

Elective arteriovenous fistula ligation for prevention of lymphedema in a patient with breast cancer before ipsilateral axillary lymph node dissection: A case report

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Abstract. Upper limb lymphedema (LE) may occur following radical treatment of breast cancer (BC), and may manifest more severely in patients with dialysis vascular access located on the ipsilateral limb. The present study reports a case of a 44-year-old female patient with patent arteriovenous fistula (AVF) in the left antecubital fossa following a third kidney transplant and the diagnosis of luminal B-like (human epidermal growth factor receptor 2-positive) BC of the left breast (clinical stage cT4bN2aM0), admitted to the Clinical Hospital of the Medical University of Silesia in Katowice (Poland) in October 2020. The patient received neoadjuvant systemic therapy, achieving partial regression of the tumor. Before a left-sided mastectomy with axillary lymph node dissection (ALND), the AVF was ligated. Following radiotherapy, trastuzumab treatment was continued for 18 cycles, along with hormonal therapy, and no upper limb LE developed. After 18 months, numerous metastases of the same biological subtype appeared in the area of the previously irradiated mastectomy scar. Palliative treatment was implemented and resulted in a complete objective response. First-line systemic treatment resulted in a partial response and disease control for 9 months. As of March 2025, the kidney graft function was stable (estimated glomerular filtration rate, 56.9 ml/min/1.73 m²) and second-line treatment with trastuzumab emtansine was terminated after 3 months due to symptomatic brain metastases. The upfront ligation of AVF located in the antecubital fossa decreased the risk of

upper limb LE, which may occur during BC treatment, ALND and chest wall and axillary region radiotherapy.

Introduction

Breast cancer (BC) is one of the most common malignant tumors in female patients with a global incidence of 2.3 million in 2022 (1). The prevalence of BC in patients with chronic kidney disease (CKD) is 11-13% (2). However, current data do not clearly support an increased incidence of BC in the CKD population, including kidney transplant recipients undergoing immunosuppressive therapy (3). In Tendulkar *et al* study 238 out of 6463 women with CKD developed BC during follow-up period of 20 years (4). In patients undergoing hemodialysis therapy for CKD, the BC treatment process must consider disturbed pharmacokinetics and elimination of drugs during the hemodialysis session (5). Dialysis arteriovenous fistula (AVF) is created surgically by directly connecting an artery to a vein, typically on the arm, to facilitate effective extracorporeal blood circulation during hemodialysis. However, this abnormal vascular connection is associated with potential complications including its obstruction, thrombosis, aneurysms and hemorrhage. Complications may also affect the limb, resulting in distal ischemia, infection and lymphedema (LE) (6). Moreover, in patients following kidney transplantation, the nephrotoxicity of therapy should be considered, in addition to potential drug-to-drug interactions with an immunosuppressive regimen, as worsening of the kidney graft function may limit the number of therapeutic options. Notably, compression should not be applied to the patent arteriovenous fistula (AVF), making the treatment of LE more difficult. Following a successful kidney transplant, the AVF is no longer required; however, it is still patent in 61% patients 5 years after transplant (7), especially in patients with a high risk of graft loss (8,9). One of the potential hazards of radical surgical treatment of BC with axillary lymph node dissection (ALND) is LE of the ipsilateral upper limb (10). During ALND, lymphatic vessels are damaged and lymph nodes are resected, which impairs lymph drainage from the

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limb. The risk of LE occurrence increases when more than 5 nodes are resected (11). The present study presents a case of a patient undergoing a third kidney transplant with AVF at the time of BC diagnosis.

Case report

A 44-year-old female patient with CKD, who had received three consecutive kidney transplants (in July 1997, Apr 2006 and Sep 2018), was admitted to Clinical Hospital of the Medical University of Silesia in Katowice (Poland) in October 2020 and diagnosed with a bifocal tumor in the left breast, with diameters of 32x30 and 25x16 mm, accompanied by widespread edema on the skin and enlarged axillary lymph nodes. Routine automated immunohistochemical examination of core biopsy revealed a non-special type G2, luminal B-like (HER2-positive) subtype carcinoma: estrogen receptor (ER) - positive in 30% of tumor cell nuclei; progesterone receptor (PR) - positive in 5% of tumor cell nuclei; human epidermal growth factor receptor 2 (HER2) - overexpression (score 3+ - intense membrane staining in >10% of tumor cells); and Ki-67 - positive in 10% of tumor cell nuclei. Mutations in the *BRCA1* and *BRCA2* genes were excluded with NGS of the tumor tissue. The cancer stage was determined with UICC TNM classification (8th edition) to be cT4bN2aM0 (12).

