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Venous thromboembolism prophylaxis after hip preservation surgery: a review and presentation of institutional experience

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ABSTRACT

Venous thromboembolism (VTE) is a serious complication after major orthopedic procedures. The best options for prevention of the VTE are still debated. The most popular evidence-based guidelines for prevention and treatment of VTE in orthopedic surgery addressed the total hip or knee arthroplasty and hip fractures as the major orthopedic surgeries. Majority of studies have evaluated the different modalities of the VTE prophylaxis in patients undergiong hip or knee arthroplasty. Hip preservation surgeries (HPS) including mini-open femoroacetabular osteoplasty, surgical dislocation of the hip, arthroscopic procedures, and periacetabular osteotomy (PAO) are gained popularity in recent two decades. The majority of these patients are young, healthy and active and may not be considered at high risk for VTE. The frequency of VTE in patients undergoing PAO seems to be low between 0 and 5%. There is a paucity of data regarding rates of VTE in young healthy patients undergoing HPS as well as the optimal prevention methods for VTE. Hence current VTE prevention guidelines do not cover HPS adequately. We aimed to review the available literature regarding VTE events and VTE prophylaxis options after HPS. We discussed the available and potential options for prophylaxis of VTE events in these procedures along with our experience in a large cohort of hip preservation surgery.

INTRODUCTION

Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), represents a serious and potentially fatal complication that has been reported after major orthopedic surgery involving the lower extremity [1]. The reported cumulative (0–35 days post-operatively) incidence of symptomatic VTE after major orthopedic procedures with no prophylaxis is 4.3% (1.50 and 2.80% for PE and DVT, respectively). Fatal PE occurs between 0.1–2% and 0.1–1.7% in patients undergoing THA and TKA, respectively [2, 3].
Hip preservation surgeries (HPS) including hip arthroscopy, mini-open femoroacetabular osteoplasty (FAO), surgical dislocation of the hip (SDH) and periacetabular osteotomy (PAO) are performed to address hip abnormalities like femoroacetabular impingement and developmental dysplasia of the hip [4–8] VTE can occur after HPS procedures. The frequency of venous thromboembolic disease during the post-operative period of patients undergoing PAO has been reported to between 0 and 5% [9–13]. Similarly the rate of VTE after hip arthroscopy has been reported to be between 0 and 9.6% [14, 15], 0.25% after mini-open FAO [16] and 0.5% after SDH [17] using different VTE prophylaxis protocols.

There is no consensus in the literature regarding most effective method of VTE prophylaxis in patients undergoing HPS. The majorities of the patients undergoing HPS are young, healthy and active and may not be considered at high risk for VTE.

The objective of this review was to evaluate all available literature related to VTE prophylaxis after HPS. In addition we present our experience with VTE prophylaxis in a large cohort of patients undergoing HPS at our institution.

RISK ASSESSMENT

Estimating the individual risk of VTE for patients undergoing orthopedic surgery is crucial in order to identify those at high risk for development of VTE, and to decide on the most optimal VTE prophylaxis. The risk for VTE consists of two categories of factors: patient-related and procedure-related factors. Patient-related risk factors include age, gender, body mass index (BMI), pregnancy, family history of VTE, recurrent VTE, thrombophilia, cancers, prolonged immobilization, consumption of contraceptive drugs or hormone replacement therapy [18]. Procedure-related factors include the invasiveness of the procedure (open or arthroscopic), need for bone osteotomy, and the duration of the procedure [18–20]. Numerous studies have evaluated risk assessment for the development of VTE events after total joint arthroplasty (TJA) [21–23] and determined multiple factors responsible for increasing the risk of VTE. Caprini *et al.* proposed the Caprini Risk Assessment Model for development of VTE in 1990 that has been modified a few times with the latest edition produced in 2005 [24, 25]. However in this model, all patients undergoing orthopedic procedures are considered to be at a very high risk for VTE and in need of a potent VTE prophylaxis. A recent study conducted at the Rothman Institute aimed to develop a risk assessment model for patients, using the National Inpatient Sample data on 1 721 806 patients, undergoing arthroplasty. Among this large cohort 15 775 (0.9%) patients developed VTE post-operatively. A large number of possible risk factors responsible for development of VTE were assessed and the relative weight for each factor was determined [21]. The analyses allowed the investigators to develop an iOS App (VTEstimator) that could be used to assign patients into low or high risk for VTE after TJA [21].

