Acta Clin Croat 2016; 55:414-421 Original Scientific Paper

doi: 10.20471/acc.2016.55.03.10

# INFLUENCE OF FONDAPARINUX *VERSUS* NADROPARIN CALCIUM THROMBOPROPHYLAXIS ON CLINICAL PARAMETERS FOLLOWING TOTAL KNEE ARTHROPLASTY

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SUMMARY – Fondaparinux has been shown to be as effective as low molecular weight heparin in orthopedic surgery, with no cases of heparin induced thrombocytopenia proven until today. The main goal of this prospective randomized controlled trial was to define whether thromboprophylaxis in patients with primary osteoarthritis of the knee undergoing total knee arthroplasty (TKA) influences clinical parameters in the same manner in patients receiving fondaparinux as in those receiving nadroparin during the first 7 postoperative days. Sixty patients with primary knee osteoarthritis underwent unilateral TKA performed by the same surgeon and were randomized into two groups of 30 patients receiving either fondaparinux or nadroparin thromboprophylaxis. Patients were compared according to the duration of operation, perioperative blood loss, laboratory results and clinical evaluation of the edema during the early postoperative period. No differences were found between the groups in the mean duration of surgery, perioperative blood loss, and most of laboratory results. The level of urea was significantly lower in the nadroparin group on the first and second postoperative day. No cases of heparin induced thrombocytopenia, deep vein thrombosis or pulmonary embolism were noted during the study. Study results showed both fondaparinux and nadroparin to have the same influence on clinical parameters during the first 7 postoperative days in patients undergoing TKA.

Key words: *Arthroplasty, replacement, knee; Anticoagulants; Fondaparinux; Nadroparin; Hemorrhage*

## Introduction

The importance of thromboprophylaxis in orthopedic surgery regarding the possible postoperative development of thromboembolic complications such as deep vein thrombosis (DVT) and pulmonary embolism (PE) is well known. The American College of Chest Physicians (ACCP) guidelines from 2012 suggest that the baseline risk in orthopedic surgery is 1% for PE and 1.8% for DVT[1]. According to some authors, the rate of DVT can be by 50% higher if no thromboprophylaxis is used in orthopedic surgery[2]. Low molecular weight heparin (LMWH) is nowadays often used for prevention of thromboembolic complications in patients undergoing TKA, with the incidence of DVT and PE reduced by 60% when compared to the control group without thromboprophylaxis[3]. The known drawbacks in LMWH treatment are the possibility of heparin-induced thrombocytopenia (HIT) in 0.2% of patients with LMWH therapy and excessive bleeding[4].

Great attention has been focused lately on developing an 'ideal' medication for prevention and treatment of thromboembolic diseases. The ideal drug should be as effective as the best known drug used to-

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Received January 9, 2015, accepted February 16, 2016

day, safe and simple to use, and widely applicable. Direct inhibitors of factor Xa are being investigated as the possible 'new generation' of anticoagulants for some time[5]. Fondaparinux is a Xa inhibitor demonstrated to be as effective as LMWH, with no cases of HIT proven until today. It inhibits factor Xa *via* antithrombin III, but is, unlike LMWH, selective for factor Xa. The main goal of this prospective randomized controlled trial was to define whether thromboprophylaxis in patients with primary osteoarthritis of the knee undergoing TKA influences clinical parameters in the same manner in patients receiving fondaparinux as in those receiving nadroparin calcium during the first 7 days following surgery.

## Patients and Methods

Our study included 60 patients with primary osteoarthritis of the knee that underwent unilateral TKA performed by the same surgeon at our Department. The patients were examined by an anesthesiologist working at our Department, 3-4 weeks before the surgery and at that time laboratory results were checked, which included complete blood count (CBC), sodium and potassium levels, blood glucose level, liver enzymes (aspartate aminotransferase (AST) and alanine aminotransferase (ALT)), as well as urea and creatinine levels. The American Society of Anesthesiologists (ASA) physical status was assessed at that time[6]. The inclusion criteria were primary knee osteoarthritis, age between 40 and 80 years, weight between 45 and 110 kg, and ASA status I and II.

