

Perioperative hypercoagulability in patients with rheumatoid arthritis: Sonoclot study

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Preoperative blood hypercoagulability and perioperative hemostasis are the risk factors of postoperative venous thromboembolism (VTE). Prosthetic surgery of the knee is one of the operations with the highest risk of VTE when it is performed without prophylactic anticoagulant therapy, according to an International Consensus Statement [1]. A high body mass index (BMI) and advanced age have been reported to be further risk factors [2], but prophylaxis must be considered according to the patients' perioperative blood coagulability in individual cases.

A number of previous studies have reported on the presence of systemic hemostatic abnormalities in patients with rheumatoid arthritis (RA), including increases in serum fibrinogen and von Willebrand factor levels [3]. Also, the therapeutic use of corticosteroids is known to accelerate hemostasis in RA patients. We need to detect hypercoagulability and to investigate the appropriate prophylaxis perioperatively in these patients.

The Sonoclot (Sienco, Morrison, CO, USA) analyzer is one of the viscoelastic measures of blood coagulation that is frequently used for intraoperative coagulation management, because it offers global assessment of whole-blood clotting in a short time. Using the Sonoclot analyzer, in this study we aimed to assess perioperative hemostatic abnormalities in patients with RA compared to patients with osteoarthritis (OA) presenting for

elective knee surgery, and we aimed to determine whether prophylaxis against thromboembolism was necessary in either of these groups of patients.

After obtaining informed consent from the patients, 16 women with RA and 13 age-matched women with OA having prosthetic surgery of the knee were enrolled. Patients with a BMI of more than 27, those receiving anticoagulant therapy, and those having a history of diabetes mellitus or cerebrovascular thrombotic diseases were excluded. All patients with RA had received corticosteroid therapy (prednisolone, 1–10 mg per day) for more than 5 years. A tourniquet was used for all patients, with a pressure of around 250 mm Hg, and the duration was between 80 and 130 min.

Patients received 0.5 mg atropine, with or without 25 mg hydroxyzine intramuscularly 30 min preoperatively. Indirect blood pressure measurement, ECG, and SpO₂ were monitored in the operation room. Spinal anesthesia was performed with 0.5% isobaric bupivacaine 2.5–3.0 ml through the L3–4 or L2–3 interspace.

The blood count, bleeding time, prothrombin time (PT), activated partial thromboplastin time (aPTT), and C-reactive protein level were measured preoperatively. About 5 ml of blood was sampled from a large vein after spinal anesthesia was performed (preoperation) and after tourniquet deflation (postoperation). Sonoclot (Sienco) analysis was immediately performed with 0.36 ml of whole blood. Parameters included Sonoclot activated clotting time (SonACT, s), gradient of the initial slope of the signature (clot rate of fibrin formation [CR], signal·min⁻¹), and the time to peak impedance (TP, min). Statistical analysis was performed with Mann-Whitney's nonparametric test, with a *P* value of less than 0.05 regarded as statistically significant.

Patients' demographic data are shown in Table 1. There were no differences in preoperative hematological indices, including platelet count, between the patients with RA and those with OA. Coagulation tests showed no difference between these two groups

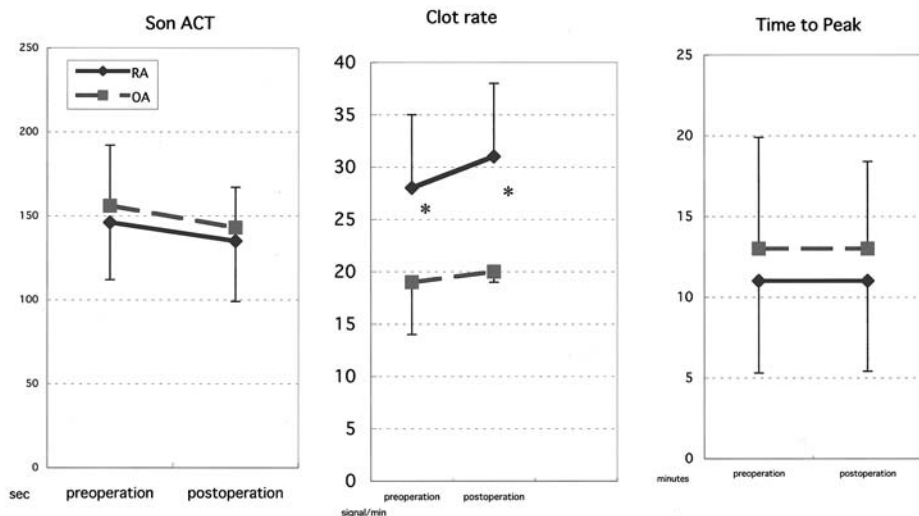


Fig. 1. Changes in Sonoclot (Sienco) activated clotting time (*Son-ACT*), clot rate, and time to peak. Data values are means (SD). * $P < 0.05$ vs osteoarthritis (OA). RA, rheumatoid arthritis

