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Original Article / Özgün Makale

Incidence and treatment of pulmonary vein stenosis after repair of total anomalous pulmonary venous connection

Total pulmoner venöz dönüş anomalisi tamiri sonrasında pulmoner ven darlığının insidansı ve tedavisi

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ABSTRACT

Background: In this study, we aimed to investigate the incidence and treatment of pulmonary vein stenosis after repair of total anomalous pulmonary venous connection.

Methods: Between December 2010 and December 2016, a total of 40 patients (25 males, 15 females; mean age 45±41 days; range, 2 days to 6 months) who underwent total anomalous pulmonary venous connection repair were retrospectively analyzed.

Results: Eighteen (45%) of the patients were supracardiac, seven (17.5%) were cardiac, eight (20%) were infracardiac, and seven (17.5%) were mixed-type anomaly. Twelve patients (30%) had obstruction of the pulmonary venous pathways. Hospital mortality was seen in three patients (7.5%). All of non-survivors received emergent surgery and the causes of death were sepsis and multiple organ failure. A total of 23 complications were seen in 20 patients (50%) mainly delayed sternal closure (n=11; 27.5%) and prolonged mechanical ventilation (n=6; 15%). The mean follow-up was 12.2±9.6 (range, 1 to 36) months in all patients, except one. Pulmonary vein stenosis developed in three patients (8.3%) after repair. All of them underwent sutureless repair.

Conclusion: Total anomalous pulmonary venous connection can be repaired with low mortality and morbidity rates and favorable mid-term outcomes. Close follow-up is necessary due to the risk of development of pulmonary vein stenosis. Sutureless repair may provide relief in such cases.

Keywords: Congenital heart surgery, infant, pulmonary vein stenosis, total anomalous pulmonary venous connection.

ÖZ

Amaç: Bu çalışmada total pulmoner venöz dönüş anomalisi tamiri sonrasında pulmoner ven darlığının insidansı ve tedavisi araştırıldı.

Çalışma planı: Aralık 2010 - Aralık 2016 tarihleri arasında total pulmoner venöz dönüş anomalisi tamiri yapılan toplam 40 hasta (25 erkek, 15 kız; ort. yaş 45±41 gün; dağılım 2 gün-6 ay) retrospektif olarak incelendi.

Bulgular: Hastaların 18'inde (%45) suprakardiyak, yedisinde (%17.5) kardiyak, sekizinde (%20) infrakardiyak ve yedisinde (%17.5) miks tip anomali mevcuttu. On iki hastada (%30) pulmoner ven yolaklarında tıkanıklık izlendi. Üç hastada (%7.5) hastane mortalitesi görüldü. Kaybedilen hastaların tümü acil ameliyata alınan hastalardı ve ölüm nedenleri sepsis ve çoklu organ yetmezliği idi. Başta gecikmiş sternum kapatılması (n=11; %27.5) ve uzamış mekanik ventilasyon (n=6; %15) olmak üzere 20 hastada (%50) toplam 23 komplikasyon gözlendi. Ortalama takip süresi, biri hariç hastaların tümünde 12.2±9.6 (dağılım, 1-36) ay idi. Tamir sonrasında üç hastada (%8.3) pulmoner ven darlığı gelişti. Bu hastaların tümüne dikişsiz tamir uygulandı.

Sonuç: Total pulmoner venöz dönüş anomalisi düşük mortalite ve morbidite oranları ve iyi orta dönem sonuçlar ile tamir edilebilir. Pulmoner ven darlığı gelişme riski açısından yakın takip gereklidir. Bu olgularda dikişsiz tamir yöntemi iyileşme sağlayabilmektedir.

Anahtar sözcükler: Konjenital kalp cerrahisi, bebek, pulmoner ven darlığı, total pulmoner venöz dönüş anomalisi.

