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Immediate postoperative transfusions after total hip arthroplasty: retrospective analysis comparing two methods of predicting post-transfusion hematocrit

Ankstyvos pooperacinės transfuzijos po klubo sąnario endoprotezavimo operacijų: dviejų potransfuzinio hematokrito prognozės metodų retrospektyvus palyginimas

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Background / objective

Total hip arthroplasty is associated with significant bleeding, which continues through early postoperative hours. Choosing the amount of packed red blood cells (PRBC) for transfusion to reach hematocrit targets is challenging. We compared two methods of predicting post-transfusion hematocrit: the new – Homeostatic Blood States' Method, patent pending – USA, referred to as method A, and the conventional "Rule of Thumb" (Habibi et al.) referred to as method B.

Patients and methods

The retrospective investigation of immediate postoperative blood transfusions included sixteen adult patients who were ASA physical status II, five of them males and eleven females, mean age 64.75±10.427 (range, 45–79 yr) after total hip arthroplasty. Patients received routine procedures: venous blood samples taken just before starting transfusion (20 minutes after stopping all infusions), then 20 minutes after transfusion. Eight patients received one PRBC unit, others received two. The amount of wound drainage was measured. Perioperative infusion and transfusion data, timing, blood test results, urine output and drainage amounts were recorded using a new type of chart – HBS Nomogram (Copyright © 2005 by Audrius Andrijauskas). We calculated post-transfusion hematocrit predicted by both methods. Method A deploys mathematical formulas for calculating hematocrit-specific homeostatic circulating erythrocyte mass. Corrections for simultaneous blood loss were applied to calculations by method A protocol A-cor. Corrections are not applicable to method B, which accounts only for units transfused: protocol B1 predicts 3%, B2 4% and B3 5% hematocrit increase.

Results

Method B-1 ($p = 0.019$) predicted hematocrit better than method A, but method A did it better than B-2 ($p = 0.04$), B-3 ($p < 0.0001$) and B-1 ($p < 0.009$), and method A-cor was the best, predicting better than A ($p < 0.0001$), B-1 ($p < 0.009$), B-2 ($p < 0.0001$) and B-3 ($p < 0.0001$). Method B does not account for simultaneous bleeding, and there are no criteria for choosing a proper protocol – B1, B2 or B3, therefore the overall advantage was given to method A and its modification A-cor.

Conclusion

The new method is a promising tool for transfusion amount selection, therefore further investigations are purposeful.

Key words: bleeding, blood, hematocrit, transfusion, new method, nomogram

Įvadas / tikslas

Klubo sąnario endoprotezavimo operacijų metu ir ankstyvuoju pooperaciniu laikotarpiu vyksta reikšmingas kraujavimas. Sudėtinga parinkti perpilamos eritrocitų masės kiekį, siekiant hematokrito padidėjimo. Buvo palyginti du metodai, kurie padeda prognozuoti potransfuzinį hematokritą: naujas homeostazinis kraujo būklių metodas, apsaugotas parengtinio JAV patento, toliau vadinamas A metodu, ir praktikoje labai dažnai naudojamas apytikslės taisyklės (Habibi et al.) metodas, arba B metodas.

Ligoniai ir metodai

Retrospektyviai ištirta 16 ankstyvųjų pooperacinių kraujo perpylimų, atliktų ASA-2 fizinės klasės pacientams po klubo sąnario endoprotezavimo operacijų: iš jų 5 vyrams ir 11 moterų, kurių amžiaus vidurkis 64,75±10,427 (nuo 45 iki 79 metų). Visiems buvo taikytas toks pat rutininis gydymo reglamentas: veninio kraujo hematokrito tyrimai paimti tiesiogiai prieš transfuzijos pradžią (20 min. po infuzijų sustabdymo), vėliau – 20 min. nuo transfuzijos baigimo. Aštuoniems buvo perpiltas vienas eritrocitų masės vienetas, o kitiems aštuoniems – du vienetai. Perioperaciniai infuzinės terapijos ir transfuzijų duomenys, tyrimų rezultatai, diurezė ir netekimas per drenus buvo registruojami naujo tipo apskaitos lape – HBS nomogramoje (Autorystės teisės © 2005, Audrius Andrijauskas). Naudojant abu metodus apskaičiuotas prognozuojamas potransfuzinis hematokritas. Metodu A matematiškai apskaičiuojamas hematokrito vertėms būdingas homeostazinis cirkuliuojančios eritrocitų masės tūris. Skaičiavimų korekcija atlikta tik metodo A (A-cor), atsižvelgiant į transfuzijos metu vykusį nukraujavimą per žaizdos drenus, nes antrasis metodas tokiai korekcijai nepritaikytas. Metodo B yra trys prognoziniai protokolai: B1 numato hematokrito padidėjimą trimis hematokrito procentais (3%), B2 – 4% ir B3 – 5%.

