

Review Article

Application and clinical value of percutaneous VSD closure guided by echocardiography alone

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Abstract: The application and clinical value of transcatheter ventricular septal defect (VSD) closure guided by echocardiography alone were explored. A total of 48 children undergoing percutaneous VSD closure guided by ultrasound were collected as a study group, and 52 children undergoing percutaneous VSD closure guided by conventional radiation were enrolled as a control group (con group). The operation time, occluder diameter, equipment cost, and total cost of the study group were lower than those of the con group, and the NT proBNP level in the two groups reached the peak 24 h after treatment and began to decrease 48 h later, and the water level of NT proBNP in the study group was lower than that in the con group. Additionally, there was no significant difference in serum CK-MB between the two groups before and after treatment, and the serum cTnI level in the study group was lower than that in the con group. The IL-10 level in the two groups increased after treatment, and the level in the study group was significantly higher than that in the con group. Moreover, both groups showed improved heart function indexes, and there was no significant difference in cardiac function and the total incidence of postoperative complications between the two groups. VSD diameter, occluder diameter, superior margin to aortic valve, and operation time were independent risk factors for complications of VSD patients. Percutaneous VSD closure guided by echocardiography alone can significantly improve the cardiac function and alleviate myocardial injury, which has good clinical value. The size of VSD, diameter of occluder, distance between the upper edge and aortic valve, and operation time are all factors that affect the postoperative complications.

Keywords: Echocardiography, radiation, transcatheter closure of VSD, clinical value, risk factors

Introduction

Ventricular septal defect (VSD), which occurs in all ages, is a prevalent congenital heart disease, accounting for appropriate 40% of congenital heart disease [1]. VSD is mainly formed due to the abnormal development of ventricular septum during the embryonic period, resulting in the abnormal traffic between the ventricles, which mainly occurs in the membranous septum and muscular septum or its boundary [3]. At present, there are many studies on different treatments for VSD closure. Conventional open heart surgery is the traditional treatment for patients with VSD, which can solve many kinds of deformities. However, because the open chest surgery is to repair VSD directly under the assistance of cardiopulmonary bypass, the trauma is relatively large,

which may bring about serious mental and physical injury [4]. Since the first application of transcatheter VSD closure in 1988, with the continuous development of medical closure devices and deployment technologies, transcatheter VSD closure has been widely applied in many institutions around the world [5-7]. Percutaneous VSD closure does not require thoracotomy and cardiopulmonary bypass, but it may cause radiation damage to patients and doctors due to the use of radiation, and the use of contrast agents may cause renal failure and allergy [8]. However, ultrasound-guided percutaneous VSD closure overcomes these shortcomings, which has the characteristics of no incision, avoiding the use of radiation, minimally invasive, and no need of cardiopulmonary bypass [9, 10]. NT proBNP is one of the biomarkers of cardiovascular disease [11], and it

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can be used as an assistant marker for comprehensive diagnosis, screening, management and follow-up of heart failure caused by various congenital and acquired heart diseases [12]. Studies have shown that mechanical stimulation of ventricular wall and pressure changes can affect the synthesis and release of NT ProBNP in cardiomyocytes [13]. Creatine kinase isoenzyme (CK-MB) is a common clinical myocardial enzyme spectrum, which mainly exists in the cytoplasm of myocardial cells. When myocardial cells are damaged, the activity of CK-MB increases significantly. With high sensitivity and rapid change, CK-MB can be used as a biochemical marker in serum after myocardial injury [14, 15]. CTnI is an inhibitory subunit, which belongs to the troponin complex (TN), and is an inhibitor of ATPase in the transverse bridge of myocardial fiber. It can participate in the down regulation of the relaxation and contraction of myocardial fiber in Ca^{2+} together with other subunits in TN complex. The expression of cTnI is related to the severity of myocardial injury and can be used as a marker of myocardial injury [16, 17]. Interleukin-10 (IL-10) is one of the anti-inflammatory factors, which can inhibit the migration and activation of inflammatory cells, and can inhibit a variety of nuclear transcription factors [18]. Some studies have verified the importance of IL-10 in the pathogenesis of experimental myocarditis [19]. However, the clinical value of percutaneous VSD closure guided by echocardiography alone and its influence on NT proBNP, CK-MB, cTnI and IL-10 need further exploration.

The study aimed to explore the clinical significance of percutaneous VSD closure under the guidance of echocardiography and the influencing factors of complications by comparing the effect and complications of percutaneous VSD closure under the guidance of echocardiography and traditional radiation.

Method

General information

A total of 48 patients undergoing percutaneous VSD closure guided by ultrasound were selected as the study group, including 27 males and 21 females, with an average age of 12.56 ± 5.11 years, average weight of 31.78 ± 10.12 kg, and VSD diameter 4.76 ± 0.81 mm. A total of 52 children undergoing percutaneous closure

guided by conventional radiation were selected as the control group (con group), including 30 males and 22 females, with a mean age of 13.62 ± 5.09 years, a mean weight of 32.06 ± 10.87 kg, and a VSD diameter of 5.03 ± 0.96 mm.

This study was approved by the Medical Ethics Committee of Affiliated Children's Hospital of Xi'an Jiaotong University and met the standard set in the Declaration of Helsinki. All family members signed the informed consents after understanding the study.

Inclusion criteria: Patients with complete clinical data, patients with good compliance, patients whose age of VSD was more than 3 years, and the diameter of VSD was 3-10 mm, and those without pulmonary hypertension or other cardiac malformations.

Exclusion criteria: Patients with infective endocarditis, patients with cardiac malformations that require surgical treatment, patients with other infectious diseases, patients suffering from other bleeding diseases, patients with severe liver or kidney dysfunction, and those intolerable to operation.