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Total anomalous pulmonary venous connection (TAPVC), in which pulmonary veins are connected to an abnormal location rather than the left atrium, was first described by Wilson in 1798.[1] The incidence of TAPVC has been reported as 5.9 to 7.1 per 100,000 live births, accounting for about 0.8% of all congenital heart defects. Intervention-free survival is 50% for the first three months and 20% for one year.[2,3] In the literature, the first surgical correction was performed by Müller in 1951.[4]

Supracardiac TAPVC is the most common type, accounting for about 40 to 45% of the total cases, followed by the cardiac type as the second most common type. In contrast, in some series, infracardiac type has been reported as the second most common type, accounting for about 20 to 26%.[2] Mixed type is the least common type in almost all series.[2,5] The relationship between the types of TAPVC and outcome is still controversial. However, the presence of obstruction of the pulmonary venous pathways is universally deemed as a surgical emergency and the results are usually less satisfactory.[2,5]

With the introduction of advances in the field of cardiac surgery, surgical mortality is currently below 5 to 10% with favorable mid- and long-term results. However, pulmonary vein stenosis (PVS) may develop after cardiac repair and can be difficult to manage. The incidence of PVS has been reported as 0 to 18%.[5] It has been suggested that PVS usually develops two to six months after primary repair and the results are usually poor.[6] Sutureless repair for PVS has been previously introduced as a sutureless connection of the pulmonary veins to the left atrio-pericardial sac with dramatically improved results.[7]

In the present study, we aimed to investigate the incidence and treatment of PVS after TAPVC repair.

PATIENTS AND METHODS

Between December 2010 and December 2016, a total of 40 patients (25 males, 15 females; mean age 45±41 days; range, 2 days to 6 months) who underwent TAPVC repair were retrospectively analyzed. In two patients, ventricular septal defects (VSDs) were intervened as additional anomalies. Those with heterotaxy syndromes were excluded from the study. A written informed consent was obtained from each parent. The study protocol was approved by the ATADEK 2018/13 Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

Operations were performed under cardiopulmonary bypass (CPB), aortic-bicaval cannulation, moderate hypothermia (28 to 32°C), and isothermic blood cardioplegia. Pulmonary venous anastomoses were performed using 7/0 polydioxanone stitch materials.

There were a retrocardiac common chamber in all 18 patients with supracardiac type TAPVC. Fourteen of them were connected to the innominate vein via left-sided vertical vein and one of them had obstruction. In the remaining four patients, common chamber was connected to the superior vena cava via right-sided vertical vein and two of them had obstruction. The incidence of obstruction was higher in right-sided connection than usual left-sided connection with the vertical vein. All but one of the patients were repaired using the superior approach (Tucker's technique). One patient underwent the Schumaker procedure.

In seven patients with cardiac type TAPVC, the superior wall of the coronary sinus was resected after coronary sinus cut-back and atrial reseptation was performed using a glutaraldehyde-treated autologous pericardial patch in six patients and Schumaker procedure was needed in one patient. In eight patients with infracardiac TAPVC, the common chamber was anastomosed to the left atrium via posterior approach. A 4-mm patent foramen ovale was left open in all patients.

All pulmonary veins were connected to the left atrium in all patients with mixed type TAPVC by using suitable techniques. All patients received milrinone (0.5 μg/kg/min) and adrenaline (0.05 μg/kg/min) infusion at the end of CPB. Doses were adjusted according to the patient's hemodynamic condition, and dopamine was added, when necessary.

Statistical analysis

Statistical analysis was performed using the web-based GraphPad software version Prism 8 (GraphPad Software Inc., CA, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max), or number and frequency. The Fisher's exact test was used for intragroup comparisons of the categorical data, while the chi-square test was used for the analysis of nominal data. A p value of <0.05 was considered statistically significant.