Table 1. Preoperative demographic characteristics of the patients

	RA patients (n = 16)	OA patients (n = 13)
Age (years)	60 ± 11	70 ± 4
BMI (kg/m ²)	23 ± 2	25 ± 1
Hemoglobin (g/dl)	11 ± 2	12 ± 1
Hematocrit (%)	34 ± 2	35 ± 3
Platelet count (×10000/μl)	31 ± 6	24 ± 6
C-reactive protein (mg/dl)	1.45 ± 1.1*	0.26 ± 0.4*
Bleeding time (min)	2.0 ± 0.6	1.9 ± 0.9
Prothrombin time (s)	11.7 ± 0.6	11.8 ± 0.5
Activated partial thromboplastin time (s)	24.8 ± 3.0	27.9 ± 4.1

* $P < 0.05$

Values are means ± SD

RA, rheumatoid arthritis; OA, osteoarthritis; BMI, body mass index

of patients. The C-reactive protein level was higher in patients with RA.

The Sonoclot results showed no differences in SonACT and TP between the two groups of patients either pre- or postoperatively. The CR was significantly ($P < 0.05$) higher in patients with RA, both preoperatively and postoperatively, and it tended to increase postoperatively, but not significantly (Fig. 1).

Our result showed an accelerated clot rate in RA patients who were receiving steroids compared with patients with OA. Significant elevations in several thrombotic predictors of cardiovascular disease (fibrinogen, von Willebrand factor, tissue plasminogen activator antigen, and fibrin D-dimer) were found in patients with RA, a chronic inflammatory disease with vasculitis [4,5]. The use of corticosteroids increases the risk of thrombotic events in RA, because these drugs promote atherosclerosis, increase von Willebrand

factor, and accelerate platelet aggregation [6,7]. RA patients treated with corticosteroids are considered to have a hemostatic tendency, but, there are no studies about the differences in hemostatic condition between RA patients with and without corticosteroid treatment. Multi-center, prospective, and epidemiological studies in Japanese patients undergoing total knee arthroplasty show a 50% prevalence of deep venous thrombosis in those without prophylactic anticoagulant therapy [2]. This kind of operation, with the use of an air tourniquet, seems to have a high risk of postoperative thromboembolism for RA patients receiving corticosteroids.

In this study, we detected postoperative blood hypercoagulability in patients with RA compared with patients with OA. A high CR means accelerated fibrinogenesis and clot formation. The increased preoperative serum level of C-reactive protein and fibrinogen support the findings of a high CR in patients with RA with corticosteroid therapy.

Sonoclot analysis has been shown to be valuable and reliable in monitoring intraoperative changes in coagulation and perioperative hypercoagulation state [8,9]. The usual hematological tests could not demonstrate any differences between RA and OA patients. The postoperative decrease of SonACT in both groups indicates an increase in blood clotting factors caused by operative stress. Kohro et al. [10] have demonstrated that operative stress caused by an air tourniquet increases blood coagulability under anesthesia. The increased C-reactive protein level in patients with RA supported the presence of chronic inflammation. A high CR indicates a rapid increase in viscosity due to the conversion of fibrinogen to fibrin, and it reflects the speed at which the clot is being formed. These Sonoclot data support the findings of accelerated fibrin formation in RA patients receiving corticosteroids, and explain

the increase in their risk of postoperative thromboembolism. This viscoelastic measurement of coagulation may be more appropriate for an anesthesiologist than the use of discrete laboratory tests of coagulation. To find which factor is responsible for increasing the CR, RA or corticosteroid therapy, we should have compared patients receiving corticosteroid therapy to those not receiving it. Acceleration of fibrinolysis in RA patients is still controversial, and evaluation of this parameter with the Sonoclot analyzer has not yet been conducted.

Previous Sonoclot studies show an increased CR in female patients and older patients undergoing orthopedic operations. Patients with OA tend to be older and more obese than patients with RA. We showed a higher CR in sex-, age-, and BMI-matched patients with RA compared to those with OA. Younger women who are still menstruating are less likely to have a hemostatic state than older women [11].

Recently, Iturbe et al. [12] reported the existence of a hypercoagulable state prior to prosthetic knee surgery regardless of the preoperative diagnosis. No patients in our study showed postoperative clinical evidence of thrombosis, but if they had active prophylaxis might have been considered in future cohorts. The Sonoclot analyzer offers a rapid, global assessment of whole-blood clotting, and it is useful to assess perioperative hypercoagulability. But further study is needed to measure thrombotic variables (fibrinogen, thrombin-antithrombin complex, and D-dimer) simultaneously with Sonoclot analysis.

In conclusion, patients with RA receiving corticosteroid therapy showed a higher hypercoagulable state than patients with OA in the perioperative period of total knee arthroplasty. Prophylaxis for thromboembolism must be considered for these patients. The Sonoclot

analyzer is a useful means with which to detect hypercoagulability in these patients.

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