Egyptian Journal of Anaesthesia

ISSN: (Print) 1110-1849 (Online) Journal homepage: https://www.tandfonline.com/loi/teja20

# Acute normovolemic hemodilution in spinal fusion surgery

Maha I. El-Dessouky, Salwa H. Waly & Yasser M. Nasr

**To cite this article:** Maha I. El-Dessouky, Salwa H. Waly & Yasser M. Nasr (2011) Acute normovolemic hemodilution in spinal fusion surgery, Egyptian Journal of Anaesthesia, 27:4, 249-254, DOI: 10.1016/j.egja.2011.07.004

**To link to this article:** https://doi.org/10.1016/j.egja.2011.07.004

Egyptian Journal of Anaesthesia (2011) **27**, 249–254

Egyptian Society of Anesthesiologists

**Egyptian Journal of Anaesthesia**

www.elsevier.com/locate/egja
www.sciencedirect.com

**Research Article**

# Acute normovolemic hemodilution in spinal fusion surgery

**Maha I. El-Dessouky, Salwa H. Waly *, Yasser M. Nasr**

*Department of Anesthesia, Faculty of Medicine, Zagazig University, Egypt*

Received 18 June 2011; accepted 14 July 2011

**KEYWORDS**

Autologous transfusion;
Normovolemic hemodilution;
Spinal fusion

**Abstract** *Background:* Spinal fusion surgeries are accompanied by significant blood loss. Acute normovolemic hemodilution is one of the autologous blood transfusion techniques that is proved to improve tissue perfusion through decreasing blood viscosity. However, its effect on hemodynamics, hematologic state, and coagulation profile is controversial.

*Aim of the work:* To detect safety of ANH as an alternative to allogenic blood transfusion in major surgeries.

*Patients and methods:* Forty adult patients undergoing spinal fusion surgery were randomly assigned into two groups: hemodilution group (group H: $n = 20$) and control group (group C: $n = 20$). Samples were collected five times. T1: just after the induction of anesthesia and before hemodilution starts. T2: just after the end of hemodilution or 40 min after the induction of anesthesia in the control group. T3: at the start of surgical closure.T4: before the reversal from residual neuromuscular effect. T5: 3 h postoperative. Samples included: Arterial blood gases (ABGs), Hb level, Ht%, serum Na+ and K+ levels, platelet count (Plt), bleeding time (BT), activated partial thromboplastin time (aPTT), and international neutralizing ratio (INR).

*Results:* Heart rate, arterial blood pressure and CVP showed no significant differences during intra- and postoperative times between the two groups. Reduction in Hb and Ht % occurred in both groups compared to basal and was more significantly reduced in group H compared to group C at T2. Platelets were reduced in both groups compared to basal and significantly reduced in group H at T2 compared to group C. BT, aPTT, and INR were not affected all through the study time in both groups. Serum Na+, Serum K+, and ABGs showed insignificant differences all through the study time.

* Corresponding author. Tel.: +20 124329364.
E-mail address: salwa.waly@yahoo.com (S.H. Waly).



Peer review under responsibility of Egyptian Society of Anesthesiologists.
doi:10.1016/j.egja.2011.07.004

**Production and hosting by Elsevier**

*Conclusions:* Acute normovolemic hemodilution can be considered as a safe and effective alternative for allogenic blood transfusion (avoiding all its hazards) in spinal fusion surgery.



## 1. Introduction

Adequate volume replacement during major surgeries is mandatory in order to avoid organ dysfunction and death [1]. The hazards related to homologous blood transfusion are well known, and might include: hypothermia, coagulation problems, hyperkalemia, hypocalcemia, allergic reactions, acute lung injury, hemolytic and non-hemolytic reactions, and transmitted infections [2].

Although multiple measures are performed to increase the safety of donated blood and/or products, autologous blood remains the safest source for blood transfusion [3]. Autologous blood donation may be performed by either: pre-deposit autologous transfusion (The patient donates blood 3–5 weeks before surgery to be used intraoperatively), intraoperative acute normovolemic hemodilution, or intraoperative red blood cell salvage [4].

