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Acute Limited Normovolemic Hemodilution: A Method For Avoiding Homologous Transfusion

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Preoperative normovolemic hemodilution was introduced for clinical application by Messmer and co-workers. Preoperative blood withdrawal of 1,500–2,000 ml by an isovolemic exchange with colloids or crystalloids (3 times the volume of blood withdrawn), in order to maintain a constant circulating volume, is offset by an adequate increase of cardiac output and an unchanged systemic oxygen transport capacity despite a decreased oxygen content. Patients lose fewer red cells and more plasma intraoperatively. The retransfusion of autologous blood follows in the reverse order of collection after hemostasis is restored. The procedure is a safe and feasible method, which is not beset with the logistical problems of autologous blood predeposit and has the added advantage that fresh autologous blood is available at once for retransfusion. Provided that the contraindications are observed, the technique helps to reduce or even avoids the risks of homologous blood transfusion. The need for stored blood can be reduced by 20% to 90%, depending on the surgical procedure.

The average blood loss in some elective surgical procedures ranges from 1,500 to 2,000 ml and, in most instances, 2–3 units of homologous blood are given intra- and postoperatively. For a long time blood was thought to be the ideal volume-replacing substance in cases of acute blood loss. Although the administration of blood is usually regarded as a safe procedure, intraoperative tranfusion is not without hazard. Potential complications include errors of typing, cross-matching, and administration, as well as allergic reactions, alloimmunization to blood elements, and exposure to transmissible diseases including hepatitis, syphilis, malaria, cytomegalovirus, and acquired immunodeficiency syndrome. Patients who are able to serve as their own blood donors, therefore, receive the safest of all possible transfusions—autologous blood. Increased safety alone would sufficiently justify autologous transfusion programs. One alternative to avoid or reduce the administration of homologous blood is autologous blood transfusion by means of acute preoperative hemodilution [1–7].

Arguments for Hemodilution

At the time of its clinical introduction in the early 1970's, the main reason for hemodilution during surgical procedures was to save donor blood in order to reduce the risk of transmissible diseases, especially hepatitis. The incidence of posttransfusion hepatitis in West Germany is assumed to range from 0.02 to 0.2% [8]. It must be stressed that hospital-acquired hepatitis is often a hospital infection rather than a transfusion-related disease [9, 10]. Nevertheless, the risk of transfusion-related hepatitis cannot be excluded.

Increasing interest in avoiding homologous transfusion concerns immunologic aspects, i.e., alloimmunization of the patients to constituents of transfused blood especially in young patients, which gives rise to problems with later blood transfusions [11–13].

Severe hemolytic reactions have been described and the lethality of such reactions is reported to be 1:30,000 [14]. Other arguments in favor of autologous transfusion are the biochemical changes that homologous blood undergoes during storage, i.e. loss of clotting factors, platelets, and 2,3-diphosphorglycerate. Homologous (banked) blood is known to cause a decrease of P_{50}, resulting in a shift of the oxyhemoglobin dissociation curve to the left [15]. P_{50} is one of the important factors that influence the supply of oxygen to the tissues when there is a decrease in blood flow, as occurs in major vascular surgery. Intentional hemodilution does increase P_{50} and it is concluded that this procedure is beneficial to patients having major vascular surgery by increasing P_{50} of the blood and facilitating oxygen supply to the tissues [16].

Undoubtedly one main impetus for reexploring hemodilution has come from increasing evidence in the past few years that even a normal or high hemoglobin or hematocrit level represents an important cardiovascular risk factor. This lends support to what may at first seem an unlikely hypothesis, namely, that the normal range of hematocrit is not necessarily the optimal range. Hemodilution by no means treats the primary cause of ischemia, but it may compensate in some measure for narrowing of the vessels. Improved rheological properties of diluted blood under hemodilution allow better tissue perfusion. Lowering the blood viscosity by isovolemic hemodilution, therefore, has a wide range of clinical applications in obstructive diseases of the veins and arteries and their surgical repair [17–22].

