The Contegra Valved Bovine Conduit: A Biomaterial for the Surgical Treatment of Congenital Heart Defects

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Abstract

Contegra, a bovine jugular vein graft, has been widely used as a preferable biomaterial in the surgical treatment of congenital heart defects, especially as a conduit for the right ventricular outflow tract reconstruction. This article aims to make a comprehensive review on the clinical outcomes of Contegra.

Reports of Contegra published since 2002 were comprehensively retrieved, collected and analyzed. There were 1718 Contegra, applied in 1705 patients. The sizes of the conduits were 8-22 mm. The patients aged from newborn to 74.5 years, prevailed by pediatrics. The primary diagnosis was congenital heart defects in all cases, with Tetralogy of Fallot, truncus arteriosus and pulmonary atresia being the first three diagnoses, representing 25.6%, 16.7%, and 13.1%, respectively.

Contegra was used as a tube graft in the pulmonary position in 1635 (95.9%) patients, as a monocuspid patch in 12 (0.7%), as a graft in the position of the pulmonary valve or a monocusps in 40 (2.3%), and as an inferior vena cava-pulmonary artery conduit in the Fontan procedure in 18 (1.1%) patients, respectively. Conduit reimplantation was performed in 141 (8.3%) patients 33.8 ± 37 (8.6-106.8) months after the initial conduit insertion. Conduit plasty was necessary in 6 (0.4%), and reintervention in 83 (4.9%) patients. Indications for conduit reimplantation included severe stenosis of the distal anastomosis, pseudoaneurysm of the proximal anastomosis and severe conduit regurgitation.

As for the good performance, availability and longevity, Contegra is a biomaterial suitable for the right ventricular outflow tract reconstruction and for patch repair for ventricular septal defect, but not apt for Fontan procedure.

Introduction

Contegra, a bovine jugular vein graft, is a valved xenograft conduit developed by Medtronic1. Limitation of availability in quantity and sizes, actual conduit longevity and patient survival of the homo- and otherwise xenografts made the clinical utilization of Contegra grafts for the right ventricular outflow tract reconstruction for the patients with complex congenital defects possible2. Patients with congenital heart defects requiring right ventricular outflow tract reconstruction or other operations with the use of Contegra are often very young. Majority of them were newborns or infants with low body weight, and only minority were adults3. These risk factors were inevitably associated with the postoperative conduit problems, including conduit stenosis, insufficiency and degeneration, etc, hence leading to further catheter intervention, reoperation, or even mortality4.

Materials and methods

Reports with a patient series of ≥10 cases, who received a Contegra conduit published since 2002 were comprehensively retrieved, collected and analyzed in terms of patients' information, Contegra conduit size, surgical indications, conduit dysfunction, conduit explantation, catheter intervention, freedom from the postoperative events and patient survival, etc.

Data were expressed in mean ± standard deviation and student t test was used to evaluate intergroup differences. p ≤ 0.05 was considered of statistical significance.

Results

Totally 33 reports with a patient series of ≥10 cases, who received a Contegra conduit published since 2002 were collected135. The reports included 1718 conduits, applied in 1705 patients. The sizes of 758 Contegra conduits that were used for the surgical treatment of congenital heart defects were recorded ranging between 8 and 22 mm. The size distribution was depicted in Figure 1. The mean conduit sizes were 14-20.4 mm from different reports16,17,20,31,32,35 (Figure 2). The median sizes were reported to be 16 mm19, and 20 mm35. Graft size ≤ 20 mm was utilized in 51.8% of the patients35.

Nine hundred and sixty-seven patients had their gender expressed in the reports, including 474 (49.0%) males and 493 (51.0%) females, with an equivalent gender predominance.

The patients aged from newborn to 74.5 years. Of the 33 reports, pediatric patients were described in 9 (27.3%) reports with 5 of them included purely infants, adult patients were dealt with in 1 (3.0%), and both pediatrics and adults were reported in 22 (66.7%), and patients' ages were not mentioned in 1 (3.0%) report.

