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Higher preoperative D-dimer value remain high postoperatively in patients with rheumatoid arthritis compared with those with osteoarthrosis

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Abstract
The differences in hemostatic condition between patients with inflammatory rheumatoid arthritis (RA) and noninflammatory osteoarthrosis (OA) were studied. Twenty-six patients undergoing total knee arthroplasty were enrolled. Compared with OA patients, RA patients showed a higher platelet count and D-dimer value preoperatively, and D-dimer remained high for 1 week after the operation. Patients with OA showed popular DD change, with the lowest value observed before the operation, and a gradual increase for 1 week after the operation. The highest value of thrombin–antithrombin complex was observed immediately after the operation. Fibrinogen and the clot rate at 1 week after operation were higher in both patient groups. We concluded that patients with RA showed different perioperative hemostatic change than patients with OA.

Key words Total knee replacement · D-dimer · Hemostasis

Introduction

Prosthetic surgery of the knee is one of the operations with the highest risk of postoperative venous thromboembolism. Preoperative hypercoagulability because of higher age, obesity, or other factors in these patients has been reported [1]. Intraoperative use of an air tourniquet may accelerate venous stasis. Total knee arthroplasty (TKA) is indicated both for patients with inflammatory rheumatoid arthritis (RA) and those with noninflammatory osteoarthrosis (OA). Perioperative hemostatic differences between patients with RA and OA have not been much discussed before. We have already reported increased coagulability in preoperative patients with RA compared with patients with OA, measured by celite-activated thromboelastography (Sonoclot; Sienco, Morrison, CO, USA) in patients of the same age and with the same body mass index (BMI) [2]. In this study, we report further differences in perioperative coagulation changes 1 week postoperatively in patients with RA or OA, determined by a serum hemostatic markers analysis and Sonoclot.

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Patients and methods

After informed consent was obtained, 26 women aged 40 to 81 years undergoing elective TKA were enrolled. Twelve patients were diagnosed with RA and 14 with OA. Premedication with 0.5 mg atropine, with or without 2–2.5 mg midazolam, was administered intramuscularly 30 min before the patient entered the operation room. Indirect blood pressure, the electrocardiogram, and S_{PO_2} were monitored in the operation room. Spinal anesthesia with 2.5–3.0 ml of plain bupivacaine 0.5% was performed through the L2/3 or L3/4 interspace. An air tourniquet was used for all patients intraoperatively for 60–90 min.

The blood cell count, including the platelet count, bleeding time, prothrombin time (PT), activated prothrombin time (aPTT), and C-reactive protein (CRP) were measured preoperatively. Fibrinogen (Fib), D-dimer (DD), thrombin–antithrombin complex (TAT) were measured and the Sonoclot analysis was performed after spinal anesthesia (preoperation), after tourniquet deflation at the end of the operation (postoperation), and 1 week after the operation (1 week). The Sonoclot analysis was performed with 0.36 ml of whole blood immediately after the blood sample was obtained. 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). Fib was measured by the coagulation method, DD by the latex coagulation method, and TAT

Table 1. Patient characteristics

	Rheumatoid arthritis (RA) $n = 12$	Osteoarthrosis (OA) $n = 14$
Age (years)	61 ± 9	74 ± 7*
BMI ($kg \cdot m^{-2}$)	23 ± 2	27 ± 5*
CRP ($mg \cdot dl^{-1}$)	1.1 ± 0.9	0.7 ± 1.0
Bleeding time (min)	1.4 ± 0.3	1.7 ± 1.0
PT (s)	11.3 ± 0.4	11.1 ± 0.6
APTT (s)	29.7 ± 4.5	28.2 ± 3.5
Operation time (min)	120 ± 32	123 ± 19

Values are means ± SD
BMI, body mass index; CRP, C-reactive protein; PT, prothrombin time; APTT, activated prothrombin time
* $P < 0.05$