Patients with secondary osteoarthritis of the knee, patients awaiting revision TKA, patients with malignancies, autoimmune diseases, coagulation disorders, cardiovascular diseases (uncontrolled hypertension, unstable angina pectoris, acute myocardial infarction and/or cerebrovascular insult up to 6 months prior to surgery), gastrointestinal bleeding that had been present for up to 6 months prior to surgery, and patients taking immunosuppressive or cytostatic drugs or anticoagulants were not included in the study.

Upon approval by the Hospital Ethics Committee, patients were randomized using the random number table into two groups consisting of 30 patients each. The first group of patients received thromboprophylaxis with fondaparinux (Arixtra®, GlaxoSmithKline-GSK, Brentford, United Kingdom) at a dose of 2.5 mg in subcutaneous injections. The first dose was administered 6 hours after the surgery and the same dose was administered each day during the remaining hospital stay at 10 a.m.

The second group received thromboprophylaxis with nadroparin calcium (Fraxiparine®, GlaxoSmith-Kline-GSK, Brentford, United Kingdom) at a dose of 0.4 mL in subcutaneous injections. The first dose was administered 12 hours before the surgery, the second dose 8 to 10 hours after the surgery, and then the same dose was administered every 24 hours during the hospital stay.

All patients received thromboprophylaxis during the first 6 postoperative weeks, which included thromboprophylaxis using either fondaparinux or nadroparin calcium throughout the hospital stay, which usually ended after the patients achieved at least 90° of flexion and full extension of the operated knee. Upon discharge from the hospital, thromboprophylaxis differed based on whether they were discharged to a rehabilitation center or home. If the patients were transferred to a rehabilitation center, they received thromboprophylaxis as suggested by the orthopedic surgeon in the discharge letter. In cases they were discharged home, their thromboprophylaxis was converted to oral warfarin at a dose adjusted by the attending physician.

Upon admission to the hospital, blood pressure was measured, as well as heart frequency and weight. At that time, blood sample was obtained to determine CBC, activated partial thromboplastin time (aPTT) and prothrombin time (PT). This was repeated at 24 hours, 3 days and 7 days after the surgery. The level of D-dimers was assessed at 24 hours and 7 days after the surgery.

All surgeries were performed with the patients in spinal anesthesia. All patients preoperatively received antibacterial prophylaxis with first-generation cephalosporins or clindamycin, which is in accordance with recent guidelines[7,8]. A thigh tourniquet was inflated at 250-300 mm Hg before the beginning of surgery. Total knee arthroplasty was performed in a standard fashion in all patients, using the cemented total knee endoprosthesis Multigen Plus (Lima Coorporate spa®, Udine, Italy). The tourniquet was deflated after the original components had been implanted, followed by detailed hemostasis and placement of two surgical drains intra-articularly before suturing the wound. Surgical drains were connected to the autotransfusion

Drentech Surgical blood salvage system (REDAX®, Poggio Rusco, Italy), which was used during the first 6 hours postoperatively. Upon removal of the blood salvage system, surgical drains were connected to the standard 'free-fall' system.

Postoperative care was taken by anesthesiologists in the Orthopedic Intensive Care Unit (ICU) for 24 or 48 hours following the surgery, after which the patients were transferred back to the orthopedic department. Intensive care included fluid resuscitation and continuous use of analgesics. Monitoring of the blood pressure, heart and respiratory function and oxygen saturation was performed and any complications were noted.

Intraoperative and postoperative bleeding was measured and local hemorrhage and hematoma was noted if present. Intraoperative bleeding implied the blood that was aspirated after deflation of the tourniquet and before suturing the wound. It also included the blood volume that was present in cheesecloths and compresses used during the operation, which was measured by weighing them and calculating the difference between the used and unused ones.

Total postoperative bleeding consisted of two components. Early postoperative bleeding implied the blood volume that was collected by the blood salvage system during the first 6 hours after the surgery and was used for postoperative autotransfusion. On the other hand, late postoperative bleeding was the blood volume that was drained from the joint in the first 48 hours after the operation, i.e. until surgical drains were removed. Total perioperative bleeding was simply counted as intraoperative and postoperative bleeding together.

Postoperative rehabilitation was started in the ICU with respiration and circulation exercises and was continued after removal of surgical drains, 48 hours after the surgery, and included use of the continuous passive motion machine (CPM) and individual exercises. Rehabilitation was performed in the same way in all patients and was continued upon their discharge from the hospital in another institution with stationary rehabilitation.

