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Red Blood Cells Morphology Monitoring to Predict Hyperfunction of Subclavian-Pulmonary Anastomosis in Patients with Fallot Tetralogy

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ABSTRACT

Hyperfunction of subcluvian-pulmonary anastomosis in patients with tetralogy of Fallot (TOF) is known to be a rather common condition in the early post-operative period. It resulted in development of hypervolemic pulmonary circulation and edema. Morphometry of peripheral blood cells of 81 TOF post-operative patients revealed an increase in the number of pathologically shaped red blood cells (PS RBCs) in 14 of them. Mainly these were the ones with a ridge-like structure on their surface. The hick drop express-technique (TDET) enables to evaluate the correlation of normal RBCs/ PS RBCs for 10-15 min for the entire procedure. The progressive deterioration of RBCs morphological features is suggested to be a predictor of the anastomosis hyperfunction due to changed blood rheology. In addition the correlation of normal and pathological forms of erythrocytes can be an evaluation criterion of effectiveness of patient management tactics of cardiologic intensive care.

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INTRODUCTION

Tetralogy of Fallot is one of the most common congenital heart disorders across the world. For instance, the centers for disease control and prevention (CDC) estimate that each year about 1,660 babies in the United States are born with this pathology [1, 2]. If left untreated, TOF children face additional risks that include paradoxical emboli leading to stroke, pulmonary embolus, and subacute bacterial endocarditis [3]. In most of these children, the causes of stroke, along with thromboemboli, have been related to prolonged hypotension, anoxic polycythemia.

Most TOF infants require surgery and a lot of surgical series have reported excellent short-term clinical results since the time when the first classic Blalock-Taussig shunt between the subclavian artery and the pulmonary artery was made. Primary repair of tetralogy of Fallot is known to have low surgical mortality; however, some patients still experience significant postoperative morbidity [4, 5]. Several attempts have been

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made recently to find out predictors of early post-operative complications in TOF patients depending on the surgery profile [5-10].

One of the main problems of patients, who undergone cardiosurgery, in particular the ones with congenital heart defects due to impaired blood circulation, is a considerable change in delivery of O_2 to tissues [4, 8]. Unfortunately, adequate attention has not been paid so far to the change in the hemorheology status and transfusion indicators during post-operative adaptive transformation of hemodynamics as well as to the methods of their evaluation and monitoring.

The research was focused on evaluating the efficiency of thick-drop technique of scanning electron microscopy in predicting and monitoring the hyperfunction of subclavian-pulmonary anastomosis in TOF patients at the early post-operative period.

MATERIAL AND METHODS

Eighty one TOF patients aged 1 - 22 years (mean age 8.7 ± 0.9), including 43 males (53%), 38 females (47%), have been operated in Republican Specialized Center of Surgery named after academician V.Vakhidov (Tashkent, Uzbekistan) from 2015 to 2017. In all the cases, the modified subclavian-pulmonary anastomosis (SPA) was performed. Artificial lung ventilation was carried out to the SPA patients in the standard regimes in early post-operative period. The relative predictors of intensive care unit (ICU) stay and morbidity were age and weight of the patients, while the surgery profile suggested the duration of mechanical ventilation. Hyperfunction of the anastomosis in the early post-operative period developed in 14 patients (17.3%). The median duration of their mechanical ventilation was 19 hours. The ICU stay ranged from 2 to 14 days. Five of these patients were randomly selected to form the study group; 8 patients with no SPA hyperfunction were matched by age, sex and concomitant conditions to compose the comparison group.

To monitor the RBC status, scanning electronic microscopy (SEM) was used since it enables to differentiate and count precisely normal RBCs having the shape of biconcave discocytes (D) from pathologically shaped RBCs (PS RBC). Usually, the most frequent PS RBCs found are echinocytes, i.e. RBCs with numerous processes, stomatocytes, RBCs with a ridge-like structure, and considerably changed PS RBCs or so called irreversible RBCs.

