Laboratory characteristics and clinical utility of post-operative cell salvage: washed or unwashed blood transfusion?

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Introduction

The development of complex surgical procedures for the treatment of a number of diseases has increased the demand for allogeneic blood. In hospitals, up to 50% of transfused blood units are used in the surgical setting and up to 60% of all transfusions are given to patients over 65 years old, an age group of patients who are excluded from altruistic blood donation in some countries[1,2]. The demand for allogeneic blood often exceeds the supply. The safety of allogeneic blood transfusion (ABT) in developed countries has improved dramatically, especially as a result of more restrictive criteria for donor selection and increased analytical screening of donated blood which have led to a decrease in the rate of transfusion-transmitted infections. However, "clerical mistakes" or administration of "wrong blood" are still too frequent (1/15,000-20,000 units)[3,4]. Liberal transfusion protocols (pre-transfusion haemoglobin [Hb] concentration > 9-10 g/dL) should, therefore, be avoided to further reduce the risk of infection and other complications such as incompatible haemolytic reactions, Graft-versus-Host Disease, metabolic disorders, Transfusion-Related Acute Lung Injury, and transfusion related immuno-modulation[3,4]. As for immuno-modulation, the results of three extensive studies involving more than 22,000 patients undergoing orthopaedic surgery strongly suggest that peri-operative ABT is associated with an increase in the risk of post-operative infection[5-7].

Overall concerns about the adverse effects of ABT have prompted the review of transfusion practices and the search for transfusion alternatives, such as pre-operative autologous blood donation, haemodilution, peri-operative cell salvage, recombinant human erythropoietin (rHuEPO) and iron, or anti-fibrinolytic administration[8]. The ultimate objective is to minimise exposure to ABT and, therefore, ABT-associated risks. The main objective of this review is to provide updated evidence on the quality, safety and efficacy of post-operatively salvaged shed blood (PSB) after major surgery. However, the results of a systematic review indicate that reinfusion of unwashed filtered PSB after cardiac surgery produces only a marginal benefit[9] and can also cause significant adverse effects, so its use is not recommended[10]. We, therefore, shall focus mainly on the use of PSB in orthopaedic surgery, especially lower limb joint replacement.

Are post-operative drains needed after major orthopaedic surgery?

The use of closed-suction drainage systems after total joint replacement is common practice. The theoretical advantage of the use of such drains is a reduction in the occurrence of wound haematoma and infection. However, there are at least three unanswered questions in this regard. The first question is whether post-operative drains are efficacious in achieving this goal. In a recent meta-analysis of 36 studies involving 5,464 participants undergoing different types of orthopaedic surgery, pooling of results indicated no statistically significant difference in the incidence of wound infection, haematoma, dehiscence or re-operations, but a significantly greater need for ABT in patients managed with a post-operative drain (relative risk [RR], 1.25; 95% CI, 1.04-1.51)[11]. Thus, the authors concluded that there is insufficient evidence from randomised trials to support the routine use of closed-suction drainage in orthopaedic surgery[11]. An alternative reading of this conclusion is that further randomised trials with larger numbers of patients and full reporting of outcomes are indicated

before the absence of any benefit from the use of drains, particularly for the outcome of wound infection, can be proven. However, it is worth noting that reinfusion of PSB was not performed in these studies.

Nevertheless, if a postoperative drain is to be used, the second question is whether to use a low-vacuum or a high-vacuum drain. Very recently, Slappendel *et al*.[12] presented data from an open, prospective and single-centre comparison of blood loss, post-operative haemoglobin levels and allogeneic blood transfusions of 179 patients scheduled for revision of total hip surgery who were randomised to either the Bellovac ABT (autologous blood salvage, low vacuum) or the Medinorm AG (high vacuum) drainage systems. No statistically significant differences were detected between the two drainage systems with regards to blood loss, ABT rate and post-operative adverse events. These results are in agreement with those previously reported by Benoni and Fredin[13] comparing the effect of low-vacuum and high-vacuum drains on these outcomes in a randomised study of 73 patients undergoing primary hip arthroplasty. In contrast, a recent study in patients undergoing a hemi-arthroplasty for subcapital hip fracture repair showed that the use of a low-vacuum drain resulted in a lower post-operative ABT rate when compared to the use of a high-vacuum drain[14].

This raises a third question, i.e. whether to use low vacuum re-infusion drains (ConstaVac CBCII, BelloVac ABT, Solcotrans, Suretrans, Donor, etc.). Of course, if no drain is used, there is no need for re-infusion. However, it can be postulated that if post-operative drains are to be used, low-vacuum salvage/re-infusion drains, which produce less haemolysis, may be preferred, as they might be beneficial to the patient in the event of high post-operative blood loss. We shall try to answer this question in the next section.

Nevertheless, there are two additional aspects which must be borne in mind. First, in most studies the location of drains is not mentioned, and this is an important issue. In some studies subcutaneous drains were used, and this led to a low volume of blood saving, thus compromising the efficacy for reducing ABT. Second, revision hip surgery is totally different from primary hip surgery or hip fracture repair surgery. So, best response for PBS in knee surgery rather than in primary and revision hip and spine surgery is still under debate when looking for reductions in ABT.

Are low-vacuum re-infusion drains useful?

Post-operative cell salvage and re-infusion, with or without washing, must be restricted to elective orthopaedic procedures with an anticipated post-operative blood loss between 750 - 1,500 mL, allowing for the recovery of at least the equivalent of one unit of packet red cells. This blood conservation technique may, therefore, be especially useful after total knee arthroplasty, total hip arthroplasty, and instrumented spine surgery, but generally not after hip fracture repair. We will review some recent studies in which PSB re-infusion was used in conjunction with a defined ABT protocol.

Total knee arthroplasty

In patients undergoing primary total knee arthroplasty, salvage and re-infusion of PSB reduced the relative risk of receiving ABT by 60% when compared with the risk in a control group, but not the number of units transfused per patient (2 units/patient)[15-22]. This reduction of transfusion rates, which was not observed in all studies, was independent of whether washed (relative risk reduction [RRR]: 63%)[15,16] or unwashed PSB (RRR: 62%)[17-22] was re-infused (Table I). Interestingly, after stratification of patients by pre-operative haemoglobin concentration, a controlled observational study including 953 patients suggested that those with a haemoglobin concentration between 12 and 14 g/dL would benefit most from PSB as a unique blood conservation technique. This would not be necessary in patients with a haemoglobin greater than 14 g/dL and should be associated with other blood-saving techniques (e.g., iron, rHuEPO) in patients with a haemoglobin concentration less than 12 g/dL[22]. In addition, there is an ongoing multicentre randomised study comparing the re-infusion of unwashed PSB with infusion of hydroxyl ethyl starch (Voluven®) in patients undergoing total knee arthroplasty with a pre-operative haemoglobin between 11 g/dL and 14 g/dL, and a low-vacuum post-operative drain, draining at least 400 mL in the first 6 hours after the operation. Preliminary data from this study strongly suggest that re-infusion of unwashed PSB is superior to infusion of hydroxyl ethyl starch in reducing the requirements for ABT (Muñoz *et al*., unpublished data).

Thus, reduction of post-operative blood loss and/or treatment of peri-operative anaemia could also be

Table I - Some recent studies on post-operative cell salvage after total knee replacement.