To our knowledge, there is no study that evaluates the risk factors for development of VTE in patients undergoing HPS.

Laboratory individual risk assessment methods

Genetic tests

The genetic risk factors are classified into two main categories: loss of function mutations (such as deficiencies of antithrombin, protein C, protein S, ABO blood group, factor V Leiden and prothrombin G20210A) and gain of function mutations (such as prothrombin mutation G20210A, factor V Leiden) [26, 27]. Pre-operative genomic profiling will likely improve pre-operative risk stratification for VTE and could also lead to the development of newer prophylactic and may be therapeutic interventions. Inherited thrombophilia may be involved in up to 40% of VTE cases [28, 29]. The detection of hereditary thrombophilia is recommended for children with purpura fulminans, pregnant women at risk of VTE and may be useful in risk assessment for recurrent thrombosis in patients presenting with VTE at a young age and patients with a strong family history of VTE [27].

Thromboelastography

Thromboelastography (TEG) is a whole-blood assay that can identify both hypocoagulable and hypercoagulable states [30, 31]. Elevated levels of the TEG assay at admission have been found to be predictive of PE in general trauma patients [31]. However, in a recent study on 101 patients who underwent THA or TKA, or surgery for hip fractures, pre-operative assessment of the patients' coagulation status using TEG did not predict the risk of subsequent VTE [32]. Thus, TEG as a predictor of subsequent VTE has been abandoned for the most part in clinical practice.

DIAGNOSIS

Wells clinical prediction criteria is a combination of physical exam and risk factors scoring system that establishes whether a patient has a low, intermediate or high risk factor for VTE development [33–35]. However, Wells criteria are not definitive and should be used to predict the probability of VTE when combined with other diagnostic tests [36]. Venous ultrasonography is the imaging test of choice for diagnosing of DVT [37]. There are two methods for identifying the DVT by means of US, Proximal US and the whole leg US. When attempting to diagnose proximal DVT, either of these two methods could be administered. Proximal venous ultra-sonography has been reported to have a sensitivity and specificity of 97 and 98%, respectively [36]. However, proximal venous US cannot rule out a distal DVT, hence a comprehensive ultra-sonographic examination of the lower extremity may be necessary in order to evaluate the more distal veins [38–40]. Patients with low pre-test probability combined with a negative US may not require any VTE prophylaxis [33]. D-dimer is a very sensitive laboratory test and useful in ruling out the presence of DVT and PE [41, 42]. The sensitivity and specificity of D-dimer depends on the assay which may be used in laboratories. In multiple assays, the test has been reported to be highly sensitive while the specificity remains low [43, 44]. A positive D-dimer in the setting of

suspected PE necessitates further imaging such as computed tomographic pulmonary angiography or ventilation-perfusion scan [45]. Alternative diagnostic strategies have suggested a potential role for MRI in diagnosis of PE [46]. Research has also focused on single-photon emission CT in this setting [47], but additional investigation is necessary to confirm the role of these novel tests for diagnosis of VTE.

MODALITIES FOR PREVENTION OF VTE

Pharmacologic and mechanical modalities have been recommended as prophylactic agents after major orthopedic procedures. Pharmacologic agents presently include warfarin, unfractionated heparin, LMWH, fondaparinux, aspirin, rivaroxaban, dabigatran, apixaban and some other agents. Mechanical modalities are graduated compression stockings, intermittent pneumatic compression device (IPCD) and the venous foot pumps (VFP) [48]. Although these modalities have been evaluated in joint arthroplasty and other major orthopedic procedures, the literature related to the use of these agents in patients undergoing HPS is relatively scarce.

GUIDELINES

The American college of chest physicians (ACCP) and The American Academy of Orthopaedic Surgeons (AAOS) have both developed evidence based guidelines for prevention of VTE following total joint arthroplasty and hip fracture [3, 49]. These guidelines also posit recommendations related to knee arthroscopy.