RESULTS

Before the operation, eight patients (20%) were dependent on mechanical ventilatory support and emergent surgery was performed. Obstructive type

Table 1. TAPVC types and obstruction rates

TAPVC types	n	%	Obstructive (n)	%
Supracardiac	18	45	3	16.6
Cardiac	7	17.5	3	42.8
Infracardiac	8	20	5	62.5
Mixed	7	17.5	1	14.2
Total	40		12	30

TAPVC: Total anomalous pulmonary venous connection

TAPVC was observed in a total of 12 patients (30%) and most of them were infracardiac type. Eighteen (45%) of the patients were supracardiac, seven (17.5%) were cardiac, eight (20%) were infracardiac, and seven (17.5%) were mixed-type anomaly. Types of TAPVC and pulmonary venous pathway obstruction are shown in Table 1. Anatomic details of seven patients with mixed-type TAPVD are shown in Figures 1 and 2.

Hospital mortality was seen in three patients (7.5%). All of non-survivors received emergent surgery and the causes of death were sepsis and multiple organ failure. The rate of early mortality was higher in the patients with obstructive type of TAPVC (3/12; 25% vs. 0/28; 0%, respectively) (p=0.022).

A total of 23 complications were seen in 20 patients (50%) mainly delayed sternal closure (n=11; 27.5%) and prolonged mechanical ventilation (>7 days) (n=6; 15%) (Table 2).

The mean follow-up was 12.2±9.6 (range, 1 to 36) months in all patients, except one. Echocardiographic examinations were performed before hospital discharge, at one month, three months, and six months. No patient developed PVS during discharge. One patient, who was discharged with tracheostomy, died from pneumonia in the eighth postoperative month.

Pulmonary vein stenosis developed in three patients (8.3%) after repair. All of them underwent sutureless repair. The duration for the development of PVS varied from 2.5 to 4 months. One patient had non-obstructive supracardiac type. Other two patients had obstructive

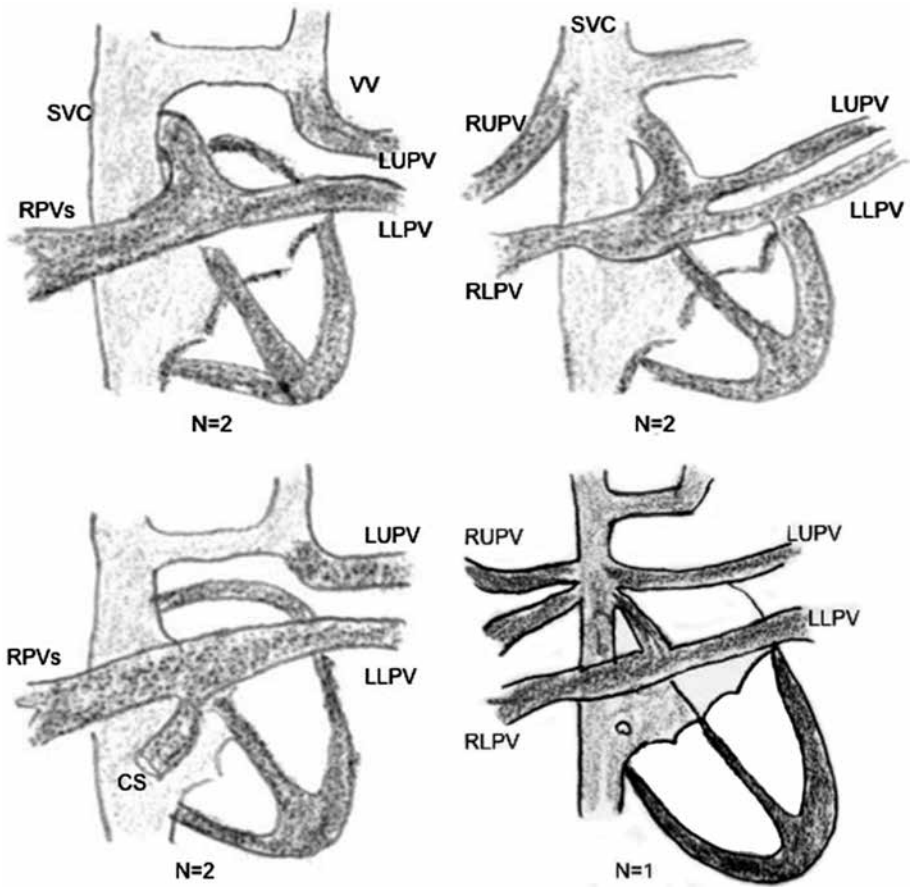

Figure 1. Different configurations of mixed-type of TAPVCs.