Author, year (Reference)	Study type	Patients (n)	Salvaged blood (re-infused volume)	Transfusion protocol	ABT (%)	
					Cell salvage	Control
Amin, 2008 (20)	RCT	178	Unwashed PSB (481 mL)	Hb < 8 g/dL ± symptoms	12/92 (13.0%)	13/86 (15.1%)
Moonen, 2007 (19)	RCT	77	Unwashed PSB (378 mL)	Hb 8.1, 8.9 or 9.7 g/dL according to ASA score	1/45 (2.2%)	5/32 (15.6%)
Abuzakuk, 2007 (18)	RCT	104	Unwashed PSB (439 mL)	Hb < 9 g/dL	13/52 (25%)	12/52 (23.1%)
Zacharopoulus, 2007 (17)	RCT	60	Unwashed PSB (564 mL)	Hb < 9 g/dL ± symptoms	5/30 (16.7%)	10/30 (33.3%)
Cheng, 2005 (16)	RCT	60	Unwashed PSB (425 mL)	Hb < 9 g/dL ± symptoms	4/26 (15.4%)	13/34 (38.2%)
Steinberg, 2004 (21)	Observational	365	Unwashed PSB	Hb < 8 g/dL ± symptoms	37/194 (19.1%)	89/171
Muñoz , 2008 (22)	Observational	953	Unwashed PSB (487 mL)	Hb < 9 g/dL	60/688 (8.7%)	80/265 (30.2%)
Thomas, 2001 (14)	RCT	231	Washed PSB	Hb < 9 g/dL ± symptoms	12/115 (10.4%)	33/116 (28.4%)
Carrero, 2006 (15)	Observational	220	Washed PSB (283 mL RBC Hct 66%)	Hb < 8 g/dL ± symptoms	21/115 (18.3%)	53/105 (50.5%)

ABT: allogeneic blood transfusion; RCT: randomised controlled trial; PSB: post-operatively salvaged blood; ASA: American Society of Anesthesiology physical score; Hb: haemoglobin.

efficacious in reducing ABT after total knee arthroplasty. In this regard, a recent retrospective analysis found that, with respect to management in a control group (n=209), routine administration of tranexamic acid during total knee arthroplasty to patients without a history of thrombo-embolic disease (n=199) was associated with a 67% reduction in ABT rate and, in those transfused, with a reduction in the number of units administered, but not with an increase in thrombo-embolic complications (2.9% versus 1.5%, for control and tranexamic acid, respectively)[23]. In another study, drain clamping with intra-articular injection of saline with adrenaline was shown to be as efficacious as PSB return for avoiding ABT after total knee arthroplasty[24]. Similarly, pre-operative rHuEPO with iron supplementation has been proven to be useful in preventing ABT in knee, hip and spine surgery[25,26], although the Food and Drug Administration had alerted that the frequency of deep venous thrombosis in patients treated with rHuEPO was more than twice that in patients who received usual blood conservation care (4.7% versus 2.1%, respectively) (http://www.fda.gov/medwacht/report.htm), and the minimal effective dose of rHuEPO has not been clearly defined[27,28]. In this regard, in anaemic patients undergoing total knee arthroplasty, peri-operative intravenous iron (400 mg) plus a single dose of rHuEPO (40,000 IU), in combination with a restrictive transfusion protocol, dramatically reduced transfusion requirements with respect to those needed in a historical control series[29,30]. No additional reduction of ABT rate was obtained by the addition of PSB re-infusion to this blood-saving protocol (9% versus 3%, respectively)[29]. Moreover, in an observational study administration of pre-operative haematinics (oral iron, vitamin C and folic acid) for 30-45 days before elective total knee arthroplasty, plus a restrictive post-operative transfusion protocol, significantly reduced both ABT rate (5.8% versus 32%; $p<0.01$) and ABT volume (1.8 versus 2.2 units/patient; $p<0.05$) with respect to a control group[31].

Total hip arthroplasty

In patients undergoing primary total hip arthroplasty, re-infusion of unwashed PSB reduced the relative risk of receiving ABT compared with control (RRR 40%), but not the number of units per patient transfused (2 units/patient)[20,32-34] (Table II). In contrast, in the study by Slappendel *et al.*[12] no significant differences were found in ABT rates between patients managed either with a low-vacuum drain and receiving re-infusion of PSB or with a high-vacuum drain (10% versus 16%, p=0.268). However, it is worth noting that in this study anaemic patients were treated pre-operatively with rHuEPO to optimise haemoglobin levels, intra-operative cell salvage was used in all procedures, and a well-defined ABT protocol was implemented. Thus, the possible contribution of PSB reinfusion to ABT saving is difficult to evaluate.

On the other hand, re-infusion of washed blood salvaged peri-operatively (intra-operatively and post-operatively) has also been shown to effective in reducing both ABT rate and ABT volume in primary total hip arthroplasty[35] and in revision total hip arthroplasty[36] (Table II), although patients undergoing the latter procedure could benefit from association with any other blood-saving technique, such as pre-operative autologous blood donation[37,38] or administration of tranexamic acid[39].

Instrumented spine surgery

The effectiveness of peri-operative blood salvage in spine surgery is controversial and its use is recommended only for selected operations with high intra-operative blood loss[8]. A study of the effect of a blood-saving programme for these procedures involved the use of a ConstaVac CBCII blood conservation canister (Stryker, Kalamazoo, MI, USA). The initial study group comprised 28 consecutive patients who had undergone lumbar spinal fusion and from whom unwashed PSB was collected and re-infused (group B). In comparison with a previous series of 31 patients (group A), the procedure reduced ABT requirements in group B patients by nearly 30% ($p<0.05$) without any increase in post-operative complications[40]. Despite these positive results, it became evident that the exclusive use of PSB re-infusion was not enough to avoid ABT and treatment was complemented with a short-time autologous

Table II - Some recent studies on peri-operative cell salvage in total hip replacement.

Author, year (Reference)	Study type	Patients (n)	Salvaged blood (re-infused volume)	Transfusion protocol	ABT (%)	
					Cell salvage	Control
Moonen, 2007 (20)	RCT	83	Unwashed PSB (203 mL)	Hb 8.1, 8.9 or 9.7 g/dL according to ASA	4/35 (11.4%)	10/48 (20.8%)
Smith, 2007 (32)	RCT	158	Unwashed PSB (252 mL)	Hb < 8 g/dL ± symptoms	6/76 (7.9%)	21/82 (25.6%)
Mirza, 2007 (33)	Observational	218	Unwashed PSB (200-400 mL)	Hb < 8 g/dL ± symptoms	10/109 (9.2%)	33/109 (30.3%)
Sturdee, 2007 (34)	Observational	86	Unwashed PSB (441 mL)	Hb < 8 g/dL	2/43 (4.7%)	10/43 (23.3%)
Trujillo, 2008 (35)	Observational	108	Washed Intra-op & post-op (336 mL RBC, Htc 63%)	Hb < 8 g/dL ± symptoms	9/60 (15.0%)	13/48 (27.1%)
Bridgens, 2007 (36)	Observational	94	Washed Intra-op (590 mL RBC)	Hb < 9 g/dL ± symptoms	36/47 (76.6%)	46/47 (97.9%)
Philips, 2006 (39)	Observational	80	Washed IntraOP + Tranexamic acid	Hb <7g/dL or Hb <8g/dL if cardiac disease	20/40 (50%)	37/40 (92.5%)

ABT, allogeneic blood transfusion; RCT, randomised controlled trial; PSB, post-operatively salvaged blood; Intra-op, intra-operative; post-op, postoperative; ASA, American Society of Anesthesiology physical score; Hb, haemoglobin.

blood donation protocol. The next 64 patients undergoing instrumented lumbar spinal fusion were included in this new protocol (group C). On the one hand, despite a greater peri-operative blood loss, due to a increased proportion of revision surgery, 80% of patients avoided exposure to ABT with this blood-saving strategy and post-operative complications were reduced by 50%[41]. On the other hand, 96% of donated units were transfused and the overall transfusion rate was higher than in group A[41], suggesting a tendency to more liberal transfusion criteria when autologous blood is available[42]. Hence, salvage and re-infusion of washed or unwashed PSB might be of use to complement intra-operative cell salvage for reducing ABT requirements, as well as the number of autologous donations, especially in patients undergoing extensive instrumented spine fusion in which post-operative blood loss is substantial.

