The Neurocognitive Outcomes of Hemodilution in Adult Patients Undergoing Coronary Artery Bypass Grafting Using Cardiopulmonary Bypass

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ABSTRACT

Objective: The study aimed to evaluate the effect of mild and moderate hemodilution during CPB on the neurocognitive dysfunction in patients undergoing coronary artery bypass grafting.

Design: A randomized clinical study.

Setting: Cardiac center.

Patients: 186 patients scheduled for cardiac surgery with cardiopulmonary bypass.

Intervention: The patients were classified into 2 groups (each = 93), Mild hemodilution group: The hematocrit value was maintained >25% by transfusion of packed-red blood cells plus hemofiltration during CPB. Moderate hemodilution group: the hematocrit value was maintained within the range of 21-25%.

Measurements: The monitors included the hemofiltrated volume, number of transfused packed red blood cells, and the incidence of postoperative cognitive dysfunction.

Main Results: The hemofiltrated volume during CPB was too much higher with mild hemodilution compared to the moderate hemodilution (p = 0.001). The number of the transfused packed red blood cells during CPB was higher with mild hemodilution compared to the moderate hemodilution (p = 0.001), but after CPB, the number of the transfused packed red blood cells was lower with the mild hemodilution group than the moderate hemodilution (p = 0.001). The incidence of total postoperative neurological complications was significantly lower with the mild hemodilution group than moderate hemodilution (p = 0.033). The incidence of neurocognitive dysfunction was significantly lower with mild hemodilution group than moderate hemodilution (p = 0.042).

Conclusions: The mild hemodilution was associated with a significant decrease in the incidence of neurocognitive dysfunction compared to moderate hemodilution in patients undergoing coronary artery bypass grafting. Also, the transfused packed red blood cells increased during CPB and decreased after CPB with the mild hemodilution than moderate hemodilution.

Keywords: Cardiopulmonary bypass, coronary artery bypasses grafting, hemodilution, neurocognitive dysfunction.
INTRODUCTION

Hemodilution during cardiopulmonary bypass (CPB) was used to improve the microcirculatory flow\(^1\) and counteract the adverse effects of hypothermia such as increased viscosity and red cell rigidity.\(^5\)

However, hemodilution may reduce the perfusion pressure which increases the risk of adverse neurologic outcome after CPB,\(^6\) and also it increases the cerebral blood flow, and therefore it may increase the incidence of microemboli to the brain. Also, hemodilution reduces the oxygen-carrying capacity of blood and, in combination with the effect of the hypothermia; the hemodilution may decrease the oxygen delivery to brain tissues.\(^7,8\)

We hypothesized that hemodilution during CPB will increase the risks of neurocognitive dysfunction after cardiac surgery.

The aim of the present study was to evaluate the effect of mild and moderate hemodilution during CPB on the neurocognitive dysfunction in patients undergoing coronary artery bypass grafting.

PATIENTS

After obtaining informed consent and approval of local ethics and research committee in the cardia center (45/2017, 15/01/2017), a prospective randomized study included 186 patients undergoing coronary artery bypass grafting using cardiopulmonary bypass. The inclusion criteria were patients with ischemic heart disease, hypertension, diabetes, ejection fraction $\geq 50\%$. Exclusion criteria included patients with valvular surgery, previous neurologic diseases, congestive heart failure, acute myocardial infarction, atrial fibrillation or obstructive cardiomyopathy, off-pump coronary artery bypass grafting (CABG), renal, hepatic impairment or patients with hematocrit (HCT) value $<21\%$. The patients were randomly allocated (the concealment of allocation was done by using random numbers generated through excel) into two equal groups (n = 93 each).

Mild hemodilution group
The hematocrit value was maintained $>25\%$ by hemofiltration plus transfusion of packed-red blood cells during CPB.

Moderate hemodilution group
The hematocrit value was maintained within the range of 21-25% by hemofiltration plus transfusion of packed-red blood cells during CPB.

