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Original Article

The hybrid approach – current knowns and unknowns: the perspective of cardiology

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Abstract The hybrid approach to the treatment of patients with hypoplastic left heart syndrome most commonly includes transcatheter placement of a stent in the arterial duct and surgical placement of bands on the branch pulmonary arteries via median sternotomy. This manuscript will review the concept of hybrid palliation and discuss topics related to several time intervals: peri-procedural, post-procedural, interstage, and comprehensive stage 2.

Keywords: Congenital cardiac disease; hypoplastic left heart syndrome; hybrid procedure; arterial duct stenting; retrograde coarctation; Norwood; Comprehensive Stage 2; single ventricle; functionally univentricular heart

The management of patients with hypoplastic left heart syndrome has come quite a long way in the recent past. This relatively common cause of functionally univentricular heart was once thought uniformly fatal. However, with the initial remarkable and courageous work of Norwood for surgical reconstruction and Bailey for cardiac transplantation, that dogmatic belief was shattered.[1,2] Initial results of both approaches were limited with only a few large centres having promising early results for Norwood staged reconstruction and issues related to the availability of donor organs limiting the more expanded use of transplantation. In the 1990s, a few groups took a different approach to early palliation. Their goal was to create the same physiology of

- controlling the flow of blood to the pulmonary circulation,
- securing systemic output, and
- opening up the atrial septum

as for a child following the Norwood (Stage 1) operation, but without the marked stress of a lengthy, complicated, and difficult neonatal operation. The potential advantages espoused by those in favour of this approach were several and compelling to some and include

- the avoidance of cardiopulmonary bypass or circulatory arrest in a neonate,
- the avoidance of one or two bypass runs,
- the value of allowing patients to get better from other medical problems,
- the value of allowing for growth of premature neonates, and
- the value of allowing for the possibility of avoiding exposure to blood products for a neonate.

Ruiz et al[3] described stenting the arterial duct alone as a means of discontinuing prostaglandin in patients with hypoplastic left heart syndrome awaiting transplant in 1993. The largest series of early results of stenting the arterial duct and placement of bands on the pulmonary arteries were published by Schranz in 2002 and 2003.[4,5] Their technique included first the percutaneous placement of the stent in the arterial duct followed a few days later by surgical placement of bands on the branch pulmonary arteries via median sternotomy. They were able to utilise this approach as

- a bridge to a combined Norwood and bidirectional superior cavopulmonary anastomoses – bidirectional Glenn;

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- a bridge to eventual two ventricle repair; and
- a bridge to cardiac transplantation.

Chan et al[6] demonstrated in 2006 the concept of a completely transcatheter hybrid palliative strategy. They placed flow restrictors in each of the branch pulmonary arteries followed by stenting the arterial duct in a single procedure in the catheterisation laboratory. This idea did show initial promise, however, the implantation of the flow restrictors was technically challenging and stressful for the patient. The total transcatheter palliation was shown to be an effective bridge to transplant for some patients, and allowed them to avoid the multiple problems of chronic venous access and infusion of prostaglandin. The flow restrictors are not currently available, and therefore the wider acceptance of this approach is currently not feasible.

Cheatham and Galantowicz[7] took these early outcomes and expanded and added structure to the concept of hybrid palliation. They combined the physiological goals into a single procedure via median sternotomy: first surgically placing the bands, and then delivering the stent in the arterial ductal via a purse-string in the pulmonary trunk (main pulmonary artery). Although early results were promising, it was clear that the expanded use of the concept of hybrid palliation had both a learning curve and a host of issues that needed to be studied and understood at several periods of time: peri-procedural, post-procedural, interstage, and post-comprehensive stage 2.[8–10]

As of today, the use and application of the hybrid palliation is clearly limited and not primarily offered at most centres.[11,12] Some have taken to offering this approach for patients deemed high-risk for standard surgical palliation, and we have begun to see at least small comparisons of outcomes for similar groups of patients.[9,13]

Current approach for performing the hybrid

Selection of patients remains a bit unclear in most centres, and ours is no exception. We are currently offering this approach only to patients who are deemed high-risk using the criteria most others would consider,[14,15] which include

- patients with weight less than 2 kilograms,
- neonates with gestational age less than 36 weeks,
- patients with more than mild tricuspid regurgitation or more than mild right ventricular dysfunction,
- patients with an intracranial bleed,
- patients with genetic anomalies, and
- patients with pulmonary venous obstruction.