Most scanning electron microscopes are comparatively easy to operate, with user-friendly interfaces. Many applications require minimal sample preparation and data acquisition is rapid (less than 5 min/image). The thick-drop express-technique (TDET) has been elaborated at the NSCS for practical and research purposes. This technique and relevant software have been developed and patented in Uzbekistan [3, 6]. One of advantages of the technique is that it preserves the natural condition of RBCs and quickly evaluates the correlation of D/ PS RBCs (for 10-15 min).

Ethical approval

The review board and ethics committee of Republican Specialized Center of Surgery named after academician V.Vakhidov approved the study protocol and gave permission for study.

RESULTS AND DISCUSSION

The TDET enabled to monitor the RBCs morphologic condition and evaluate the hemodynamic changes in the early post-operative period of 14 TOF patients, in particular the development of hypervolemia of the pulmonary circulation and pulmonary edema. The proportion of the PS RBCs in TOF-SPA patients' blood significantly increased. Studying the RBC profile in patients with cyanotic TOF (CTOF) demonstrated that the discocyte count in the early post-operative period made 40% with 85% reference value. The most part of the rest RBCs (60%) was presented by the population of pathologicaly-shaped and lysed cells (Figures 1 and 2).

The echinocyte population of adult patients with CTOF was more remarkable; it included 26% of echinocytes of class I; 8% of the second class echinocytes and 5% of the third class cells. The number of stomatocytes and hydrocytes proved to be larger than in children with CTOF. It made 3% of stomatocytes of class I, while the stomatocytes of the second and third classes made 7% and 5%, respectively. The population of discocytes with a ridge-like structure was distributed as follows: small ridges were found in 1.5-2%, the medium-sized ones were found in 1-1.5%, and 0.5% of the discocytes had large ridges.

The morphological cell variability reflected differences in the physical condition and compensation-adaptation mechanism of the patients. It is worth mentioning that children elder than 10 years need to be monitored more closely due to a notable increase in the number of pathologically shaped erythrocytes before the surgery. It should be taken into consideration at the next stages of treatment, in particular during the surgery, anesthetic management and perfusion.

After the SPA-surgery the proportion of discocytes decreased while that one of PS RBCs increased; at the same time number of echinocytes increased, as well as the number of irreversibly altered RBCs. Two hours after the surgery, the proportion of pathologically shaped RSCs increased, mainly those ones with ridges and echinocytes (Figure 3). Twelve hours after the surgery the number of discocytes in the blood significantly increased with a considerable drop in the number of RSCs with ridge and echinocytes.

The TDET used to evaluate alterations in the RBC shape in TOF patients before and after the surgery enabled to estimate the discocytes/PS RBC within 15 min after the surgery and conduct rather large hemomorphologic study. The TDET evaluation of RBCs in the comparison group demonstrated significant domination of discocytes. In addition to the characteristic shapes of the biconcave discs, they had a smooth external membrane with no processes, folds and depressions (Table 1).

The TDET made to TOF patients before the surgery showed a considerable increase in the PS RBC proportion. They made 1/3 of the RBCs, 61% of them were discocytes, but RBCs with a ridge dominated (Table 1, Figure 4). Immediately after the surgery, a lot of PS RBCs were found with higher proportion of echinocytes (Table 1). Two hours after the surgery the counts of discocytes and stomatocytes tended to diminish while the number of RBCs with ridge increased (Figure 5).

When anastomosis hyperfunction has developed, the clinical changes are manifested by pulmonary edema with an increase in PS RBC count in peripheral blood and a decrease in the number of discocytes up to 49%. The RBCs with ridge composed up to 16%, and echinocytes of classes 1 and 2 made 14%. Stomatocytes, the cells with coarse echinocyte transformations, and irreversibly shaped cells were presented in relatively equal numbers: 6%, 7% and 8%, respectively (Table 1).

