



Recent Updates of the Diagnosis and Prevention of Venous Thromboembolism in Patients with a Hip Fracture

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Venous thromboembolism (VTE) is a potentially fatal complication that is relatively common after hip surgery. Since patients with a hip fracture have a higher risk of preoperative VTE due to an inability to ambulate after injury and aggravation of underlying age-related conditions, it may be difficult to effectively prevent VTE using only conventional approaches. Very few studies have been published reporting on the prevalence and prevention of VTE in patients with a hip fracture compared to those with hip arthroplasty. For this reason, we aimed to share recent updates on the diagnosis and prevention of VTE in patients with a hip fracture. Preoperative screening tests to diagnose VTE need to be performed more actively following hip fracture and indirect multidetector computed tomography venography is considered the most effective test for this purpose. As the risk of VTE appears to increase with time following a hip fracture, preventive measures should be taken as soon as possible in patients with a hip fracture. A wide variety of mechanical and pharmacological options are available for prophylaxis. When considering patient compliance and preventive impact, intermittent pneumatic compression devices and foot pumps are recommended as mechanical modalities. Of the available preventive medications for patients with a hip fracture, low molecular weight heparin seems to be the most appropriate option because of its short half-life and fast onset of action. Surgery should be performed as soon as possible in patients with hip fractures, and we recommend mechanical and pharmacological methods as active interventions immediately after injury to prevent VTE.

Key Words: Hip fractures, Venous thromboembolism, Diagnosis, Prevention

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INTRODUCTION

Hip fractures are the most common type of fracture in an aging population. Older adults, in particular, have higher morbidity and mortality rates following a hip fracture because of prolonged periods confined to a bed, postoperative aggravation of underlying conditions and others^{1,2}. Venous thromboembolism (VTE) is the second most common complication following hip fracture surgery³; pulmonary embolism (PE) is the fourth common cause of death in these patients⁴. Without thromboprophylaxis following a hip fracture, the incidences of VTE, proximal thromboembolism, and fatal PE range between 42-50%, 20-27%, and 0.6-7.5%, respectively⁵⁻⁸. In comparison, VTE occurs at a rate of 20-30% after hip arthroplasty^{9,10}. The risk of VTE in patients with a hip fracture has been recognized for many years, and prevention of VTE has been emphasized by American College of Chest Physicians (ACCP)¹¹, National Institute for Health and Clinical Excellence (NICE)¹², Scottish Intercollegiate Guidelines Network (SIGN)¹³, Korean Hip Society¹⁴ and many other associations. A recent study has reported a relatively high prevalence of preoperative VTE in patients for whom surgery was delayed for more than 24 hours after hip fracture⁸. Since patients with a hip fracture have a higher risk of preoperative VTE because of their inability to ambulate after injury and aggravation of age-related underlying conditions, it may be difficult to prevent VTE effectively using only conventional approaches. Also, only a few studies are available in the literature reporting on the prevalence and prevention of VTE in patients with a hip fracture compared to those with hip arthroplasty. Therefore, we aimed to share recent updates on the diagnosis and prevention of VTE in patients with a hip fracture.

PREVALENCE AND RISK FACTORS

Studies report varying incidences of VTE following hip fractures and its prevalence after surgery ranges up to 80%¹⁵. To date, most studies have focused on postoperative VTE in patients with a hip fracture; few studies have explored the preoperative prevalence of VTE after hip fracture¹⁶⁻¹⁹. The results of previous studies suggest that patients with a hip fracture have a considerably high prevalence of VTE preoperatively, ranging from 9% to 12.7%¹⁶⁻¹⁹. Older patients are more likely to experience fractures of the hip than in other parts of the body and they often have other concomitant conditions (e.g., venous

thrombosis or other internal diseases). The high likelihood of a patient with a hip fracture experiencing VTE is related to the extended bed rest before surgery¹⁸. Furthermore, a delay in surgery following a hip fracture, which may occur for various reasons, contributes significantly to the increased prevalence of preoperative VTE¹⁵⁻¹⁹. A delay more than 48 hours in surgical intervention after hip fracture has been shown to increase the prevalence of preoperative VTE to as high as 54% to 62%^{18,20}. A recent study using indirect multidetector computed tomography (MDCT) venography has shown that, in patients who experienced a greater than 24-hour delay to surgery following an injury, the prevalence of preoperative VTE was 11.1%, despite mechanical and pharmacological prophylaxis⁸. Other factors known to increase the risk of preoperative VTE are female gender, subtrochanteric femur fractures, lung diseases and past history of VTE.