Treatment plan

Study Group: All children were examined by echocardiography before operation, and the VSD was measured and its location was determined. The right femoral artery of the patient was punctured in supine position after anesthesia, and then catheter and guide wire were inserted. Under the guidance of echocardiography, the guide wire and catheter were sent to the ascending aorta and then to the left ventricle. Under the guidance of echocardiography, the occluder was gently fed into the right ventricle, and then the right ventricular side umbrella disc of the occluder was released. Under the guidance of ultrasound, the right ventricular opening of VSD was pressed tightly, the transport sheath was removed, and the left ventricular side of the packer was opened. Echocardiography was used to check whether the occluder had residual shunt and was far away from the aortic valve. In case of eccentric occluder, the direction of umbrella wheel should be adjusted under the guidance of ultrasound. If the sealing effect was satisfactory, release the packer under ultrasonic monitoring, take

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out the delivery system, apply hemostasis bandage, and complete the operation.

Control group: Anesthesia puncture was carried out on each child, and left ventricle and ascending aorta were imaged before catheter was inserted. The morphology and size of VSD were evaluated, and then the left and right cardiac catheters were examined. Subsequently, a guide-wire track was constructed, and the occlusion process was monitored by ultrasound and fluoroscopy, during which the occluder was released through femoral vein after the shape and position of the occluder were determined to be good. After operation, the ascending aorta and left ventricle were repeatedly imaged, and reexamined through ultrasound. Both groups of children were followed up and reviewed regularly.

Serum determination

Fasting venous blood (3 ml) was sampled from each child before treatment, 6 h, 24 h, and 48 h after treatment. The blood was centrifuged at 4000 R/min for 10 min. Then the serum in the test tube was carefully sucked to obtain the serum, and the serum was stored in a refrigerator at -80°C for later analysis. The contents of NT-proBNP, CK-MB, cTnl, and IL-10 were detected through a double anti sandwich enzyme-linked immunosorbent assay (ELISA) using a mk-3 automatic enzyme-linked analyzer purchased from Shanghai Yilian medical instrument development Co., Ltd., and NT-proBNP, CK-MB, cTnl and IL-10 kits provided by Shanghai Kanglang Biotechnology Co., Ltd., with product numbers of ls-f29630, kl-e111114, kl00503 and dl-il10-hu, respectively. Standard at different concentrations (50 µl) was added into the standard hole; 10 µl sample and 40 µl diluents were added into the sample hole to be tested respectively; 50 µl distilled water was added into the blank hole (the same as other steps, but without enzyme standard reagent and sample), and 50 µl enzyme standard reagent was added into the standard hole and sample hole. The reaction hole was sealed with sealing membrane, and washed after incubation in 37°C water bath for 1 h. Substrate A and B (50 µl each) were added into each hole, and the liquid in each hole was mixed gently, and developed at 37°C for 15 min without light. Termination solution (50 µl) was added into each hole, and within 15 min, the blank hole was taken as the ref-

erence value for zero adjustment, and the OD of each hole at the 450 nm wavelength was measured. The content of NT-proBNP, CK-MB, cTnl, and IL-10 were calculated.

Outcome measures

The success rate, hospitalization time, operation time, occluder diameter, equipment cost, and total cost of the two groups were evaluated. The levels of NT proBNP, CK-MB, cTnl, and IL-10 were compared before and after treatment. The left ventricular end diastolic diameter (LVEDd), left ventricular end systolic volume (LVESV), left ventricular end diastolic volume (LVEDV), and left ventricular ejection fraction (LVEF) were analyzed. In addition, the complications of the two groups were compared and the influencing factors were explored.

Statistical analysis

Spss20.0 (IBM Corp, Armonk, NY, USA) was employed for statistical analysis, and Graphpad Prism 7 (Graphpad Software Co., Ltd., San Diego, USA) was used to draw figures of the collected data. The count data was expressed as [n (%)], and compared between groups using the Chi square test. The measurement data were expressed as the mean ± standard deviation ($\bar{x} \pm SD$), and compared between groups using the T test. Single factor analysis of variance was adopted for multi-group comparison, and LSD-t test for post test. Multivariate logistic regression was adopted for analysis on risk factors of patients with heart failure and renal insufficiency. $P < 0.05$ indicates a significant difference.

Result

Comparison of general clinical data

The general clinical data of the two groups were analyzed (**Table 1**). There was no significant difference between the two groups with regard to sex, average age, average weight, VSD diameter, right ventricular end diastolic diameter, left ventricular end diastolic diameter, left ventricular ejection fraction, blood creatinine and leukocyte (all $P > 0.05$).

Comparison of operation conditions between the two groups

The operation conditions of the two groups were compared (**Table 2**). In the study group, 2

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Table 1. Comparison of general clinical data between the two groups ($\bar{x} \pm SD$)/n [%]

	Study group (n = 48)	Con group (n = 52)	χ^2/t	P
Sex			0.02	0.88
Male	27 (56.25)	30 (57.69)		
Female	21 (43.75)	22 (42.31)		
Average age (years)	12.56±5.11	13.62±5.09	1.04	0.30
Average weight (kg)	31.78±10.12	32.06±10.87	0.13	0.89
VSD diameter (mm)	4.76±0.81	5.03±0.96	1.51	0.13
Hemoglobin (g/L)	130.91±10.23	131.26±9.98	0.17	0.86
Platelet ($\times 10^9/L$)	170.24±23.18	171.13±21.73	0.20	0.84
Blood creatinine (umol/L)	29.35±15.65	30.97±14.36	0.54	0.59
Leukocytes ($\times 10^9/L$)	8.57±2.43	7.85±2.65	1.41	0.16
Platelet aggregation function (mm)	64.27±5.56	65.09±5.38	0.75	0.46

