Effectiveness of Minimal Acute Normovolemic Hemodilution in Elective Adult Cardiac Surgery

Ahmad Fathy Abd El-Latef[a], Essam Ahmad Mohammad[a]*, Mohamed Abd-Elbary[b], Salah Mostafa Asida[a], Hatem Saber Mohamed[c]

[a]Anaesthesia &ICU Department, Faculty of Medicine, South Valley University, Qena, Egypt.
[b]Cardiothoracic Surgery Department, Faculty of Medicine, South Valley University, Qena, Egypt.
[c]Anaesthesia &ICU Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt.

Abstract

Background: The haematological care of cardiac surgery patients necessitates a careful equilibrium between excessive anticoagulation and the restoration of normal hemostasias following the operation.

Objectives: The purpose of this study was to evaluate the impact of mild acute normovolemic hemodilution on blood transfusion needs and reopening in planned adult cardiac surgical intervention.

Patients and methods: A prospective randomized observational research was carried out on one hundred patients that were planned to undergo planned adult cardiac surgery, aged from 40-65 years old. Participants were assigned randomly to 2 groups: acute normovolemic hemodilution group and controls. All participants were subjected to preoperative preparations and standard monitoring (pulse oximetry, lead II and V5 of the ECG).

Results: haemoglobin, haematocrit had a significant increase in acute normovolemic hemodilution group than Controls in 2nd and 3rd ($P<0.05$). Platelet count showed significant increase in the study group than controls in 3rd ($P = 0.042$). Patient transfused with packed red blood cells, patient transfused with fresh frozen plasma, and chest tubed drainage were lower in study group than control group ($P = 0.017$, 0.028 and <0.001respectively).

Conclusion: In this study, for patients undergoing elective coronary artery bypass graft surgery, minimal acute normovolemic hemodilution technique using 6% hydroxyethyl starch 130/0.4 (Voluven) reduces the need of allogenic blood transfusion, fresh frozen plasma transfusion, packed red blood cells and platelets. so, it decreases postoperative bleeding in patients underwent heart surgery. However, this technique had no effect on patients transfused with platelet concentrate.

Keywords: Minimal Acute Normovolemic Hemodilution; Elective Adult; Cardiac Surgery; Blood Transfusion.

***Correspondence**: essamhamad30@hotmail.com

DOI: 10.21608/SVUIJM.2023.182990.1479
Received: 29 December, 2022.
Revised: 16 January , 2023.
Accepted: 18 January , 2023.
Published: 24 May, 2024
Cite this article as: Ahmad Fathy Abd El-Latef, Essam Ahmad Mohammad, Mohamed Abd-Elbary, Salah Mostafa Asida, Hatem Saber Mohamed.(2024). Role of Growth Differentiation Factor15 in pediatric cardiac patients. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 1, pp: 911-918.

Introduction

In Acute Normovolemic Hemodilution (ANH), a whole blood sample is taken right before or right after the anesthesia starts. As blood is taken out, large amounts of either crystalloid (3:1 ratio with blood volume taken away) or colloid (1:1 ratio with blood volume taken away)) are infused to keep the blood volume the same. Colloid may be better, though. The amount of blood that is taken out is supposed to bring the hematocrit level down to about 28%, but sometimes more drastic steps are taken to bring down the level of hematocrit. There are formulas that can be used to figure out how much blood can be taken from patients with different starting hematocrits and different weights to get a final hematocrit of 30%. Some good things could come from ANH **(Nistal-Nuño, 2021)**.

The hematologic care of patients undergoing heart surgery requires a delicate balance between excessive anticoagulation and normal hemostasis. These two distinct pathways must be closely managed and changed according to pre-existing disease condition, time of cardiac surgery, extracorporeal circulation usage, and anticipated hemostatic result **(L, 2003)**.

Talented surgery coupled with blood-conserving techniques and vigilant monitoring of blood coagulation will aid in minimising needless blood loss and the need for transfusions. Hypovolemia, hemodynamic instability, anaemia, and decreased tissue oxygen supply result from excessive surgical bleeding, leading to an increase in postoperative morbidity and death **(Mahdy et al., 2004)**.

Blood grouping incompatibility, sepsis, febrile responses, immunosuppression, and viral transmission are among the dangers associated with the transfusion of allogenic blood products **(Shander et al., 2005)**.

