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ORIGINAL ARTICLE

Study on the correlation of modified Blalock Taussig duct occlusion and platelet parameters in congenital heart disease

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Platelet count;
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Platelet distribution width

Summary *Background:* Platelet parameters play an important role in thrombosis. This study investigates the role of platelet parameters in the occlusion of modified Blalock Taussig (BT).
Objectives: To investigate the association between mean platelet volume (MPV), platelet distribution width (PDW) and BT conduit obstruction and to evaluate the role of MPV and PDW in BT conduit obstruction.
Methods: 388 patients with modified BT shunt in the Pediatric Heart Center, Anzhen Hospital From January 1, 2008 to December 30, 2014 were divided into BT obstruction group (OBS) 11 cases and BT non-obstruction group (N-OBS) 377 cases according to whether the BT tube was occluded. The platelet count, mean platelet volume and platelet distribution width in the both groups were measured. The BT pipe occlusion related risk factors were analyzed.
Results: There was no significant difference in PC value of OBS group [(221 $\pm$ 28.4) $\times$ 109/L] and that of N-OBS group [(198 $\pm$ 69.1) $\times$ 109/L). MPV [(15 $\pm$ 6.8) fL] and PDW (20 $\pm$ 6.4)% in OBS group were significantly higher than those in N-OBS group [(8 $\pm$ 3.2) fL, (15 $\pm$ 2.1)%] ($P < 0.05$). Logistic regression showed that BT occlusion was not related to the tube diameter and PC value ($P > 0.05$). Abnormal increases of MPV and PDW increased the risk of ductal occlusion [(OR = 2.1, 95%CI:1.47–2.49, $P < 0.05$), (OR = 2.4, 95%CI:1.71–3.87, $P < 0.05$)].
Conclusion: Improved BT postoperative occlusion are closely related to MPV and PDW. Increased MPV and PDW can increase the risk of postoperative BT occlusion.

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1. Introduction

In 1944, Blalock and Taussig first reported on the successful implementation of classic Blalock-Taussig (BT) shunt in children with tetralogy of Fallot (TOF), thereby initiating systemic-pulmonary shunt of cyanotic congenital heart disease (CHD).[1] However, the obvious shortcoming of classic BT lies in that upper limb ischemia appears in some children after operation. With the development of artificial blood vessel technology, the modified BT shunt has not only made pulmonary blood flow well controlled, but also overcomes the shortcoming of the classic ones, which has been widely promoted and applied in clinical practice. Modified BT shunt can improve children's hypoxia, activity and life expectancy and promote the further development of pulmonary artery. Thus, BT shunt is a safe and effective phase I operation for the phase II radical ones.[2,3] However, thrombosis and even obstruction of artificial blood vessels are still the main reasons for the failure of surgery despite the continuous improvement in the materials of artificial blood vessels and the increasing emphasis on anticoagulant antiplatelet therapy.[4–6] As we all know, platelets play a major role in the pathophysiology of thrombosis. The mean platelet volume (MPV) and platelet distribution width (PDW) are important indicators of platelet activation.[7–9] This study aimed to investigate the association between MPV, PDW and BT conduit obstruction and to evaluate the role of MPV and PDW in BT conduit obstruction.

2. Patients and methods

2.1. Subjects

A total of 388 children who were admitted to Pediatric Cardiac Center of Anzhen Hospital from January 1, 2008 to December 30, 2014 and underwent modified BT shunt were enrolled in this study. Inclusion criteria: children undergoing phase I modified BT shunt. Exclusion criteria: ① children without height recording; ② children without body mass recording; ③ children undergoing modified BT shunt with obstruction after BT shunt; ④ children with surgical incision of right posterolateral or left posterolateral approach; ⑤ children with preoperative pneumonia; ⑥ children with preoperative routine blood test suggesting abnormalities in platelet count (PC), MPV and PDW. Children undergoing modified BT shunt were divided into obstruction (OBS) group and non-obstruction (N-OBS) group according to the condition of the artificial conduit. The diameter of BT conduit was stratified into D4mm and D5mm. For PC stratification, PCI$\leq$150 $\times$ 109/L, 150 $\times$ 109/L $<$ PCII$<$250 $\times$ 109/L, PCIII$\geq$250 $\times$ 109/L; for MPV stratification, MPVI$\leq$5fL, 5fL $<$ MPVII$<$10fL, MPVIII$\geq$10fL; for PDW stratification, PDWI$\leq$12%, 12% $<$ PDWII$<$17%, PDWIII$\geq$17%. Venous blood samples were collected postoperatively in EDTA-C anticoagulant tubes, and detected by blood samples including PC, MPV and PDW were detected by Sysmex XE-2100 automatic hematology analyzer and matched reagents for routine blood test, including PC, MPV and PDW.

