

# Non-Activated Autologous Platelet-Rich Plasma for the Prevention of Inguinal Wound-Related Complications After Endovascular Repair of Abdominal Aortic Aneurysms

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**Abstract:** The endovascular repair (EVAR) of abdominal aortic aneurysms (AAAs) usually involves the surgical exposure and catheterization of the femoral arteries. Several inguinal surgical wound-related complications have been reported postoperatively. The aim of this report was to evaluate the safety and efficacy of intraoperative application of autologous platelet-rich plasma (PRP) for the prevention of wound-related complications in AAA EVAR. The authors conducted a patient- and assessor-blinded controlled trial involving 100 subjects undergoing EVAR of an AAA. PRP was produced using an autologous platelet separator and was applied, without prior thrombin activation, in 50 patients eligible for inclusion. The results were compared with a control group of 50 patients who underwent AAA EVAR within the same time period. The primary outcome was the difference in postoperative hospital stay. Secondary outcomes included subjective assessment of wound healing and

wound-related complications. Age, sex, and other comorbidities related to wound healing were not significantly different between cases and controls. One patient treated with PRP developed a unilateral wound infection with lymphorrhea, and two patients developed a bi-lateral superficial infection. Twelve patients within the control group developed a wound-related complication. The postoperative hospitalization was significantly lower in the PRP group. The overall surgical wound-related complications rate was also significantly lower in the PRP group. Application of non-thrombin-activated PRP seems to prevent major postoperative wound-related complications ( $p = .026$ ) and shorten postoperative hospital stay duration after femoral artery exposure and catheterization for AAA EVAR (mean,  $4.48 \pm 0.48$  vs.  $6.14 \pm 0.39$  days). **Keywords:** platelet-rich plasma, endovascular, abdominal aortic aneurysm, wound-related complications. *JECT. 2008;40:52–56*

There are a number of reports justifying the use of platelet derivatives, such as platelet-rich plasma (PRP), as a means of accelerating tissue regeneration and wound healing (1–6). These derivatives contain a high concentration of transforming growth-factor- $\beta$  and platelet-derived growth factor, which may aid in soft tissue healing. Endovascular repair (EVAR) emerged in the early 1990s as a promising alternative treatment option to open surgical repair in various fields of vascular surgery, including abdominal aortic aneurysms (AAAs). In most cases grafting for an AAA is performed after surgical exposure and catheterization of the common femoral arteries. Percutaneous catheterization of the vessels is not widely applied, because of the relatively large diameter of the introducing devices. The reported wound-related complications rates after surgical exposure and catheterization of the common femoral arteries for AAA EVAR include hematoma, seroma, infection, pseudoaneurysm formation, and arterial bleeding (7–10). The aim of this report was to evaluate the safety and efficacy of the subcutaneous injection of au-

tologous non-thrombin-activated PRP in patient inguinal surgical wounds after EVAR of an AAA, in terms of prevention of wound-related complications and postoperative hospital stay duration. The primary outcome was the difference in postoperative hospitalization. The secondary outcome included the subjective assessment of postoperative wound healing and wound-related complications (hematomas, seromas, infection, etc.).

## MATERIALS AND METHODS

### Patient Selection

Written informed consent was obtained from all patients undergoing EVAR and PRP application. Institutional review board approval was also obtained. The PRP was applied in 50 consecutive patients (46 men; mean age,  $71.4 \pm 7.26$  years) who met the exclusion and inclusion criteria of this analysis (Table 1) and were subjected to EVAR of an AAA in our department (1st Department of Surgery, Aristotle University of Thessaloniki, Thessaloniki, Greece), located in a tertiary hospital, during a period of 7 months (November 2005 to May 2006). All operators involved in the study had previous experience with the endografts that were used (10–13), having performed a total of 280 grafting procedures for AAAs during the past 3 years.

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**Table 1.** Inclusion and exclusion criteria.

