

■ HIP

Reduction of blood loss with the use of a new combined intra-operative and post-operative autologous blood transfusion system compared with no drainage in primary total hip replacement

W. G. Horstmann,
M. J. Swierstra,
D. Ohanis,
R. M. Castelein,
B. J. Kollen,
C. C. P. M. Verheyen

From Isala Clinics,
Zwolle, the
Netherlands

■ W. G. Horstmann, MD, PhD,
Orthopaedic Surgeon
Kennemer Gasthuis,
Department of Orthopaedic
Surgery, Boerhaavelaan 22,
2035 RC Haarlem, the
Netherlands.

■ M. J. Swierstra, MD, Resident
Orthopaedic Surgery
■ D. Ohanis, MD, Resident
Orthopaedic Surgery
■ C. C. P. M. Verheyen, MD,
PhD, Orthopaedic Surgeon
Isala Clinics, PO Box 10500,
8000 GM Zwolle, the
Netherlands.

■ R. M. Castelein, MD, PhD,
Orthopaedic Surgeon,
Professor
University Medical Center
Utrecht, PO Box 85500, 3508 GA
Utrecht, the Netherlands.

■ B. J. Kollen, PhD,
Epidemiologist
University of Groningen,
University Medical Center
Groningen, Department of
General Practice, University of
Groningen, PO Box 196, 9700
AD Groningen, the
Netherlands.

Correspondence should be sent
to Dr W. G. Horstmann; e-mail:
wghorstmann@kg.nl

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Autologous retransfusion and no-drainage are both blood-saving measures in total hip replacement (THR). A new combined intra- and post-operative autotransfusion filter system has been developed especially for primary THR, and we conducted a randomised controlled blinded study comparing this with no-drainage.

A total of 204 THR patients were randomised to autologous blood transfusion (ABT) (n = 102) or no-drainage (n = 102). In the ABT group, a mean of 488 ml (SD 252) of blood was retransfused. The mean lowest post-operative haemoglobin level during the hospital stay was higher in the autotransfusion group (10.6 g/dl (7.8 to 13.9) vs 10.2 g/dl (7.5 to 13.3); p = 0.01). The mean haemoglobin levels for the ABT and no-drainage groups were not significantly different on the first day (11.3 g/dl (7.8 to 13.9) vs 11.0 g/dl (8.1 to 13.4); p = 0.07), the second day (11.1 g/dl (8.2 to 13.8) vs 10.8 g/dl (7.5 to 13.3); p = 0.09) or the third day (10.8 g/dl (8.0 to 13.0) vs 10.6 g/dl (7.5 to 14.1); p = 0.15). The mean total peri-operative net blood loss was 1464 ml (SD 505) in the ABT group and 1654 ml (SD 553) in the no-drainage group (p = 0.01). Homologous blood transfusions were needed in four patients (3.9%) in the ABT group and nine (8.8%) in the no-drainage group (p = 0.15). No statistically significant difference in adverse events was found between the groups.

The use of a new intra- and post-operative autologous blood transfusion filter system results in less total blood loss and a smaller maximum decrease in haemoglobin levels than no-drainage following primary THR.

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It has been reported that total hip replacement (THR) is associated with a mean total blood loss of 1500 ml and a post-operative decline in haemoglobin (Hb) levels of a mean of 3.0 g/dl.¹ Lower post-operative Hb levels following THR are associated with a lower functional score, longer hospital stay and an increased homologous blood transfusion rate.^{2–4} Homologous blood transfusions (HBT) are also related to poorer outcomes following THR, such as higher post-operative infection rates, delayed wound healing and prolonged hospital stay.^{5–8}