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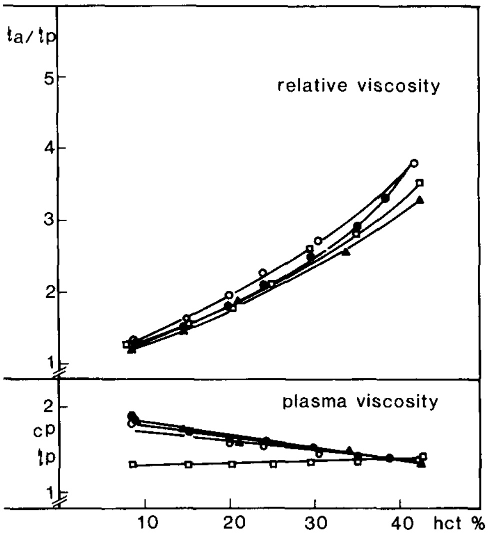

Fig. 1. Changes in relative apparent viscosity (*above*) and plasma viscosity (*below*) from hemodilution in vivo. □ = values from low-molecular-weight gelatin, ○ = hydroxyethyl starch, ▼ = high-molecular-weight gelatin, ● = dextran 60 [21]. Reprinted with permission of publisher.

Definition

The term *acute preoperative limited normovolemic hemodilution* is applied to a hematocrit reading of not less than 27%. Acute preoperative extreme hemodilution designates a hematocrit level lower than 20%.

Physiological Aspects of Hemodilution

The normal hematocrit level of 45% provides optimal oxygen transport only at rapid flow rates. In all low-flow states it reduces O_2 transport because of marked increases in blood viscosity. Acutely lowering hematocrit under isovolemic conditions not only favors recovery from such low-flow states, but at the same time improves the curtailed oxygen transport. The changes of whole blood viscosity must be regarded as the basic mechanism in controlling cardiac output (Fig. 1) [21]. Thus, maximum oxygen transport capacity coincides with the hematocrit ratio of 30%. It can be stated that limited hemodilution is a procedure for the safe improvement of the flow properties of the blood without jeopardizing oxygen transport [21, 23–26]. The connection between viscosity, oxygen transport, and flow rates has supplied the basis for the concept of therapeutic hemodilution.

Method of Preoperative Normovolemic Hemodilution

The technique of acute preoperative hemodilution is as follows: Prior to or after induction of anesthesia immediately before surgery, depending on the patient's hematocrit reading which should be above 36% (> 12 g/100 ml Hb), 1,500–2,000 ml blood are withdrawn into standard collection bags and stored as CPD blood at room temperature. The amount of blood withdrawn is replaced by simultaneous isovolemic infusion of colloids [human albumin 5%, dextran 60–70, hydroxyethyl starch (HES) 200 or 450] or with Ringer's lactate solution in a volume 3 times that of the blood withdrawn to maintain normovolemia [2, 3]. In this way the circulating blood volume is kept constant, since the reduction of red cell mass is made up for by an increase in plasma volume. Under these conditions it is evident that, in comparison to a patient with a normal hematocrit ratio, a patient who has undergone hemodilution will lose fewer red blood cells (RBCs) with an identical operative blood loss because his blood loss mainly entails plasma. Blood loss during surgery is immediately replaced with colloids or crystalloids down to a hematocrit ratio of 27%, depending on the patient's condition. Reinfusion of the autologous blood should begin when hemostatis is restored. The units should be retransfused in the reverse order of collection without a filter, so as to ensure maximum retransfusion of the platelets in the autologous blood. Postoperative hematocrit values of 28–30% are tolerable under normovolemic conditions.

The Compensatory Mechanisms of Preoperative Acute Limited Normovolemic Hemodilution

The acute dilutional reduction of hematocrit demands the action of compensatory mechanisms. Oxygen content of arterial blood critically depends on cardiorespiratory function and the circulatory blood volume. As long as normovolemia is provided, 3 mechanisms are activated to maintain systemic oxygen transport despite the lowering of the arterial oxygen content of the blood: (a) increase in total and local blood flow rates, (b) increase in oxygen extraction, and (c) reduction of hemoglobin oxygen affinity by shifting the oxygen dissociation curve to the right. The first mechanism prevails for limited normovolemic hemodilution (hematocrit reading not lower than 27%). The most constant finding in patients in an awake state or under anesthesia is that the cardiac output rises when the hematocrit level is acutely reduced, if blood volume is maintained in the normal range [1, 2, 4–7, 21, 27, 28].