Acute normovolemic (isovolemic) hemodilution (ANH) is a blood conservation technique which involves intraoperative removal and storage (at room temperature) of blood from a patient, just before or shortly after the induction of anesthesia, with simultaneous adding of a replacement volume of crystalloid and/or colloid [5]. This blood is transfused again to the same patient when intra-operative blood loss is controlled, or when necessary [6].

ANH is indicated when blood loss is expected to be more than 1 l or expected to exceed 20% of the patients' blood volume [4].

Spinal surgeries might range from cervical to lumbosacral levels. Spinal fusion might involve distractive forces and/or fixation by special instruments of multiple spinal levels. Application of these devices may be associated with clinically significant blood loss [7].

The aim of the present study is to reveal the efficacy and safety of acute normovolemic hemodilution compared to homologous blood transfusion in spine surgery patients.

## 2. Patients and methods

After local ethics committee approval and an informed written patient consent, 40 adult ASA I-II patients of both sexes (aged between 25 and 40 years), undergoing spinal fusion surgery were included in the current study. Exclusion criteria included: patients with cardiac disease, uncontrolled hypertension, respiratory impairment ($PaO_2 < 60$ mm Hg on room air), impaired renal (creatinine > 1.5 mg/dl) or hepatic function (serum bilirubin > 1.5 mg/dl or doubled AST), hemoglobin (Hb) level < 12 gm/dl, and coagulopathies (platelet count < $100 \times 10^3$/cc, INR > 1.2).

Patients were randomly assigned into two groups: hemodilution group (group H: $n = 20$) and control group (group C: $n = 20$). Randomization was done by closed envelopes.

### 2.1. Anesthetic technique

For both groups general anesthesia was performed. Patients were premedicated with 0.1 mg/kg midazolam and 0.5 mg atropine intramuscularly 1 h before surgery. Anesthesia was induced with fentanyl 1 μg/kg and thiopental sodium 6 mg/kg. Atracurium 0.5 mg/kg i.v. was given and 100% oxygen via a face mask for 2–3 min was applied. Appropriate size cuffed endotracheal tube was inserted. Anesthesia was maintained with isoflurane and muscle relaxation was maintained using incremental doses of atracurium (0.05 mg/kg) as required. Repeated doses of fentanyl were given intraoperatively as needed. Patients were ventilated to maintain an end-tidal $Pco_2$ of 35–40 mm Hg throughout the whole procedure. Depth of anesthesia was monitored by clinical signs and hemodynamic responses to surgical stimuli. All patients were put in prone position. Controlled hypotension was done by reducing systolic arterial pressure not more than 30% less than the initial values or maintaining mean arterial pressure (MAP) at 60 mm Hg. This was achieved by gradual increasing of the maintenance isoflurane (0.5% every 5 min) until targeted MAP was achieved. This was accompanied by hyperventilation in which the rate adjusted to achieve targeted PaCO2 of 30–35 mm Hg (provided that the minute ventilation was held constant).

Arterial cannula (20 G) was inserted in non dominant hand of the patient after performing Allen's test. This cannulation aimed for arterial blood sampling to detect oxygenation and acid–base status and for continuous blood pressure monitoring.

Central venous catheter was applied into internal jugular vein under complete aseptic conditions.

For all patients intraoperative monitoring included pulse oximetry, ECG, End tidal $CO_2$, CVP, and arterial blood pressure monitoring.

All patients were reversed with i.v. Neostigmine 0.05 mg/kg and Atropine 0.02 mg/kg then extubated.

### 2.2. Postoperative follow up

Patients were carefully monitored for 3 h postoperatively. It was planned to transfuse autologous blood if volume expansion was needed.

### 2.3. Estimated allowable blood loss (EBL)

It was calculated from the following formula [8]:

$$EBL = EBV \times (\text{initial Hb} - \text{targeted Hb})/\text{mean Hb}$$

where EBV = estimated blood volume; Hb = hemoglobin; mean Hb = arithmetic mean of initial Hb, and the targeted Hb.

EBV is calculated for all patients as 70 ml × body weight. The targeted Hb level in the current study was 9 gm/dl and the lowest hematocrit (Ht) allowed was 25%.

