Atrial cardiomyoplasty in a Fontan circulation

Bernhard Vossa,*, Falk-Udo Sackb, Werner Saggauc, Siegfried Haglb, Rüdiger Langea

aDepartment of Cardiac Surgery at the German Heart Centre of Munich, Lazaretstrasse 36, 80636 Munich, Germany
bDepartment of Cardiac Surgery at the University Hospital of Heidelberg, Heidelberg, Germany
cDepartment of Cardiac Surgery at the Heart Centre, Ludwigshafen, Germany

Received 18 September 2001; received in revised form 20 December 2001; accepted 17 January 2002

Abstract

Introduction: The Fontan circulation is a direct connection between the systemic veins and the pulmonary artery (PA). Consequently, the pulmonary flow is passive due to the gradient between the right and left atrial pressure. In patients with increased pulmonary vascular resistance, the surgical procedure of atrio-pulmonary connection is therefore prone to failure. The goal of this experiment was to increase the pulmonary flow in an experimental model of a Fontan circulation by performing a right atrial cardiomyoplasty (ACMP). Methods: In 19 Foxhounds the left m. latissimus dorsi (LD) was mobilised and transferred as a pedicle into the chest. After sternotomy a ‘Fontan circulation’ was created under cardiopulmonary bypass (CPB) by connecting the right atrium (RA) with the PA by a valveless conduit. The tricuspid valve was closed with a patch. In 11 dogs (group 1) a valve was implanted in the inferior vena cava (IVC) and pulmonary inflow impedance was increased by partial occlusion of the conduit to a gradient of 10 mmHg between RA and PA. In the other eight dogs (group 2) no valve was implanted, but flowmeters were placed in the IVC and the superior vena cava (SVC). In all dogs the RA was enlarged by a fascia lata patch before the LD was wrapped over the RA and stimulated synchronously to the R-wave with burst impulses. Results: After coming off CPB, relatively high central venous pressures (22.5 ± 5.8 mmHg) were necessary to maintain haemodynamic stability. With LD-stimulation in a 1:3 mode in group 1, RA pressure (P) increased from 23.1 ± 7.7 to 45 ± 10.5 mmHg (P < 0.001), pulmonary atrial pressure (PAP) from 15.5 ± 4.3 to 25.5 ± 7.6 mmHg (P < 0.001) and central venous pressure increased to 33.1 ± 11.3 mmHg (P < 0.05). Stroke volume increase from 11.4 ± 4.7 to 17.2 ± 4.3 ml and peak conduit-flow from 1286.3 ± 880.3 to 2329 ± 1173 ml/min (all P < 0.001). In a 1:1 stimulation mode a pulsatile pressure/flow profile was obtained in the PA-conduit. Furthermore, at higher frequencies of about 120 beats/min muscle relaxation was still fast enough as not to interfere with the RA filling. In group 2 caval flow without stimulation occurred mainly during diastole. However, with LD-stimulation, a strong backflow into IVC and SVC was observed resulting in a less pronounced pressure/flow increase in the PA. Conclusions: Our experimental model demonstrates the possibility of a ‘ventricularisation’ of the RA by using the force of the LD. However, the haemodynamic benefit of ACMP was achieved only, when a valve was implanted in the IVC. © 2002 Published by Elsevier Science B.V.

Keywords: Cardiomyoplasty; Atrial cardiomyoplasty; Fontan procedure

1. Introduction

The principle of the Fontan operation has been applied for 30 years as a palliative treatment of most forms of functional single ventricle (e.g. tricuspid atresia, hypoplastic left heart syndrome). This operation places the pulmonary and systemic circulation in series by connecting the systemic venous blood flow directly to the pulmonary arteries. Initially, the right atrium (RA) has been believed to act as a pump for the maintenance of an adequate pulmonary circula-

lation [1]. But soon it became obvious that the relatively weak right atrial contraction was inefficient and even detrimental in a Fontan circulation, because of a turbulent flow profile [2,3]. Hence, the amount of pulmonary flow is primarily determined by the gradient between right and left atrial pressure [4]. In order to improve the flow pattern in the Fontan circulation changing concepts led to new operative techniques, such as the cavo-pulmonary connection instead of the ‘classic’ atrio-pulmonary connection [5].

If a careful patient selection is made, a poor functional outcome after the Fontan operation is uncommon. However, it becomes more frequent with increasing duration of follow-up [6]. Some of the patients, especially those with a ‘classic’ Fontan circulation, are physically impaired and suffer from an entity which may be called the ‘Fontan-
disease’ [7]. For patients with increased pulmonary pressure and decreased function of the ‘systemic’ ventricle the Fontan operation is a priori associated with a higher risk and poor long-term outcome [8].