The patients were evaluated by trained neuropsychiatrist using a battery of tests that is composed of a comprehensive assessment of the cognitive status, including the memory, attention, language, executive function, and motor speed, on the day before surgery, the 2\(^{nd}\), 4\(^{th}\), and 6\(^{th}\) postoperative days for the diagnosis of neurological complications. The neuropsychiatrist was blinded for all patients of the two groups.

Anesthetic technique
For all patients and under local anesthesia, a radial arterial cannula and central venous line were inserted guided by ultrasound before the operation to enable continuous hemodynamic monitoring. Induction was done by intravenous Fentanyl (3-5 µg/kg), Etomidate (0.3 mg/kg), Rocuronium (0.8 mg/kg). The anesthesia was maintained with oxygen/air (50%), Fentanyl infusion (1-3 µg/kg/hr), Cisatracurium (1-2 µg/kg/min), and Sevoflurane or Propofol according to the study medication protocol. Epiaortic ultrasound scanning using a transducer applied directly to the ascending aorta and the aortic arch after opening the chest to enable the detailed visualization of the aortic wall and to show the distribution of calcified atherosclerotic lesions and also to determine the optimal and safe location for aortic cannulation. At the end of surgical intervention, the patients were prepared for weaning from CPB. If there was difficulty to wean from CPB, pharmacological support (dopamine or epinephrine or norepinephrine, or nitroglycerine), mechanical support (IABP), or pacing were started. At the end of the surgery, the patients were transferred to the cardiac surgery ICU with full monitoring.

Cardiopulmonary bypass
The pump (Roller pump, Stockert S5 Germany) was primed with 1000 ml of ringer lactate, 300 ml hetastarch 6%, 100 ml albumin 20%, 50 meq of sodium bicarbonate, 5000 IU of heparin and 200 ml of mannitol 20%. Cardiopulmonary bypass was established with cannulation of the ascending aorta and right atrium. The patients received cold blood cardioplegia in the standard ratio (4:1) four parts of blood from the cardiopulmonary bypass circuit, and one part potassium-rich crystalloid named Plegisol (Hospira, Inc, Lake Forest, IL, USA). The initial dose was 30 ml/kg, and subsequent doses were 20 ml/kg given every 20 min. The temperature was reduced to 28-32°C and pump flow rates 2-2.4 L/min/m² was used to maintain the perfusion pressure of 100-125 mmHg. The arterial blood gases monitoring was done using alpha-stat PH-stat strategy during cardiopulmonary bypass.

In the two groups, cardioplegia solution was given two-thirds through the antegrade and one-third through
the retrograde route, and a hot shot (warm blood) antegrade dose was given just before the myocardium reperfusion. After the initiation of CPB and stabilizing the hemodynamics according to the standardized parameters during CPB, the hemofiltration was started and continued up to 10 min before weaning from CPB. The hemofiltration and the packed red blood cells transfusion were done to maintain the hematocrit value either >25% or 21-25% according to the study protocol.

**Monitoring of patients**
Hemodynamic monitoring included the heart rate; mean arterial blood pressure (MAP), a continuous electrocardiograph with automatic ST-segment analysis (leads II and V), central venous pressure, and cerebral near-infrared spectroscopy (NIRS) to measure the regional cerebral oxygen saturation. The patients with postoperative neurological complications were assessed by a neuropsychiatrist through the 2nd, 4th, and 6th postoperative days for the diagnosis of neurocognitive dysfunction or stroke. Postoperatively, the CT scan or MRI brain was done in patients with neurological complications.

Hemodynamic values were serially collected at the following timepoints: T0: Baseline reading; T1: 15 minutes after induction; T2: before cardiopulmonary bypass; T3: 30 minutes after cardiopulmonary bypass; T4: at ICU admission; T5: 6th hour after ICU admission; T6: 12th hour after ICU admission; T7: 24th hour after ICU admission. In addition to the previous timepoints, regional cerebral oxygen saturation was assessed during CPB at the 15th, 30th minute after initiation of CPB and five minutes before weaning of CPB. The neurological functions were evaluated before surgery, the 2nd, 4th, and 6th postoperative.

