Feasibility of transcatheter techniques for intracardiac and extracardiac cavocaval connection in principle for Fontan completion in chronic animal models

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Abstract

OBJECTIVES: We report the safety and feasibility of various transcatheter techniques of cavocaval connection in principle for the completion of Fontan circulation in viable, chronic and ovine heart models. Surgically simulated preparations of both intracardiac and extracardiac cavocaval connections were studied.

METHODS: Sixteen sheep were divided into two groups per the type of surgical preparation. All animals underwent standard right thoracotomy with interposition of a 20-mm Gore-tex® conduit between the superior vena cava (SVC) and the right atrium (RA). Nitinol rings were placed around the SVC and the inferior vena cava (IVC). In Group I (intracardiac, n = 10), the SVC-RA junction was closed using a polytetrafluoroethylene (PTFE) membrane 1 cm below the SVC-Gore-tex® anastomosis. In Group II (extracardiac, n = 6), a 20-mm Gore-tex conduit de-aired and filled with heparinized saline was anastomosed to connect the SVC and the IVC. The IVC end was anastomosed in a termino-lateral fashion and the SVC end in a termino-terminal fashion; both the ends were occluded with a PTFE membrane. Animals were scheduled for transcatheter cavocaval connection after a variable healing period.

RESULTS: Four animals in Group I died; three early and one late after surgical preparation. After a median interim period of 1 month (0–9 months), five sheep from Group I and six from Group II underwent successful transcatheter cavocaval connection. Perforation of the PTFE membrane was successful in all animals. Covered stents were deployed precisely and with good stability ensured by the nitinol rings. All animals survived transcatheter completion and were sacrificed after a median follow-up of 4 months (0–8 months) per protocol. No stent migration, thromboembolic events, residual shunts or paraprosthetic leak was noticed on angiographic evaluation or at autopsy in any animal.

CONCLUSIONS: Transcatheter techniques for completion of cavocaval connection in surgically simulated, chronic animal models is safe and feasible. Both techniques were equally successful with no failures or short-term complications. Such techniques should work in principle for completion of intracardiac and extracardiac Fontan circulation.

Keywords: Fontan circulation • Transcatheter completion • Hybrid approach • Congenital heart diseases

INTRODUCTION

Significant improvements in the management of children with various single ventricle morphologies have led to better long-term survival over the last couple of decades [1–5]. In the absence of septation or biventricular repair the goal of surgery is to separate pulmonary and systemic circulations; at first by connecting the superior vena cava (SVC) and the pulmonary artery and finally by connecting the inferior vena cava (IVC) to the pulmonary artery commonly known as the Fontan pathway [6]. However, repeated surgeries increase cost, morbidity, mortality and significantly impact the quality of life of these patients with poor cardiopulmonary reserve [7, 8]. The need to reduce the number of surgeries prompted various groups to try some creative and indigenous transcatheter techniques [9]. However some concerns on the long-term effectiveness have been highlighted [10]. Our prior study described an improvement with the introduction of an occluded stent near the SVC-right atrium (RA) junction to enhance the stability and avoid accidental covering of the right pulmonary artery (RPA) with the strands of the covered stent placed during subsequent transcatheter completion [11, 12]. The present study describes newer, simplified surgical preparations, with the intention of transcatheter completion of cavocaval connection in viable, chronic ovine heart models.
METHODS

All animals received humane care in compliance with the European convention on animal care. After approval by the local institutional ethics committee (INRA, Paris, France), 16 sheep underwent surgical techniques as described below.

Surgical model

A viable, chronic model was created as described in our previous article [11]. Standard premedication, anaesthesia induction, endotracheal intubation and ventilation were achieved in 16 sheep weighing 55 ± 7 kg. Anaesthesia was maintained using halothane (1.5–2.5%) with continuous monitoring of arterial pressure, oxygen saturation and cardiac rhythm. The animal was placed in left lateral decubitus and the heart exposed via right axillary thoracotomy. A Gore-tex® conduit of 20 mm was anastomosed between the SVC and the RA after closing the azygos vein. Further modification of the surgical technique was based on study design and the type of pathway proposed: intracardiac or extracardiac for cavocaval connection. After the surgical preparation, animals from both groups were extubated and allowed to heal at the sheepfold for a variable interim period: median of 1 month (range 0–9 months), without any anticoagulation.

