Medical Research Journal

METHODS OF PREVENTION OF VENOUS THROMBOEMBOLIC COMPLICATIONS AFTER HIP JOINT ARTHROPLASTY

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Abstract: The prevention of venous thromboembolic complications (VTE) after orthopedic surgery remains a key component of postoperative management. The choice of pharmacological agent should be based on patient characteristics, adherence potential, ease of administration, and economic factors. Low-molecular-weight heparins (LMWH) and unfractionated heparin (UFH) remain the standard agents for pre- and early postoperative prophylaxis. However, the introduction of new oral anticoagulants (NOACs) — such as dabigatran etexilate, rivaroxaban, and apixaban — has provided effective and convenient alternatives that do not require routine laboratory monitoring. The minimum duration of pharmacological prophylaxis after total hip replacement is 10–14 days, while extended therapy for 35 days or longer significantly reduces the risk of late-onset deep vein thrombosis and pulmonary embolism. An individualized, prolonged, and well-monitored approach to VTE prevention improves outcomes and ensures long-term patient safety.

Keywords: venous thromboembolism, deep vein thrombosis, anticoagulant prophylaxis, low-molecular-weight heparin, direct oral anticoagulants, rivaroxaban, dabigatran, apixaban, duration of therapy, orthopedic surgery.

МЕТОДЫ ПРОФИЛАКТИКИ ВЕНОЗНЫХ ТРОМБОЭМБОЛИЧЕСКИХ ОСЛОЖНЕНИЙ ПОСЛЕ ЭНДОПРОТЕЗИРОВАНИЯ ТАЗОБЕДРЕННОГО СУСТАВА

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Аннотация: Профилактика венозных тромбоэмболических осложнений (ВТЭО) после ортопедических операций является важнейшим элементом послеоперационного ведения пациентов. При выборе лекарственного средства необходимо учитывать индивидуальные особенности больного, приверженность лечению, удобство введения и экономические факторы. Стандартом остаются низкомолекулярные гепарины (НМГ) и нефракционированный гепарин (НФГ), применяемые в пред- и раннем послеоперационном периоде. Внедрение новых пероральных антикоагулянтов (дабигатрана этексилат, ривароксабан, апиксабан) открыло возможности для эффективной и безопасной профилактики без необходимости лабораторного контроля. Минимальная продолжительность профилактики составляет 10–14 дней, а оптимальная — до 35 дней и более. Продолжительный курс достоверно снижает риск позднего тромбоза глубоких вен и тромбоэмболии легочной артерии. Индивидуализированный подход к выбору препарата и длительности терапии обеспечивает высокую эффективность и безопасность лечения.

Ключевые слова: венозные тромбоэмболические осложнения, тромбоз глубоких вен, антикоагулянтная профилактика, низкомолекулярные гепарины, прямые пероральные антикоагулянты, ривароксабан, дабигатран, апиксабан, длительность терапии, ортопедическая хирургия.

CHANOQ-SON BO‘G‘IMI ENDOPROTEZIDAN KEYIN VENOZ TROMBOEMBOLIK ASORATLARNING OLDINI OLISH USULLARI

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Annotatsiya:
Ortopedik jarrohlikdan keyingi venoz tromboembolik asoratlarning (VTE) oldini olish bemorlarni operatsiyadan keyingi boshqarishning muhim bosqichidir. Antikoagulyant tanlashda bemorning individual xususiyatlari, davoga rioya qilish darajasi, dori qo‘llash qulayligi va iqtisodiy omillar hisobga olinadi. Past molekulyar og‘irlikdagi geparinlar (NMH) va nofraksion geparin (NFG) hali ham standart vositalar bo‘lib qolmoqda. So‘nggi yillarda yangi og‘iz orqali qabul qilinadigan antikoagulyantlar — dabigatran eteksilat, rivaroksaban va apiksaban — samarali va xavfsiz profilaktika imkonini bermoqda. Profilaktika minimal muddati 10–14 kunni, tavsiya etilgan muddati esa 35 kun va undan ko‘proqni tashkil etadi. Davomli profilaktika chuqur venalar trombozi va o‘pka emboliyasining kechki rivojlanish xavfini kamaytiradi. Dori vositasini tanlash va profilaktika davomiyligini individual tarzda belgilash yuqori samaradorlik va xavfsizlikni ta’minlaydi.
Kalit so‘zlar: venoz tromboembolik asoratlar, chuqur vena trombozi, antikoagulyant profilaktika, past molekulyar og‘irlikdagi geparin, to‘g‘ridan-to‘g‘ri og‘iz antikoagulyantlari, rivaroksaban, dabigatran, apiksaban, davolash davomiyligi, ortopedik jarrohlik.