To evaluate postoperative swelling of the operated leg, the knee and lower leg circumference was measured. The lower leg circumference was measured at two levels, 10 and 15 cm distally to the inferior pole of the patella, while the knee circumference was measured at the level of the middle third of the patella. Both measurements were repeated 24, 48 and 72 hours after the surgery, as well as 7 days postoperatively.

Statistical analysis was performed using the Smirnov-Kolmorgorov testing with ANOVA and Kruskal-Wallis test for quantitative variables. The $\chi^2$-test and Fisher exact test were used on analysis of qualitative variables. The STATISTICA ver. 9.1 software was employed. The t-test and Wilcoxon test were used to test differences, as well as Student's t-test and Mann Whitney test. The level of statistical significance was set at $p<0.05$.

## Results

Sixty patients were included in our study (24 male and 36 female). Sex distribution of study patients was comparable in both groups, with 11 male and 19 female patients receiving fondaparinux *versus* 13 male and 17 female patients receiving nadroparin calcium ($\chi^2$-test, p=0.743). The mean age was 66.3 and 66.5 years in the fondaparinux group and nadroparin calcium group, respectively (Student's t-test, p=0.749). There was no statistically significant between-group difference in BMI (Student's t-test, p=0.390) and weight (Student's t-test, p=0.270).

The mean duration of surgery was similar in both groups with a mean of 103 minutes in the fondaparinux group and 113.3 minutes in the nadroparin calcium group (Student's t-test, p=0.239). The mean volume of intraoperative bleeding, postoperatively autotransfused blood, late postoperative bleeding and perioperative bleeding, as well as the mean volume of transfused blood are shown in Figure 1.

Blood test results were similar in both groups when comparing red blood cell (RBC) count, hemoglobin and hematocrit level (Table 1). The dynamics of hemoglobin level differed between the groups, with a continuous decrease in the fondaparinux group and an increase in the nadroparin calcium group at 72 h postoperatively. Platelet level was similar in both groups, decreasing during the first 48 h postoperatively, followed by a continuous increase thereafter. No cases of HIT were recorded in the study.

Between-group differences in the AST and ALT levels did not reach statistical significance. Nevertheless, different dynamics was observed, with an increase during the first 48 h postoperatively in the nadroparin

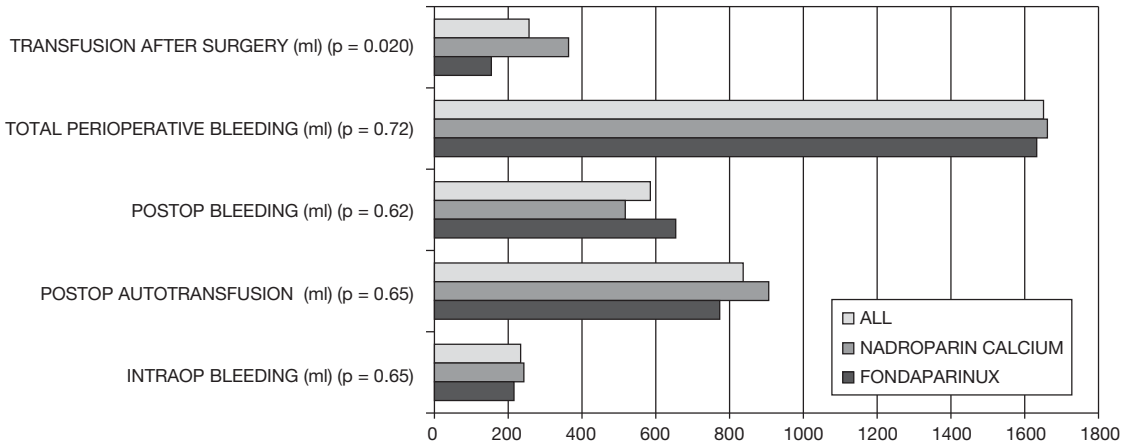


*Fig. 1. Perioperative blood loss: chart showing the mean volume of intraoperative bleeding, postoperative autotransfused blood, postoperative bleeding, total perioperative bleeding and postoperative allotransfusion in each group, and the mean in all patients.*

calcium group, followed by a decrease of AST and ALT levels *versus* continuous decrease in AST and ALT levels in the fondaparinux group throughout the hospital stay. A statistically significant between-group difference was found in the level of urea, which was significantly lower in the nadroparin calcium group on the first and second postoperative day (p=0.028 and p=0.048, respectively), as shown in Table 2. The levels of D-dimers were higher in the nadroparin calcium group at both 24 h and 7 days after the surgery, but it was not statistically significant (Table 3). The clinical signs of the knee and lower leg edema were similar in both groups with no statistically significant differences.