Rezultatai

Metodu A prognozuojama prasčiau negu B1 ($p = 0,019$), bet geriau negu B-2 ($p = 0,04$) ir B-3 ($p < 0,0001$), o A-cor buvo tiksliausia, lyginant su A ($p < 0,0001$), B-1 ($p < 0,009$), B-2 ($p < 0,0001$) ir B-3 ($p < 0,0001$). Metodas B neatsižvelgia į transfuzijos metu vykstantį nukraujavimą ir neturi kriterijų, kurie nurodytų, kada ir kurį prognozinį protokolą reikėtų naudoti. Dėl to ne tik modifikuotu metodu A-cor, bet ir metodu A potransfuzinis hematokritas prognozuojamas geriau negu metodu B.

Išvada

Naujasis metodas gali būti naudingas parenkant perpilamos eritrocitų masės kiekį, todėl tikslinga jį plačiau ištirti.

Reikšminiai žodžiai: kraujavimas, kraujas, hematokritas, transfuzija, naujas metodas, nomograma

Introduction

The lack of simple, but at the same time objective dynamic methods for defining blood component resuscitation measures is an ongoing deficiency. It makes blood transfusion amount selection strategies complex and challenging, frequently leading to overzealous transfusion practices. Overestimated blood transfusions are a common result in clinical practice. It negatively effects the overall cost of treatment, having in mind the increasing cost of blood products (according to Cremieux the cost of one PRBC unit in USA was 646-717 USD in year 2003) [1]. Post-transfusion blood tests fre-

quently reveal overestimated transfusion volumes leading to inappropriately high hemoglobin concentrations [2]. The draft of the new American Society of Anesthesiologists (ASA) Guidelines for transfusion of allogeneic red blood cells or autologous blood has defined that adequate quantities of red blood cells (RBCs) should be transfused to maintain organ perfusion [3]. However, these draft recommendations do not offer new tools for tailoring transfusion amounts.

Knowing the circulating blood volume (BV) would be of great value, however, direct methods of measuring red cell mass (RCM) have a limited clinical applicability due to steady state requirements, complicity, radiation hazards, mostly invasive character, limited onsite availability, lack of precision and reliability along with labor and time consuming patterns. Ideal blood (IBV) and plasma volume (IPV) can be theoretically estimated by formulas, like the widely preferred formula by Nadler et al. [4] which utilizes two individual specific physical variables – body height and weight. Pearson et al. have demonstrated that calculations based solely on body weight were inappropriate, particularly because approximately half of the male and female populations could be regarded as overweight or obese [5].

In the current clinical environment, the amount of RCM and plasma volume (PV) is approximate estimates obtained by indirect parameters such as Hct or hemoglobin concentration (Hb). Simplified blood transfusion guidelines based on Hct and Hb are helpful, especially in urgent situations. The rule of thumb as suggested by Habibi et al. is that the administration of one unit of packed RBCs (PRBC) will increase hematocrit by 3–5% [2]. This method is referred to as method B in the present study. However, a common dilemma occurs when the desired hematocrit (Hct) increase is 9% and more: should it be 2 or 3 units of PRBC to be transfused for achieving 9% Hct increase? In fact, clinical practice is currently the basis for most schemes used.

Overestimated transfusions induce unnecessary risk for the patient and raise the cost of treatment. More precise tools and guidelines are needed to optimize blood transfusions. The recently introduced new method addresses these deficiencies. It is part of the new theory – the Homeostatic Blood States' theory (HBS Theory), which has been developed by one of the authors. The new method (HBS Method, patent pending – USA) is introduced in part for the first time in this article and referred to as method A. Total hip arthroplasty is associated with a significant bleeding, which continues through early postoperative hours [6]. The goal was to determine which method – A or B – was better in predicting post-transfusion Hct in patients receiving immediate postoperative blood transfusions after total hip arthroplasty.

