Clinical Dossier: **DVT PROPHYLAXIS**

Evidence Supporting Use of the VPULSE™ System as Prophylaxis for Patients Undergoing Surgical Procedures

COTHERA

I. Introduction: Dangers of DVT Following Surgery, Morbidity, Mortality

Deep vein thrombosis (DVT) refers to the development of blood clots in a deep vein of the body. These clots, or thrombi, typically form in the lower limbs and can block circulation in the vein, leading to pain, swelling, and discoloration. Though the majority of these symptoms dissipate with identification and treatment, approximately 30% of patients suffer more painful swelling, skin breakdown and ulcers. However, the most significant complication associated with DVT is a pulmonary embolism (PE), which occurs when a portion of the clot loosens and travels through the bloodstream and into the lungs. Pulmonary embolism has been reported to occur in over one-third of DVT patients.[1] Frequently pulmonary embolism causes sudden death, and even those who do survive may have lasting ramifications and chronic respiratory and cardiovascular issues. Ten to thirty percent of individuals with venous thromboembolism VTE will die within one month of diagnosis.[1,2]

Deep vein thrombosis and pulmonary embolism (collectively referred to as venous thromboembolism) affect thousands of Americans each year. The National Center for Health Statistics estimates that DVT is an underlying cause of death in over 10,000 cases annually.[3] Some estimates place the number of persons affected between 350,000 and 600,000, with as many as 100,000 annual deaths occurring within the United States.[2] The precise number of deaths attributable to VTE is difficult to ascertain, due largely to challenges in identifying and diagnosing the condition. In fact, some studies suggest that incidence rate may be significantly higher than estimates suggest, approximating that nearly half of the cases of VTE remain undiagnosed.[1,4] Those who survive a VTE event are often plagued by serious, long-lasting complications due to the damage the clot does to the valves of the affected vein.[2]

With serious and often chronic complications and estimated fatalities rivaling rates associated with breast cancer, motor vehicle incidents and AIDS, the prevention of VTE has become a major health concern. Furthermore, because the incidence of DVT increases markedly with age, it is possible that the growth in total number of VTE cases will outpace the growth of the population, due to the increasing average age of the U.S. population.[1] Thus, it is particularly critical that appropriate methods of prevention and treatment be identified and implemented in a timely manner.

Though VTE previously received little attention by the medical community, there has been a more recent increase in the number of initiatives devoted to increasing knowledge and awareness of this condition. In fact, the Centers for Disease Control (CDC) has recently named the prevention of clotting disorders as a top internal priority based on burden and unmet need.[5] Because DVT is a preventable condition and one that been identified as the most common preventable cause of hospital death, much of this outreach has focused on methods of prophylactic treatment and on identifying risk factors thought to contribute to the occurrence of DVT.[6,7]

Some of the risk factors identified for VTE vary slightly based upon age, race and gender. Still, certain risk factors have been well-documented and described, including: obesity, cancer, immobility, pregnancy, use of hormone therapy, smoking, history of genetic clotting disorders, and recent hospitalization for trauma or major surgery.[1,2] The risk of developing DVT is greatest between two and five days after surgery, with a second peak development period occurring about ten days after surgery, after the patient has been discharged. Additionally, approximately one-third of individuals who have had a DVT will have a recurrence within ten years.[2,8]

Published clinical evidence demonstrates the increased probability of a DVT event (non-fatal or fatal) due to certain risk factors and combinations of risk factors, regardless of anatomy. Evidence-based clinical practice guidelines have also addressed the increased probability of VTE where certain high risk factors are present through recommending multimodal approaches and extending the duration of prophylaxis. Despite the identification of these various risk factors, DCD estimates that one-third to one-half of VTE events occur without any known risk factors.

