

# Effectiveness of autologous fibrin tissue adhesive in reducing postoperative blood loss during total hip arthroplasty: a prospective randomised study of 100 cases

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## ABSTRACT

**Purpose.** To evaluate the effectiveness of autologous fibrin tissue adhesive (auto-FTA) in reducing blood loss during cementless total hip arthroplasty (THA).

**Methods.** From September 2000 to August 2001, 100 patients who pre-donated 400 ml of autologous blood were randomised to undergo either standard treatment with auto-FTA (auto-FTA group) or standard treatment alone (control group). The volume of postoperative blood loss and the decrease in haemoglobin level were measured. All patients were followed up for 3 years to evaluate the rate of bone ingrowth and heterotopic ossification.

**Results.** The mean postoperative blood loss was 580 ml (standard deviation [SD], 240 ml) in the auto-FTA group and 810 ml (SD, 341 ml) in the control group; the difference was significant (230 ml,  $p < 0.001$ ). The decrease in haemoglobin concentration was 17 g/l (SD, 11 g/l) in the auto-FTA group and 22 g/l

(SD, 12 g/l) in the control group. The difference was significant (5 g/l,  $p = 0.03$ ). The percentage of total blood loss of >1200 ml in any single patient was significantly lower in the auto-FTA group (4%) than in the control group (20%) [ $p = 0.01$ ].

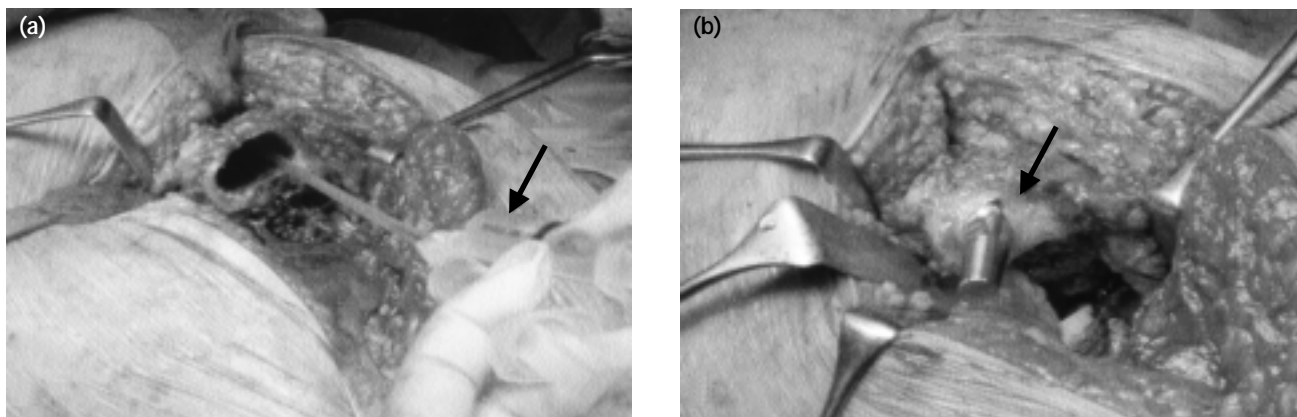
**Conclusion.** Auto-FTA is a safe and effective means of reducing perioperative blood loss in THA.

**Key words:** arthroplasty, replacement, hip; blood loss, surgical; blood transfusion, autologous; fibrin tissue adhesive; hemostasis, surgical; postoperative complications; postoperative hemorrhage

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## INTRODUCTION

Total hip arthroplasty (THA) is associated with a considerable amount of perioperative blood loss ranging from 700 ml to 1700 ml,<sup>1-4</sup> and blood transfusion is often required. Methods of blood conservation are sought to minimise the risks associated with transfusion of homologous blood,



**Figure 1** Fibrin tissue adhesive (arrows) is sprayed into (a) the proximal femoral canal and (b) around the stem caller.

including transfusion reactions and the transmission of viral diseases such as human immunodeficiency virus,<sup>5</sup> hepatitis,<sup>6,7</sup> and cytomegalovirus.<sup>8,9</sup> These methods include preoperative haemodilution,<sup>10</sup> preoperative autologous blood donation,<sup>4,11-15</sup> hypotensive anaesthesia,<sup>16</sup> and intra-operative and postoperative blood salvage and reinfusion.<sup>17,18</sup>

An alternative approach is to use fibrin tissue adhesive (FTA) as a haemostatic agent during surgery.<sup>19,20</sup> Despite its extensive use in other specialties,<sup>21-23</sup> FTA is not widely used in orthopaedic surgery. Commercial FTA products carry a potential risk of infection because they are manufactured from pooled human plasma and are expensive for routine use.

Preoperative autologous blood donation is commonly performed in patients undergoing THA to avoid homologous transfusion. Preparation of FTA from autologous blood does not require special instruments and is cost-effective.<sup>24,25</sup> During total joint replacement surgery, 10 ml of FTA (obtained from 400 ml of predonated blood) is usually used. This prospective randomised study aimed to evaluate the effectiveness and safety of autologous FTA (auto-FTA) obtained from 400 ml of predonated autologous blood in patients undergoing THA.