Retransfusion of blood that is lost during and after surgery has been introduced to reduce peri-operative net blood loss, maintain higher post-operative Hb levels and reduce the use of HBT. The results of a recent Cochrane review on peri-operative cell salvage show that autologous retransfusion reduced HBT requirements by 54%

compared with regular drains in orthopaedic procedures.⁹ Post-operative autologous blood transfusion (ABT) filter systems for the retransfusion of filtered drained blood are often used in primary THR. However, the currently available intra-operative cell-saver devices wash the blood, separate the various cells and permit retransfusion of the red blood cells. Unfortunately, they are expensive to run and are often reserved for revision surgery. As a result, the 500 ml or so of blood that is generally lost during primary THR is not used for retransfusion. Therefore, a new system has been developed for primary THR, which filters the intra-operatively collected blood, in the same manner as the filters in post-operative ABT systems. This intra-operative retransfusion filter system is claimed to be easier to handle and less expensive than intra-operative washing/separating devices, and therefore suitable for use in

primary THR. It is combined with a post-operative retransfusion unit to retransfuse as much as possible of the lost blood.

Another approach to blood-sparing THR is the avoidance of drains altogether. A Cochrane review reported that no-drainage following THR leads to a reduction in HBT requirements compared with conventional closed-suction drains.¹⁰

We propose that the use of a combined intra- and post-operative autologous blood transfusion system would reduce peri-operative blood loss and the need for HBT, and diminish the reduction in post-operative Hb levels in primary THR. The purpose of this study was therefore to conduct a blinded randomised controlled trial evaluating the effects of this new intra-operative autologous blood retransfusion filter system combined with a post-operative ABT filter unit, and compare it with no-drainage following primary THR. The primary endpoint was the Hb level on the first post-operative day.

Patients and Methods

Between August 2009 and April 2011 we undertook an open double-blind randomised controlled single-centre study with two parallel groups at the Isala Clinics, Zwolle, the Netherlands. Approval for the study was obtained from our institutional medical ethics committee, and all patients provided informed written consent. Patients were enrolled if the following exclusion criteria were absent: coagulation disorders, including deep-vein thrombosis and pulmonary embolism; malignancy; ongoing infections; untreated hypertension; unstable angina pectoris; myocardial infarction within the past 12 months; coronary bypass surgery within the past 12 months; renal dysfunction; or the use of anticoagulants.

A total of 204 patients scheduled for primary THR were randomised either to the ABT group (Sangvia, autologous blood salvage, low vacuum, 100 to 150 mmHg; Astratech, Mölndal, Sweden) (n = 102) or to the no-drainage group (n = 102). In the ABT system, blood collected in the sucker bottle intra-operatively, and post-operatively drained blood, was retransfused after sequential filtering through 200 µm, 80 µm and 40 µm filters.

Formal randomisation by concealed allocation took place prior to the operation. Numbered sealed opaque envelopes containing pre-randomised cards with either 'autologous transfusion group' or 'no-drainage group' were available in the operating theatre. Blood lost intra-operatively was collected via a sucker for all 204 patients. The surgeons (including CCPMV) were blinded to group allocation until the end of surgery, just before closure of the wound, at which time the envelope was opened and the patient's group allocation was disclosed.

In the ABT group a drain with a post-operative retransfusion unit was inserted and the blood that had been collected during the operation was subsequently retransfused within six hours of surgery. In accordance with the manufacturer's guidelines it was not permissible to retransfuse > 1500 ml of intra-operatively collected blood and 1000 ml

of post-operatively drained blood. The drains were removed 24 hours post-operatively. In the no-drainage group the intra-operative blood loss was not retransfused and no drain was inserted.

Cemented hip prostheses (SP-2 stem and Fal acetabular component; Link, Hamburg, Germany), uncemented (Bimetric stem and Recap acetabular component; Biomet, Warsaw, Indiana) and hybrid prostheses made from these components were used in the patients in this study. Cefazolin was used as routine antibiotic prophylaxis (2 g intravenously 15 to 30 minutes pre-operatively, and 1 g three times in first 24 hours post-operatively). The primary endpoint of the study was the Hb level on the first post-operative day. Secondary endpoints included Hb levels on the day of surgery, the second and third days, the lowest post-operative level, any HBT requirement, adverse events, and total blood loss. Other measurements were the volume of intra-operatively collected and retransfused blood, and the volume of retransfused blood collected in the drains. Total blood loss was calculated according to Gross,¹¹ based on the maximum peri-operative decrease in Hb level and the patients' pre-operative blood volume: Blood loss = pre-operative blood volume × [(Hb pre-operatively – Hb lowest)/mean Hb]. Pre-operative blood volume was calculated as 65 ml/kg. The mean Hb was taken as the mid-point between the pre-operative level and the lowest post-operative level.¹¹