We are also following the experience of leading hybrid centres and not offering the hybrid in patients with identified pre-procedural retrograde aortic arch obstruction.[16] Some of those patients are going on to Norwood palliation and some are listed for transplant.

Hybrid palliation is best approached in a "hybrid capable operating room" or an "operating room capable cardiac catherisation laboratory". The most important issues in deciding where to perform the Hybrid procedure is evaluating, given the physical and infrastructural constraints of your centre, where this procedure can best be accomplished. The procedural space must have room for both congenital interventional equipment and the standard set-up for median sternotomy. It is also vitally important that imaging be the best possible and not simply adequate. Doing this procedure in an operating room with a simple C-arm for guidance of the placement of the stent in the arterial duct is simply much less than ideal and will likely lead to a suboptimal result.

More important than infrastructure, however, is developing the teamwork and communication necessary but inherently and naturally not present between the staff from the catheterisation laboratory and the staff from the operating room. These teams do not regularly work together and have different training, experience, and skillsets. They do not all naturally get along, anticipate the needs of one another, or understand the concerns of each other. It is for these reasons that preparatory sessions for pre-procedural planning are absolutely essential. Whether this preparation is done with meetings of the group or procedural simulation, or "dry runs", should be up to the operators who know their people best. These events allow everyone to know the expected sequence of events, issues that may develop, and common problems to be avoided. It is vitally important for all to be aware of all the simple things, which include

- positioning of the patient,
- control of the temperature of the patient,
- how the fluoroscopic gantries fit next to the patient,
- where the tables that hold the surgical instruments for the sternotomy fit,
- how to drape, and
- where monitoring equipment can be viewed.

Members of the staff of the hospital are used to their own zones of comfort and what they are used to seeing and doing. Helping everyone involved to have an appropriate expectation for the procedure helps to diminish the anxiety inherent in performing procedures far different from what they commonly see. Going over the expected steps of the procedure, expected duration of parts of the procedure, and what is difficult about certain parts of the procedure is vital. Understanding simple things such as how the systemic arterial pressure

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and the levels of oxygen are likely to change while placing the bands on the pulmonary arteries and after placing the bands is very helpful.

One of the simple things we have found is that the typical table for equipment in the cardiac catheterisation laboratory is usually superfluous for hybrid procedures. The part of the team from the cardiac catheterisation laboratory will need only a few pieces of equipment. Removing that table makes it easier for staff, and one less object is in the room to walk around and avoid. Minimising staff in the room to only those who need to be present is also very helpful. Many members of the staff of the hospital will naturally flock to new, interesting, and exciting procedures; they can stop by the control room but keep them out of where the procedure is happening.

The actual interventional equipment needed includes just a few items including

- short sheaths, 5 or 7 centimetres long, in 6 or 7 French,
- both balloon expandable and self-expanding stents in several diameters and lengths,
- the appropriate guide wires for the stents, and
- a few diagnostic end-hole and angiographic catheters.

We typically have on hand pre-mounted stents in diameters 5–10 millimetres and lengths of 12–29 millimetres. The types of pre-mounted stents we have usually used are Formula (Cook, Bloomington, Indiana, United States of America) and Genesis (Cordis, Miami, Florida, United States of America). Self-expanding stents should be available in diameters of 6–10 millimetres, but we typically only stock their shortest length, which is 20 millimetres. We typically stock the Zilver (Cook) self-expanding stents. One also needs the appropriate guide wires for the stents. Generally speaking, because the distance the balloons and stents have to travel is so short, one should try to use the shortest available shafts for balloons and stents. It is also best to have available a few diagnostic end-hole and angiographic catheters, which usually include balloon angiographic catheters, Judkins Right catheters, and angled glide catheters.

In general, we tend to perform hybrids at least 2–3 days after delivery to allow for the pulmonary vascular resistance to drop a bit and to optimise the patient medically and complete postnatal evaluations of other organ systems. We usually try to keep the arterial duct large and unrestrictive but use the lowest possible dose of prostaglandin to achieve this goal. We do not stop prostaglandin or decrease its rate of infusion before the procedure. As with most centres, we typically place umbilical lines following delivery and try to avoid pre-procedural mechanical ventilation whenever possible. The more rarely one performs this procedure, the more important it is that this procedure is performed as a first case of the day. The patient is brought to the procedural room and prepped and draped for the median sternotomy. It is very important during prepping and draping that the part of the team from the catheterisation laboratory is present and makes sure the drapes will function with the fluoroscopic gantries. The staff from the catheterisation laboratory will also have to help with the controls of the table to ensure manipulation of the table is as the surgeon prefers it.