## MATERIALS AND METHODS

From September 2000 to August 2001 inclusive, in 220 patients at the Saga University Hospital, 250 THAs were performed. The ethics committee of the hospital approved this investigation and informed consent was obtained from each patient prior to enrolment in the study. All male patients or patients with bleeding diathesis, or on anticoagulant therapy or

haemodialysis, or with revision THA, femoral osteotomy, dislocated hip, ankylosed hip, or haemoglobin concentration of <100 g/l were also excluded. A total of 100 patients were recruited. Using a computer-generated randomisation list, 50 were assigned to receive treatment with FTA (auto-FTA group) and 50 to treatment without FTA (control group). A single senior surgeon performed all the operations, using a cementless prosthesis (Kyocera AMS cup, PerFix stem, HWMPH liner, 26-mm head). During surgery and just prior to the possible application of the auto-FTA, the surgeon was notified via a study monitor whether the patient was to receive FTA treatment. This was to minimise the possibility of bias that would occur if the surgeon deviated from standard haemostatic techniques and practices because of prior knowledge about which study group the patient was in.

All patients donated 400 ml of blood (for autologous transfusion) 3 weeks prior to surgery. Patients then received oral iron supplements (200 mg ferrous fumarate) for 3 weeks. Erythropoietin products were not administered. The auto-FTA was prepared as previously reported<sup>24</sup>: the whole blood was centrifuged, separated plasma was collected and stored at -40°C and then thawed by storage at 4°C for 24 hours. The freeze-and-thaw process was repeated twice. The plasma was centrifuged after the second thawing, and an autologous cryoprecipitate (auto-Cryo) was obtained. The auto-Cryo was stored at -40°C and thawed just prior to surgery (solution A). Solution A was delivered to the operating room where solution B (thrombin 5000 IU + 5 ml of 2% calcium chloride + aprotinin 50 000 IU) was prepared. Solutions A and B were individually filled into a double-syringe spray device and used as auto-FTA. The volume of auto-FTA was approximately 10 ml.

**Table 1**  
Preoperative status of auto-FTA group and control group

Preoperative status	Auto-FTA group*, n=50	Control group*, n=50	p value	
			Two-sample <i>t</i> test	Mann-Whitney <i>U</i> test
Age (years)	60 (11)	60 (10)	0.99	0.71
Weight (kg)	55 (12)	54 (7)	0.57	0.88
Predonation haemoglobin (g/l)	132 (10)	130 (12)	0.46	0.59
Red blood cell (x10 <sup>6</sup> /l)	406 (36)	405 (42)	0.92	0.81
Haemoglobin (g/l)	124 (9)	123 (11)	0.77	0.69
Haematocrit (%)	36.8 (2.7)	36.9 (3.2)	0.88	0.71
Platelets (x10 <sup>4</sup> /l)	25.7 (7.0)	24.6 (5.9)	0.38	0.26
PT activity (%)	94.0 (8.3)	91.4 (8.6)	0.13	0.14
APTT activity (%)	106.1 (17.6)	101.2 (16.1)	0.15	0.71
Fibrinogen (mg/l)	328.2 (73.1)	341.3 (66.8)	0.36	0.59

\* Values are given as mean (standard deviation)

**Table 2**  
Peri-operative outcome of the auto-FTA group and control group

Peri-operative outcome	Auto-FTA group*, n=50	Control group*, n=50	p value		% saved, (B-A)/B
			Two-sample <i>t</i> test	Mann-Whitney <i>U</i> test	
Operating time (minutes)	35 (6)	35 (7)	0.79	0.87	-
Intra-operative blood loss (ml)	216 (100)	212 (111)	0.86	0.75	-
Postoperative blood loss (ml)	(A)	(B)			-
1 hour	56 (36)	108 (62)	<0.001	<0.001	48.1%
24 hours	526 (223)	726 (278)	<0.001	<0.001	27.5%
48 hours	580 (240)	810 (341)	<0.001	<0.001	28.4%
Total blood loss (ml)	788 (268)	1017 (364)	<0.001	<0.001	-
Decrease in haemoglobin level on day 1 (g/l)	17 (11)	22 (12)	0.03	0.03	-

\* Values are given as mean (standard deviation)

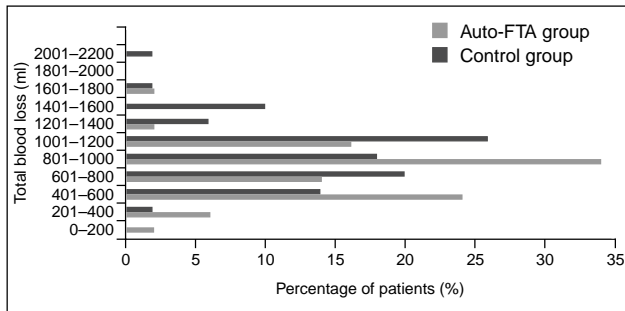
Surgery was performed on all patients under spinal anaesthesia in a complete lateral position. The posterolateral approach and cementless THA were used. The auto-FTA was sprayed into the proximal femoral canal after rasping, and around the stem-collar after the stem was inserted to seal the canal (Fig. 1). A drain was placed in the joint and was connected to a high-vacuum suction unit. Intra-operative blood loss was evaluated by measuring the volume in the suction apparatus and by estimating the amount of lost blood in the swabs. Postoperative blood loss was recorded by measuring the volume of blood in the suction drain and the gauze drain at hour 1, 6, 12, 24, and 48. Total postoperative blood loss was evaluated for 48 hours. All patients were transfused with 400 ml of autologous blood on the day of surgery. No anti-thrombotic therapy was prescribed postoperatively.

