Postoperative Arterial Thromboembolism Causing Acute Limb Ischemia and Amputation Following Gynecologic Oncology Malignancy Surgery: Presentation of Two Cases

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ABSTRACT

This case report presents two rare cases and aims to highlight arterial thromboembolism (ATE) as a rare but potentially devastating complication following gynecologic oncology surgery. Chronic kidney disease (CKD) has been demonstrated to heighten susceptibility to thrombotic events through a variety of mechanisms, including endothelial dysfunction, uremia-associated platelet activation, impaired fibrinolysis, and systemic inflammation. In addition, other systemic and perioperative risk factors-including advanced age, malignancy-associated hypercoagulability, smoking history, hypertension, atherosclerosis, sepsis, and perioperative hemodynamic instability-may also contribute to the development of arterial thromboembolism. This report presents two rare cases of early postoperative ATE leading to acute limb ischemia, amputation, and death in patients with advanced ovarian malignancy and concomitant CKD.

In the first instance, a 51-year-old female patient was diagnosed with end-stage CKD and required long-term dialysis. She subsequently underwent a surgical procedure for high-grade serous ovarian carcinoma. Severe postoperative ATE manifested on postoperative day 1, rapidly progressing to extensive ischemia. Despite escalating treatment from prophylactic to therapeutic anticoagulation and vasodilator therapy, the patient's condition continued to deteriorate, ultimately resulting in the need for amputation. The patient succumbed on postoperative day 35 due to complications from sepsis and multi-organ failure. In the second case, a 71-year-old woman with advanced-stage CKD (non-dialysis-dependent) underwent primary cytoreductive surgery for ovarian mucinous carcinoma. Bilateral lower-extremity arterial thrombosis developed on postoperative day 2, with absent distal perfusion. Despite aggressive anticoagulation and prostacyclin therapy, thigh-level amputation was necessary, and the patient succumbed on postoperative day 18 due to multi-organ failure.

These cases suggest that CKD may increase susceptibility to postoperative arterial thromboembolism and may be an important predisposing factor rather than an independent causal risk factor. ATE development in this setting is likely multifactorial and should not be interpreted as a direct cause-effect relationship based on two cases. In this high-risk population, ATE may progress rapidly and remain refractory to medical therapy. Early postoperative peripheral perfusion monitoring and multidisciplinary management are essential.

Keywords: Acute limb ischemia; Amputation; Arterial thromboembolism; Chronic kidney disease; Gynecologic oncology surgery; Postoperative complications

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Introduction

Arterial thromboembolism (ATE) following gynecologic cancer surgery is a rare but potentially devastating complication. It may result in acute limb ischemia, amputation, and mortality (1). In contrast to venous thromboembolism, a condition well recognized in oncologic patients, postoperative arterial thrombotic events are far less frequently reported and are mainly described in case reports and small case series (2). However, when such events do occur, they are frequently accompanied by rapid clinical deterioration and limited therapeutic options (1). Therefore, the current evidence is limited and largely hypothesis-generating rather than confirmatory.

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Malignancy-associated hypercoagulability plays a central role in thrombotic complications in gynecologic oncology (3). While this prothrombotic state predominantly predisposes patients to venous thromboembolic events, population-based data also suggest an increased risk of arterial thromboembolism in patients with cancer (4). In gynecologic malignancies, extensive cohort and registry-based studies have delineated the incidence and risk factors for venous thromboembolism (VTE) (5,6). Prophylactic strategies, including those employed during neoadjuvant chemotherapy for ovarian cancer, have also been evaluated (7).

Chronic kidney disease (CKD) has been increasingly recognized as a condition associated with heightened thrombotic susceptibility through multiple mechanisms, including endothelial dysfunction, impaired fibrinolysis, platelet hyperreactivity, chronic inflammation, and accelerated atherosclerosis (8-10). In patients with advanced CKD, particularly those reliant on dialysis, these alterations may contribute to both venous and arterial thrombotic events. However, the contribution of CKD to postoperative arterial thromboembolism in gynecologic oncology patients remains unclear, and the current evidence is limited (3). Accordingly, any proposed relationship should be interpreted as an association rather than a proven independent causal effect.

