



The use of direct oral anticoagulants (DOACs) for thromboprophylaxis during neoadjuvant chemotherapy and after interval debulking surgery in ovarian cancer patients – Maximizing prevention of venous thromboembolism (VTE)

Venous thromboembolism (VTE) can occur in up to one-fourth of gynecologic oncology patients and can lead to delays in treatment, morbidity, and mortality (Cohen et al., 2017). Therefore, it is important to evaluate when and what type of prophylactic anticoagulation to utilize in these patients. In this month's edition of *Gynecologic Oncology Reports*, there are three manuscripts discussing the importance of thromboprophylaxis for patients with gynecologic malignancies. First, Abdelkhalek et al. described the prevalence and risk factors for the development of asymptomatic VTEs in ovarian cancer patients who underwent interval debulking surgery. (Abdelkhalek et al., 2024). This observational trial included 107 patients with ovarian cancer who received neoadjuvant chemotherapy (NACT) without clinical evidence of VTE. Seven (6.5 %) patients developed an asymptomatic VTE, as documented by bilateral Doppler ultrasound in the pre- and post-operative settings. Interestingly, all seven patients diagnosed with VTE did not have significant medical comorbidities. This study highlights the fact that patients with ovarian cancer undergoing neoadjuvant chemotherapy are at increased risk for VTE.

These results fall in line with increasing data demonstrating the risk of VTE in patients with ovarian cancer. Earlier this year, Shafa et al. described the rates of VTE in patients with advanced ovarian cancer who received NACT (Shafa et al., 2023). Thirty-three of the 154 (21.4 %) patients experienced a VTE. Four (2.6 %) occurred at the time of cancer diagnosis, nine (5.8 %) between cancer diagnosis and initiation of NACT, 13 (8.4 %) between initiation of NACT and interval debulking, and 7 (4.5 %) within 180 days after interval debulking. There were no statistically significant differences in risk factors between patients with VTE and without VTE. The authors concluded that two-thirds of the VTEs could have been prevented with thromboprophylaxis as they occurred between the diagnosis of ovary cancer and interval debulking. These two studies support then use of thromboprophylaxis in patients with advanced ovary cancer undergoing NACT.

Also, in this month's edition, Diamond et al. describe a retrospective cohort study of patients who underwent exploratory laparotomy for a gynecologic cancer at an urban academic medical center (Diamond et al., 2024). The objective was to compare outcomes of patients who received thromboprophylaxis with low molecular weight heparin (LMWH) versus apixaban, a direct oral anticoagulant (DOAC). The primary outcome was a VTE event within 90 days of surgery and secondary outcomes were major and minor bleeding events. Two-hundred and fifteen patients were included in the study; 65 were discharged home on LMWH and 150 on apixaban. There were no significant differences between the two groups. Rates of any VTE event within 90 days of surgery

were similar for apixaban and LMWH (3.3 % vs. 4.6 %, $p = 0.6$). The rate of a major bleeding event was also similar between groups (1.3 % vs. 3.1 %, $p = 0.4$). The authors concluded that apixaban was effective and safe as postoperative VTE prophylaxis in this patient population.

Guntupalli et al. previously published comparable results with the use of apixaban (Guntupalli et al., 2020). This was a multicenter, randomized trial that enrolled 400 patients undergoing surgery for suspected or confirmed gynecologic cancer to either postoperative oral apixaban (2.5 mg twice daily) or subcutaneous enoxaparin (40 mg daily). There was no difference detected in the study's primary outcome of major bleeding events (0.5 % vs. 0.5 %). Furthermore, there was no statistically significant difference reported in radiologically confirmed VTE (1.0 % vs. 1.5 %). Notably, patients in the apixaban group reported significantly higher satisfaction compared with the enoxaparin group, specifically regarding the ease of taking the medication (98.9 % vs. 58.8 %, $p < 0.0001$).

Finally, Ketch et al. published a quality mini review on using DOACs for postoperative VTE prophylaxis in patients with gynecologic malignancies (Ketch et al., 2024). Historically, guidelines have recommended 28 days of LMWH or unfractionated heparin for extended VTE prophylaxis after major abdominal and pelvic surgery for gynecologic malignancies. DOACs have emerged as an attractive alternative to injectable anticoagulants. The updated Society for Gynecologic Oncology (SGO) clinical practice statement and the enhanced recovery after surgery (ERAS) guidelines support consideration of DOACs for extended post-operative VTE prophylaxis in patients with a gynecologic cancer (Gressel et al., 2021, Nelson et al., 2023).

These three studies highlight the importance of understanding when to use thromboprophylaxis for VTEs in women with gynecologic malignancies. There seems to be emerging, promising data to support DOACs in these patients and increased utilization may lead to an improved patient experience, higher rates of treatment compliance, and increased cost savings.

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