The postoperative course was uneventful in all study patients, with no cases of DVT or PE in the early postoperative period.

## Discussion

Many studies have shown the beneficial effects of fondaparinux in the prevention of thromboembolic diseases in orthopedic surgery[5,9-13]. Our study results were in favor of these data, showing both fondaparinux and nadroparin calcium to be safe and efficient during the first 7 days after TKA.

Nevertheless, caution is advised by the ACCP guidelines in patients weighing less than 45 kg and the elderly when applying fondaparinux because of the increased bleeding risk. Demographic data showed that there were no significant differences among study patients at the beginning of the study; the mean body weight was 85.7 kg, with lowest weight of 65 kg in both groups.

The duration of the surgery was expectedly similar in both groups because of the same type of osteoarthritis (primary), similar age, BMI, and the same orthopedic surgeon performing all the operations with the same endoprosthesis model. The tourniquet was used in the same fashion in all patients, which is one of the main factors influencing the duration of TKA and possible intraoperative and postoperative complications[14].

We used nadroparin calcium in the control group because LMWH is usually the first choice for perioperative thromboprophylaxis in orthopedic surgery. In this way, fondaparinux was compared to the standard of care in our country and region. According to ACCP, the application of LMWH in orthopedic surgery is advised at least 12 h before (preoperative application) or 12 h after the surgery (postoperative application). In our department, we have good experience with preoperative application of LMWH and that was the reason why we decided to use this type of thromboprophylaxis. This could also explain the larger intraoperative bleeding in patients receiving LMWH due to the anticoagulant effect that is present during the operation.

Following the surgery, the blood salvage system collects the blood for the first 6 h after the surgery and then autotransfusion is initiated. Only at that time, when the blood salvage system is disconnected, the first dose of fondaparinux was administered, which could

*Table 1. Complete blood count*

| | Hemoglobin concentration (g/L) | | | Hematocrit level (%) | | | RBC count (x$10^{12}$/mL) | | | Platelet count (x$10^{9}$/L) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p |
| Preop. | 139.9 | 135.45 | 0.261 | 0.41 | 0.41 | 0.567 | 4.56 | 4.62 | 0.7 | 237.25 | 229.55 | 0.637 |
| Op. day | 112.2 | 109.05 | 0.352 | 0.32 | 0.31 | 0.591 | 3.44 | 3.58 | 0.249 | 183.15 | 195.2 | 0.394 |
| 24 h postop. | 107.15 | 104.7 | 0.437 | 0.3 | 0.3 | 0.859 | 3.29 | 3.45 | 0.16 | 170.3 | 182.45 | 0.384 |
| 48 h postop. | 91.45 | 90.6 | 0.816 | 0.28 | 0.26 | 0.192 | 3.02 | 3.01 | 0.915 | 157.65 | 159.2 | 0.904 |
| 72 h postop. | 88.8 | 97 | 0.204 | 0.27 | 0.26 | 0.861 | 2.97 | 3.04 | 0.556 | 187.3 | 170.4 | 0.347 |

Values are expressed as mean except where stated differently; RBC = red blood cell; Preop. = preoperatively; Op. day = day of operation; postop. = postoperatively