Coagulopathy is frequent after cardiopulmonary bypass (CPB), platelet dysfunction, low clotting factor activity, inadequate heparin inactivation, and aggressive fibrinolysis are the primary reasons of post-CPB nonsurgical bleeding **(Zisman et al., 2009)**.

ANH prior to a major operation is a very easy, inexpensive, and successful method for avoiding or reducing the need for allo-blood transfusions. However, the anesthesiologist must have knowledge of ANH's practical applications. In addition, deep understanding of the physiologic hemostatic mechanisms that occur during ANH and their limitations is required for the proper use of this life-saving treatment **(Zisman et al., 2009)**.

There are added advantages of ANH not shared by other auto-transfusion methods. Blood stored in the same operation room eliminates the possibility of clerical mistake. Platelets and coagulation factors, Blood acquired via ANH, on the other hand, degrades minimally since it is stored at room temperature and is often reinfused within 8 hours **(Mahoori et al., 2009).**

The primary purpose of this study is to assess the impact of limited ANH on blood transfusion needs and re-opening in elective adult heart operations while, the secondary goal is to assess the impact of limited ANH on postoperative ICU stay and hospital stay.

Patients and Methods

Prospective randomized research was done on one hundred patient who planned to undergo planned adult cardiac surgery, aged from 40-65 years old. The study was conducted at Qena University Hospital (**Fig.1**).

The research was conducted with the agreement of the Qena University Ethics Board from April 2018 to April 2021. All participants provided their written informed permission.

Exclusion criteria were major cardiac function disability, left ventricular ejection fraction less than 40%, unstable angina pectoris in combination with coronary artery disease and severe aortic stenosis, Euro score II of greater than 2%, pump time of greater than 2.5 h, known haematological problems, extensive chronic kidney disease (serum creatinine >2 mg/dl), hepatic cirrhosis or inflammation, preoperative hematocrite < 34%, and hypersensitivity to colloid.