Introduction. Methods of prevention are generally divided into **mechanical** and **pharmacological** approaches. Mechanical methods include **elastic compression (EC)** of the lower extremities, **sequential intermittent pneumatic compression (SIPC)**, **electroneuromyostimulation**, **restoration of circulating blood volume**, and **therapeutic physical exercise**. Pharmacological methods, on the other hand, involve the use of drugs that affect various components of the **coagulation cascade**, such as **anticoagulants** and **antiplatelet agents**.
Use of Elastic Compression of the Lower Extremities. There are conflicting opinions regarding the effectiveness of elastic compression. Researchers from a **British Vascular Center**, after conducting studies among different groups of hospitalized patients, concluded that **elastic compression (EC)** is an effective method for reducing the risk of **deep vein thrombosis (DVT)** [1]. However, a **systematic review of randomized clinical trials published in 2012** did not find a significant difference in DVT incidence between patients using **calf-level** compression and those using **thigh-level** compression [2].
A **meta-analysis** was conducted based on studies indexed in **Medline, Embase, and the Cochrane Library**. The studies included groups of **orthopedic patients** who received pharmacological prophylaxis—such as **low molecular weight heparin (LMWH)**, **unfractionated heparin (UFH)**, **rivaroxaban**, and **dabigatran**—in accordance with the **NICE 2010 guidelines**, with or without additional elastic compression. The authors concluded that in orthopedic patients, **elastic compression used in combination with modern anticoagulant prophylaxis does not significantly reduce the risk of venous thromboembolic events (VTE)** [3]. Elastic compression of the lower limbs is effective primarily during the **acute phase of DVT** (within the first week), but it does not contribute to thrombus resolution, improvement of **valvular competence**, or prevention of **post-thrombotic syndrome** one year after the event [4].

Sequential Intermittent Pneumatic Compression

In 1989, **H. C. K. Wuh** published a study in which **intraoperative ultrasound examinations** demonstrated that blood flow in the **common femoral vein** decreases or even ceases entirely when the hip is rotated internally or externally beyond **45 degrees** [5]. When **sequential intermittent pneumatic compression (SIPC)** was applied during surgery, blood flow was preserved in **four out of five** patients examined. In 1982, **J. T. Hartman** reported a **significant reduction in the incidence of deep vein thrombosis (DVT)** after surgery when SIPC was used, from **19% down to 2%** [6]. According to **J. Urbankova et al. [7]**, the use of SIPC in various postoperative patient groups reduced the frequency of DVT by **60%** compared with patients who did not receive prophylaxis. However, in cases of **moderate or high risk** of venous thromboembolic events (VTE), using SIPC **alone** is considered **insufficient** as a preventive measure. **T. Schwarz et al.** conducted a study involving two groups of patients with **distal DVT**.

- The **first group** received **therapeutic doses of low molecular weight heparin (LMWH)** for 10 days combined with SIPC.
- The **second group** received **SIPC only**.

Progression of thrombosis occurred in **1 out of 52 patients** in the first group and in **13 out of 32 patients** in the second group. These results underscore the importance of maintaining **anticoagulant therapy** in patients with distal lower limb DVT [8]. Researchers from **Japan** concluded that in their population, the use of **SIPC after total hip replacement** is both **safe and effective** for thrombosis prevention, even **without anticoagulant therapy** [9]. According to **D. A. Forsh et al. [10]**, the total incidence of DVT with pharmacological and mechanical prophylaxis was **similar**, but the **distribution differed**: when SIPC was used, the proportion of **proximal (more dangerous)** thromboses increased compared with **distal (less severe)** ones. Specifically, **warfarin** use resulted in **15 DVT cases** (5 proximal), while SIPC use resulted in **16 cases**, **14 of which were proximal**. These findings indicate that **anticoagulant therapy remains essential**, even when mechanical methods such as SIPC are applied.