Patients and methods

Records of immediate postoperative blood transfusions administered after total hip arthroplasty were retrospectively investigated in sixteen patients who were ASA physical status II, five of them males and eleven females, mean age 64.75±10.427 (range, 45–79 yr). Patients were selected from the latest list of those operated on by the same two surgery and anaesthesia teams, excluding only patients who were physical status other than ASA II. All patients had undergone similar routine procedures. Baseline venous blood hematocrit (tHct) tests were obtained just before starting PRBC transfusion 20 minutes after stopping maintenance rate intravenous crystalloid infusion for equilibration of plasma dilution. Blood samples were obtained through peripheral intravenous catheter after flushing it with 3 ml of withdrawn blood, which was later returned to the vein. Post-transfusion hematocrit (ptHct) tests were obtained 20 minutes after commencing transfusion and before restarting crystalloid infusion. Eight patients received transfusions of one PRBC unit, while another eight received two units. The standard PRBC transfusion rate was one unit in 30 minutes. All blood Hct tests have been processes by the same laboratory equipment: hematological analyzer COULTER®HmX, Beckman Coulter, Inc. USA, 2004. The amount of wound drainage was measured before and after the transfusion. Criteria of transfusion decision-making were not investigated. Perioperative infusion and transfusion data, timing, blood test results, urine output and drainage amounts were recorded on the new type of chart – HBS Nomogram (Copyright © 2005 by Audrius Andrijauskas) (Figure 1). This chart includes HBS Graphics – a new graphical method for recording