**Outcomes**
The primary outcome was the effect of mild hemodilution and moderate on the incidence of neurocognitive dysfunction symptoms such as the inability to concentrate, amnesia, confusion, anxiety, the feeling of imbalance, changes in vision, and abnormal behavior of the patients. Secondary outcomes were the requirement and safety of blood product transfusion which was assessed by the occurrence of any adverse events.

**Sample size calculation**
Power analysis was performed using the Chi-square test for independent samples on the frequency of patients associated with neurocognitive dysfunctions because it was the main outcome variable in the present study. A pilot study (10 patients in each group) was done before starting this study because there is no available data in the literature for the comparison of the neurocognitive function of mild hemodilution and moderate hemodilution in patients undergoing coronary artery surgery. The results of the pilot study showed that the incidence of postoperative neurological complications was 20% in the mild hemodilution group, and 50% in the moderate hemodilution group. Taking power 0.8, alpha error 0.05, and beta 0.2, a minimum sample size of 93 patients was calculated for each group.

**Statistical analysis**
Data were statistically described in terms of mean ± standard deviation (± SD), or frequencies (number of cases) and percentages when appropriate. A comparison of numerical variables between the study groups was done using the student t-test for independent samples. Repeated measure ANOVA was used to compare the hemodynamics and regional cerebral oxygen saturation at different follow-up intervals. For comparing categorical data, Chi-square (χ²) test was performed. Exact test was used instead when the expected frequency is less than 5. P values less than 0.05 were considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

**RESULTS**
Table 1 shows no significant differences regarding the demographic data, co-morbidities, preoperative medications, hematocrit, NYHA class, Euroscore, and the ASA physical status score (p > 0.05).

Table 2 shows the changes in the hemodynamics of patients during the procedure and through the first 24 hours in the ICU. There was no significant difference in the perioperative heart rate, mean arterial blood pressure, and central venous pressure between the patients of the two groups (p > 0.05).

Table 3 shows the changes in regional cerebral oxygen saturation. There was no significant difference in the right or left regional cerebral oxygen saturation as measured by cerebral near-infrared spectroscopy before, during, or after the CPB between the two groups (p > 0.05).

Table 4 shows the intraoperative data and the outcomes of patients of the two groups. There was no difference in the number of coronary artery grafts, cardiopulmonary bypass time and temperature, cross clamping time, blood loss, intraoperative fluid, urine output, blood sugar, postoperative renal complications, allergic reactions, ICU
Table 1: Preoperative Data of Patients (Data are Presented as Mean±SD, Number, %)

| Variable                      | Mild Hemodilution Group (n=93) | Moderate Hemodilution Group (n=93) | P     |
|-------------------------------|--------------------------------|-----------------------------------|-------|
| Age (year)                    | 59.6±4.70                     | 57.8±3.45                        | 0.376 |
| Weight (Kg)                   | 87.7±10.63                    | 88.4±12.40                       | 0.492 |
| Gender Male:Female            | 69:24                         | 73:20                            | 0.604 |
| Diabetes mellitus             | 74                             | 80                                | 0.331 |
| Hypertension                  | 79                             | 72                                | 0.260 |
| Ischemic heart disease        | 93                             | 93                                | 1.000 |
| Atrial fibrillation           | 28                             | 23                                | 0.510 |
| Pulmonary hypertension        | 22                             | 17                                | 0.471 |
| Ejection fraction (%)         | 55.4±3.75                     | 54.8±3.48                        | 0.112 |
| Angiotensin-converting-enzyme inhibitors | 62 | 55                  | 0.362 |
| Beta-blockers                 | 77                             | 81                                | 0.538 |
| Calcium channels-blockers     | 24                             | 15                                | 0.436 |
| Aspirin                       | 93                             | 93                                | 1.000 |
| Statins                       | 82                             | 87                                | 0.308 |
| Hematocrit (%)                | 39.7±3.65                     | 38.9±3.53                        | 0.112 |
| Carotid stenosis <50%         | 15                             | 8                                 | 0.181 |
| Unilateral                    | 9                              | 5                                 | 0.404 |
| Bilateral                     | 6                              | 3                                 | 0.494 |
| Smoking                       | 55                             | 60                                | 0.546 |
| NYHA                          |                                |                                   |       |
| II                            | 19                             | 21                                | 0.858 |
| III                           | 67                             | 62                                | 0.524 |
| IV                            | 7                              | 10                                | 0.610 |
| ASA                           |                                |                                   |       |
| III                           | 79                             | 85                                | 0.256 |
| IV                            | 14                             | 8                                 | 0.256 |
| Euroscore (%)                 | 12.8±2.97                     | 12.3±2.10                        | 0.204 |
| Body surface area (m²)        | 1.75±0.19                     | 1.78±0.16                        | 0.245 |