In a study of 25 patients undergoing abdominal surgery, hemodynamics were measured during acute limited normovolemic hemodilution [5, 7]. Figure 2 shows the mean cardiac output percent (CO) of the 25 patients, using different solutions. During acute normovolemic hemodilution, the decrease in hematocrit and consequent decrease in O_2-carrying capacity are offset by an increase in CO, which remains elevated throughout the operation period. Comparing the hemodynamic effects of 4 different diluents, no statistically significant difference could be determined between the groups. It appears, however, that the use of dextran alone for hemodilution should be limited by the total amount of infused dextran because of its influence on coagulation (1.5 g/kg per 24 hours).

As a result of the increase in cardiac output, the systemic oxygen transport capacity (product of cardiac output and arterial oxygen content) does not fall parallel to the dilutional fall in hematocrit. Based on theoretical considerations, Hint [18] predicted that systemic oxygen transport would result in a peak hematocrit ratio of approximately 30% (Fig. 3). Sunder-Plassmann et al. were able to confirm that maximum oxygen transport did not coincide with the animals' control hematocrit ratio but with a ratio of about 30% [20, 26]. The increase in oxygen transport was explained by the enhancement of cardiac output being proportionally greater than the corresponding fall in arterial oxygen content of the blood.

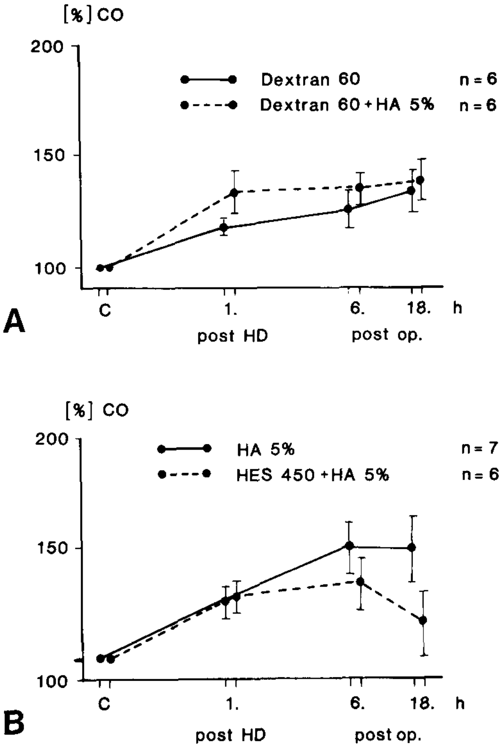

Fig. 2A. Changes of cardiac output (CO, percent) when using dextran 60 (*solid line*), dextran 60 and human albumin 5% (*dotted line*). **B.** Changes of cardiac output when using human albumin 5% (*solid line*), starch and human albumin 5% (*dotted line*). C = control values = 100%, after hemodilution 1, postoperatively 6 hr and 18 hr [5, 7]. Reprinted with permission of publisher.

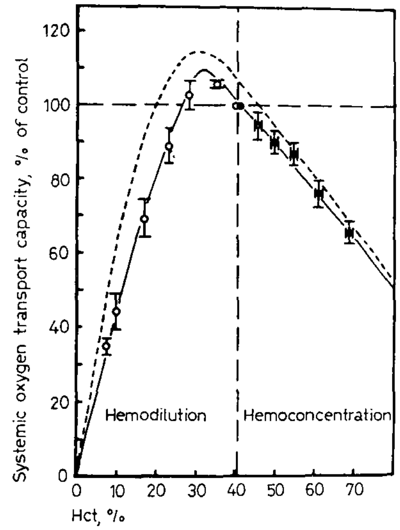

Fig. 3. Systemic oxygen transport capacity during normovolemic hemodilution with dextran 60 and normovolemic hemoconcentration with packed red cells in dogs. The dotted line represents the behavior of the curve predicted by Hint [18]. The solid circles represent values obtained during isovolemic hemoconcentration by means of homologous packed red cells. The open circles represent values obtained during isovolemic hemodilution by means of dextran 60 [26]. Reprinted with permission of publisher.