DIAGNOSIS

Patients with VTE may experience leg swelling, pain, erythema and local heating, dyspnea and other symptoms, but differential diagnosis of VTE can be difficult due to: i) an overlap in symptoms associated with a hip fracture (e.g., swelling and severe pain) or ii) no presenting symptoms. Moreover, in addition to postoperative VTE, VTE may occur preoperatively in association with hip fracture or may exist as an underlying disease before injury. Since following a hip fracture VTE may progress to proximal complications such as intra- or postoperative fatal PE, more active screening than in ordinary surgical patients is warranted. VTE is currently diagnosed via blood test, Doppler ultrasound and CT scan, and can also be diagnosed using contrast venography.

One representative blood test is the D-dimer in which a negative result means the absence of deep vein thrombosis (DVT). The D-dimer test may be used to help rule out the possibility of DVT, however, results should be interpreted carefully because a positive result may be observed in cases of liver disease, inflammation, malignant tumor, pregnancy, trauma, and even after recent surgery. Since older patients with a hip fracture may show elevated levels of D-dimer due to their underlying diseases and trauma regardless of VTE, there are limitations to singular use of the D-dimer test for confirming the presence of DVT.

Imaging tests for VTE include, but are not limited to, ultrasonography, contrast venography, and CT venography. Ultrasonography is the first-line imaging test and preferred

diagnostic approach for diagnosing DVT particularly in the proximal portion of leg veins (Fig. 1)^{14,21,22}. Ultrasonography is non-invasive, can be performed immediately and easily used as a component of follow-up exams. However, according to a recent meta-analysis, ultrasonography showed a sensitivity of 94.2% and a specificity of 93.8% in femoral vein and popliteal vein DVT, whereas it revealed a relatively low sensitivity at 67.0% in below knee DVT in the distal veins²². Moreover, ultrasonography may be affected by the skill

level of the operator. Additionally, ultrasonography requires position changes during the examination and is can be difficult to be perform to patients with a hip fracture who may experience pain if required to change positions. Furthermore, additional tests should be conducted for the diagnosis of PE. Venography using contrast medium is recognized as a relatively accurate diagnostic test of DVT (Fig. 2). However, this method is not the preferred first-line imaging test for VTE because it is invasive, causes

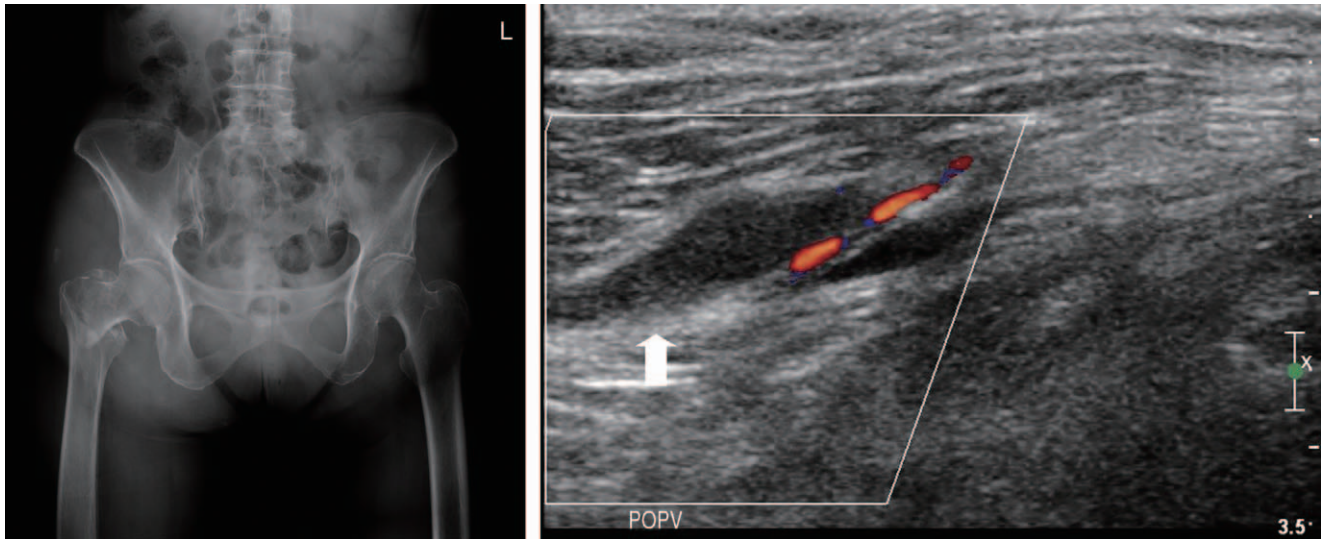


Fig. 1. The ultrasonography showed deep vein thrombosis at a popliteal vein [arrow] in a patient with intertrochanteric femoral fracture.