Exclusion criteria
General contraindications for endovascular surgery
Connective tissue disease
Mycotic AAA
Groin infection within the last 6 months
Systemic inflammation or signs of infection at admission
Lupus or idiopathic thrombocytopenia purpura
Ruptured aneurysm
Abnormal platelet count at admission
Cardiovascular instability
Thrombophilia
Uncontrolled diabetes
Excessive obesity (BMI at admission >32 kg/m <sup>2</sup> )
Current systemic steroid use
Patient positive for methicillin-resistant <i>Staphylococcus aureus</i>
Concurrent sepsis in the lower limbs
Current statin use
Inclusion criteria
Given consent for the application of the PRP and the endovascular procedure
Had not undergone previous femoral artery catheterization within the last 6 months
Ability to receive anti-platelet treatment postoperatively, consisting of clopidogrel and aspirin

A control group consisting of 50 patients who met the same inclusion and exclusion criteria (Table 1) was also identified. All patients included in the control group were referred to our department for an AAA within the same time period (November 2005 to May 2006). All comorbidities and demographics for cases and controls were collected on admission and are listed on Table 2. There was no statistically significant difference between comorbidities that could significantly affect the postoperative wound-healing process (age, sex, current smoking status, obesity, hyperlipidemia, diabetes mellitus, and arterial hypertension). None of the patients in either group were treated immediately after an aneurysmal rupture. Patients with isolated common iliac aneurysms were also excluded from this analysis. The size of the aneurysms and the type of the endograft(s) deployed were not a criterion for patient selection. The preoperative evaluation and all the anatomical measurements were based on contrast-enhanced computed tomographic angiography (CTA) with three-dimensional reconstruction or magnetic resonance angiography (MRA). Preoperative abdominal CT slices were also obtained in all cases. The median aortic aneurysm diameter was 6.1 cm (range, 5.6–13.2 cm) within the control group and 6.4 cm within the PRP group (range, 5–11 cm). The selection of the graft to be deployed in each case was dependent on the anatomical measurements and the patient's co-morbidities. In case a bifurcated endoprosthesis was contraindicated because of anatomical restrictions, such as a narrow terminal aorta and a tortuous, narrow, or calcified contralateral iliac artery, an aorto-mono-iliac graft with femoro-femoral crossover bypass was preferred (EndoFit stent-graft; Le Maitre Vascular, Burlington, MA). Four patients within the treatment

**Table 2.** Co-morbidities and demographics.

	Control Group	Platelet Plasma Group
Sex		
Male	47	46
Female	3	4
Type of procedure—endograft		
AAA aorto-mono-iliac EndoFit + fem-fem bypass	8	16
AAA Endologix	2	5
AAA straight EndoFit	3	7
AAA Talent	34	6
AAA Anaconda	2	10
AAA Gore Excluder	1	6
Total	50	50
Number of common femoral arteries that were surgically exposed	98	95
Co-morbidities		
Arterial hypertension	28	21
Current smoking habit or quit smoking ≤12 months ago (≥10 pack-years)	24	29
Current smoking habit or quit smoking ≤12 months ago (≤10 pack-years)	2	6
Ex-smoker = quit smoking ≥12 months ago	8	1
Chronic renal insufficiency	0	2
Hostile abdomen	0	1
Chronic obstructive pulmonary disease	5	3
Previous stroke	3	1
Diabetes mellitus	5	4
Coronary artery disease	23	19
Previous acute myocardial infarction	11	12
Hyperlipidemia at admission (total serum cholesterol ≥240 mg/dL and serum LDL ≥130 mg/dL)	23	27

group and three patients in the control group were concurrently treated for a common iliac or femoral artery aneurysm with the deployment of an additional endoprosthesis.