The patient had a medical history of glomerulonephritis diagnosed at 16 years old and a total of >8.5 years of hemodialysis therapy. Comorbidities included arterial hypertension, hepatitis C virus infection (successfully treated with direct-acting antiviral drugs since December 2015) and a parathyroidectomy in March 2010. There was no history of jugular or subclavicular vein catheterization. The last AVF was created in 2017 and was not ligated following the last transplantation, partly due to the increased immunological risk of premature graft loss. The patient received 250 mg antithymocyte globulin in the induction therapy after the third transplant. The immunosuppressive therapy included tacrolimus (initially 0.01 mg/kg of body mass twice daily, with a gradually reduced dose under control of trough levels to 3 mg twice daily), mycophenolate mofetil (500 mg twice daily), and steroids (prednisone 15 mg at discharge, reduced to 5 mg during follow-up).

As the kidney graft function was adequate [estimated glomerular filtration rate (eGFR), 63.5 ml/min/1.73 m²], the patient underwent standard neoadjuvant chemotherapy with doxorubicin (60 mg/m²) and cyclophosphamide (600 mg/m²) every 3 weeks - four cycles, followed by combination therapy with molecular targeted therapy and chemotherapy with pertuzumab (840 mg initial dose, followed by 420 mg intravenous) and trastuzumab (600 mg subcutaneously) and docetaxel (75 mg/m²) every 3 weeks (six cycles). After completing the therapy, a helical CT scan (Toshiba Aquilion 64 CT Scanner, 1 mm slice thickness) revealed a regression of the breast tumor (May 2021). After the oncological surgeon confirmed multifocal disease, persisted skin edema, positive ALN, the patient underwent left breast radical mastectomy with left-sided standard ALND, involving the removal of lymph nodes from levels I and II. Due to the risk of LE, the still-functioning AVF in the left antecubital fossa was closed 2 weeks before the radical mastectomy. Postoperative histological examination

confirmed partial response to implemented therapy and metastasis in a single lymph node (ypT2N1a). There were no complications during the healing of the mastectomy wound and fistula ligation scar. After one month, chest wall irradiation involving the surgical scar and post-treatment tissue areas using intensity-modulated radiation therapy (RT; 40.5 Gy in 15 fractions) was performed. There were no signs of LE following treatment.

The patient completed adjuvant anti-HER2 therapy with trastuzumab (600 mg every 3 weeks up to 12 cycles) followed by hormonal therapy with letrozole (2.5 mg daily). No drug toxicity symptoms were noted, and no metastases were detected. At that time, T-DM1 therapy was not covered by the National Health Fund as an adjuvant treatment. The immunosuppressive regimen remained unchanged during the BC treatment.

Numerous metastases of the same biological subtype (ER, 60%; PR, negative; HER2, +++; Ki-67, 40%) appeared in the skin and subcutaneous tissue in the area of the previously irradiated mastectomy scar 18 months after completion of therapy, measured by ultrasound (Fig. 1). Palliative combination therapy with molecular-targeted agents and chemotherapy with trastuzumab (600 mg on day 1, subcutaneously), pertuzumab (840 mg initial dose, followed by 420 mg on day 1 of the cycle, intravenous) and docetaxel (60 mg/m² on day 1 of the cycle, intravenously, 6 cycles) was started as recommended by the National Comprehensive Cancer Network guidelines (13) and supported by results of the CLEOPATRA trial (14). Palliative treatment resulted in a partial response and disease control for ~9 months (14 cycles). Due to multiple soft tissue and skin metastases, the treatment was changed to trastuzumab emtansine (T-DM1 at a dose of 3.6 mg/kg on day 1 of the cycle, intravenously) and continued due to the occurrence of brain metastases after 3 months (4 cycles). Following stereotactic RT, the patient started third-line therapy with trastuzumab deruxtecan (5.4 mg/kg on day one of the cycle, intravenously).

The kidney graft function was stable as of March 2025, the eGFR value was 56.9 ml/min/1.73 m², and despite chest wall skin recurrence of the scar tissue, the patient has not developed upper limb LE, based on monitoring limb circumferences at each oncology visit. The total follow-up duration was 4.5 years from the initial breast cancer diagnosis.