Is re-infusion of unwashed shed blood safe?

PSB has a very variable red blood cell content and may be contaminated with tissue and chemical debris (fat particles, free haemoglobin, activated coagulation factors, fibrin degradation products, activated white blood cells or inflammatory mediators)[41], and some authors have questioned the quality and safety of this transfusion product, suggesting that it should be washed prior to be returned to the patient[43,44], even though few serious side effects have been witnessed after its re-infusion (e.g., acute cardiorespiratory dysfunction, respiratory distress and upper airway oedema)[45,46]. Beside these reported complications, there are numerous clinical studies that seem to support the notion that re-infusion of unwashed PSB is safe. In an evaluation of 1,819 patients receiving unwashed PSB after elective lower limb arthroplasty in 38 Dutch hospitals, the frequency of serious adverse events (0.1%; one patient had a brief asystole during re-infusion which responded quickly to medication; and the other, with a history of deep vein thrombosis, had pulmonary embolism) and minor adverse events (3.5%, mostly fever or shivering) was similar to that in other smaller clinical studies[47]. Nine (0.5%) patients were re-transfused with volumes above 1,500 mL, without adverse events. Based on the low incidence of side effects in this large cohort of orthopaedic patients, post-operative PSB after elective arthroplasty is considered to be clinically safe.

In addition, the results of a number of laboratory studies by our group and others strongly suggest that most of the potential adverse effects of unwashed PSB re-infusion after orthopaedic procedures are no more than theoretical. Nevertheless, it seems reasonable to set an upper limit on the volume of unwashed PSB to be re-infused (although the most accepted figure of approximately 1,000 mL is arbitrary)[48]. We shall briefly analyse these topics in the next sections.

Haematological characteristics of post-operatively salvaged shed blood

Usually, samples of unwashed PSB obtained in the first 6 post-operative hours have lower red blood cell and platelet counts as well as lower haemoglobin and haematocrit values than blood drawn from the patient in the pre-operative period (Table III). Red blood cells in unwashed PSB have a normal osmotic fragility and normal energy metabolism, as reflected by normal adenosine triphosphate (3.5 - 4.5 mmol/g Hb) and glucose uptake levels. In addition, PSB red blood cells have normal diphosphoglycerate levels (11 - 13 mmol/g Hb), leading to an oxygen-delivery capacity even superior to that of blood stored for more than 15 days[40,49]. All together, laboratory data strongly suggest that shed red cells are not significantly damaged, maintain their functionality, exhibit viability comparable to that seen in blood collected during the pre-operative and intra-operative period, and have excellent rheological properties[50].

Haemolysis

The amount of free haemoglobin in the plasma has been used as an index of haemolysis and, certainly, the amounts in unwashed PSB were above the normal limits[40,49,51] (Table III). However, it was previously reported that, for a total unwashed salvaged blood volume of 1,000 - 1,500 mL, there is enough circulating haptoglobin to bind the re-infused plasma free haemoglobin, thereby circumventing possible renal damage[41]. Re-infusion of unwashed PSB should, however, be avoided when the blood is grossly haemolysed and/or in patients with overt renal or hepatic dysfunction.

Fat particles

Return of fat probably increases the risk of fat embolism syndrome, which is mostly associated with

Table III - Haematological and biochemical characteristics of peri-operatively salvaged unwashed autologous blood.

	Post-operative shed blood	Post-operative shed blood	Post-operative shed blood	Leucodepleted post-operative shed blood
Reference #	98	40	41,62	41,62
Patients (n)	20	20	14	14
Surgery	CABG	Spine	TKA	TKA
Haemoglobin (g/dL)	11.1 ± 2.3	9.8 ± 0.8	10.6 ± 1.1	11.4 ± 1.2
Haematocrit (%)	34 ± 9	29 ± 2	33 ± 3	34 ± 4
Leucocytes ($x10^9$/L)	2.5 ± 0.7	6.7 ± 0.6	9.5 ± 2.0	3.3 ± 0.9
Platelets ($x10^9$/L)	32 ± 5	63 ± 5	22 ± 15	1704 ± 465
Plasma free Hb (g/dL)	1.9 ± 0.3	2.0 ± 0.2	0.5 ± 0.3	0.6 ± 0.3
K^+ (mmol/L)	6.5 ± 0.6	6.4 ± 0.5	ND	ND
Haptoglobin (g/dL)	ND	101± 14	80 ± 42	69 ± 35
IL-1 (pg/mL)	17 ± 2	11 ± 2	< 2	< 2
IL-6 (pg/mL)	110 ± 25	1335 ± 490	515 ± 402	377 ± 339
IL-8 (pg/mL)	ND	ND	271 ± 196	175 ± 244
TNF-α (pg/mL)	<2	<2	22 ± 15	18 ± 6

Data are mean ± SD; ND: not determined; TKA: total knee arthroplasty; CABG: coronary artery bypass grafting; Spine: instrumented lumbar-sacral spinal fusion; IL: interleukin; TNF: tumour necrosis factor.

acute lung injury. Hence, even when no adverse effects have been clearly reported, the return of fat particles should be minimised, or, even better, it should be avoided because of the potential toxicity of these particles. In this regard, a method was validated, based on the use of different haematology cytometers, which allows for detection of fat particles in unwashed PSB and verification of their elimination by means of several leucocyte filters, thereby avoiding the potential side effects of these particles[52-54]. There are also data supporting the efficacy of these filters in the elimination of tumour cells and amniotic membranes[55,56], although some authors recommend washing combined with irradiation of salvaged blood when blood is salvaged from patients undergoing oncological surgery[57].

Haemostasis

Unwashed PSB contains certain activated coagulation factors as well as fibrinogen degradation products so that its re-infusion could lead to a coagulopathy. In two recent studies, it was found that the re-infusion of unwashed PSB was associated with activation of blood coagulation in patients undergoing total knee arthroplasty. The authors concluded that the clinical relevance of this activation must be tested in prospective studies of adequate size[58,59]. However, in 13 studies including almost 700 orthopaedic patients, those who received an average of 560 mL of unwashed salvaged blood experienced neither clinically significant coagulopathy nor an increase in post-operative bleeding[60]. As stated above, the re-infusion of unwashed PSB after cardiac surgery can cause significant derangements in haemostasis, so its use is not recommended in this setting[10].

Inflammatory mediators and immune responses

As regards the presence of inflammatory mediators, we and other investigators found increased serum levels of interleukin (IL)-1β, IL-6, IL-8, tumour necrosis factor (TNF)-α and anaphylatoxins in unwashed salvaged blood[40,50,61-63]. The use of a leucocyte filter between the wound and the drain blood container reduces the IL-8 and TNF-α content in unwashed PSB, but at the same time triggers complement activation[50], whereas such a filter has a negligible effect when intercalated in the PSB-giving set[62]. It should be remembered that these cytokines are also present in stored blood, sometimes at levels even higher than those in unwashed salvaged blood[61,64].

