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Efficacy of Eliquis Administration v Lovenox Administration in Postoperative Care for Total  
Knee/Hip Replacement

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### Abstract

In 2005, the number of individuals who received total hip replacement was 285000 while those who received total knee replacement were 523000.<sup>[21]</sup> It is expected that approximately 4 million patients will require total knee and hip replacement by 2030 and this calls for better postoperative management practices. In hip and knee replacement surgeries, if a thromboprophylaxis procedure is not carried out, the prevalence of deep vein thrombosis is 18 – 36% in hip replacement and 5 – 22% in knee replacement (Zachary, 2013). The prevalence of pulmonary embolism in the same treatment scenario is 0.9 – 28% after hip replacement and 1.5 – 10% after knee replacement. Various methods of prophylaxis reduced the number of VTE cases post total arthroplasty. For decades, physicians have used only low molecular weight heparins and mechanical methods to prevent thromboembolism. However, this does not resolve the problem as the complications still occur in 1.3 – 10% of patients who receive the operation. In the recent past, the pharmaceutical companies have produced an anti-Xa inhibitor known as Apixaban which is marketed as Eliquis. A 2482 patient trial indicated that 73 of the 829 patients (8.8%) who took a placebo died. However, there were only 14 of the 840 patients<sup>[2]</sup> (1.7%) who died in the group that received 2.5 mg of Apixaban and 14/813 in 5mg Apixaban. This shows that the anticoagulant is significantly effective in reducing VTE post-arthroplasty.

Keywords: Eliquis [Apixaban], Lovenox [enoxaparin], efficacy, Safety, Deep Venous

Thromboembolism

## INTRODUCTION

Hip and Knee complications affect thousands of patients in the United States. In 2005, the number of individuals who received total hip replacement was 285000 while those who received total knee replacement were 523000 (Zachary, 2013). The general demographical tendencies for developing economies show an aging population. Older people are more vulnerable to accidents and illnesses that require knee and hip replacements.<sup>[21]</sup> With the current aging trends, it is expected that approximately 4 million patients will require total knee and hip replacement by 2030 (Zachary, 2013). The prognosis of such a huge segment of the population is important to the healthcare system. This makes the management of postoperative management practices after total knee/hip arthroplasty essential.

The majority of complications after arthroplasty procedures are likely to occur post-operation, especially when switching care and medication. Venous thromboembolism (VTE) is established as one of the greatest cause of mortality in both cases of knee and hip replacement (Zachary, 2013).<sup>[28]</sup> In an attempt to resolve this challenge, numerous anti-coagulation techniques have been approved through the Food and Drug Administration (FDA) authority. This paper intends to analyze the performance of two anticoagulants so as to determine the best standard practice for post OP for knee and hip replacement procedures.

### Problem Statement

The number of mortalities resulting from venous thromboembolism (VTE) has remained the approximately the same for about two decades. This stagnation is contrary to the expectation that advances in medicine would result in a decline in any disease related mortalities. It alludes to the fact that newer medicines do not increase efficiency in resolving coagulation problems. Additionally, previous methods have been administered in intrusive ways and therefore raising

demand for orally administered drugs. Apixaban, which is sold as Eliquis, is one of the new anti-coagulation medications that are prescribed for (VTE) Prophylaxis.

### Background

Coagulation to prevent blood loss during surgeries can cause complications after surgery. Patients are therefore often offered some sort of prophylaxis to counter these effects. In hip and knee replacement surgeries, if a thromboprophylaxis procedure is not carried out, the prevalence of deep vein thrombosis is 18 – 36% in hip replacement and 5 – 22% in knee replacement (Zachary, 2013). The prevalence of pulmonary embolism in the same treatment scenario is 0.9 – 28% after hip replacement and 1.5 – 10% after knee replacement (Zachary, 2013). These complications result in up to 2% fatality rates in patients who receive total hip/knee replacement (Zachary, 2013). To manage these complications, physicians administer anticoagulants. This can be either low molecular weight heparin (LMWH) regimens, unfractionated heparin – UFH) which are rapid-onset parenteral anticoagulants or the direct oral anticoagulant (DOAC). Apixaban (Eliquis) is one of the anticoagulants administered orally. The decision to prescribe a particular anticoagulant is determined by various factors. Although anticoagulants perform an important task, the improper administration can lead to fatal hemorrhaging in the patient. Some of the factors that are checked when administering these drugs are therefore safety and efficacy, ease of administration, required special procedures and the expected results. These factors are checked against the cost-effectiveness of a drug so as to determine whether its use is viable.