Intracardiac surgical preparation (Group I)

Ten sheep underwent further surgical preparation to simulate a cavocaval connection of an intracardiac Fontan on completion using transcatheter totalization. The proximal 2 cm of SVC between the Gore-tex® anastomotic site and the junction of RA was transection in its middle, occluded by a polytetrafluoroethylene (PTFE) membrane and re-sutured. Two nitinol rings spaced 1 cm apart were fixed around the proximal SVC stump on either side of the interrupted zone, just below the Gore-tex® anastomosis. Finally, two nitinol rings were fixed around the IVC near its entry into the RA (Fig. 1A).

Extracardiac surgical preparation (Group II)

Six sheep underwent further surgical preparation to simulate cavocaval connection of an extracardiac Fontan on completion using transcatheter totalization. A 20-mm Gore-tex® conduit, de-aired and filled with heparinized saline was anastomosed between SVC and the IVC (Figs 1B and 2). The IVC anastomosis was done in a termino-lateral fashion and the SVC end in a termino-terminal fashion. The SVC and the IVC end of the Gore-tex® conduit was occluded using a PTFE membrane. Nitinol rings were stretched and positioned on either sides of the SVC and IVC anastomotic line and also on the Gore-tex® conduit to identify its course with respect to the PTFE membrane on fluoroscopy.

Interventional catheter completion

All cardiac interventions were performed under general anaesthesia with right femoral and internal jugular vein (IJV) accesses (7Fr) obtained in all. All animals underwent an initial angiogram to confirm flow across the SVC to RA conduit and create a road...
map for the precise placement of covered stents. In Group I, a 5-Fr right Judkins catheter was placed under fluoroscopy from the right IJV, in contact with the PTFE membrane separating the SVC and RA. The stiff end of a 0.035 guide wire was advanced through its lumen to perforate the membrane. The use of a radio-frequency wire for perforation was kept as a backup; however, it was never required. The catheter was advanced in the RA over the wire and the soft end of the guide wire was advanced into the IVC. A 16-Fr Mullins sheath was advanced over the guide wire into the IVC. Using this as the delivery sheath, a mean of three covered stents grafts (CP, Numed Inc. or Atrium V12) were placed between the SVC and IVC nitinol rings; precise placement was ensured to avoid little margin for error in accidentally covering the anastomosis between SVC and Gore-tex® conduit above and the hepatic vein drainage below.

In Group II, a 5-Fr right Judkins catheter was placed from the right IJV access under fluoroscopy, in contact with the PTFE membrane separating the SVC from the saline filled cavocaval Gore-tex® conduit. Through its lumen, the stiff end of a 0.035 guide wire was advanced to perforate the membrane. The catheter was advanced in the Gore-tex® conduit and the PTFE membrane at the IVC end perforated as well. The catheter was advanced over the wire and the wire was then reversed to advance the soft end further into the IVC. The occluding membranes were dilated with a balloon catheter to facilitate stent placement. Thereafter, a 16-Fr Mullins sheath was advanced over the guide wire into the IVC. Through this long sheath, covered stents grafts were placed between the nitinol rings completely occluding the native IVC ostium and redirecting flow into the cavocaval Gore-tex® conduit as in the extracardiac Fontan procedure and also at the superior connection with the SVC.

Follow-up after transcatheter completion

All animals were sacrificed per study protocol at last follow-up with a median of 4 months (range 0–8 months). Before the sacrifice, selective angiographies were performed to confirm (i) the absence of native flow from SVC and IVC into IVC, (ii) absence of para-prosthetic leakages, (iii) intracardiac or extracardiac leaks from the neo-conduit, (iv) patency of initial SVC-RA Gore-tex® conduit with no overlap by the strands of the covered stent, (v) patency of the hepatic venous drainage and (v) analyse haemodynamic flow into the montage.