Literature review

The present systematic review was based on a search of PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) performed in November 2024, using the following search algorithm: ['Kidney dialysis' OR 'Arteriovenous fistula' OR 'Vascular access' AND ('Mastectomy' OR 'Breast Cancer')]. Initially, 60 records were obtained and screened for the content of the abstract. Reviews, systemic reviews, meta-analyses and case reports not associated with the topic were excluded. Finally, four papers were included in the present review (Fig. 2) (15-18). Each study was reviewed to assess patient age, AVF location, LE occurrence and the time of AVF creation relative to the mastectomy. Additionally, use of the AVF, including its active or inactive status and the duration of use, was evaluated.

The age of the analyzed patients ranged from 57 to 76 years. Out of six patients, four had an AVF localized in the

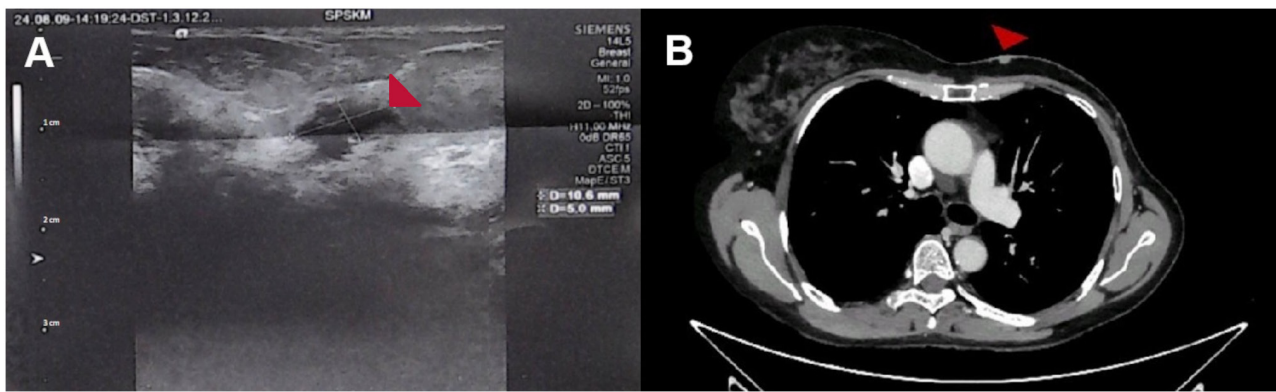


Figure 1. Ultrasound imaging and computed tomography of chest wall skin recurrence of breast cancer. Local recurrence of breast carcinoma (arrow) in the area of the mastectomy scar of the chest wall in (A) ultrasound imaging with 11 MHz linear probe and (B) contrast-enhanced computed tomography scan of the chest.