Pharmacological Prevention of Venous Thromboembolic Complications Unfractionated Heparin (UFH). One of the most widely used anticoagulants in traumatology is **unfractionated heparin (UFH)**, discovered in 1916. UFH exerts its effect by binding to **antithrombin (AT) III** [19]. The interaction between UFH and AT III alters the structure of the latter, converting it into a rapid inhibitor of several coagulation cascade factors. Due to its **short half-life**, UFH must be administered **subcutaneously several times per day**. The most common prophylactic regimen is **5,000 IU three times daily**. However, UFH use may be accompanied by complications such as **heparin-induced thrombocytopenia (HIT)**, **cutaneous reactions**, and, in rare cases, **osteoporosis** or **hypersensitivity reactions**. **Low-Molecular-Weight Heparins (LMWHs).** By the end of the 20th century, **low-molecular-weight heparins (LMWHs)**—such as **enoxaparin sodium**, **dalteparin sodium**, and **nadroparin calcium**—had largely replaced UFH in clinical practice [20]. These drugs have a **longer half-life**, allowing for **once-daily administration**. In a comparative study by **L. J. McGarry et al.**, the incidence of **pulmonary embolism (PE)** was **reduced by 74%** in the LMWH group compared to UFH, with **no significant difference** in adverse effects, hospital mortality, or overall treatment costs [11].

LMWHs may **accumulate in patients with renal insufficiency**, increasing the risk of bleeding. Therefore, for patients with a **creatinine clearance below 30 mL/min**, **dose reduction** rather than standard dosing is recommended. It should also be noted that the **baseline antithrombin III level** is reduced in approximately **40% of patients with lower limb DVT** [12]. In such cases, **heparin-based prophylaxis may be ineffective**, and **alternative anticoagulants** should be considered.

Vitamin K Antagonists (Warfarin). Warfarin **reduces plasma concentrations of** vitamin K-dependent coagulation factors (II, VII, IX, and X) **by inhibiting their synthesis in the liver [13]. The** onset of action **occurs within** 36–72 hours**, with full anticoagulant effect developing after** 5–7 days **of therapy. When used as prophylaxis after** total hip replacement surgery (THR)**, warfarin decreased the** overall incidence of DVT by 60% **and** proximal DVT by 70% **[14].**

However, the main difficulty with warfarin therapy lies in the need for individualized dosing **and the risk of** cumulative effects **over several days. Numerous** foods **and** medications **can influence warfarin efficacy, necessitating frequent** blood monitoring **to maintain the** international normalized ratio (INR) **within the** therapeutic range of 2–3**, reflecting the desired level of anticoagulation.**

Fondaparinux. Fondaparinux **is an** indirect factor Xa inhibitor **administered subcutaneously, with** 100% bioavailability **and a** half-life of approximately 17 hours**. Its use has been shown to reduce the** relative risk of venous thromboembolic events (VTE) **by** more than 50% **compared to enoxaparin [24].** Although **major bleeding** occurred more frequently with fondaparinux, there were **no statistically significant differences** between groups regarding **clinically significant bleeding**, **fatal outcomes**, or the need for **reoperation** [15].

Because **UFH**, **LMWH**, and **fondaparinux** are available **only as injectable formulations**, their use in **outpatient settings** can be challenging and less convenient for long-term prophylaxis.

New Oral Anticoagulants. At the beginning of the 21st century, **new oral anticoagulants (NOACs)** were introduced into clinical practice as alternatives to traditional heparins and vitamin K antagonists. These agents, which include **dabigatran etexilate**, **rivaroxaban**, and **apixaban**, offer predictable pharmacokinetics, fewer food and drug interactions, and no need for routine coagulation monitoring, making them especially convenient for postoperative prophylaxis following orthopedic surgery.