The purpose of atrial cardiomyoplasty (ACMP) is to increase the pulmonary flow by ‘ventricularisation’ of the RA. Especially in the population of failing Fontan patients or those with increased pulmonary resistance the ACMP may be helpful in delaying or reversing the development of the ‘Fontan disease’. The technical feasibility of an ACMP in a Fontan circulation was already proven by Chachques et al. [9] and Loumet et al. [10]. The aim of this study was focussed on the question whether ACMP could be effective in a Fontan model with increased pulmonary resistance.

2. Material and methods

Nineteen Foxhounds weighing between 18.4 and 26 kg were used for the experiment. General anaesthesia was induced with an intravenous bolus of 20 mg/kg body weight (BW) and maintained by continuous infusion of phenobarbital (3 mg/kg/h) and piritramid (0.4 mg/kg/h). All animals received human care in compliance with the ‘Guide for the Care and Use of Laboratory Animals’ published by the National Institute of Health (NIH publication 85-23, revised 1985). The experimental part of this study was carried out at the University of Heidelberg.

2.1. Harvesting of the M. latissimus dorsi

In the right lateral position the left latissimus dorsi (LD) was dissected, taking care to preserve the thoracodorsal neurovascular bundle. Two intra-muscular stimulation electrodes were implanted in the proximal part of the LD flap. The bulk of the LD flap was then passed into the thorax through a window created by dissection of the second rib. Then the wound was closed. An external stimulation device (Model 3076, Medtronic, Inc., Minneapolis, MN, USA) was used for electrical muscle stimulation.

2.2. Fontan circulation

The heart was exposed through a median sternotomy. After heparinisation (3 mg/kg BW), a normothermic cardiopulmonary bypass (CPB) was instituted between both femoral veins, the right jugular vein and the ascending aorta. The vena azygos and hemiazygos were ligated. Between the right atrial (RA) appendage and the distal pulmonary artery (PA) trunk a valveless conduit with an integrated flowmeter was inserted. The conduit was partially occluded to achieve a gradient of 5–10 mmHg between the RA and PA. After introduction of a vent in the right ventricle the proximal trunk of the PA was closed by a pursestring suture. In order to simulate a tricuspid valve atresia the tricuspid valve was exposed through a right atriotomy and closed with a dacron patch. In 11 Foxhounds (group 1) a mechanical valve (Medtronic Hall 16 mm) was implanted at the inferior cavo-atrial junction. In the other eight dogs (group 2) no valve was implanted, but flowmeters were placed in the inferior and superior caval veins. In all dogs a fascia lata patch was used to enlarge the RA. The experimental designs of both groups are illustrated in Figs. 1 and 2.

2.3. Atrial cardiomyoplasty

After completion of the atriopulmonary connection the transposed left LD was placed over the RA (Fig. 2). In order to get an optimal LD size for the ACMP it was necessary to shorten the LD by cutting 2–3 cm of the outer muscle board. Then the distal muscle part was fixed in the area of the intra-atrial groove on the pericardium with interrupted 4-0 prolene sutures. Special care was taken so that the LD did not obstruct the RA–PA conduit. A sensing lead (model SP 6500, Medtronic, Inc., USA) was implanted into the ventricular wall and connected to the sensing channel of
the external cardiomyostimulator. The LD muscle leads were coupled with the pacing channel of the stimulator. In order to increase the RA output the LD was stimulated synchronously with the heartbeat in a 1:3 or 1:1 mode. Burst impulses were delivered by the cardiomyostimulator using the following parameters: pulse amplitude 3–6 V, pulse width 210 μs, burst rate 30 Hz, burst duration 185 msec and heart-to-muscle synchronisation delay 4 msec.

2.4. Haemodynamic measurement

Micro-Tip catheters (Millar Instruments, Inc., Housten, TX, USA) for blood pressure monitoring were placed in the superior caval vein, the RA, the PA and the left ventricle. Flow studies were performed using electromagnetic flowmeters in the RA–PA conduit (group 1 + 2) and in the superior and inferior caval vein (only group 2). Electrocardiogram (ECG), central venous pressure, right atrial pressure (RAP), pulmonary atrial pressure (PAP), left ventricular pressure (LVP), dp/dt, pulmonary flow and caval veins flow (only group 2) were monitored and recorded simultaneously on a multi-channel printer (Astro-med MT 9500, Warwick, RI, USA). Stoke volumes were calculated by planimetry of the flow curves. Haemodynamic variables were assessed in each experiment with and without stimulation of the LD. Statistical analysis was performed using a Student’s t test. A P-value of less than 0.05 was considered statistically significant.