RESULTS

Early results after surgical preparation

In Group I, three animals died in the early postoperative period after the initial surgical preparation. One animal died of haemorrhage in the operating room secondary to anastomotic failure between SVC and the 20 mm Gore-tex® conduit. Technical difficulties of thoracotomy exposure and end-to-side SVC to Gore-tex® conduit diameter mismatch were some problems encountered. The second animal died from a SVC syndrome secondary to haemodynamically significant stenosis at the level of Gore-tex® conduit to RA anastomosis due to stretched pectinate muscle bands. The third animal died of a large haemothorax secondary to laceration of an intercostal artery while closing the thorax. Over time and after a short learning curve the procedure was standardized with no further complications noted in this group. Group II showed no mortality and the Gore-tex® conduit was anastomosed easily with the SVC and IVC.

Late results of initial surgery and interim period

In Group I, one animal died 4 months after the surgical preparation at the sheepfold secondary to pyothorax. Finally, six sheep survived the operative procedure and recovered uneventfully. One animal was considered as a control of this step and autopsied 12 months later to study the isolated effects of surgery without transcatheter instrumentation. There was no thrombus in the distal or proximal SVC stump; the Gore-tex® conduit between SVC and RA was widely patent with neo-endothelialization as expected; there was no displacement of nitinol rings with no evidence of transmural erosion. In Group II, all six animals survived the initial surgical procedure; however, one underwent early totalization in view of recurrent pneumothoraces.

Early results after transcatheter completion of intracardiac cavocaval connection

Among the remaining five animals in Group I, all underwent transcatheter completion after a median interim period of 9 months (range 1–9 months). The three to four covered stents were precisely deployed between the two nitinol rings with no compromise or covering of the of the SVC-RA conduit ostium, a surrogate for the RA-PA anastomosis as in a classic Fontan (Fig. 3).

Figure 3: Angiograms after transcatheter cavocaval connection in Group I. (A) Covered stents have been placed between in SVC and IVC rings. (B) Dye injection in the pathway. (C) Still frame focusing on the IVC junction. The dye is diverted within the intracardiac pathway. (D) Angiogram showing the SVC connection with the RA.
Early results after transcatheter completion of extracardiac cavocaval connection

All six sheep in Group II underwent perforation of the PTFE membranes, opening of the Gore-tex® conduit and closing the native ostium of the IVC to simulate an extracardiac Fontan-like circulation after a median interim period of 1 month (range 0–1) (Figs 4 and 5). A single covered stent was required to effectively occlude the native ostium of the IVC and channelize flow into the conduit.

All animals in both groups demonstrated good flow dynamics in the SVC–RA conduit; no gradients or shunts were noted between IVC, SVC and RA. All left the cardiac catheterization laboratory alive with no complications. Only one animal in Group I showed a moderate gradient (3 mmHg) at the level of the Gore-tex® conduit–RA anastomosis secondary to uncut and stretched pectinate muscles.

Outcomes at last follow-up after transcatheter completion

In Group I, all animals were followed for a median follow-up of 5 months (range 1–8 months) before sacrifice. No late technical, haemodynamic or thrombotic complications were noted. The concluding angiograms did not show any stent migration, in situ thrombus or leakage across the device. The gross examination showed proximal and distal stents well anchored by the nitinol rings with no displacement.

In Group II, four animals were followed for a median follow-up of 3 months before the sacrifice. No technical, haemodynamic or thrombotic complication was noted in any animal. The concluding angiograms showed a widely patent extracardiac conduit, without any gradients at any level. The covered stent was well deployed with no IVC to RA leakage. The gross examination showed a well neo-endothelialized extracardiac Gore-tex conduit® and complete disruption of the PTFE membrane. The PTFE strands were seen below the stent or against the prosthetic wall. The stents were securely moulded on the nitinol anchoring rings and Gore-tex® conduit.