### 2.4. Hemodilution technique (for group H)

The technique applied in the current study followed the guidelines for autologous transfusion by Napier et al. [9] [British Committee for Standards in Haematology Blood Transfusion Task Force].

After applying all monitoring devices and before putting the patient in prone position, hemodilution was started just after the induction of anesthesia. Two units of whole blood were withdrawn and collected via ante-cubital vein into standard blood collecting bags [Citrate – phosphate – dextrose – Adenine anticoagulant bag (CPD – A)]. The blood was sealed, and labeled with patient identification and time of collection. ''Untested blood for autologous use only'' was written on all blood bags' labels. Harvested blood was stored at room temperature in the operating room.

Concomitantly, Voluven® (6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride injection) [Fresenius Kabi, Germany] was infused into the central line in a rate equal to the blood collection rate (1:1 volume).

At the proper time all harvested blood was re-infused to the patient in the reverse order of collection (2nd bag infused first).

During the time of hemodilution, continuous invasive blood pressure and continuous ECG monitoring were performed. CVP was measured and recorded every 10 min.

### 2.5. Time of blood transfusion

In the hemodiluton group (group H): all patients were re-infused with their blood after surgical hemostasis was performed or when maximum calculated allowable blood loss was reached. It was planned to use allogenic blood in this group if blood loss exceeded 500 ml more than harvested blood.

In the control group (group C): allogenic blood transfused when maximum calculated allowable blood loss was reached or when the Hb $\leqslant$ 9 gm/dl and/or Ht $\leqslant$ 25 %.

### 2.6. Sampling

Samples were collected at five times.

**T1**: just after the induction of anesthesia and before hemodilution starts.
**T2**: just after the end of hemodilution or 40 minutes after the induction of anesthesia in the control group.
**T3**: at the start of surgical closure (surgical hemostasis was achieved).
**T4**: before the reversal from residual neuromuscular effect (end of surgery).
**T5**: 3 hours postoperative.

Samples included: Arterial blood gases (ABGs), Hb level, Ht%, serum $Na^+$ and $K^+$ levels. Hemostasis was also investigated through: platelet count (Plt), bleeding time (BT), activated partial thromboplastin time (aPTT), and international neutralizing ratio (INR).

### 2.7. Statistical analysis

Data entry and statistical analysis were performed using the SPSS software (SPSS, Chicago, IL, USA). Qualitative data were presented as a number or ratio, while quantitative data were presented as mean ± standard deviation (SD). The chi-square test ($\chi^2$) was used to test associations between variables of qualitative data. Two-way repeated measure analysis of Variance was used for continuous variables as HR and MAP and the differences were then calculated by Newman–Keuls test. Paired and non-paired *t*-tests, Mann Whitney U, and Wilcoxon tests were applied. Differences were considered significant at ($P < 0.05$).

## 3. Results

Patients' data including: age, weight, gender, duration of surgery, estimated blood volume, estimated allowable blood loss, and actual blood loss; showed insignificant differences between the two groups (Table 1).

Regarding cardiovascular data, heart rate and CVP showed no significant differences during intra- and postoperative times in both groups. Blood pressure was significantly lower than basal levels just before skin incision and for one hour later in both groups which may be attributed to a controlled hypotension technique employed within the maneuver at this time of surgery (Table 2).

There were significant reductions in both Hb and Ht % in both groups during intra-operative time and 3 h postoperatively compared to the basal levels. During the time of hemodilution (T2), the reduction in Hb and Ht % was more significant in hemodilution group compared to the control group (Table 3).

Platelet count was significantly reduced compared to the basal level in both groups during intra-operative and 3 h after the end of surgery. Significant reduction was encountered in the hemodilution group at T2 (time of hemodilution) compared to the control group. Thrombocytopenia was defined as PLT $< 100 \times 10^3/\mu L$. Bleeding time, activated partial thromboplastin time (aPTT), and INR were not affected all through the study time in both groups (Table 4).

Serum $Na^+$ and $K^+$ showed insignificant differences all through the study time (Table 5).

Regarding patients' oxygenation and ventilation as shown by ABGs, collected data revealed insignificant variations between the two groups (Table 6).

None of the patients in group H needed homologous transfusion neither during intra-operative, nor postoperative periods.

