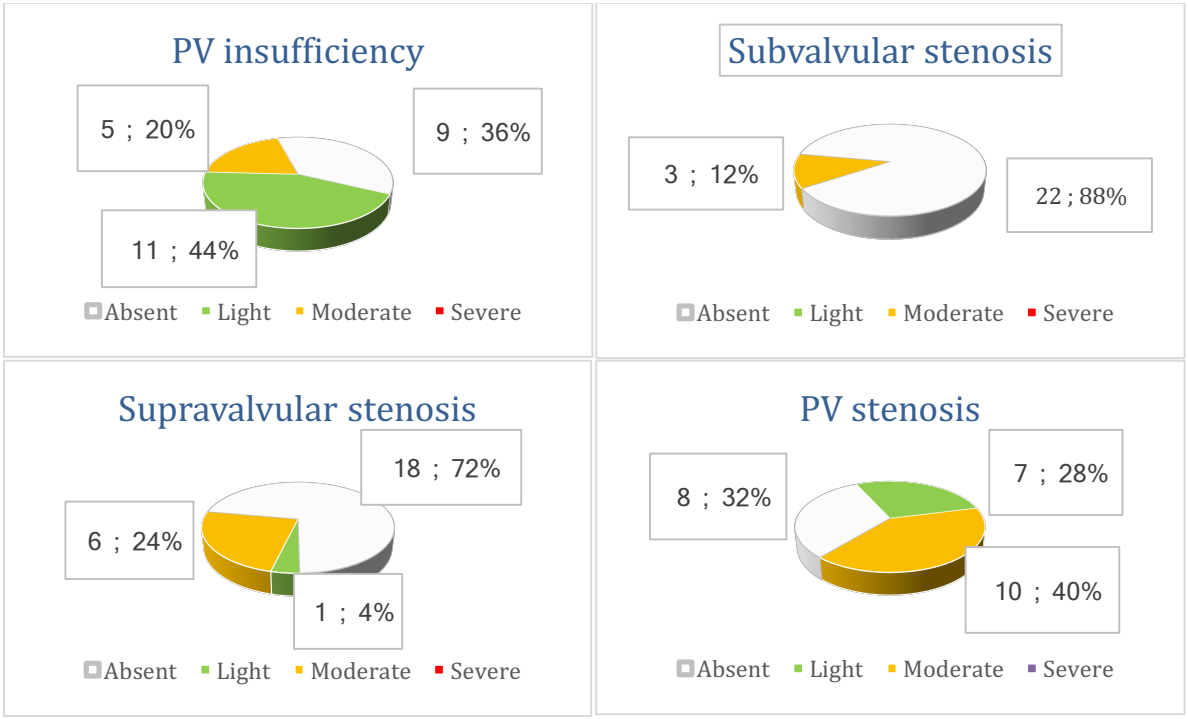
There was no mortality. No major adverse cardiac and cerebrovascular events were observed. None of the patients required implantation of a permanent pacemaker.
The mean duration of mechanical ventilation was 28.7±19.6 h (range: 7-76). The length of ICU stay was 4.8±2.4 days (2-10), and the total length of hospital stay was 11.7±4.5 days (range: 4-25).
A Budd Chiari syndrome occurred in a 27 months girl after surgery.
A surgical reintervention was necessary in two cases. One patient underwent reoperation due to a residual significant RVOT stenosis at 2 days after total correction; a second patient required placement of a perdicardial drain due to a postcardiotomy syndrome at 20 days postoperatively. The same patient showed a severe endocarditis of the PV 2 month later, necessitating implantation of a RVOT conduit (20mm Contegra).

Last follow-up was performed at 1 month postoperatively. Follow-up echocardiography demonstrated a residual mean RV/PA gradient of 34.6±14.8mmHg; normal biventricular function in all cases; postoperative oxygen saturation was 98% (range: 95-100%).
A residual **pulmonary valve stenosis** was mild in 28%, moderate in 40% of cases. A moderate residual **subvalvular PS** was observed in 12% of the patients. A mild residual **supravalvular PS** was noticed in 4% and at a moderate level in 24% patients.

Concerning **pulmonary valve insufficiency;** a mild insufficiency was observed in 44%, a moderate in 20% of the patients.

Table 4 : postoperative characteristics	Value	Range
Mortality	0%	
RV/PA gradient (mmHg)	34.6 ±14.8	11.0-60.0
Pacemaker	0%	
LOS (days)	11.7 ±4.54	4-25
Days in ICU	4.8 ±2.35	2-10
Mechanical ventilation (hours)	28.7 ±19.6	7-76

Charts 2



PV : pulmonal valve ; **PS** : pulmonal stenosis

Discussion

Correction of TOF is part of the standard spectrum of congenital cardiac surgery. During the last decades, excellent results are reported with a low mortality and morbidity rate. There is general consent that the recommended age for correction is during infancy, with most of the cases undergoing surgery at 6 to 9 months of age.