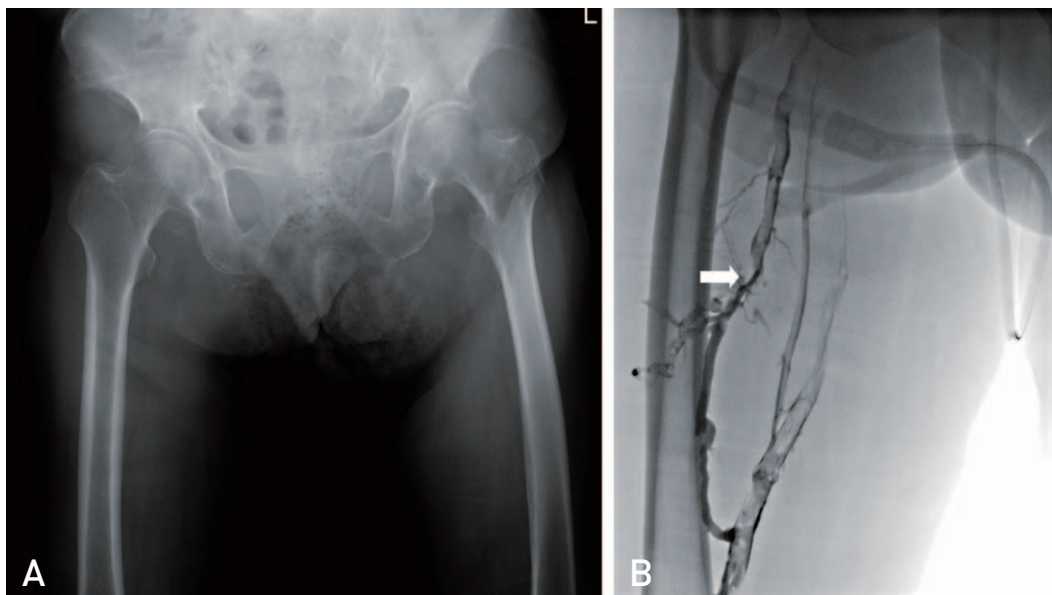


Fig. 2. (A) This plain radiograph showed an intertrochanteric femoral fracture in a 77-year-old women. (B) The venography was performed due to suspicion of deep vein thrombosis. The narrowing of deep femoral vein was observed because of deep vein thrombosis (arrow).

patient discomfort, restricted to patients with renal insufficiency and contrast hypersensitivity, and challenging to use when diagnosing PE^{23,24}). CT venography has emerged as an alternative method of ultrasonography because it ensures short examination time and has high sensitivity and specificity at 100% and 96.6%, respectively^{25,26}). In recent years, high-resolution indirect MDCT venography has enabled more accurate and prompt diagnosis of VTE, and has been acknowledged as a useful technique for evaluating VTE in hip fracture patients^{8,26-28}). Indirect MDCT venography can detect both DVT and PE with relatively easy screening process and no change in patients' positioning by obtaining combined images of lower-extremity venography and pulmonary angiography^{8,26-29}) (Fig. 3). Briefly, indirect MDCT venography is a combined imaging study examining the subdiaphragmatic deep-vein system at the time of CT pulmonary angiography. CT pulmonary angiography is obtained in the craniocaudal direction, ranging from the apex to the adrenal gland, during a single inspiratory breath-hold. Indirect CT venography is performed from the kidneys to the feet to detect DVT after a thoracic scan. However, there are concerns about equipment cost, additional radiation during the exam and adverse effects of contrast media. On a study on radiation dose, the mean radiation dose for indirect MDCT venography was 5.2 ± 0.5 mSv, indicating a lower amount of radiation compared to that of CT of the chest and abdomen or CT venography²⁹). This method appears to be a relatively safe test taking into consideration that most hip fracture patients are older adults with more limited concerns about the effect of additional radiation on the reproductive system³⁰). Nevertheless, precautions are warranted when performing indirect MDCT venography in patients predicted to have side effects induced by contrast

media. Since indirect MDCT venography should be used selectively due to contraindications, careful attention is needed in patients with elevated serum creatinine levels (serum creatinine >1.5 mg/dL), those with renal disease or hyperthyroidism and pregnant women³¹⁻³³).

In summary, a relatively high prevalence preoperative VTE has been observed in patients with a hip fracture. Even though VTE may occur after a fracture, it may also exist as an asymptomatic underlying condition. This form of VTE may progress to fatal complications such as intra- or postoperative fatal PE. Considering hip fracture-induced bed rest and age-related risk factors, more active screening tests are needed to diagnose preoperative VTE after hip fracture; indirect MDCT venography seems to be the most effective imaging option.