## 4. Discussion

Blood loss during spinal fusion surgery is expected to be 10–30 ml/kg because of the rich vasculature of the area besides

**Table 1** Patients' demographic data.

| | Group C ($n = 20$) | Group H ($n = 20$) |
|---|---|---|
| Age (yr) | 39.2 ± 8.3 | 38.9 ± 9.2 |
| Weight (kg) | 82.1 ± 7.4 | 80.6 ± 8.9 |
| Male/female | 16/4 | 17/3 |
| Length of surgery (min) | 148.3 ± 39.2 | 159.9 ± 43.8 |
| EBV (ml) | 5676 ± 459 | 5873 ± 372 |
| EABL (ml) | 1500 ± 244 | 1633 ± 183 |
| BL (ml) | 1200 ± 400 | 1300 ± 350 |

Data were expressed as mean (±SD) or ratio.

**Table 2** Intra- and postoperative cardiovascular data.

| | | 24 hours before surgery (basal) | Just after induction of anesthesia | Just before skin incision | 60 min after skin incision | At the start of surgical closure | 3 hours post-operative |
|---|---|---|---|---|---|---|---|
| HR | Group C | 84.0 ± 8.7 | 81.0 ± 12.6 | 81.6 ± 11.4 | 81.4 ± 10.7 | 82.9 ± 10.7 | 81.5 ± 10.9 |
| | Group H | 83.8 ± 9.3 | 82.8 ± 9.9 | 81.8 ± 10.1 | 83.8 ± 9.9 | 81.9 ± 11.1 | 82.1 ± 11.2 |
| MAP | Group C | 88 ± 13 | 86 ± 15 | 68 ± 8* | 67 ± 9* | 81 ± 11 | 88 ± 15 |
| | Group H | 86 ± 16 | 84 ± 12 | 68 ± 10* | 65 ± 11* | 82 ± 8 | 86 ± 14 |
| CVP | Group C | 7.01 ± 1.2 | 6.8 ± 1.3 | 6.5 ± 1.7 | 6.7 ± 1.4 | 6.69 ± 1.5 | 6.8 ± 1.2 |
| | Group H | 6.95 ± 1.1 | 6.7 ± 1.2 | 6.5 ± 1.8 | 6.6 ± 1.6 | 6.68 ± 1.4 | 6.9 ± 1.6 |

HR = heart rate (beat/min), MAP = mean arterial blood pressure (mm Hg), CVP = central venous pressure (cm water).
Data were expressed as mean ± SD; significant, $P > 0.05$.
* Significantly lower as compared to basal data within the same group

**Table 3** Intra- and postoperative hemoglobin and hematocrit.

| | | T1 (basal) | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|---|
| Hb (gm/dl) | Group C | 13.3 ± 0.7 | 12.2 ± 1.3* | 12.0 ± 1.5* | 12.2 ± 1.1* | 12.4 ± 0.9* |
| | Group H | 13.1 ± 1.1 | 11.9 ± 0.3*,† | 12.0 ± 0.2* | 12.2 ± .3* | 12.2 ± 1.6* |
| Ht (%) | Group C | 38.6 ± 1.6 | 36.6 ± 2.4* | 35.5 ± 1.1* | 36.3 ± 1.8* | 36.2 ± 1.3* |
| | Group H | 39.2 ± 1.1 | 33.3 ± 0.2*,† | 34.9 ± 1.4* | 35.9 ± 1.9* | 36.7 ± 1.2* |

Hb = hemoglobin, and Ht = hematocrit.
Data were expressed as mean ± SD; significant, $P > 0.05$.
* Significantly lower as compared to basal data within the same group.
† Significantly lower as compared to the data obtained in the same time within the other group.