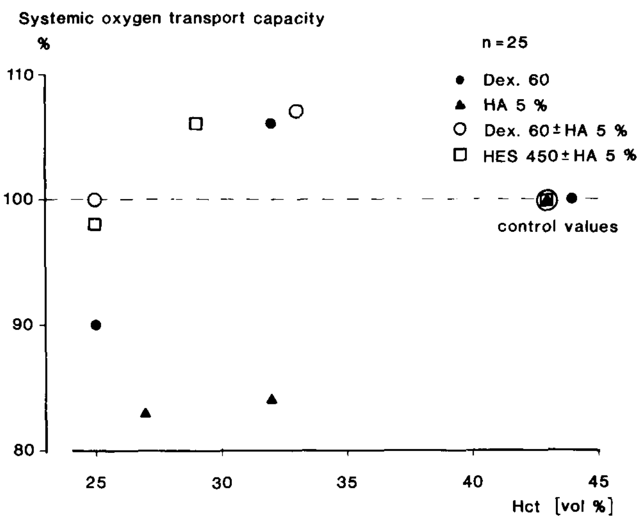

Fig. 4. Calculated systemic oxygen transport capacity after hemodilution at different hematocrit ratios with 4 dilution solutions in 25 patients [5, 7]. Reprinted with permission of publisher.

Figure 4 presents the calculated mean values of the systemic oxygen transport capacity for the above-mentioned study with different diluents [5]. The control values were set as 100% with a hematocrit reading in the range of 43% or 44%. A calculated oxygen transport capacity of 106% or 107% of the control values was found between hematocrit ratios of 29% and 33% with dextran 60, and dextran 60 or HES in combination with human albumin 5%. Plasma substitute (HA 5%) alone resulted in lower oxygen transport capacity values. The slightly hyperoncotic effect of dextran and HES explains the difference as compared to plasma. Laks et al. [4, 29], when using hemodilution on surgical patients, found a systemic oxygen transport of 110% at a hematocrit ratio of 27%. In contrast to Lundsgaard-Hansen who criticized the "fundamental curve" first published by Hint and Sunder-Plassmann, the results shown in Fig. 4 confirm the concept of hemodilution [30]. It must, however, be stressed that the concept of hemodilution is based on the fact that the oxygen transport rate and tissue oxygenation can be maintained in the control range despite considerable reductions in hematocrit, and the peak oxygen transport rate is never of major importance [6, 27, 31].

Indications and Contraindications for Hemodilution

Preoperative hemodilution has been used routinely in many surgical fields, such as cardiac surgery [32–38], vascular surgery [16, 17, 19, 39–42], orthopedic surgery [4, 22, 28, 43–47], and major general surgery [1, 2, 5, 7, 22, 43, 48–51]. Furthermore, it is especially indicated in patients with polycythemia since, in addition to providing autologous blood in these patients, hemodilution per se has beneficial effects [23, 52, 53].

Anemia, cardiac dysfunction, severe coronary artery disease, and severe hepatic disease are all relative contraindications to elective hemodilution. Furthermore, patients with pulmonary emphysema or obstructive lung disease are not good candidates for hemodilution because blood oxygenation could be endangered.

Coronary artery disease per se limits the potential and effectiveness of the compensatory mechanisms necessary to tolerate hemodilution. Gisselsson et al. demonstrated that, during hemodilution, the decrease in oxygen content in arterial blood after hemodilution was compensated by an increase of cardiac output (34%) and an increase of myocardial blood flow of 59% [46]. Thus, the myocardial blood flow increased proportionally more than the cardiac output, resulting in a virtually unchanged oxygen tension in coronary sinus blood in healthy patients. It could be shown that blood loss of up to 20% of the total volume can be replaced by dextran solutions without a significant decrease in the myocardial oxygen supply. Coronary artery disease otherwise leads to impaired perfusion of the myocardium, causing diffuse necrosis of the heart muscle with scar formation or myocardial infarction. This can diminish the pumping function of the left ventricle so that the ventricle is not able to increase cardiac output sufficiently during hemodilution.

A significant stenosis of a coronary artery also limits the compensatory increase of coronary blood flow during hemodilution. In myocardial regions distal to a coronary artery stenosis where the oxygen supply is already borderlined at normal hemoglobin concentration, acutely reduced hemoglobin concentration in the presence of an unchanged coronary blood flow will cause a severe oxygen deficit and impairment of regional myocardial function [54].