*Table 2. Liver and kidney function*

| | Prothrombin time | | | Activated partial thromboplastin time (s) | | | Urea (mmol/L) | | | Creatinine (μmol/L) | | | AST (U/L) | | | ALT (U/L) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p | Fonda-parinux | Nadro-parin calcium | p |
| Preop. | 0.997 | 0.972 | 0.521 | 28.17 | 26.76 | 0.121 | 6.16 | 6.33 | 0.793 | 79.6 | 77.35 | 0.594 | 19.9 | 18.72 | 0.371 | 19.05 | 20.31 | 0.503 |
| 24 h postop. | 0.905 | 0.908 | 0.93 | 27.53 | 28.37 | 0.325 | 5.03 | 4.12 | 0.028 | 84.58 | 86.95 | 0.729 | 18.45 | 25.15 | 0.138 | 15.95 | 23.15 | 0.169 |
| 48 h postop. | 0.826 | 0.888 | 0.204 | 28.37 | 27.84 | 0.534 | 4.69 | 3.7 | 0.048 | 84.4 | 83.2 | 0.826 | 16.45 | 19.8 | 0.057 | 14.2 | 16.15 | 0.41 |
| 72 h postop. | 0.846 | 0.943 | 0.076 | 26.13 | 26.92 | 0.59 | 4.1 | 3.47 | 0.134 | 82.1 | 88.15 | 0.303 | 16.4 | 19.15 | 0.174 | 13.4 | 18.45 | 0.075 |

Values are shown as mean except where stated differently; AST = aspartate aminotransferase; ALT = alanine aminotransferase; Preop. = preoperatively; Op. day = day of operation; postop. = postoperatively

*Table 3. Inflammation markers and D-dimers*

| | Erythrocyte sedimentation rate (mm/h) | | | C-reactive protein concentration (mg/L) | | | D-dimers (ng/L) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Fonda-parinux | Nadroparin calcium | p | Fonda-parinux | Nadroparin calcium | p | Fonda-parinux | Nadroparin calcium | p |
| 24 h postop. | 20 | 26.15 | 0.246 | 60.38 | 52.29 | 0.497 | 9.24 | 13.35 | 0.075 |
| 7 days postop. | 73.85 | 78.15 | 0.666 | 97.91 | 74.93 | 0.238 | 4.1 | 5.62 | 0.013 |

Values are shown as mean except where stated differently; postop. = postoperatively

explain the lower volume of postoperatively autotransfused blood in the fondaparinux group. In addition, in patients on fondaparinux, there is no risk of the possible development of spinal hematoma. We hypothesize that the late postoperative bleeding was greater in this group for the same reason. The statistically significant difference was found only in the volume of allotransfused blood, which was on average greater in the nadroparin calcium group. This could lead to a conclusion that patients on fondaparinux have less need for postoperative allotransfusion due to the less intraoperative and early postoperative bleeding.

A recent study by Hosaka *et al.*[10] confirmed the opinions from previous studies that excessive bleeding can be expected in patients undergoing surgery and receiving fondaparinux[5,12,15-17]. In their study, Hosaka *et al.* assessed the safety of fondaparinux *versus* enoxaparin after TKA in Japanese patients and concluded that thigh swelling and subcutaneous hematomas were greater in the fondaparinux group. They hypothesize that it is due to the same dose (2.5 mg daily) which all patients receive regardless of their body mass and the fact that Japanese patients are smaller than Western populations[10]. In our study, we found no differences in the knee or lower leg swelling between the groups, suggesting that no excessive bleeding was found in the fondaparinux group, which could partly be explained by the fact that most of our patients undergoing TKA were overweight with the mean BMI of 29.4 (range, 21.6-42) kg/m$^2$.

In addition, we recorded the levels of hemoglobin and hematocrit preoperatively and during the first 3 days after the surgery and found no statistically significant difference between the groups, which also confirmed that there was no excessive bleeding in the fondaparinux group. Different dynamics of hemoglobin levels, with an earlier increase in the nadroparin calcium group could be explained again by earlier initiation of thromboprophylaxis in this group. The platelet level decreased in both groups during the first 48 h of the surgery, which could be explained by fluid resuscitation the patients received in the ICU and subsequent hemodilution.

Some anticoagulants have been withdrawn from the market because of their side effects on the liver function[18]. Our results showed an increase in AST and ALT levels immediately after the surgery in the patients receiving nadroparin calcium, while in the patients receiving fondaparinux the levels of AST and ALT decreased throughout their hospital stay. Although it is known that LMWH can lead to an increase of ALT level, it is hypothesized that this increase does not pose a problem for liver function, but is simply a reaction to direct stimulation of hepatocytes, immunoreaction, or a transient increase of LMWH half-life[19]. None of our patients developed any symptoms regarding liver function and no further examination was needed regarding this issue.