Operation time, surgical approach, type of anaesthesia and temperature at the end of surgery were also assessed because of their potential influence on blood loss. Creatinine, urea levels and the estimated glomerular filtration rate using the MDRD formula (modification of diet in renal disease)¹² were recorded.

A pre-operative creatinine level > 125 µmol/l was the exclusion criterion for renal dysfunction. Adverse events were registered during the hospital stay and the first three months post-operatively. The independent physicians undertaking post-operative examinations in outpatients at six weeks and three months post-operatively were blinded to group allocation. No patients were lost to follow-up.

A blood management protocol was implemented for this study: venous thromboembolism prophylaxis was carried out using fondaparinux (2.5 mg/0.5 ml) starting six to eight hours after the operation at the day of surgery, continued for five weeks once daily. Non-selective non-steroidal anti-inflammatory agents (NSAIDs) were stopped one day pre-operatively. The selective Cox-2 inhibitor meloxicam was used in all patients for pain management. Additional HBTs were given according to the Dutch HBT guidelines.¹³ The trigger for HBT was an Hb 6.4 g/dl for American Society of Anesthesiologists (ASA)¹⁴ grade 1 patients, 8.0 g/dl for ASA 2/3 patients, and 9.6 g/dl for ASA 4 patients (and in patients who failed to increase their cardiac output to compensate for dilution).

Statistical analysis. Based on a clinically relevant difference in Hb levels of 0.5 g/dl (10.9 g/dl *vs* 11.4 g/dl; standard

Table I. Patient characteristics

Characteristic	Autotransfusion	No-drainage	p-value
Number	102	102	
Mean (SD) age (yrs)	67.3 (9.3)	67.6 (9.4)	0.82*
Female:male	74:28	73:29	1.00†
Mean (SD) body mass index (kg/m ²)	28.3 (4.1)	27.9 (4.7)	0.57*
Indication (n)			0.50†
Primary osteoarthritis	102	100	
Post-traumatic	0	1	
Osteonecrosis	0	1	

* Student's *t*-test

† chi-squared test

Table II. Surgical factors affecting blood loss

Factors	Autotransfusion	No-drainage	p-value
Anaesthesia (n, %)			0.44*
Spinal	71 (69.6)	76 (74.5)	
General	31 (30.4)	26 (25.5)	
Mean (SD) body temperature at end of operation (°C)	36.0 (0.6)	36.0 (0.5)	0.62†
Surgeon (n, %)			0.47*
Consultant orthopaedic surgeon	59 (57.8)	65 (63.7)	
Trainee	43 (42.2)	37 (36.3)	
Approach, posterolateral/anterolateral			0.76*
Posterolateral	73 (71.6)	70 (68.6)	
Anterolateral	29 (28.4)	32 (31.4)	
Hip replacement (n, %)			0.51*
Cemented	57 (55.9)	65 (63.7)	
Uncemented	31 (30.4)	24 (23.5)	
Hybrid	14 (13.7)	13 (12.7)	
Mean (SD) operating time (mins)	68 (13)	68 (16)	0.97†

* chi-squared test

† Student's *t*-test**Table III.** Peri-operative blood loss and retransfusion

Mean (SD) blood loss (ml)	Autotransfusion	No-drainage	p-value
Total intra-operative suctioned	459 (220)	431 (220)	0.37
Post-operative drain 24 hours	384 (248)	-	-
Retransfusion intra-operative	287 (146)	-	-
Retransfusion post-operatively collected drained blood < 6 hours	201 (183)	-	-
Total retransfused blood loss	488 (252)	-	-

deviation (SD) 1.3), α of 0.05 and a power of 80.8%, on the first post-operative day, a sample size of 204 patients (102 per group) was required for this study. Study data were collected using dedicated case report forms and entered into a computerised database. Statistical analysis was conducted with SPSS v 17.0 (SPSS Inc., Chicago, Illinois). Categorical data were expressed as proportions. Continuous data were expressed as means and SD. Based on an intention-to-treat analysis, differences were analysed using chi-squared exact tests for categorical data and Student's *t*-tests for continuous data. The Levene test was used

to check for test assumptions. A two-sided p-value < 0.05 was considered to be statistically significant.