Table 2. Comparison of basic operation conditions between the two groups ($\bar{x} \pm SD$)/n [%]

	Study group (n = 48)	Con group (n = 52)	χ^2/t	P
Success rate of operation	45 (93.75%)	49 (94.23%)	0.01	0.92
Operation time (min)	41.23±12.32	53.82±12.11	5.15	< 0.05
Length of stay (d)	3.76±0.77	3.69±0.78	0.45	0.65
Intraoperative application of radiation	0	100%	-	-
Occluder diameter (mm)	6.22±2.13	6.98±1.63	0.55	0.04
Equipment cost (10000 yuan)	2.23±0.45	2.87±0.83	4.74	< 0.05
Total cost (10000 yuan)	3.45±0.75	4.61±0.91	6.92	< 0.05

cases were converted to transthoracic VSD, because the catheter failed to pass through VSD along the guide wire. Because the residual shunt was more than 2 mm in one child, it was repaired by surgery. In the con group, 1 patient had unstable occluder, 2 patients could not establish the orbit successfully, and all patients changed to conventional surgical repair. There was no significant difference between the study group and the con group in the success rate of operation and the length of stay ($P > 0.05$). The operation time, occluder diameter, equipment cost and total cost of the study group were statistically lower than those of the con group ($P < 0.05$).

Comparison of serum factor levels between the two groups before and after treatment

There was no significant difference in the levels of NT proBNP, CK-MB, cTnI and IL-10 between the two groups before treatment ($P > 0.05$). After treatment, no significant change was found in serum CK-MB in the two groups ($P > 0.05$), and there was no remarkable difference between the two groups ($P > 0.05$). After

treatment, the NT proBNP level in serum was significantly higher than that before treatment, and the highest level of NT proBNP was seen 24 h after treatment, and it began to decrease 48 h later. The water level of NT proBNP in the study group was lower than that in the con group at each time point after treatment ($P < 0.05$). The level of serum cTnI in the study group was lower than that in the con group ($P < 0.05$). The level of IL-10 in the two groups was greatly higher than that before treatment ($P < 0.05$). The peak was reached at 6 h after treatment, and it was greatly higher in the study group than in the con group ($P < 0.05$). There was no remarkable difference between the two groups at 24 h and 48 h after treatment ($P > 0.05$) (**Figure 1; Table 3**).

Changes of cardiac function in the two groups before and after treatment

The changes of cardiac function indexes before and after treatment were shown in **Table 4**. There was no remarkable difference between the two groups ($P > 0.05$). After treatment, LVEDd, LVEDV, LVESV and LVEF in the two

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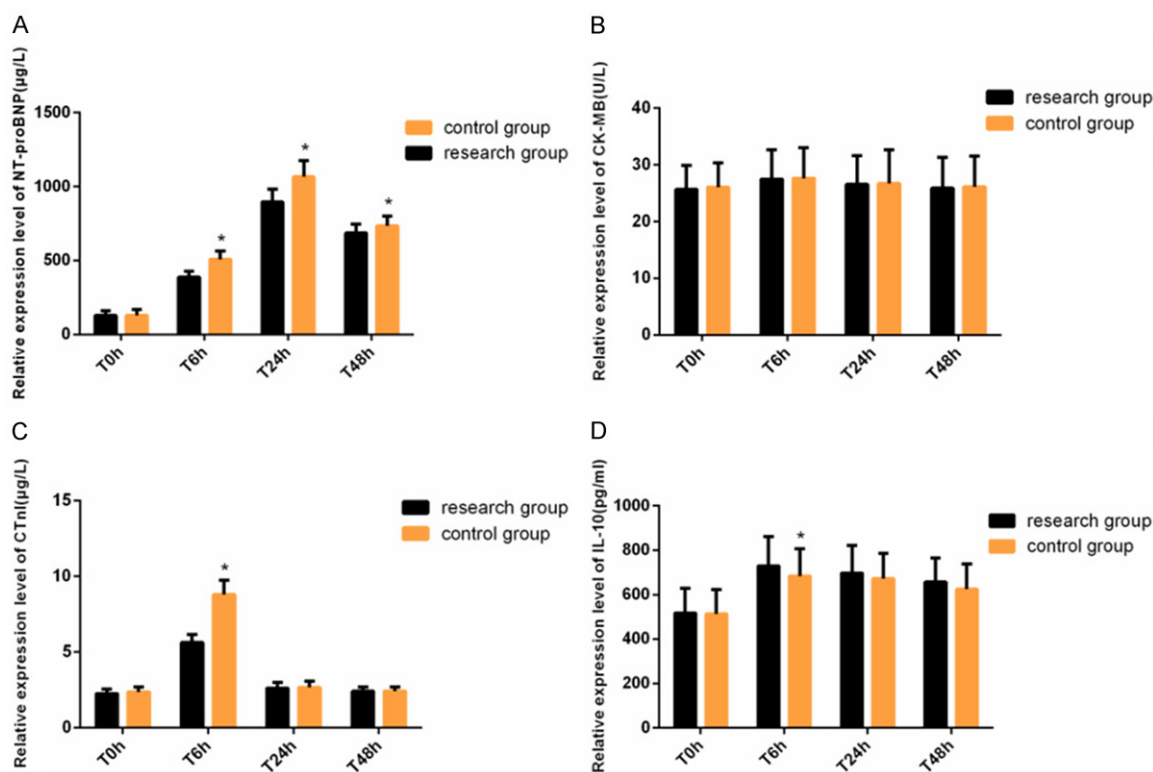