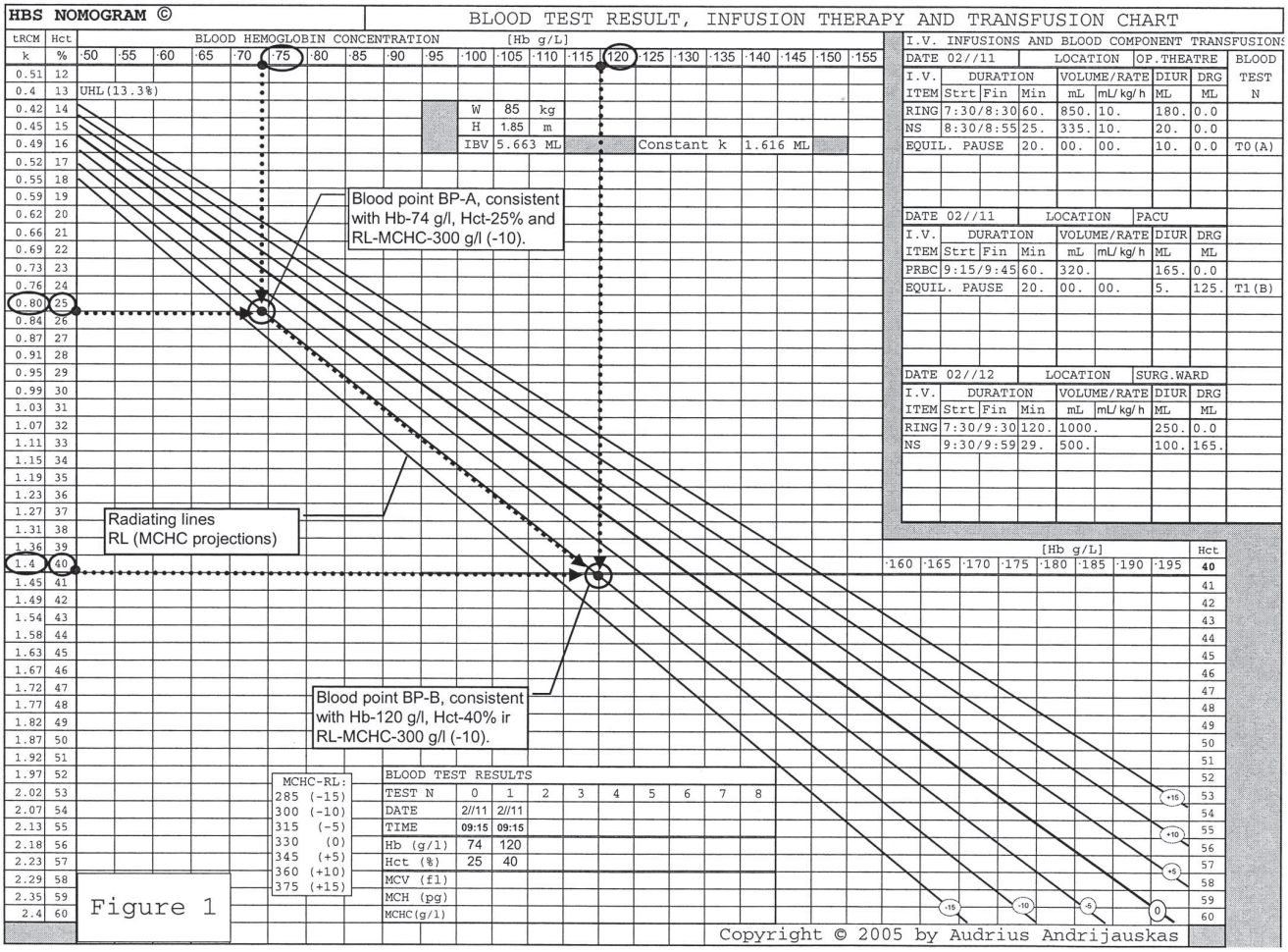

Figure 1. The HBS Nomogram

blood Hb, Hct and mean corpuscular hemoglobin concentration (MCHC), which also enables evaluation of osmolality (Osm) dynamics in plasma [7].

The predicted post-transfusion Hct values were compared as calculated by two methods: method A (HBS Method, Andrijauskas A) and method B (Rule of thumb, Habibi et al.). Calculation corrections that account for the amount of simultaneous blood loss through drainage were applied only to method A. The corrections are referred to as the modified method A or method A-cor. Blood loss corrections are not applicable to method B.

Method A

This method is based on the new HBS Theory which describes hematocrit-specific homeostatic target states of blood. According to the theory, the body strives to maintain circulating RCM and consequently the Hct value specific homeostatic target blood (tBV) and plasma (PV) volume. The overall homeostatic setting that maintains tBV as part of the homeostatic target is referred to as target state. Target state is characterized by target RCM, tBV and tPV in combination with tOsm and target mean corpuscular volume (tMCV), which correlates with target MCHC (tMCHC).

The HBS Theory considers that in the setting of normal sympathetic tone only extremely high-rated isoosmotic crystalloid infusions can residually override the target Hct value, meanwhile it is much more vulnerable to dehydration. When tRCM changes due to a loss of RBCs or their introduction into circulation, target states maintain different tHct values. However, tBV and tPV accommodate to fit the specific circulating tRCM volume as follows: the tBV homeostatically decreases with decreasing tRCM. This concept is supported by a recent volume turnover study by Dr.

Norberg and his colleagues on hemorrhaged sheep, who have not found evidence of endogenous plasma expansion exceeding its loss in order to restore the lost erythrocyte mass and prehemorrhage blood volume. Such findings suggest that homeostasis prevents excessive plasma expansion during erythrocyte loss by means of blood volume reduction and fluid extravasation.

The HBS Theory describes target states as Hct-specific target values – tBV, tPV, tRCM and tOsm – that maintain equal absolute deviations from IBV and IPV. Meanwhile the latter are homeostatically maintained as target state's parameters only at Hct of Ideal Total Match (ITM), which is considered to be 40%. This concept is based on the discovery that target states at physiologically critical limits of hematocrit, which are 13.3% and 60%, maintain equal absolute sum deviations from the BV and PV values that are inherent only to tHct-40%. That sum deviation is referred to as Constant k, which is equal to 0,3·IBV. Mathematically the target state is described in the formulas below:

$$tBV = 0.5 \cdot (IBV + IPV + tRCM), \quad [1]$$

where IBV – ideal blood volume – can be calculated by any preferred method and tRCM is tHct specific, meanwhile IPV (ideal plasma volume) is originally described as follows:

$$IPV = IBV \cdot (1 - tHct_{ITM}), \quad [2]$$

where Hct_{ITM} is hematocrit of the Ideal Total Match, which is considered universally equal to 0.4; consequently:

$$IPV = 0.6 \cdot IBV. \quad [3]$$

The formula for calculating tRCM is as follows:

$$tRCMn = Cn \cdot (IBV + 0.6 \cdot IBV \cdot (1 - tHct_n)^{-1})) \cdot \cdot Hct_n, \quad [4]$$

where tRCM is the red cell mass in target state at target Hct value n, and Cn is the coefficient inherent to the target Hct value n:

$$Cn = ((IBV + IPV) \cdot (2 - Hct_n)^{-1}) \div \div (IBV + IPV \cdot (1 - Hct_n)^{-1}) = = ((IBV + 0.6 \cdot IBV) \cdot (2 - Hctn)^{-1}) \div \div (IBV + 0.6 \cdot IBV \cdot (1 - Hct_n)^{-1}). \quad [5]$$

Consequently, the predicted post-transfusion eHctA value was calculated by method A as follows:

$$eHctA = (tRCMn + PRBC) \cdot tBVx^{-1} = = 2 \cdot (tRCMn + PRBCx) \cdot (tRCMn + + PRBC + 1.6 \cdot IBV), \quad [6]$$

where tRCMn is the red cell mass at pre-transfusion Hct value n, assuming that the homeostatic target state is being maintained at the time of blood sampling, which has been obtained after a 20 minutes long equilibration pause of maintenance rate isotonic crystalloid infusion, and PRBC is the volume of transfused packed red blood cells.