PREVENTION

1. Start Time and Duration of Prevention

Early surgery is considered a key factor for reducing morbidity and mortality in patients with a hip fracture^{13,34-37}). Most treatment guidelines suggest medical assessment of patients and immediate surgical intervention, and recommend early surgical treatment within the first 48 hours of admission^{12,34,38}). Nevertheless, delayed surgery is often unavoidable during the preoperative evaluation by internal medicine physicians or during transfer to a tertiary hospital after a hip fracture. Most previous studies have focused on the prevention of postoperative VTE, but the risk of VTE appears to increase immediately after injury before undergoing surgery in patients with a hip fracture^{2,39-41}). It has to be taken into account that VTE may exist not only after hip fracture, but also as an underlying disease prior

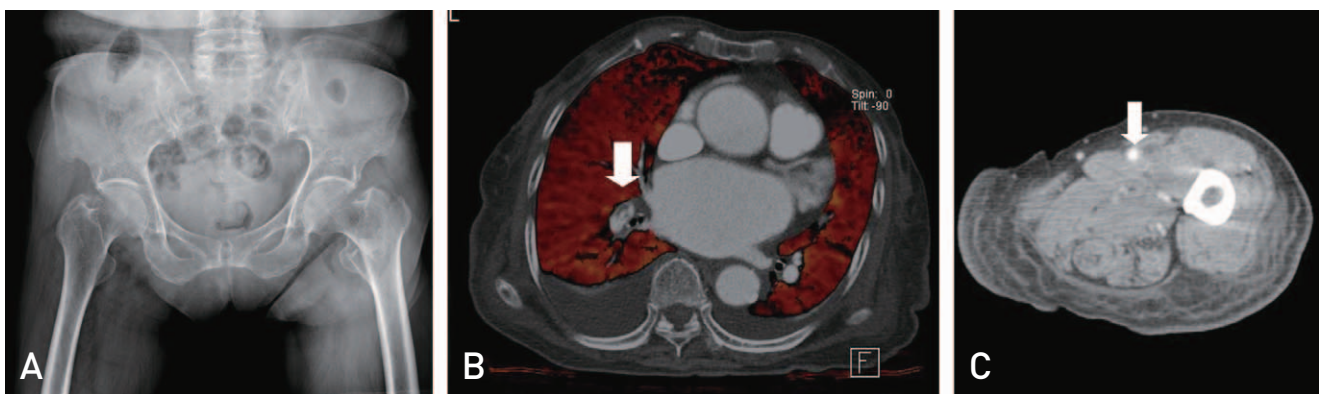


Fig. 3. Both pulmonary embolism and deep vein thrombosis were observed on indirect multidetector computed tomographic venography preoperatively in an 89-year-old female patient with intertrochanteric femoral fracture.

to injury^{8,13}). Since delays in surgery increase the risk of VTE, measures to prevent VTE should be taken as soon as possible after the injury and before surgery. Unless contraindications exist, the SIGN, NICE and Korean Hip Society recommend preoperative pharmacological prophylaxis in patients with a hip fracture¹²⁻¹⁴). The time to initiation of postoperative pharmacological prevention varies from the 6 to 12 hours after surgery and the duration recommended by clinical practice guidelines vary (between 28 to 35 days). The exact duration of prevention are likely to be informed by the presence of underlying conditions, intraoperative findings, postoperative status of the wound and others¹¹⁻¹³).

2. Mechanical Prophylaxis

Mechanical prophylaxis aims to prevent venous congestion and has drawn an increasing amount of attention as recent studies have reported the risk of bleeding and complications in the patient group that received pharmacological prophylaxis⁴²). Mechanical prophylaxis includes, among others, compression stockings, elastic bandages, foot pumps, and intermittent pneumatic compression (IPC) devices. Of these, foot pumps and IPC devices are advised considering patient compliance and preventive effects. However, mechanical prophylaxis alone is not recommended to patients with a hip fracture^{12,13}), and this seems to be attributable to the usefulness of pharmacological prophylaxis and patient compliance. The biggest advantages of mechanical prophylaxis with no risk of bleeding are usability without specific treatment from the preoperative period and applicability when bleeding is detected or pharmacological prophylaxis is constrained¹³).

