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Original Contributions

ORAL THROMBOPROPHYLAXIS IN PELVIC TRAUMA: A STANDARDIZED PROTOCOL

Daniel Godoy Monzon, MD,* Kenneth V. Iserson, MD, MBA,† Alberto Cid, MD,‡ and Jorge A. Vazquez, MD*

*Hospital Italiano de San Justo, "Centro Agustin Rocca" (HICAR), San Justo, Provincia de Buenos Aires, Argentina, †Arizona Bioethics Program, University of Arizona, Tucson, Arizona, and ‡Salud Ocupacional Integral (SOI) and Centro Medico Fitz Roy, Ciudad de Buenos Aires, Argentina

Corresponding Address: Kenneth V. Iserson, MD, MBA, Arizona Bioethics Program, University of Arizona, 4930 N. Calle Faja, Tucson, AZ 85718

☐ **Abstract—Background: Thromboprophylaxis for deep vein thrombosis (DVT) after lower-extremity trauma could include rivaroxaban, an oral medication that does not need laboratory monitoring. Objective: To assess rivaroxaban's efficacy in preventing DVTs after pelvic trauma compared to its historical incidence. Materials and Methods: All patients admitted with pelvic fractures in a 12-month period followed a standardized thromboprophylaxis protocol: 1) rivaroxaban 10 mg/day within 24 h of injury or upon hemodynamic stability; 2) pre-operative, post-operative, and 30-day extremity ultrasound; 3) ventilation-perfusion scintigraphy for clinical signs of pulmonary embolus; and 4) a 45-, 90-, and 120-day re-evaluation. Rivaroxaban administration ceased the day of surgery and restarted 12 h post-operatively or upon hemodynamic stability, continuing for 30 days. Excluded patients had severe neurological or hepatosplenic injuries, heparin hypersensitivity, or hemodynamic instability. Results: Of 113 patients assessed, 84 patients (66 males), average age 46.6 years (range 19–69 years), were included. They had isolated pelvic trauma (n = 37), associated lower limb injuries (n = 47), average Injury Severity Score 21.4 (range 16–50), and average Glasgow Coma Scale score 13.6 (range 9–15). Patients receiving thromboprophylaxis soon after their fracture (n = 64) had a lower incidence of DVT than those receiving delayed thromboprophylaxis (n = 20) ($p = 0.02$). One patient (1.2%) died from a pulmonary embolus; 13 had asymptomatic below-the-knee DVTs. Rivaroxaban did not increase intra- or post-operative bleeding in surgical wounds. Conclusions: DVT incidence after pelvic fractures is reduced by administering antithrombotics within 24 h of injury or, if the patient is hemodynamically unstable, 24 h after stabilization. Rivaroxaban is a safe and effective method of providing this thromboprophylaxis.**

☐ **Keywords—rivaroxaban; deep vein thrombosis; thromboprophylaxis; pelvic trauma; lower-extremity trauma**

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INTRODUCTION

The incidence of deep vein thrombosis (DVT) after pelvic trauma varies between 35% and 61% (1,2). Patients with pelvic trauma are at high risk of thromboembolic complications. Though effective methods of prophylaxis have yet to be accepted and adopted widely.

A variety of thromboprophylactic regimes have been recommended in trauma patients (1,3–5). Low-dose or intermittent pneumatic compression devices alone are not always effective in preventing DVT (6–8). Although low-molecular-weight heparin agents have been shown to reduce the rate of DVT in patients with injury to the pelvis or lower limbs, they require parenteral administration (1,3,9,10).

A new oral thromboprophylactic medication, rivaroxaban (Xarelto®, Bayer AG, Manheim, Germany), was recently approved in Argentina for use in patients with

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lower limb fractures. In September 2008, both Health Canada and the European Commission approved rivaroxaban for the prevention of DVT in patients who have undergone elective total hip or knee replacement. The U.S. Food and Drug Administration's Cardiovascular and Renal Drugs Advisory Committee has voted to recommend approval (11).