Table 2. Hematological data

	RA			OA		
	Preoperation	Postoperation	1 week postoperation	Preoperation	Postoperation	1 week postoperation
Hb ($g \cdot dl^{-1}$)	11.3 ± 1.4	9.3 ± 1.2*[b]	9.3 ± 1.3*[b]	12.1 ± 1.3	10.3 ± 1.7*[b]	9.1 ± 1.8*[b,c]
Ht (%)	33.8 ± 4.8	27.7 ± 3.3*[b]	28.6 ± 4.0	35.5 ± 3.7	30.3 ± 5.1*[b]	27.2 ± 5.2*[b,c]
Platelet (×10000/μl)	32.7 ± 6.6*[a]	27.9 ± 6.4*[a,b]	35.5 ± 6.3*[c]	23.1 ± 9.1*[a]	17.9 ± 4.9*[a,b]	30.2 ± 10.5*[c]
Fib ($mg \cdot dl^{-1}$)	349 ± 49	325 ± 42	386 ± 18*[c]	343 ± 75	303 ± 78	471 ± 130*[b,c]
TAT ($ng \cdot ml^{-1}$)	7.9 ± 8.2	37.6 ± 15*[b]	15.5 ± 3.7*[c]	7.9 ± 5.5	39.6 ± 22*[b]	21.2 ± 9.0*[c]
DD ($\mu g \cdot ml^{-1}$)	12.9 ± 10*[a]	13.5 ± 8.2	12.4 ± 9.1	2.8 ± 3.5*[a]	4.7 ± 4.2	11.9 ± 7.1*[c]

Values are means ± SD
Hb, hemoglobin; Ht, hematocrit; Fib, fibrinogen; TAT, thrombin–antithrombin complex; DD, D-dimer
* $P < 0.05$
[a] RA vs. OA
[b] vs. preoperation
[c] vs. postoperation

by an enzyme immunoassay. Statistical analysis was performed with Student's *t* test or the Mann-Whitney Test, with a *P* value of less than 0.05 regarded as statistically significant.

Results

Patient characteristics are shown in Table 1. Age and BMI were higher in the patients with OA than in those with RA. The preoperative blood cell count showed that the platelet count was higher in RA patients. The hemoglobin concentration and hematocrit and platelet counts decreased postoperatively because of bleeding. The hemoglobin concentration and hematocrit remained low for 1 week after the operation, but the platelet count increased significantly to a value comparable to the preoperative value at 1 week in both groups. Hemostatic measurements showed no differences in the preoperative values of Fib and TAT between the two groups. Fib increased gradually and showed the highest value at 1 week, but TAT was the highest immediately after the operation in both patient groups. Perioperative DD changes showed the greatest difference between patients with OA and RA. In OA patients, DD was lowest before the operation and gradually increased for 1 week after the operation. In RA patients, however, preoperative DD was significantly higher than in OA patients, and it did not change immediately after the operation or after 1 week (Table 2). In both groups of patients, preoperative TAT and DD values were higher than normal. There were no differences in the Sonoclot results (SonACT, CR, or TP) between patients with RA and OA throughout the time course. CR increased at 1 week in both groups (Table 3).

Discussion

Patients with RA showed a significantly higher preoperative platelet count than patients with OA. TAT and DD were higher than normal preoperatively in both groups of patients: DD in RA patients was ten times normal. Iturbe et al. [1] reported a hypercoagulable state prior to prosthetic hip or knee surgery regardless

Table 3. Sonoclot data

	RA			OA		
	Preoperation	Postoperation	1 week postoperation	Preoperation	Postoperation	1 week postoperation
SonACT (s)	155 ± 34	175 ± 23	183 ± 10	186 ± 37	146 ± 29*	177 ± 22
Clot rate (signal/min)	21 ± 4.8	25 ± 3.5	28 ± 3.9*	19 ± 5.0	22 ± 4.3	26 ± 7.8*
Time to peak (min)	15 ± 7.6	14 ± 6.5	11 ± 2.8	17 ± 5.5	13 ± 3.1	14 ± 10.7