Figure 1. Comparison of serum factor levels before and after treatment. A. The level of NT proBNP in the two groups reached the peak 24 h after treatment, and began to decrease 48 h later, and the water level of NT proBNP in the study group was lower than that in the con group ($P < 0.05$). B. There was no remarkable difference in serum CK-MB between the two groups after treatment and before treatment, and there was no remarkable difference between the two groups in it ($P > 0.05$). C. The serum cTnI level of the two groups was the highest 6 h after treatment, and the serum cTnI level of the study group was lower than that of the con group ($P < 0.05$). D. The serum IL-10 level in the two groups was greatly higher than that before treatment ($P < 0.05$), and reached the peak at 6 h after treatment, and the level in the study group was greatly higher than that in the con group ($P < 0.05$). There was no remarkable difference between the two groups at 24 h and 48 h after treatment ($P > 0.05$). Note: t0 h: before treatment, t6 h: 6 h after treatment, t24 h: 24 h after treatment, t48 h: 48 h after treatment; * indicates that in contrast to the study group, $*P < 0.05$.

groups were improved compared with those before treatment ($P < 0.01$), and there was no remarkable difference between the two groups ($P > 0.05$).

Comparison of postoperative complications between the two groups

Among the 45 children who had successfully transcatheter VSD closure guided by ultrasound, 5 children suffered from early residual shunt, 2 suffered from slight arrhythmia, and 3 suffered from tricuspid regurgitation. The total incidence of complications was 22.22%. Among the 49 children who had successfully transcatheter closure of VSD, 4 children suffered from early residual shunt, 3 suffered from slight arrhythmia and 5 suffered from tri-

cuspid regurgitation, with a total incidence of 24.49%. There was no remarkable difference in the incidence of postoperative complications between the two groups ($P > 0.05$) (Table 5).

Influencing factors of complications

A total of 94 cases of successful percutaneous VSD closure guided by ultrasound and radiation were divided into two groups according to complications. Data of the two groups were analyzed by univariate analysis, as shown in Table 6. There were differences in VSD diameter, occluder diameter, superior margin to aortic valve and operation time between the two groups ($P < 0.05$). Indexes with differences in univariate analysis were included in the assign-

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Table 3. Comparison of serum factor levels before and after treatment ($\bar{x} \pm SD$)

	NT-proBNP ($\mu\text{g/L}$)	CK-MB (U/L)	CTnl ($\mu\text{g/L}$)	IL-10 (pg/ml)
Research Group				
T0 h	127.65 \pm 34.38	25.69 \pm 4.23	2.26 \pm 0.28	518.26 \pm 110.37
T6 h	387.46 \pm 40.87	27.47 \pm 5.21	5.63 \pm 0.54	729.87 \pm 131.87
T24 h	896.38 \pm 87.32	26.59 \pm 5.02	2.62 \pm 0.37	698.21 \pm 124.39
T48 h	687.37 \pm 57.72	25.88 \pm 5.47	2.40 \pm 0.29	658.28 \pm 106.32
F	1581.00	1.25	840.50	29.67
P	< 0.01	0.29	< 0.01	< 0.01
Con group				
T0 h	129.31 \pm 38.79	26.04 \pm 4.32	2.37 \pm 0.33	513.78 \pm 109.29
T6 h	508.47 \pm 55.76*	27.66 \pm 5.34	8.79 \pm 0.96*	684.79 \pm 123.27*
T24 h	1067.38 \pm 109.67*	26.71 \pm 5.96	2.67 \pm 0.41	673.28 \pm 113.24
T48 h	735.21 \pm 64.12*	26.11 \pm 5.42	2.42 \pm 0.27	624.97 \pm 114.21
F	1558.00	1.043	1628.00	23.90
P	< 0.01	0.38	< 0.01	< 0.01

Note: *indicates that in contrast to the study group, *P < 0.05.

Table 4. Changes of cardiac function indexes before and after treatment in two groups ($\bar{x} \pm SD$)

	LVEDD (mm)	LVEDV (ml)	LVESV (ml)	LVEF (%)
Research Group				
Before treatment	57.98 \pm 7.71	114.01 \pm 8.12	97.77 \pm 6.42	37.12 \pm 7.01
After treatment	48.72 \pm 6.11	91.32 \pm 6.14	80.23 \pm 5.34	47.12 \pm 6.04
t	6.23	15.12	13.77	7.25
P	< 0.01	< 0.01	< 0.01	< 0.01
Con group				
Before treatment	58.23 \pm 7.53	113.79 \pm 8.02	96.49 \pm 7.09	46.79 \pm 6.31
After treatment	52.02 \pm 6.72	91.89 \pm 5.99	82.01 \pm 5.13	37.81 \pm 6.93
t	5.14	15.45	12.04	6.43
P	< 0.01	< 0.01	< 0.01	< 0.01

ment (see **Table 7**), and the results of risk factor Logistic regression analysis are shown in **Table 8**. It can be seen that VSD diameter (HR: 0.109, 95% CI: 0.026-0.448), occluder diameter (HR: 5.231, 95% CI: 1.310-20.888), superior margin to aortic valve (HR: 6.538, 95% CI: 1.633-26.188), operation time (HR: 0.912, 95% CI: 0.865-0.963) were independent risk factors for complications of VSD patients.

Discussion

With the development of science and technology, treatment, anesthesia and postoperative nursing, the prognosis of VSD after surgical closure has improved significantly over time. However, residual shunt, conduction system

disorder, nerve injury, and postoperative mortality are still the main postoperative complications, especially in children with malnutrition [20, 21]. At present, percutaneous VSD closure has become a crucial treatment of VSD [22]. However, due to the use of contrast media and radiation, the traditional interventional therapy will increase the risk and damage of treatment [8]. In recent years, the application of echocar-

diography in interventional therapy instead of radiation has become one of the key measures to improve percutaneous therapy [23]. At present, the risk and severity of postoperative complications of VSD are considered as the key indicators to evaluate the value of surgical treatment [24]. Therefore, it is of great significance to study the influencing factors of postoperative complications of VSD.