CURRENT EVIDENCES REGARDING PREVENTION OF VTE AFTER HPS

Despite the presence of a few recent studies, the most optimal mode of VTE prevention after HPS remains largely unknown (Table I). Routine screening for diagnosis of VTE is not endorsed by any guidelines. VTE prophylaxes after hip preservation procedures are not addressed by ACCP and AAOS or any other guidelines. Hence specific VTE prevention protocols are required to implement optimum prophylaxis method after HPS.

VTE prophylaxis after PAO

PAO is a major orthopedic procedure with extensive soft tissue dissection and multiple pelvic bone cuts [4, 11]. Unlike TJA, intramedullary reaming is not required during HPS. However, multiple bone osteotomies during PAO may predispose patients for subsequent bleeding and a potent anticoagulation may increase the risk of bleeding [50, 51]. On the other hand, because of the partial or non-weight bearing status of the patient after this procedure, some degree of inactivity and limb swelling occurs that may predispose the patients to VTE [16, 52].

In a retrospective study from Japanese Registry, Sugano *et al.* [53], evaluated the effect of mechanical prophylaxis in 70 patients undergoing pelvic or femoral osteotomies [53]. Epidural anesthesia, intraoperative calf bandage, early mobilization and IPCD were implemented post-operatively for thromboprophylaxis in the latter cohort. Patients who were taking aspirin before surgery, stopped it 1 week before surgery and resumed it after surgery. These patients were not excluded from the study. For mechanical prophylaxis against VTE, a VFP was used post-operatively for 1–2 days until the patient started to walk with aids. Thigh-high compression stockings were used for 2 weeks. Post-operatively, no VTE occurred in these patients whose average age was 30.2 years.

Thawrani *et al.* conducted a retrospective study on 76 patients ($n = 83$ hip) who underwent a Bernese PAO. The mean age of patients was 15 ± 2.4 years. They employed no VTE prophylaxis. The authors reported no thromboembolic events in their patients [7]. Similarly, Ito *et al.* [8] investigated the intermediate to long-term results of PAO in patients in two groups of younger and older than 40 years of age. The older group included 36 patients (range 41 hips), and the younger group included 103 patients (117 hips). The overall average age of the patients at the time of surgery was 32 years (range 12–56). Prophylaxis against VTE was not routinely administered. Only high-risk patients with a previous history of thrombosis were managed with aspirin for 2 weeks post-operatively. One patient developed PE after operation and he was more than 40 years. This patient died 4 days after surgery. The study is not focusing on VTE, but low rate of VTE is in agreement with other studies evaluating VTE after PAO [53, 54].

Zaltz *et al.* [13] investigated the incidence of VTE after PAO in 1067 patients from six North American centers. They included patients younger than 18 years with a mean age for the patients in their cohort being 24 years (range 13–56 years). Multiple types of DVT prophylaxis method were employed, including mechanical only, chemical only or combination of mechanical and chemicals. There were four cases of PE and seven cases of DVT. The crude incidence of clinically symptomatic VTE was 9.4/1000. In two centers, both chemical and mechanical prophylaxis employed for prophylaxis of VTE. The crude incidence of VTE after PAO per 1000 patients was 6.73 (2/297) and 8.51 (2/235), respectively, in these two centers. Other two centers administered either only chemical or only mechanical agents for VTE prophylaxis. The crude incidence was 9.37 (3/32) and 12.05 (3/249), respectively. Interestingly in other two children hospitals the crude incidence was

Table I. Data extracted from studies, which addressed VTE after open hip preservative surgeries