It is imperative to acknowledge that patients undergoing gynecologic cancer surgery frequently exhibit a multitude of concomitant thrombotic risk factors that extend beyond CKD. These additional risk factors may include advanced age, hypertension, a smoking history, chronic pulmonary disease, malignancy-related hypercoagulability, perioperative sepsis, and hemodynamic instability. Consequently, postoperative ATE is presumably the consequence of a multifactorial interaction rather than a solitary isolated risk factor (4). Thus, arterial thrombotic events in this population are more likely to arise from the combined influence of several systemic and perioperative factors.

In this report, we present two cases of patients with advanced ovarian malignancy and advanced-stage chronic kidney disease who developed fulminant postoperative arterial thromboembolism leading to acute limb ischemia, amputation, and death, despite the absence of pelvic lymph node dissection. The objective of these cases is twofold: first, to underscore the potential role of combined systemic risk factors in the development of postoperative arterial thrombotic events, and second, to emphasize the importance of early recognition and close postoperative vascular monitoring in high-risk gynecologic oncology patients (1,2). These cases are intended to generate clinical awareness rather than to establish causality.

Therefore, this report should be interpreted as hypothesis-generating rather than evidence-establishing, aiming to increase clinical awareness rather than demonstrate causality.

Case 1

A 51-year-old postmenopausal woman with stage 5 chronic kidney disease (dialysis-dependent) and hypertension presented with abdominal distension, anorexia, and symptoms of ileus. The patient's medical history revealed the presence of two non-functional kidneys, a prior renal transplantation that occurred 22 years prior, followed by 10 years of non-functioning of the transplanted kidney. This was subsequently followed by a period of regular dialysis for the last 10 years. The patient reported no history of bleeding or known hereditary thrombophilia. The clinical presentation included abdominal distension, anorexia, and signs of ileus.

Preoperative chest computed tomography revealed no evidence of metastatic involvement. Whole-abdominal dynamic diffusion-weighted magnetic resonance imaging revealed widespread intraabdominal disease and ovarian mass lesions, along with conglomerate lymph nodes surrounding the inferior vena cava and aorta. The patient's tumor markers were elevated, with CA-15.3 at 173.1 U/mL and CA-125 at 468.5 U/mL. Serum creatinine was 3.79 mg/dL. After undergoing anesthesia and consulting with the nephrology department, the patient was deemed to be in a stable condition before undergoing surgery. The patient was informed in detail about the options of primary cytoreductive surgery and neoadjuvant chemotherapy. The patient accepted the risks and opted for primary surgery.

Subcutaneous administration of 4,000 international units of unfractionated heparin was initiated for preoperative prophylaxis against thromboembolism. During the intraoperative period, severe hypotension developed after anesthesia induction and abdominal entry, and norepinephrine infusion was initiated. Due to the high tumor burden and hemodynamic instability, primary debulking could not be performed. The patient underwent a wide omental biopsy, intra-abdominal fluid drainage, and a loop colostomy due to previous ileus symptoms. The frozen section pathology result was reported as high-grade serous ovarian carcinoma. Due to the high risk of morbidity associated with the procedure, the patient was admitted to the postoperative intensive care unit.

On postoperative day 1, the patient exhibited severe pain in the right lower extremity. Prophylactic-dose anticoagulation was continued at that time; on postoperative day 2, marked coldness, pallor, and cyanotic discoloration developed in the right lower extremity. The right femoral artery catheter was subsequently removed. Color Doppler ultrasonography demonstrated intimal thickening and atherosclerotic plaques in multiple arterial segments. Although the vessels were patent, monophasic flow patterns suggested compromised distal perfusion, which may also reflect the known limitations of Doppler imaging in patients with advanced CKD and vascular calcification. On the same day, prophylactic anticoagulation was escalated to therapeutic-dose enoxaparin (1 mg/kg/day) following multidisciplinary consultation with cardiovascular

surgery and nephrology due to progressive signs of acute arterial ischemia. Because therapeutic LMWH use in dialysis-dependent CKD remains controversial and no standardized guidelines exist, this decision was individualized. Vasopressor doses were subsequently reduced, and warming measures were implemented. Concurrently, the C-reactive protein level was 512 mg/L, and an infectious diseases consultation was performed, yielding a preliminary diagnosis of sepsis. Consequently, the treatment regimen was initiated with imipenem and vancomycin. The patient was subsequently placed on continuous veno-venous hemodialysis (CVVHD).

