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Original Research

Percentage of hematocrit decrease after the initiation of cardiopulmonary bypass—clinical implications and affecting factors

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Decrease of patient's hematocrit level is a natural process which occurs during the initiation of cardiopulmonary bypass. To some extent it is a beneficial occurrence, but excessive hematocrit decrease can lead to many complications and increase patient's demand for blood transfusion. In this study authors investigated the causes and clinical implications of $\geq$30% hematocrit decrease after the initiation of cardiopulmonary bypass. Retrospective analysis of 172 patients undergoing elective cardiac surgery procedures was conducted. It was concluded that 30% or greater hematocrit decrease (comparing to preoperative level) after the initiation of cardiopulmonary bypass, is associated with an increased demand for blood transfusion. The most important factors influencing hematocrit decrease after the initiation of cardiopulmonary bypass proved to be: lower BMI, female gender, more advanced age and the usage of priming fluid of higher volume and lower osmolality.

Keywords

Cardiac surgery; Hematocrit decrease; Cardiopulmonary bypass

1. Introduction

Decrease in patient's hematocrit level is a natural process which occurs during the initiation of cardiopulmonary bypass and its primary cause is the volume of fluid that fills the perfusion pump (priming). In certain boundaries that is a beneficial occurrence, as the hemodilution decreases the viscosity of blood, thus improving its rheological properties and reducing vascular resistance. That allows to increase the organ perfusion and oxygen supply for the tissues [1]. However, if the hematocrit level is too low it may result in complications originating from poor tissue oxygenation, such as impaired renal function, increased risk of myocardial damage, perioperative stroke, prolonged time of mechanical ventilation or increased mortality [2, 3]. Additionally, an excessive decrease of hematocrit level creates the need for blood transfusion, which also results in increased complications risk [4–7].

Numerous articles were published concerning nadir hematocrit level during cardiopulmonary bypass [2, 8, 9]. The authors of this publication have yet been unable to find any articles analysing the percentage of hematocrit decrease after the initiation of cardiopulmonary bypass (compared to the initial value), its causes and clinical implications.

For the needs of this study hypothesis was formulated, that more significant decrease of hematocrit level in certain patients may be due to preoperative fluid overload. Such an overload might originate from slight or moderate renal failure, right heart ventricle dysfunction or tricuspid valve regurgitation. Sudden drop of pressure in vascular bed during cardiopulmonary bypass might result in seepage of fluid back into the vessels from the extravascular space, according to the Starling's equation [10]. Clearly any of the preceding factors in adequate intensity could cause a severe fluid overload with its many clinical manifestations, such as the lower extremities oedema, dilatation of jugular veins or transudation in pleura, pericardium and peritoneum. The problem, however, is to identify patients with mild water retention caused by some of the previously mentioned factors, but moderately intensified. Such patients will most probably demonstrate no clinical signs of fluid overload and thus no actions will be taken to remove that excessive fluid, such as forcing diuresis pharmacologically. Identifying those patients was one of the secondary objectives of this study.

The time period from the initiation of cardiopulmonary bypass to the first hematocrit measurement is critical, as patient's hematocrit level during that time is unknown. If it proves to be too low, it requires time to take actions in order to rise the hematocrit level. Accessible means in such situation are blood transfusion, pharmacologically forced diuresis and intraoperative hemofiltration. The possibility of foreseeing excessive hematocrit decrease, basing on the preoperative tests results, might enable to prevent such a decrease. There are of course equations designed for predicting

the drop in hematocrit level, based on the assumption of constant red cells amount and known perfusion volume (sum of the estimated blood volume and priming volume). However, the actual intravascular volume which determines hematocrit value (given the constant amount of red blood cells), is the resultant of numerous factors [11]. These factors are for example: pressure gradient within the capillaries (which determines the direction of fluid seepage between the intravascular and extravascular space), urine excretion, perspiration or patient's preoperative hydration state. For this reason the authors believe that the use of such predictive equations is limited, thus giving the ground for this investigation.

The main objective of this study was to assess the clinical implications of $\geq$30% hematocrit decrease (comparing to preoperative level), after the initiation of cardiopulmonary bypass and to identify the factors on which that decrease depends.