Author	Year	Procedure	Sample size	Inc. of VTE	DVT	PE	Age	Prophylaxis	Dosage	Duration	Screen	Major bleeding
Sugano	2009	PAO	70	0	0	0	30.2	MCD+ASA[a]	NA	2 wks.	Clinical	No
Thawrani	2010	PAO	83	0	0	0	15.6±2.4	No prophylaxis	NA	NA	Clinical	No
Ito	2011	PAO	158	1/158 (0.6%)	0	1	32 (20–56)	ASA[b]	NA	2 wks.	Clinical	No
Zaltz	2011	PAO	1067	9.4/1000 (0.94%)	7	4	24 (13–56)	Multiple	NA	NA	NA	No
Polkowski	2014	PAO	134	1.3%	2	0	30 (18–60)	ASA+MCD	325 mg bid	6 wks.	US	No
Wassilew	2015	PAO	48	0	0	0	31.7±10.1	LMWH	NA	Na	Clinical	No
Wingerter	2015	PAO	50	0	0	0	28 (13–49)	ASA+MCD	325 mg bid	6 wks.	Clinical	No
Bryan	2016	PAO	75	1.33%	1	0	28±9.2	ASA/MCD	325 mg bid	6 wks.	Clinical	No
Yamanaka	2016	PAO	144	2.1%	3	0	32.2±11.4	MCD±LMWH	NA	NA	MDCT/US	No
Tischler	2014	Mini open FAO	407	1/407 (0.25%)	1	0	34.5±11.1	ASA	325 mg daily	14–28	Clinical	No
Sink	2011	Surg. Dx. FAO	334	2/334 (0.59%)	2	0	26 (8–61)	Multiple	NA	NA	NA	No

[a]Chemical prophylaxis was applied only for a few patients. [b]ASA administered for patients who were high risk for thrombosis.
PAO, periacetabular osteotomy; FAO, femoroacetabular osteoplasty; Surg Dx, surgical hip dislocation; DVT, deep vein thrombosis; PE, pulmonary embolism; MCD, mechanical compression devices; ASA, aspirin; LMWH, low molecular weight heparin; US, ultra sound; MDCT, multi detector CT; NA, not applicable.

Table II. **Data extracted from studies, which addressed VTE after arthroscopic hip preservative surgeries**

Author	Year	Procedure	Inc. of VTE	DVT	PE	Sample size	Age	Prophylaxis	Dosage	Duration	Screen	Major bleeding
Clarke[a]	2003	Arthroscopy	0	0	0	1054	37 (6–80)	No	NA	NA	Clinical	No
Philippon[b]	2009	Arthroscopy	0	0	0	112	40.6±2.9	No	NA	NA	Clinical	No
Salvo	2010	Arthroscopy	3.7%	3	0	81	32.2 (14–59)	No	NA	NA	Clinical	No
Chan	2013	Arthroscopy	0.8%	2	0	236	37±13	No	NA	NA	Clinical	No
Alaia	2014	Arthroscopy	1.4%	2	0	139	37±12	No	NA	NA	US	No
Larson	2016	Arthroscopy	0.2%	2	1	1502	30.5±18.5	MCD	NA	NA	Clinical	No
Fukushima	2016	Arthroscopy	6.94%	5	0	72	46.3±1.7	No	NA	NA	US	No
Mohtadi	2016	Arthroscopy	4.3%	5	0	115	35.4±10.3	No	NA	NA	US	No

All Other studies performed for FAO or labral tear or miscellaneous problems.
[a]Procedure performed for pain (41%), osteoarthritis (21%), labral tears (18%), removal of loose bodies (7%) and other miscellaneous conditions (13%).
[b]Procedure performed only for FAO.
MCD, mechanical compression devices; US, ultra sound; NA, not applicable.

0/1000 while they used mechanical prophylaxis for majority of the patients in one and no prophylaxis for the other children center.

Polkowski *et al.* [55], in a retrospective cohort, indicated that the risk of symptomatic DVT associated with PAO is low (1%) with use of aspirin 325 mg two times daily along with mechanical compression prophylaxis for 6 weeks. Furthermore, routine post-operative screening did not detect any patients with an asymptomatic DVT.