3. Results

After the Fontan operation high venous filling pressures (22.5 ± 5.8 mmHg) were needed to maintain satisfactory haemodynamics. The heart rate was 102 ± 20 beats/min, the LVP 91 ± 14.1 mmHg, LVEDP 12.2 ± 7.3 mmHg and the dp/dt max 1871 ± 831 mmHg/s. All dogs were in sinus rhythm. The partial occlusion of the RA–PA conduit increased the pulmonary inflow gradient to about 10 mmHg. The ACMP could be performed in every case without problems. All muscle flaps were longer than necessary and were shortened by cutting 2–3 cm of the distal border. The LD was not preconditioned and muscle fatigue began as expected 5–10 min after induction of the electrostimulation. The contraction of the LD which was fixed between the chest wall and the inter-atrial groove resulted in a compression of the enlarged free atrial wall, reducing the atrial cavity upon the burst impulse. In group 1 the muscle stimulation performed in a 1:3 mode caused a significant increase of central venous pressure (CVP), RAP, PAP and pulmonary flow (Table 1 and Fig. 3A). Heart rate and LVPs remain unchanged. Fig. 3B shows a short episode of a 1:1 mode stimulation: Without stimulation the pulmonary flow and pressure profile were approximately monophasic, which is typical in a Fontan circulation. When the stimulation started, flow and pressure pattern became pulsatile. In this example the registration reveals an early diastolic backflow in the PA. Despite this insufficiency of the valveless RA–PA conduit the forward flow was still significantly higher than without stimulation.

In group 2, the point of interest was to look at the change of flow characteristics after atrio-cardiomyoplasty in a valveless system. Under the condition of atrio-pulmonary connection the main blood flow in the superior and inferior caval veins took place in the early diastole of the left ventricle, when the muscle was not stimulated. During the ventricular systole a slight backflow was seen into the caval veins. The contraction of the LD, synchronous to the left ventricle, caused a large backflow in both caval veins (Fig. 3C). Thereby a larger amount of volume was distributed into the inferior caval vein. Immediately after that a disproportional forward flow into the RA took place. In the PA the flow pattern was nearly inverse to that in the caval veins: without muscle stimulation the maximal forward flow took place during atrial contraction and in ventricular systole. In early diastole regurgitation of flow in the valveless conduit was observed (Fig. 3D). Despite the wave of pressures recorded in the RA and PA, no significant change was recorded in the pulmonary flow.

4. Discussion

The Fontan operation was introduced in 1971, by Fontan and Baudet [1] as a surgical therapy for tricuspid atresia. The operation results in the separation of the systemic and pulmonary circulation, directing the venous return into the PA without passing through a ventricle. Subsequently, this technique has been applied to the treatment of most forms of functional single ventricle. It was on the basis of the pump-
ing function of the RA that Fontan performed the first atrio-pulmonary connection. With great precision he described the mechanical requirements for a contractile chamber to act as a pump, namely, a power source generating sufficient stroke work, an inlet valve and an outlet valve. But soon it became evident, that inlet and outlet valves were dispensable and that the importance of the RA as a pump in the Fontan circulation had to be questioned [2]. It was shown that the relatively weak contraction of the Fontan RA induces significant turbulence in blood flow and hence increases flow resistance [3]. Chronic atrial distension was seen as a cause for long-term arrhythmias [11] and thromboembolic events [12]. Many modifications of the Fontan circulation aimed at improving flow dynamics. The atrio-pulmonary connection has subsequently been abandoned in favour of the total cavopulmonary connection. With this technique, the superior caval vein is connected directly end to side to the PA and the inferior caval vein is tunnelled through the atrium or through an extracardiac conduit to the pulmonary circulation [3]. This cavo-pulmonary connections exhibit a better haemodynamic design than the atrio-pulmonary connection, but the pulmonary flow remains non-pulsatile.