This study reports the findings of correction of TOF in older children with an average age of 71 months, which is higher than the international standards. The oldest patients, who benefited from total TOF correction (without a previous BT-shunt) had even been older than 10 years of age. The mean BMI was found to be 14.6±1.9 kg/m2 (range: 10.9- 19.3) and the mean weight was 17.7±10.2 kg (range: 9 – 53.9) revealing a reduced general health condition with chronic malnutrition, hypoxia and growth retardation(1). Malnutrition is common in children with CHD, and “studies from developed countries have documented normalization of somatic growth when corrective surgery for CHD is performed early” (19). It is also known that 25% of the children continue to have persistent malnutrition even after corrective intervention especially if the total correction is performed late (19).

Another characteristics of these children was the higher percentage (32%) of major aorto-pulmonary collateral arteries (MAPCAs) compared to the international average (2%) in the paediatric population with TOF (20). This finding can be explained by a response to the chronically decrease pulmonary blood flow and cyanosis (20)(11). To confirm this, the percentage of MAPCAs in unrepaired adults is between 13% and 25%, and unlikely in patients who had correction before 6 months of age (20)(11). In addition, MAPCAs can result in several complications including gross enlargement with erosion of the bronchi, massive haemoptysis, postoperative pulmonary oedema, prolongation of postoperative ventilation and

ICU stay (20). In this study, 26% of the children underwent transcatheter closure just prior to surgical correction to avoid associated perioperative complications. With this strategy, it was possible to successfully manage intraoperative collaterals vessels and postoperative therapy. A more frequent occurrence of coronary abnormality was found compared to the international average for TOF (4). Nevertheless, it was possible to perform correction without placement of a RVOT conduit due to an aberrant coronary artery.

Regarding mortality after TOF correction, the Society of Thoracic Database reports a rate of 7.5% at discharge after a palliation with a BT-shunt , 0.9% after a total repair with a previous palliation, and 1.3% following correction without a previous shunt (6). However, the patients of this study were much older than the international median age at total repair surgery, and furthermore, came from a difficult socioeconomic-situation. Consequently, we have to compare our results with two studies who analysis a more similar cohort (older age at surgery, origin from developing countries). Benbrik et *al.* compared foreign patients with a, median age of 57.61± 38months who underwent a total correction of TOF to a control population (median age: 8.3±9.1 months, local origin from France) who underwent timely complete repair of TOF between January 2007 and December 2013. They report a mortality of 4,2%, with no difference between foreign and local patients. They lost a 20-month-old girl who suffered from a severe postoperative RV failure due to the residual distal PA stenosis, and a 5-years-old boy who died of a cardiac arrest 6h after surgery (1). The second study, Raj et *al.* analysis perioperative complications after total correction of TOF (median age: 72 months, coming from India). They showed a mortality of 2% with the death of a 3-years-old male patient who underwent a TAP for RVOT obstruction (21). In our study, we observed no mortality. Beside the low number of patients, we conclude that it appears that **the early mortality rate after total repair of TOF in older patient from developing countries does not differ from the rate of patients operated "timely" and coming from "industrialized" countries.**

For the intraoperative results, cardiopulmonary bypass (CPB) time was 93± 22 minutes (range: 35-140), with an aortic cross-clamp time of 56±16 minutes (range: 21- 93). The longest CPB time was performed in a case, who underwent a valve-sparing procedure and a RVOT muscle resection which required a second aortic-cross clamp after intraoperative TEE demonstrated a significant residual RVOT obstruction. To compare with other studies: Hirsh and *al. reported* a median CPB time of 71± 26 minutes, with an aortic cross clamp time of 45±15 minutes (22), Li et *al.* (n=821, median age= 12month, China) found a CPB time of 122.75±42.47 minutes with an aortic cross-clamp of 83.12±28.52 minutes for total corrective surgery of TOF (23). Concerning the two humanitarian studies : Benbrik et *al* showed a median CPB time of 136±45 min, with an aortic cross-clamping of 80±34 min and affirmed the fact that the mean cross-clamp time did not differ between the foreign and local patients (1). In the second study, Raj R and colleagues showed a CPB time of 160±54 min, aortic cross-clamp of 110±50 min (21). Given those studies and the reported findings w**e conclude that correction of older TOF patients does not require longer CBP and aortic cross clamp times compared to "standard" cases.**