Nevertheless, despite the high concentration of

certain pro-inflammatory cytokines in unwashed PSB, which produces a temporary increase in circulatory levels after the infusion, no differences were observed between re-infused and non re-infused patients in most measured cytokines 12 - 24 hours post-infusion[40,62]. In addition, co-incubation of post-operative venous blood with unwashed PSB in the presence of endotoxin resulted in a significant depression of TNF-α synthesis, without significant effects on IL-10 synthesis. However, no differences were observed for endotoxin-stimulated cytokine release in peri-operative blood samples from patients who did or did not receive unwashed PSB. These data suggest that unwashed PSB contains an anti-inflammatory agent. However, at the actual re-transfusion rate, unwashed PSB does not seem to further enhance the immunosuppression that follows total knee arthroplasty[63].

The influence of re-infused unwashed PSB on cellular immune responses has not been extensively studied. In a study of 40 consecutive patients undergoing total knee arthroplasty, all patients showed a post-operative decrease in T-cell and natural killer cell counts, but not in B-cell counts, and there were no significant differences between patients who did or did not receive unwashed PSB with regards to cellular immune response parameters, post-operative infection or hospital stay[65]. Moreover, data from previous reports seem to indicate a positive effect of unwashed PSB on cellular immunity, namely significant increases in the production of reactive oxygen species by the neutrophils[66] and in natural killer cell precursor frequency[67] in patients who received unwashed PSB. These findings add to the clinical experience that post-operative unwashed PSB, as a source of autologous blood, is safe, and question the beneficial effect of washing the blood.

Bacterial and cancer cell contamination

Bacterial contamination may occur during cell salvage, generally as a result of inappropriate use of the device or skin contamination. Overall, bacterial growth, whenever it occurs, is tolerated by the immunocompetent patient under antibiotic prophylaxis and does not lead to the development of sepsis[60]. Another source of bacteria or cancer cells is the presence of infection or tumour at the operative site, which has been considered an absolute contraindication to blood salvage. However, as stated above, there are data supporting the efficacy of filters in the elimination of tumour cells[55], and also bacteria, although some authors recommend washing and irradiating blood salvaged from patients undergoing oncological surgery[57]. Nevertheless, most surgeon and anaesthesiologists are still reluctant to used blood salvaged in the presence of infection or cancer at the operative site, and its potential benefit should be carefully weighed against its potential adverse effects. In addition, re-infusion of PSB should be avoided in patients with viral hepatitis B, hepatitis C or human immunodeficiency virus infection, to reduce the risks for infection in healthcare givers.

Does a washing procedure improve the quality of post-operatively salvaged shed blood?

In spite of all the above stated evidence regarding its efficacy and safety, unwashed PSB is viewed less favourably than washed PSB, which is somehow arbitrarily thought to be safer, because the washing procedure eliminates complement anaphylotoxins, pro-inflammatory cytokines, activated coagulation and fibrinolysis factors, fat particles, activated leucocytes and free haemoglobin to variable degrees (Table IV), yielding a concentrated RBC suspension in normal saline[68-77]. In addition, as there is not an upper limit on the volume of washed PSB that can be re-infused, it is also thought to be associated with a greater blood-sparing effect.

From a haematological point of view, all the different cell processing devices are able to effectively cleanse (greater than 90% removal of proteins and potassium ions) and concentrate blood (haematocrit increased from 20-25% to 40-65%), with 50-90% of the RBC mass being recovered. The reduction in RBC mass is most probably due to the loss of intact RBC during the procedure and to a certain degree of haemolysis induced by blood aspiration, centrifugation and washing, and also by the use of citrate as an anticoagulant[78]. However, most haemolysis products are removed, as reflected by the reductions of potassium ions and free haemoglobin in the plasma (Table IV).

Regarding overall removal of white blood cells and platelets, the OrthoPAT device showed a removal capacity similar to that of Sequestra (Medtronic), CATS (Sorensen), and Autolog (Medtronic), but

higher than that of Brat 2 (Cobe) or Cell Saver 5 (Haemonetics) (Table IV). In this regard, Reents *et al*.[72] have questioned the quality of wound blood washed by a cell-saving device, because the washing procedure failed to remove pro-inflammatory cytokines completely and spared activated leucocytes, particularly monocytes, which could produce a pro-coagulant state in the patient, and polymorphonuclear leucocytes, which might produce endothelial damage. To reduce the likelihood of these detrimental effects, it might be useful to remove monocytes from the wound washed blood by using a leucocyte filter. However, at least for orthopaedic surgery, the beneficial effects of special leucocyte-removing filters are controversial[62,79].

Another point of controversy regarding unwashed PSB is the content of fat particles which, when re-infused, may produce acute lung injury and has also be reported to cause neurological deficits after orthopaedic and cardiac surgery[80,81]. In the setting of cardiac surgery, the use of a cell saver to scavenge shed blood during cardiopulmonary bypass decreased cerebral lipid micro-embolisation, measured as small capillary and arteriolar dilations[81]. The Fresenius continuous autotransfusion system seems to be more efficient than any of the discontinuous autotransfusion systems, whereas there were no significant differences in the density of small capillary and arteriolar dilations with leucocyte filtration or with the various arterial-line filters[81]. In contrast, it has recently been shown that blood from a cardiotomy reservoir processed with the Brat 2 cell-saving device appears to have an abundance of fat particles that are completely eliminated by using a 21 mm arterial filter in series with the cardiotomy reservoir[82]. However, as far as we know, data regarding fat particle elimination using a cell saver in orthopaedic surgery are scant[77,83]. Nevertheless, it must be remembered that fat particles can be completely eliminated using a leucocyte filter[52,84].

The percent removal of cytokines from activated blood was around 90% for all cell processing devices (Table III). Particularly, for cardiac surgery, Amand *et al*.[74] examined the quality of PSB before and after processing with five different devices (BRAT2, Sequestra, Compact Advanced, Cell Saver 5, Continuous Autologous Transfusion System) and found that the attenuation rate of IL-6 and TNF-a (95%) was optimal for all the investigated blood salvage systems. After total knee arthroplasty there were no differences in patients' IL-6 and IL-8 blood levels, regardless of whether they received autologous predeposited blood or PSB processed with the OrthoPAT devices[85], but it is worth noting that similar results were obtained after re-infusing unwashed PSB with or without leucocytes[62].

Transfusion of washed or unwashed post-operatively salvaged shed blood?

In summary, processing PSB in a cell saver device improves the quality of blood, and this seem to translate into clinical benefits for patients undergoing cardiac surgery, whereas the controversy of washed versus unwashed PSB in orthopaedic surgery still persists, although with different possible solutions. As intra-operative cell salvage is often successfully

Table IV - Comparative evaluation of different salvaged blood processing systems.