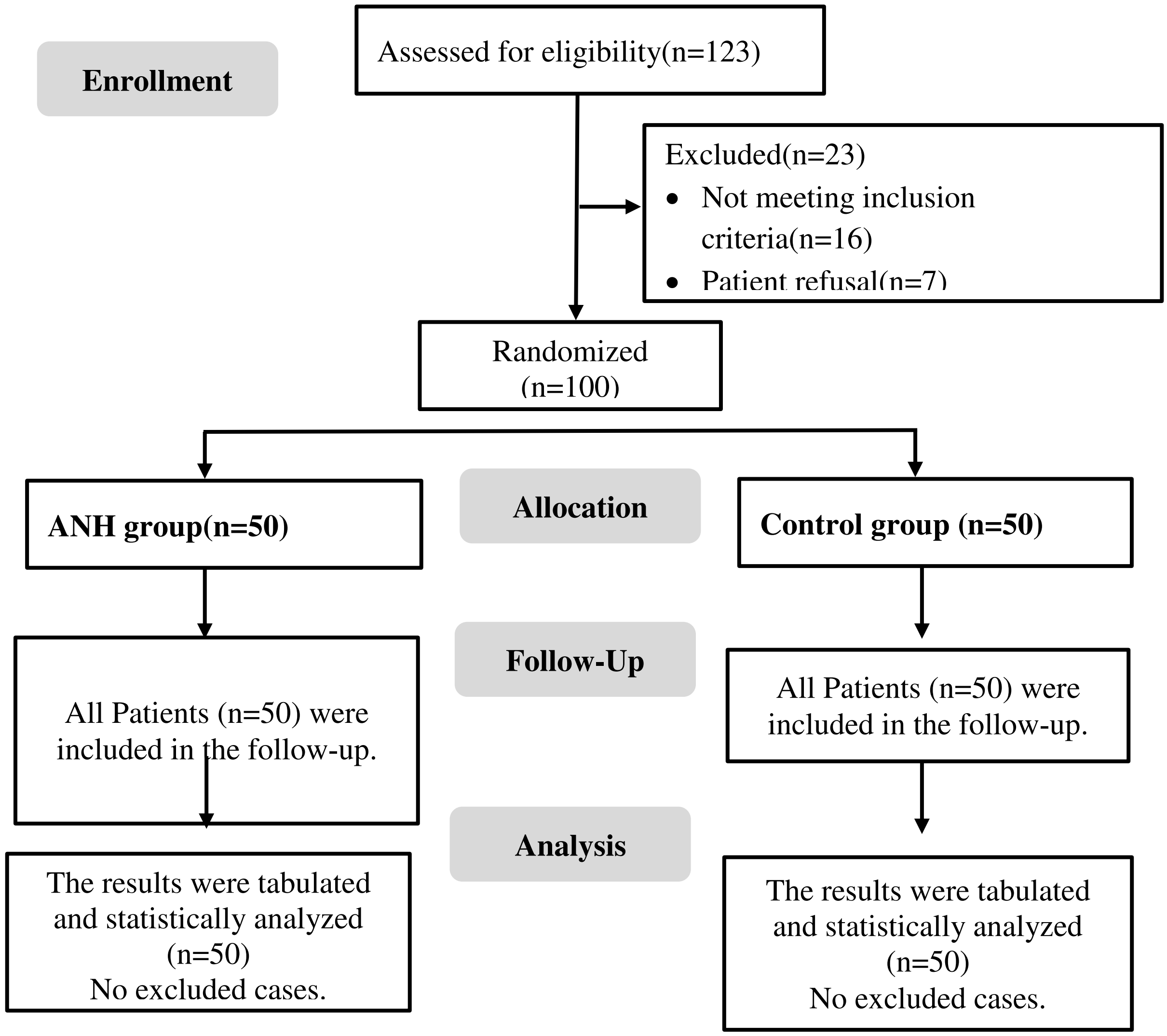

Fig. 1. CONSORT flowchart of the enrolled patients (ANH; Acute Normovolemic Hemodilution).

Cases were allocated into two groups at random: ANH group and controls.

All patients were subjected to complete history taking, preoperative preparations and standard monitoring (pulse oximetry, lead II and V5 of the ECG).

Primary outcome of this study is to evaluate the effectiveness of the use of minimal ANH for blood transfusion requirements and re-opening in elective adult cardiac surgery.

Secondary outcome: is to evaluate the effectiveness of minimal ANH on postoperative ICU stay and hospital stay after cardiac surgery.

Acute Normovolemic Hemodilution

About 5 to 8 ml/kg of auto-whole blood was extracted prior to anaesthetic administration and systemic heparinization for the ANH group. An equal amount of

Colloid (6% hydroxyethyl starch (HES) 130/0.4; Voluven) was administered as blood was re-infused after CPB surgery. For the control group, no hemodilation was performed. For both groups, the total amount of allo-packed red blood cells (PRBC), fresh frozen plasma (FFP), and platelet concentrates (PLTC) transfusions, as well as the number of cases undergoing re-surgery due to severe haemorrhage, were determined.

Anesthetic techniques

Pulse oximetry leads II and V5 of the electrocardiogram (ECG), automated segment trend analysis, end tidal capnography, and continuous measurement of (venous pressure) CVP, invasive blood pressure, nasopharyngeal temperature, and urine output were performed. Also done were serial blood gas analysis and serum electrolytes.

Anesthesia was administered using fentanyl 2–5 mic/kg, propofol 1–2 mg/kg, atracurium 0.5 mg/kg, and breathed isoflurane 0.5–1%. End-Tidal Carbon Dioxide (ETCO2) was kept between 30 and 35 mmHg by artificially ventilating patients. After heparinization (300 IU/kg), cardiopulmonary bypass (CPB) was administered with non-pulsatile flow (2.2–2.5 l/min/m^2) and hypothermia (28–30°C).

The goal range for mean arterial pressure was between 50 and 80 mmHg, using a -stat control for acid–base management. Protamine was supplied at the conclusion of cardiopulmonary bypass to neutralise heparin (1:1); additional doses were provided if the blood coagulation time was longer than the baseline.

Operative techniques

All patients had surgery at our institution using normal procedures. Before the chest was closed, mediastinal and pleural drains were placed and a low-grade suction was initiated.

ICU management

All patients were moved to the ICU, where intubation was done and put on mechanical ventilation until extubation was possible, when stable circulatory condition and no major bleeding were noted.

Blood conservation techniques

Whole blood was obtained with a wide bore cannula (14 G) introduced in the external jugular vein and allow blood flow without negative pressure. The collected blood was stored in citrate phosphate dextrose collection bags, kept on a rocking platform shaker, preserved at room temperature under sterile conditions, and labelled appropriately for patient identification.

All collected blood was returned to the patients before leaving the operation room. Samples were taken from the central venous catheter for evaluation of hemoglobin (Hb), hematocrit, Platelet count, prothrombin time (PT), and activated partial thromboplastin time (aPTT), which were carried out at the following times: before anaesthesia (1st), on arrival in ICU (2nd), 24 hours after the arrival in ICU (3rd), 48 h after ICU admission (4th), and at discharge from ICU (5th). During surgery, serial arterial blood analysis was performed to determine Hb, hematocrit, electrolytes, and blood gases.