NT ProBNP is primarily released by ventricular myocytes. In children with heart disease, the decrease of LVEF and increase of left ventricular end systolic pressure will enhance the mechanical stimulation of blood volume on the heart wall, thus promoting the synthesis and release of NT ProBNP [25, 26]. The results

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Table 5. Comparison of postoperative complications between the two groups n [%]

		Early residual shunt	Arrhythmia	Tricuspid regurgitation	Complete atrioventricular block	Total incidence rate
Research Group	45	5 (11.11)	2 (4.44)	3 (6.67)	0 (0.00)	22.22%
con group	49	4 (8.16)	3 (6.12)	5 (10.20)	0 (0.00)	24.48%
X ²						0.11
P						0.74

Table 6. Single factor analysis [n (%)]/($\bar{x} \pm SD$)

	Occurrence group (n = 22)	Non-occurrence group (n = 72)	t/X ²	P
Gender			0.10	0.75
Male	12 (54.55)	42 (58.33)		
Female	10 (45.45)	30 (41.67)		
Age (years)			0.45	0.50
< 12	14 (63.64)	40 (55.56)		
≥ 12	8 (36.36)	32 (44.44)		
weight (kg)			0.00	0.96
< 30	9 (40.91)	29 (40.28)		
≥ 30	13 (59.09)	43 (59.72)		
VSD diameter (mm)			9.14	0.00
< 5	6 (27.27)	46 (63.89)		
≥ 5	16 (72.73)	26 (36.11)		
Occluder diameter (mm)			6.13	0.01
< 7	17 (77.27)	34 (47.22)		
≥ 7	5 (22.73)	38 (52.78)		
Superior margin aortic valve (mm)			4.26	0.04
< 3	15 (68.18)	31 (43.06)		
≥ 3	7 (31.82)	41 (56.94)		
Type of occluder			0.15	0.70
Symmetric type	14 (63.64)	49 (68.06)		
Asymmetric type	8 (36.36)	23 (31.94)		
Operation time (min)	55.72±12.56	40.13±12.11	5.24	< 0.05
NT-proBNP (μg/L)	128.15±34.09	128.67±36.31	0.06	0.95
CK-MB (U/L)	25.01±7.56	25.94±8.23	0.47	0.64
CTnl (μg/L)	2.33±0.31	2.29±0.52	0.34	0.73
IL-10 (pg/ml)	515.16±103.11	514.67±97.18	0.02	0.98

Table 7. Assignment table

Factor	Assignment
VSD diameter	< 5 mm: 1, ≥ 5 mm: 2
Occluder diameter	< 7 mm: 1, ≥ 7 mm: 2
Superior margin aortic valve	< 3 mm: 1, ≥ 3 mm: 2
Operation time	Data belongs to continuous variable analysis with original data

revealed that the NT proBNP level in serum reached the peak at 24 h after treatment and began to decrease at 48 h, and the water level

of NT proBNP in the study group was lower than that in the con group (P < 0.05). It has been reported that NT ProBNP will be up-regulated in

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Table 8. Multi factor analysis

	β	SD	X^2	P	HR (95% CI)
VSD diameter	-2.220	0.723	9.433	0.002	0.109 (0.026-0.448)
Occluder diameter	1.655	0.706	5.486	0.019	5.231 (1.310-20.888)
Superior margin aortic valve	1.878	0.708	7.034	0.008	6.538 (1.633-26.188)
Operation time	-0.092	0.027	11.176	0.001	0.912 (0.865-0.963)

the early stage after interventional treatment of ASD, and it will return to normal value during further follow-up [26], which suggests that NT ProBNP can reflect myocardial injury and NT ProBNP can reflect myocardial injury. CK-MB mainly exists in myocardium, which is of great significance in the diagnosis of myocardial injury. It can catalyze ATP and creatine to produce creatine phosphate as the energy reserve of cardiomyocytes. When myocardial ischemia injury occurs, CK-MB can catalyze the reverse reaction of adenosine triphosphate and creatine, leading to the first reduction of creatine phosphate level. Additionally, the enzyme is released into the blood due to the damage of myocardial cells [27-29]. There was no significant difference in CK-MB level among the three volatile anesthetics used in children with VSD closure [30]. The results of this study showed that there was no significant difference in serum CK-MB between the two groups after treatment and before treatment, and there was no significant difference between the two groups ($P > 0.05$). Cardiac troponin (CTN), a muscle contraction regulating protein, exists in the form of complex in vivo. When cTnI maintains the stability of tropomyosin by binding to actin and blocks the entry of its myosin binding site, the cardiac diastolic function is relaxed. There are 6%~8% free cTnT in the cytoplasm of cardiomyocytes. When myocardial injury occurs, cTnT is released into the blood and the level of Serum cTnT increases [31, 32]. Saraiya [33] found that serum cTnI was significantly increased in neonates after cardiac surgery, and showed a peak value 6-24 h after surgery. The results showed that the serum cTnI level of the two groups was the highest at 6 h after treatment, and the serum cTnI level of the study group was lower than that of the con group ($P < 0.05$), which suggested that cTnI level was more effective than CK-MB in reflecting myocardial damage, and VSD closure under the guidance of ECG played a better role in protecting myocardial damage. IL-10 is a strong anti-inflammatory cytokine, which is

mainly produced by Th2 lymphocytes, monocytes/macrophages and regulatory T cells. It can inhibit the production of pro-inflammatory factors by Th1 lymphocytes, thus improving the proliferation, survival and antibody production of B lymphocytes. It can also regulate the effect by inhibiting the activation of T cells and reducing the expression of antigens [34]. Fang [35] found that the level of IL-10 in valved bovine jugular catheter was significantly higher than that in valved bovine jugular catheter. It has been reported in the literature that the level of serum IL-10 in patients with congenital heart disease after transcatheter closure and implantation of domestic occluder is significantly increased [36]. This study showed that the level of IL-10 in the two groups significantly increased after treatment ($P < 0.05$), with the peak at 6 h after treatment, and the level of IL-10 in the study group was significantly higher than that in the con group at 6 h after treatment ($P < 0.05$), but there was no significant difference between the two groups 24 h and 48 h after treatment ($P > 0.05$), which suggested that the two treatments can improve the level of IL-10, so as to relieve the tissue damage caused by inflammation and reduce the risk of bleeding.