When post-SPA hyperfunction developed, the set of intensive therapy interventions procedures included application of the regulating cuff. It contributed to restoration of the peripheral blood RBCs shape in 120-180 minutes with the increase in discocyte count from 49% to 55%, while the number of PS RBCs decreased by 6% (Figures 6 and 7).

Twelve hours after the surgery we noted the tendency to an increase in the number of discocytes and a decrease in the PS RBC number (Table 1). The dynamics of morphological monitoring is as follows: at hours 12-15 after SPA hyperfunction development the number of discocytes in peripheral blood is increasing because of the restoration of pathologically changed erythrocytes (Table 1).

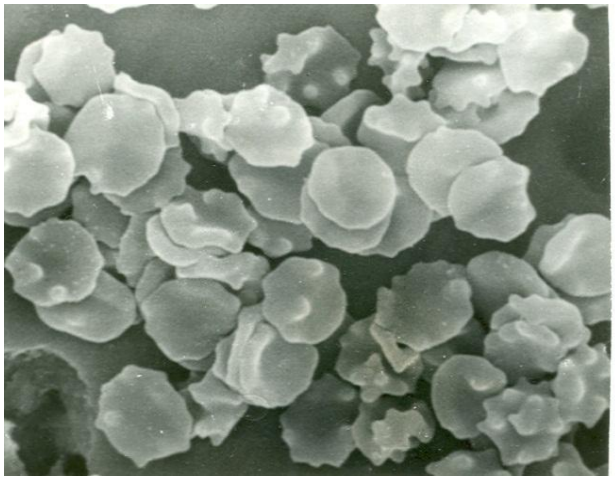

Figure 1. The blood sample of the CTOF patient. The evident domination of pathologically shaped RBCs. SEM × 1.000

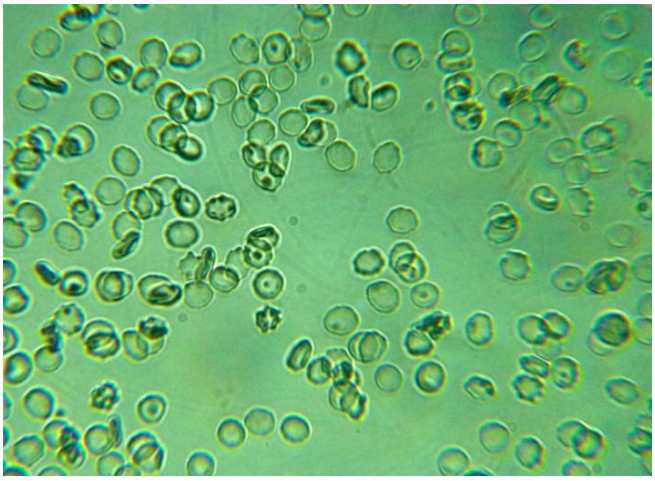

Figure 2. The blood of the same patient. Numerous echinocytes, cells with ridges and stomatocytes. TDET 10 × 60.

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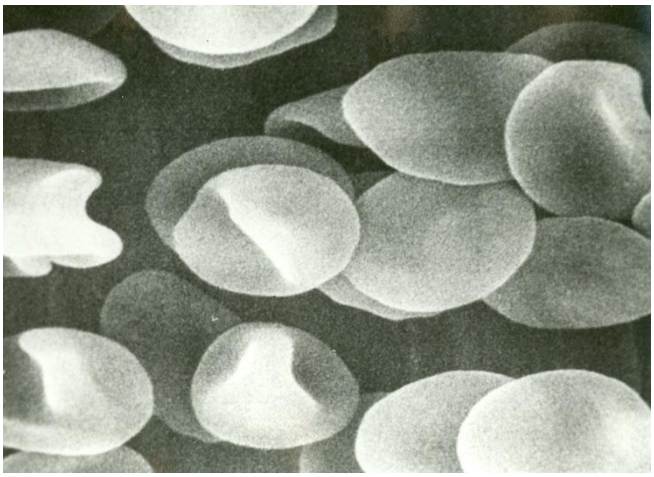