Keywords

Heart defects, congenital / surgery; bioprosthesis; vascular grafting; tetralogy of Fallot / surgery; transplantation, heterologous.
Figure 1 - The sizes of 758 Contegra conduits

Figure 2 - The mean conduit sizes reported from different reports
The Contegra was used as a tube graft in the pulmonary position in 1635 (95.9%) patients, of whom a patch closure of the VSD using a segment from the same Contegra material was done in 11 patients\textsuperscript{26}. The Contegra was tailored as a monocuspid valved transannular patch in 12 (0.7%) patients\textsuperscript{22}, as a tube graft in the position of the pulmonary valve for pulmonary valve replacements and as a monocusp in 40 (2.3%)\textsuperscript{33}, and as an inferior vena cava-pulmonary artery conduit in the Fontan procedure in 18 (1.1%) patients\textsuperscript{27}, respectively.

The primary diagnosis was congenital heart defects in all cases. Of the 1416 patients receiving a tube graft in the pulmonary position, Tetralogy of Fallot, truncus arteriosus and pulmonary atresia with ventricular septal defect were the first three involved congenital heart defects, representing 25.6%, 16.7%, and 13.1%, respectively (Table 1).

The conduit insertion was a primary surgery in 1079 (63.3%), with previous palliative or repair surgery in 584 (34.3%), with previous interventional therapy in 42 (2.5%) patients, respectively.

The patients were at a mean follow-up of 31.8 ± 21.1 (3-74) months (n = 26), and a maximal follow-up of 69.4 ± 44.6 (25-193.2) months (n = 24). The peak transconduit pressure gradient was 14.1 ± 3.5 (8.5-36.5) mmHg (n = 6) at discharge, and 18.7 ± 7.9 (10.4-20) mmHg (n = 17) at follow-up. There was no significant difference in the transconduit pressure gradient between discharge and follow-up (p = 0.1872).

Contegra conduit reimplantation was performed in 141 (8.3%) patients 33.8 ± 37 (8.6-106.8) months after the initial conduit insertion. Conduit plasty was necessary in 6 (0.4%), and reintervention to the conduit or to the pulmonary arteries in 83 (4.9%) patients. The conduit reimplantation was due to severe stenosis (excessive gradient) of the distal anastomosis refractory to interventional treatment\textsuperscript{9,14,24,33,35}, (pseudo)aneurysm of the proximal anastomosis\textsuperscript{19}, progressive right ventricular dysfunction caused by severe conduit regurgitation\textsuperscript{18,20,31}, endocarditis\textsuperscript{11,35} or graft degeneration\textsuperscript{15}.

During the follow-up period, conduit valve was absent of regurgitation in 17.2-77.5\%\textsuperscript{6,9,13}, trivially regurgitant in 31-79.4\%\textsuperscript{8,13}, mildly regurgitant in 24-58.3\%\textsuperscript{8,13}, and moderately regurgitant in 3.4-8.6\%\textsuperscript{13,21,23,24,31} patients, respectively. Significant conduit dilation (DD% >30%) was observed in 27.5\% patients\textsuperscript{31}.

There were 58 and 37 early and late deaths with an early mortality of 3.4% and a late mortality of 2.2%. The mortality were sometimes unrelated to the conduit\textsuperscript{5,31,32}, but caused by septicemia and endocarditis\textsuperscript{11}.

Freedoms from severe stenosis at the distal anastomosis, catheter intervention, conduit reoperation, and reoperation after intervention were satisfactory in several reports (Table 2). The actuarial survival rate was 85.7% at 5 years\textsuperscript{21}, 93.1% ± 3.6% at 6 years\textsuperscript{18}, and 91.5% ± 2.3% at 8 years\textsuperscript{22}.