Parameter	Sequestra* (Medtronic)	BRAT 2* (Cobe)	CATS* (Fresenius)	Cell Saver* (Haemonetics)	AUTOLOG* (Medtronic)	OrthoPAT* (Haemonetics)	Colloid ** sedimentation
RBC recovery; %	65 - 76	71 - 93	51 - 87	64 - 94	79	80	90
WBC removal; %	31 - 78	30	45 - 80	22 - 55	78	72	60
PLT removal; %	87 - 93	68	92 - 96	86 - 87	99	88	48
PFHB removal; %	89	63	65 - 95	85 - 93	92	96	53
TP or ALB removal; %	97 - 98	91 - 93	93 - 99	NA	NA	97	76
K^+ removal; %	92	90	90 - 98	91	89	97	NA
Cytokine removal; %	95	95	95	91 - 95	NA	90	70 - 77

Values are minimum – maximum interval. CATS: continuous autotra nsfusion system; RBC: red blood cells; WBC: leucocytes; PLT: platelets; PFHB: plasma free haemoglobin; TP: total protein; ALB: albumin. NA: not assessed. References: * (68-77), ** (51).

used in major hip or spine surgery, the use of a blood-processing device during the operation and in the post-operative period would seem to offer a solution to the dilemma about washed versus unwashed blood. Most conventional peri-operative cell salvage systems are bulky and require an operator, whereas systems such as the OrthoPAT® (Haemonetics, Braintree, MA, USA) are computer-automated systems, specifically designed to adapt to the peri-operative intermittent blood loss experienced by patients undergoing orthopaedic surgery. Such devices can be attached to an intravenous drip stand and can be moved with the patient from the operating theatre to the ward[35,77]. The adaptability of OrthoPAT® in providing washed salvaged autologous blood in both the intra-operative and post-operative settings suggests that it might help reduce the need for ABT without the added cost of an unwashed re-infusion drain system. Very recently, a new device (Sangvia, AstraTech) has been marketed for the salvage of intra- and post-operative unwashed blood and its re-infusion, but only preliminary data on blood quality are available[86], and its clinical efficacy is currently under evaluation (NCT00822588: Comparison in need for bank blood between patients undergoing total hip surgery that either receive their own blood back or not).

This controversy is more difficult to resolve in knee surgery because such surgery is usually performed using a tourniquet and blood salvaged is limited to the early post-operative period (the first 6 hours). Consequently, low-vacuum re-infusion drains are generally preferred, as blood processing devices are expensive and/or require trained personnel. In the search for an alternative solution to this problem, a validated, simple, low-cost procedure has been developed, for improving and standardising the quality of unwashed PSB; this procedure employs a colloid solution in a closed system[51] and is based on the ability of colloids to counteract the negatively charged repulsive forces of RBC, leading to RBC aggregation, rouleaux formation and accelerated sedimentation, and the consequent upward plasma flow[87-89]. In these experiments, unwashed PSB samples (Hb 10.9 g/dL) were drawn from the re-infusion bag and mixed with a hydroxy-ethyl starch or gelatine solution (15%-30%, colloid volume/total volume). PSB red blood cells were allowed to settle by gravity for 30 min, the supernatant was evacuated and the RBC concentrate analysed. Samples from leucodepleted allogeneic packed RBC were also analysed as a comparator group. After colloid treatment, 90% of RBC were recovered, and the haemoglobin content of the PSB was similar to that of leucodepleted packed RBC (18.9 g/dL versus 19.6 g/dL, respectively). In addition, the procedure reduced the amount of leukocytes (60%), platelets (48%), total protein (76%), cytokines (70-77%) and plasma free haemoglobin (53%) in the PSB, without major differences between colloids (see Table III for comparison with PSB washing). In conclusion, processing PSB with commercially available colloid solutions might be a feasible, low cost alternative for improving and standardising the quality of unwashed PSB prior to returning it to the patient, thus increasing the patient's safety and allowing the inclusion of this transfusion product in a quality management programme (see below). However, more clinical research is needed to ascertain the impact of this procedure on patients' outcome and whether this method applies to intra-operatively salvaged blood.

Are there European regulations regarding the transfusion of salvaged blood?

Directive 2002/98/EC of the European Parliament and of the Council (known as the Blood Directive) set comprehensive binding standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components. Three additional directives have since been implemented to develop the blood directive: Directive 2004/33/EC, regarding certain technical requirements for blood and blood components; Directive 2005/61/EC, regarding traceability requirements and notification of serious adverse reactions and events; and Directive 2005/62/EC, regarding quality standards and specifications relating to a quality system for blood establishments. Regulations regarding pre-operative autologous blood donation are now covered by the above-mentioned European Directives, which contain several references to "autologous donation" and "autologous transfusion". Although they do not mention the terms "pre-operative", "pre-operative autologous donation" or "pre-operative autologous blood donation", the context in which they are used clearly signifies that these are to be included[90].

However, the clinical use of allogeneic or

autologous blood is not so regulated, being more subject to professional judgement and clinical need. This clinical need has to be defined by Guidelines, such as the ones issued by the Scottish Intercollegiate Guideline Network[42], the British Society of Haematology[91], the Spanish Society for Blood Transfusion[92], and the Italian Society of Transfusion Medicine and Immunohematology[93].

In contrast, as for peri-operative cell salvage, there are only regulations regarding the marketing of cell salvage devices (Directive 93/42/CEE, amended by Directive 2007/47/EC), safety (Directive 2001/95/CE), liability for defective products (as provided for by Council Directive 85/374/EEC), and certain recommendations on indications and implementation[8,42,94]. In this regard, the provisions of Directive 2005/62/ CE need to be taken into account: these state: "In order to ensure the highest quality and safety for blood and blood components, guidance on good practice should be developed to support the quality system requirements for blood establishments taking fully into account the detailed guidelines referred to in Article 47 of Directive 2001/83/EC so as to ensure that the standards required for medicinal products are maintained".

On the other hand, there is a lack of regulations regarding the product yielded by these devices; i.e., unlike for pre-operative autologous blood donation, there are no quality standards for the blood obtained during peri-operative cell salvage and this may be a matter of concern for the clinicians, especially when using unwashed shed blood. However, current standard requirements for red blood cell units suggested in the recommendations of the European Council are also based on the level of haemolysis (below the threshold of 0.8% at the end of the storage period)[95]. Furthermore, in Italy, for example, transfusion medicine standards require that "the coordination and organisation of autologous transfusion activities except predeposit should also comprise interventions aimed at assessing both the quality and safety of blood products deriving from the perioperative cell salvage procedures (e.g. excess of activation of coagulation factors, excess of haemolysis, contaminants from the surgical field)[96].

In addition, if no quality oversight is mandatory a possible underreporting of side effects after re-administration of peri-operative shed blood might cause a lack of observation and auditing of more serious untoward effects of unwashed blood which in any case could/would be effectively prevented/avoided by simply processing the blood. We, therefore, believe that, to meet with European Directives on transfusion safety, the development of quality standards and good practice guidelines for post-operative cell salvage, as well as its inclusion in haemovigilance programmes, are urgently needed. In this regard, a new subgroup has recently started to work with SHOT to develop a reporting questionnaire for adverse incidents relating to cell salvage, including device-related incidents if a blood component was transfused to the patient[3], whereas we are still waiting for initiatives to develop the above-mentioned quality standards and good practice guidelines.

Summary recommendations

- Post-operative cell salvage and reinfusion must be restricted to elective procedures with an anticipated post-operative blood loss between 750 - 1,500 mL, allowing for the recovery of at least the equivalent of one unit of packed red cells (e.g., total knee arthroplasty, total hip arthroplasty, instrumented spine surgery, coronary artery bypass grafting), and used in conjunction with a defined ABT protocol.
- Reinfusion of PSB, with or without washing, after orthopaedic procedures is safe, economic and clinically beneficial, as it can reduce the requirements for ABT and ABT-associated risks. The superiority of washed PSB over unwashed PSB in these procedures has not been demonstrated.
- In contrast, for cardiac surgery PSB should be washed prior to re-infusion, as re-infusion of unwashed PSB after cardiac surgery produces only a marginal benefit and can also cause significant adverse effects.
- Surgical teams, anaesthetists and nursing staff should be familiar with the use of the different devices, ensure strict sterility, re-transfuse salvaged blood with 6 hours after the start of collection, and use a 40-mm filter intercalated in the re-infusion line. Thus, occasional use of this technique should be avoided and comprehensive education should be provided by manufacturers.
- Records involving every case of PSB re-infusion should be started prospectively to comply with

traceability regarding disposables and/or the machine used. In addition, quality control samples should be sent at regular intervals to the Blood Bank, and any adverse events should be reported to the National Haemovigilance Reporting System via the Hospital Transfusion Committee or the Blood Bank responsible (as is now requested by SHOT).