2. Materials and methods

The patients' data were retrospectively extracted from the database of the cardiac surgery clinic. 172 patients were enrolled into the study (137 males and 35 females), who underwent cardiac surgeries in a 12 months period. The inclusion criteria were: age 50–70 years and qualification for elective cardiac surgery proceudre with the use of cardiopulmonary bypass. The exclusion criterion was intraoperative blood transfusion.

All patients included in this study were in good clinical condition prior to the prodecure (ASA Physical Status Classification System: II). None of these patients required blood transfusion before the surgery. Preoperative hematocrit measurement was performed within 24 hours before the surgery.

The intraoperative hematocrit decrease was assessed referring to the preoperative hematocrit level and the first intraoperative measurement, which took place 10–15 minutes after the initiation of cardiopulmonary bypass. Hematocrit measurement was always performed prior to cardioplegia infusion, thus it did not influence the hematocrit value.

The patients were divided into the study group and the control group, based on the percentage of hematocrit decrease after the initiation of cardiopulmonary bypass. Patients who experienced 30% or greater hematocrit decrease were assigned to the study group (47 patients), while the rest of the patients formed the control group (125 patients). As there is no literature available analysing the percentage of hematocrit decrease after the initiation of cardiopulmonary bypass, a working hypothesis was assumed. The criterion of $\geq$30% hematocrit decrease after the initiation of cardiopulmonary bypass was established based on the data regarding the hypovolemic shock. Hypovolemic shock occurs after the loss of at least 1/3 of the blood volume. The pathomechanism of hypovolemic shock involves the loss of intravascular volume and subsequent organ malperfusion, thus it is not directly caused by the red blood cells loss and hematocrit decrease. The shock itself, however, is defined as an imbalance between oxygen delivery and tissue demand [12]. During cardiopulmonary bypass the priming fluid provides an adequate perfusion volume, but the oxygen-carrying capacity of the blood is decreased. Extrapolating from the fact that loss of 1/3 of the blood volume can cause shock, the authors hypothesised that decreasing the oxygen-carrying capacity of the blood by 30% (30% decrease of hematocrit level) can exceed the compensatory mechanisms of human body and cause tissue ischemia.

Two types of priming fluid were used in the patients included in this study. One type had the volume of 1500 mL and consisted of 500 mL of colloid solution, 250 mL of 20% mannitol and 750 mL of Ringer's solution (higher osmolality priming). The other priming solution had the volume of 1750 mL and consisted of 1500 mL of Ringer's solution and 250 mL of 20% mannitol (lower osmolality priming). The choice of priming solution was based on the perfusionist's preferences. There were no medical indications to favour one type of priming solution over the other.

Statistical analysis was conducted using the licenced Statistica 12.0 software (StatSoft, Inc. Tulsa, OK, USA). Evaluation of the normality of distribution of the analysed variables was conducted using Shapiro – Wilk test. The analysis of the quantitative data was conducted using U Mann – Whitney test. Qualitative data were analysed using the chi^2 test. If the subgroup size was insufficient, the Yates's correction was applied. The logistic regression was implemented for potentially distorting variables (sex, age, BMI). Significance level $p \leq 0.05$ was assumed.

3. Results

The patients' preoperative characteristics differed in terms of: age (64.43 $\pm$ 4.14 years in the study group vs 62.18 $\pm$ 4.84 years in the control group, $p = 0.006$), sex (there were 19 females in the study group – 40.43% vs 16 females – 12.8% in the control group, $p < 0.001$) and BMI (27.75 $\pm$ 4.36 in the study group vs 29.76 $\pm$ 4.62 in the control group, $p = 0.019$) – Table 1. The priming volume of 1750 mL has been used significantly more frequently in the study group (25 patients – 53.19% vs 39 patients – 31.2 % in the control group, $p = 0.008$). In the study group there was a lower percentage of patients who had diabetes (8 patients – 17.02% vs 40 patients – 32% in the control group), however this result did not obtain statistical significance ($p = 0.051$). The comparison of HbA1C hemoglobin levels revealed that blood sugar control was very similar in both groups (HbA1C = 6.04 $\pm$ 0.82 % in the study group vs 6.11 $\pm$ 0.87 % in the control group, $p = 0.485$).

A positive correlation was observed between the patient's age and inclusion in the study group ($r = 0.211$, $p = 0.005$), while there was a negative correlation between the inclusion in the study group and patient's weight ($r = -0.345$, $p < 0.001$). Preoperative parameters which could influence fluid retention were compared in both groups, in a search of the

Table 1. Patients' preoperative characteristics.