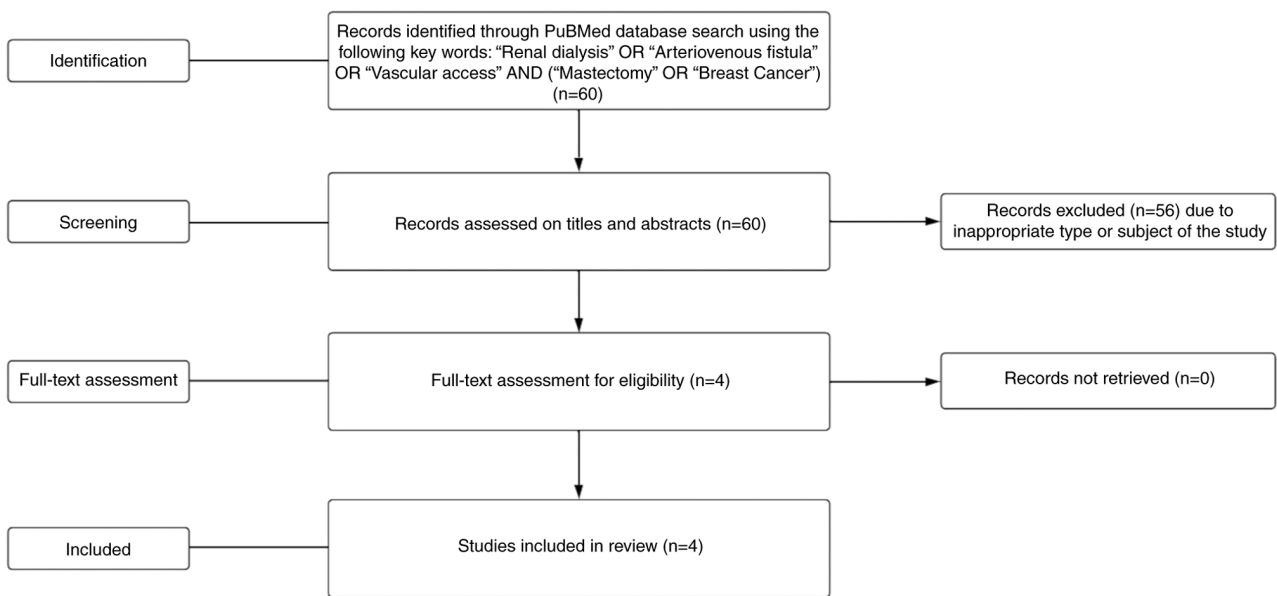


Figure 2. Flowchart of the systemic literature review.

cubital fossa, and one had an AVF in the forearm (Table I). The AVF data for one patient were unavailable. All AVFs were located on the ipsilateral arm. A total of two AVFs were created before BC development, while four were post-mastectomy with ALND. All six AVFs were active, and the length of their use ranged between 2 months and 8 years. A total of two out of six patients developed LE.

Discussion

The present study describes a patient with BC who had undergone a kidney transplant. The elective antecubital fossa AVF closure was performed before the planned cancer treatment, which included mastectomy with ALND, followed by chest wall irradiation involving surgical scar and post-treatment tissue areas. A patent AVF, especially in antecubital fossa on the ipsilateral limb, notably increases the risk of complications, including LE (6). Even functioning AVF in the antecubital fossa (for example, with higher blood flow compared with the

forearm localization markedly increases the venous pressure, promoting the development of LE, and often generates turbulent flow which may result in endothelium damage (19).

Among patients who undergo breast-conserving therapy (BCT) with adjuvant RT or mastectomy, 10 and 23% developed LE of the upper extremity, respectively (20,21). ALND increases the risk of LE occurrence by impairing lymph drainage. The development of upper limb LE following ALND in patients with BC is reported in 16-40% of cases (22). Similarly, post-mastectomy RT increases the risk of upper limb LE due to decreased lymphatic proliferation, interstitial fibrosis compressing lymphatic vessels, and mechanical insufficiency of the lymphatic system (23). In the present study, a mastectomy was performed due to contraindications to BCT. Mastectomy with RT to the chest wall is recommended by NCCN, even in cases responding well to induction chemotherapy (13).

Furthermore, LE may cause other complications, including cellulitis, tissue fibrosis, recurrent bacterial and fungal

Table I. Patient characteristics evaluated in previous studies.

First author, year	Age, years	AVF location	Ipsilateral location	Mastectomy	Type of mastectomy	ALND	AVF creation relative to mastectomy	Activity of AVF	Fistula usage time	Lymphedema occurrence (Refs.)
Özçete and Eyigör, 2020	57	ND	Yes	Yes	T	Yes	Before	Active	8 years	Yes (15)
Chou <i>et al</i> , 2013	48	Cubital fossa	Yes	No	NA	NA	Before cancer diagnosis	Active	12 years	Yes (16)
Olsha <i>et al</i> , 2012	67	Forearm	Yes	Yes	P	Yes	After	Active	20 months	No (17)
Olsha <i>et al</i> , 2012	76	Cubital fossa	Yes	Yes	T	Yes	After	Active	76 months	No (17)
Olsha <i>et al</i> , 2012	58	Cubital fossa	Yes	Yes	P	Yes	After	Active	2 months	No (17)
Ali <i>et al</i> , 2016	65	Cubital fossa	Yes	Yes	T	Yes	After	Active	9 months	No (18)

ND, data not available; NA, not applicable; AVF, arteriovenous fistula; T, total; P, partial; ALND, axillary lymph node dissection.

infection, skin ulcers and angiosarcomas in rare cases (24). Patients receiving immunosuppressive treatment may also have increased risk of the aforementioned adverse events (25). In addition, the onset of pain, restricted mobility and psychological repercussions following LE development markedly impact the quality of life (24).

The potential hazards of patent AVF in patients with BC in the context of LE occurrence and treatment have been described previously (10). Özçete and Eyigör (15) described a 57-year-old female patient after a mastectomy with ALND who developed LE on the left upper limb with functioning vascular access. Due to contraindications to the use of excessive compression on the AVF, laser therapy and kinesio taping were used, which partially decreased the size of LE, allowing the continuation of concomitant hemodialysis treatment. A similar result was obtained in the case described by Chou *et al* (16), where a 48-year-old female patient developed LE on the arm with functioning AVF due to BC metastases to axillary nodes. The patient underwent kinesio taping, which resulted in a marked decrease of LE, allowing further treatment with hemodialysis.