2.2. Surgical methods and postoperative anticoagulant and antiplatelet therapy

All children underwent the connection between off-pump subclavian artery-pulmonary artery. We performed median sternotomy, dissected subclavian artery, left or right pulmonary artery, connected subclavian artery-pulmonary artery with a 4 mm or 5 mm Gore-Tex artificial blood vessel according to pulmonary artery development and body mass, conducted anticoagulation with add-on heparin of 0.3–0.5 mg/kg to maintain ACT about 200 s, conducted antiplatelet therapy with aspirin on day 2 after the surgery, and administered aspirin alone on day 3 until the stoppage of anticoagulation and antiplatelet therapy one week before the second surgery.

2.3. Color Doppler flow imaging

Philips SONOS-7500-based ultrasonic system with the probe frequency of 2–4 MHz were used in this study. After all children were placed in the supine position in a sedated state, we performed examinations via subxiphorid, apical, parasternal and suprasternal acoustic windows. At least 10 ultrasonic cross-section views were showed for each children, including the short axis view of the great vessels, inferior and superior vena cava short axis view, subxiphorid four-chamber view, apical four-chamber view, apical two-chamber view, apical five-chamber view, apical left ventricle inflow-outflow tract view, parasternal left ventricle long axis view, parasternal right ventricle inflow view, parasternal aortic short axis view, parasternal left ventricle short axis view at the mitral valve and papillary muscle levels, and suprasternal aortic arch long axis view. The section at the suprasternal fossa section or under the right/left sternoclavicular joint was used to observe the vascular patency of the artificial blood vessels.

2.4. Statistical analysis

All data were processed by SPSS 16.0 software. Normally distributed measurement data were expressed as mean $\pm$ standard deviation. Comparison between the two groups was performed using t test and the influences of confounding factors were eliminated by covariance analysis. Measurement data of non-normal distribution were expressed as the median (quartile range). Comparison was performed using rank-sum test between the two groups and using χ^2 test between the enumeration data. The risk factors for modified BT conduit obstruction were assessed by Logistic regression. $P < 0.05$ was regarded as statistically significant differences.

3. Results

3.1. Clinical outcomes after modified BT shunt

A total of 388 children undergoing modified BT shunt were enrolled in this study, including 203 males and 185 females with a mean age of 1.05 (0.56, 2.90) years, an average height of 72.0 (66.0, 88.3) cm, and mean body mass of [9.0 (7.0, 12.0)] kg. Primary diseases for modified BT shunt include pulmonary atresia (PA), TOF, transition of great artery (TGA), double outlet right ventricle (DORV), single ventricle (SV) and tricuspid atresia (TA). The classification of diseases is shown in Table 1. Hospital deaths included 3 cases of TOF and 2 cases of PA for severe postoperative pulmonary infection and secondary disseminated intravascular coagulation. During the hospitalization, 11 cases (2.8%) underwent second modified BT shunt due to obstruction of the artificial blood vessels, and improved after the second surgery. The rest of the patients recovered well.

3.2. Comparison of platelets between the OBS group and N-OBS group

The postoperative values of PC, MPV, PDW in the OBS group and N-OBS group are shown in Fig. 1. No significant differences in PC value were found between the two groups $[(221 \pm 28.4) \times 109/L$ vs $(198 \pm 69.1) \times 109/L$, $P > 0.05)$. MPV value was significantly higher in OBS group than in control group (8 ± 3.2fL vs 15 ± 6.8fL, $P < 0.05$). The differences in PDW value between the two groups were statistically significant (15 ± 2.1% vs 20 ± 6.4%, $P < 0.05$).

Logistic regression analysis of risk factors for BT conduit obstruction showed that 4 mm conduit did not increase the risk of obstruction as compared to the 5 mm ones. PC is not associated with the risk of obstruction. The risk of conduit obstruction was obviously increased in parallel with the abnormal increases in MPV and PDW values postoperatively. $^*P < 0.05$ as compared to the control group (Table 2).

Table 1 The distribution of diseases for modified BT shunt (%).