On postoperative day 3, cyanosis manifested prominently in the right lower extremity, which was noted to be cold and pale. Distal pulses were not palpable. Physical examination revealed color change due to ischemia, motor deficit, and sensory loss at the distal phalanx level of the right foot. A palpable pulse was identified in the left lower extremity. Pentoxifylline infusion was initiated. However, acute surgical revascularization was deemed inappropriate by the cardiovascular surgery team, who cited concomitant sepsis and advanced CKD as key factors in this decision. According to the Rutherford classification, the presence of motor deficit, sensory loss, and absent distal pulses was consistent with class IIb–III acute limb ischemia, indicating an immediately threatened or irreversible limb.

On postoperative day 5, transtibial amputation was planned by the orthopedic team due to the demarcation line becoming apparent; however, the surgical procedure was postponed due to the presence of ongoing sepsis and general deterioration. Subsequent clinical follow-up revealed the progression of extremity necrosis.

On postoperative day 7, after achieving partial clinical stabilization, lower extremity CT angiography was performed for further evaluation. Imaging revealed widespread stenosis in the bilateral iliac arteries, multi-level peripheral artery disease, and markedly reduced distal flow. These findings were considered consistent with clinically progressive acute limb ischemia. Consequently, antiplatelet therapy, comprising acetylsalicylic acid and clopidogrel, was initiated, while the ongoing anticoagulation regimen was maintained. Despite multi-level endovascular interventions by interventional radiology, the ischemic damage in the distal tissues remained irreversible.

Despite the implementation of comprehensive care measures and continuous monitoring in the surgical ward, the patient exhibited a progressive clinical degeneration that culminated in death on the 35th postoperative day, due to sepsis and multiorgan failure.

Case 2

A 71-year-old woman presented with clinical and radiological findings suggestive of ovarian malignancy. Her medical history included advanced age, long-term smoking (a duration of 53 years), hypertension, chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD). The patient reported no history of bleeding or known thrombophilia. The patient's surgical history revealed a prior open hysterectomy.

In the preoperative period, the patient's serum creatinine level was measured at 2.32 mg/dL, and the patient was evaluated as having stage 4 CKD (advanced CKD, non-dialysis dependent, not meeting criteria for end-stage kidney disease). No metastatic involvement was observed on chest computed tomography. A subsequent abdominal computed tomography scan revealed the presence of free fluid and septated ovarian mass lesions extending from both adnexal areas to the midline of the abdomen, up to the umbilical level. No pathological lymph nodes were detected in the paraaortic, paracaval, and interaortocaval regions. Colonoscopy and upper gastrointestinal endoscopy showed no pathology. After a thorough evaluation of the clinical and radiological findings, the patient met the criteria for primary cytoreductive surgery.

The patient underwent a series of surgical procedures, including open bilateral salpingo-oophorectomy, total omentectomy, pelvic paracolic peritonectomy, and appendectomy. The intraoperative frozen section result was consistent with primary ovarian mucinous carcinoma. Lymph node dissection was not performed because no lymph node involvement was observed in preoperative and intraoperative imaging. No additional surgical complications occurred during the operation.

On postoperative day 1, the patient exhibited complaints of pain, coldness, and pallor in the right and left feet. A subsequent bilateral lower extremity venous system color Doppler ultrasound revealed patent venous structures with no evidence of thrombus.

On postoperative day 2, a marked temperature difference developed between both lower extremities, accompanied by ecchymotic changes, more pronounced on the right side. Bilateral dorsalis pedis pulses were absent on palpation. Arterial Doppler ultrasonography demonstrated thrombus formation in both superficial femoral arteries with absent flow in the popliteal, posterior tibial, and dorsalis pedis arteries, consistent with acute arterial insufficiency. Contrast-enhanced CT angiography could not be performed due to impaired renal function (serum creatinine 2.78 mg/dL), and the risk of contrast-induced nephropathy was considered prohibitive. On the same day, therapeutic anticoagulation was initiated with enoxaparin (0.8 mg twice daily) following multidisciplinary consultation with cardiovascular surgery and nephrology. Pentoxifylline and iloprost infusion were added as adjunct vasodilator therapies. The patient received analgesia and active limb-warming measures and was closely monitored for acidosis and systemic deterioration. Because anticoagulation strategies in advanced CKD are not standardized, treatment decisions were individualized. Concurrently, inflammatory mark-

ers surged (CRP: 323 mg/L). After consultation with infectious diseases specialists, ceftriaxone was discontinued, and meropenem and linezolid were initiated. A comprehensive orthopedic consultation revealed widespread ecchymosis in both lower extremities, necrotic areas in the anterior-distal region of the right crus and around the lateral malleolus, and limited joint movement and sensory loss in the right ankle.