3. Pharmacological Prophylaxis

The most common prophylactic drugs for VTE are aspirin, heparin, vitamin K antagonists (warfarin) and factor Xa inhibitors. Aspirin in particular has been shown to be a relatively safe option for the prevention of VTE. According to the results of a comparative study on low molecular weight heparin (LMWH) and aspirin in patients with a hip fracture, the incidence of postoperative DVT was higher in the aspirin group than in the LMWH group. The use of aspirin alone appears to be less effective in the prevention of postoperative VTE among patients with a hip fracture compared to other pharmacological prophylaxis⁴³). A large number of recent studies on VTE prevention methods have suggested the use of LMWH^{11-14,30,44}). The ACCP, NICE, SIGN, Thrombosis

Interest Group of Canada and many other associations recommend the use of LMWH for preventing preoperative VTE after admission to hospital^{11-13,30,44}) (Table 1). Although active pharmacological prophylaxis are required for thromboprophylaxis immediately after injury in patients with a hip fracture⁸), there are limitations in the choice of administered drugs because undergoing surgery within the earliest possible time also needs to be considered concurrently. In this regard, LMWH, with a short elimination half-life (4.5 hours) and fast onset of action is thought to be an appropriate drug for preventing preoperative VTE in patients with a hip fracture. Warfarin and vitamin K antagonists are economic and effective oral anticoagulants, but limitedly used to prevent preoperative VTE in hip fracture patients due to their long half-life and slow onset of action (international normalized ratio [INR] range, 2.0-3.0). In addition, these anticoagulants cannot be administered to pregnant women and have food interactions. In the clinical practice guidelines of multiple medical associations, the use of warfarin in hip fractures is an evidence-based approach for postoperative prevention, but is not recommended as a preoperative measure^{12,13,44}). Fondaparinux is most commonly used factor Xa inhibitor and suggested as a primary option by the NICE and SIGN for prevention of postoperative VTE after hip fractures^{12,13}). In a previous study, fondaparinux and LMWH (enoxaparin) were randomly given to 1,711 patients with a hip fracture after surgery at a daily dose of 2.5 mg. The rates of VTE were 8.3% and 19.1%, respectively ($P < 0.001$) and the incidences of proximal DVT were 0.9% and 4.3% ($P < 0.001$)³⁹). However, no differences were found in symptomatic DVT and fatality rates. Furthermore, the preoperative use of fondaparinux is not advised due to its long half-life (17-21 hours) and slow onset of action^{12,13}).

4. Inferior Vena Cava (IVC) Filter

To prevent PE, insertion of the IVC filter through the catheter can be considered in patients with acute DVT. However, the recurrence rate of DVT was higher in the group with permanent IVC filter compared to the group without, and no difference was found in the survival rate between the groups during the 2-year follow-up⁴⁰). The use of permanent IVC filters is not recommended for short-term effects^{45,46}), and the ACCP does not recommend IVC filters for primary prophylaxis of PE. The indications for IVC filter placement have broadened with the recent development of new retrieval IVC filters. Nevertheless,

Table 1. Summary of Venous Thromboembolism (VTE) Prophylaxis in Patients with a Hip Fracture

Association	Aspirin	Heparin (LMWH)	Warfarin	Fondaparinux	Mechanical prophylaxis	Duration of treatment
ACCP (9th edition) ¹¹⁾	Not recommended as sole prophylaxis	Preoperatively (especially if delay to surgery) or postoperatively	Target INR, 2.5	Commence 6-8 hr after surgery or next day	Recommended if high risk of bleeding, and added to/substituted with pharmacologic VTE prophylaxis after high bleeding risk decreases	35 days
NICE ¹²⁾	Not recommended as sole prophylaxis	Starting at admission, stopping 12 hr before surgery and restarting 6-12 hr after surgery	Not recommended routinely	Not recommended preoperatively; commence 6 hr after surgical closure	Recommends compression stockings, foot impulse devices, and IPC	Continue pharmacologic VTE prophylaxis for 28-35 days and mechanical prophylaxis until patient no longer has markedly reduced mobility
SIGN ¹³⁾	Not recommended as sole prophylaxis	Preoperatively If delay to surgery; may be used for duration of treatment if necessary	Not recommended routinely	Recommended as primary VTE prophylaxis; commence 6 hr after surgery; not recommended preoperatively because of potential for spinal hematoma after spinal/epidural anesthesia	Consider only for suitable patients	28 days
BOA (September 2007) ³⁵⁾	No agreed consensus	No agreed consensus	No agreed consensus	No agreed consensus	No agreed consensus	No agreed consensus
TIGC ⁴²⁾	Not recommended as sole prophylaxis	Preoperatively If delay to surgery; recommended for sole VTE prophylaxis	Recommended for sole VTE prophylaxis	Commence 12 hr after surgery	Not recommended as sole prophylaxis	14-35 days

LMWH: low-molecular-weight heparin, ACCP: American College of Chest Physicians, INR: international normalized ratio, NICE: National Institute for Health and Clinical Excellence, IPC: intermittent pneumatic compression devices, SIGN: Scottish Intercollegiate Guidelines Network, BOA: British Orthopaedic Association, TIGC: Thrombosis Interest Group of Canada; TIGC recommends against rivaroxaban and dabigatran for VTE prophylaxis after hip fracture until additional studies that assess their efficacy are carried out.