SVC: Superior vena cava; VV: Vertical vein; RPVs: Right pulmonary veins; LUPV: Left upper pulmonary vein; LLPV: Left lower pulmonary vein; RUPV: Right upper pulmonary vein; RLPV: Right lower pulmonary vein; CS: Coronary sinus.

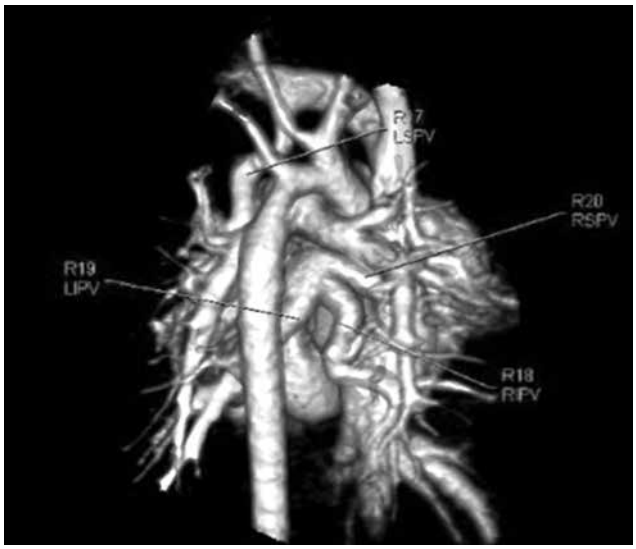

Figure 2. A computed tomography angiography image of mixed-type total anomalous pulmonary venous connection, in which right and left lower pulmonary veins drain to coronary sinus; left upper pulmonary vein connecting to innominate vein via left vertical vein (posterior view).

LSPV: Left superior pulmonary vein; LIPV: Left inferior pulmonary vein; RSPV: Right superior pulmonary vein; RIPV: Right inferior pulmonary vein.

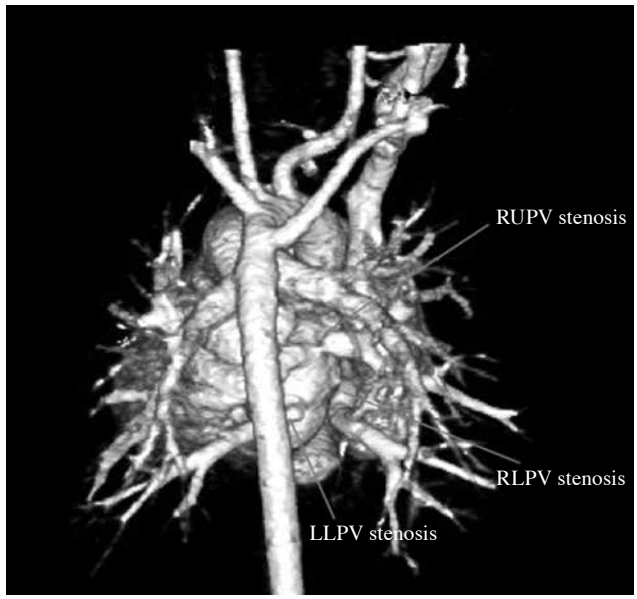

Figure 3. Pulmonary vein stenosis at postoperative three months. A computed tomography angiography image (posterior view).

