Apixaban vs Enoxaparin for Postoperative Prophylaxis: Safety of an Oral Alternative for the Prevention of Venous Thromboembolism

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Postoperative venous thromboembolism (VTE) pharmacologic prophylaxis is recommended for patients with cancer by the American Society for Clinical Oncology (ASCO) and the American Academy of Chest Physicians, as well as in the Gynecologic Oncology Enhanced Recovery After Surgery (ERAS) recommendations.1-3 Malignancy and radical pelvic surgery are known risk factors for the development of VTE, highlighting the distinct need for effective and tolerable prophylactic strategies for women with gynecologic cancers. Deep vein thrombosis (DVT) and pulmonary embolism (PE) are associated with significant morbidity and mortality in this population.4 Recent investigations have demonstrated that prolonged VTE prophylaxis up to 28 days postoperatively in a gynecologic population was associated with fewer VTE events.5 The randomized clinical trial of apixaban vs enoxaparin for postsurgical prophylaxis against VTE in women with suspected gynecologic cancer by Guntupalli et al6 adds valuable data to this emerging practice that may optimize postoperative outcomes for women undergoing gynecologic surgery.

Subcutaneous low-molecular-weight heparin is an established standard that has been extensively studied for preoperative and postoperative VTE prophylaxis in surgical populations.5 A significant limitation to widespread use has been the need for daily subcutaneous injections along with a high cost, leading to decreased patient compliance and satisfaction when compared with oral medication.7 In another trial, oral apixaban (a factor Xa inhibitor) was compared with injectable fractionated heparins for the treatment of VTE in populations with cancer and demonstrated noninferior recurrence rates of VTE.8 These data provide rationale for investigating whether oral factor Xa inhibitors may represent a safe and effective option for the prevention of postoperative VTE that could also improve patient compliance and quality of life.

Dr Guntupalli and colleagues addressed these questions in this 2-site randomized clinical trial of apixaban vs enoxaparin prophylaxis in a postoperative gynecologic oncology population.6 This trial enrolled 400 women undergoing surgery for known or suspected gynecologic malignancies. Once deemed stable following surgery, each patient was randomized 1:1 to either apixaban 2.5 mg orally twice a day or enoxaparin 40 mg subcutaneously daily for 28 days. Primary outcomes demonstrated safety of apixaban prophylaxis compared with enoxaparin; both major bleeding events (0.5% vs 0.5%, respectively; P > .99) and clinically relevant nonmajor bleeding events (5.4% vs 9.7%, respectively; P = .11) were not different between the groups. VTE was assessed for drug efficacy and showed no difference between the groups, with 1.0% in the apixaban group and 1.5% in the enoxaparin arm (P = .68). Importantly, patient satisfaction was significantly higher in the apixaban group compared with the enoxaparin group, 98.9% vs 58.8% (P < .001).

Guntupalli and colleagues’ trial6 provides important and provocative pilot data regarding the practice of extended VTE prophylaxis in a gynecologic oncology surgical population. Given the historically high rate of postoperative VTE noted in these women, it is imperative to explore safe and acceptable prophylaxis options. Patients in the past have demonstrated lower adherence with injectable prophylaxis, and patient preference for an oral medication is clear in the findings of this trial. Notably, this study was done in an unselected surgical population without strict inclusion and exclusion criteria for the types of patients undergoing surgery performed by a gynecologic oncologist. While the broad inclusion criteria limits conclusions about apixaban efficacy for a specific...
oncology indications, this feature makes these data easy to apply in the clinic and could be extrapolated to a broad oncologic surgical population.

These data demonstrate feasibility and likely safety of apixaban for postoperative prophylaxis in women undergoing surgery with gynecologic oncologists. While the very low rate (0.5%) of major bleeding events and postoperative VTE observed in this study suggest safety of both of these prophylaxis choices in this gynecologic oncology population, the unanticipated lack of events makes the trial underpowered to detect any significant differences. The broad surgical case inclusion was likely responsible for the lower observed event rate, and it may be that future trials limited to high risk patients and surgeries may demonstrate differences in apixaban performance. Efficacy is a critical outcome in this population, and because this study was not designed with a primary outcome of efficacy, larger randomized investigations will be required to validate the promising signal observed in this trial.

For women who cannot or will not perform self-injection with enoxaparin, Guntupalli and his colleagues have demonstrated that an alternative, oral VTE prevention strategy with apixaban in the postoperative setting is feasible, and possibly as safe with similar VTE outcomes. As more data are acquired through general use and repeated clinical trials, we are likely to see the emergence of a new standard of care for these women that improves patient satisfaction and may improve compliance. In light of these data, a noninferiority trial designed to assess efficacy of VTE prevention will be required to change standard of care for all women in this patient population, and this study provides the scientific rationale to launch such an investigation.

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REFERENCES