### Purpose

The purpose of the research is to determine the gold standard procedure for postoperative care in patients recovering from total knee or hip arthroplasty. In specific, the paper aims to compare the efficacy of Eliquis which is also known as Apixaban and Lovenox known as enoxap-

arin. To do this, the article will compare various factors such as the two regimens efficiency, cost, and ease of use, the results, safety and complications. The ultimate goal is to establish the drug that ensures a better prognosis for arthroplasty patients between Eliquis and Lovenox.

#### The Nature of the Project

This project would be carried out through a systematic literature review. A cross-section of previous literature was selected for analysis. The criteria for choosing relevant articles were publication date [between 2013 – present], peer-reviewed and published in medicine or scholarly journal and relevance of content.

#### Research Question(s)

1. Should healthcare institutions use an Eliquis anticoagulant for postoperative care in patients who have had total hip or knee arthroplasty so as to prevent DVT and PE?
2. What are advantages and limitations of using Eliquis, Lovenox and aspirin anticoagulants in post OP for knee or hip surgery?

P= Patients in postoperative care for total knee/hip replacement.

I= Administration of either Eliquis (Apixaban) or Lovenox (Enoxaparin)

C= Patients who received Eliquis vs. Patients who received Lovenox treatment.

O= the more recent Eliquis has better anticoagulation effects and more effective in preventing the development of DVT and PE than Lovenox after total knee/hip replacement surgery.

#### Summary

Venous thromboembolism (VTE) is a major concern during postoperative hip and knee replacement management. It causes up to 2% mortality rates amongst these patients. Various treatment methods have been commissioned by FDA as methods of reducing the chances of

these complications. However, 1.3 – 10% of patients who undergo total knee and hip replacement experience the complications. Considering the number of patients who undergo the procedure annually, this is a significant number of mortality rates. There is still need for research into proper management practices for patients recovering from the surgery. Among these practices include administration of Apixaban or enoxaparin which are discussed in this article.

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## LITERATURE REVIEW

### Introduction

#### 1. Historical Overview

Historically, methods used to prevent venous thromboembolism can be divided into two. There are mechanical methods on one hand and pharmacological interventions. Mechanical methods include special stockings, foot pumps and either continuous or intermittent compression devices. The pressure exerted by these devices results in an increased velocity of blood in the limbs and therefore prevents thromboembolism after hip/knee arthroplasty. These methods are usually advantageous because they have very low monitoring requirement and do not pose any threat to hemorrhaging of the patient. They are also non-intrusive and therefore desirable. However, the methods are not cost effective especially on a large-scale operation.

Pharmacological interventions, on the other hand, can be easily administered to a larger population. For decades, the only pharmacological option has been unfractionated heparins and LMWH. Among LMWH's administered is enoxaparin. These anticoagulants work by preventing the circulation of the formed thrombi. However, the drugs are not able to break down the clots that have already been formed (Nutescu, Burnett, Fanikos, Spinler & Wittkowsky, 2016). The bioavailability of enoxaparin for anti-Xa activity is usually 100% after about 3 to 4 hours of administration (Nutescu, Burnett, Fanikos, Spinler & Wittkowsky, 2016). After the action, the drug is eliminated through depolymerization and desulfation by the liver. This results in particles with lower molecular weight and therefore lesser bioactivity in the body. Up to 10% of enoxaparin is excreted through renal systems and may accumulate in case of renal failure.

Apixaban, on the other hand, has a bioavailability of up to 50% (Nutescu, Burnett, Fanikos, Spinler & Wittkowsky, 2016). It is easily absorbed through the stomach and the intestines. It

reaches the maximum concentration in between 1 – 3 hours. The concentration of Apixaban in the patient's circulatory system is determined by the administration of anti-Xa factor assay that is prepared with HemosIL Liquid Heparin kit (Ikeda & Tachibana, 2016). This will determine whether an additional dose of the drug is required. This is a Xa-dependent chromogenic assay which works by measuring the amount of unstructured LWMH available (Ikeda & Tachibana, 2016).