NYHA: New York Heart Association; ASA: American Society of Anesthesiologists Physical Status Score

or hospital length of stay, and mortality between the two groups (p > 0.05). There was no difference in the hematocrit before or after the CPB between the two groups (p > 0.05), but during the CPB, the hematocrit was significantly higher in the patients of the mild hemodilution group compared to the moderate hemodilution group (p < 0.05). The hemofiltrated volume during CPB was too much higher in the patients of the mild hemodilution group compared to the moderate hemodilution group (p = 0.001).

The number of the transfused packed red blood cells during CPB was higher in the patients of the mild hemodilution group compared to the moderate hemodilution group (p = 0.001), but after the CPB, the number of the transfused packed red blood cells was lower in the patients of the mild hemodilution group compared to the moderate hemodilution group (p = 0.001).

The weaning from CPB was easier in patients of the mild hemodilution group compared to the moderate hemodilution group. Patients of the mild hemodilution group needed smaller doses of pharmacological support (Dopamine, Epinephrine, Norepinephrine, and Nitroglycerine) than the moderate hemodilution group (p < 0.05), and the requirement for mechanical support (IABP) and the pacing was lower in patients of the mild hemodilution group compared to the moderate hemodilution group (p < 0.05). The total number of patients who suffered from postoperative neurological complications was significantly lower in patients of the mild hemodilution group compared to the moderate hemodilution group (p = 0.001). The incidence of neurocognitive dysfunction was significantly lower in patients of the mild hemodilution group compared to the moderate hemodilution group (p = 0.003). The incidence of stroke was lower in the patients of the mild hemodilution group than the moderate hemodilution group, but the difference was insignificant (p = 0.650). The number of patients who suffered from pulmonary edema and required postoperative mechanical ventilation was lower in the mild hemodilution group compared to the moderate hemodilution group, but the difference was insignificant (p = 0.164). There was...
In the present study, the hematocrit value was maintained >25% in the mild hemodilution group and in the range of 21-25% in the moderate hemodilution group by hemofiltration plus transfusion of packed-red blood cells during CPB. The incidence of neurocognitive dysfunction symptoms such as the delirium, inability to concentrate, amnesia, confusion, anxiety, the feeling of imbalance, changes in vision, and abnormal behavior of the patients was significantly lower in the mild hemodilution group compared to the moderate hemodilution group (18.72% vs. 32.25% respectively).

Progressive hemodilution is associated with a progressive decrease in the oxygen-carrying capacity and viscosity of the blood,[11,12] and it leads to a reduction in the tissue oxygen delivery and organ dysfunction.[13-15] This finding is supported by other observational studies that showed a direct relationship between the severity of hemodilution and the risk of intra- and postoperative renal, hepatic, and central nervous system dysfunction, as well as mortality.[9,16-23]

McCusker et al.[24] and Vijay et al.[25] showed that higher intraoperative hematocrit between 25 and 30% is required to maintain an adequate regional cerebral oxygen saturation during CPB and other studies showed the association of postoperative neurological complications and the intraoperative cerebral desaturation during CPB.[26-28] Esper et al.[29] reported that moderate to severe hemodilution can result in impaired oxygen-carrying capacity and tissue ischemia despite a decrease in the basal metabolic rate and affect the outcomes after cardiac surgery.