II. Treatment Options and Methods of Prevention

Asymptomatic DVT has been estimated to develop in 40%-60% of total hip or total knee arthroplasty patients who do not receive prophylaxis. [9,10] Given this staggering figure, several professional societies and key stakeholders have identified various methods for preventing and minimizing the impact of DVT and PE. These prophylactic measures range from general recommendations related to diet, exercise and ambulation, to more intense mechanical and pharmacologic treatment typically overseen by a physician. An abundance of evidence-based clinical practice guidelines have been issued to advise clinicians in their administration of these various treatment methods. In fact, the National Quality Forum (NQF) endorsed a set of 20 voluntary consensus standards related to model policies and performance measures intended to promote the prevention of VTE.[1] These standards include a policy statement recommending that facilities institute written procedures related to treatment, diagnosis and prophylactic care.[11] Despite these consensus standards and clinical guidelines, there is still some disparity amongst evidence-based guidelines regarding when and how to issue prophylactic treatment.

Ambulation and Compression Stockings

Early ambulation is recommended across the board for patients who have undergone major surgery. Patients are encouraged to regain mobility as soon as possible after surgery, and should be automatically advised to do so by clinicians.[12] Compression stockings or graduated compression stockings may also be recommended to help prevent DVT. Stockings are worn on the lower limb from the foot to the knee and are intended to reduce pain and swelling, thereby preventing the chances that blood will pool and clot. Compression stockings are typically recommended for at least one year, but may need to be worn for two years or more where there is a diagnosis of DVT.[2,13] Notably, the use of compression stockings in conjunction with mechanical devices is debatable, as certain specialty societies recommend against the combined use of these treatment methods.[14]

Pharmacologic

Medication is the most commonly instituted course of prophylactic treatment. Anticoagulants, or blood thinners, are widely utilized due to their success in preventing coagulation and their ability to stop current clots from enlarging.[2] Anticoagulants can be administered via IV, injection, or may be taken orally. Their effectiveness has been confirmed in a variety of clinical studies, but the risk of bleeding has also been well-documented.[1] Because of this risk of bleeding, patients receiving certain types of pharmacologic prophylactic treatment must be monitored closely and must submit to frequent blood tests.[2]

Mechanical

More recently mechanical devices, and in particular pneumatic compression devices, have been recommended for DVT prophylaxis. Mechanical devices include foot and calf pumps, as well as calf and thigh pumps for standard pneumatic compression, rapid inflation compression, or sequential compression.[15] These devices improve circulation and blood flow by distributing variable gradations of pressure on the affected limb.[1] The majority of evidence-based guidelines recommend the use of IPC devices where anticoagulants are contraindicated.[14,16] Many of these guidelines also recommend a combination of IPC devices with pharmacologic treatment, depending on the type of surgery, and for varying duration. [17, 18] Additionally, these devices have demonstrated clinical efficacy in reducing VTE events.[22]

Filters

In select patients who are unable to comply with pharmacologic treatment due to urgent surgery or increased risk of bleeding, permanent or retrievable filters may be implanted in the vena cava. These filters are not intended to prevent DVT. Rather, they are specifically designed to trap blood clots and still permit blood flow. These implants prevent PE in patients who are at high risk of DVT, and are not intended for DVT prophylaxis.

III. Role of Ambulation

The lack of mobility certainly puts a patient at increased risk of developing a DVT, yet published clinical literature and professional society guidelines make clear that the ability to ambulate should not necessitate the removal or discontinuance of prophylactic treatment. In fact, doing so may put the patient at greater risk, given the critical points of developing a DVT.

Published clinical evidence identifies one of the critical post-operative time points to be 40-45 following surgery, which would occur after ambulation regardless of anatomy and surgery type. Other studies demonstrate risk up to 90 days.[19,20] Finally, a study by Hingorani determined that 21% of patients diagnosed with an upper extremity DVT developed acute lower extremity DVTs.[21] For patients who have undergone an upper extremity procedure, ambulation occurs shortly after surgery, yet the risk of experiencing a VTE event (in either an upper or lower extremity) remains great despite the patient's mobility.