**Table 4** Intra- and postoperative coagulation parameters.

| | | T1 (basal) | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|---|
| PLT ($\times 10^3$ μ/L) | Group C | 311 ± 37 | 230 ± 42* | 201 ± 22* | 222 ± 29* | 211 ± 33* |
| | Group H | 315 ± 34 | 183 ± 33*,† | 191 ± 34* | 212 ± 34* | 205 ± 39* |
| BT (min) | Group C | 1.8 ± 0.4 | 1.7 ± 0.6 | 1.7 ± 0.6 | 1.6 ± 0.7 | 1.7 ± 0.7 |
| | Group H | 1.9 ± 0.2 | 1.7 ± 0.5 | 1.6 ± 0.6 | 1.7 ± 0.5 | 1.7 ± 0.8 |
| aPTT (s) | Group C | 38 ± 3 | 37 ± 4 | 36 ± 6 | 37 ± 3 | 36 ± 5 |
| | Group H | 38 ± 2 | 36 ± 3 | 36 ± 5 | 37 ± 4 | 37 ± 5 |
| INR | Group C | 1.1 ± 0.05 | 1.1 ± 0.06 | 1.1 ± 0.01 | 1.1 ± 0.03 | 1.1 ± 0.05 |
| | Group H | 1.1 ± 0.04 | 1.1 ± 0.04 | 1.1 ± 0.03 | 1.1 ± 0.05 | 1.1 ± 0.06 |

PLT = platelet count, BT = bleeding time (normal: 1–3 min), aPTT = activated partial thromboplastin time (normal: 25–40 s), INR = international neutralizing ratio (normal: 1).
Data were expressed as mean ± SD; significant, $P > 0.05$.
* Significantly lower as compared to basal data within the same group.
† Significantly lower as compared to data obtained in the same time within the other group.

**Table 5** Intra- and postoperative serum $Na^+$ and $K^+$.

| | | T1 (basal) | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|---|
| $Na^+$ (meq/L) | Group C | 141.1 ± 3.3 | 142.0 ± 2.8 | 141.1 ± 4.1 | 141.1 ± 3.0 | 142.3 ± 5.9 |
| | Group H | 141.4 ± 3.3 | 140.9 ± 3.2 | 142.0 ± 5.6 | 141.4 ± 2.9 | 140.9 ± 2.3 |
| $K^+$ (meq/L) | Group C | 4.0 ± 0.4 | 3.8 ± 0.3 | 3.8 ± 0.3 | 3.9 ± 0.1 | 3.8 ± 0.3 |
| | Group H | 4.0 ± 0.4 | 3.9 ± 0.2 | 3.9 ± 0.4 | 3.9 ± 0.2 | 3.9 ± 0.2 |

Data are expressed as mean (±SD).

the extensive trauma associated with multiple spinal levels fusion [10].

Acute normovolemic hemodilution in this clinical study demonstrated stable hemodynamics, with non-significant alteration in hematologic state, hemostatic condition, serum electrolytes, or arterial blood gases when compared to allogenic blood transfusion. Thereby, homologous blood transfusion can be avoided by applying ANH technique.

**Table 6** Intraoperative arterial blood gas analysis (ABG) on 100% $O_2$.

| | | T1 (basal) | T2 | T3 | T4 |
|---|---|---|---|---|---|
| $SaO_2$ (%) | Group C | 99.6 ± 0.3 | 99.5 ± 0.3 | 99.5 ± 0.2 | 99.5 ± 0.1 |
| | Group H | 99.5 ± 0.4 | 99.4 ± 0.2 | 99.4 ± 0.1 | 99.5 ± 0.4 |
| $PaO_2$ | Group C | 446.4 ± 16.1 | 440.3 ± 21.9 | 439.4 ± 39.8 | 433.8 ± 23.9 |
| | Group H | 442.0 ± 36.2 | 434.4 ± 34.6 | 436.9 ± 34.4 | 444.5 ± 63.5 |
| $PaCO_2$ | Group C | 37.1 ± 2.4 | 33.1 ± 2.8 | 35.6 ± 2.1 | 36.0 ± 2.9 |
| | Group H | 37.2 ± 2.3 | 33.7 ± 2.5 | 35.2 ± 2.7 | 36.6 ± 2.7 |
| Arterial (pH) | Group C | 7.42 ± 0.04 | 7.39 ± 0.04 | 7.37 ± 0.03 | 7.43 ± 0.06 |
| | Group H | 7.43 ± 0.04 | 7.44 ± 0.05 | 7.42 ± 0.05 | 7.42 ± 0.05 |
| $HCO_3$ | Group C | 26.4 ± 2.6 | 27.6 ± 2.2 | 27.2 ± 2.2 | 27.8 ± 2.3 |
| | Group H | 26.3 ± 2.3 | 25.4 ± 2.3 | 25.2 ± 1.3 | 27.9 ± 2.2 |
| BE | Group C | 3.0 ± 2.7 | 4.1 ± 2.4 | 3.3 ± 2.7 | 3.7 ± 2.8 |
| | Group H | 2.8 ± 1.4 | 1.6 ± 1.9 | 0.5 ± 1.5 | 4.0 ± 2.4 |