RUPV: Right upper pulmonary vein; RLPV: Right lower pulmonary vein; LLPV: Left lower pulmonary vein.

type of cardiac and infracardiac TAPVC. Although not statistically significant, the incidence of development of PVS during follow-up was higher in the obstructive types of TAPVCs than the non-obstructive types (22.2% vs. 3.5%, respectively) (p=0.14).

The diagnosis of PVS was made by echocardiographic examination. Newly developed severe pulmonary hypertension, pulmonary venous flow acceleration, and increased gradient were detected. All three patients had tachypnea and feeding difficulty. All of them were hospitalized, when PVS was detected. Inotropic support and diuretics were initiated. One patient (repaired supracardiac type) was intubated and underwent cardiac catheterization. During catheterization, cardiac arrest occurred, and the patient were resuscitated successfully. A detailed anatomical study was performed with computed tomography (CT) angiography in all patients (Figure 3). In two patients (repaired supracardiac and cardiac type), all pulmonary veins were affected. Severe stenosis was detected at the entry point of pulmonary veins to the left atrium. The last patient

Table 2. Postoperative complications

	n	%
Delayed sternal closure	11	27.5
Long intubation	6	15
Tracheostomy	3	7.5
Neurological problem	2	5
Bleeding revision	1	2.5

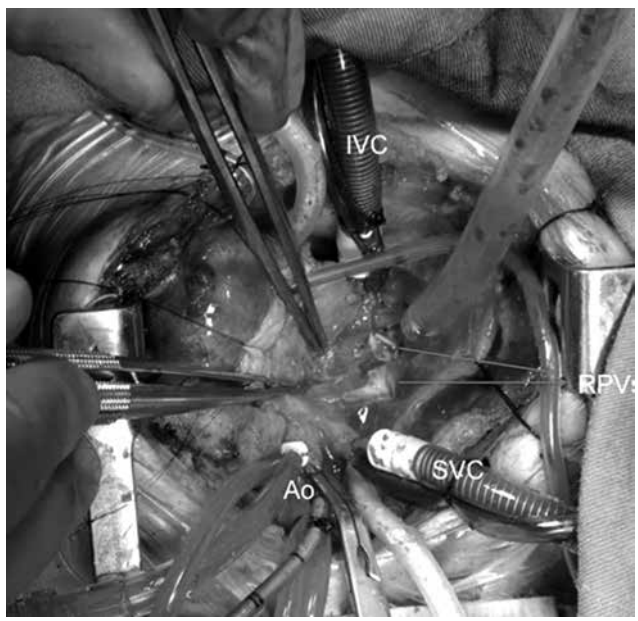

Figure 4. Stenosis at right pulmonary veins relieved with incision until reaching healthy pulmonary vein orifices (An intraoperative image).

IVC: Inferior vena cava; SVC: Superior vena cava; Ao: Aorta; RPVs: Right pulmonary veins.

(infracardiac type) had only right pulmonary vein stenosis.

Sutureless repair

All patients underwent open heart surgery with resternotomy. After aortic and bicaval cannulation CPB was commenced. Hypothermia 24°C was obtained. No extensive dissection was performed around the left pulmonary veins. Right atrium was opened after cardioplegic arrest. The atrial septum was incised vertically. The pulmonary vein orifices were explored under low-flow perfusion. In two patients with left PVS, ostial endovenectomy was performed. Pulmonary vein orifices were pulled back into the left atrium with a fine mosquito clamp and resected by the Potts scissors. All fibrous tissues were removed and the left pulmonary veins were left in the posterior mediastinum draining directly into the left atrium as a controlled bleeding. For the right pulmonary veins, the pulmonary vein confluence was incised transversely across its entire length. The incision was carried into each pulmonary vein until reaching healthy pulmonary vein orifices (Figure 4). Fibrous tissues were resected at the junction of the left atrium. Neoatrialization was performed with an autologous fresh or pedicled (n=1) pericardial patch, which was sutured away from the pulmonary veins (Figure 5). This creates a neo-left atrium by suturing the incised left atrial edge to the pericardium adjacent to the incised pulmonary veins. The atrial septum was, then, closed with a new pericardial patch leaving a 4-mm fenestration. After cessation of CPB, right ventricular-to-left ventricular ratio was measured which was below 0.6 at the end of the procedures in all patients.