A few studies have attempted to evaluate the effect of tranexamic acid (TXA) on the rate of thrombotic or hemorrhagic events after PAO [51, 56, 57]. In one study by Bryan *et al.* [51] 150 patients undergoing PAO were investigated. Of these, 75 patients received intravenous TXA and 75 patients did not receive TXA. All patients received aspirin 325 mg two times daily for 6 weeks and mechanical prophylaxis while they were in the hospital after osteotomy. They reported the VTE event rate of 2 of 75 (2.67%) in patients who received TXA and 1 of 75 (1.33%) in group who did not receive TXA. Wingerter *et al.* [56] investigated the incidence of VTE as well as other complications after PAO in patients who received TXA and controlled them with the same PAO group who did not receive TXA (50 hips in each group). Patients younger than 18 years did not receive prophylaxis. Older patients received a contralateral mobile IPCD intraoperatively and bilateral IPCD for 10 days post-operatively. All patients received aspirin 325 mg two times daily for 6 weeks. No patient in either group had signs or symptoms of VTE. In a same study, Wassilew *et al.* [57] performed PAO on consecutive 48 patients who received TXA and 48 who did not. All patients were screened for symptoms of VTE on discharge and at the sixth, 12th, and 18th week post-operatively. Weight-based LMWH was administered to the patients starting 12 h before surgery with further doses 6 and 12 h after surgery. LMWH was continued in daily dose till full weight bearing was allowed (12 weeks after surgery). They showed no patient undergoing PAO had symptomatic post-operative DVT or symptomatic PE in either group.

Yamanaka *et al.* [52] investigated the incidence of VTE in patients undergoing major hip surgeries including primary or revision hip arthroplasties, hip fractures and PAOs in 820 hips. Of these, 144 underwent PAO. VTE was detected by multidetector computed tomography (MDCT) and by US, 10–14 days post-operatively. Seventy-nine patients received chemoprophylaxis (Enoxaparin or Edoxaban) with compression devices and 65 patients only received compression device (compression stocking and devices) for 3 days after PAO. No significant difference was found between two methods $P = 0.43$). We should keep in mind that small sample size limits the accuracy of incidence report one out of the three patients with VTE was under chemoprophylaxis while two patients received only MCDs. This would make it impossible to judge the effect of chemoprophylaxis.

VTE prophylaxis for hip arthroscopy
Hip arthroscopy has been used to treat various disorders of the hip [58–61]. The incidence of VTE after hip

arthroscopy has been reported to be between 0 and 6.94% [14, 15, 62–67] (Table II). In a recent systematic review on VTE after hip arthroscopy, Haldane *et al.* [68], reported the overall pooled proportion of VTE events after hip arthroscopy in 2985 hips to be 2.0% with a total of 3 PEs and 22 DVTs. By removing the studies, which did not utilize ultrasound for the diagnosis of DVT, the rate of thrombotic events increased to 4.2%. In 6 studies (1542 hips) which did not use any kind of VTE prophylaxis, the incidence of VTE was 2.3% and by removing a single large study that that did not use VTE prophylaxis in the patients, and had no VTE event, the rate of VTE increased to 3.6% compared with 2% for studies with 1443 hips in which VTE prophylaxis was used.

Similarly Salvo *et al.* [14] conducted a study in 81 patients who underwent hip arthroscopy and reported that 3 patients (3.7%) developed clinically symptomatic DVTs. No patient developed symptomatic pulmonary emboli. No chemical or mechanical prophylaxis were used intra or post-operatively. They did not use regular screening method, and diagnosis was based on symptoms of VTE. Another study by Alaia *et al.* [15] reported a VTE rate of 1.4% on 139 patients after hip arthroscopy. No chemical or mechanical prophylaxis was used intra or post-operatively. They intended to screen all patients post-operatively for DVT, using bilateral venous duplex ultrasound at 2 weeks post-operative time point but only 81 patients could be screened. There was no case of asymptomatic DVT in those screened.

Fukushima *et al.* [63] retrospectively evaluated 72 patients for the incidence of DVT after hip arthroscopy who did not receive any VTE prophylaxis. Five patients (6.94%) had DVT while none of them was symptomatic. Clinical diagnosis of DVT was confirmed through US performed pre-operatively and 3 days post-operatively. Additionally, D-dimer levels were measured pre-operatively and on post-operative days one and three. Although not significant, mean D-dimer levels were higher in patients with DVT than in those without DVT. Interestingly, they recommend routine screening for diagnosis of DVT after hip arthroscopy. The latter has not been endorsed by any guideline body or other study.