Transfusion guidelines were as follows: During CPB, PRBCs were given if the patient's haemoglobin level was below 7 g/dL and hematocrit level was below 25%. In addition, following bypass surgery and during hospitalisation if the patient's Hb value dropped below 9 g/dL and hematocrit dropped below 27%. If the prothrombin time value was 1.5 times normal, FFP was injected following protamine administration or in case of ongoing blood loss in dose of 15 ml/kg. PLTC was transfused if platelets count was < 50 000/mm^3 in presence of ongoing blood loss and given as 1 U/10 kg body weight.

Surgical re-exploration: The quantitative chest tube drainage reoperation criteria were: >500 ml/h in the first hour, >800 ml during two consecutive hours, >900 ml during three consecutive hours, or total bleeding >1200 ml after five hours.

Statistical analysis

SPSS v26 was used to do statistical analysis (IBM Inc., Armonk, NY, USA). Comparing the two groups using an unpaired Student's t- test, quantitative data were provided as mean and standard deviation (SD). When applicable, qualitative variables were given as frequency and percentage (%) and analysed with the Chi-square test or Fisher's exact test. A two-tailed P value less than or equal to 0.05 was deemed statistically significant.

Results

Patients' characteristics (age, sex, height, weight, and body mass index (BMI)), risk factors (hypertension, diabetes mellitus and smoking) and left ventricular ejection fraction (EF) had insignificant difference in the two groups (**Table.1**).

Table 1. Patients' characteristics, risk factors and left ventricular ejection fraction of the studied groups

Variable*		ANH group (n=50)	Control group (n=50)	P value
Age (years)		52.42±8.65	51.8±7.93	0.710
Sex	Male	32 (64%)	29 (58%)	0.682
	Female	18 (36 %)	21 (42 %)	
Height (m)		1.65 ± 0.05	1.64 ± 0.05	0.208
Weight (kg)		71.92 ± 6.47	72.68 ± 6.14	0.548
BMI (Kg/m^2)		26.4 ± 2.65	27.02 ± 2.15	0.203
Risk factors				
Hypertension		27 (54%)	22 (44%)	0.423
Diabetes mellitus		21 (42%)	17 (34%)	0.536
Smoking		36 (72%)	30 (60%)	0.291
Left ventricular ejection fraction (%)		51.57 ± 0.89	51.62 ± 0.85	0.774

* Data are presented as mean ± SD or frequency (%), ANH: acute normovolemic hemodilution, BMI: body mass index

Hemoglobin, Hematocrit were significantly higher in ANH group than controls in 2nd and 3rd (P<0.05) and had insignificant difference in the two groups in 1st, 4th, and 5th. Platelets count showed significant increase in ANH group than controls in 3rd (P = 0.042) and had insignificant difference in the two groups in 1st, 2nd,4th, and 5th. aPTT had insignificant difference in the two groups in 1st, 2nd, 3rd, 4th and 5th. PT showed significant increase in ANH group than Controls in 2nd (P <0.001) and had insignificant difference in the two groups in 1st, 3rd, 4th, and 5th (**Table.2**).

Table 2. Hemoglobin, haematocrit, platelet count, aPTT and PT (s) of the studied groups

Hemoglobin (g/dl)	1st	2nd	3rd	4th	5th
ANH group (n = 50)	11.420±0.772	11.224±0.784	10.942±0.856	8.164±1.100	7.584±0.847
Control group (n = 50)	11.204±0.731	10.656±0.828	10.384±1.187	8.224±0.981	7.544±0.990
P value	0.154	0.001*	0.008*	0.774	0.829
Hematocrit (%)					
ANH group (n = 50)	41.20±6.82	39.82±6.67	39.24±6.93	33.18±6.52	32.42±6.62
Control group (n =	39.06±6.15	37.04±6.15	36.14±6.13	31.80±6.12	31.38±6.29