a recent randomized, open-label, blinded end point trial (PREPIC 2, Prevention of Recurrent PE by Vena Cava Interruption) have addressed that the use of a retrieval IVC filter is an invasive procedure with no confirmed effectiveness in the treatment of acute PE compared to the use of medication alone^{8,47}. A 6-month follow-up study of 17 French centers investigated 200 acute PE patients with a combination of anticoagulation therapy and retrieval IVC filters and 199 patients with the use of anticoagulants alone. In the filter group, the filter was successfully inserted in 193 patients and was retrieved as planned in 153 of the 164 patients in whom retrieval was done at 3 months. By 3 months, recurrent PE had occurred in 6 patients (3.0%) in the filter group and in 3 (1.5%) in the group with anticoagulation alone. Among the 193 patients in the filter group, access site hematoma occurred in 5 patients (2.6%), filter thrombosis in 3 (1.6%) and retrieval failure due to mechanical reasons in 11 (5.7%). A single patient experienced cardiac arrest during filter insertion. These outcomes imply that there is no clear evidence showing efficacy of retrieval IVC filter implantation for treatment of patients with acute PE. The above clinical findings suggest that IVC filters should be used for patients with recurrent PE despite of sufficient use of anticoagulants or with contraindication to anticoagulants^{47,48}. When DVT is detected in preoperative study after injury in patients with a hip fracture, associated complications include intra- or postoperative fatal PE. Preoperative insertion of retrieval IVC filters may be considered in a limited number of patients (e.g., those for whom pharmacological treatment for thrombus removal cannot be sustained for a sufficient length of time until

surgical intervention or drug therapy is not applicable) (Fig. 4). When determining the placement of retrieval IVC filters, medical cost, patient's cardiovascular function, presence of IVC thrombosis, mechanical thrombectomy and others must be taken into consideration.

SUMMARY

Different thromboprophylaxis modalities should be considered for patients undergoing surgery for hip fracture, unlike patients undergoing ordinary hip surgery. Additionally, since hip fracture-induced factors increase the risk of VTE over time, mechanical and pharmacological VTE-prophylactic measures should be initiated immediately after injury unless contraindicated. Among the available preventive drugs, LMWH, with a short half-life and fast onset of action appears to be most appropriate for preoperative thromboprophylaxis in patients with a hip fracture. Enoxaparin, one of the most widely used LMWHs, is injected subcutaneously once daily at a dose of 4,000 IU immediately after injury to 12 hours before surgery. When VTE is diagnosed in preoperative examination, enoxaparin is injected subcutaneously twice daily at a dose of 100 IU/kg regardless of symptoms. Prevention of postoperative VTE can be initiated with the same methods applied to patients undergoing ordinary hip surgery.

CONCLUSION

VTE is a common complication in patients with a hip fracture, and the risk of VTE increases immediately after injury unlike in other ordinary hip surgery. Since hip fractures



Fig. 4. (A) This plain radiograph showed an intertrochanteric femoral fracture in an 81-year-old man. (B) Deep vein thrombosis (arrow) of femoral vein was observed on preoperative indirect multidetector computed tomographic venography. (C) Inferior vena cava filter was inserted preoperatively.

frequently occur in older patients, VTE is more likely to develop as an underlying condition prior to hip fractures. Thrombi located distally before surgery can migrate proximally during or after surgery and may result in fatal complications. Therefore, more active screening is crucial to diagnose preoperative VTE after hip fracture; indirect MDCT venography is thought to be a useful imaging option. We strongly recommend that surgical intervention in patients with a hip fracture is performed as soon as possible following injury and that mechanical and pharmacological prophylaxis are used concomitantly immediately after injury.

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CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest relevant to this article.