**Discussion**

**Clinical features**

For the pulmonary position Contegra, it was orthotopic when Ross procedure, replacement after a prior tetralogy of Fallot or double outlet right ventricle repair was performed, while it was heterotopic in truncus arteriosus repair, Rastelli operation, and severe pulmonary atresia\textsuperscript{32}. The Contegra has

**Table 1 - The primary diagnosis or operation of 1416 patients receiving a Contegra material**

<table>
<thead>
<tr>
<th>Primary diagnosis or operation</th>
<th>Case (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetralogy of Fallot</td>
<td>362 (25.6)</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>236 (16.7)</td>
</tr>
<tr>
<td>Pulmonary atresia with ventricular septal defect</td>
<td>185 (13.1)</td>
</tr>
<tr>
<td>Conduit failure</td>
<td>168 (11.9)</td>
</tr>
<tr>
<td>Double outlet right ventricle with pulmonary stenosis</td>
<td>100 (7.1)</td>
</tr>
<tr>
<td>Tetralogy of Fallot + pulmonary atresia</td>
<td>58 (4.1)</td>
</tr>
<tr>
<td>Transposition of the great arteries with ventricular septal defect and pulmonary stenosis</td>
<td>58 (4.1)</td>
</tr>
<tr>
<td>Aortic disease</td>
<td>27 (1.9)</td>
</tr>
<tr>
<td>Pulmonary stenosis/insufficiency</td>
<td>19 (1.3)</td>
</tr>
<tr>
<td>Corrected transposition of the great arteries</td>
<td>14 (1.0)</td>
</tr>
<tr>
<td>Pulmonary atresia with intact septum</td>
<td>11 (0.8)</td>
</tr>
<tr>
<td>Tetralogy of Fallot + atioventricular canal</td>
<td>3 (0.2)</td>
</tr>
<tr>
<td>Taussig-Bing anomaly</td>
<td>2 (0.1)</td>
</tr>
<tr>
<td>Rare complex abnormalities</td>
<td>6 (0.4)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>17 (1.2)</td>
</tr>
<tr>
<td>Ross procedure</td>
<td>142 (10.0)</td>
</tr>
<tr>
<td>Rastelli procedure</td>
<td>8 (0.6)</td>
</tr>
</tbody>
</table>
been praised for its good subvalvular and valvular performance with good freedom from explantation in comparison to homografts (Table 3), however, supravalvular events may occur in Contegra as well\(^5\).

Nevertheless, long-term follow-up revealed no calcification in the Contegra conduit\(^23\). Contegra is a promising alternative patch material for ventricular septal defect repair\(^26\). The potential relevant advantages of using the Contegra conduit between the inferior vena cava and the pulmonary artery were excellent off-the-shelf availability, large range of available sizes, easy tailoring and suturing, no need for proximal or distal extension, and presence of a valve\(^27\). The patent conduit with the valve competency may support better pulmonary forward flow\(^27\).

Freedom from conduit events and survival of Contegra was satisfactory as described above. Rastan et al.\(^20\) reported freedom from reoperation was 77.6% and 59.3% at 1 and 4 years for patients less than 1 year of age compared with 93.5% and 87.4% for patients older than 1 year of age. By comparison, the actuarial freedom from reoperations was 90.7% at 7 years for Contegra conduits significantly superior to the overall freedom from reoperations for cryopreserved valved homografts (81.3%)\(^24\). Right ventricle to left ventricle pressure ratio development and freedom from explantation/redo were equal for the Contegra conduits and homografts\(^1\). The 3-year freedom from replacement for in-conduit stenosis was 96 ± 4% for the Contegra and 69 ± 8% for allograft\(^28\).

### Conduit failure

Conduit dysfunction is defined as a peak conduit gradient greater than 40 mm Hg or greater than 2+ regurgitation and conduit failure was defined as the need for conduit replacement or the need for catheter lab conduit reintervention\(^16\). Of the entire patient setting, 141 (8.3%) patients required conduit reimplantation at 8.6-106.8 months after the initial conduit insertion. It illustrated that Contegra showed good durability requesting an explantation up to 106.8 months after the primary surgery.