Several evidence-based clinical guidelines further support the continued use of DVT-prophylaxis once the patient becomes ambulatory. The American College of Chest Physicians (ACCP) recommends a 10-14 day administration of either chemical prophylaxis or IPD devices in patients undergoing certain orthopedic surgeries. Furthermore, pharmacologic treatment should be extended for up to 35 days from the day of surgery in patients undergoing total hip, total knee or hip fracture surgery. AACP guidelines highlight this critical period during which prophylaxis treatment is particularly crucial and during which the patient is more than likely mobile. Though the American Academy of Orthopedic Surgeon (AAOS) does not make definitive statements as to optimal duration of prophylaxis, they do suggest that patients and physicians fully discuss the duration of prophylaxis. These guidelines also recommend that patients undergo early mobilization following hip and knee arthroplasty, yet nowhere in the guidelines is it suggested that the detailed prophylactic care they prescribe be discontinued once the patient is ambulatory. Thus, early ambulation and use of prophylaxis are not mutually exclusive. Because of these guidelines and because of the lengthy period during which a patient is at risk of developing a DVT, coverage for DVT prophylaxis should not be limited to or dependent upon the patient's immobility.

IV. Introduction to the VPULSE™ System

Overview of the VPULSE™ System

The VPULSE™ System is a single user durable medical device that employs a combination of therapeutic mechanisms considered critical to effective rehabilitation and the prevention of complications associated with DVT. This unique technology is intended for use in reducing post-operative pain and swelling, and to prevent hospital-acquired VTE. The VPULSE™ System provides multiple therapies, including:

- Controlled cold therapy in order to reduce pain and swelling;
- Dynamic pneumatic compression (DPC) to further reduce pain and swelling;
- Intermittent sequential pneumatic compression (IPC), a DVT prophylaxis that prevents hospital-acquired venous thromboembolism

Each of these separate therapies is considered critical in preventing complications and conducting effective post-operative rehabilitation. By combining these treatment modalities, the VPULSE™ optimizes the treatment process for the patient.

Necessity of the VPULSE™ System

The VPULSE™ System fulfills the critical need for postoperative treatment and prevention of DVT, all within one full feature therapeutic set. The risk of developing DVT is greatest between two and five days after surgery, with a second peak development period occurring about ten days after surgery, after the patient has been discharged.

V. Evidence by Anatomy

Overview

The vast majority of clinical literature on VTE prophylaxis is devoted to studying orthopedic surgery involving the hip and knee, so it is not surprising that there is an abundance of evidence-based guidelines discussing prophylaxis recommendations for these procedures. However, as the awareness of the serious risks and costs associated with VTE become more well-known, and as additional clinical publications turn their attention to different parts of the anatomy, this concept of "major surgery" for which DVT prophylaxis is recommended and covered, should be expanded.

Based upon the published clinical literature, as well as an analysis of evidence-based clinical practice guidelines issue by professional societies, "major surgery" should also include shoulder and elbow replacement and hip fracture surgery. Total ankle replacement procedures should also be considered, as the small amount of existing evidence still supports appropriate utilization of DVT prophylaxis in these patients, particularly given the seriousness of this lower limb procedure. Finally, partial knee and partial hip procedures appear to pose a similar danger for DVT/PE as their total replacement counterparts, so that coverage expansion for these procedures may also be warranted.

While the evidence supporting DVT prophylaxis following less invasive arthroscopic procedures is not particularly robust, use of prophylaxis in patients who are otherwise identified as high risk (based on previously outlined risk factors) may still be necessary. Yet surgeon need and anecdotal utilization of prophylaxis following these arthroscopic procedures makes evident the appropriateness of this preventative treatment.

Total and Partial Knee Arthroplasty Procedures

Venous thrombolic disease is the leading factor for hospital readmission following total knee arthroplasty, and is the most common complication associated with this procedure.[22,23] The clinical community generally agrees that the use of various prophylactic regimes is appropriate and necessary given the extremely high incidence of VTE events following total knee arthroplasty. Given the comparable dangers associated with partial or unicompartmental knee replacement, DVT prophylaxis following this procedure may also be appropriate.