The median sternotomy is performed in the typical manner and the bands are placed. We usually place a surgical right atrial line to minimise the need for percutaneous central venous access. Our surgeons typically use silk ties or silastic strips for the bands and place them in such a way that they can be dilated a bit by a balloon in the future. Often in our experience, the systemic levels of oxygen do not immediately drop even with bands that are pretty tight angiographically. A purse-string is then placed in the pulmonary trunk (main pulmonary artery), a needle hole is made in the middle of the purse-string, and the short sheath and dilator are advanced and secured. We try to avoid advancing the sheath more than a centimetre into the pulmonary artery to try to ensure that the sheath does not wind up interfering with delivery of the stent and thereby need to be repositioned during deployment. This positioning is done by measuring a centimetre from the end of the sheath and marking it clearly with suture. The sternal retractor is then removed, and a member of the team constantly manually controls the sheath.

We perform an angiogram with injection by hand through the sheath and measure the diameter and length of the arterial duct. On this same angiogram, the bands should be closely scrutinised to ensure they are not obviously too tight or loose. *The most important issue with delivering the stent is ensuring the entire arterial duct is stented, as any unstented area will of course become an area of obstruction when the prostaglandin is discontinued*. This goal always means the stent will need to protrude a bit into the proximal descending aorta and distal pulmonary trunk – distal main pulmonary artery. One should always be willing to put in an additional stent, or rarely two, if it is possible that a segment of the arterial duct is not stented. It is common that the estimates of the length of the arterial duct are a bit shorter than what is found once the initial stent is placed and the arterial duct is straightened. We tend to select a diameter of the stent that is a millimetre or two larger than the diameter of the arterial duct to ensure apposition to the wall. The appropriate wire is advanced via the sheath and down the

arterial duct to the descending aorta, and the stent is advanced over it and positioned. More angiograms are performed to ensure precise placement and the stent is deployed. Repeat angiograms are performed. If the bands and stent are in good position, the sheath is removed, a mediastinal chest tube is placed, and the chest is closed.

The patient returns to the intensive care unit and is weaned to extubation over the next few days, and enteral feedings are started as soon as it appears possible. Daily aspirin is initiated when enteral feedings are tolerated at 3–5 milligrams per kilogram per day. We have commonly found many of the same issues with feeding in babies following hybrid as those following a Norwood (Stage 1) operation, and the need for supplemental feedings via a nasogastric tube or gastric tube is common. We tend to make a decision about the need for neonatal atrial septal intervention about a week after the hybrid, as some of these patients do wind up needing a balloon septostomy or balloon atrial septoplasty before discharge.

Interstage management

Outpatient follow-up during the interstage period is quite rigorous, and when things are well we see these patients on a biweekly basis. Frequent echocardiograms are markedly important as subtle findings regarding right ventricular systolic function or tricuspid insufficiency in particular may be the harbinger of important anatomical issues including obstruction in the proximal or distal arterial duct or retrograde obstruction of the aortic arch. The atrial septum and bands on the pulmonary arteries also have to be closely followed as the development of restriction to flow across the atrial septum or the development of advanced obstruction of a branch pulmonary artery are both possible. Remember in particular that up to 24% of patients will develop retrograde obstruction of the aortic arch, and this finding can be difficult to sort out by surface echocardiography due to artefact from the stent.[16] It is for all of these reasons that development of even mild changes in the saturation of oxygen, right ventricular function, tricuspid regurgitation, atrial septal gradient, or gradient across the band on the pulmonary artery should usually prompt admission to the hospital, further evaluation, and often urgent catheterisation. The need for interstage intervention is common, and these interventions between stages need to be expected as part of the process of caring for any patient undergoing the hybrid approach.