The Fontan operation and its modifications have dramatically improved the functional outcome for most patients with single ventricle physiology [6,13,14]. Recent reports, however, have emphasised a continuing risk of late failure and poor functional outcome in some long-term survivors. Exercise capacity is reduced, atrial arrhythmias are common and pulmonary arterio-venous fistulae are frequent [7]. The occurrence of thromboembolic complications with neurologic or cognitive deficits has been reported to be up to 20% [15]. Protein-losing enteropathy is a serious complication and occurs as well in up to 20% of the reported series.
An increasing number of patients with poor functional outcome are being recommended for cardiac transplantation [6,14]. Hence, it has been suggested that although the Fontan procedure is an excellent palliative operation, it is not a curative one [13].

The main problem of a Fontan circulation is the absence of the ventricle for pulmonary blood flow. This circulation can only succeed with slightly elevated systemic venous pressure, low pulmonary vascular resistance and low left atrial pressure [4]. The ‘systemic’ ventricle in the Fontan circulation is chronically underloaded as in mitral stenosis. This probably accounts for the diastolic dysfunction demonstrated in these patients. Macé et al. [17] demonstrated in an experimental model, that increasing degrees of right heart bypass are associated with a significant decrease of the single ventricle performance. A long-term atriotomy related to the ‘Fontan state’ appeared to be the natural history of that circulation [5]. Especially in the case of patients with increased pulmonary resistance the Fontan procedure is prone to failure.

Mechanical devices to support the failing circulation after right ventricular exclusion by phasic external body compression [18] or by a right atrial balloon pump could only be used temporarily. For high-risk Fontan candidates, ACMP could be an alternative for long-term support. By using the force of a stimulated skeletal muscle the RA could be ‘ventricularised’ to work in accordance with Fontan and Baudet’s original idea as an effective ‘pumping-chamber’. The muscle may also prevent the distension of the atrial tissue.

The use of an electro-stimulated skeletal muscle to improve the pump function of the RA was first proposed by Nakamura and Glenn in 1964 [19]. In 1987 Macoviaik et al. [20] presented the anatomical replacement of the right ventricle by using a neoventricle chamber assisted by a stimulated latissimus dorsi. Bridges et al. [21] described an experimental right heart bypass with skeletal muscle neoventricles in 1989. They concluded that skeletal muscle ventricles were capable of performing the work of the right ventricle with nearly physiological filling pressures. However, they needed the presence of a prosthetic chamber as neoventricle. With regard to the treatment of congenital heart anomalies the use of neoventrices would involve the impossibility of growth in young patients. In contrast, the technique of ACMP performed in this study avoids the use of prosthetic neochambers and allows the growth of the skeletal muscle in proportion to the heart [22]. Loumet et al. [10] were the first to apply experimental ACMP in a Fontan circulation using the right LD in dogs. With the help of muscle stimulation right atrial and pulmonary pressures increased significantly. Despite an implanted valve in the inferior vena cava (IVC), however, no changes in pulmonary flow were seen. In a different experiment Chachques et al. [9] used the left LD, instead of the right: In five goats the RA was connected to the distal part of the PA with a valveless conduit and the proximal pulmonary trunk was ligated. In another five goats a bioprothetic valve was implanted into the inferior caval vein and the tricuspid orifice was closed. In both groups the left LD was sutured over the RA. LD stimulation restored a pulsatile pressure pattern in the PA and increased significantly the cardiac output. This observation was much more evident in the model with a valve in the inferior caval vein. Chekanov and Shatalov [23] used a diaphragm muscle flap for ACMP. They showed remarkable haemodynamic improvements in an experimental Fontan circulation in dogs when the flap was electrically stimulated. This approach, however, seemed not practical in patients, because the lack of diaphragm function may lead to severe respiratory insufficiency.

Our experiment differs in two aspects from previous studies: first, we used an experimental ‘Fontan model’ with increased pulmonary inflow impedance. Second, we enlarged the RA with a fascia lata patch. With this approach we succeeded in increasing the RAP by the LD contraction. Consequently, the pulmonary flow was significantly improved, when a valve was implanted in the IVC. When muscle stimulation started, the pulmonary flow and pressure pattern changed from non-pulsatile to pulsatile. This shows, that the skeletal muscle contraction converted the RA into an efficient ‘pumping-chamber’. In comparison, the effect of ventricular cardiomyoplasty, which has been performed in more than 1000 patients world-wide, on systolic ventricular function, was considerably less pronounced [24]. The different working conditions of the LD in atrial and ventricular cardiomyoplasty may be the reason for this. Physiologically, the LD works by shortening in a linear fashion, thereby reducing its length and developing a pulling force. Once wrapped around the ventricles, it has to produce radial shortening in order to generate pressure. Ninety percent of the power expanded to produce linear work is thereby wasted [25]. In ACMP mechanical traction arising from the left chest wall attachment is blocked on the distal attachments of the LD-flap (inter-atrial groove and pericardium) and the free atrial wall lying under the LD is compressed [9]. Thereby the linear muscle contraction could ideally be transformed to reduce the atrial cavity and create ‘systolic activity’. The patch enlargement of the RA increases the volume shift in ACMP.