The significantly lower levels of urea in the nadroparin calcium group on the first and second postoperative day were noted, although there were no differences between the groups preoperatively. Although low, the values of urea were within the reference values throughout the hospital stay, with the lowest urea value of 3.47 mmol/L, and there were no between-group differences in creatinine levels. We believe that the lower levels of urea may have been caused by iatrogenic hyperhydration during the early postoperative period in the ICU.

Increased levels of D-dimers can be a sign of serious complications such as DVT or PE, but can also be expected to increase after surgery because of the local tissue trauma. Although in other studies blood vessel echo was performed to check for the possible intraluminal signs of thrombosis, the treatment policy of our department is to perform this type of imaging only in symp-

tomatic patients, and none of our patients developed symptoms suggesting development of DVT or PE[5,10].

The main limitation of this study was a relatively small number of patients. However, the study was performed in a single center, by a single surgeon, and only in patients undergoing elective TKA, which limited the number of different factors influencing the results of this study. In addition, power analysis was performed to determine the sample size needed for the study with acceptable power level (80%).

No cases of DVT or PE were recorded in our study, and there was no case of excessive perioperative bleeding or the need for revision of the wound. We therefore believe that both fondaparinux and nadroparin calcium are safe and effective in thromboprophylaxis during the first 7 days after surgery in patients undergoing TKA, with the same influence on clinical parameters in both groups. Additional studies in a greater number of patients should clarify the issue whether there is less need for postoperative transfusion in patients receiving fondaparinux.

## References


1. Arcelus JI, Villar JM, Munoz N. Should we follow the 9th ACCP guidelines for VTE prevention in surgical patients? Thromb Res. 2012;130 Suppl 1:S4-6. doi:10.1016/j.thromres.2012.08.260
2. Prevention and treatment of venous thromboembolism. International Consensus Statement (guidelines according to scientific evidence). Int Angiol. 2006;25:101-61.
3. Mismetti P, Laporte S, Darmon JY, Buchmuller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. Br J Surg. 2001;88:913-30. doi:10.1046/j.0007-1323.2001.01800.x
4. Martel N, Lee J, Wells PS. Risk for heparin-induced thrombocytopenia with unfractionated and low-molecular-weight heparin thromboprophylaxis: a meta-analysis. Blood. 2005;106:2710-5. doi:10.1182/blood-2005-04-1546
5. Bauer KA, Eriksson BI, Lassen MR, Turpie AG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after elective major knee surgery. N Engl J Med. 2001;345:1305-10. doi:10.1056/NEJMoa011099
6. ASA Physical Classification System. American Society of Anesthesiologists. Available from: http://www.asahq.org/clinical/physicalstatus.
7. Hansen E, Belden K, Silibovsky R, Vogt M, Arnold WV, Bicanic G, *et al.* Perioperative antibiotics. J Arthroplasty. 2014;29 Suppl 2:S29-48. doi:10.1016/j.arth.2013.09.030
8. Bicanic G, Crnogaca K, Barbaric K, Delimar D. Cefazolin should be administered maximum 30 min before incision in total knee arthroplasty when tourniquet is used. Med Hypotheses. 2014;82:766-8. doi:10.1016/j.mehy.2014.03.020
9. Eikelboom JW, Quinlan DJ, O'Donnell M. Major bleeding, mortality, and efficacy of fondaparinux in venous thromboembolism prevention trials. Circulation. 2009;120:2006-11. doi:10.1161/CIRCULATIONAHA.109.872630
10. Hosaka K, Saito S, Ishii T, Sumino T, Ryu K, Suzuki G, *et al.* Safety of fondaparinux *versus* enoxaparin after TKA in Japanese patients. Orthopedics. 2013;36:e428-33. PubMed PMID: 23590781. doi:10.3928/01477447-20130327-17
11. Li H, Wang J, Xiao J, Shi Z. Efficacy and safety of fondaparinux *versus* enoxaparin for preventing venous thromboembolism after major orthopedic surgery: a meta-analysis. Nan Fang Yi Ke Da Xue Xue Bao. 2013;33:370-5. (in Chinese)
12. Lassen MR, Bauer KA, Eriksson BI, Turpie AG. Postoperative fondaparinux *versus* preoperative enoxaparin for prevention of venous thromboembolism in elective hip-replacement surgery: a randomised double-blind comparison. Lancet. 2002;359:1715-20. doi:10.1016/S0140-6736(02)08652-X
13. Argun M, Oner M, Saglamoglu M, Karaman I, Guney A, Halici M, *et al.* Fondaparinux *versus* nadroparin for prevention of venous thromboembolism after elective hip and knee arthroplasty. Curr Ther Res Clin Exp. 2013;74:49-53. doi:10.1016/j.curtheres.2013.02.003
14. Yi S TJ, Chen C, Chen H, Huang W. The use of pneumatic tourniquet in total knee arthroplasty: a meta-analysis. Arch Orthop Trauma Surg. 2014;134:1469-76. doi:10.1007/s00402-014-2056-y
15. Turpie AG, Bauer KA, Eriksson BI, Lassen MR. Postoperative fondaparinux *versus* postoperative enoxaparin for prevention of venous thromboembolism after elective hip-replacement surgery: a randomised double-blind trial. Lancet. 2002;359:1721-6. doi:10.1016/S0140-6736(02)08648-8
16. Eriksson BI, Bauer KA, Lassen MR, Turpie AG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. N Engl J Med. 2001;345:1298-304. doi:10.1056/NEJMoa011100
17. Agnelli G, Bergqvist D, Cohen AT, Gallus AS, Gent M. Randomized clinical trial of postoperative fondaparinux *versus* perioperative dalteparin for prevention of venous thromboembolism in high-risk abdominal surgery. Br J Surg. 2005;92:1212-20. doi:10.1002/bjs.5154
18. Agnelli G, Eriksson BI, Cohen AT, Bergqvist D, Dahl OE, Lassen MR, *et al.* Safety assessment of new antithrombotic agents: lessons from the EXTEND study on ximelagatran. Thromb Res. 2009;123:488-97. doi:10.1016/j.thromres.2008.02.017
19. Harrill AH, Roach J, Fier I, Eaddy JS, Kurtz CL, Antoine DJ, *et al.* The effects of heparins on the liver: application of mechanistic serum biomarkers in a randomized study in healthy volunteers. Clin Pharmacol Ther. 2012;92:214-20. doi:10.1038/clpt.2012.40