However, some Contegra conduits had poor durability and failed in as short as 8.6 months. Therefore, the standard deviation of the conduit reimplantation interval was as long as 37 months. Indications for conduit surgery were conduit obstruction (n = 128), conduit regurgitation (n = 3), and a combination of both (n = 6)\(^29\). Severe graft incompetence,
progressive supravalvular stenosis, or combined were the main causes of conduit explantation after Contegra implantation\textsuperscript{26}. Distal anastomosis obstruction seemed to be a major problem responsible for the reoperation for the conduit early postoperatively\textsuperscript{11}. Stenosis of the proximal pulmonary arteries or diminutive pulmonary arteries was also indicated for the conduit explantation of the Contegra, in particular in pulmonary atresia and truncus arteriosus\textsuperscript{11}. Fibrous pannus formation at the distal anastomotic site or due to thrombus formation leading to conduit obstruction was an alternative condition requiring a conduit replacement\textsuperscript{11}. It was observed that gradients during follow-up were located at the anastomotic site between the Contegra conduit and the pulmonary arteries\textsuperscript{11}.

Corno et al.\textsuperscript{37} described that reoperation was non-conduit-related in all 26 cases included in their study. Peri-conduit infection, abscess or endocarditis, was often seen\textsuperscript{37}. Structural deterioration of the Contegra graft may be seen in small number of patients (5.1%)\textsuperscript{11}. Necessity for reoperations within the first 2 years was significantly lower for Contegra grafts than for non-blood group compatible cryopreserved homografts, 2 of 78 (2.6%) and 8 of 20 (40.0%), respectively\textsuperscript{13}. Contegra grafts had reoperations due to insufficiency in only 6%, however, reoperations were mainly due to peripheral pulmonary stenosis at the distal anastomosis and aneurysms\textsuperscript{14}.

Graft valve regurgitation ≥ 3 + was associated with age < 1 year at surgery, Contegra conduit size < 14 mm, and the right ventricle to left ventricle pressure ratio ≥ 0.6\textsuperscript{11}. The rate of overall conduit replacement was 25% for the Shelhigh pulmonic xenograft versus 26% for Contegra with a mean time to replacement of 18 ± 9 months for the Shelhigh pulmonic xenograft versus 42 ± 4 months for Contegra with no significant difference (p = 0.25)\textsuperscript{11}.

Conduit valve stenosis

Dave et al.\textsuperscript{12} reported that 28.2% of their 163 survivors of Contegra implantation developed Contegra conduit stenosis, of which 19.6% were at the proximal anastomotic, 32.6% were at the valvular, and 47.8% at the distal anastomotic level. Distal anastomosis stenosis with supravalvular conduit dilation was also found a cause for conduit stenosis\textsuperscript{14}. Corno et al.\textsuperscript{38} reported that postoperative intervention was due to twisted or stenotic conduit in 2 of 5 patients. Rastan et al.\textsuperscript{26} observed that stenosis at the distal anastomosis occurred in 25% of their patients with a mean transconduit gradient increased from 15 to 23 mmHg at follow-up. When the Contegra was ring-supported, the transconduit gradient became a bit elevated\textsuperscript{16}. At 38-month follow-up, mean pulmonary pressure gradient was 14.5 ± 7.9 mmHg (Ross procedure: 14.1 ± 8.8 mmHg, Tetralogy of Fallot: 15.8 ± 6 mmHg, isolated pulmonary valve disease: 12.5 ± 3.5 mmHg, dilated cardiomyopathy: 10 mmHg, double outlet right ventricle: 24 mmHg)\textsuperscript{30}.