Disease	Case	Percentage
PA	205	52.8
TOF	119	30.7
TGA	25	6.5
DORV	18	4.6
SV	15	3.9
TA	6	1.5
Total	388	100.0

4. Discussion

CHD children with inadequate pulmonary blood and pulmonary dysplasia tend to undergo BT shunt palliative surgery and then the radical surgery. Modified BT shunt can not only improve the clinical status of hypoxia in children, but also promote the further development of pulmonary artery. However, artificial vascular obstruction is still the main reason for surgical failure. Increasing evidence supports the important role of platelets in thrombotic diseases. In clinical practice, we often value the clinical significances of increased or decreased PC, while neglecting the clinical values of MPV and PDW. MPW is the mean platelet volume measured by hematology analyzer, while PDW is the variation of platelet volume obtained after data processing of platelet distribution by hematology analyzer, and represents the dispersion of platelet size in blood, and often expressed as CV%. Previous reports have showed that increased MPV is related to myocardial infarction, coronary collateral

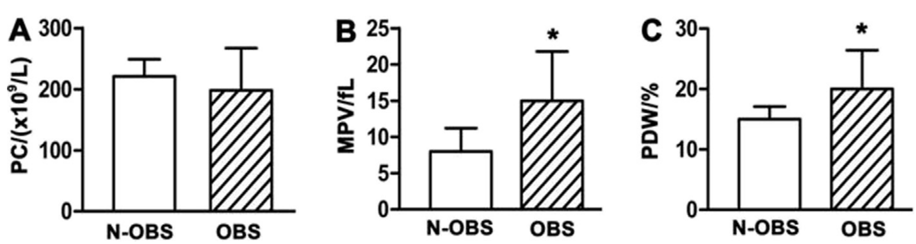

Figure 1 Comparison of PC, MPV and PDW values between the OBS group and N-OBS group. Note: $^*P < 0.05$ for the comparison between the two groups.

Table 2 Logistic regression analysis of risk factors for BT conduit obstruction.

Variable	Risk stratification	OR (95% CI)	*P* value
Diameter	D_{5mm}	1.0	
	D_{4mm}	1.1 (0.82–1.43)	0.58
PC	$PC_I \leq 150 \times 10^9/L$	1.0	
	$150 \times 10^9/L < PC_{II} < 250 \times 10^9/L$	0.96 (0.74–1.23)	0.29
	$PC_{III} \geq 250 \times 10^9/L$	1.5 (0.69–2.54)	0.11
MPV	$MPV_I \leq 5fL$	1.0	
	$5fL < MPV_{II} < 10fL$	1.3 (0.81–1.58)	0.17
	$MPV_{III} \geq 10fL$	2.1 (1.47–2.49)[a]	0.03
PDW	$PDW_I \leq 12\%$	1.0	
	$12\% < PDW_{II} < 17\%$	1.6 (0.86–2.02)	0.08
	$PDW_{III} \geq 17\%$	2.4 (1.71–3.87)[a]	0.01

[a] MPV increased, the hazard ratio for BT conduit obstruction enhanced. PDW also functioned as a risk factor for BT conduit obstruction.

dysplasia, stroke and venous thromboembolism.[10–12] In addition, elevated MVP is also associated with infective endocarditis, rheumatoid arthritis, and diabetes,[13–15] and elevated PDW is significantly associated with myeloproliferative disorders, diabetes, and various cardiovascular diseases.[12,14] Larger volumes of platelets contain more dense particles and tend to be more active which can release more substances including 5-HT and thrombomodulin, thereby easy to promote thrombosis. PDW values are significantly increased during platelet activation. Due to the interaction between actin filaments and myosin thick filaments, activated platelets have morphological changes, including transition from normal disciform to napiform, pseudopodium on the cell surface and platelet aggregation, triggering thrombotic disease. Beyan et al[16] believe that the PDW value should not be used as an independent indicator of platelet activation, since great morphological changes in platelets can be clinically observed in many cases, such as hemorrhagic disease and myelodysplastic syndrome, without complication of coagulation activation. But PDW and MPV increase simultaneously, suggesting platelet activation. The results of this study suggest that modified BT conduit obstruction is significantly associated with elevated MPV and PDW but not with PC. Thus, MPV and PDW can better reflect changes in prethrombotic platelets than does PC, speculating that MPV and PDW changes are likely to be earlier than the changes in PC, and PC changes only in the later stages of severe thrombotic disease with relative lagging behind the trend of change. Therefore, patients with increased MPV and PDW in the peripheral blood may have timely detection of platelet aggregation and platelet activation markers such as TXB2, DH-TXB2 and PAI-1. If these indicators are significantly increased, we need to strengthen anticoagulant and antiplatelet therapy, and adjust the doses of heparin and aspirin.

The diameter of artificial blood vessels affects the postoperative patency rate, resulting in the multiple choices of artificial blood vessels in various heart centers when most of the choices are made based on the experience of the surgeon. Thin artificial vessels can reduce the load on the heart and may have some advantages in protecting cardiac function, but if the vessel is too thin, it is easier to be blocked and weak in promoting the further development of pulmonary artery. Too thick one may bring shortcomings, including excessive shunt, increased cardiac load, diastolic heart insufficiency, and influences on myocardial contraction.[17] As reported, 3 mm conduit can promote pulmonary artery development without increase in the obstruction rate.[18] However, other scholars found that 4–5 mm artificial blood vessels can better promote pulmonary artery development, while decreasing obstruction rate without significant increased mortality rate. The majority of CHD patients in our center were treated with 4 mm and 5 mm conduit with satisfactory outcomes, showing that 4 mm or 5 mm artificial vessels are not associated with postoperative obstruction.