Several influential professional societies have issued parallel recommendations for administering prophylaxis following knee arthroplasty. AAOS recently approved new clinical practice guidelines on preventing DVT in patients undergoing elective knee arthroplasty, suggesting mechanical and/ or pharmacologic prophylaxis, and both methods where the patient has previously experienced a VTE event.[24] Patients with a known bleeding disorder are explicitly advised to utilize mechanical compressive devices. While this guideline does not directly address partial knee replacement procedures, AAOS's description of unicompartmental knee replacement identifies blood clots such as DVT as the leading complication associated with procedure, noting that blood thinners can help prevent this serious complication.[25]

ACCP and NICE clinical practice guidelines similarly recommend dual prophylaxis following elective knee arthroplasty. ACCP advises that prophylaxis continue for at least 10-14 days and that pharmacologic treatment continue for up to one month following surgery.[17,18] For patients at risk of bleeding, use of an IPC device is recommended, rather than pharmacologic treatment.[18]

Given the well-documented risk of developing a DVT following knee arthroplasty, the use of prophylaxis is undisputed, and

much of the clinical literature has sought to determine the best method and duration of prophylaxis. In order to determine the actual benefits of prophylaxis, Januel and colleagues meta-analyzed 47 randomized controlled trials and observational studies. The authors concluded that the pooled rates for DVT and PE amongst patients who received VTE prophylaxis following total or partial knee replacement were .63% and .27%, respectively.[35] These incidence rates are quite distinct from the documented 40%-60% of patients who develop DVT without the use of prophylaxis.

Clinical studies and published literature investigating the use of mechanical compression devices have noted the ability of these devices to effectively enhance blood flow in the veins.[22] While a multimodal approach to prophylaxis has been deemed effective by both professional societies and clinical publications[26,27], pharmacologic prophylaxis is undoubtedly linked with increased bleeding complications.[28]

One large meta-analysis sought to determine and compare the efficacy of the various prophylactic regimes. Pooled incidence of DVT was 53% in the aspirin group, 45% in the warfarin group, 29% in the low molecular weight heparin group, and only 17% in the pneumatic compression device group. There were no reported incidences of symptomatic PE in the pneumatic compression group.[29] Two randomized studies have also compared the effectiveness of pharmacologic prophylaxis. Though Blanchard et al's study of 108 patients noted a statistically significant difference in favor of low molecular weight heparin utilization, Tamir and colleagues reported an absence of DVT events for both treatment groups, but found a significant reduction in lower limb swelling and pain in patients treated with the mechanical compression device.[30,31] These high-quality studies demonstrate the effectiveness of IPC devices when used either in conjunction with pharmacologic prophylaxis, or as stand-alone methods of prevention.

Total Hip Arthroplasty and Hip Fracture Procedures

Asymptomatic DVT reportedly occurs in 40%-60% of patients undergoing total hip arthroplasty without subsequent DVT prophylaxis.[9,32] DVT has been shown to be the leading cause of death following total hip replacement.[33] Because of this well-known risk, one supported by a wealth of clinical literature, professional societies and surgeons generally agree that prophylaxis is necessary following this orthopedic procedure. What is slightly less robust is the benefit of prophylaxis amongst patients undergoing partial hip replacement and hip fracture procedures. Because these procedures appear to pose similar danger for developing DVT and PE, coverage for prophylaxis following partial hip replacement and hip fracture procedures should be permitted.

Both AAOS and the ACCP directly recommend pharmacologic or mechanical compression devices for patients undergoing elective hip arthroplasty.[24,34] AAOS recommends a multimodal prophylactic strategy, particularly where the patient has experienced a previous VTE.[24] ACCP advises use of dual prophylaxis for patients undergoing major orthopedic surgery, defined as total hip arthroplasty, total knee arthroplasty and hip fracture surgery. Both societies advise that patients with a known bleeding disorder use mechanical compressive devices for prevention. While AAOS does not make definitive statements regarding duration of prophylaxis, or optimal prophylaxis strategies, ACCP is more detailed as to these issues. Specifically, patients undergoing total hip replacement are instructed to receive prophylaxis for 10-14 days, with pharmacologic treatment extended for up to 35 days from the date of surgery. Furthermore, only the use of portable, battery-powered IPC devices capable of recording daily wear time is recommended for inpatients and outpatients.