Some studies reported the association of ischemia and inflammatory tissue injury with greater hemodilution and these findings to explain the improved neurological outcomes with high hematocrit[15,30] and other studies reported the increased incidence of complications with the increased hemodilution severity.[20,31,32]

Mathew et al.[33] found that extreme hemodilution was associated with severe postoperative neurocognitive impairment among older patients undergoing cardiac surgery. Karkouit et al.[34] found that the odds of neurological complications increased by 10% for each 1% decrease in hematocrit during CPB.

Habib et al.[9] showed that the adverse outcomes and the neurological complications after CPB were related to the degree of hemodilution severity and they are recommending to minimize on-pump hemodilutional anemia and to maintain the hematocrit value >24.5-27% to improve the outcomes after cardiac surgery.

Wypij et al.[35] showed that hematocrit ≥24% was associated with higher psychomotor development index scores

### Table 3: Regional Cerebral Oxygen Saturation of Patients (Data are presented as %)

| Variable | Mild hemodilution group (n=93) | Moderate hemodilution group (n=93) | P  |
|----------|-------------------------------|-----------------------------------|----|
| T0       | 68.15±4.36                   | 67.15±3.92                        | 0.101|
| T1       | 71.29±2.53                   | 70.7±2.47                         | 0.150|
| T2       | 71.9±2.80                    | 72.11±2.94                        | 0.618|
| CPB      |                               |                                   |     |
| 15 min   | 64.4±3.58                    | 65.25±4.52                        | 0.156|
| 30 min   | 65.53±6.73                   | 65.85±5.52                        | 0.452|
| 5 min before weaning | 65.37±5.62              | 64.64±4.70                        | 0.337|
| T3       | 71.2±0.82                    | 70.77±4.25                        | 0.599|
| T4       | 70.79±3.54                   | 71.15±3.64                        | 0.495|
| T5       | 72.30±3.83                   | 71.76±3.66                        | 0.326|
| T6       | 70.37±3.48                   | 70.73±3.60                        | 0.489|
| T7       | 71.50±4.30                   | 70.75±3.74                        | 0.206|
| Left regional cerebral oxygen saturation (%) |                               |                                   |     |
| T0       | 71.13±3.55                   | 70.85±3.10                        | 0.567|
| T1       | 70.54±3.34                   | 70.08±3.17                        | 0.336|
| T2       | 71.44±4.37                   | 70.95±3.75                        | 0.412|
| CPB      |                               |                                   |     |
| 15 min   | 66.13±3.34                   | 65.79±2.76                        | 0.450|
| 30 min   | 65.53±3.65                   | 65.30±3.43                        | 0.458|
| 5 min before weaning | 66.86±3.87              | 66.24±4.10                        | 0.290|
| T3       | 72.40±3.48                   | 71.92±3.27                        | 0.333|
| T4       | 72.74±3.72                   | 72.55±3.64                        | 0.725|
| T5       | 72.07±3.47                   | 71.79±3.87                        | 0.644|
| T6       | 70.72±2.15                   | 71.15±3.20                        | 0.283|
| T7       | 71.45±3.50                   | 71.24±3.71                        | 0.691|

CPB: cardiopulmonary bypass. T0: Baseline reading; T1: Reading 15 minutes after induction; T2: before initiation cardiopulmonary bypass; CPB 15 min: 15 minutes after initiation of cardiopulmonary bypass; CPB 30 min: 30 minutes after initiation of cardiopulmonary bypass; CPB 5 min: five minutes before weaning of cardiopulmonary bypass; T3: 30 minutes after cardiopulmonary bypass T5: 30 minutes after cardiopulmonary bypass; T6: at ICU admission; T9: 6th hour after ICU admission; T10: 12th hour after ICU admission; T7: 24th hour after ICU admission