Some scholars believe that the surgical incision may be related to modified BT obstruction. To exclude the influence of the surgical incision approach, we performed median sternotomy in all patients undergoing modified BT shunt. The results of this study suggest that the differences in MPV and PDW may be the important factors affecting the obstruction in children with similar surgical incision approach and matched gender, age and body mass. In such a retrospective and a single-center study, the sample size of the OBS group is relatively small and further studies with large multicenter samples are still be expected.

Disclosure of conflict and interest

The authors declare that they don't have any conflict and interest.

Author's contributions

Yaobin Zhu and Zhiqiang Li both participated in the study design, manuscript drafting and data interpretation. Yaping Zhang and Nan Ding was responsible for recruitment of the patients. Yang Liu and Xing Fan was involved in analyzing part of the data.

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References

1. Vricella LA, Jacobs ML, Cameron DE. The birth of a new era: the introduction of the systemic-to-pulmonary artery shunt for the treatment of cyanotic congenital heart disease. *Cardiol Young*. 2013;23:852–857.
2. McKenzie ED, Khan MS, Samayoa AX, et al. The Blalock-Taussig shunt revisited: a contemporary experience. *J Am Coll Surg*. 2013;216:699–704.
3. Ahmad U, Fatimi SH, Naqvi I, et al. Modified Blalock-Taussig shunt: immediate and short-term follow-up results in neonates. *Heart Lung Circ*. 2008;17:54–58.
4. Sivakumar K, Anil SR, Ravichandra M, et al. Emergency transcatheter balloon recanalization of acutely thrombosed modified Blalock-Taussig shunts. *Indian Heart J*. 2001;53:743–748.
5. Al Jubair KA, Al Fagih MR, Al Jarallah AS, et al. Results of 546 Blalock-Taussig shunts performed in 478 patients. *Cardiol Young*. 1998;8:486–490.
6. Gillespie MJ, Rome JJ. Transcatheter treatment for systemic-to-pulmonary artery shunt obstruction in infants and children. *Cathet Cardiovasc Interv*. 2008;71:928–935.
7. Kamath S, Blann AD, Lip GY. Platelet activation: assessment and quantification. *Eur Heart J*. 2001;22:1561–1571.
8. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. *Hippokratia*. 2010;14:28–32.
9. Tsiara S, Elisaf M, Jagroop IA, Mikhailidis DP. Platelets as predictors of vascular risk: is there a practical index of platelet activity? *Clin Appl Thromb Hemost*. 2003;9:177–190.

10. Şahin İ, Karabulut A, Kaya A, et al. Increased level of red cell distribution width is associated with poor coronary collateral circulation in patients with stable coronary artery disease. *Turk Kardiyol Dernegi Arsivi*. 2015;43:123—130.
11. Chu SG, Becker RC, Berger PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemostasis*. 2010;8:148—156.
12. Khandekar MM, Khurana AS, Deshmukh SD, Kakrani AL, Katdare AD, Inamdar AK. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. *J Clin Pathol*. 2006;59:146—149.
13. Yazici S, Yazici M, Erer B, et al. The platelet indices in patients with rheumatoid arthritis: mean platelet volume reflects disease activity. *Platelets*. 2010;21:122—125.
14. Bozkurt N, Yilmaz E, Biri A, Taner Z, Himmetoğlu O. The mean platelet volume in gestational diabetes. *J Thromb Thrombolysis*. 2006;22:51—54.
15. Xu Wenliang, Hui Bo, Wu Yue, et al. Mean platelet volume in coronary heart disease patients with type 2 diabetes mellitus and its relevance of blood glucose and lipids. *J Cardiovasc Pulm Dis*. 2013;32:286—290.
16. Beyan C, Kaptan K, Ifran A. Platelet count, mean platelet volume, platelet distribution width, and plateletcrit do not correlate with optical platelet aggregation responses in healthy volunteers. *J Thromb Thrombolysis*. 2006;22:161—164.
17. Xu Zhaojun, Lan Song, Yin Xiaoqing. Modified Blalock-Taussing shunts for patients with congenital heart diseases of diminutive pulmonary blood. *Chin J Clin Thorac Cardiovasc Surg*. 2015;22:450—453.
18. Pace Napoleone C, Oppido G, Angeli E, et al. Adjustable aorto-pulmonary shunt to prevent temporary pulmonary over-circulation. *Eur J Cardio Thorac Surg*. 2006;29:253—254.