The predictive values of post-transfusion Hct_x were calculated by the formulas [4], [5] and [6], where patient physical state specific IBV value was calculated by Nadler's formula:

$$IBV = 0.3669 \cdot H^3 + 0.03219 \cdot W + 0.6041, \quad [7]$$

where H is body height in meters and W is body weight in kilograms.

The measured and calculated results are presented in Table.

Method A-cor (Modified method A)

An appropriate correction to calculations by method A was made accounting for the recorded simultaneous blood loss through the wound drainage during the transfusion:

$$eHctA\text{-}cor = 2 \cdot (tRCMn + PRBC - cLEM) \cdot (tRCMn - cLEM + PRBC + 1.6 \cdot IBV), \quad [8]$$

where cLEM is the calculated loss of erythrocyte mass through the wound drainage. It is calculated as follows:

$$cLEM = MDM \cdot dmHct, \quad [9]$$

where MDM is the measured drainage mass and dmHct is the Hct of the drainage mass. However, measuring dmHct is not a routine practice in our institution, therefore a pilot test for dmHct had been made. It revealed that dmHct was in the midst of the interval between the measured baseline (tHct) and post-transfusion (ptHct) values. Therefore an assumption of dmHct as the mean value of tHct and ptHct was made. Thus, the calculation of the corHct value was made by calculating the cLEM value:

$$cLEM = 0.5 \cdot MDM \cdot (ptHct - tHct). \quad [10]$$

Table. The numeric data deployed for comparing the two methods of predicting the post-transfusion hematocrit

	PATIENT SPECIFIC					POST-OPERATIVE PRBC						BLOOD	BLOOD	BLOOD LOSS				METHOD A									METHOD B		
	PHYSICAL PARAMETERS					TRANSFUSION PROTOCOL						TEST TIMING	HEMATOCRIT	DURING TRANSFUSION				CALCULATED VALUES									CALCULATED VALUES		
Row	GENDER		Age	H	W	PRBC		Duration		TU	Day	Time interval		tHct	ptHct	MDM	dmHct	cLEM		k	tRCM		ptRCM		cPRBC		eHctA	eHctA-cor	eHctB-1	eHctB-2	eHctB-3
N	M	F	Yrs	m	kg	ml	k	30'	60'	units	Nr	<60min	>12 h	%	%	ml	%	ml	k		ml	k	ml	k	ml	k	%	%	%	%	%
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
1		1	52	1.68	65	243	0.19	1		1	0	1		33.7	36.1	230	35	80	0.06	1,267	1,438	1.14	1,563	1.23	125	0.10	38.3	36.8	36.7	37.7	38.7
2	1		47	1.76	86	203	0.13	1		1	0	1		35.0	38.9	135	37	50	0.03	1,534	1,823	1.19	2,076	1.35	252	0.16	38.2	37.4	38.0	39.0	40.0
3		1	72	1.75	100	193	0.12	1		1	0	1		36.9	39.2	140	38	53	0.03	1,653	2,096	1.27	2,258	1.37	162	0.10	39.6	38.9	39.9	40.9	41.9
4		1	61	1.58	86	213	0.15	1		1	0	1		31.2	36.3	115	34	39	0.03	1,376	1,425	1.04	1,710	1.24	285	0.21	35.0	34.4	34.2	35.2	36.2
5	1		61	1.70	79	233	0.16	1		1	0	1		35.2	37.7	215	36	78	0.06	1,413	1,692	1.20	1,840	1.30	148	0.10	39.1	37.8	38.2	39.2	40.2
6		1	73	1.60	83	233	0.17	1		1	0	1		30.9	33.4	205	32	66	0.05	1,364	1,397	1.02	1,533	1.12	136	0.10	35.1	34.0	33.9	34.9	35.9
7		1	67	1.59	78	223	0.17	1		1	0	1		34.9	37.8	125	36	45	0.03	1,310	1,552	1.18	1,711	1.31	159	0.12	38.9	38.1	37.9	38.9	39.9
8		1	74	1.60	60	193	0.17	1		1	0	1		32.6	34.0	275	33	92	0.08	1,153	1,258	1.09	1,323	1.15	65	0.06	36.7	34.8	35.6	36.6	37.6
9		1	68	1.64	93	406	0.27		1	2	0	1		35.6	40.8	280	38	107	0.07	1,489	1,807	1.21	2,139	1.44	332	0.22	41.9	40.3	41.6	43.6	45.6
10	1		45	1.70	80	423	0.30		1	2	0	1		39.0	47.0	120	43	52	0.04	1,422	1,931	1.36	2,449	1.72	518	0.36	45.6	44.8	45.0	47.0	49.0
11		1	79	1.50	89	406	0.30		1	2	0	1		39.9	44.8	280	42	119	0.09	1,344	1,877	1.40	2,174	1.62	297	0.22	46.5	44.6	45.9	47.9	49.9
12		1	74	1.62	70	416	0.33		1	2	0	1		34.7	39.6	320	37	119	0.09	1,261	1,484	1.18	1,745	1.38	261	0.21	42.4	40.3	40.7	42.7	44.7
13	1		55	1.81	95	353	0.21		1	2	0	1		35.4	38.7	285	37	106	0.06	1,667	2,009	1.21	2,241	1.34	232	0.14	40.4	38.9	41.4	43.4	45.4
14		1	66	1.60	79	386	0.29		1	2	0	1		38.3	42.0	385	40	155	0.12	1,328	1,762	1.33	1,978	1.49	215	0.16	44.8	42.3	44.3	46.3	48.3
15	1		76	1.83	84	378	0.24		1	2	0	1		43.5	48.6	105	46	48	0.03	1,586	2,471	1.56	2,854	1.80	383	0.24	48.5	47.9	49.5	51.5	53.5
16		1	66	1.50	60	476	0.44		1	2	0	1		35.5	41.1	420	38	161	0.15	1,077	1,303	1.21	1,562	1.45	259	0.24	45.5	42.3	41.5	43.5	45.5