Sažetak

## UTJECAJ TROMBOPROFILAKSE FONDAPARINUKSOM U USPOREDBI S NADROPARIN KALCIJEM NA KLINIČKE PARAMETRE NAKON UGRADNJE POTPUNE ENDOPROTEZE KOLJENA

*Z. Mihaljević, D. Dimnjaković, B. Tripković, M. Buljan, A. Aljinović, D. Delimar* i *G. Bićanić*

Fondaparinuks se pokazao jednako učinkovitim u ortopedskim operacijama kao i heparin niske molekularne težine, bez slučajeva heparinom izazvane trombocitopenije do danas. Glavni cilj ovoga prospektivnog randomiziranog istraživanja bio je pokazati utječe li tromboprofilaksa fondaparinuksom na bolesnike s primarnom gonartrozom koji su podvrgnuti operacijskom zahvatu ugradnje totalne endoproteze koljena na jednaki način kao i nadroparin tijekom prvih 7 dana nakon operacije. Ukupno 60 bolesnika kod kojih je jednostranu ugradnju totalne endoproteze koljena izveo jedan te isti operater randomizirani su u dvije skupine po 30 bolesnika te je jedna skupina dobivala tromboprofilaksu fondaparinuksom, a druga nadroparinom. Bolesnici su uspoređivani prema trajanju operacije, perioperacijskom gubitku krvi, laboratorijskim nalazima te kliničkoj evaluaciji edema tijekom ranog poslijeoperacijskog razdoblja. Nisu nađene razlike u trajanju operacijskog zahvata, perioperacijskom gubitku krvi niti prema većini laboratorijskih nalaza. Razina ureje je bila značajno niža u skupini s nadroparinom tijekom prva dva poslijeoperacijska dana. Nije zabilježen niti jedan slučaj heparinom izazvane trombocitopenije, duboke venske tromboze ili plućne embolije tijekom ovog istraživanja. Naši rezultati pokazali su da fondaparinuks i nadroparin na isti način utječu na kliničke parametre tijekom prvih 7 poslijeoperacijskih dana od ugradnje totalne endoproteze koljena.

Ključne riječi: *Artroplastka koljena; Antikoagulansi; Fondaparinuks; Nadroparin; Krvarenje*