Retrograde stenosis of the aortic arch is particularly difficult and challenging. Echocardiographic imaging of the arch upstream of a stented arterial duct in an unsedated infant can be challenging. The stent itself creates extensive artefact. It is often pretty easy to see the stented area, note unexciting Doppler patterns there, and accept that things are fine. In fact, they often are not fine. Take the example of a 2-month-old boy. His initial diagnosis was hypoplastic left heart syndrome with aortic atresia, mitral stenosis, and sinusoidal communication between the coronary artery and left ventricle. He underwent a hybrid because of his high-risk status for Norwood palliation. Clinically, he was doing well, had no symptoms of congestive heart failure, was feeding and growing on full oral feedings, and had good saturations of oxygen. His pulses in his hands and feet were equal as were his systemic arterial pressures measured by cuff. Routine echocardiographic imaging showed normal right ventricular function and mild tricuspid regurgitation, but his retrograde flow in the aortic arch was difficult to image. Taking the time to very carefully evaluate that part of the arch, however, demonstrated findings suggestive of aortic coarctation, but coarctation – with a peak Doppler gradient in the high 60s and diastolic flow continuation – travelling retrograde towards the ascending aorta, not the descending aorta. This anatomy was best seen in a modified high left upper sternal border view. At cardiac catheterisation, he was found to have a gradient measured between the descending aorta and ascending aorta – with the ascending aorta being lower – of 22 millimetres of mercury. This patient underwent implantation of an additional balloon expandable stent perpendicular to the stent already in his arterial duct and extending into the distal transverse arch, abolishing the angiographic narrowing and gradient (Figs 1 and 2). This patient underwent comprehensive stage 2 operation at 6 months of age and did well.

Obstruction within the stented arterial duct can also be subtle, as will be illustrated by the following vignette. The initial diagnosis of this patient was critical aortic stenosis with a borderline small left ventricle and restrictive atrial septum. He underwent transcatheter atrial septoplasty with a cutting balloon within hours of birth followed by transcatheter aortic valvuloplasty with a balloon a week later. He failed to wean successfully from prostaglandin and underwent an uneventful hybrid procedure at 3 weeks of age. He was discharged home a week later. At 3 months of age, he developed mild right ventricular systolic dysfunction and worsening tricuspid regurgitation. The tricuspid regurgitation went from trivial to mild to moderate. No worrisome Doppler gradient was noted in his arterial duct or retrograde aortic arch. He was asymptomatic with equal upper and lower extremity pressures and pulses.

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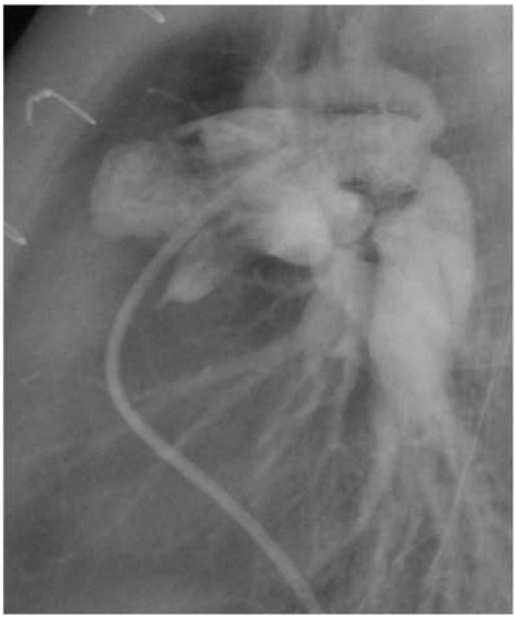

Figure 1.
Retrograde obstruction of the aortic arch.

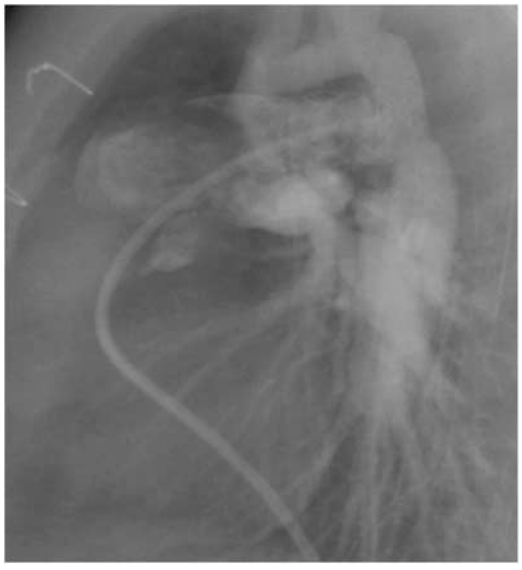

Figure 2.
Retrograde obstruction of the aortic arch, post stent.

At catheterisation a few days later, he was found to have a mild angiographic narrowing at the distal end of his stented arterial duct, with a 15 millimetres of mercury gradient measured at catheterisation. An additional stent was placed with abolition of the gradient (Figs 3 and 4,). His right ventricular systolic function normalised in the next few days, and his tricuspid regurgitation diminished back to trivial. At 9 months of age, he underwent surgical biventricular repair.