Conduit dilation

Dilation of the right ventricular outflow patch and conduit may progress\textsuperscript{14,20}. In an attempt to maintain conduit valve geometry and competency, a ring-supported Contegra can be an alternative. At the time of discharge and at follow-up, the degree of conduit valve insufficiency and the gradient across the conduit was not significantly different from the patients who received non-ring-supported Contegra conduit\textsuperscript{20}. In the patients with severe regurgitation, Contegra structures may change involving completely vanished valve leaflets and rudiments of the commissures\textsuperscript{20}. High right ventricle to left ventricle pressure ratio, distal conduit stenosis\textsuperscript{14}, and pulmonary artery branch obstruction or pulmonary hypertension\textsuperscript{11}. The grade of the graft valve regurgitation did not change over time in some patients\textsuperscript{32}. Interventions, sometimes on an urgent basis, included the dilation and/or stenting of the distal anastomosis in more patients, and dilation occurred at the subvalvular level of the conduit, and concomitant major aortopulmonary collateral arteries coil occlusion in a few\textsuperscript{20}.

Thrombosis

Thrombus formation at the distal anastomosis was one of the indications for Contegra conduit explantation\textsuperscript{31}. All three patients with a Contegra conduit for total cavopulmonary connection experienced serious complications of conduit thrombosis, implying the thrombogenicity of the Contegra and it was recommended not being used as a conduit for total cavopulmonary connection\textsuperscript{18}.

Basic research

Histologic examination of the explanted conduits revealed excessive intimal peel formation forming an annular membrane at the level of the distal anastomosis with infiltrations of lymphocytes and macrophages\textsuperscript{11,14,20,34}. Severe perigraft scarring reaction was also observed\textsuperscript{11}. Similar chronic inflammatory reaction was also observed in the Contegra, but not as strong as in the Shelhigh pulmonic xenograft group\textsuperscript{14}. The pathological changes were in line with the better performance of the Contegra conduit. A computational fluid dynamic study demonstrated more homogeneous pressure, velocity and shear stress distributions for elliptical compared to circular anastomosis at the pulmonary artery bifurcation, and preferential flow in left pulmonary artery, suggesting that the elliptical anastomosis with larger cross-sectional area than the circular may reduce incidence and degree of distal stenosis, particularly for small size conduits\textsuperscript{38}.

Risk factors

Risk factors for

- reoperation were age less than 1 year, correction of truncus arteriosus, conduit size of 12 mm, and persistently elevated right-ventricular-to-left ventricular pressure ratio greater than 0.6\textsuperscript{20};
- percutaneous right ventricular outflow tract reintervention were small conduit size 12 and 14 mm, and truncus arteriosus correction, and right ventricle to left ventricle pressure ratio in the immediate post-operative period\textsuperscript{20};
Conduit stenosis were younger age, graft size and indication, which did not change over time; pulmonary artery obstruction were younger age (< 1 year) at operation and small graft size (< 14 mm); valve regurgitation was always secondary to dilation in the presence of severe distal stenosis.

However, Tiete et al. did not observe any significant correlation between younger age (≤ 6 months) or small graft size (≤ 14 mm) and a gradient at the distal anastomosis after implantation and at last follow-up, which was supported by Schoenhoff et al. The multivariable analysis confirmed that graft size ≤ 20 mm, the non-anatomical position of the graft, and the use of the Contegra conduit were predictive of conduit explantation. Niemantsverdriet et al. noted Contegra conduits and aortic homografts showed earlier failure than pulmonary homografts, but the time to conduit failure could be extended after transcatheter intervention.

In conclusion, right ventricular outflow tract reconstruction with Contegra can result in better hemodynamics, longevity and long-term survival than other biomaterials in most of the situations of congenital heart defect repair. It can also be used as a monocusp material in congenital heart defect repair.

However, it should be avoided using as an inferior vena cava-pulmonary artery conduit in Fontan operation. The common risk factors younger age at operation, smaller size of the conduits and higher right ventricle to left ventricle pressure ratio that were in charge of the postoperative conduit events including conduit dysfunction and the subsequent conduit explantation and catheter intervention should be taken into consideration in the decision-making of the surgical treatment. In the operation, an elliptical anastomosis is preferred in order to prevent anastomotic stenosis.

### References