The 2 groups were compared with regard to age, weight, haemoglobin value before donation and

perioperative laboratory data, namely, red blood cell count, haemoglobin concentration, haematocrit, platelet count, prothrombin time, activated partial thromboplastin time, and fibrinogen level. The haemoglobin concentration was measured on postoperative day 1.

The occurrences of complications such as infection, deep vein thrombosis, or pulmonary embolism were recorded. Patients were followed up for 3 years to evaluate the rate of bone ingrowth or heterotopic ossification.

Demographic data and other baseline parameters were analysed to ascertain the comparability of the 2 study groups. Efficacy was evaluated by determining the significance of differences in the results between the 2 groups. The two-sample *t* test and the nonparametric Mann-Whitney *U* test were used to compare the 2 groups. A probability value of  $p < 0.05$  was considered significant.



**Figure 2** Two (4%) patients in the auto-FTA group and 10 (20%) patients in the control group with total blood loss of >1200 ml ( $p=0.01$ ).

## RESULTS

No significant differences were observed between the 2 groups with regard to age, weight, preoperative haemoglobin concentration, and bleeding parameters (Table 1) or mean operating time and intra-operative blood loss (Table 2).

The mean postoperative blood loss at hour 1, 24, and 48 in the auto-FTA group was significantly less than that in the control group ( $p<0.001$ ). The mean postoperative blood loss at 48 hours was 580 ml (range, 133–1290 ml) in the auto-FTA group and 810 ml (range, 155–1811 ml) in the control group; this difference (230 ml) was statistically significant ( $p<0.001$ ).

The mean postoperative decrease in haemoglobin concentration at day 1 was 17 g/l (range, 6–40 g/l) in the auto-FTA group and 22 g/l (range, 1–47 g/l) in the controls; this difference (5 g/l) was statistically significant ( $p=0.03$ , Table 2).

The percentage of patients with total blood loss of >1200 ml was significantly lower in the auto-FTA than control group, based on cross tables and Chi squared test ( $p=0.01$ ). Only 2 (4%) of the patients in the auto-FTA group had postoperative blood loss of >1200 ml, compared to 10 (20%) in the control group (Fig. 2).

No patient in either group required homologous transfusion or developed major complications such as infection, severe deep vein thrombosis, or pulmonary embolism. No significant differences were observed between the 2 groups in the rate of bone ingrowth and heterotopic ossification at their 3-year follow-up.

## DISCUSSION

The present study is the first controlled study of

patients undergoing cementless THA with auto-FTA treatment. To minimise variability and reduce bias, the study population was restricted to female patients, since they are less likely to have intra-operative complications and extensive blood loss. The differences in the mean postoperative blood loss at 48 hours and mean decrease in haemoglobin concentration at day 1 were similar to those of a previous study that used commercial FTA to reduce postoperative bleeding in THA.<sup>21</sup> The efficacy of FTA treatment in reducing the extent of blood loss was slightly lower in the present study. This may be attributed to the standardisation of the patient population and the surgical procedure. Thus, greater benefit from FTA treatment may be gained by males than females.<sup>21</sup> To standardise the intra-operative use of FTA, we restricted its use by spraying only the femoral side. If both the acetabular and femoral sides were sprayed with FTA, an even greater decrease in postoperative bleeding may have resulted. The surgeon's experience is another critical factor in the successful use of FTA.<sup>22</sup>

The percentage of patients having a blood loss of >1200 ml was significantly lower in the auto-FTA group than in the controls; no allogeneic transfusion was required for patients in either group. Orthopaedic surgery involves dissection of the soft tissue and bone such that bleeding cannot be controlled by conventional surgical techniques alone. In addition, the use of prophylactic anticoagulants to prevent deep vein thrombosis and pulmonary embolism may hinder control of postoperative blood loss. Thus, the use of a haemostatic agent such as FTA is especially beneficial.

Predonation of blood for autologous transfusion requires a special programme and schedule prior to surgery. Some patients cannot predonate a large volume of blood and require treatment with erythropoietin, which is a very expensive agent. In the present study, all patients were able to donate 400 ml of blood 3 weeks prior to surgery without the need for erythropoietin. The decrease in haemoglobin concentration as a result of predonation did not result in any adverse effects. Predonation for autologous blood transfusion is therefore a safe and cost-effective technique, despite being time-consuming.

## CONCLUSION

Perioperative blood loss and decrease in haemoglobin level after THA involving adjunctive haemostasis with auto-FTA is significantly decreased, and such treatment is safe and effective.

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