- Due the relatively low haemoglobin concentration in unwashed PSB, a rise in the patient's haemoglobin levels should not be expected after re-infusing this product. In fact, re-infusion of unwashed PSB is a method of volume replacement that allows most patients to maintain their haemoglobin levels above the transfusion trigger until bleeding stops, thus avoiding ABT.
- Contraindications to PSB re-infusion include contamination of the surgical field by agents not for parenteral use (e.g., betadine, chlorhexidine, hydrogen peroxide, topical antibiotics), patients with overt hepatic or renal failure (especially so for unwashed PSB), sickle cell disease, sickle cell trait or other red cell disorders, the presence of infection or malignancy in the operative field (relative contraindication for washed PSB), and patients who decline the use of the technique.
- Finally, although this technique may be effective on its own in many procedures, the aim of performing major surgical procedures without the use of ABT and without placing the patient at risk of anaemia-related complications may be better accomplished by combining several blood conservation strategies into a defined algorithm[97].

References

1) Stanworth SJ, Cockburn HA, Boralessa H, Contreras M. Which groups of patients are transfused? A study of red cell usage in London and Southeast England. Vox Sang 2002; **83**: 352-7.
2) García-Erce JA, Giralt M, Campos A, Muñoz M. Blood donation and blood transfusion in Spain (1997 –2006): the effects of demographic changes and universal leucoreduction. Blood Transfusion 2010; **8**:100-6.
3) The Serious Hazards of Transfusion Steering Group. Annual Report 2006. http://www.shotuk.org/SHOT_report_2006.pdf.
4) Klein HG, Spahn DR, Carson JL. Red blood cell transfusion in clinical practice. Lancet 2007; **370**: 415-26.
5) Carson JL, Altman DG, Duff A, et al. Risk of bacterial infection associated with allogeneic blood transfusion among patients undergoing hip fracture repair. Transfusion 1999; **39**: 694-700.
6) Bierbaum BE, Callaghan JJ, Galante JO, et al. An analysis of blood management in patients having a total hip or knee arthroplasty. J Bone Joint Surg Am 1999; **81**: 2-10.
7) Rosencher N, Kerkkamp HE, Macheras G, et al; OSTHEO Investigation. Orthopedic Surgery Transfusion Haemoglobin European Overview (OSTHEO) study: blood management in elective knee and hip arthroplasty in Europe. Transfusion 2003; **43**: 459-69.
8) Leal-Noval R, Muñoz M, Páramo JA, García-Erce JA, for the Spanish Expert Panel on Alternatives to Allogeneic Blood Transfusion. Spanish consensus statement on alternatives to allogeneic transfusions: the 'Seville document'. Transfus Altern Transfus Med 2006; **8**: 178-202.
9) Carless P, Moxey A, O'Connell D, Henry D. Autologous transfusion techniques: a systematic review of their efficacy. Transf Med 2004; **14**: 123-44.
10) Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Anesthesiologists Special Task Force on Blood Transfusion. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg 2007; **83**(5 Suppl): S27-86.
11) Parker MJ, Livingstone V, Clifton R, McKee A. Closed suction surgical wound drainage after orthopaedic surgery. Cochrane Database Syst Rev 2007; CD001825.
12) Slappendel R, Horstmann W, Dirksen R, van Hellemondt GG. Wound drainage with or without blood salvage? An open, prospective, randomized, single-center comparison of blood loss, postoperative hemoglobin levels and allogeneic blood transfusions after major hip surgery. TATM 2008; **10**: 174-81.
13) Benoni G, Fredin H. Low- or high-vacuum drains in hip arthroplasty? A randomized study of 73 patients. Acta Orthop Scand 1997; **68**: 133-7.
14) Iglesias D, Cuenca J, García-Erce JA, et al. Is there a role for cell salvage in patients undergoing surgery for hip fracture repair? An observational cohort study. Tranfus Alter Transfus Med 2010; **11** (Suppl 2): 29-30.
15) Thomas D, Wareham K, Cohen D, Hutchings H. Autologous blood transfusion in total knee replacement surgery. Br J Anaesth 2001; **86**: 669-73.
16) Carrero A, Trujillo MM, Muñoz M. Postoperative washed red cell reinfusion reduces allogeneic transfusion requirements after total knee replacement. Transfus Alter Transfus Med 2006; **8**: 203-9.
17) Cheng SC, Hung TS, Tse PY. Investigation of the use of drained blood reinfusion after total knee arthroplasty: a prospective randomised controlled study. J Orthop Surg (Hong Kong) 2005; **13**: 120-4.
18) Zacharopoulos A, Apostolopoulos A, Kyriakidis A. The effectiveness of reinfusion after total knee replacement.

