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Changes in Blood Coagulation–Fibrinolysis Markers By Pneumatic Tourniquet During Total Knee Joint Arthroplasty With Venous Thromboembolism

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ABSTRACT

This study investigated changes in blood coagulation–fibrinolysis markers during total knee arthroplasty (TKA). Preoperative 16-row multidetector row computed tomography (MDCT) revealed no asymptomatic venous thromboembolism (VTE) in the 42 patients recruited. Using MDCT postoperatively, patients were divided into thrombus (asymptomatic VTE, 19 patients) and no-thrombus (23 patients) groups. Blood taken at intervals before and after pneumatic tourniquet release revealed increased plasminogen activator inhibitor type-1 (PAI-1) at 30 s for both groups and at 90 s (both $P = 0.01$) in the thrombus group. D-dimer levels were highest at 30 and 90 s for both groups ($P = 0.01$). PAI-1 and D-dimer levels were strongly correlated at both time points in the thrombus group. Inactivating fibrinolysis due to PAI-1 may lead to asymptomatic VTE after TKA.

In orthopedic surgery, it is extremely important to prevent the development of postoperative venous thromboembolism (VTE), particularly symptomatic, fatal pulmonary embolism (PE), after total knee arthroplasty (TKA) [1]. Antithrombotic therapies using agents such as unfractionated or low-molecular-weight heparin have been administered to patients after surgery. Despite the implementation of aggressive antithrombotic protocols, however, the incidence of fatal PE remains at 0.15% [2] and that of symptomatic PE remains at 0.41% [3], with no changes in mortality rates since the 1990s [4]. Furthermore, in a cohort in Korea, the presence of asymptomatic VTE was 35.7% after TKA, as determined using multidetector row computed tomography (MDCT) [5]. Although it is thought that prophylactic antithrombotic treatments are necessary to prevent postoperative fatal and symptomatic PE, previous reports have found no difference in the incidence of these two entities or of asymptomatic VTE, regardless of whether prophylactic antithrombotic therapy was given [2–7]. In addition, reports indicate that the infection rate in prophylactically treated patients is increased owing to hematoma caused by hemorrhage [8–10] and coagulation abnormalities [11] associated with the therapy early after surgery. It is important for orthopedic surgeons to avoid these complications because such infections can last a lifetime. Even if patients achieve remission, they are prone to infection relapse. The routine administration of prophylactic antithrombotic treatment is not recommended in East Asia [12]. Based on these observations, to reduce postoperative infections associated with the overuse of antithrombotic treatment in low-risk patients, we have considered it clinically important to be able to detect early asymptomatic VTE that may cause fatal or symptomatic PE after surgery in patients who are not administered prophylactic antithrombotic treatments. Also, we start antithrombotic therapy only in those patients who need it [6,13]. There are currently no blood coagulation–fibrinolysis markers available for early detection of postoperative asymptomatic VTE following TKA.

Since 2005, some studies have indicated that VTE is affected by the use of the pneumatic tourniquet, causing particular postoperative changes in coagulation–fibrinolysis pathways [14–17]. Therefore, we hypothesized that detecting changes in blood coagulation–fibrinolysis markers in patients with asymptomatic VTE immediately after the pneumatic tourniquet is released might be used to indicate whether patients require antithrombotic therapy. This information could help prevent postoperative bleeding after administering antithrombotics to patients who were at low risk of developing VTE. The purpose of this study was to investigate the changes of blood coagulation–fibrinolysis markers in asymptomatic VTE immediately after release of the pneumatic tourniquet during surgery.

The Conflict of Interest statement associated with this article can be found at http://dx.doi.org/10.1016/j.arth.2013.08.011.

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Materials and Methods

Patients

The study protocol was approved by the Ethics Review Board of our university. This prospective, single-center study enrolled patients who underwent TKA at our institution between April 2007 and March 2009 and gave consent to participate in the study. As exclusion criteria, patients with a past history of symptomatic VTE, cerebral hemorrhage, cerebral infarction, cardiac infarction, or drug allergy to a contrast medium were excluded from the study. In addition, patients with liver disease, renal disease, and/or congenital clotting factor deficiencies and those undergoing antithrombotic therapy or hemodialysis were excluded from the study. Patients with asymptomatic VTE by preoperative MDCT were also excluded.

We enrolled 42 patients who underwent TKA for osteoarthritis (30 knees) or rheumatoid arthritis (12 knees). The cohort comprised 1 male and 41 female patients, with a mean age of 71 years (range 49–84 years). TKA was performed under general anesthesia in all patients, and a pneumatic tourniquet was used. Its pressure was raised before surgery while the leg was exsanguinated and lowered about 90 min later. The tourniquet was used only one time. The patients wore an elastic stocking on the unaffected leg during surgery. Later, they wore them on both affected and unaffected legs and used an intermittent pneumatic compression device until walking training was initiated, in accordance with the Japanese Guidelines for Prevention of Venous Thromboembolism [18]. No postoperative prophylactic antithrombotic therapy was administered. If the patients developed symptomatic VTE and/or if VTE was detected by MDCT, aggressive antithrombotic therapy was initiated.