After creating the Fontan circulation, we needed a high systemic venous pressure to maintain a stable haemodynamic situation. A limitation in this acute experiment was the use of unconditioned skeletal muscles, which allowed only short periods of muscle stimulation. This could be a reason, why we failed to decrease venous pressure by longer periods of continuous muscle stimulation.

In accordance to the experiments of Chachques et al. [9] we found that a significant increase of pulmonary flow in ACMP is only achieved under the condition, that at least one valve is implanted in the caval system. The implantation of a second valve in the RA–PA conduit would cause a further increase in flow by preventing pulmonary regurgitant flow.
However, it has been shown that the use of valves in the Fontan circulation is often associated with the risk of thrombosis and valvular dysfunction, probably the result of low flow and pressure condition. Problems with implanted valves may be less frequent with the application of ACMP because the muscle stimulation increases the flow and pressure levels. As a potential alternative to intravascular valves, a synchronised extraluminal occlusion of the caval veins with a separately stimulated part of the LD or with an intercostal muscle could theoretically be considered.

Good haemodynamics of a normal circulation are characterised by a low caval pressure, in particular, in the inferior cava (<10 mmHg) and a PAP of at least 15 mmHg (mean) to keep the pulmonary vasculature patent. The paradox of the Fontan circulation is that it imposes a caval hypertension and a pulmonary atrial hypotension [5]. This study showed that with ACMP it is possible to step up the pulmonary pressure and flow even in the presence of an increased pulmonary inflow impedance. Further long-term studies with transformed skeletal muscles have to prove if it is also possible to step down the caval pressure by ACMP and thus to reverse the Fontan paradox.

References


Appendix A. Conference discussion

Mr A. Tang (Southampton, UK): The Achilles heel with skeletal muscle circulatory support has been the way the muscles were obviously deployed, and there are two major aspects to that: one is the way the muscle is conditioned to achieve an optimal compromise between power output and fatigue resistance, second is to prevent long-term and medium-term ischemic damage. Now, in your study, have you addressed the issue of muscle transformation, and if not, why not?

And secondly, what steps do you take to try to minimise ischemic damage to the muscle, and if not, why not?

Dr Voss: The experiment was done with non-conditioned muscles. Non-conditioned muscles are only able to contract for a short period of time. When you do this in a chronic model, you have to condition the muscle before. It is correct, if you have a conditioned muscle, the muscle loses power, but not to an amount that it loses the haemodynamic effect. In ventricular cardiomyoplasty you definitely see effects with conditioned muscles, and I think in the low pressure system, the force of a conditioned muscle is even more sufficient to support the atrial contraction.
Dr F. Lacour-Gayet (Hamburg, Germany): The results of many centers which have attempted to increase the contraction of the RA or the low pressure atrium has not been very good, and one of the observations has been that the diastolic relaxation of the muscle is not good. Could you comment on that?

Dr Voss: In our experience, the muscle relaxation time didn’t impair filling of the heart chambers, neither in ventricular nor in ACMP.

Dr L. Lapanshivili (Winterthur, Switzerland): What kind of equipment do you use for muscle contraction, what kind of stimulation do you use?

Dr Voss: We used an external cardiomyostimulator constructed only for experimental work. You know that at the moment no cardiomyostimulators are commercially available because Medtronic stopped the work on cardiomyoplasty. But perhaps next year new cardiomimators, developed by another company, will be available again.

Summarising, I don’t intend to go back to the atriopulmonary connection because TCPC is a good treatment for most patients with a functional single ventricle. But ACMP could perhaps be used in patients with a failed ‘classic Fontan’ or in patients with increased pulmonary resistance. I don’t want to combine this operation with TCPC. That is not necessary.

Dr Lapanshivili: I want to say that cardiomyoplasty must be done. I am engaged in development of various auto muscular (invasive and non-invasive) systems of assisted circulation since 1980 in different institutes of Tbilisi (Georgia), Moscow and now of Switzerland. It looks, that the results in this field could be very, very significant. The twenty years’ experience gives me the confidence to approve, that cardiomyoplasty is one of the real ways in cardiovascular surgery. The only question is how to do it, which way of stimulating the muscles with what kind of equipment.