A prospective randomised controlled study. Int Orthop 2007; **31**: 303-8.
19) Abuzakuk T, Senthil Kumar V, Shenava Y, et al. Autotransfusion drains in total knee replacement. Are they alternatives to homologous transfusion? Int Orthop 2007; **31**: 235-9.
20) Moonen AF, Knoors NT, van Os JJ, et al. Retransfusion of filtered shed blood in primary total hip and knee arthroplasty: a prospective randomized clinical trial. Transfusion 2007; **47**: 379-84.
21) Amin A, Watson A, Mangwani J, et al. A prospective randomised controlled trial of autologous retransfusion in total knee replacement. J Bone Joint Surg Br 2008; **90**: 451-4.
22) Muñoz M, Ariza D, Florez A, Campos A. Reinfusion drains reduce postoperative transfusion requirements after primary total knee replacement surgery. Transfus Med 2008; **18**: 269-71.
23) Lozano M, Basora M, Peidro L, et al. Effectiveness and safety of tranexamic acid administration during total knee arthroplasty. Vox Sang 2008; **95**: 39-44.
24) Tsumara N, Yoshiya S, Chin T, et al. A prospective comparison of clamping drain or post-operative salvage of blood in reducing blood loss after total knee arthroplasty. J Bone Joint Surg Br 2006; **88**: 49-53.
25) Feagan BG, Wong CJ, Kirkley A, et al. Erythropoietin with iron supplementation to prevent allogeneic blood transfusion in total hip joint arthroplasty. Ann Intern Med 2000; **133**: 845-54.
26) Weber EW, Slappendel R, Hémon Y, et al. Effects of epoetin alfa on blood transfusions and postoperative recovery in orthopaedic surgery: the European Epoetin Alfa Surgery Trial (EEST). Eur J Anaesthesiol 2005; **22**: 249-57.
27) Rosencher N, Poisson D, Albi A, et al. Two injections of erythropoietin correct moderate anaemia in most patients awaiting orthopedic surgery. Can J Anesth 2005; **52**: 160-5.
28) Gonzalez-Porras JR, Colado E, Conde MP, et al. An individualized pre-operative blood saving protocol can increase pre-operative haemoglobin levels and reduce the need for transfusion in elective total hip or knee arthroplasty. Transfus Med 2009; **19**: 35-42.
29) García-Erce JA, Solano VM, Cuenca J, Ortega P. La hemoglobina preoperatoria como único factor predictor de las necesidades transfusionales en la artroplastia de rodilla. Rev Esp Anestesiol Reanim 2002; **49**: 254-60.
30) Cuenca J, García-Erce JA, Martínez F, et al. Peri-operative intravenous iron, with or without erythropoietin, plus restrictive transfusion protocol reduce the need for allogeneic blood after knee replacement surgery. Transfusion 2006; **46**: 1112-29.
31) Cuenca J, García-Erce JA, Martínez F, et al. Pre-operative haematinics and transfusion protocol reduce the need for transfusion after total knee replacement. Inter J Surg 2007; **5**: 89-94.
32) Smith LK, Williams DH, Langkamer VG. Post-operative blood salvage with autologous retransfusion in primary total hip replacement. J Bone Joint Surg Br 2007; **89**: 1092-7.
33) Mirza SB, Campion J, Dixon JH, Panesar SS. Efficacy and economics of postoperative blood salvage in patients undergoing elective total hip replacement. Ann R Coll Surg Engl 2007; **89**: 777-84.
34) Sturdee SW, Beard DJ, Nandhara G, Sonanis SV. Decreasing the blood transfusion rate in elective hip replacement surgery using an autologous drainage system. Ann R Coll Surg Engl 2007; **89**: 136-9.
35) Trujillo MM, Carrero A, Muñoz M. The utility of the perioperative autologous transfusion system OrthoPAT in total hip replacement surgery: a prospective study. Arch Orthop Trauma Surg 2008; **128**: 1031-8.
36) Bridgens JP, Evans CR, Dobson PM, Hamer AJ. Intraoperative red blood-cell salvage in revision hip surgery. A case-matched study. J Bone Joint Surg Am 2007; **89**: 270-5.
37) Bierbaum BE, Callaghan JJ, Galante JO, et al. An analysis of blood management in patients having a total hip or knee arthroplasty. J Bone Joint Surg Am 1999; **81**: 2-10.
38) Feagan BG, Wong CJ, Johnston WC, et al. Transfusion practices for elective orthopedic surgery. CMAJ 2002; **166**: 310-4.
39) Phillips SJ, Chavan R, Porter ML, et al. Does salvage and tranexamic acid reduce the need for blood transfusion in revision hip surgery? J Bone Joint Surg Br 2006; **88**: 1141-2.
40) Sebastián C, Romero R, Olalla E, et al. Postoperative blood salvage and reinfusion in spinal surgery. Blood quality, effectiveness and impact on patient blood parameters. Eur Spine J 2000; **9**: 458-65.
41) Muñoz M, García-Vallejo JJ, Ruiz MD, et al. Transfusion of postoperative shed blood: laboratory characteristics and clinical utility. Eur Spine J 2004; **13**(Suppl.1): S107-13.
42) Scottish Intercollegiate Guidelines Network. Perioperative Blood Transfusion for Elective Surgery. A National Clinical Guideline, 2001 (Update in 2004). Accessed at http://www.sign.uk.
43) Hansen E, Pawlik M. Reasons against the retransfusion of unwashed wound blood. Transfusion 2004; **44**(Suppl. 1): 45S-53S.
44) Waters JH, Dyga RM. Postoperative blood salvage: outside the controlled world of the blood bank. Transfusion 2007; **47**: 362-5.
45) Murray DJ, Gress K, Weinstein SL. Coagulopathy after reinfusion of autologous scavenged red blood cells. Anesth Analg 1992; **75**: 125-9.
46) Woda R, Tetzlaff JE. Upper airway oedema following autologous blood transfusion from a wound drainage system. Can J Anaesth 1992; **39**: 290-2.
47) Horstmann WG, Slappendel R, Van Hellemondt GG, et al. Safety of retransfusion of filtered shed blood in 1819 patients after total hip or knee arthroplasty. Tranfus Altern Tranfus Med 2010; **11**: 57-64.
48) Hamer A. Postoperative cell salvage. In: Thomas D, Thompson J, Ridler B (eds.). *A Manual for Blood Conservation*. Tfm Publishing Ltd., Shrewsbury, 2005;123-32.
49) Muñoz M, Sánchez-Arrieta Y, García-Vallejo JJ, et al.

Autotransfusión pre y postoperatoria. Estudio comparativo de la hematología, bioquímica y metabolismo eritrocitario en sangre predonada y sangre de drenaje postoperatorio. Sangre (Barc) 1999; **44**: 433-50.
50) Engstrom KG. Inflammatory mediators in autotransfusion drain blood after knee arthroplasty, with and without leucocyte reduction. Vox Sang 2003; **85**: 31-9.
51) Muñoz M, García-Segovia S, Ariza D, et al. A sedimentation method for improving and standardizing the quality of postoperatively salvaged unwashed shed blood in orthopaedic surgery. Br J Anaesth 2010 (Advanced access July 16; doi:10.1093/bja/aeq174)
52) Ramírez G, Romero A, García-Vallejo JJ, Muñoz M. Detection and removal of fat particles from postoperative salvaged shed blood in orthopedic surgery. Transfusion 2002; 42: 66-75.
53) Muñoz M, Romero A, Campos A, Ramírez G. Detection of fat particles in postoperative shed blood from orthopaedic surgery using haematologic cell counter. Transfusion 2004; **44**: 620-2.
54) Muñoz M, Romero A, Ariza D, et al. Capacidad de los filtros leucoreductores en la eliminación de partículas de grasa en sangre recuperada. Un estudio in vitro. Rev Esp Anestesiol Reanim 2005; **52**: 81-7.
55) National Institute for Health and Clinical Excellence. Interventional procedure guidance 258: intraoperative red blood cell salvage during radical prostatectomy or radical cystectomy. Issue date: April 2008.
56) Sullivan I, Faulds J, Ralph C. Contamination of salvaged maternal blood by amniotic fluid and fetal red cells during elective Caesarean section. Br J Anaesth 2008; **101**: 225-9.
57) Hansen E, Bechmann V, Altmeppen J. Intraoperative blood salvage in cancer surgery: safe and effective? Transfus Apheresis Sci 2002; **27**:153-7.
58) Biagini D, Filippucci E, Agnelli G, Pagliaricci S. Activation of blood coagulation in patients undergoing postoperative blood salvage and re-infusion of unwashed whole blood after total knee arthroplasty. Thromb Res 2004; **113**: 211-5.
59) Muñoz M, García-Erce JA, Cuenca J, Solano VM. Course of D-dimer concentrations after total knee replacement surgery: effect of allogeneic and unwashed drainage blood transfusion. Transfus Alter Transfus Med 2006; **8**: 135-43.
60) Muñoz M, García Vallejo JJ, López-Andrade Jurado A, et al. Autotransfusión postoperatoria en cirugía ortopédica. Un análisis de la calidad, seguridad y eficacia de la sangre recuperada de los drenajes postoperatorios. Rev Esp Anestesiol Reanim 2001; **48**: 131-40.
61) Jacobi KE, Wanke C, Jacobi A, et al. Determination of eicosanoid and cytokine production in salvaged blood, stored blood cell concentrates, and whole blood. J Clin Anesth 2000; **12**: 94-9.
62) Muñoz M, Cobos A, Campos A, et al. Impact of postoperative shed blood transfusion, with or without leukocyte reduction, on acute phase response to surgery for total knee replacement. Acta Anaesthesiol Scand 2005; **49**: 1182-90.
63) Muñoz M, Muñoz E, Navajas A, et al. Impact of post-operative unwashed shed blood retrieved after total knee arthroplasty, on endotoxin-stimulated tumour necrosis factor alpha release in vitro. Anesthesiology 2006; **104**: 267-72.
64) Kristiansson M, Soop M, Saraste L, Sundqvist KG. Cytokines in stored red blood cell concentrates: promoters of systemic inflammation and stimulators of acute transfusion reactions? Acta Anaesthesiol Scand 1996; **40**: 496-501.
65) Muñoz M, Cobos A, Campos A, et al. Postoperative unwashed shed blood transfusion does not modify cellular immune response to surgery for total knee replacement. Acta Anaesthesiol Scand 2006; **50**: 443-50.
66) Gharehbahian A, Haque G, Truman C, et al. Effect of autologous salvaged blood on post-operative natural killer cell precursor frequency. Lancet 2004; **363**: 1025-30.
67) Iorwerth A, Wilson C, Topley N, Pallister I. Neutrophil activity in total knee replacement: implications in preventing post-arthroplasty infection. Knee 2003; **10**: 111-3.
68) Szpisjak DF, Edgell DS, Bissonnette B. Potassium as a surrogate marker of debris in cell-salvaged blood. Anesth Analg 2000; **91**: 40-3.
69) Serrick CJ, Scholz M, Melo A, et al. Quality of red blood cells using autotransfusion devices: a comparative analysis. J Extra Corpor Technol 2003; **35**: 28-34.
70) Nitescu N, Bengtsson A, Bengtson JP. Blood salvage with a continuous autotransfusion system compared with a haemofiltration system. Perfusion 2002; **17**: 357-62.
71) Shulman G. Quality of processed blood for autotransfusion. J Extra Corpor Technol 2000; **32**: 11-9.
72) Reents W, Babin-Ebell J, Misoph MR, et al. Influence of different autotransfusion devices on the quality of salvaged blood. Ann Thorac Surg 1999; **68**: 58-62.
73) Walpoth BH, Eggensperger N, Walpoth-Aslan BN, et al. Qualitative assessment of blood washing with the continuous autologous transfusion system (CATS). Int J Artif Organs 1997; **20**: 234-9.
74) Amand T, Pincemail J, Blaffart F, et al. Levels of inflammatory markers in the blood processed by autotransfusion during cardiac surgery associated with cardiopulmonary bypass circulation. Perfusion 2002; **17**: 117-23.
75) Flom-Halvorsen HI, Øvrum E, Øystese R, Brosstad F. Quality of intraoperative autologous blood withdrawal used for retransfusion after cardiopulmonary bypass. Ann Thorac Surg 2003; **76**: 744-8.
76) Bottner F, Sheth N, Chimento GF, Sculco TP. Cytokine levels after transfusion of washed wound drainage in total knee arthroplasty: a randomized trial comparing autologous blood and washed wound drainage. J Knee Surg 2003; **16**: 93-7.
77) Muñoz M, Ariza D, Romero A, et al. Evaluación del