## 2. Current Findings

The administration dosage for enoxaparin is 40mg administered once in a day. Apixaban, on the other hand, is administered 2.5mg 2 times every day. Both enoxaparin and Apixaban have a considerably high level of effectiveness. However, Apixaban has been proven to be more effective compared to enoxaparin in both safety and reduction of DVT and PE occurrences after total arthroplasty (Solayar & Shannon, 2014). Budhiparama et al., find that Eliquis administered at 2.5 mg twice daily was the most effective dosage (Budhiparama, Abdel, Ifran & Parratte, 2014). This dosage performed much better than a 40 mg dosage of enoxaparin administered once a day (Budhiparama, Abdel, Ifran & Parratte, 2014). However, there was not much difference in the results of patients who received 2.5 mg of Apixaban and those who received 30 mg of enoxaparin twice a day (Budhiparama, Abdel, Ifran & Parratte, 2014). Apixaban should be administered for 12 days for individuals who have undergone knee replacement and 35 days for a hip replacement and should be started between 12 – 24 hours after the surgery completion (Sunkara et al., 2016). The effectiveness of anti-Xa treatments was unfortunately restricted to the prevention of deep vein thrombosis. Other complications that result from total hip/knee arthroplasty such as pulmonary embolisms, wound infections and mortality rate remained constant. Enoxaparin is administered through an intravenous injection while Apixaban is administered through direct

oral administration. In ease of use, it is, therefore, easier to interact with Eliquis than Lovenox.

Non-intrusive medications are always more preferable to intrusive counterparts.

However, increased effectiveness is often an indication of the increased level of complications. The main complication that is associated with Apixaban is excessive bleeding. In case of a hemorrhage onset during the administration of the drug, it is not understood how the process can be stopped. The drug is also not favorable to individuals with any hepatic problems. Sunkara et al., (2016) write that the medication dosage should be adjusted in patients who have mild hepatic impairments (Sunkara et al., 2016). The drug should be avoided altogether in patients who have moderate to severe renal challenges. The treatment regimen is also deemed to be harmful, during pregnancies (Sunkara et al., 2016). The HWM particles are very small. These particles can pass through the placenta and impact gravely on the development of the child. Apixaban poses risks to an individual with a BMI that is greater than  $40\text{kg/m}^2$  and anyone who is above 120kg (PINEO et al., 2013). Such individuals are more likely to experienced increased excessive bleeding. The drug is only partially eliminated through the kidneys [about 27%]. However, this means that it can accumulate in people who are suffering from renal failure and therefore cause more damages. 1% of the individuals also experience allergic reactions such as skin rashes and edema.

For enoxaparin, the main complication is extended duration for the healing of the fracture. It is also known to cause thrombocytopenia and osteoporosis when the use is extended. Enoxaparin also has a risk of increased bleeding. When evaluated for safety, it was discovered that Apixaban had a reduced risk of bleeding as compared to enoxaparin (Hur et al., 2017). Aspirin is also used in VTE prevention. Aspirin prevents the body from forming of thromboxane. This is a necessary ingredient to the bonding of platelets in blood clotting. One of the reasons for

the extensive use of aspirin is that it is tolerated by a wider segment of the population. It, therefore, requires minimal monitoring. It is administered orally and is therefore non-intrusive (Hur et al., 2017). Although it is deemed just as effective when used alone, it is advocated to use it in conjunction with other prophylaxis medication. In most cases, it is used alongside an LMWH such as enoxaparin. Agaba et al (2017) demonstrated that it is aspirin causes the highest level of bleeding for post OP care for arthroplasty among the other anticoagulant drugs. Previous research has demonstrated that aspirin slows down wound healing processes. This is as a result of its interaction with keratinocytes by slowing their migration which reduces the speed of wound healing. This causes wounds to drain longer and therefore longer hospital stays after total knee/hip arthroplasty. According to the same rescue, the results indicate that Apixaban, also known as Eliquis is the best in reducing VTE.

The cost of a 30mg/0.3ml dosage of Lovenox is approximately \$268 for a 3ml supply ("Prices and Coupons for Lovenox", 2018). This is approximately 26.8 dollars per administration syringe. Eliquis costs approximately \$446 for 60 tablets of the 2.5mg dosage ("Prices and Coupons for Eliquis", 2018). This is approximately 8 dollars per 2.5mg tablet. The latter drug is therefore much more expensive. None of the medication requires any special procedures. The expensive nature of Apixaban can serve as a deterrent towards its use. However, this is misleading. The additional cost can be easily mitigated by the reduced hospitalization and better health-related quality of life (HRQoL) after the arthroplasty. The reduced hospital stay reduces the overall medical expenditure for the procedure. Improved HRQoL renders the patient more productive after the surgery and therefore counters the additional cost of the drugs. The Unit should always target better prognoses for its patients. For this reason, the financial implications of more expensive but more effective medication should be ethical and applicable.