Results

The two groups were statistically homogeneous (Table I). There were no significant differences between them with regard to anaesthetic and surgical parameters that could affect blood loss (Table II).

Peri-operative blood loss, autologous transfusion, haemoglobin levels. The volume of intra-operative blood loss collected via the sucker was similar in both groups ($p = 0.37$,

Table IV. Peri-operative haemoglobin levels (Student's *t*-test)

Mean haemoglobin levels (g/dl) (SD; range)	Autotransfusion	No-drainage	p-value
Day -1	14.1 (1.0; 12.0 to 17.1)	14.0 (1.1; 10.7 to 16.6)	0.49
Day 0	11.5 (1.1; 9.0 to 14.2)	11.2 (1.2; 7.5 to 14.2)	0.20
Day 1	11.3 (1.1; 7.8 to 13.9)	11.0 (1.2; 8.1 to 13.4)	0.07
Day 2	11.1 (1.2; 8.2 to 13.8)	10.8 (1.4; 7.5 to 13.3)	0.09
Day 3	10.8 (1.2; 8.0 to 13.0)	10.6 (1.3; 7.5 to 14.1)	0.15
Lowest	10.6 (1.2; 7.8 to 13.9)	10.2 (1.3; 7.5 to 13.3)	0.01

Table V. Pre-operative blood volume, calculated blood loss, homologous blood transfusions (Student's *t*-test)

	Autotransfusion	No-drainage	p-value
Mean (SD) pre-operative blood volume (ml)	5135 (976)	5153 (1004)	0.90
Mean (SD) total blood loss (ml)	1464 (505)	1654 (553)	0.01
Homologous transfusion (n, %)	4 (3.9)	9 (8.8)	0.15

Table VI. Adverse events during hospital stay (chi-squared test)

Event	Autotransfusion	No-drainage	p-value
Fever (> 37.5°C)	34	22	0.06
Hypotension (BP sys < 90 or dias < 50)*	24	34	0.12
Bradycardia (heart rate < 50/min)	3	1	0.31
Chest pain	2	1	0.56
Atrial fluttering	2	1	0.56
Dyspepsia	19	18	0.86
Urinary tract	4	3	0.70
Pneumonia	2	0	0.16
Renal dysfunction	1	0	0.32
Technical failures autologous blood transfusion	2	0	0.16

* BP, blood pressure; sys, systolic; dias, diastolic

Student's *t*-test) (Table III). In the ABT group a mean of 488 ml (SD 252; 100 to 1500) of lost blood was retransfused. The mean lowest Hb level after THR was higher in the ABT group (10.6 g/dl (7.8 to 13.9) *vs* 10.2 g/dl (7.5 to 13.3); $p = 0.01$) (Table IV). The lowest Hb level was recorded on day 0 in 43 patients (22 ABT, 21 no-drainage), on day one in 27 patients (17 ABT, 10 no-drainage), on day two in 40 patients (18 ABT, 22 no-drainage) and on day three in 94 patients (45 ABT, 49 no-drainage). The maximum decline in Hb level was 3.5 g/dl and 3.9 g/dl, respectively ($p = 0.01$, Student's *t*-test). There was no significant difference in mean Hb levels between the groups on the pre-operative day ($p = 0.49$), the day of operation ($p = 0.20$), or the first, second and third post-operative days ($p = 0.07$, 0.09 and 0.15, respectively). The mean total peri-operative net blood loss was less in the ABT group compared with the no-drainage group (1464 ml (SD 505) *vs* 1654 ml (SD 553); $p = 0.01$) (Table V). Homologous blood transfusions were needed in four patients (3.9%) in the ABT group and nine patients (8.8%) in the no-drainage group ($p = 0.15$, Student's *t*-test). The mean transfusion trigger in the ABT group was 8.3 g/dl (SD 0.7; 7.8 to 9.3), on post-operative days one, two, three and nine, and in the no-drainage group