REFERENCES

- Kannus P, Niemi S, Parkkari J, Palvanen M, Vuori I, Järvinen M. Hip fractures in Finland between 1970 and 1997 and predictions for the future. *Lancet*. 1999;353:802-5.
- Roberts SE, Goldacre MJ. Time trends and demography of mortality after fractured neck of femur in an English population, 1968-98: database study. *BMJ*. 2003;327:771-5.
- McLaughlin MA, Orosz GM, Magaziner J, et al. Preoperative status and risk of complications in patients with hip fracture. *J Gen Intern Med*. 2006;21:219-25.
- Perez JV, Warwick DJ, Case CP, Bannister GC. Death after proximal femoral fracture--an autopsy study. *Injury*. 1995;26:237-40.
- Powers PJ, Gent M, Jay RM, et al. A randomized trial of less intense postoperative warfarin or aspirin therapy in the prevention of venous thromboembolism after surgery for fractured hip. *Arch Intern Med*. 1989;149:771-4.
- Agnelli G, Cosmi B, Di Filippo P, et al. A randomised, double-blind, placebo-controlled trial of dermatan sulphate for prevention of deep vein thrombosis in hip fracture. *Thromb Haemost*. 1992;67:203-8.
- Hamilton HW, Crawford JS, Gardiner JH, Wiley AM. Venous thrombosis in patients with fracture of the upper end of the femur. A phlebographic study of the effect of prophylactic anticoagulation. *J Bone Joint Surg Br*. 1970;52:268-89.
- Shin WC, Woo SH, Lee SJ, Lee JS, Kim C, Suh KT. Preoperative prevalence of and risk factors for venous thromboembolism in patients with a hip fracture: An indirect multidetector CT venography study. *J Bone Joint Surg Am*. 2016;98:2089-95.
- Kim YH, Choi IY, Park MR, Park TS, Cho JL. Prophylaxis for deep vein thrombosis with aspirin or low molecular weight dextran in Korean patients undergoing total hip replacement. A randomized controlled trial. *Int Orthop*. 1998;22:6-10.
- Yoo MC, Kang CS, Kim YH, Kim SK. A prospective randomized study on the use of nadroparin calcium in the prophylaxis of thromboembolism in Korean patients undergoing elective total hip replacement. *Int Orthop*. 1997;21:399-402.
- Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e278S-e325S.
- National Institute for Health and Clinical Excellence. Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital. Clinical Guideline 92 [Internet]. London: National Institute for Health and Clinical Excellence; 2010 Jan [updated 2015 June; cited 2017 April 2]. Available from: <https://www.nice.org.uk/guidance/cg92>.
- Scottish Intercollegiate Guidelines Network. Management of hip fracture in older people: a national clinical guideline [Internet]. Edinburgh: Scottish Intercollegiate Guidelines Network; 2009 June [cited 2017 April 2]. Available from: <http://www.sign.ac.uk/assets/sign111.pdf>.
- Park YS. Guideline for the Prophylaxis of Venous Thromboembolism in hip surgery patients. *J Korean Orthop Assoc*. 2011;46:95-8.
- Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J Med*. 1994;331:1601-6.
- Girasole GJ, Cuomo F, Denton JR, O'Connor D, Ernst A. Diagnosis of deep vein thrombosis in elderly hip-fracture patients by using the duplex scanning technique. *Orthop Rev*. 1994;23:411-6.
- Smith EB, Parvizi J, Purtill JJ. Delayed surgery for patients with femur and hip fractures-risk of deep venous thrombosis. *J Trauma*. 2011;70:E113-6.
- Hefley FG Jr, Nelson CL, Puskarich-May CL. Effect of delayed admission to the hospital on the preoperative prevalence of deep-vein thrombosis associated with fractures about the hip. *J Bone Joint Surg Am*. 1996;78:581-3.
- Roberts TS, Nelson CL, Barnes CL, Ferris EJ, Holder JC, Boone DW. The preoperative prevalence and postoperative incidence of thromboembolism in patients with hip fractures treated with dextran prophylaxis. *Clin Orthop Relat Res*. 1990;(255):198-203.
- Zahn HR, Skinner JA, Porteous MJ. The preoperative prevalence of deep vein thrombosis in patients with femoral neck fractures and delayed operation. *Injury*. 1999;30:605-7.
- National Institute for Health and Clinical Excellence, National Clinical Guideline Centre. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing [Internet]. London:

- National Clinical Guideline Centre at the Royal College of Physicians; 2012 June [updated 2015 Nov; cited 2017 April 2]. Available from: <http://www.nice.org.uk/guidance/cg144/>.
22. Goodacre S, Sampson F, Thomas S, van Beek E, Sutton A. Systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis. *BMC Med Imaging*. 2005;5:6.
 23. Lensing AW, Prandoni P, Büller HR, Casara D, Cogo A, ten Cate JW. Lower extremity venography with iohexol: results and complications. *Radiology*. 1990;177:503-5.
 24. McLachlan MS, Thomson JG, Taylor DW, Kelly ME, Sackett DL. Observer variation in the interpretation of lower limb venograms. *AJR Am J Roentgenol*. 1979;132:227-9.
 25. Watanabe H, Sekiya H, Kariya Y, Hoshino Y, Sugimoto H, Hayasaka S. The incidence of venous thromboembolism before and after total knee arthroplasty using 16-row multidetector computed tomography. *J Arthroplasty*. 2011;26:1488-93.
 26. Loud PA, Katz DS, Klippenstein DL, Shah RD, Grossman ZD. Combined CT venography and pulmonary angiography in suspected thromboembolic disease: diagnostic accuracy for deep venous evaluation. *AJR Am J Roentgenol*. 2000;174:61-5.
 27. Cham MD, Yankelevitz DF, Shaham D, et al. Deep venous thrombosis: detection by using indirect CT venography. The Pulmonary Angiography-Indirect CT Venography Cooperative Group. *Radiology*. 2000;216:744-51.
 28. Perrier A, Roy PM, Sanchez O, et al. Multidetector-row computed tomography in suspected pulmonary embolism. *N Engl J Med*. 2005;352:1760-8.
 29. Monreal M, Lafoz E, Navarro A, et al. A prospective double-blind trial of a low molecular weight heparin once daily compared with conventional low-dose heparin three times daily to prevent pulmonary embolism and venous thrombosis in patients with hip fracture. *J Trauma*. 1989;29:873-5.
 30. Richman PB, Wood J, Kasper DM, et al. Contribution of indirect computed tomography venography to computed tomography angiography of the chest for the diagnosis of thromboembolic disease in two United States emergency departments. *J Thromb Haemost*. 2003;1:652-7.
 31. Lightfoot CB, Abraham RJ, Mammen T, Abdolell M, Kapur S, Abraham RJ. Survey of radiologists' knowledge regarding the management of severe contrast material-induced allergic reactions. *Radiology*. 2009;251:691-6.
 32. Andreucci M, Solomon R, Tasanarong A. Side effects of radiographic contrast media: pathogenesis, risk factors, and prevention. *Biomed Res Int*. 2014;2014:741018.
 33. Katz DS, Loud PA, Bruce D, et al. Combined CT venography and pulmonary angiography: a comprehensive review. *Radiographics*. 2002;22:S3-19; discussion S20-4.
 34. Shiga T, Wajima Z, Ohe Y. Is operative delay associated with increased mortality of hip fracture patients? Systematic review, meta-analysis, and meta-regression. *Can J Anaesth*. 2008;55:146-54.
 35. Moran CG, Wenn RT, Sikand M, Taylor AM. Early mortality after hip fracture: is delay before surgery important? *J Bone Joint Surg Am*. 2005;87:483-9.
 36. Uzoigwe CE, Burnand HG, Cheesman CL, Aghedo DO, Faizi M, Middleton RG. Early and ultra-early surgery in hip fracture patients improves survival. *Injury*. 2013;44:726-9.
 37. Association of Anaesthetists of Great Britain and Ireland, Griffiths R, Alper J, et al. Management of proximal femoral fractures 2011: Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia*. 2012;67:85-98.
 38. British Orthopaedic Association. The care of patients with fragility fracture. London: British Orthopaedic Association; 2007. 32-4.
 39. Eriksson BI, Bauer KA, Lassen MR, Turpie AG; Steering Committee of the Pentasaccharide in Hip-Fracture Surgery Study. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med*. 2001;345:1298-304.
 40. Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prévention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. *N Engl J Med*. 1998;338:409-15.
 41. Rosencher N, Vielpeau C, Emmerich J, Fagnani F, Samama CM; ESCORTE Group. Venous thromboembolism and mortality after hip fracture surgery: the ESCORTE study. *J Thromb Haemost*. 2005;3:2006-14.
 42. Lieberman JR, Pensak MJ. Prevention of venous thromboembolic disease after total hip and knee arthroplasty. *J Bone Joint Surg Am*. 2013;95:1801-11.
 43. Gent M, Hirsh J, Ginsberg JS, et al. Low-molecular-weight heparinoid organon is more effective than aspirin in the prevention of venous thromboembolism after surgery for hip fracture. *Circulation*. 1996;93:80-4.
 44. Thrombosis Canada. Thromboprophylaxis: orthopedic surgery [Internet]. Whitby, ON: Thrombosis Canada; 2016 Dec 7 [cited 2017 April 2]. Available from: http://thrombosiscanada.ca/?page_id=18&search=VTE#.
 45. Imanaka S, Aihara S, Yoshihara K, Kato A, Matsumoto K, Kudo S. Use of a temporary caval filter in a young man with pulmonary embolism to prevent migration of massive caval thrombus during an attempt of caval thrombolysis. *J Atheroscler Thromb*. 2000;6:18-21.
 46. Protack CD, Bakken AM, Patel N, Saad WE, Waldman DL, Davies MG. Long-term outcomes of catheter directed thrombolysis for lower extremity deep venous thrombosis without prophylactic inferior vena cava filter placement. *J Vasc Surg*. 2007;45:992-7; discussion 997.
 47. Wärntges S, Konstantinides SV. Progress in the management of acute pulmonary embolism. *Curr Opin Pulm Med*. 2015;21:417-24.
 48. Mismetti P, Laporte S, Pellerin O, et al; PREPIC2 Study Group. Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. *JAMA*. 2015;313:1627-35.