		Study group	Control group	*p*-value
		n = 47	n = 125	
Sex (n)	Male	28	109	**<0.001**
	Female	19	16	
Age [years] (mean ± SD)		64.43 ± 4.14	62.18 ± 4.84	**0.006**
BMI (mean ± SD)		27.75 ± 4.36	29.76 ± 4.62	**0.019**
NYHA, n (%)		I—3 (11.54%) II—11 (42.31%) III—11 (42.31%) IV—1 (3.85%)	I—6 (7.32%) II—40 (48.78%) III—34 (41.46%) IV—2 (2.44%)	0.863
LVEF (mean ± SD)		48.32 ± 9.75	47.43 ± 11.77	0.773
ES II (mean ± SD)		2.18 ± 2.38	2.08 ± 1.98	0.729
Hypertension, n (%)		31 (65.96%)	90 (72%)	0.439
Persistent AF, n (%)		15 (31.91%)	37 (29.6%)	0.768
Myocardial infarction, n (%)		16 (34.04%)	46 (36.8%)	0.737
Renal failure, n (%)		5 (10.64%)	13 (10.4%)	0.964
Stroke, n (%)		4 (8.51%)	8 (6.4%)	0.628
Other neurological conditions (transient ischemic attack, carotid arteries stenosis and mental disorder) , n (%)		9 (19.15%)	14 (11.2%)	0.172
Diabetes, n (%)		8 (17.02%)	40 (32%)	0.051
Neoplasm, n (%)		5 (10.64%)	14 (11.2%)	0.917
COPD, n (%)		1 (2.13%)	2 (1.6%)	0.814
CK-MB0 (mean ± SD)		35.32 ± 34.40	32.48 ± 28.73	0.593
eGFR0 (mean ± SD)		78.4 ± 20.68	83.62 ± 16.58	0.143
Ht0 (mean ± SD)		40.6 ± 3.62	41.55 ± 3.81	0.179

Legend: CK-MB0, initial plasma CK-MB concentration [IU/L]; COPD, chronic obstructive pulmonary disease; eGFR0, initial eGFR level [mL/min/1.73 m^2]; ES II, EuroSCORE II scale; Ht0, initial hematocrit level [%]; LVEF, left ventricular ejection fraction [%]; Persistent AF, persistent atrial fibrillation.

Table 2. Parameters potentially influencing fluid retention.

	Study group	Control group	*p*-value
	n = 47	n = 125	
Ht0 (mean ± SD)	40.6 ± 3.62	41.55 ± 3.81	0.179
eGFR (mL/min/1.73 m^2) (mean ± SD)	78.4 ± 20.68	83.62 ± 16.58	0.143
RVSP (mmHg) (mean ± SD)	33.26 ± 14.96	35.73 ± 17.6	0.416
TVP/R, n (%)	3 (6.38%)	17 (13.6%)	0.294

Legend: eGFR0, initial eGFR level; Ht0, initial hematocrit level [%]; RVSP, right ventricle systolic pressure; TVP/R, patients qualified for annuloplasty or replacement of the tricuspid valve.

cause of higher hematocrit decrease in the study group. No significant differences were found (Table 2).

It was noted that the first hematocrit level obtained during the cardiopulmonary bypass,was at the same time the lowest hematocrit value during the whole procedure in 88.02% of the study population (95.74% in the study group vs 85% in the control group, $p = 0.097$).

Postoperative outcomes in both groups did not reveal any statistically relevant differences (Table 3), apart from the perioperative myocardial infarction which occurred more frequently in the study group (6.38% vs 0.8% in the control group, $p = 0.030$). However, after adjusting the results for potentially distorting factors (sex, age, BMI), this result was proven to be statistically insignificant.

Patients from the study group more often required a blood transfusion (24 patients – 51.06% vs 33 patients – 26.4% in the control group; OR = 2.217 (1.030–4.772), $p = 0.042$). The percentage of nephrological complications which did not require hemodialysis was higher in the study group (12 patients – 25.53% vs 19 patients – 15.2% in the control group), although this result was not statistically relevant ($p = 0.116$). The patients included in this study underwent different kinds of cardiac surgery procedures (Table 4). The cardiopulmonary bypass time and aortic cross-clamp time were compared. Results were as follows: cardiopulmonary bypass time in the study group was 67.81 ± 31.91 minutes, comparing to 78.18 ± 34.33 minutes in the control group ($p = 0.059$) and aortic cross-clamp time in the study group was 44.77 ± 26.11 minutes, comparing to 51.7 ± 26.53 minutes in the control group ($p = 0.104$).