These influential society positions echo recommendations issued by the National Institute for Health and Clinical Excellence.[17] NICE guidelines specifically advocate for combined VTE prophylaxis (mechanical and pharmacologic methods) for patients undergoing elective hip replacement. Like ACCP, these guidelines recommend that pharmacologic treatment be continued for 28 to 35 days. Notably, NICE has issued identical recommendations for patients undergoing hip fracture surgery.[17]

The clinical literature unequivocally supports DVT prophylaxis following major hip procedures. Given the well-known risk of developing a DVT following these orthopedic procedures, much of the published literature is more focused on examining the effectiveness of particular prophylactic methods, rather than studying incidence rates of DVT without the use of this life-saving treatment.

One large meta-analysis of randomized clinical trials and observational studies proposed to estimate VTE event rates prior to discharge in patients who received recommended anticoagulant prophylaxis following total or partial hip replacement. The authors pooled rates of symptomatic DVT and PE and concluded that approximately 1 in 200 patients undergoing "TPHA (total or partial hip replacement) develop symptomatic VTE when using pharmacologic prophylaxis. [35] This figure is easily contrastable with the 40%-60% incidence rate reported without the use of prophylaxis. Notably, the meta-analysis did not distinguish partial from total hip replacement procedures, lending support to the belief that the dangers associated with the two procedures are comparable.

While several studies have compared the various methods of prophylaxis in an attempt to identify an optimal treatment strategy, the ideal agent for prophylaxis has not been ascertained.[36] While Lieberman's review of the literature asserts that anticoagulants are the more effective form of prophylaxis following hip arthroplasty, other studies have demonstrated that intermittent pneumatic compression devices are just as effective in preventing VTE.[36,37] Woolson's evaluation of 289 patients' post-opera-

tive experiences with IPC devices following total hip arthroplasty demonstrated a 6% incidence of proximal DVT, as well as a complete lack of any clinically detectable PE or major bleeding complications. Intraoperative and post-operative IPC utilization was deemed effective in preventing VTE, with prevalence rates similar to those reported for pharmacologic prophylaxis, but without the risk of major bleeding complications.[37]

One randomized clinical trial directly compared the safety and effectiveness of pharmacologic prophylaxis with mechanical compression devices following total hip replacement.[38] DVT was detected in 3% of patients utilizing the foot pump and 6% of patients receiving chemical prophylaxis. Patients randomized to the foot pump treatment group also experienced significantly fewer soft-tissue and bleeding complications.[38] These high-quality findings confirmed the safety and effectiveness of mechanical prophylaxis following hip replacement surgery.

The published clinical literature investigating hip fracture surgery supports AAOS, ACCP and NICE evidence-based guidelines recommending various forms of prophylaxis for patients undergoing this procedure. Yen and Weiss's analysis of pharmacologic prophylaxis compared effectiveness of this prevention method following certain knee and hip procedures.[39] The incidence of DVT development was comparable in patients undergoing total knee replacement, total hip replacement and hip fracture surgery, as were rates of pulmonary embolism. Mehta and his colleagues studied over 400 patients admitted to their facility for hip fracture surgery.[40] Nearly all patients received mechanical prophylaxis, while 37% also received pharmacologic prophylaxis. Symptomatic VTE developed in 13 patients and, while eight patients developed bleeding complications, none of the patients experienced complications related to the pneumatic calf pump.[40] Investigators concluded that mechanical prophylaxis is an appropriate method of prophylaxis in patients undergoing hip fracture surgery.