M- male gender
F- female gender
W- body weight
H- body height

PRBC- actual volume of transfused packed RBC
k- volume value expressed in fractions of Constant k
TU- units of transfused packed red blood cells
NA- data not available
Day- postoperative day (0- means day of surgery)

tHct- measured baseline hematocrit
ptHct- post-transfusion hematocrit
MDM- measured drainage mass volume
dmHct- drainage mass hematocrit
cLEM- calculated loss of erythrocyte mass

k- Constant k
tRCM- pretransfusion volume of circulating PRBC
ptRCM- post-transfusion volume of RBC
ctPRBC- calculated volume of transfused PRBCs

eHctA- expected Hct after transfusion of PRBCs volume (column N7)
eHctA-cor- the same, but corrected to loss of RBC volume (column N19)
eHctB1- expected Hct value, assuming 3% increase per PRBC unit
eHctB2- expected Hct value, assuming 4% increase per PRBC unit
eHctB3- expected Hct value, assuming 5% increase per PRBC unit

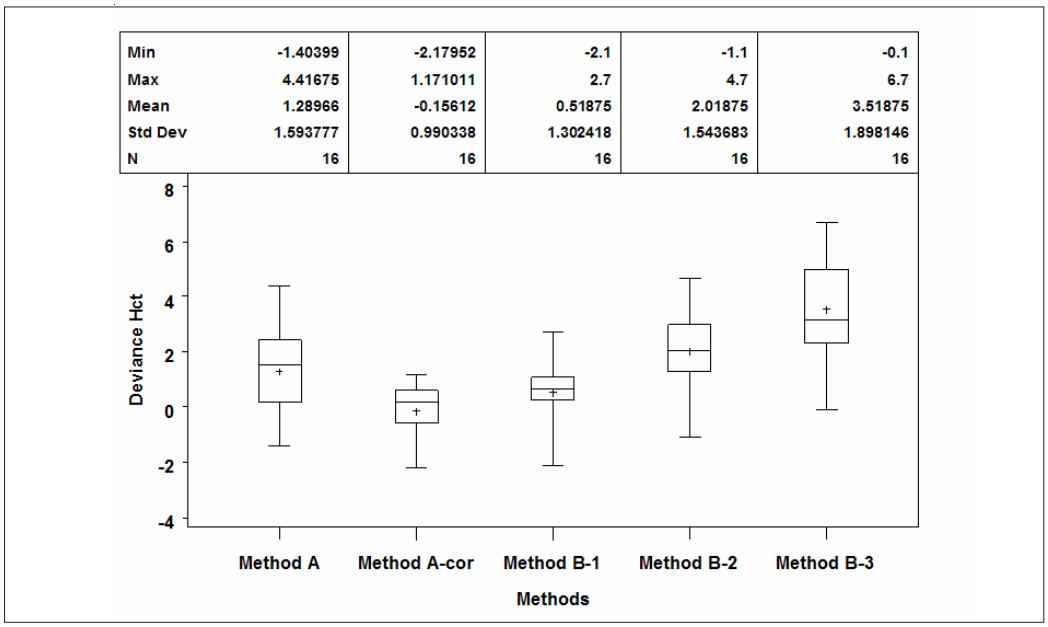

Figure 2. The chart of statistic analysis

Method B

Method B accounts only for transfused PRBC units: the rule of thumb predicts that administration of one unit of PRBC will increase Hct by 3–5%. Therefore three different protocols of this method were determined: protocol B1 predicted a 3%, B2 4% and B3 5% hematocrit increase. The predicted values were calculated as follows:

$$eHctB1 = tHct + 3 \cdot NU, \quad [11]$$

$$eHctB2 = tHct + 4 \cdot NU, \quad [12]$$

$$eHctB3 = tHct + 5 \cdot NU, \quad [13]$$

where eHct-B1 (B2, B3) is the predicted (expected) post-transfusion Hct value, tHct is the baseline or the pre-transfusion Hct value, and NU is the number of transfused PRBC units.

Results

Statistical analysis was performed with SAS/STAT® 9.0. Continuous variables were analyzed and presented as mean ± SD. The normal distribution of the collected data was first verified by the Kolmogorov–Smirnov test. A hypothesis on distribution normality for all variables wasn't rejected, therefore the parametric t test for paired samples was used to compare the means of deviance Hct between method A and method B. A value of $p = 0.05$ was considered to be significant in tests. The difference between all the methods was significant: method B-1 ($p = 0.019$) predicted hematocrit better than method A, but method A did it better than B-2 ($p = 0.04$), B-3 ($p < 0.0001$) and B-1 ($p < 0.009$), and method A-cor was the best, predicting better than A ($p < 0.0001$), B-1 ($p < 0.009$), B-2 ($p < 0.0001$) and B-3 ($p < 0.0001$) (Figure 2).

Considering that method B has no criteria of choosing a proper protocol – B1, B2 or B3 – and does not account for simultaneous bleeding during the transfusion, we concluded that both method A and its modification A-cor predicted post-transfusion hematocrit better than method B.

Discussion

Blood component resuscitation is an integral part of perioperative care. There is a significant advance in determining PRBC transfusion triggers, but it is not the case when it comes to choosing the right amount of transfusion in order to reach the goals of hematocrit increase. To the best knowledge of the authors, none of the existing methods of predicting post-transfusion hematocrit increase take into account the volume of transfused PRBC, especially with a simultaneous blood loss. Meanwhile the new method – the HBS Method as part