#### Technique—Graft Deployment and PRP Application

All manipulations in both groups were carried out by the same team of vascular surgeons and anesthesiologists. All operators involved had previous experience on the specific endografts (10–13) and femoral catheterization. All operations were carried out in a fully equipped operating room, and standard patient monitoring was available (electrocardiogram, blood pressure, and pulse oximetry). Cefuroxime (1500 mg) was administered intravenously preoperatively in all patients in both groups, as a broad spectrum prophylactic antibiotic 30 minutes before the operation. The skin was dressed with Steri-Drape Incise Drapes (3M, St. Paul, MN) in all cases. The patients were placed under regional or general anesthesia before surgically accessing the common femoral arteries (CFA) bilaterally. Heparin (5000–7000 units) was administered intravenously. All manipulations were carried out under fluoroscopic control using a portable C-arm (Siemens Siremobil; Siemens Medical Solutions, Malvern, PA). The type and affiliations of the endografts that were deployed are listed in Table 4.

The detailed steps of each grafting procedure have been

**Table 3.** Types of AAA endografts that were deployed.

Type of Endograft Deployed	Number of Graphs	Number of Graphs
Aorto-mono-iliac EndoFit (LeMaitre Vascular, Burlington, MA)	8	16
Endologix AAA graft (Endologix, Irvine, CA)	2	5
Tubular EndoFit (LeMaitre Vascular, Burlington, MA)	3	7
Talent (World Medical; Medtronic, Sunrise, FL)	34	6
Anaconda AAA graft (Vascutek, Glasgow, UK)	2	10
Gore Excluder (Gore, Flagstaff, AZ.)	1	6
Total	50	50

**Table 4.** Postoperative (< 30 days) surgical wound-related complications.

	Control Group	Platelet Plasma Group
Postoperative complications related to wound healing expressed in no. of patients)	Number of Patients	Number of Patients
Wound hematoma requiring surgical repair	1	0
Superficial wound infection (treated with antibiotics)	3	1
Lymphorrhea	1	0
Deep wound hematoma + lymphorrhea + fever	1	0
Wound inflammation + lymphorrhea	0	1
Superficial inflammation of the access site + fever	3	0
Total	9	2
Postoperative complications related to wound healing (expressed in no. of surgical wounds)		
Wound hematoma requiring surgical repair	1	0
Superficial wound infection (treated with antibiotics)	6	2
Lymphorrhea	1	0
Deep wound hematoma + lymphorrhea + fever	1	0
Wound inflammation + lymphorrhea	0	1
Superficial inflammation of the access site + fever	3	0
Total	12	3
Mean postoperative hospitalization (days)	6,14 (range: 12)	4,48 (range: 15)

published in previous articles (10–13). A completion angiography verified the exclusion of the aortic aneurysm and ruled out the possibility of endoleak or other graft-related complication in all cases. The maximum diameter of the devices inserted into the femoral vessels (sheaths and guide wires) was 22 F. The mean fluoroscopy time was 19 minutes in the PRP group and 14 minutes in the control group (Mann-Whitney test,  $p < .001$ ). None of the patients required blood transfusion in either group. The mean operative time was 126 minutes in the PRP group and 98 minutes in the control group; the mean quantity of con-

trast medium used was 167 mL in the PRP group and 156 mL in the control group, and mean blood loss was 350 mL in the control group and 410 mL in the PRP group (Mann-Whitney test,  $p < .001$ ). Closure was performed by a single attending vascular surgeon in all cases, using Vicryl (Johnson & Johnson, New Brunswick, NJ) for subcutaneous tissues and staples for the skin. The subcutaneous tissues were closed in two layers. Vacuum drains were used in all cases where the femoral artery was surgically exposed. The drains were removed by the nursing staff when appropriate.