Hemodilution during CPB results from the mixing of pump crystalloid and colloid prime solution with the blood of the patients and these two mixed volumes plus to the pre-CPB hematocrit determine the degree of hemodilution.[9] The hemodilution during CPB is classified into three groups: mild (Hct >25%), moderate (Hct 21-25%), and severe (Hct <21%).[9]

In the present study, the hematocrit value was maintained >25% in the mild hemodilution group and in the range of 21-25% in the moderate hemodilution group by hemofiltration plus transfusion of packed-red blood cells

no incidence in the anaphylactic reaction, disseminated intravascular coagulopathy, postoperative graft occlusion and acute myocardial infarction, and central nervous system dysfunction, or mortality in the two groups.

**DISCUSSION**

Hemodilution during CPB results from the mixing of pump crystalloid and colloid prime solution with the blood of the patients and these two mixed volumes plus to the pre-CPB hematocrit determine the degree of hemodilution.[9] The hemodilution during CPB is classified into three groups: mild (Hct >25%), moderate (Hct 21-25%), and severe (Hct <21%).[9]
in infants undergoing cardiac surgery and also, it was associated with a reduction in the lactate level that indicates better tissue perfusion during CPB.

Richard A[36] showed that the hematocrit was the only CPB parameter that has an important effect on the cognitive outcome and suggested that a hematocrit of 25% be considered the lowest acceptable level with normal flow rates for adults during CPB and the same results were reported by other studies.[34–38]

There are some recommendations to minimize the incidence of severe hemodilution during CPB:

1. controlling preoperative blood loss during routine preoperative phlebotomy and cardiac catheterization;