Figure 3. The RBC of the TOF patient 2 hours after the surgery: the increasing proportions of PS RBC, RBCs with ridge and echinocytes.
SEM × 4.000

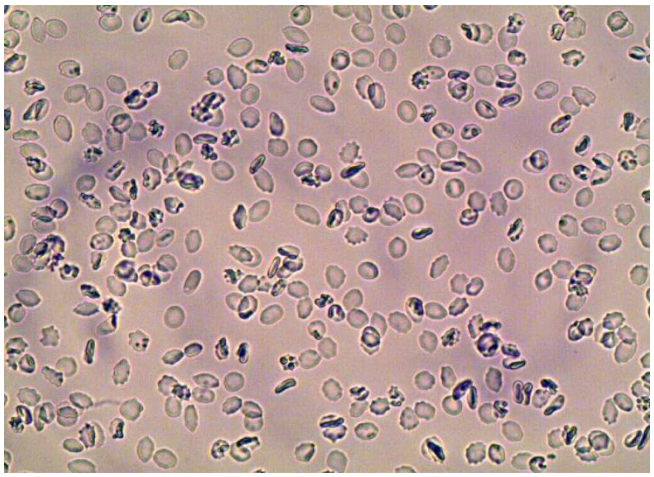

Figure 4. The RBCs of the TOF patient before the surgery: domination of PS RBCs, RBCs with ridge in particular. TDET 10 × 40

Table 1. Dynamics of the subclavian-pulmonary anastomosis effect on peripheral blood RBCs of TOF patients (%)

Items	Comparison group n=8	Before the surgery n=10	Immediately after the surgery n=10	120 min. after the surgery n=5	Anastomosis hyper-function Pulmonary edema, n=5	120 min. after RSPA n=5	12 hr after the surgery n=5	12 hr after the RSPA n=5
Discocytes	85±1.2	59±1.1	57±2.5*	56±2.3**	49±2.9**	55±2.4 **	61±2.2***	64±2.4***
Echinocytes	2±0.1	7±0.2	10±0.6*	11±0.7**	14±1.3**	12±0.8 **	10±0.6***	9±0.5***
Stomatocytes	3±0.2	8±0.4	7±0.4*	4±0.3**	6±0.6**	5±0.4**	4±0.4***	4±0.3***
With ridge	4±0.2	19±0.2	14±0.3*	17±0.3**	16±0.5**	15±0.3 **	15±0.3	12±0.4
Echinocytes rough	4±0.3	5±0.4	6±04	7±0.3	7±04	7±04	5±0.3	4±0.3
Irreversible cells	2±0.1	2±0.7	6±0.5	5±0.3	8±0.5	6±0.8	5±0.4	7±0.3

*significant difference (P<0.05) from the previous group; **significant difference (P<0.05) from group*; *** significant difference (P<0.05) from group**; RSPA= Regulated subclavian-pulmonary anastomosis.

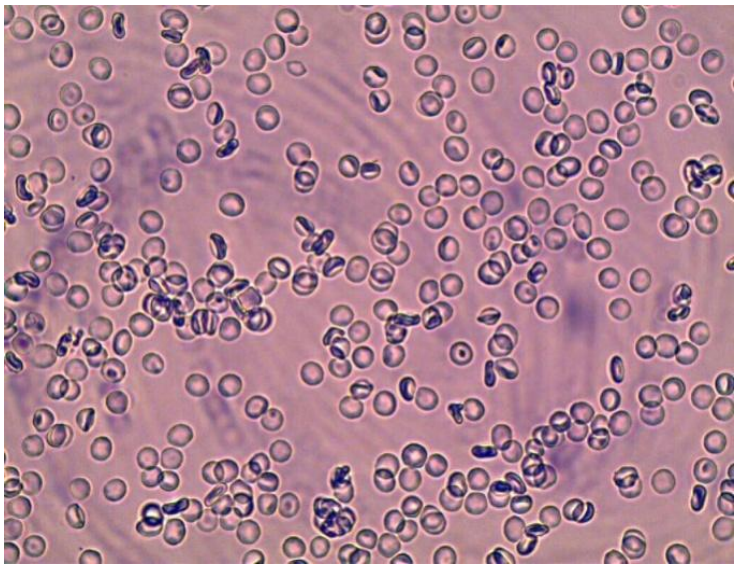

Figure 5. Two hours after SPA. A higher proportion of pathologically shaped RBCs, RBCs with ridge and echinocytes. TDET 10 × 40