Mohtadi *et al.* [62] conducted a prospective cohort about incidence of VTE after hip arthroscopy that had multiple superiorities comparing to former studies. They excluded patients with previous risk factors for VTE, employed ultrasound and MDCT in order to screen for VTE and found asymptomatic patients and also tried to stratify the surgical risk factors for VTE. The subjects were not given any pharmacologic or mechanical thromboprophylactic agent, but were encouraged to mobilize as soon as possible. The rate of DVT after elective hip arthroscopy as diagnosed by US was 4.3% (5/115 patients). Only one patient was asymptomatic. There was no statistically individual/surgical significant factor associated with the occurrence of a DVT. They concluded that routine prophylaxis or screening may not be necessary in low risk patients undergoing elective hip arthroscopy.

Based on available literature, the incidence of VTE after hip arthroscopy appears to be low. In patients who are not otherwise at high risk for VTE, either no agent for VTE is needed or administration of effective agents such as aspirin that does not require blood monitoring and is less likely to cause surgical site bleeding is justified [69].

Collins *et al.* [70] reported the rate of VTE after hip arthroscopy to be 6.9% in their cohort. They used Aspirin 325 mg daily for 2 weeks as prophylaxis. Domb *et al.* [71] administered aspirin 325 mg two times daily for 2 weeks after hip arthroscopy as VTE prophylaxis. The incidence of DVT and PE was 0.5% (5 patients) and 0.2% (2 patients), respectively, in their cohort.

VTE prophylaxis for mini-open FAO

The only study that evaluates the incidence of VTE after min-open FAO is by Tischler *et al.* [16]. In a prospective case series of 407 consecutive patients who underwent mini-open FAO procedure, the rate of symptomatic VTE was 0.25% when aspirin at 325 mg daily dose was administered. Majority of patients included in this cohort were young, healthy and active, and were ambulated within hours of their surgery. Patients in this series were not subjected to routine screening for DVT or PE.

VTE prophylaxis after surgical hip dislocation

As a complication of surgical hip dislocation, the incidence of VTE was reported by Sink *et al.* They analyzed the data on 355 hips (323 patients) from 8 different North American centers. The rate of VTE was 0.5%. There was not a consistent method of VTE prophylaxis between eight centers. Two patients complicated with DVT and both had received a combination of chemical and mechanical VTE prophylaxis with the exact details of prophylaxis missing. The findings of the study suggest that the rate of VTE after SDH in the young and healthy adults is acceptably low.

OUR INSTITUTIONAL EXPERIENCE

At our institution patients undergoing mini-open FAO or PAO initially received Coumadin then they received aspirin 325 mg and lastly aspirin 81 mg in recent years. We have evaluated the incidence of VTE in a series of 603 patients (643 hips) undergoing FAO and 80 patients (87 hips) undergoing PAO. The mean age of the patients

was 34.3 years (range 14.3–68.1 years). The administered prophylaxis was warfarin in 44 cases aspirin at 325 mg two times daily in 448 cases and aspirin 81 mg two times daily in 238 cases for four weeks post-operatively. The complications of PE, DVT and major bleeding events within 90 days of surgery were documented. Patients were not routinely screened for VTE. Lower extremity ultrasound and chest CT/VQ scans were only performed in cases of suspected symptomatic VTE. The overall incidence of a VTE within 90 days following FAO was 0.16% (1/643). The overall incidence of VTE complication after PAO was 1.1% (1/87). No major bleeding events developed in-patient undergoing FAO or PAO. There was no difference between ASA 325 mg and ASA 81 mg in our cohort. Based on our institutional experience we believe that aspirin 81 mg two times daily is a safe and an effective modality in minimizing the risk of VTE in patients undergoing hip preservation surgery including PAO.

CONCLUSION

Based on the available literature, the incidence of symptomatic VTE after HPS appears to be very low. One of the major reasons for the latter finding may relate to the fact that these patients are often young, healthy, and active who return to their activity levels fairly soon after the hip surgery. The available evidence, including data from our institution on a large cohort of patients undergoing HPS, suggests that aspirin or mechanical prophylaxis is adequate for majority of patients undergoing HPA. Potent agents, that place the patients at a higher risk of bleeding, should be reserved for patients who are at high risk of VTE based on family history or prior history of VTE.

CONFLICT OF INTEREST STATEMENT

None declared.

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