### Table 4: Intraoperative Data and Outcome of Patients (Data are Presented as Mean±SD, Number, %)

| Variable                               | Mild hemodilution group (n=93) | Moderate hemodilution group (n=93) | P     |
|----------------------------------------|-------------------------------|-----------------------------------|-------|
| Number of coronary artery grafts       |                               |                                   |       |
| 2                                      | 17                            | 20                                | 0.713 |
| 3                                      | 19                            | 24                                | 0.486 |
| 4                                      | 48                            | 45                                | 0.769 |
| 5                                      | 5                             | 2                                 | 0.441 |
| 6                                      | 4                             | 2                                 | 0.678 |
| CPB time (minute)                      | 118.3±20.57                   | 115.6±18.40                      | 0.363 |
| Cross clamping time (minute)           | 89.1±14.50                    | 86.7±13.90                       | 0.262 |
| CPB temperature (°C)                   | 29.0±1.14                     | 29.1±1.17                        | 0.813 |
| Hematocrit (%)                         |                               |                                   |       |
| 10 min before CPB                      | 36.1±3.5                      | 36.46±3.62                       | 0.553 |
| 15 min during CPB                      | 27.2±1.46                     | 23.8±1.09                        | 0.001*|
| 30 min during CPB                      | 28.35±1.17                    | 23.40±1.24                       | 0.001*|
| 5 min before weaning                   | 27.30±1.22                    | 24.02±0.65                       | 0.001*|
| 15 min after weaning                   | 29.27±1.78                    | 26.75±1.60                       | 0.001*|
| End of surgery                         | 32.10±2.30                    | 28.18±2.14                       | 0.001*|
| Hemofiltrated volume during CPB (ml)   | 1808.2±253.54                 | 1294.7±250.32                    | 0.001*|
| Transfused P-RBC (unit)                |                               |                                   |       |
| During CPB                             | 2.65±0.83                     | 2.23±0.58                        | 0.001*|
| After CPB                              | 1.15±0.45                     | 1.66±0.81                        | 0.001*|
| Blood loss (ml)                         |                               |                                   |       |
| Intraoperative (ml)                     | 2184.60±252.55                | 2250.75±268.40                   | 0.085 |
| Postoperative (ml/24 hr)               | 548.7±131.10                  | 576.8±145.17                     | 0.168 |
| Intraoperative fluids                   |                               |                                   |       |
| Crystalloids (ml)                       | 2992.5±497.43                 | 3120.8±527.30                    | 0.089 |
| Hesteril 6% (ml)                        | 625.7±155.30                  | 652.2±143.55                     | 0.197 |
| Dopamine (µg/kg/min)                    | 6.30±2.50                     | 7.15±2.90                        | 0.033*|
| Epinephrine (µg/kg/min)                 | 0.05±0.02                     | 0.06±0.03                        | 0.008*|
| Norepinephrine (µg/kg/min)             | 0.04±0.01                     | 0.07±0.02                        | 0.001*|
| Nitroglycerine (µg/kg/min)             | 0.7±0.40                      | 0.6±0.35                         | 0.071 |
| Intra-aortic balloon pump              | 12                            | 27                               | 0.011*|
| Pacing                                 | 17                            | 30                               | 0.042*|
| Intraoperative urine output (ml)        | 2142.6±181.80                 | 2181.2±218.30                    | 0.192 |
| Intraoperative blood sugar levels (mmol/L) | 8.19±1.30                 | 8.02±1.23                        | 0.360 |
| Postoperative neurological complications|                               |                                   |       |
| Total                                   | 19 (20.43%)                   | 33 (35.48%)                      | 0.033*|
| Neurocognitive dysfunction              | 17 (18.72%)                   | 30 (32.25%)                      | 0.042*|
| Stroke                                  | 2                             | 3                                 | 0.650 |
| Postoperative renal impairment          | 6                             | 9                                 | 0.793 |
| Postoperative renal failure             | 4                             | 3                                 | 0.700 |
| Postoperative dialysis                  |                               |                                   |       |
| Temporarily                             | 2                             | 2                                 | 1.000 |
| Permanent                               | 2                             | 1                                 | 0.560 |
| Pulmonary edema                         | 4                             | 10                                | 0.164 |
| Postoperative mechanical ventilation    | 4                             | 10                                | 0.164 |
| Allergic reaction                      | 4                             | 2                                 | 0.678 |
| Hepatic complications                   | -                             | -                                 |       |
| Anaphylactic reaction                   | -                             | -                                 |       |
| Disseminated intravascular coagulopathy| -                             | -                                 |       |
| Thromboembolism                         | -                             | -                                 |       |
| Infection                               | -                             | -                                 |       |
| ICU length of stay (days)               | 2.78±1.17                     | 3.02±1.24                        | 0.176 |
| Hospital length of stay (days)          | 8.15±2.53                     | 8.32±2.41                        | 0.639 |
| Mortality                               | 4                             | 3                                 | 0.700 |
(2) minimizing the size of CPB circuits according to patient BSA;
(3) minimizing of the tubing size by minimizing the length and diameter of the tubes connecting the patient and pump;
(4) returning the collected blood to the circulating volumes;
(5) controlling the intraoperative blood loss and fluid administration;
(6) using of retrograde autologous priming of the CPB circuit, which has been shown to reduce hemodilution and transfusion requirements\(^{[39,40]}\);
(7) The acceptable hematocrit levels during CPB must be determined according to the age and co-morbidities of the patient\(^{[29]}\);
(8) Transfusion of packed red blood cells is reasonable and indicated if the hemoconcentration is not possible or is ineffective to maintain the hematocrit above the required levels.\(^{[41]}\)

There are limitations to the present study. First, the study was not a blinded study; and second, it was done in a single center.

**CONCLUSION**

The mild hemodilution was associated with a significant decrease in the incidence of neurocognitive dysfunction compared to moderate hemodilution during CPB in patients undergoing coronary artery bypass grafting. Also, the transfused packed red blood cells increased during CPB and decreased after CPB with the mild hemodilution more than moderate hemodilution.

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**Conflicts of interest**

There are no conflicts of interest.

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