it was 8.0 g/dl (SD 0.5; 7.5 to 8.8) on day one ($n = 4$), day two ($n = 3$) and day three ($n = 2$). All patients identified for transfusion received two units of homologous blood.

Adverse events, kidney function. Adverse events during the hospital stay and afterwards up to three months post-operatively were similar in the two groups (Tables VI and VII). There were three deep infections of the hip prostheses, all in the no-drainage group. In all, 23 patients had a pre-operative MDRD < 60, which might be considered a suboptimal glomerular filtration rate (GFR) (Table VIII). One patient in the ABT group was successfully treated for acute renal failure. No statistically significant differences were noted in creatinine levels, urea levels or estimated glomerular filtration rate using the MDRD formula during the hospital stay.

Hospital stay. The mean hospital stay was 4.8 days (SD 1.7) in the ABT group and 5.1 days (SD 2.3) in the no-drainage group ($p = 0.20$, Student's *t*-test).

Discussion

In this study the use of a new intra-operative autotransfusion filter system combined with a post-operative ABT system resulted in less total blood loss and a smaller maximum decrease in Hb levels compared with no-drainage

Table VII. Adverse events from discharge up to three months post-operatively (chi-squared test)

Event	Autotransfusion	No-drainage	p-value
Deep infection, re-operation, irrigation	0	3	0.08
Haematoma, suspected deep infection (not proven), re-operation, irrigation	0	1	0.32
Dislocated total hip replacement	2	2	1.00
Deep-vein thrombosis	0	1	0.32

Table VIII. Creatinine and urea levels, glomerular filtration rate (GFR). Good kidney function is assumed when creatinine level is < 125 µmol/l and glomerular filtration rate (GFR) using the MDRD (modification of diet in renal disease) formula is ≥ 60 ml/min/1.73 m²

	Autotransfusion	No-drainage	p-value
Mean (SD) creatinine level (µmol/l)			
Pre-operative	73 (14)	74 (19)	0.65*
Post-operative day 1	63 (17)	62 (16)	0.57*
Post-operative day 2	67 (28)	67 (24)	0.94*
Post-operative day 3	67 (28)	67 (24)	0.97*
Patients with GFR MDRD* < 60 ml/min/1.73 m ² (n, %)			
Pre-operative	10 (9.8)	13 (12.7)	0.51†
Post-operative day 1	3 (2.9)‡	5 (4.9)	0.72†
Post-operative day 2	5 (4.9)‡	9 (8.8)	0.41†
Post-operative day 3	6 (5.9)‡	9 (8.8)	0.59†
Mean (SD) urea level (mmol/l)			
Pre-operative	6.4 (1.7)	6.5 (1.8)	0.73*
Post-operative day 1	5.0 (1.7)	4.8 (1.6)	0.33*
Post-operative day 2	4.8 (1.8)	4.8 (2.0)	0.87*
Post-operative day 3	5.2 (1.9)	5.6 (2.5)	0.24*

* Student's *t*-test

† chi-squared test

‡ one patient received treatment for acute renal failure. Their GFR MDRD was > 60 pre-operatively, 24 on day 1, 13 on days 2 and 3, 20 on day 4, 37 on day 7, and returned to > 60 at six weeks

following primary THR. Nevertheless, the mean Hb level on the first post-operative day – the primary endpoint of the study – was not significantly different ($p = 0.07$).