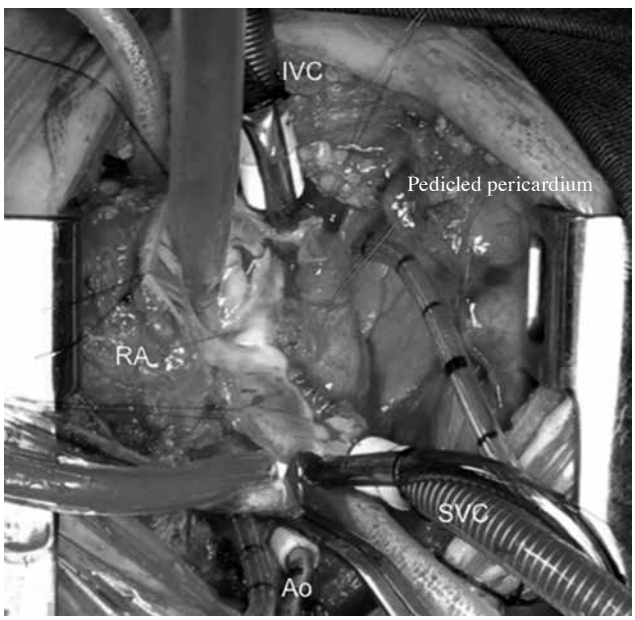

Figure 5. An intraoperative image of sutureless repair. Neoseptation with pedicled pericardium.
IVC: Inferior vena cava; SVC: Superior vena cava; Ao: Aorta; RA: Right atrium.

Two patients were discharged without any major problems. One had transient neurological complication. Other patient (supracardiac type with bilateral stenosis) developed recurrent, diffuse PVS one month after the repair. Due to the diffuse nature of the disease, no further intervention was able to be performed and the patient unfortunately died. Other patients were in a good clinical condition at one year after the repair. Echocardiographic examination revealed mild left PVS in one patient without pulmonary hypertension.

DISCUSSION

Total anomalous pulmonary venous connection is a rare congenital heart disease with a great morphological diversity. Although echocardiography is usually enough for the diagnosis, CT angiography is very helpful to demonstrate the detailed anatomy in cases with any suspicion. Angiography is rarely needed.[2,5] In our study, most of the patients underwent repair according to the echocardiographic findings. Of note, it should be kept in mind that the findings should be confirmed by operative inspection. Nevertheless, all patients with mixed-type of TAPVC needed CT angiography to delineate the detailed anatomy and plan the repair.

Early outcomes with conventional repair techniques are usually excellent after TAPVC repair. The majority of patients who survive after TAPVC surgery are followed in the New York Heart Association (NYHA) Class I. However, the focus of efforts has been oriented on the development of PVS and related mortality (5 to 18%) and morbidity in the mid- and long-term.[2,5,6]

Sutureless repair for PVS treatment after TAPVC repair is a featured operation defined by Najm et al.[6] and Lacour-Gayet et al.,[7] and the outcomes of PVS repair have been dramatically improved since then. Based on the studies showing that PVS is associated with late morbidity and mortality, surgeons have attempted to use sutureless repair for primary correction of TAPVC.[8,9]

Potential advantages of sutureless technique include the prevention of mobilization and stretching of the common chamber, the avoidance of often small pulmonary venules in the suture line, limited

reactive intimal hyperplasia, and prevention of anastomotic fibrous scarring. Therefore, when properly implemented, sutureless repair results in adequate venous opening and optimal flow.[6-9]