It has been confirmed that the transcatheter atrial septal defect guided by ultrasound and electrocardiography can be used as an alternative to fluoroscopy guided surgery, which has high application value [37]. In this study, by observing the operation of the two groups, it was found that there was no significant difference between the study group and the con group in the success rate of operation, length of stay and other basic conditions ($P > 0.05$). The operation time, occluder diameter, equipment cost, and total cost of the study group were lower than those of the con group ($P < 0.05$), which implied that percutaneous VSD closure guided by echocardiography can effectively reduce the operation time and cost, and has a high clinical value. This is similar to the

research results of Liu [23], and it is suggested that the operation of the ultrasound guided group is relatively simple. It does not need intraoperative high-pressure angiography, femoral vein puncture and special equipment. The results showed a remarkable difference between VSD patients and healthy people ($P < 0.05$) [38]. Some studies have found that the cardiac function of children changes after VSD closure via catheter using speckle tracking echocardiographer [39]. Yuan [40] revealed that transcatheter closure of ASD could significantly improve the cardiac function indexes such as LVEDd, LVEDV, LVESV, and LVEF. This study revealed that there was no significant difference in cardiac function between the two groups before treatment. After treatment, LVEDd, LVEDV, LVESV, and LVEF in the two groups were improved compared with those before treatment, and there was no significant difference in LVEDd, LVEDV, LVESV and LVEF between the study group and the con group after treatment ($P > 0.05$). It is suggested that echocardiography and percutaneous VSD closure under the guidance of radiation can improve the heart function of children and restore the left ventricular function with little difference. Residual shunt is the main complication of VSD transcatheter closure, with an incidence of 25.5%. Other complications include cardiac arrest, aortic valve and tricuspid regurgitation [23]. Complete atrioventricular block is the most serious complication, with the incidence of 0-5.7% [41, 42]. It has been found in the study of transcatheter closure of atrial septal defect under the guidance of transthoracic echocardiography in foreign countries that this method has high safety and few complications [43]. The results showed that the incidence of residual shunt and tricuspid regurgitation was higher, and the incidence of complete atrioventricular block was 0%. There was no significant difference between the complications of ultrasound-guided percutaneous VSD closure and that of radiation-guided percutaneous VSD closure ($P > 0.05$). The risk factors of arrhythmia after transcatheter closure of congenital perimembranous ventricular septal defect were studied, and it was found that eccentric, large occluder and long fluoroscopy time were the risk factors of postoperative complications. One study by Zhang et al. [44] on analysis of risk factors for arrhythmia after VSD occlusion

in children showed that the size of occluder, male, body weight, asymmetric occluder placement, and foreign occluders were all related to the occurrence of postoperative complication of arrhythmia. The results of logistic regression analysis revealed that the diameter of VSD, the diameter of occluder, the distance between the upper margin and aortic valve, and the operation time were all independent risk factors for the complications of VSD patients.

This paper has mainly discussed the application and clinical value of percutaneous VSD closure guided by echocardiography, but there are still some limitations. Because of the small sample size, a large number of multicenter studies are needed. Moreover, in this study, there are few observation indexes, which may be missed in the analysis of related factors that cause complications, and further research is needed. In the future research, we should follow up the long-term curative effect and complications of the children, so as to reduce the complications to a greater extent and improve the therapeutic effect.

Conclusion

Percutaneous VSD closure guided by echocardiography alone can significantly improve the cardiac function and reduce myocardial injury, which has a good clinical value. The size of VSD, the diameter of occluder, the distance between the upper margin and aortic valve, and the operation time are all the factors influencing the postoperative complications.

Disclosure of conflict of interest

None.

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References

- [1] Zhao LJ, Han B, Zhang JJ, Yi YC, Jiang DD and Lyu JL. Postprocedural outcomes and risk factors for arrhythmias following transcatheter closure of congenital perimembranous ventricular septal defect: a single-center retro-