$SaO_2$ = $O_2$ saturation, $PaO_2$ = arterial partial pressure of oxygen, $PaCO_2$ = arterial partial pressure of carbon dioxide, $HCO_3$ = bicarbonate, and BE = base excess.
Data are expressed as mean (±SD).

The results obtained in the current study was in accordance with the results obtained by a study performed by Hur et al. [11] who found that the technique of ANH reduced the demand for allogenic blood transfusion in spinal surgery.

In the present study, the heart rate stability in both groups reflects proper anesthetic technique and intraoperative fluid management (rate and volume). This was in contrast to the results obtained by Weiskopf et al. [12] who demonstrated that the technique of ANH was accompanied by tachycardia. The hemodynamic stability in the present was in agreement with the results obtained by other studies performed by Ickx et al. [13] and Bak et al. [14].

In the current study, both groups have shown reduction in Hb and Ht %. In the hemodilution group, this could be attributed to the technique itself; while in the control group, this could be explained by surgical blood loss with concomitant administration of crystalloids. Such reduction in hematologic parameters was not accompanied by disturbances in acid base balance and did not fall below the values shown to be accepted for adequate oxygen delivery to various organs especially the brain (Hb of 11.3 mg/dl and Ht of 30%) [15].

A study conducted by Deem et al. [16] reviewed other studies evaluating the relationship between normovolemic hemodilution and arterial $O_2$ and $CO_2$ tensions in rabbits and concluded that such parameters where not affected by ANH. This was in agreement with the results obtained by the present study. Moreover, Szegedi et al. [17] demonstrated that ANH is not a safe procedure regarding the issue of ventilation if patients were not properly selected according to their pulmonary functions and those with poor lung performance were excluded.

Two factors have been accused within the subject of coagulation disorders that might occur with ANH: Extreme hemodilution (Ht $\leqslant$ 20%) with concomitant decrease in coagulation factors [18], and the type of the replacement fluid used [19]. Since hemostatic disorders were not encountered in the current study; therefore, these results supported the guidelines of ANH which state that Ht % should be kept between 25% and 30% [9]. McLaughlin et al. [18] recommended fresh frozen plasma as a replacement fluid if extreme hemodilution is to be performed. Many studies that found HES to cause impaired hemostasis were conducted upon first-generation HMW HES [20–22]. LMW HES (HES 130/0.4) has a better effect on the hemostatic condition [19] that may be attributed to its different physicochemical properties than hetastarch [23] which was found to affect both the coagulation factors and the platelet aggregation [22].

## 5. Conclusion

Acute normovolemic hemodilution is a safe, effective alternative for allogenic blood transfusion in spinal fusion surgery with consequent avoidance of the expected hazards of homologous blood.