Shoulder and Upper Extremity Procedures

The incidence of pulmonary embolism caused by upper extremity thrombosis reportedly ranges from 12% to 36%, with a reported 16% of cases resulting in fatalities.[41] Despite these rates, most patients in the U.S. do not routinely receive prophylaxis when at risk for upper extremity DVT.[42] Though the majority of clinical literature investigating incidence of DVT and use of prophylaxis has focused on the knee and hip joints, more recently professional societies, surgeons and clinical investigators have turned their attention to the shoulder and elbow joints, as well as other upper extremity procedures.

Although the National Institute for Health and Clinical Excellence (NICE) 2010 Clinical Guidelines recommend against routinely offering VTE prophylaxis to patients undergoing upper limb surgery, patients undergoing a surgery longer than 90 minutes, or who have otherwise been determined to be at an increased risk of VTE based upon stated risk factors, may appropriately be prescribed a combination of mechanical and pharmacologic prophylaxis.[17]

In contrast, AAOS's 2009 guidelines on treating osteoarthritis of the shoulder joint directly recommend utilizing DVT prophylaxis for patients undergoing shoulder arthroplasty.[43] The guideline advises that physicians use perioperative mechanical and/or pharmacologic prophylaxis to prevent VTE for the treatment of shoulder arthroplasty patients, unless the risk of bleeding outweighs the risk of VTE. Though the published clinical evidence is somewhat scarce, AAOS believes that mechanical prophylaxis for shoulder arthroplasty patients intra-operatively and immediately following the procedure places minimal additional risk or discomfort and may ultimately help prevent the "potentially catastrophic" complications associated with DVT.[43]

There has been a recent surge in clinical publications examining rates of DVT and use of prophylaxis following upper extremity procedures and shoulder arthroplasty in particular. Several of these studies have noted incidence rates comparable to those associated with hip and knee procedures, which are currently prophylactic-controlled.[44,45] In fact, Willis et al's prospective observational study of 100 prosthetic should replacement surgeries (total and hemiarthroplasty) reported a DVT prevalence of 10.0% at two days following surgery, and 6.0% at week 12, for an overall prevalence of 13.0%.[44] Nonfatal pulmonary embolism occurred in 2.0% and one fatal PE incidence was reported.

Though one international database review found extremely low incidence and mortality rates, the majority of published literature noted incidence rates high enough to warrant a recommendation that prophylaxis be prescribed.[46] Smith et al's systematic review of upper extremity deep vein thrombosis noted the highest incidence rates following shoulder surgeries and concluded that, although a less common complication, the severity of DVT complications warranted a patient-specific assessment by the treating physician as to the appropriateness of prophylaxis.[41] Lyman's retrospective database review specifically compared hospital admission for DVT following shoulder, hip and knee arthroplasties. The frequency of DVT was 5.0 per 1,000 patients (shoulder), 15.7 per 1,000 (hip) and 26.9 per 1,000 (knee). [47] Though rates of VTE complications were lower following shoulder arthroplasties, a greater percentage of these complications were pulmonary embolism, highlighting the need for prophylaxis following shoulder arthroplasty.[47]

Additionally, upper extremity DVT has been associated with coexistent lower extremity DVT. Hingorani's prospective examination of patients found that 21% of patients diagnosed with an upper extremity DVT developed acute lower extremity DVTs, and an additional 5% developed a thrombosis at a later follow-up date.[21]

These case reports and more recent studies suggest that DVT following upper extremity arthroplasty is not as rare as previously thought and necessitate the conclusion that DVT prophylaxis may be appropriate following these procedures.[48] Given the severe consequences associated with DVT, as well as the frequent coexistence of upper and lower extremity DVT, it is imperative that coverage be expanded so that complications and fatalities can be prevented through appropriate use of prophylaxis.