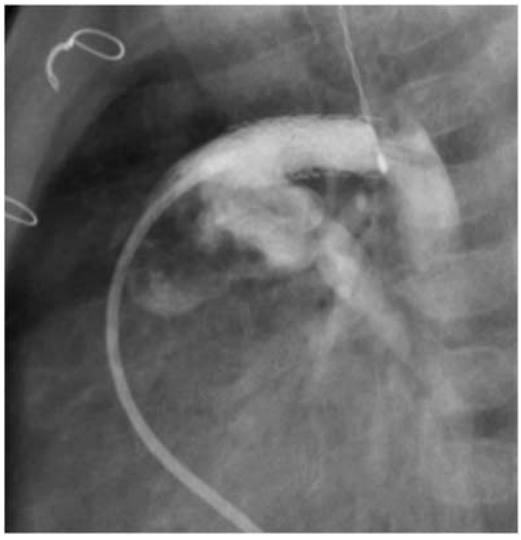

Figure 3.
Stenosis of the distal arterial duct.

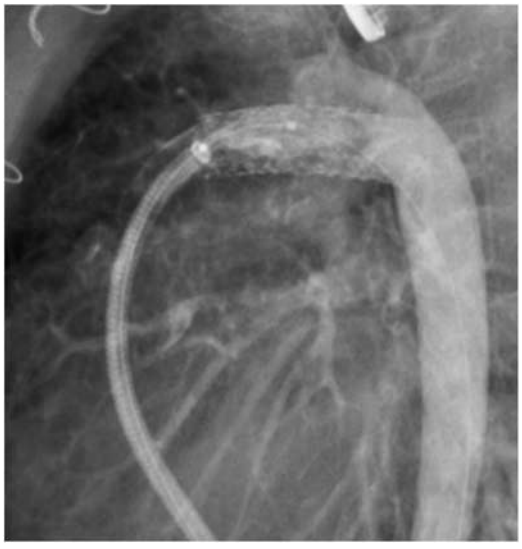

Figure 4.
Stenosis of the distal arterial duct, post added stent.

Diminished levels of systemic oxygen imply recurrent restriction at the atrial septal level or progressive stenosis of the banded pulmonary arteries. A change in the levels of systemic oxygen should prompt further evaluation for either of these potential aetiologies and likely early interstage catheterisation as well.

The interstage period following hybrid palliation is full of pitfalls and potentially lethal haemodynamic derangements. Given the limited global experience with children who undergo this procedure, one should have a low clinical threshold for

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extensive, non-invasive, and invasive evaluation of these patients.

Conclusions

What is known about the hybrid approach is that it can be accomplished safely and effectively and that it can provide effective palliation for some patients with hypoplastic left heart syndrome. It can be offered to many patients at high risk and at the absolute extremes of size and age.[17] The overall technical simplicity of this procedure has led to it being offered in a developing country.[18] It is also known that post-procedural care and interstage management are both complicated and arduous and require close follow-up and commonly unpredicted additional interstage interventions. Interstage mortality and morbidity, although uncommon, do occur. Unanticipated interventions are not rare and should not be seen as such. It is also known that the comprehensive stage 2 palliation is a large and difficult operation. The arch reconstruction in particular is by necessity more challenging than in a newborn because it is a repeat sternotomy and the stent must be removed.

What is unknown is whether any of the currently proposed benefits of the hybrid procedure will be borne out in the future.

- What if the rate of late right ventricular failure is markedly lower in long-term follow-up after a hybrid approach? What if it is higher?
- What if avoiding exposure to cardiopulmonary bypass as a neonate leads to fewer neurodevelopmental problems, a higher intelligence quotient, and better performance at school?
- What if the comprehensive stage 2 operation makes it more likely that late coronary stenosis develops?

As with any relatively new procedure, the unknowns far outnumber the knowns. Given the benchmark outcomes for Norwood palliation and cardiac transplantation, we will have to continue to compare outcomes after the hybrid approach to contemporary results for mainstream surgical approaches. Over the coming years, it is our hope that we will begin to answer some of these questions with greater procedural experience and with the expanded use of clinical trials and databases in congenital cardiac disease. What would clearly be best would be comparing standard risk and high-risk patients separately, ideally in a randomised fashion, but at least in such a way that the outcomes of similar risk patients can be compared in a more structured fashion.

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