## References

[1] Mythen MG, Webb AR. Intra-operative gut mucosal hypoperfusion is associated with increased post-operative complications and costs. Intensive Care Med 1994;20:99–104.
[2] Rosenblatt MA. Strategies for minimizing the use of allogeneic blood during orthopedic surgery. Mt Sinai J Med 2002;69(1-2):83–7.
[3] Murray D. Acute normovolemic hemodilution. Eur Spine J 2004;1:S72–5.
[4] Vanderlinde ES, Heal JM, Blumberg N. Clinical review: autologous transfusion. Br Med J 2002;324:772–5.
[5] Lee D, Chapman J, Contreras II M, et al. Perioperative haemodilution and cell salvage. British Committee for Standards in Haematology Blood Transfusion Task Force. Br J Anaesth 1997;78:768–71.
[6] Duguid JKM. Autologous blood transfusion: review. Clin Lab Haematol 1999;21:371–6.
[7] Raw DA, Beattie JK, Hunter JM. Anaesthesia for spinal surgery in adults. Br J Anaesth 2003;91(6):886–904.
[8] Gross JB. Estimating allowable blood loss: corrected for dilution. Anesthesiology 1983;58:277–80.
[9] Napier JA, Bruce M, Chapman J, Duguid JK, Kelsey PR, Knowles SM, Murphy MF, Williamson LM, Wood JK, Lee D, Contreras M, Cross N, Desmond MJ, Gillon J, Lardy A, Williams FG. Guidelines for autologous transfusion. II. Perioperative haemodilution and cell salvage. British Committee for Standards in Haematology Blood Transfusion Task Force. Autologous transfusion working party. Br J Anaesth 1997;78(6):768–71.
[10] Zheng Jr F, Cammisa FP, Sandhu HS, Girardi FP, Khan SN. Factors predicting hospital stay, operative time, blood loss, and transfusion in patients undergoing revision posterior lumbar spine decompression, fusion, and segmental instrumentation. Spine 2002;27:818–24.

[11] Hur SR, Huizenga BA, Major M. Acute normovolemic hemodilution combined with hypotensive anesthesia and other techniques to avoid homologous transfusion in spinal fusion surgery. Spine 1992;17:867–73.
[12] Weiskopf RB, Feitner J, Hopf H, Viele MK, Watson JJ, Lieberman J, Kelley S, Toy P. Heart rate increases linearly in response to acute isovolemic anemia. Transfusion 2003;43:235–40.
[13] Ickx BE, Rigolet M, Van der Linden PJ. Cardiovascular and metabolic responses to acute normovolemic anemia: effects of anesthesia. Anesthesiology 2000;93:1011–6.
[14] Bak Z, Abilgard L, Lisander B, Sjöberg J. Transesophageal echocardiographic hemodynamic monitoring during preoperative acute normovolemic hemodilution. Anesthesiology 2000;92:1250–6.
[15] Han SH, Ham BM, Bahk JK, Bahk JH, Ro YJ, Do SH, Park YS. The effect of acute normovolemic hemodilution on cerebral oxygenation. Int J Clin Pract 2004;5810:903–6.
[16] Deem S, Alberts MK, Bishop MJ, Bidani A, Swenson ER. $CO_2$ transport in normovolemic anemia: complete compensation and stability of blood $CO_2$ tensions. J Appl Physiol 1997;83:1240–6.
[17] Szegedi LL, Van der Linden P, Ducart A, Cosaert P, Poelaert J, Vermassen F, Mortier EP, d'Hollander AA. The effects of acute isovolemic hemodilution on oxygenation during one-lung ventilation. Anesth Analg 2005;100:15–20.
[18] McLaughlin TM, Fontana JL, Alving B, Mongan PD, Biinger. Profound normovolemic hemodilution: hemostatic effects in patients and in a porcine model. Anesth Analg 1996;83: 456–9.
[19] Boldt J, Haisch G, Suttner S, Kumle B, Schellhaass A. Effects of a new modified, balanced hydroxyethyl starch preparation (Hextend®) on measures of coagulation. Br J Anaesth 2002;89(5):722–8.
[20] Cope JT, Banks D, Mauney MC, Lucktong T, Shockey KS, Kron IL, Tribble CG. Intraoperative hetastarch infusion impairs hemostasis after cardiac surgery operations. Ann Thorac Surg 1997;63:78–82.
[21] Boldt J, MuÈller M, Heesen M, Heyn O, Hempelmann G. Influence of different volume therapies on platelet function in the critically ill. Intensive Care Med 1996;22:1075–81.
[22] deJonge E, Levi M. Effects of different plasma substitutes on blood coagulation: a comparative review. Crit Care Med 2001;29:1261–7.
[23] Waitzinger J, Bepperling F, Pabst G, Opitz J, MuÈller M, Baron JF. Pharmacokinetics and tolerability of a new hydroxyethylstarch (HES) specification (HES 130/0.4) after single-dose infusion of 6% or 10% solution in healthy volunteers. Clin Drug Invest 1998;16:151–60.