Arthroscopic Shoulder Procedures

Arthroscopy is one of the most commonly performed orthopedic procedures.[49] Yet published evidence documenting the incidence of DVT following arthroscopic shoulder surgery is less abundant, thereby explaining the lack of clinical guidelines advising clinicians to utilize DVT prophylaxis after these procedures. The few clinical articles published on this specific part of the anatomy are mindful of the potentially fatal consequences of DVT, but all state that the occurrence of DVT following shoulder arthroscopy is less common that rates following certain well-studied orthopedic procedures. [50,51,52]

Kuremsky's case series attempted to identify incidence and risk factors associated with thromboembolic phenomena after shoulder arthroscopy by way of a retrospective database review over a five-year period. Of the 1,908 patients who underwent shoulder arthroscopy, only six patients experienced either a DVT or a PE following shoulder arthroscopy, with no deaths documented over this five year period.[50] The authors did note that DVT lesions occurred on the operative side and that three were upper extremity lesions and two were lower extremity lesions. Despite the potentially fatal consequences of VTE, this study found only a .31% reported incidence.[50]

A recent literature review reiterated the rareness of DVT after shoulder arthroscopy, noting the nonexistence of guidelines recommending the use of DVT prophylaxis. [52] Based upon two case series and a literature review, and noting that the number of patients undergoing arthroscopic procedures will likely increase, the authors concluded that additional clinical studies are necessary to determine the true risk of VTE, but urged clinicians to consider anti-coagulant treatment in higher risk patients.

Complications following arthroscopic shoulder surgery are less documented in the literature, but consequences are undoubtedly serious. Pharmacologic prophylaxis in higher risk patients may help prevent thromboembolic complications. [51,52] Additionally, anecdotal evidence describing surgeon need and reported utilization demonstrate the need for coverage expansion of DVT prophylaxis following arthroscopic shoulder procedures.

Anterior Cruciate Ligament Knee Procedures

Anterior cruciate ligament (ACL) surgery involves either the repair of a torn ACL through suturing, or the removal of a torn ACL and subsequent reconstruction of the ligament using a tissue graft replacement. These procedures are typically performed arthroscopically, and involve small incisions and a shorter surgery time.[53]

The incidence of DVT following arthroscopic ACL procedures has been studied fairly frequently, with some variance in reported rates.

Arthroscopic Knee Procedures

The incidence of deep venous thrombosis (DVT) in patients undergoing knee arthroscopy is reported to be 0.6% to 17.9% depending on the diagnostic method used. [54] Many of the evidence-based clinical practice guidelines do not directly address DVT prophylaxis following arthroscopic knee procedures. Those that do address this issue typically advise against the routine use of thromboprophylaxis, unless the patient has had a prior DVT or is otherwise considered at high risk.[18] The evidence stemming from clinical literature does not reach a definitive conclusion regarding the need for DVT prophylaxis subsequent to knee arthroscopy, but surgeon experience suggests the need for this preventative care.

Ramos and his colleagues sought to assess the safety and effectiveness of thromboprophylaxis in reducing the occurrence of DVT in patients undergoing knee arthroscopy. Selection criteria included all types of interventions used in preventing DVT. The relative risk of thrombotic events was determined to be 0.16% when comparing low molecular weight heparin versus placebo. No strong evidence was found to conclude that thromboprophylaxis was effective in preventing thromboembolic events for people with unknown risk factors for thrombosis.[54]

Egermayer's review of over 10,000 arthroscopic knee procedures noted a similarly low incidence rate, reporting an overall complication rate of 1.68%, with 6.9% of these complications clinically recognized as a thromboembolic disease. [55] This equated to a total incidence of thromboembolic events of.0012%, with an "un-measurably small" mortality rate. In contrast, the mortality associated with pharmacologic treatment was 1 per 1,000 and 5 per 1,000 when IV anticoagulation treatment was used, prompting the author's conclusion that the risks associated with prophylactic treatment seemed greater than the risk of developing DVT.[55] This conclusion was more recently countered by Flanigan and his colleagues, who retrospectively evaluated complication rates amongst 20 patients who had undergone arthroscopic procedures (10 knees and 10 shoulders) and had been administered anticoagulants.[49] None of these patients experienced serious bleeding complications, and no VTE events were reported.