### PRP Preparation and Application

After the patient was placed on the operating room table and regional or general anesthesia had been induced, 55 mL of venous blood was drawn by the anesthesiologist from a venous puncture in the upper arm. The syringe contents were centrifuged (1 cycle) using the portable tabletop Magellan Autologous Platelet Separator (Medtronic, Minneapolis, MN) and PRP was produced. The PRP was preserved on the platelet separator and was eventually drawn into a 10-mL sterile syringe right before application. After the completion of the grafting procedure and once adequate hemostasis of the surgical wounds had been obtained, the PRP was injected bilaterally into the subcutaneous tissues simultaneously with the closure procedure. A final layer of PRP was injected percutaneously while closing the skin using staples. A total of 10 mL of PRP was injected in the surgical wounds in all cases. The PRP was not activated using thrombin, either autologous or bovine. All the disposables used during the PRP preparation and application were supplied in the Magellan Autologous Platelet Separator Disposables Kit (Medtronic).

A technician appointed by the distributor of the Platelet Separator (Medtronic) was present in all cases in which the PRP was applied.

### Postoperative Care

Cefuroxime (1500 mg) was administered 3 hours after surgery, aspirin was administered the day of the procedure, and clopidogrel (7 mg daily) was added on the first postoperative day in both groups. The patients ambulated on postoperative day 2, and a plain abdominal radiogram was performed to document graft integrity and positioning. The patients on average were discharged at day 4 postoperatively, unless additional hospitalization was required because of a postoperative complication. During hospitalization, all surgical wounds were evaluated on a daily basis (every 24 hours) by a clinical examiner (attending vascular surgeon) who was not involved in the initial grafting procedure and the application of the PRP. The postoperative care protocol during hospitalization was the same in both groups, making all efforts to minimize bias. The assessor and the nursing staff were not aware whether the patient had received the PRP or not. The surgeons

who performed the grafting procedures and the application of the PRP were not directly involved in the postoperative care of the surgical wounds while the patients remained hospitalized. The follow-up involved an abdominal CT scan performed after postoperative month 1 and then every 6 months.

### Statistical Analysis

The data were analyzed using SPSS 13.0 (SPSS, Chicago, IL) for Windows XP. Continuous variables were tested for normality (Kolmogorov-Smirnov test) and analyzed using a two-sample Wilcoxon rank-sum (Mann-Whitney) test for non-parametric data. The  $p$  value was set at  $<.05$ .

### RESULTS

The deployment of the stent-graft(s) was feasible in all cases; no procedure was converted to open repair in either group, and no graft-related complications were noted on the completion angiography. None of the patients required blood transfusion, and no intraoperative deaths occurred. The heparin dose did not exceed 7000 IUs in any case, and heparin was not reversed in any patient (target activated clotting time was  $>200$  seconds). The preparation and the application of the PRP were successful in all cases (100% technical success), and no immediate PRP-associated complications were observed. The subjects were clinically reviewed on postoperative months 1, 3, and 6 in our department's clinic. All surgical wounds were re-evaluated by the same assessor who was responsible for recording wound-related complications during the postoperative hospitalization on the first follow-up visit. No patient was lost to follow-up.

One diabetic patient within the treatment group developed a unilateral deep wound inflammation with lymphorrhea, and two patients developed a bi-lateral superficial wound infection, all treated with antibiotics (the overall wound-related complication rate in the PRP group was 6%, 3/50 patients). None of the patients in the treatment group developed fever or a wound complication that needed surgical repair. Twelve patients (24%) in the control group developed a wound-related complication (Table 4). Two patients developed a deep wound hematoma with significant bruising needing surgical exploration, both within 3 days after the grafting procedure. The mean postoperative hospital stay duration was 4.48 days (range: 12) in the PRP group (median: 3; SE: 0.39) and 6.14 days (range: 15) in the control group (median: 5; SE: 0.48). The postoperative hospitalization was significantly lower in the PRP group ( $p = .001$ , Mann-Whitney U test). The wound-related complication rate was also significantly lower in the PRP group ( $p = .026$ , Mann-Whitney U test). No device-related or other peripheral vascular complications were observed in the PRP treat-

ment group. Other procedure-related complications observed in the control group included the following: thrombosis of the femoro-femoral graft (aorto-mono-iliac graft group) occurred in one case during the immediate postoperative period. One tunnel hematoma (femoro-femoral crossover bypass) occurred in the aorto-mono-iliac graft group (sixth postoperative month) and was treated conventionally (surgical repair).