Dabigatran Etexilate. Dabigatran is a **direct thrombin inhibitor** [16]. It is administered **1–4 hours after completion of total hip replacement surgery (THR)** at **half the daily dose**. From the **second postoperative day**, patients take **two capsules (220 mg total)** once daily. The course continues for **28–35 days**. **Two dosage strengths are available:** 75 mg **and** 110 mg per capsule**. A** reduced daily dose of 150 mg (two 75 mg capsules) **is recommended for** elderly patients (over 75 years old) **and those with** moderate renal impairment (creatinine clearance 30–50 mL/min)**. Food intake does not affect the drug's absorption or efficacy. Dabigatran can also be used in the** treatment of deep vein thrombosis (DVT)**. In cases of** bleeding**, adequate** diuresis **should be maintained; if necessary,** fresh frozen plasma transfusion **and** surgical hemostasis **are performed as indicated.**

Rivaroxaban. Rivaroxaban is a **direct inhibitor of factor Xa** in the coagulation cascade. Its **superior efficacy** in DVT prevention compared to **enoxaparin** has been well established. The drug is administered **6–10 hours after surgery**, at a dose of **10 mg once daily**, independent of meals. The treatment course lasts **35 days**, and **dose adjustment is not required**. **There are limited data regarding its use in** severe renal impairment**. Rivaroxaban is also approved for the** treatment of DVT**. According to a study published in the** New England Journal of Medicine (December 2010)**, rivaroxaban demonstrated** similar efficacy to enoxaparin and warfarin **in DVT treatment,** without an increased risk of bleeding **[17].**

Apixaban. Apixaban, another **oral factor Xa inhibitor**, has shown **comparable efficacy to enoxaparin** for DVT prevention after elective total hip replacement, **without an elevated risk of bleeding** [18]. **No studies have yet evaluated its use in** emergency orthopedic procedures **or in patients with** severe hepatic impairment**. The recommended dose is** 2.5 mg twice daily**, with the** first dose taken 12–24 hours postoperatively**. Apixaban is currently** not approved for the treatment of DVT**, only for** prophylactic use **following major orthopedic surgery.**

Aspirin**, in** low doses (50–100 mg daily)**, functions as a** platelet aggregation inhibitor**. A large European study on** pulmonary embolism (PE) prevention **included** 13,356 patients with knee arthroplasty **and** 4,088 patients with total hip replacement**. Approximately** 40% **of the participants received** UFH or LMWH **in addition to aspirin. In the hip replacement group, the** incidence of DVT decreased by 25%**, but** no significant reduction in PE frequency **was observed** [19]. **Thus, the study did** not demonstrate clear advantages **of using aspirin as a** primary method of VTE prophylaxis **in patients undergoing hip joint replacement.**

Selection of Antithrombotic Agents and Duration of Venous Thromboembolism (VTE) Prophylaxis. When selecting a specific drug for pharmacological prevention of venous thromboembolic complications, several factors must be considered: patient preferences, treatment

adherence, ease of administration, and local economic conditions, including the availability and cost of pharmacological agents within particular healthcare institutions.

For patients undergoing major orthopedic surgery such as total hip replacement (THR), prophylaxis of deep vein thrombosis (DVT) should begin upon hospital admission and continue through the preoperative period using low-molecular-weight heparins (LMWH) or unfractionated heparin (UFH) [20, 21]. These agents remain the standard of care for hospitalized patients, especially during the immobilization phase before surgery. In recent years, the introduction of **new oral anticoagulants (NOACs)** — such as **dabigatran etexilate**, **rivaroxaban**, and **apixaban** — has significantly expanded the options for safe and effective prophylaxis. These drugs do **not require routine laboratory monitoring**, have **predictable pharmacokinetics**, and demonstrate **comparable efficacy and safety** to LMWHs. All NOACs are initiated **after surgery**, with the possibility of switching to **therapeutic doses** if DVT develops during follow-up. The **minimum duration** of pharmacological prophylaxis after **total hip replacement** is **10–14 days**, while the **recommended duration** is **up to 35 days or longer**. Clinical evidence suggests that after discontinuation of **short-term prophylaxis**, new cases of **lower limb DVT** may still occur. Consequently, **extended-duration prophylaxis** provides a **more pronounced and sustained reduction in VTE risk** compared to short-term regimens. Long-term prophylaxis is particularly justified in patients with additional risk factors — such as advanced age, obesity, previous VTE episodes, malignancy, or prolonged immobility — as these populations demonstrate a higher likelihood of thromboembolic recurrence after early cessation of anticoagulant therapy.

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