The application value of VSD closure under ultrasonic guidance

- spective study. *Chin Med J (Engl)* 2017; 130: 516-521.
- [2] Zhang J, Ko JM, Guileyardo JM and Roberts WC. A review of spontaneous closure of ventricular septal defect. *Proc (Bayl Univ Med Cent)* 2015; 28: 516-520.
- [3] Liu SP, Li L, Yao KC, Wang N and Wang JC. Investigation of membranous ventricular septal defect complicated with tricuspid regurgitation in ventricular septal defect occlusion. *Exp Ther Med* 2013; 5: 865-869.
- [4] Zhou Y, Liu LX, Zhao F, Tang SH, Peng HL and Jiang YH. Effects of transthoracic device closure on ventricular septal defects and reasons for conversion to open-heart surgery: a meta-analysis. *Sci Rep* 2017; 7: 12219.
- [5] Nguyen HL, Phan QT, Doan DD, Dinh LH, Tran HB, Sharmin S, Thottian JJ, Won H, Lee WS, Shin SY, Nguyen TQ and Kim SW. Percutaneous closure of perimembranous ventricular septal defect using patent ductus arteriosus occluders. *PLoS One* 2018; 13: e0206535.
- [6] Chen ZY, Lin BR, Chen WH, Chen Q, Guo XF, Chen LL and Ge JB. Percutaneous device occlusion and minimally invasive surgical repair for perimembranous ventricular septal defect. *Ann Thorac Surg* 2014; 97: 1400-1406.
- [7] Yang J, Yang L, Wan Y, Zuo J, Zhang J, Chen W, Li J, Sun L, Yu S, Liu J, Chen T, Duan W, Xiong L and Yi D. Transcatheter device closure of perimembranous ventricular septal defects: mid-term outcomes. *Eur Heart J* 2010; 31: 2238-2245.
- [8] Bu H, Gao L, Zhang W, Wu Q, Jin W, Tang M and Zhao T. Application of perimembranous ventricular septal defects closure solely by femoral vein approach under transesophageal echocardiography guidance. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2017; 42: 802-807.
- [9] Zhu D, Gan C, Li X, An Q, Luo S, Tang H, Feng Y and Lin K. Periventricular device closure of perimembranous ventricular septal defect in pediatric patients: technical and morphological considerations. *Thorac Cardiovasc Surg* 2013; 61: 300-306.
- [10] Vasilyev NV, Melnychenko I, Kitahori K, Freudenthal FP, Phillips A, Kozlik-Feldmann R, Salgo IS, del Nido PJ and Bacha EA. Beating-heart patch closure of muscular ventricular septal defects under real-time three-dimensional echocardiographic guidance: a preclinical study. *J Thorac Cardiovasc Surg* 2008; 135: 603-609.
- [11] Stanciu AE, Stanciu MM and Vatasescu RG. NT-proBNP and CA 125 levels are associated with increased pro-inflammatory cytokines in coronary sinus serum of patients with chronic heart failure. *Cytokine* 2018; 111: 13-19.
- [12] Feliciano M, Uscategui RR, Maciel GS, de Almeida VT, Silveira MF, de Oliveira G and Vicente W. Serum levels of cardiac markers NT-pro-ANP and NT-proBNP in brachycephalic bitches at different gestational stages. *Reprod Domest Anim* 2016; 51: 346-350.
- [13] Wu P and Wang YJ. Relationship of NT-ProBNP in early cardiovascular dysfunction assessment in children with ventricular septal defect. *Journal of Pediatric Pharmacy* 2016; 8: 4-6.
- [14] Ye XD, He Y, Wang S, Wong GT, Irwin MG and Xia Z. Heart-type fatty acid binding protein (H-FABP) as a biomarker for acute myocardial injury and long-term post-ischemic prognosis. *Acta Pharmacol Sin* 2018; 39: 1155-1163.
- [15] Poyhonen P, Kylmala M, Vesterinen P, Kivisto S, Holmstrom M, Lauerma K, Vaananen H, Toivonen L and Hanninen H. Peak CK-MB has a strong association with chronic scar size and wall motion abnormalities after revascularized non-transmural myocardial infarction - a prospective CMR study. *BMC Cardiovasc Disord* 2018; 18: 27.
- [16] Wei H and Jin JP. A dominantly negative mutation in cardiac troponin I at the interface with troponin T causes early remodeling in ventricular cardiomyocytes. *Am J Physiol Cell Physiol* 2014; 307: C338-348.
- [17] Kluser L, Maier ET and Wess G. Evaluation of a high-sensitivity cardiac troponin I assay compared to a first-generation cardiac troponin I assay in doberman pinschers with and without dilated cardiomyopathy. *J Vet Intern Med* 2019; 33: 54-63.
- [18] Garikipati VN, Krishnamurthy P, Verma SK, Khan M, Abramova T, Mackie AR, Qin G, Benedict C, Nickoloff E, Johnson J, Gao E, Losordo DW, Houser SR, Koch WJ and Kishore R. Negative regulation of miR-375 by interleukin-10 enhances bone marrow-derived progenitor cell-mediated myocardial repair and function after myocardial infarction. *Stem Cells* 2015; 33: 3519-3529.
- [19] Kaya Z, Dohmen KM, Wang Y, Schlichting J, Afanasyeva M, Leuschner F and Rose NR. Cutting edge: a critical role for IL-10 in induction of nasal tolerance in experimental autoimmune myocarditis. *J Immunol* 2002; 168: 1552-1556.
- [20] Shi G, Chen H, Sun Q, Zhang H and Zheng J. Mattress stitch—a modified shallow stitching in the surgical closure of large perimembranous ventricular septal defect in infants. *Ann Thorac Cardiovasc Surg* 2015; 21: 282-288.
- [21] Aydemir NA, Harmandar B, Karaci AR, Sasmazel A, Bolukcu A, Saritas T, Yucel IK, Coskun FI, Bilal MS and Yekeler I. Results for surgical closure of isolated ventricular septal defects in