Rivaroxaban is an oral, direct Factor Xa inhibitor with high oral bioavailability, a rapid onset of action, and predictable pharmacokinetics (half-life of 5–9 h) (12,13). It is excreted rapidly, mostly through the kidney (66%; 36% of the dose excreted unchanged), but also via the biliary/fecal route (13). Single doses of rivaroxaban have pharmacodynamic effects that persist for 24 h and significantly inhibit peak and total amounts of thrombin generated for 24 h after administration (12,14). It has been shown to be as safe and effective in preventing DVTs as enoxaparin when administered after orthopedic surgery, and has been successfully used in a once-a-day dosage after total hip and knee replacement surgery (15,16).

This led to the following study to assess rivaroxaban's efficacy in preventing DVTs after major lower-extremity trauma. The study's aim was to determine the use of thromboprophylactic therapy with this protocol, patient compliance and complications, and the incidence of DVT and pulmonary embolus (PE) in the treated patients.

MATERIAL AND METHODS

Between June 2009 and June 2010, all patients admitted to our trauma center with pelvic or acetabular fractures received a standardized protocol for DVT prophylaxis. Informed consent for inclusion in the study was obtained from patients or their surrogate decision-makers. The Institutional Review Board approved this study.

Enrolled patients were evaluated with laboratory tests (complete blood count, hematocrit, electrolytes, liver and kidney function, coagulation). Vital signs (heart rate, respiratory rate, and mean arterial pressure), the Injury Severity Score (ISS), and Glasgow Coma Scale score (GCS) were recorded. Patients excluded from this study included those with the presence of a severe neurological injury (GCS $\leq$ 8), spinal cord injury, identifiable hepatic or splenic injuries, a known hypersensitivity to heparin, and hemodynamic instability secondary to continued bleeding.

Each study patient had an ultrasound evaluation for DVT of all lower-extremity veins from the groin to the foot at the time of admission, within 48 h after surgery, and 30 days post-surgery. The same imaging team for all patients identified the location and size of any thrombi. All patients with pelvic trauma were treated with a standardized protocol for thromboprophylaxis consisting of: 1) the administration of rivaroxaban (Xarelto, Bayer), 10 mg, orally once a day within 24 h of injury or upon the establishment of hemodynamic stability; 2) preoperative, post-operative, and 30-day investigation for DVT using duplex ultrasound; 3) a ventilation-perfusion scintigraphy (V/Q lung scan) if the patient showed clinical signs of PE; and 4) a clinical evaluation at 45, 90, and 120 days.

All patients received treatment with rivaroxaban, with the last dose being given the day before surgery and restarted within 12 h after surgery or when hemodynamic stability was achieved post-operatively. Rivaroxaban prophylaxis was continued for 30 days post-operatively. After surgery, patients were mobilized within 48 h, depending on the complexity of their associated injuries. They generally walked short distances with partial weight-bearing. At the conclusion of the study, all patients were asked about their compliance with the medication and any post-hospitalization complications.

RESULTS

Of 113 patients initially assessed, 29 were excluded (Table 1); 84 patients (66 males [78.6%] and 18 females [21.4%]), average age 46.6 years (range 19–69 years) were included in the study group. Of these, 37 presented with isolated pelvic trauma, whereas 47 had associated injuries of their lower limbs (60%). The types of pelvic and acetabular fractures are shown in Table 2 (17,18). All subjects' average ISS was 21.4 (range 16–50 points) and they had an average GCS of 13.6 (range 9–15 points). The 65 patients that initially presented to our hospital had an average wait of 4.8 days until they had acetabular or lower-extremity surgery. The other 19 patients were transferred to us from other hospitals. They waited an average of 9.4 days after their injury for surgery due to delayed transfers (Mann-Whitney U test, $p < 0.001$). A delay of < 5 days post-injury is standard practice in Argentina.

Of the 65 patients accepted directly into our institution, 57 (87.7%) started prophylaxis within 24 h; it was

Table 1. Patients Excluded from the Study

Reason for Exclusion	Number of Patients
Referred to another hospital (due to patient/family request or medical insurance requirements)	8
Died on admission (due to multiple non-orthopedic injuries)	5
Had proximal DVT on admission (2 had history of femoral intravenous catheter; thrombosis resolved after its withdrawal)	7
GCS < 8	9
Total excluded	24

DVT = deep vein thrombosis; GCS = Glasgow Coma Scale score.