50)					
P value	0.102	0.033*	0.020*	0.278	0.422
Platelet count ($10^3/mm^3$)					
ANH group (n = 50)	270.08±77.05	264.36±76.87	258.12±77.41	213.66±70.91	200.08±73.74
Control group (n = 50)	278.34± 68.00	251.30±68.72	228.52±65.84	225.72 65.72	216.10 66.43
P value	0.571	0.373	0.042*	0.380	0.257
aPTT (s)					
ANH group (n = 50)	34.10±4.56	32.74± 4.53	31.56±4.53	32.50±4.64	32.54±4.60
Control group (n = 50)	33.38±4.96	31.92±5.03	31.90±5.00	31.86±4.92	31.82±5.03
P value	0.571	0.452	0.394	0.722	0.505
PT (s)					
ANH group (n = 50)	11.81±0.50	13.78±0.47	13.79±0.48	11.80±0.44	11.65±0.48
Control group (n = 50)	11.70±0.49	13.24±0.74	13.84±0.50	11.77±0.18	11.54±0.33
P value	0.264	<0.001*	0.567	0.720	0.184

Data are presented as mean ± SD, * Significant as P value <0.05, aPTT: activated partial thromboplastin time, PT: prothrombin time

Intraoperative data (cross clamp time (CCT), duration of the operation) had insignificant difference in the two groups (**Table.3**).

Table 3. Intraoperative data of the studied groups.

Variable *	ANH group (n=50)	Controls (n=50)	P value
CCT (min)	74.98 ± 33.34	72.26 ± 28.01	0.660
Duration of the operation (min)	264.6 ± 46.3	271.48 ± 53.45	0.493
Collected autologous blood (ml)	461.06 ± 50.6	---	---

*Data are presented as mean ± SD, CCT: cross clamp time

Patient transfused with PRBC, patient transfused with FFP, and chest tube drainage were significantly lower in ANH group than Controls (P = 0.017, 0.028 and <0.001 respectively). Patient transfused with PLTC and reexplored had insignificant difference in the two groups (**Table.4**).

Table 4. Perioperative allogenic blood transfusion and postoperative data of the studied groups.

Variable	ANH group (n=50)	Control group (n=50)	P value
Patient transfused with PRBC	4 (8%)	14 (28%)	0.017*
Patient transfused with FFP	7 (14%)	18 (36%)	0.028*
Patient transfused with PLTC	6 (12%)	10 (20%)	0.413
Chest tube drainage (ml)	519.4 ± 49.3	779.2 ± 42.37	<0.001*
Patients reexplored	2 (4%)	6 (12%)	0.269

FFP: fresh frozen plasma, PLTC: platelet concentrate, PRBC: packed red blood cell

Discussion

Several studies have investigated the effect of blood transfusion strategies, such as preoperative auto-blood donation, hypotensive anaesthesia, ANH, and intraoperative cell salvage system, on haemorrhage and bleeding in cardiac surgery patients **(Li et al., 2022)**.

In our study, haemoglobin and hematocrit were considerably greater in the ANH group than the controls on the second and third occasions, but had insignificant difference in first, fourth, and fifth occasions. Therefore, ANH was related with less RBC transfusions.

Multiple possible pathways may contribute to this positive effect. First, minimising the frequency of RBC transfusions may indirectly improve the prognosis of the patient. Red blood cell transfusions may worsen postoperative chest infection in CABG subjects **(Min et al., 2014)**. Second, the levels of interleukin-10 and neutrophil elastase as inflammatory mediators in ANH blood was lower than in auto-blood transfusion **(Kotake et al., 2009)**. Thirdly, due to the increase in blood viscosity caused by hemodilution, this may be responsible for a better oxygen supply-consumption equilibrium **(Licker et al., 2007)**.

(Xu et al., 2022) who conducted a randomised controlled experiment on a total of 1200 subjects receiving lumbar fusion surgery, reached the same conclusion. Subjects were divided into two distinct groups. A control and a group receiving preoperative auto-blood donation (PABD). In the PABD group, the quantity of allo-blood transfusion linked with increased haemoglobin and hematocrit levels was significantly lower than in the controls.

In this study, Platelets count, and PT were considerably greater in the ANH group than in the controls on the third occasion, but had insignificant difference on the first, second, fourth, and fifth occasions. The aPTT had insignificant difference in the two groups on the first, second, third, fourth, and fifth occasions.

(Crescini et al., 2018) discovered that the administration of ANH was linked with preserving platelets count and function during cardiac surgery. Similarly, the ANH group exhibited better preservation of platelets function following surgery.

In contrast, **(Mahoori et al., 2009)** observed no difference in platelets count between the controls and the ANH group.

Patients receiving PRBC transfusions, FFP transfusions, and chest tube drainage were considerably lower in the ANH group in comparison to controls. Those transfused with PLTC and subjects who were re-examined did not vary substantially.