According to Klövekorn et al. [36], the contraindications for hemodilution in patients undergoing coronary bypass surgery are: (a) Hb concentration < 140 g/L, (b) unstable angina, preinfarction syndrome, (c) abnormal left ventricular function, ejection fraction < 0.5, cardiac index < 2.5 l/m^2 per min, (d) left main coronary artery stenosis, (e) ischemic electrocardiogram changes at rest, and (f) impaired lung function. The recommendation to advocate preoperative hemodilution only for patients with coronary artery disease when they undergo coronary bypass surgery would help to avoid considerable problems due to hemodilution, which may complicate the intra- and postoperative course.

Avoidance of Homologous Transfusion by Hemodilution

In the literature regarding hemodilution, a reduction in homologous blood transfusion has been reported varying from 18% to 90% [1, 2, 5, 7, 17, 32, 34–37, 39, 40, 42, 44, 47, 48, 50, 51, 55, 56]. Preoperative hemodilution (in which blood is removed before surgery and is replaced with cell-free solutions) as well as intraoperative hemodilution (in which blood loss is replaced during surgery with cell-free solutions) are both unable to avoid homologous blood transfusion completely. In attempting to achieve this, extreme hemodilution, i.e., hemodilution below a hematocrit ratio of 20%, was performed [33, 35, 36, 38, 50, 51]. In order to decrease further the need for homologous blood, especially in children undergoing dorsal spinal fusion, a study was conducted to evaluate the saving effect of extreme hemodilution [57]. Table 1 presents data of 26 patients undergoing Harrington's instrumentation. Fourteen patients were diluted to a hematocrit ratio of below 20% (EHD); 12 patients served as controls, receiving homologous blood transfusion corresponding to their intraoperative blood losses. The 2 groups were comparable in age, body-surface area, body weight, and anesthesia time.

Table 1. Data of patients selected for study of extreme hemodilution (EHD) [57].[a]

	Control group	EHD group
No. of patients	12	14
Age (yr)	13.8	13.7
Range	11–18	12–17
Body surface area (m^2)	1.44	1.55
Body weight (kg)	46	53
Anesthesia (min)	309	316

[a]Numbers in both control group and EHD group are mean figures. Reprinted with permission of publisher.

Table 2. Transfusion therapy of patients selected for extreme hemodilution (EHD) study [57].

	Control group	EHD group
Homologous blood		
Intraoperative	4,120 (ml)	250 (ml)
Postoperative	250 (ml)	500 (ml)
Total	4,370 (ml)	750 (ml)

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The need for homologous transfusion is shown in Table 2. The intraoperative demand for homologous transfusion averaged 4,120 ml in the control group in contrast to 250 ml in the EHD cohort. The total need for homologous blood at the time of discharge was nearly 6-fold higher in the control group.

Acutely induced extreme hemodilution can be tolerated very well by these patients, thanks to an enormous capacity in these young people to offset the hemodilution by maintaining a constant circulating blood volume. Under special conditions with extensive and invasive monitoring, it is possible to cut down the use of excessive quantities of donor blood by extreme hemodilution and to diminish the severe clinical problems associated with massive homologous blood transfusions. Nevertheless, the procedure should only be performed in young healthy people. Furthermore, it inevitably requires monitoring of filling pressures of the heart as well as cardiac output. For this reason, extreme hemodilution is not suitable for routine use. Intraoperatively performed, extreme hemodilution was reported by Henling et al. in 110 children of the Jehovah's Witness faith who underwent operations for complete repair of congenital heart disease with cardiopulmonary bypass [35]. They did not receive any blood or blood products during hospitalization. The authors conclude that cardiac operations can be safely performed in children whose parents have denied them transfusion and suggest that hemodilution techniques might be used more extensively in children undergoing cardiac surgery.

Combined Autologous Transfusion Programs with Hemodilution

Only rarely can banked blood transfusion be avoided completely; therefore, the combination of different autotransfusion techniques has been proposed [33, 35, 47]. Ninety-three patients undergoing scoliosis surgery were studied in order to examine the efficiency of a combined autotransfusion program, namely, frozen blood products from preoperative donations,

Table 3. Transfusion therapy of patients selected for autologous transfusion programs [58].