Beside the Society of Thoracic Surgeons Database suggests that "primary repair in infancy remains the most prevalent therapeutic approach" in TOF patients. (6) Another important consideration regarding corrective strategy presents the management of the pulmonary valve. It is well recognized that a total repair of TOF, and even if it may be associated with a certain degree of pulmonary stenosis, should aim towards the preservation of the pulmonary valve (13)(6). The valve sparring procedure may preserve the competence of the pulmonary valve. In contrarious, the former liberal application of a transannular patch placement increases the incidence of the pulmonary regurgitation, increase the persistent RV

hypertension/ chronic RV volume loading. Short-term benefits of the valve sparing procedure is observed by a shorter time of mechanical ventilation than patient with TAP (12). In This study, in 96% a valve sparing approach was possible. Comparing to other studies, Benbrik et al. performed a TAP in 35% of patients, with the same percentage in foreign and in local patient (French) and *Raj et al.* found that a native valve can be preserved in only 30% of their patient (1)(21). In those two studies the percentage of valve sparing approach was clearly lower than our results. There are cases when a valve sparing approach might be impossible due to a very hypoplastic PV. However, both studies report also a certain percentage of TAP among their local children. Further follow-up is necessary to demonstrate if our strategy might be too aggressive and might potentially lead to recurrent pulmonary valve stenosis and subsequent potential reintervention.

As said before, a valve sparing procedure is associated with a shorter time of mechanical ventilation than for patient undergoing TAP placement (12). The time of mechanical ventilation varies among the studies: Hirsch et *al. report* a duration of 163.2 hours of mechanical ventilation after a complete repair of TOF in neonates (22); Edge et al. found a median duration of 19h (range: 0-136) for children with less than 12 months of age. In this study, the time of mechanical ventilation was 28.7±19.6 hours (range: 7-76).

The ICU length of stay was 4.8±2.4 days (range: 2-10) with a total length of hospital stay of 11.7±4.5 days (range: 4-25). The longest time of ICU stay (10 days) was due to the occurrence of a severe arrhythmia starting 3 days postoperatively in one patient and a Budd Chiari syndrome in a 2 years old patient. In comparison to a similar cohort; *Benbrik et al.* found a mechanical ventilation time of 48±89hrs (foreign)/ 67±97hrs (French), with a ICU stay of 93±81hrs (foreign)/172±329hrs (French) for a total length of stay of 11±6 days (foreign)/ 15±15 days (French). Even if the number of patients is relatively limited, N. Benbrik et *al* concluded that the older age tended to "decrease the durations of mechanical ventilation, stay in ICU and in hospital".
Raj et al. reported mechanical ventilation time of 34±28hrs; ICU days of stays 6.86±6.32 days for a total length of stay about 11.8±6 days (21). **Even if the results vary according to the studies, we observed no prolonged necessity of ventilation and extended length of stay of older TOF patients compared to other studies and findings reported for infants.**

Finally, even if the postoperative outcome after a total repair of TOF are determined by a numbers of factors, the most important of which is postoperative right-ventricular function (24). Due to the advanced right ventricle hypertrophy in these children, they might have a restrictive right ventricular function (1). "Even today a definitive information about optimal surgical strategies for primary repair to preserve RV function, reduce arrhythmia and optimize functional status are lacking" (25). After a TOF repair, the biventricular systolic function is usually normal but the diastolic right ventricular diastolic function may be reduced and require serial surveillance *(26)*(25). In this study echocardiography only allowed to estimate the early postoperative systolic/ diastolic function of the RV, which was good in all patients (EF>60%). However, this is very limited and ideally, a long-term follow-up with RV assessment would be in these patients.

Conclusion

Late correction of TOF can be safely performed in older children with good early postoperative results and a low morbidity rate, comparable to reported results for "timely" correction in infants. A valve-sparing correction might be possible in the majority of those

patients. Follow-up study for the evaluation of the development of right ventricular and pulmonary valve dysfunction is needed and under way.

Limitation

A potential limitation of this study presents a patient selection bias. Most of the children had passed infancy without the requirement of an operation, meaning that they present cases with a potential less severe TOF pathology. Furthermore, the children were chosen as “suitable candidates” for participation at the humanitarian program. In addition, the number of patients is relatively limited. Therefore, it is difficult to draw strong conclusions. Moreover, follow-up and cardiac function assessment was made by echocardiography. Ideally, MRI studies would be preferable but the financial aspects coming along with a humanitarian program are withholding its application.

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Reference of the Figures

Figure 1 illustration by L.G.

Figure 2 ADAM Education, *http://aia5.adam.com/content.aspx?productId=117&pid=1&gid=001567*

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Figure 6-7-8 illustration by L.G.

Calculs de Z-core: *Regression equations for calculation of z scores of cardiac structures in a large cohort of healthy infants, children, and adolescents: an echocardiographic study. Pettersen MD, Du W, Skeens ME, Humes RA. J Am Soc Echocardiogr. 2008 Aug;21(8):922-34.*