In accordance with this conclusion, **(Crescini et al., 2018)** found that the administration of FFP and PRBCS was decreased in the ANH group compared to controls.

(Zhou et al., 2017) discovered no difference between intraoperative FFP and PLTC transfusions, as well as postoperative and total perioperative allo-transfusions.

It was single-center research; therefore, the results may differ in other locations. The sample size was rather modest. Brief follow-up period

Conclusions:

In this study, minimum ANH approach employing 6% HES 130/0.4 (Voluven) lowers the demand for allo-RBCs, fresh frozen plasma transfusion, PRBCs, and platelets in subjects having elective CABG surgery. Therefore, it reduces postoperative haemorrhage in adults undergoing heart surgery. Nonetheless, this approach had no effect on PLTC-transfused individuals.

Financial support and sponsorship: Nil

Conflict of Interest: Nil

References

- **Crescini W, Muralidaran A, Shen I, LeBlanc A, You J, Giacomuzzi C, et al.** (**2018**). The use of acute normovolemic hemodilution in paediatric cardiac surgery. Acta Anaesthesiologica Scandinavica (62)**:** 756-64.

- **Kotake Y, Yamamoto M, Matsumoto M, Yamada T, Nagata H, Morisaki H, et al.(2009**). Difference in autologous blood transfusion-induced inflammatory responses between acute normovolemic hemodilution and preoperative donation. Journal of Anesthesia (23)**:** 61-6.
- **L S-L. (2003**). Hematologic aspects of cardiac surgery. 54th Annual Refresher Course Lectures, clinical updates and basic science reviews. American Society of Anesthesiologists (5)**:** 422–8.
- **Li Y, Zhang Y, Fang X. (2022**). Acute normovolemic hemodilution in combination with tranexamic acid is an effective strategy for blood management in lumbar spinal fusion surgery. Journal of Orthopaedic Research (17)**:** 1-9.
- **Licker M, Sierra J, Kalangos A, Panos A, Diaper J, Ellenberger C. (2007**). Cardioprotective effects of acute normovolemic hemodilution in patients with severe aortic stenosis undergoing valve replacement. Transfusion (47)**:** 341-50.
- **Mahdy A M, Webster N R. (2004**). Perioperative systemic haemostatic agents. British Journal of Anaesthesia (93)**:** 842-58.
- **Mahoori A, Heshmati F, Noroozinia H, Mehdizadeh H, Salehi S, Rohani M. (2009**). Intraoperative minimal acute normovolemic hemodilution in patients undergoing coronary artery bypass surgery. Middle East Journal of Anesthesiology (20)**:** 423-9.
- **Min J, Nam K, Kim T, Kim H, Seo J, Hwang H, et al. (2014**). Relationship between early postoperative C-reactive protein elevation and long-term postoperative major adverse cardiovascular and cerebral events in patients undergoing off-pump coronary artery bypass graft surgery: a retrospective study. British Journal of Anaesthesia (113)**:**391-401.
- **Nistal-Nuño B.(2021**). Euthyroid sick syndrome in paediatric and adult patients requiring extracorporeal circulatory support and the role of thyroid hormone supplementation: a review. Perfusion (36)**:** 21-33.
- **Shander A, Rijhwani T S. (2005**). Clinical outcomes in cardiac surgery: conventional surgery versus bloodless surgery. Anesthesiology Clinics of North America (23)**:** 327-45.
- **Xu N, Zhang Y, Tian Y, Li B, Qiao H, Zhang X, et al.** (**2022**). Prospective study of preoperative autologous blood donation for patients with high risk of allogeneic blood transfusion in lumbar fusion surgery: a study protocol of a randomised controlled trial. BMJ Open (12)**:** 846-9.
- **Zhou Z-f, Jia X-p, Sun K, Zhang F-j, Yu L-n, Xing T, et al. (2017**). Mild volume acute normovolemic hemodilution is associated with lower intraoperative transfusion and postoperative pulmonary infection in patients undergoing cardiac surgery--a retrospective, propensity matching study. BMC anesthesiology (17)**:** 1-9.
- **Zisman, E., Eden, A., Shenderey, A., Meyer, G., Balagula, M., Ammar, R., et al.** *(***2009***).* The effect of acute autologous blood transfusion on coagulation dysfunction after cardiopulmonary bypass. European Journal of Anaesthesiology (26)**:** 868-73.