	No autotransfusion	Intraoperative autotransfusion	Preoperative donation, intraoperative autotransfusion, preoperative hemodilution
No. of patients	17	39	37
Intraoperative blood loss (L)	4.8 ± 1.6	4.7 ± 1.4	4.8 ± 1.8
Autologous transfusion (units)	–	6.0 ± 2.3	3.1 ± 0.8 5.9 ± 2.6
Homologous transfusion (units)	8.4 ± 2.4	3.9 ± 2.1	1.4 ± 1.6
Patients without homologous transfusion	0/17	1/39	15/37

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preoperative moderate hemodilution, and intraoperatively salvaged red cells after separation, washing, and concentration (Hemonetics Cell-Saver III) (Table 3) [58].

A profound reduction in homologous transfusion was achieved by the combination of autotransfusion techniques. In 40% of group 3, the manifold risks of homologous transfusion was completely avoided at the time of discharge. Beside the saving of blood, the better quality of the autologous blood must be considered. The freezing of red blood cells and plasma greatly enhances the shelf life and the functional viability of preoperatively donated blood. In addition to the autologous blood products obtained, the patients gain the benefits of stimulated erythropoesis and a strong motivation resulting from involvement in their own medical care.

Summary

Preoperative and intraoperative hemodilution is a part of a total approach to blood conservation and can be well tolerated to hematocrit ratios of 25% under a constant circulating normovolemic volume. It helps to reduce homologous blood transfusion, improves nutritional capillary flow, and prevents thromboembolic complications. For maximum effectiveness in avoiding homologous blood transfusion it should be combined with autologous blood predeposit, intraoperative scavenging, and postoperative autologous retransfusion. The key for acceptance of hemodilution is appreciation of the fact that a hematocrit reading of 30% is adequate to prevent a tissue oxygen deficit in the operative patient. Acceptance of these principles may reduce demands for blood and protect patients from complications of homologous blood transfusion.

Résumé

L'hémodilution normovolémique pré-opératoire a été instaurée en chirurgie par Messmer et ses collaborateurs. Le prélèvement de sang du malade immédiatement avant le début de l'acte chirurgical, lors de l'induction de l'anesthésie, de 1,500 à 2,000 ml de sang, et leur remplacement isovolémique par des colloïdes ou des cristalloïdes (3 fois le volume de sang soustrait) dans le but de maintenir un volume circulatoire constant, est compensé par une élévation adéquate du débit cardiaque et par une capacité inchangée du transport de l'oxygène en dépit d'une diminution de sa saturation. De ce fait, les opérés perdent moins d'hématies mais plus de plasma au cours de l'intervention. La retransfusion du sang autologue prélevé est effectuée en ordre inverse des prélèvements sanguins dés que l'hémostase est assurée. La méthode est praticable et sans danger. Elle n'est pas en but aux problèmes logistiques posés par la transfusion de sang autologue prélevé avant la date de l'intervention et conservé. Elle a, pour avantage supplémentaire, le fait que le sang frais prélevé au début de l'intervention est disponible d'emblée pour la retransfusion. A condition que les contre-indications soient respectées, cette technique aide à réduire ou même à éviter les risques inhérents à la transfusion du sang homologue. Les besoins en sang conservé peuvent ainsi être réduits de 20% à 90% en fonction de l'intervention chirurgicale pratiquée.

Resumen

La hemodilución normovolémica preoperatoria fue introducida a la aplicación clínica por Messmer y colaboradores. La remoción preoperatoria de 1,500–2,000 ml mediante un intercambio isovolémico con coloides o con cristaloides (3 veces el volumen extraido), para mantener un volumen circulatorio constante, es compensado por el adecuado aumento en el gasto cardíaco y una mantenida capacidad sistémica de transporte de oxígeno a pesar del disminuido contenido de oxígeno. Los pacientes pierden menos globulos rojos y mayor cantidad de plasma intraoperatoriamente. La retransfusión de la sangre autóloga se hace en el orden inverso al de su recolección una vez que la hemostasis haya sido restablecida. El procedimiento representa un método seguro y factible que no se acompaña de los problemas logísticos del predepósito de la sangre autóloga y que posee la ventaja adicional que significa la disponibilidad inmediata de sangre autóloga para retransfusión. Teniendo en cuenta la debida observación a las contraindicaciones, esta tecnica ayuda a reducir, y aún a eliminar, los riesgos de la transfusión sanguínea autóloga. La necesidad de sangre almacenada puede ser reducida en 20% a 90%, según el procedimiento quirúrgico.

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