### DISCUSSION

Endografting of the abdominal aorta is typically performed through surgical exposure and catheterization of the common femoral arteries, because the relatively large diameter of the introducing devices prohibits percutaneous vessel catheterization in most cases. Wound-related complications after surgical exposure and catheterization of the femoral arteries for the exclusion of aortic aneurysms with the deployment of an endograft include arterial bleeding, pseudoaneurysm formation, wound hematoma, lymphorrhea, arteriovenous fistula, thromboembolism, and wound or groin infection (8–10,14–16). These complications may occasionally be limb or life threatening. Most patients chosen to undergo endovascular exclusion of an aortic pathology through a femoral approach are of high surgical risk and typically present with severe comorbidities (including diabetes, arterial hypertension, and obesity) that may affect the healing process of the surgical wounds. The postoperative anti-platelet therapy (consisting of clopidogrel and/or aspirin) administered in those patients may constitute an additional cause for poor wound healing (17). Finally, these patients typically undergo consecutive percutaneous femoral catheterizations after the EVAR to obtain post-procedural angiographies and/or treat other vascular pathologies (18). Consequently, the specific patient group may benefit greatly from the application of a serum that would accelerate surgical wound healing and prevent groin infections.

The application of thrombin-activated PRP, also known as platelet-gel (PG), was described in the early 1990s as an alternative to fibrin sealant for the control of hemostasis in cardiac surgery (19,20). Since then, PG and other platelet derivatives have been used for the optimization of soft tissue healing and bone regeneration in various clinical applications (21–26). The majority of the clinical studies concerning the use of thrombin-activated platelet derivatives have documented a significantly improved effect on soft tissue healing and a reduced incidence of infections and postoperative blood loss (23–26). As far as non-thrombin-activated PRP applications are concerned, Mishra and Pavelko (27) showed that patients with chronic elbow tendinosis benefited from treatment with PRP that had not been mixed with any activating agent, such as thrombin. Previous reports have also documented that PRP, besides having a high concentration of non-

activated platelets, contains the following factors associated with tissue healing: transforming growth factor  $\beta$ , basic fibroblast growth factor, platelet-derived growth factor, epidermal growth factor, vascular endothelial growth factor, and connective tissue growth factor (21). Most of these growth factors in the PRP have mitogenic actions that increase the population of various healing cells and therefore promote wound healing (21). As a result, we postulate that injecting non-activated PRP in a surgical wound would accelerate the healing process. An important benefit of non-thrombin-activated PRP is the fact that it enhances wound healing even in patients under anti-platelet therapy (28), such as those undergoing EVAR.

In this report, we tried to evaluate the safety and efficacy of the intraoperative application of autologous PRP after endovascular treatment of AAAs. The postoperative hospitalization was significantly lower in the PRP group ( $p = .001$ , Mann-Whitney U test). The overall wound-related complications rate was also significantly lower in the treatment group ( $p = .026$ , Mann-Whitney U test). In addition to this, the complications observed in the control group were of greater extent and severity. These results document that the application of non-activated PRP on surgical wounds after femoral artery catheterization may enhance the healing process and prevent severe wound-related complications.

The limitations of this analysis include the following. The evaluation of the inguinal wounds postoperatively was subjective (assessor-dependent) and not based on an objective scale. Thrombin-activated PRP was not applied; therefore, we are unable to comment on whether thrombin-activated PRP (platelet gel) would further facilitate the healing process in these patients.

## CONCLUSION

Our study confirms previous reports (28) that an application of PRP during a surgical procedure seems to have the ability reduce and/or prevent postoperative wound infection complications and to decrease hospital stay.

Further controlled blind studies are needed to confirm the benefits of PRP application on surgical wounds after endovascular repair.

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