Other studies have reported significantly higher incidence rates than those reported by Ramos and Egermayer. Delis et al studied 102 patients who underwent elective unilateral knee

arthroscopy without active prophylaxis.[56] His findings revealed ipsilateral calf DVT in 7.8% of patients, with higher risk noted in patients with previous thrombosis (relative risk of 8.2) and with two or more risk factors for DVT (relative risk 2.94). A Level II meta-analysis reporting on patient populations not receiving DVT prophylaxis reported incidence rates between 3.1% and 17.9%, while the incidence rate of proximal DVT ranged from 0 to 4.9%.[57] Combining the six studies yielded a total DVT incidence of 9.9% following knee arthroscopy, and a proximal DVT incidence of 2.1%.

Because of the range in incidence rate, as well as the general scarcity of clinical literature available for this part of the anatomy, documented surgeon experience and utilization of prophylaxis are particularly influential in this context. Given the frequency with which arthroscopic procedures are performed, and the reported surgeon experience with DVT prophylaxis following arthroscopic knee procedures, payors should consider extending coverage for this surgical procedure.

Foot and Ankle Procedures

There is a lack of published clinical literature documenting the effectiveness of DVT prophylaxis following certain foot and ankle procedures. While DVT is a possible complication following ankle arthrodesis, no clinical publications were identified that specifically investigated issues related to prevalence or prophylaxis effectiveness. The existing publications related to total ankle arthroplasty have sought to determine the incidence of VTE among this select group of patients, reporting variant incidence rates. As with arthroscopic procedures, anecdotal physician experience with prophylaxis following foot and ankle procedures will help support the existing clinical literature.

Barg and his colleagues aimed to determine DVT incidence amongst 701 ankles undergoing total ankle replacement. All patients received pharmacologic prophylaxis, yet 3.9% developed symptomatic DVT.[58] Barg concluded that the incidence of symptomatic DVT following total ankle arthroplasty and use of anticoagulants was comparable to that in patients undergoing total knee or hip replacement.

Martin and Hardy's literature review cited to the lack of data on DVT incidence and VTE prophylaxis usage following foot and ankle surgeries, and ultimately sought to provide useful information for foot and ankle surgeons.[59] The authors noted the significant dangers associated with VTE, stating that untreated proximal DVT has a 40-50% rate of pulmonary embolism and that 10% of proximal DVTs massively or fatally embolize. However, this review identified the higher frequency of DVT following knee and hip surgery as compared with incidence rates of 3.5% and mortality rates of .037% following foot and ankle procedures.[60,61]

These disparate findings still highlight both the significance of ankle joint surgery and the seriousness and grave consequences associated with DVT. The actual preventative actions taken by foot and ankle surgeons supplement the findings in these clinical publications and provide support for increased coverage of DVT prophylaxis following total ankle arthroplasty.

V. Health Economics Considerations

Cost of Adverse Events and Resource Utilization

Circulatory diseases, including heart disease, stroke, and DVT, are the most common reason for hospital admission, other than pregnancy.[62] Though two-thirds of VTE episodes are nonfatal, these incidences still result in hundreds of thousands of hospitalizations annually, which carry associated costs ranging from $3,000 to $10,000 for DVT and up to $20,000 for pulmonary embolism.[63,64] The cost to a health plan of patients experiencing DVT has been estimated at over $10,000, with costs increasing by 30% over the six month period following discharge.[65]

According to AHRQ's Healthcare Cost and Utilization Project, "thrombophlebitis, phlebitis and thromboembolism" result in 155,900 hospitalization stays, averaging 5.2 days per stay and costing facilities an aggregate $2.2 billion each year.[66] A second study reported a 22% increase in average number of outpatient visits and a 74% increase in average number of emergency room visits for patients experiencing DVT following discharge.[67]

The impact of DVT on resource utilization is significant and highlights the need for prophylactic treatment, and particularly treatment that may be administered outside of the facility setting.

Cost-Effectiveness Analyses

Discharging patients from the hospital without prophylaxis, even when no additional risk is present, is not cost-effective.[36]

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