Values are means ± SD
* $P < 0.05$ vs. preoperation

of the preoperative diagnosis. Obesity and higher age in OA, and chronic inflammation in RA may contribute to this hypercoagulable state. The postoperative increases in the platelet count and in the serum Fib level at 1 week in both groups indicate that coagulation accelerated after total knee replacement for at least for 1 week. Sonoclot is a method for the viscoelastic measurement of blood coagulation, showing coagulation factor activity (SonACT), the fibrin formation rate (CR), and platelet function (TP). The CR increase at 1 week after the operation was compatible with the increase of Fib at 1 week postoperatively. Production of thrombin during the operation caused TAT to peak at the end of operation, which was followed by an increase in DD 1 week afterward in OA patients. This is a common change in homeostasis after general orthopedic operations [3]. However, preoperative DD in RA patients was significantly higher than in patients with OA, without any changes for 1 week after the operation. Elevated DD reflects accelerated fibrin production or fibrinolysis. In patients with chronic arthritis with RA, increased fibrin formation in joint tissue causes the acceleration of fibrinolysis, resulting in a high DD level. Recently, DD measurement has been used to diagnose deep vein thrombosis (DVT). A high DD concentration is also associated with smoking status or advanced cancer without DVT. But old age and obesity have not been reported to be associated with a high DD level. Increases in coagulation and inflammation markers such as Fib and CRP also cause a high DD level, but they do not indicate DVT in these patients, as they do in patients with RA [4]. In a prior study using a Sonoclot analysis, we reported a perioperative CR increase in RA patients compared with OA patients at controlled age and BMI. Compared with OA patients who were neither old nor obese, RA patients with high CRP showed a hypercoagulation state. In this study, OA patients with higher age and BMI had CRs similar to those of RA patients with normal CRP. Preoperative higher CRP in the groups of RA patients might have contributed to the higher CR in our prior study. Preoperative CRP and Fib concentrations were not different between the two groups of patients in this study. Inflammation might be controlled by administration of corticosteriods, but corticosteroids by themselves can increase coagulation factors such as factor VIII and accelerate hemostasis. The increased level of DD in RA patients may be a response to fibrin formation, either intravascularly or extravascularly [5]. Fibrinolysis is accelerated in RA, but fibrin formation accelerates faster, so the fibrin precipitate delays fibrinolysis preoperatively. Patients with RA cannot increase fibrinolysis to repair operative tissue damage, and postoperative thrombotic risk seems to be higher than in OA patients. We should plan different prophylaxis for postoperative thrombosis in patients with RA than for those with OA.

In conclusion, we showed a postoperative increase in hemostasis with an increase of Fib at 1 week after total knee replacement. In patients with RA, the DD level was significantly higher than in patients with OA preoperatively, and it did not change during the week after the operation because of preoperative accelerated fibrin formation and fibrinolysis.

References

1. Iturbe T, Comudella R, Miguel R (1999) Existence of a hypercoagulability state prior to prosthetic hip or knee surgery. Haematologica 84:87–88
2. Mukubo Y, Kawamata M (2004) Perioperative hypercoagulability in patients with rheumatoid arthritis: Sonoclot study. J Anesth 18:62–64
3. Lopez Y, Paramo JA, Valenti JR (1997) Hemostatic markers in surgery: a different fibrinolytic activity may be of pathophysiological significance in orthopedic versus abdominal surgery. Int J Clin Lab Res 27:233–237
4. Cushman M (2003) Fibrin fragment D-dimer and the risk of future venous thrombosis. Blood 15:1243–1248
5. McEntegart A, Capell HA, Creran D (2001) Cardiovasular risk factors, including thrombotic variables, in a population with rheumatoid arthritis. Rheumatology 40:640–644