of HBS Theory – accounts for it, and also it argues a different hematocrit increase efficacy of the same transfusion amount applicable to different pre-transfusion Hct values. This method is closely related to the theories and research findings in the field of intravenous fluid resuscitation. This approach makes the new method essentially different from the existing art, because blood component transfusion is always an integral part of IV fluid administration, therefore it should be taken into account in the administration of transfusion therapy. Such approach is reflected in the synchronized infusion therapy and blood component transfusion monitoring method – the HBS Graphics [7], which is part of our new chart for perioperative records – HBS Nomogram recently introduced into practice (Figure 1). It complements two coordinate systems – horizontal Hb and vertically descending Hct – with incorporated derivative trends of mean corpuscular hemoglobin concentration (MCHC) referred to as radiating lines (RL). Blood test derived Hb and Hct values are graphically spotted there as "Blood Points (BP)" located on a proper case-specific RL projection, i.e. BP-B derived from Hb-120 g/l and Hct-40% is located in RL-MCHC-300 g/l encoded as RL-(-10). Isoosmotic plasma dilution and erythrocyte volume shifts follow radiating lines, while osmotic shifts induce inter-trend shifts. Target Hct specific nomographic values of circulating RBC volume (tRCM) are shown in the vertical numeric column adjacent to the standard diagrams of the HBS Graphics. The target Hct-specific tRCM volumes in the nomogram are expressed in fractions of individual physical data specific unit the Constant k. These values are put on the every percent level of the physiological Hct range (13.3 to 60%) in the Nomogram tRCM column. The Constant k is the fraction of the calculated ideal blood volume, 0.3·IBV, which is the body weight and height or estimated body surface specific. It makes the tRCM values individual, too. The first thing to do when using the HBS Method with the aid of HBS Nomogram is to calculate the individual ideal blood volume. It can be done by means of any method or formula preferred by the user. Then the individual value of Constant k can be easily derived and applied to calculation of target Hct specific tRCM values. The amount of PRBC transfusion targeted to reach the proper tHct, tHb or tRCM is then easily calculated, i.e. in Figure 1 the pre-transfusion values Hb-74(g/l), Hct-25% and MCHC-300 (g/l) spotted as BP-A (blood test result T0) need to be raised by PRBC transfusion up to Hb-120(g/l), Hct-40% and MCHC-300 (g/l) spotted as BP-B in HBS Graphics; the amount of PRBC transfusion is the difference of pre-transfusion tRCM-0.8·k and the desired ptRCM-1,4k, therefore the 0.6·k (or 0.18·IBV) volume of PRBC should be transfused. Assuming the patient's body weight 85 kg and height 1.85 m, the IBV is 5.663 ml (calculated by Nadler's formula), consequently Constant k is 1.616ml and the calculated volume of PRBC is 970 ml. For the same 15% increase in Hct, the rule of thumb would suggest choosing from 3 to 5 units of PRBC instead of a proper volume of PRBC.