The application value of VSD closure under ultrasonic guidance

- patients under one year of age. *J Card Surg* 2013; 28: 174-179.
- [22] Ferraioli D, Santoro G, Bellino M and Citro R. Ventricular septal defect complicating inferior acute myocardial infarction: a case of percutaneous closure. *J Cardiovasc Echogr* 2019; 29: 17-19.
- [23] Liu Y, Guo GL, Ouyang WB, Li MZ and Pan XB. Feasibility and effectiveness of percutaneous ventricular septal defect closure under solely guidance of echocardiography. *Zhonghua Yi Xue Za Zhi* 2017; 97: 1222-1226.
- [24] Vo AT, Vu TT and Nguyen DH. Ministernotomy for correction of ventricular septal defect. *J Cardiothorac Surg* 2016; 11: 71.
- [25] Popelova JR, Kotaska K, Tomkova M and Tomek J. Usefulness of N-terminal pro-brain natriuretic peptide to predict mortality in adults with congenital heart disease. *Am J Cardiol* 2015; 116: 1425-1430.
- [26] Weber M, Dill T, Deetjen A, Neumann T, Ekinci O, Hansel J, Elsaesser A, Mitrovic V and Hamm C. Left ventricular adaptation after atrial septal defect closure assessed by increased concentrations of N-terminal pro-brain natriuretic peptide and cardiac magnetic resonance imaging in adult patients. *Heart* 2006; 92: 671-675.
- [27] Hartman MHT, Eppinga RN, Vlaar PJJ, Lexis CPH, Lipsic E, Haecck JDE, van Veldhuisen DJ, van der Horst ICC and van der Harst P. The contemporary value of peak creatine kinase-MB after ST-segment elevation myocardial infarction above other clinical and angiographic characteristics in predicting infarct size, left ventricular ejection fraction, and mortality. *Clin Cardiol* 2017; 40: 322-328.
- [28] Natsukawa T, Maeda N, Fukuda S, Yamaoka M, Fujishima Y, Nagao H, Sato F, Nishizawa H, Sawano H, Hayashi Y, Funahashi T, Kai T and Shimomura I. Significant association of serum adiponectin and creatine kinase-MB levels in ST-segment elevation myocardial infarction. *J Atheroscler Thromb* 2017; 24: 793-803.
- [29] Xu G, Lan Z and Tong X. Effect of prolonged propofol infusion on myocardial enzyme, mitochondrial cytochrome C and adenosine triphosphate in rabbits. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2016; 41: 1181-1185.
- [30] Singh P, Chauhan S, Jain G, Talwar S, Makhija N and Kiran U. Comparison of cardioprotective effects of volatile anesthetics in children undergoing ventricular septal defect closure. *World J Pediatr Congenit Heart Surg* 2013; 4: 24-29.
- [31] Chang Y, Yu T, Yang H and Peng Z. Exhaustive exercise-induced cardiac conduction system injury and changes of cTnT and Cx43. *Int J Sports Med* 2015; 36: 1-8.
- [32] Soetkamp D, Raedschelders K, Mastali M, Sobhani K, Bairey Merz CN and Van Eyk J. The continuing evolution of cardiac troponin I biomarker analysis: from protein to proteoform. *Expert Rev Proteomics* 2017; 14: 973-986.
- [33] Saraiya NR, Sun LS, Jonassen AE, Pesce MA and Queagebeur JM. Serum cardiac troponin-I elevation in neonatal cardiac surgery is lesion-dependent. *J Cardiothorac Vasc Anesth* 2005; 19: 620-625.
- [34] Zimmermann O, Homann JM, Bangert A, Muller AM, Hristov G, Goeser S, Wiehe JM, Zittrich S, Rottbauer W, Torzewski J, Pfitzer G, Katus HA and Kaya Z. Successful use of mRNA-nucleofection for overexpression of interleukin-10 in murine monocytes/macrophages for anti-inflammatory therapy in a murine model of autoimmune myocarditis. *J Am Heart Assoc* 2012; 1: e003293.
- [35] Fang Y, Hu J, Wu Z and Pu D. Changes of serum TNF-alpha, IL-6 and IL-10 level after implantation of valved bovine jugular vein conduit in complex congenital heart diseases. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 2009; 23: 877-881.
- [36] Madhok AB, Ojamaa K, Haridas V, Parnell VA, Pahwa S and Chowdhury D. Cytokine response in children undergoing surgery for congenital heart disease. *Pediatr Cardiol* 2006; 27: 408-413.
- [37] Xu W, Li J, Ye J, Yu J, Yu J and Zhang Z. Transesophageal echocardiography and fluoroscopy for percutaneous closure of atrial septal defects: a comparative study. *Medicine (Baltimore)* 2018; 97: e12891.
- [38] Maagaard M, Heiberg J, Eckerstrom F, Asschenfeldt B, Rex CE, Ringgaard S and Hjortdal VE. Biventricular morphology in adults born with a ventricular septal defect. *Cardiol Young* 2018; 28: 1379-1385.
- [39] Ali YA, Hassan MA and El Fiky AA. Assessment of left ventricular systolic function after VSD transcatheter device closure using speckle tracking echocardiography. *Egypt Heart J* 2019; 71: 1.
- [40] Yuan YQ, Huang Q, Yu L, Wang RM, Zhao YJ, Guo YX, Sun JH, Niu SQ, Sun Y, Yang XM and Mao YL. Long-term follow up of interventional therapy of secundum atrial septal defect. *Chin Med J (Engl)* 2012; 125: 149-152.
- [41] Yang J, Yang L, Yu S, Liu J, Zuo J, Chen W, Duan W, Zheng Q, Xu X, Li J, Zhang J, Xu J, Sun L, Yang X, Xiong L, Yi D, Wang L, Liu Q, Ge S and Ren J. Transcatheter versus surgical closure of perimembranous ventricular septal defects in children: a randomized controlled trial. *J Am Coll Cardiol* 2014; 63: 1159-1168.
- [42] Yang L, Tai BC, Khin LW and Quek SC. A systematic review on the efficacy and safety of

The application value of VSD closure under ultrasonic guidance

- transcatheter device closure of ventricular septal defects (VSD). *J Interv Cardiol* 2014; 27: 260-272.
- [43] Sharfi MH, Al-Ata J, Al-Kouatli A, Baho H, Al-Ghamdi L and Galal MO. Safety and efficacy of transcatheter closure of atrial septal defect type II under transthoracic echocardiographic guidance: a case control study. *J Saudi Heart Assoc* 2019; 31: 2-8.
- [44] Zhong Q, Zheng H, Zhang Z, Qian M, Xie Y and Wang S. Prevalence and risk factors of arrhythmias after transcatheter closure of ventricular septal defect in children. *Zhonghua Xin Xue Guan Bing Za Zhi* 2014; 42: 840-845.