## Cases

In a trial, 2486 patients were tested on the safety and efficacy of Apixaban. Of these 2482 were included in analyzed results. The results indicated that 73 of the 829 patients (8.8%) who took a placebo died from symptomatic recurrent VTE (Agnelli et al., 2013). However, there were only 14 of the 840 patients (1.7%) who symptomatic recurrent VTE mortalities in the group that received 2.5 mg of Apixaban (this gives a 7.2 percentage difference which is significant at a confidence interval of at 95%) and 14 of the 813 patients symptomatic recurrent VTE mortalities in patients receiving 5mg of Apixaban dosage (Agnelli et al., 2013). There was major bleeding occurring in 0.5% of the patients who received the placebo, 0.1% of the patients who received 5-mg Apixaban v 0.2% of the patients who received 2.5-mg (Agnelli et al., 2013). There was minor but clinically significant bleeding in 3.0% of the patients who received 2.5-mg group, 2.3% of the patients who received the placebo group and 4.2% of the patients who received 5-mg (Agnelli et al., 2013). This research shows that Apixaban reduces the risks associated with post-operative VTE and also reduced the risk of over bleeding.

The test to determine the efficacy of enoxaparin was conducted using 604 patients. 194 patients were given 30 mg dose twice daily 9 of 194 patients (4.6%) still got VTE (Colwell, 2018). This happened in 30 of 203 (14.8%) patients when a 40 mg dose of enoxaparin was administered once daily. When the patients received UFH (11.6%), VTE occurred in 24 out of 207 (Colwell, 2018). This shows that 30 mg dose was safer than the other choices of dosage. In the case of bleeding, 8.7%, 8.2% and 5.7% bleeding episodes were recorded in patient/s who received 40 mg enoxaparin once daily, 30 mg enoxaparin twice daily and UFH, respectively (Colwell, 2018). This study showed reduced VTE occurrence after administration of enoxaparin but with a corresponding increase in chances of bleeding.

### Conclusion

With reference to the research above, it can be concluded that Apixaban, which is sold as Eliquis should be the gold standard for the management of postoperative therapy after total knee or hip replacements. Currently, doctors still advocate for the use of enoxaparin. This has probably been as a result of little understanding of the complications that are associated with using Apixaban. However, with increased management techniques, it is becoming easier to predict any negative responses and respond to them. When all the complications are understood and addressed, the selection criteria should move towards the pure effectiveness of the drug.

### Recommendations

The post OP care unit for patients recovering from total hip and knee arthroplasty should administer Eliquis instead of Lovenox. Research has demonstrated that Apixaban is more effective in preventing DVT and PE than enoxaparin. Additionally, the drug has higher safety levels. The only inhibiting factor might be cost-effectiveness. However, the use of a more effective drug reduces hospitalization and increases HRQoL. The latter increases a patient's productive life post-surgery. A patient's well-being is the primary concern of the physician and therefore evidence that Eliquis is better should encourage its use.

Health facilities should work with pharmaceutical companies producing Eliquis, to enhance the benefits of scale related to production and hence enable them to reduce the cost of the medication.

More research should be advanced towards solving the complications and contraindications that are associated with the administration of Apixaban. Research should also include increasing efficiency in the drug production so as to make it cheaper for patients.

The unit should conduct a staff sensitization program on the benefits of replacing Enoxaparin with Apixaban and the modes of administration. This will reduce resistance among the staff.

Patient education on the benefits of using Apixaban and the particulars of self managing its administration should be conducted on patients.

The unit should produce manuals for use by the nurses, caregivers and the patients to ensure that proper dosages are given to patients. These manuals should be pinned in public places.

The unit should dedicate some of its resources to research development in the field of post-arthroplasty anti-coagulation medicine to ensure better care in the future.

#### Summary

In summary, this article finds that both enoxaparin and Apixaban have multiple benefits and multiple side effects. However, when the efficacy and safety are measured together, Apixaban has the lowest risk. Apixaban is better than enoxaparin in terms of ease of use and effectiveness. Eliquis, the Apixaban anticoagulant is administered as a single dose. This also reduces the burden of monitoring patients significantly. It, therefore, reduces chances of over/under dosing. It is, therefore, a more beneficial drug that should be adopted for use in post OP care for patients with complete knee and hip arthroplasty. Some drawbacks are associated with the drug's cost. However, when this is compared to its effectiveness and safety, it is evident that it is the future of coagulation medicine.

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