sistema de autotransfusión OrthoPAT®, utilizando modelos experimentales de simulación de recuperación de sangre intra y postoperatoria. Rev Esp Anestesiol Reanim 2005; **52**: 235-41.
78) Moltermans Y, Vermaut G, Van Aken H, et al. Quality of washed salvaged red blood cells during total hip replacement: a comparison between the use of heparin and citrate as anticoagulants. Anesth Analg 1994; **79**: 357-63.
79) Innerhofer P, Wiedermann FJ, Tiefenthaler W, et al. Are leukocytes in salvaged washed autologous blood harmful for the recipient? The results of a pilot study. Anesth Analg 2001; **93**: 566-72.
80) Ozelsel TJ, Tillman Hein HA, Marcel RJ, et al. Delayed neurological deficit after total hip arthroplasty. Anesth Analg 1998; **87**: 1209-10.
81) Kincaid EH, Jones TJ, Stump DA, et al. Processing scavenged blood with a cell saver reduces cerebral lipid microembolization. Ann Thorac Surg 2000; **70**: 1296-300.
82) Kaza AK, Cope JT, Fiser SM, et al. Elimination of fat microemboli during cardiopulmonary bypass. Ann Thorac Surg 2003; **75**: 555-9.
83) Henn-Beilharz A, Hoffmann R, Hempel V, Brautigam KH. The origin of non-emulsified fat during autotransfusions in elective hip surgery. Anaesthesist 1990; **39**: 88-95.
84) Muñoz M, Romero A, Ariza D, et al. Capacidad de los filtros leucorreductores en la eliminación de partículas de grasa en sangre recuperada. Un estudio in vitro. Rev Esp Anestesiol Reanim 2005; **52**: 81-7.
85) Bottner F, Sheth N, Chimento GF, Sculco TP. Cytokine levels after transfusion of washed wound drainage in total knee arthroplasty: a randomized trial comparing autologous blood and washed wound drainage. J Knee Surg 2003; **16**: 93-7.
86) Kvarnström A, Schmidt A, Tylman M, et al. Complement split products and proinflammatory cytokines in intraoperatively salvaged unwashed blood during hip replacement: comparison between heparin-coated and non-heparin-coated autotransfusion systems. Vox Sang 2008; **95**: 33-8.
87) Sümpelmann R, Günther A, Zander R. Haemoconcentration by gelatin-induced acceleration of erythrocyte sedimentation rate. Anaesthesia 2000; **55**: 217-20.
88) Tsang KS, Li K, Huang DP, et al. Dextran sedimentation in a semi-closed system for the clinical banking of umbilical cord blood. Transfusion 2001; **41**: 344-52.
89) Dieterich HJ, Neumeister B, Agildere A, Eltzschig HK. Effect of intravenous hydroxyethyl starch on the accuracy of measuring hemoglobin concentration. J Clin Anesth 2005; **17**: 249-54.
90) Boulton FE, James V. Guidelines for policies on alternatives to allogeneic blood transfusion. 1. Predeposit autologous blood donation and transfusion. British Committee for Standards in Haematology, Transfusion Task Force. Transfus Med 2007; **17**: 354-65.
91) British Committee for Standards in Haematology. Blood transfusion Task Force. Guidelines for the clinical use of red cell transfusion. Br J Haematol 2001; **113**: 24-32.
92) Ortiz P, Mingo A, Lozano M, et al. Guía sobre la transfusión de componentes sanguíneos. Med Clin (Barc) 2005; **125**: 389-96.
93) Velati C, Aprili G. SIMTI recommendations on the correct use of blood components and plasma derivatives. Blood Transfus 2009; **7**: 1-12.
94) British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for autologous transfusion. II. Perioperative haemodilution and cell salvage. Br J Anaesth 1997; **78**: 768-71.
95) Council of Europe. Guide to the preparation, use and quality assurance of blood components. Recommendation no R (95) 15 on the preparation, use and quality assurance of blood components. 14th ed. Strasbourg: Council of Europe Press, 2008.
96) Transfusion Medicine Standards, page 193, 2nd edition June 2010, available in Italian at: http://www.transfusionmedicine.org/linee_guida.aspx?ok=1
97) Beris P, Muñoz M, García-Erce JA, et al. Peri-operative anaemia management: consensus statement on the role of intravenous iron. Br J Anaesth 2008; **100**: 599-604.
98) Salas J, de Vega NG, Carmona J, et al. Autotransfusión postoperatoria en cirugía cardíaca. Características hematológicas, bioquímicas e inmunológicas de la sangre recuperada del drenaje mediastínico. Rev Esp Anestesiol Reamin 2001; **48**: 122-30.

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