Notably, the risk of LE is the highest during the first 2 years after ALND with post-mastectomy RT (26). To minimize the risk of LE, performing procedures on the ipsilateral upper limb following ALND is not recommended. However, Olsha *et al* (17) described three patients where vascular access was created in the ipsilateral upper limb 4-10 years after ALND. The patients did not develop LE between 2 and 76 months after AVF creation, which remained active throughout. Similarly, Ali *et al* (18) reported a case of a 65-year-old female patient following bilateral mastectomy with ALND, where a radiocephalic fistula was created on the right upper limb. The fistula was active for 9 months until patient death due to myocardial infarction. The authors did not report the occurrence of LE.

AVF created in the antecubital fossa is associated with high blood flow and an increased heart workload. Following a prolonged period with a functioning AVF, the risk of heart failure increases (27). Left ventricular mass and hypertrophy increase markedly, due to increased pressure overload and cardiac output, which can be avoided by earlier closure of the AVF following kidney transplantation (8,9). Following AVF closure, the left ventricular mass index and end-diastolic diameter are decreased (9). In clinical practice, the ligation of the AVF is associated with beneficial effects on cardiac function in patients undergoing anthracycline-based chemotherapy. Patients with AVF that cannot be closed may have a higher risk of symptomatic chemotherapy-associated cardiotoxicity than those without patent AVF. Both anthracycline and trastuzumab may lead to left ventricular dysfunction and congestive heart failure in severe cases (28,29). In the present case, the AVF was not closed after the third successful kidney transplantation due to concerns regarding the long-term graft function in the highly sensitized recipient. However, the kidney graft function was stable during the BC treatment. Furthermore, the risk of kidney graft function deterioration was relatively low, as the combined regimen of molecular targeted (anti-HER2) therapy and chemotherapy were not reported as nephrotoxic (30). In addition, there was no adverse effect on the cardiovascular system.

To the best of our knowledge, there is scarce data (15-18) on patients treated with hemodialysis following ALND and those who undergo ALND during BC treatments. Therefore,

the risk of LE development in this group has not been established. Based on the literature review, persistence of vascular access on the ipsilateral upper limb is possible. However, once LE develops, the therapeutic strategies are limited and available management methods (kinesio taping and laser therapy) may be insufficient (15,16). The severity of LE of the limb with patent AVF is hypothesized to be greater than in those without dialysis access. A functioning AVF increases venous pressure, enhancing lymph production, and may cause upper limb LE, especially in patients with ipsilateral central vein stenosis associated with previous catheterization (31). Impaired lymph drainage, due to lymph duct damage, in patients following axillary dissection is hypothesized to increase the risk of LE development (32). Therefore, in the present case, the decision to close the AVF before ALND was due to its placement in the antecubital fossa and the substantial risk of LE. The decision caused a 2-week delay in breast surgery, which is unlikely to worsen the outcome of the therapy.

The lack of information regarding previous central vein catheterization procedures and the impact of AVF closure on upper limb volume is a limitation of the present review. In the reviewed cases, there was no data available regarding kidney transplantation procedures, as the type of renal replacement therapy has a notably smaller effect on upper limb edema compared with the aforementioned factors such as ALND, post-mastectomy RT with presence of a functioning ipsilateral AVF (4,23,33).

Closure of an AVF on the ipsilateral upper limb should be considered before mastectomy and ALND. In addition, the persistence of AVF may contribute to ongoing maladaptive cardiovascular remodeling and increase chemotherapy-associated cardiotoxicity. Therefore, in patients with BC, or other types of cancer such as melanoma who underwent ALND, the AVF should be placed on the contralateral upper limb to decrease the risk of LE occurrence.

In conclusion, for patients on hemodialysis using AVF and undergoing ipsilateral BC surgery accompanied by ALND, the risk of LE may be increased. In the present case, the patient had undergone a successful kidney transplant and had maintained renal function, so the AVF could be closed at the same time as the BC surgery.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

KS, KP, KJ, WBB, AK and JC conceived the study, designed the experiments and wrote the manuscript. KS and WBB constructed figures. AK and JC confirm the authenticity of

all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for their anonymized information and accompanying images to be published in the present article.

Competing interests

The authors declare that they have no competing interests.

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