In their study, Shi et al.[10] reported a 15% PVS incidence in 768 patients who underwent either conventional or sutureless techniques at a median follow-up of 23.3 months. They found that sutureless technique was associated with a lower restenosis rate compared to conventional repair, particularly in patients with preoperative pulmonary venous obstruction which is a risk factor for the PVS development. Preoperative pulmonary venous obstruction appears to be an important risk factor for postoperative PVS development and mortality. Some authors have advocated that PVS is a progressive disease and that none of the existing perioperative or operative strategies affect the PVS incidence and its postoperative presence indicates an underlying propensity.[10-12] Our study also confirmed that the incidence of development of PVS was higher in the obstructive type TAPVCs during follow-up. Contrary to the literature, despite a high incidence of mixed-type of TAPVC in our series, we found no PVS in the patients with mixed-type TAPVC.

Lo Rito et al.[13] developed a predictive model for post-repair survival based on preoperative pulmonary vein characteristics as evidenced by CT and magnetic resonance imaging in patients who underwent PVS repair. They measured the pulmonary vein short and long cross-sectional diameters at the left atrial junction (downstream), vein bifurcation (upstream), and the narrowest point and calculated the total cross-sectional area indexed for the body surface area (PVCSAi). The authors defined three morphological subtypes of PVS. Upstream stenosis (upstream/downstream PVCSAI >1.5), downstream stenosis (upstear/downstream PVCSAI <0.5), and diffuse stenosis. In 31 patients, they found that the narrowest part of the PVS was located at the downstream (163 mm^2/m^2) in two-third of the patients. The in-hospital mortality was 9.7% in this series. They concluded that early survival was poor for patients with a higher number of stenotic veins and upstream pulmonary vein involvement. In our study, all three patients with PVS had downstream stenosis.

In the study of the Toronto group, 33 of 73 pre- and postoperative PVS were treated with sutureless repair and 40 patients with classical repair, and although there was no significant difference in the 10-year survival and follow-up rates, routine use of sutureless technique was suggested owing to its favorable results.[14] Azakie et al.[8] also reported that 18 patients with TAPVC underwent primary sutureless repair, seven with congenital PVS, and no recurrence or persistent PVS was observed in their group.

Despite favorable early and mid-term results reported for primary sutureless repair, the long-term results of this technique are still uncertain. In patients undergoing primary sutureless repair, the atrial function of non-contractile pericardial tissue between the PV vein wall and left atrium is still unknown. Other disadvantages of primary sutureless repair include phrenic nerve injury due to the suture line of atrio-pericardial anastomosis, thrombogenicity of the pericardial surface, high-pressure air embolism, or negative effects of chest compression to fragile neoatrium, as well as potential bleeding in the posterior mediastinum or pleural space from the gap between the confluence and pericardium with contusion.[11-15] Therefore, it may be appropriate to choose primary sutureless repair for high-risk infants with TAPVC associated with a single ventricular physiology, mixed-type TAPVD, obstructive type TAPVC, or in the presence of hypoplastic PVS.

Although primary sutureless repair appears to be safe and effective with a wide applicability to any type of simple TAPVC, Yanagawa et al.[12] reported that their current indications of primary sutureless repair for simple TAPVC were all infracardiac TAPVC, intracardiac TAPVC with evidence of PVS, and surgeon preference for supracardiac TAPVC. Although we lack any experience with primary sutureless TAPVC repair, we believe that this technique may be suitable for patients who are at high risk for the development of PVS, such as obstructive type of TAPVCs.

The retrospective nature and small sample size are the main limitations of this study.

In conclusion, conventional repair techniques provide favorable early and mid-term results for total anomalous pulmonary venous connection repair. Close follow-up is necessary for the development of pulmonary vein stenosis. Sutureless repair is a useful and safe technique in such cases. Primary sutureless repair may be an option for selective high-risk patients for the development of pulmonary vein stenosis, such as preoperative obstructive type of anomaly.

Declaration of conflicting interests

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