DISCUSSION

Transcatheter completion of Fontan circulation marks a new milestone in the management of patients with univentricular heart. The distinct advantage of eliminating a second prolonged surgical procedure and thus avoiding possible surgical morbidity and mortality is the key impetus for this procedure. The study by Al soufi et al. [10] appears quite promising due to the short recovery, low complications and excellent early results. Nonetheless, there are several potential disadvantages in their approach or in the other techniques attempted so far [13–16].

The initial surgical procedure must be well planned with the interventional cardiologist to allow transcatheter completion with long-term functionality of Fontan circulation. The lack of such an ideal surgical animal preparation to try and test various transcatheter techniques prompted us to do this study. In Group I animals from the current study, the surgical preparation was simple and reproducible, with a short learning curve without the use of extracorporeal cardiac circulation. Transcatheter completion of intracardiac cavocaval connection was performed without complications. The property of foreshortening of the covered stent on balloon expansion must be kept in mind to ensure complete freedom of the SVC–PA anastomotic ostium. In

Figure 4: Angiograms at various steps of the cavocaval connection in an animal from Group II. (A) Initial angiogram showing the position of the nitinol rings and the occluding SVC membrane. (B) Dye contrast going through the SVC connection with the RA. (C) Dye injection in the Gore-tex extracardiac conduit after puncture of the SVC membrane. (D) Dye injection in the IVC after opening of the IVC occluding membrane showing the connection of the IVC with the RA.

Figure 5: Angiograms at various steps of the cavocaval connection in an animal from Group II. (A) Angiogram showing balloon dilation of PTFE membrane. (B) Insertion of the CP stent at the level of the occluding SVC membrane. (C) Insertion of a covered stent (atrium) covering both the IVC membrane and the connection of IVC–RA. (D) Angiogram at final stage showing redirection of the flow within the extracardiac conduit.
view of the cited advantages of an extracardiac Fontan, we developed a chronic animal model to reproduce an extracardiac cavocaval connection. This technique may be used as an extension of the initial cavopulmonary shunt in humans. The surgical simulation of extracardiac preparation in our ovine model was simple and successful without the use of cardioplegia. Transcatheter completion of extracardiac cavocaval connection was smooth, without complications or revisions. We believe the long-term results with respect to hemodynamic flow, arrhythmia and thrombus formation may be similar to the conventional surgical extracardiac Fontan completion albeit the surgical morbidity and mortality and the prolonged post-surgical convalescence period. These encouraging results may however need additional refinements before use in humans.

LIMITATIONS

None of the animals had a true univentricular heart; the study evaluates the adequacy of transcatheter techniques to establish a cavocaval connection in principle to achieve Fontan completion. With a fully functional RV, tricuspid and pulmonary valves with pulsatile flow, thrombus formation was not anticipated. The absence of atrial septal defect also eliminated the risk of paradoxical embolization unlike true univentricular hearts where the risk may be high with instrumentation. A strong and unified approach with the surgical team for the creation of a pathway to connect the roof of the RA to the underside of the RPA by a prosthetic device is of paramount importance. There may be a learning curve and thus an anticipated increase in surgical time/morbidity in the initial phase. Extreme care must be exercised by the surgeon when working close to the SVC-RA junction; the sinus node should ideally be located to avoid permanent damage and thus the need for life-long pacing. The long-term effects of stasis and stagnation of serum saline in the extracardiac conduit are unknown. The questionable loss of kinetic energy at the level of the new channel, possible late leakages at the anastomosis line and in-situ thrombus formation in view of the large area of foreign material in the RA are some additional concerns.

CONCLUSIONS

Transcatheter techniques for completion of cavocaval connection in surgically simulated, chronic animal models are safe and feasible. Both techniques were equally successful with no failures or short-term complications. Such techniques should work in principle for the completion of intracardiac and extracardiac Fontan circulation and mark a new milestone in the management of patients with univentricular hearts. In view of better long-term outcomes reported with extracardiac Fontan, transcatheter completion of extracardiac cavocaval connection deserves special attention. With growing experience it may be possible to create a hybrid strategy and concomitant intraoperative completion of Fontan in the same setting with significant reduction of cross-clamp time and perioperative mortality. Further long-term follow-ups may be required before the clinical application of such techniques.

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REFERENCES