MDCT

For diagnosis of VTE, 16-row MDCT was performed on the 4th day before surgery and then the 4th day after surgery. These time points mark the interval at which the incidences of PE and VTE are reported to be high [19]. The latter is the earliest point at which patients could comfortably undergo MDCT during the postoperative period.

The MDCT slice thicknesses were 2 mm in the thoracic region and 5 mm from the abdomen to the lower limbs. The window levels were 40–60 and 40–50, and the window widths were 400–500 and 200–400, respectively. A single radiologist (M.D.) evaluated the MDCT images in a blinded manner before and after the surgery. The incidence of postoperative new asymptomatic VTE was calculated.

Preoperative MDCT revealed no asymptomatic VTE in any of the 42 patients included in the study. The patients were classified postoperatively via MDCT into two groups. The thrombus group was defined as patients with a new asymptomatic VTE, and the no-thrombus group was defined as those without asymptomatic VTE.

Blood Coagulation–Fibrinolysis Markers

Blood samples were taken to measure the plasma levels of plasminogen activator inhibitor-1 (PAI-1), soluble fibrin monomer complex (SFMC), D-dimer, and cross-linked fibrin degradation products by leukocyte elastase (e-XDP) immediately before and after release of the pneumatic tourniquet and then at 30, 90, and 180 s after release of the pneumatic tourniquet (Fig. 1). Citrated plasma samples were stored at −80 °C until analysis. The plasma PAI-1 levels were measured by a latex photometric immunoassay (Mitsubishi Chemical Medience Corporation, Tokyo, Japan) using the polyclonal antibody F(ab') fragment [20]. Plasma SFMC, D-dimer, and e-XDP levels were measured by latex immunoagglutination assays (Mitsubishi Chemical Medience Corporation) using the monoclonal antibodies IF-43 and JIF-23, respectively [21,22]. The plasma e-XDP levels were measured by a latex immunoagglutination assay (Mitsubishi Chemical Medience Corporation) using the monoclonal antibody IF-123 [23].

Statistical Analysis

Statistical analyses were performed using SPSS for Windows version 11.0 software (SPSS, Chicago, IL, USA). PAI-1, SFMC, D-dimer, and e-XDP levels were analyzed by the Shapiro–Wilk test if they did not fit a normal distribution. The PAI-1, SFMC, D-dimer, and e-XDP levels were compared between the thrombus and no-thrombus groups before release using the Mann–Whitney U-test. The PAI-1, SFMC, D-dimer and e-XDP levels were compared between immediately, at 30, 90, 180 s after release, respectively, and immediately before release using the Friedman test. If a significant difference was noted, the data were compared using the Wilcoxon signed rank test and corrected using Bonferroni's inequality. Spearman's rank correlation was used to determine whether blood coagulation–fibrinolysis markers that differed significantly were affected by each other. The gender and disorder distributions were compared between the thrombus and no-thrombus groups using Fisher's exact test. Age, volume of intraoperative hemorrhage, and operation time were compared using an unpaired *t*-test. The level of statistical significance was set at $P < 0.05$ for all tests.

Results

No patients developed symptomatic VTE during or after TKA in this study. Postoperative MDCT revealed asymptomatic VTE in 19 (45.2%) patients (thrombus group) and no VTE in 23 patients (54.7%) (no-thrombus group). Aggressive antithrombotic therapy was initiated in the 19 patients in whom new asymptomatic VTE was detected following postoperative MDCT (Table).

Changes in Operative Blood Coagulation–Fibrinolysis Markers Before Release of the Pneumatic Tourniquet

There were no significant differences in the preoperative PAI-1, SFMC, D-dimer, or e-XDP levels between the thrombus and no-thrombus groups ($P = 0.23$, $P = 0.23$, $P = 0.39$, and $P = 0.89$, respectively) (Fig. 2).

Operative Blood Coagulation–Fibrinolysis Markers After Release of the Pneumatic Tourniquet

The PAI-1 level showed the most significant increases at 30 s (median 27.3 ng/ml, $P = 0.01$) and 90 s (median 28.5 ng/ml, $P = 0.01$) after release of the pneumatic tourniquet in the thrombus groups and at 30 s (median 38.7 ng/ml, $P = 0.01$) after release in the no-thrombus group (Fig. 2).

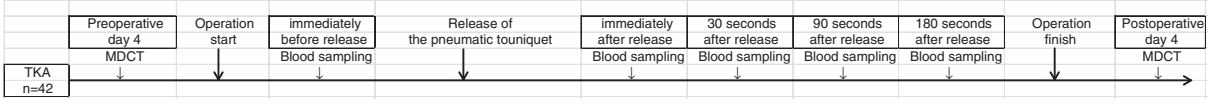

Fig. 1. Study protocol.