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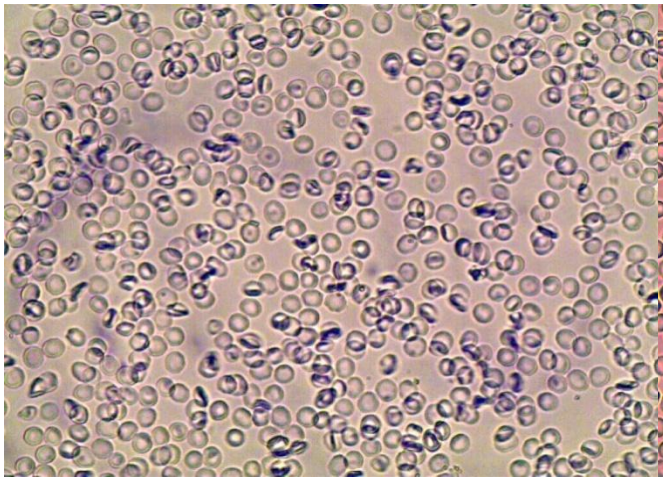

Figure 6. Two hours after application of the regulating cuff in post-SPA hyperfunction. An increase in the number of discocytes with a significantly decreased proportion of the cells with processes. TDEM 10 × 40

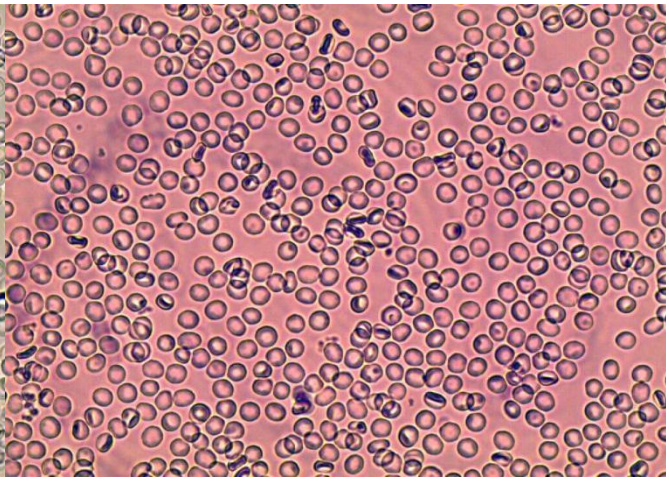

Figure 7. Two hours after application of the regulating cuff in post-SPA hyperfunction. The RBC count teds to normalize. TDEM 10 × 40

CONCLUSION

Morphological features of peripheral blood cells in patients with tetralogy of Fallot demonstrated that the number of pathologically shaped RBCs increased up to 41 %, these were mainly erythrocytes with ridge (up to 16 %). The early post-operative period after performance of subclavian-pulmonary anastomosis is characterized by the decrease of RBCs count up to 56-57%. The share of pathologically shaped RBCs in peripheral blood below 49 % is the morphological predictor of anastomosis hyperfunction development. The morphological monitoring of the correlation between normal and pathologically shaped erythrocytes after SPA-surgery for tetralogy of Fallot can provide the criterion of efficiency of the medical and diagnostic tactics in anastomosis hyperfunction development.

DECLARATIONS

Authors' Contributions

All authors contributed equally to this work.

Acknowledgements

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Competing interests

The authors declare that they have no competing interests.

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