An advantage of autologous retransfusion is the good quality of the retransfused red blood cells and the direct contribution to oxygen transport, delivery and consumption in the patient.¹⁵⁻¹⁹ This is in contrast to red blood cells in HBT, in which the optimal contribution to the oxygen consumption may take several hours because of so-called storage deficits.^{20,21} In addition, retransfusion of filtered blood is suggested to be immunostimulant.²²

Studies of intra-operative cell washing/separating devices show that intra-operative retransfusion of red blood cells reduces the requirement for HBT in primary and revision THR.²³⁻²⁷ However, intra-operative cell salvage with the currently available devices is not cost-effective in primary THR.^{25,28} The inexpensive new intra-operative ABT filter system, which is simple to use combined with a post-operative ABT system, was therefore developed for primary THR. The disposable intra-operative filter system costs approximately \$140, in contrast to about \$240 for a

disposable intra-operative washing/separating system, which is used in a cell-saver machine costing roughly \$20 000.

However, another blood-saving method that is becoming increasingly popular is no-drainage following THR. A Cochrane review showed that no-drainage after THR compared with the use of closed-suction drainage reduced the number of patients requiring HBT from 40% to 31%,¹⁰ and, together with the Cochrane review on ABT,⁹ stated the need for studies in THR comparing no-drainage with autologous retransfusion, considering the fall in Hb levels, peri-operative blood loss and HBT requirements.

In this first study on combined intra- and post-operative retransfusion compared with no-drainage following THR, a mean of 488 ml of blood was retransfused, 287 ml collected intra-operatively and 201 ml post-operatively. The results of our study show that combined retransfusion of intra- and post-operatively lost blood is more effective in reducing total blood loss and in reducing the maximum post-operative decrease in Hb levels than no-drainage in primary THR. The patient's lowest post-operative Hb level is important, as it is used to calculate blood loss,

decide on HBT, and in blood management algorithms to avoid HBT as much as possible.^{11,13,29,30} HBT was required in four patients in the ABT group and nine in the no-drainage group, but this difference was not statistically significant ($p = 0.15$). This may be affected by the strict Dutch transfusion trigger, which has already reduced the proportion of HBTs by 50%.^{13,31} In surgery, drains are commonly used in order to reduce haematoma formation and wound leakage. A drain/no-drainage Cochrane review showed significantly more bruising in the no-drainage group and reported that reinforcement of wound dressings was required 60% more often in the group managed without drains after total hip and knee replacement.¹⁰ Another drainage issue is the balance regarding infection risks between evacuating a haematoma, thereby providing less culture medium for infection, versus creating a route for bacterial entry through a drain hole. In this study there were three deep infections of the hip prostheses, all in the no-drainage group.

The cost of the combined intra- and post-operative ABT system used in this study was about \$180, whereas the cost of HBT, including cross-matching, delivery and refrigerated storage, is stated to be between \$522 and \$1183, with a mean of \$761.³² In this study, eight HBTs were given in the ABT group and 18 in the no-drainage group. The transfusion/drain costs in the ABT group were $8 \times \$761$ plus 102 (patients) $\times \$180 = \$24\,448$. For the no-drainage group the costs were $18 \times \$761 = \$13\,698$. In this study, by reducing HBTs the extra costs for the combined intra- and post-operative ABT system were reduced from approximately \$180 to \$100 (\$24 448 to \$13 698/102) per patient. A cost-effectiveness review on blood-saving measures stated that cell salvage had lower costs and slightly more quality-adjusted life years than all of the alternative blood-saving strategies except acute normovolaemic dilution, and concluded that ABT may be a cost-effective method to reduce HBT.³³ Further cost-effectiveness studies are needed to clarify this issue.

This study showed no statistically significant differences in adverse events, creatinine levels, urea levels or kidney clearance levels between the two groups.

The strengths of the study are its prospective randomised controlled design with the blinding of surgeons for patient group allocation until the end of surgery, as well as of the research physicians during follow-up, and the examination of other peri-operative factors that might affect blood loss, with no differences observed in these factors between groups. In conclusion, the use of a new intra-operative ABT filter system combined with a post-operative ABT system resulted in reduced total blood loss and a smaller maximum decrease in Hb levels than no-drainage following primary THR.

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