Subsequent Doppler ultrasonography examinations revealed the presence of thrombus material in the bilateral superficial femoral arteries, triphasic flow patterns proximal to the thrombus, and loss of flow in the distal arteries. The findings were considered consistent with clinically progressive acute limb ischemia. In light of the concomitant advanced CKD, sepsis, and systemic instability, the cardiovascular surgery team determined that surgical or endovascular revascularization was not a suitable course of action. Instead, they recommended continuing the current medical treatment regimen. Based on clinical findings of absent distal pulses, sensory impairment, and progressive tissue necrosis, the presentation was compatible with advanced (Rutherford class IIb-III) acute limb ischemia.

On postoperative day 7, despite intensive anticoagulation and vasodilator therapy, the ischemic findings did not improve. Necrosis progressed in the distal tissues, and a distinct demarcation line developed. Consequently, the patient underwent a surgical procedure involving the amputation of the thigh at the level of the right lower extremity. During postoperative follow-up, the patient's general condition exhibited a progressive deterioration, accompanied by systemic inflammation and multiple organ dysfunction. The patient ultimately succumbed to cardiac arrest on postoperative day 18.

Postoperative Timeline: Postoperative events and timing of therapeutic anticoagulation are summarized in Tables I and II to clarify the relationship between treatment and the progression of ischemic findings.

Table I: *Postoperative timeline of events -Case 1 (dialysis-dependent CKD, stage 5)*

POD 0	ICU admission after surgery; hemodynamic instability	–	Prophylactic UFH (4,000 IU SC) Prophylactic UFH continued	Stable
POD 1	Severe right leg pain	–	Escalated to therapeutic enoxa-	Symptoms progressed
POD 2	Coldness, pallor, cyanosis of right lower limb	Doppler US: patent arteries, monophasic flow, atherosclerotic change	parin (1 mg/kg/day) Pentoxifylline infusion started;	Acute limb ischemia suspected
POD 3	Motor deficit, sensory loss, absent distal pulses	Clinical evaluation consistent with Rutherford IIb–III	Enoxaparin continued; dual antiplatelet (ASA + clopidogrel) added	Limb considered threatened
POD 5	Clear demarcation line	–	–	Transtibial amputation planned but deferred due to sepsis
POD 7	Persistent ischemia	CT angiography: multilevel stenosis, poor distal flow	Medical management continued	Irreversible ischemia
POD 35	Progressive sepsis and multiorgan failure	–	–	Death

Table II: *Postoperative timeline of events – Case 2 (advanced CKD stage 4, non-dialysis)*

POD 0	Uneventful cytoreductive surgery	–	Standard prophylaxis	Stable
POD 1	Bilateral foot pain, coldness, pallor	Venous Doppler: no thrombosis	Prophylaxis continued	Symptoms persisted
POD 2	Absent dorsalis pedis pulses, temperature symmetry, ecchymosis	Arterial Doppler: bilateral SFA thrombosis, absent distal flow	Therapeutic LMWH (enoxaparin 0.8 mg BID) + pentoxifylline + iloprost infusion initiated Medical therapy continued	Acute bilateral limb ischemia
POD 3–6	Progressive necrosis	–	–	No clinical improvement
POD 7	Established demarcation	–	–	Above-knee amputation performed
POD 18	Multiorgan failure	–		Death

Discussion

The two cases under consideration illustrate that postoperative arterial thromboembolism (ATE) can result in acute limb ischemia and amputation in patients with advanced ovarian malignancy and concomitant advanced chronic kidney disease, even in the absence of pelvic lymph node dissection. However, these findings should be regarded as observational evidence suggesting increased susceptibility to arterial thrombotic events in high-risk patient groups, rather than establishing a causal relationship (3). Accordingly, these cases should be interpreted as hypothesis-generating observations rather than evidence of a direct cause–effect association.