Table 3. Postoperative complications' incidence (unadjusted for sex, age and BMI).

	Study group	Control group	*p*-value
	n = 47	n = 125	
Nephrological complications[1] (not requiring dialysis), n (%)	12 (25.53%)	19 (15.2%)	0.116
Nephrological complications (requiring dialysis), n (%)	3 (6.38%)	11 (8.8%)	0.605
Postoperative stroke, n (%)	0 (0%)	4 (3.2%)	0.215
Other neurological complications[2], n (%)	12 (25.53%)	22 (17.6%)	0.244
Postoperative circulatory failure[3], n (%)	18 (38.3%)	40 (32%)	0.436
Perioperative myocardial infarction, n (%)	3 (6.38%)	1 (0.8%)	**0.030**
Postoperative AF, n (%)	12 (25.53%)	30 (24%)	0.835
Postoperative pneumonia, n (%)	7 (14.89%)	19 (15.2%)	0.960
Surgical reintervention, n (%)	2 (4.26%)	6 (4.8%)	0.879
Blood transfusion, n (%)	24 (51.06%)	33 (26.4%)	**0.002**
Amount of transfused blood units (mean ± SD)	2.83 ± 1.37	3.03 ± 2.07	0.898
Plasma transfusion, n (%)	15 (31.91%)	49 (39.2%)	0.378
Amount of transfused plasma units, n (%)	2.87 ± 0.35	3.06 ± 1.05	0.977
Platelet transfusion, n (%)	7 (14.89%)	23 (18.4%)	0.589
Amount of transfused platelet units (mean ± SD)	5.71 ± 0.49	7.65 ± 4.32	0.168
Mortality, n (%)	1 (2.13%)	3 (2.4%)	0.916
Postoperative mechanical ventilation time [hours] (mean ± SD)	12.49 ± 7.24	12.9 ± 11.34	0.215
HtCPB (mean ± SD)	26.43 ± 2.76	33.55 ± 4.51	**<0.001**
HtCPB/Ht0 (mean ± SD)	0.65 ± 0.04	0.81 ± 0.07	**<0.001**
CRPMAX (mean ± SD)	252.47 ± 76.52	228.68 ± 68.66	0.137
CK-MBMAX (mean ± SD)	76.53 ± 122.9	58.89 ± 30.25	0.970
Hemofiltration, n (%)	11 (23.4%)	25 (20%)	0.630
Volume of hemofiltration [mL] (mean ± SD)	1659.09 ± 843.45	2108 ± 687.34	0.115
Fluid balance from the operating room [mL] (mean ± SD)	367.02 ± 790.24	347.43 ± 997	0.799

Legend: CK-MBMAX, maximal plasma CK-MB concentration [IU/L]; CRPMAX, maximal plasma CRP concentration [mg/L]; HtCPB, hematocrit level after the initiation of cardiopulmonary bypass [%]; HtCPB/Ht0, proportion of hematocrit level during cardiopulmonary bypass and initial hematocrit level; Postoperative AF, postoperative atrial fibrillation.
[1]Oliguria or anuria which did not meet criteria for introducing renal replacement therapy. [2]Consciousness disorders, psychotic syndrome. [3]Necessity of supporting the circulatory system with continuous adrenaline or noradrenaline infusion.

Table 4. Surgical procedures performed in the study population.

	Study group	Control group	*p*-value
	n = 47	n = 125	
CABG, n (%)	29 (61.7%)	53 (42.4%)	**0.024**
Valvular procedures, n (%)	7 (14.89%)	23 (18.4%)	0.753
Complex procedures and others, n (%)	11 (23.4%)	49 (39.2%)	0.053

Legend: CABG, coronary artery bypassing graft.

Coronary artery bypassing graft (CABG) procedure was performed more frequently in the study group (29 patients – 61.7% vs 53 patients – 42.4% in the control group, $p = 0.024$), while complex procedures were performed more frequently in the control group (49 patients – 39.2% vs 11 patients – 23.4% in the study group, $p = 0.053$), even though the last result was not statistically relevant.