The key element of the HBS Theory – the Hct value specific homeostatic target blood volume – is supported by numerous studies on volume kinetics and volume turnover kinetics of infused intravenous solutions. They have demonstrated the physiological target blood volume that intravascular volume will approach, usually quite rapidly after a perturbation following the intravascular volume load [8]. The related concept of target volume applicable to the expandable space of fluid distribution has been suggested by volume kinetics as follows: a fluid given by intravenous infusion at a rate k_i is distributed in an expandable space with the volume (v), which the system strives to maintain as an ideal (target) volume [9]. Plasma volume loss is known to be homeostatically compensated by a fast-acting fluid and protein-influx from peripheral tissues and lymphatics [10]. Meanwhile erythropoietin-mediated RBC recovery takes much more time. During acute hemorrhage, recovery of plasma volume by autotransfusion has been found to recover plasma, but not blood volume. It is acknowledged that only PRBC transfusion can ensure a permanent blood volume recovery. Rehm and his colleagues reported that after preoperative acute normovolemic hemodilution the plasma volume did not increase during a radical hysterectomy operation until retransfusion, despite infusing 3.389 ± 1.021 ml of crystalloid to compensate for an estimated surgical blood loss of 727 ± 726 ml [11]. A more recent volume turnover study by Dr. Norberg and his colleagues on hemorrhaged sheep has found evidence that pronounced effects on circulation, volume recruitment from interstitium and renal output during and after hemorrhage are mainly unaffected by the immediate infusion of a threefold volume of crystalloid, the latter also resulting in undesired periph-

eral edema [12]. The same study has not found any evidence of endogenous plasma expansion exceeding its loss in order to restore the lost erythrocyte mass and prehemorrhage blood volume. Such findings suggest that homeostasis prevents plasma overdilution and overexpansion in the setting of erythrocyte loss by means of blood volume reduction and extravasation of excessive fluid amount. These findings are consistent with the hypothesis of the HBS Theory which argues that the target blood volume homeostatically decreases with decreasing the erythrocyte volume. This approach is also supported by the findings of Mercuriali et al. who demonstrated that predonation of one PRBC unit at baseline Hct-40% caused a mean Hb decrease by 10 g/l and Hct by 3%, and this value was increasing with the number of predonated units [13].

The Hct-40% value inherent to Hct-ITM deployed in the formulas used by HBS Method (method A) is the well established value of ideal plasma viscosity known in human physiology [14]. The HBS Theory also argues critical homeostatic Hct limits that are derived by applying the Constant k value to the sum of absolute deviations from IBV and IPV values, which are maintained as homeostatic targets only at Hct-ITM-40%. The critical Hct limits – 13.3% and 60% – are consistent with the well established critical limits of blood viscosity in humans [15, 16]. An obvious shortcoming in the investigation of the modified method A (A-cor) is that drainage mass Hct tests were not made, so calculations of blood loss were based on the assumption that drainage mass Hct was the mean value of pre-transfusion and post-transfusion blood Hct as suggested by results of the single test for drainage mass Hct. However, the new method in general has demonstrated better prognostic features even without correction for drainage blood loss. Another concern is the body weight and height values deployed by the calculations of the new method – their accuracy could not be evaluated.

Conclusion

The present pilot study has demonstrated the applicability of the new method to the most common clinical situation when bleeding takes part simultaneously with blood component transfusion. The new method has demonstrated significant advantage over probably the most popular method – rule of thumb – used to guide the transfusion amount. These findings are supposed to encourage further investigations.

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