Thromboembolic events in gynecological malignancies are predominantly associated with the venous system. Postoperative arterial thrombosis and embolism are reported infrequently in the literature. Levenback and colleagues reported postoperative arterial occlusion and amputation in patients treated for gynecological malignancy. They emphasized that most of these cases had a history of pelvic lymph node dissection or radiotherapy (2).

Similarly, Hamilton and colleagues reported on the development and management of arterial thrombosis in gynecologic oncology patients (11). The absence of lymph node dissection in both cases indicates that ATE development cannot be attributed exclusively to surgical technique. ATE in both patients most likely resulted from a multifactorial process. Therefore, attributing the thrombotic events to a single factor would likely oversimplify the underlying pathophysiology.

Advanced age, long-term smoking, hypertension, chronic obstructive pulmonary disease, malignancy-related hypercoagulability, sepsis, systemic inflammation, hemodynamic instability, and atherosclerotic vascular changes are among the known major risk factors for arterial thrombosis. As indicated by the current literature, the risk of arterial thromboembolism in cancer patients is associated with the following factors (4). Both of our patients exhibited several of these concomitant risk factors in addition to CKD, further supporting a multifactorial mechanism.

Chronic kidney disease induces a prothrombotic state characterized by endothelial dysfunction, platelet hyperreactivity, decreased fibrinolytic activity, oxidative stress, and chronic inflammation (8,9). Furthermore, accelerated atherosclerosis and vascular calcification in chronic kidney disease patients may impair peripheral perfusion, leading to more severe arterial thrombotic events (10). Consequently, chronic kidney disease should be regarded not as an independent risk factor, but rather as a significant predisposing condition that may amplify vulnerability to arterial thromboembolism in combination with other systemic and perioperative risks.

An important observation is the discrepancy between clinically progressive ischemic findings and Doppler ultrasonography results. The sensitivity of Doppler ultrasonography may be constrained, particularly in individuals with advanced kidney disease, due to widespread vascular calcification and microvascular perfusion abnormalities (10). Advanced imaging techniques are advised when clinical suspicion is present (11). However, in patients with renal dysfunction or hemodynamic instability, CT angiography may be relatively contraindicated or delayed, which can limit early definitive vascular assessment, as observed in our cases.

In both cases, acute limb ischemia manifested clinical findings consistent with an advanced stage according to the Rutherford classification. According to the criteria established by Rutherford and colleagues, the presence of motor deficit and loss of distal Doppler signals indicates an advanced stage of acute limb ischemia (12). These objective criteria supported the decision against revascularization and favored conservative or palliative surgical approaches.

Regarding anticoagulation management, the progression of the ischemic process in both cases despite appropriate medical treatment is noteworthy. Standardized guidelines for preventing and treating postoperative arterial thromboembolism in high-risk gynecologic oncology patients remain limited, and clinical decisions are primarily informed by individual patient characteristics (11,13). Particularly in advanced CKD, the optimal dosing and choice of anticoagulant agents remain controversial, and treatment must often be individualized.

A review of the current literature reveals a paucity of clear classifications of ATE as early- or late-onset. The existing body of literature documents a range of reported cases with heterogeneous timing (2,11,14). This finding suggests that the patient-specific systemic risk profile, rather than timing, is the pivotal factor in ATE development. Thus, early postoperative occurrence, as seen in our patients, may reflect pre-existing vascular vulnerability rather than solely procedure-related injury.

In summary, the analysis of these two cases indicates that the combination of malignancy-related hypercoagulability, chronic kidney disease, and additional systemic comorbidities can result in uncommon but severe arterial thrombotic complications following gynecologic oncology surgery. It has been documented that arterial events may be more severe and the risk of amputation may increase, particularly in the presence of chronic kidney disease (13,15). Nevertheless, larger studies are required to clarify the magnitude of this association and to determine evidence-based preventive strategies.

Declarations

Ethics approval and informed consent: The local ethics committee approved the study (decision date: 08.01.2026, decision no: 1/34). Written informed consent for publication could not be obtained because both patients were deceased. All clin-

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Authors' Contributions: GES designed the study, collected the data, and drafted the manuscript. IU supervised the study; TT and IU critically revised the manuscript. All authors approved the final version.
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