4. Discussion

The primary aim for this study was to assess the clinical implications of ≥30% hematocrit decrease (comparing to preoperative level), after the initiation of cardiopulmonary bypass and to identify the factors, on which that decrease depends. Analysis of the collected data revealed that ≥30% hematocrit decrease is associated with an increased demand for red blood cells transfusion. The most significant factor influencing hematocrit decrease after the initiation of cardiopulmonary bypass proved to be patients BMI, what is consistent with the results of similar studies [2, 9, 13]. The higher hematocrit decrease is also associated with female gender (which may be related to lower estimated blood volume in females [14]), more advanced age of the patients and the usage of priming fluid of higher volume and lower osmolality.

This simple characteristics of patients predisposed to the higher hematocrit decrease enables to identify these patients more efficiently and thus to take actions, aimed at preventing the associated complications.

The population of patients included in this study was smaller than in similar studies conducted in the other facilities [2–4]. None of these publications, however, referred to the hematocrit level after the initiation of cardiopulmonary bypass, but to its lowest value during the whole procedure. The hematocrit level which sets after the initiation of cardiopulmonary bypass is crucial for several reasons. Firstly, the new hematocrit level is unknown until the first intraoperative measurement is performed and consequently it is unknown if the patient has sufficient oxygen supply for the tissues. Secondly, if the new hematocrit level proves to be too low, it requires time to take actions in order to raise that level. Moreover, it was proven in this study that the lowest hematocrit value during the whole procedure (which artibutes to the occurrence of complications [2–4]), is in most cases the first hematocrit level after the initiation of cardiopulmonary bypass. For these reasons the advantage of this study is its focusing on the critical time period between the initiation of cardiopulmonary bypass and the first hematocrit measurement.

The results of this study did not indicate any relevant differences in factors which could influence fluid retention in both groups. Nevertheless, a significantly greater hemodilution was observed in patients who received the priming fluid of higher volume and lower osmolality. This seems to support the hypothesis of fluid overload in the study group. Such hypothesis finds a substantial confirmation in the pathogenesis of formation of transudation, which is best illustrated by the Starling's equation [10]. In this study authors' opinion, it is worth to further investigate this subject since there are simple methods of removing excessive fluid from patient's organism, such as pharmacologically forced diuresis or intraoperative hemofiltration. This matter requires further, prospective studies.

The higher percentage of nephrological complications not requiring dialysis in the study group may indicate poorer preoperative kidney function. This correlates with a lower eGFR0 in this group and supports the hypothesis of fluid overload. The higher percentage of these complications may also originate from the more severe ischemic damage to the kidneys in the study group patients, resulting from higher hematocrit decrease.

The differences in kinds of procedures performed in the study group and the control group do not seem to be relevant, considering that there were no statistically significant differences in the cardiopulmonary bypass time and the aortic cross-clamp time in both groups.

As the main cause of hemodilution is the volume of priming fluid, the logical solution is to reduce that volume in patients endangered with excessive hematocrit decrease. The innovative mini – ECC (minimal extracorporeal circulation) [15] technique could be applied here. It allows to reduce the tubular length and thus to reduce the required priming fluid volume. Monitoring the fluid balance in the preoperative period, is another action that can be undertaken in order to control the fluid management, in patients qualified for surgeries with the use of cardiopulmonary bypass. Confronting the preoperative fluid balance value with patient's clinical condition, may provide the physician with vital pointers about the fluid administration during the procedure.

5. Conclusions

The 30% or greater hematocrit decrease (comparing to preoperative level) after the initiation of cardiopulmonary bypass is associated with an increased demand for blood transfusion. The most important factors influencing hematocrit decrease after the initiation of cardiopulmonary bypass are low BMI, female gender, more advanced age of the patients and the usage of priming fluid of higher volume and lower osmolality.

Author contributions

JU was the initiator and main investigator in this study, he also wrote this article. AB contributed to conceptualization of this study, provided meritorical consult and contributed to editing of this article. AS and ZK provided statistical analysis. ML provided part of the data for this study and meritorical consult.

Ethics approval and consent to participate

Due to the retrospective character of this study and full personal data confidentiality, the patient's consent was not required. Study was performed with accordance to the Good Clinical Practice guidelines.

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Conflict of interest

The authors declare no conflict of interest.

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