TURKISH JOURNAL of ONCOLOGY

Turk J Oncol 2025;40(3):233–241
doi: 10.5505/tjo.2025.4567

REVIEW

Radiotherapy in Vulvar Squamous Cell Carcinoma: Indications, Techniques, and Evidence-based Practice

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SUMMARY

Vulvar cancer constitutes around 5% of gynecological cancers within the female genital system. Approximately 90-95% of vulvar cancers are squamous cell carcinoma. This review aims to provide information about the indication, field, technique and doses of radiotherapy in vulvar SCC. Once vulvar cancer is diagnosed, the disease should be staged. Staging can be done according to TNM system or FIGO system. The principal intervention for vulvar squamous cell carcinoma is radical excision, adjuvant radiotherapy and/or chemotherapy may be recommended if there are factors that increase the risk of recurrence as a result of surgical pathology. Radiotherapy for vulvar squamous cell carcinoma will be analyzed in two categories: primary and postoperative radiotherapy. The studies indicate that definitive/neoadjuvant radiotherapy, administered concurrently with chemotherapy in patients with advanced vulvar cancer who are inoperable due to tumor or patient-related factors, demonstrates a high locoregional control rate and acceptable long-term side effects. Postoperative radiotherapy or chemoradiotherapy is recommended for cases with high risk of recurrence. It is recommended to use modern radiotherapy techniques such as IMRT as an radiation modality due to high response rates and low toxicity rates in studies. Radiotherapy and chemoradiotherapy stand out as effective and safe treatment modalities in both definitive and adjuvant treatment of vulvar cancer.

Keywords: IMRT; radiotherapy; vulvar cancer.

INTRODUCTION

Vulvar cancer constitutes around 5% of gynecological cancers within the female genital system.[1,2] Advanced age, HPV infection, vulvar inflammatory conditions, smoking, a history of pelvic radiation, and immunodeficiency are significant risk factors for the disease.[3] The illness is frequently identified between the ages of 65 and 74. High-risk HPV infections account for 30–40% of vulvar cancer cases.[3,4] The E6 and E7 oncoproteins of HPV induce carcinogenesis by inactivating tumor suppressor genes. Approximately 90–95% of vulvar cancers are squamous cell carcinoma (SCC), while the rest are tumors such as melanoma, basal cell carcinoma and sarcoma.[2,3,5] VIN (Vulvar Intraepithelial Neoplasia) is the precursor lesion of vulvar SCCs and accordingly the disease is divided into 2 main categories: HPV dependent (dVIN) and independent type (uVIN). The HPV-dependent variant is observed in younger pop-

Received: July 15, 2025
Accepted: August 07, 2025
Online: September 03, 2025

Accessible online at:
www.onkder.org

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Turk J Oncol 2025;40(3):233–241
doi: 10.5505/tjo.2025.4567

ulations and is significantly correlated with smoking. Despite a 5% progression rate to invasive SCC, it constitutes roughly 40% of vulvar SCC cases.[2,3] The HPV-independent type is caused by chronic diseases such as lichen sclerosus and lichen planus. The risk of malignant transformation is greater than that of uVIN. The keratinizing subtype constitutes 60–80% of vulvar squamous cell carcinoma cases, while the remaining subtypes are warty and basaloid SCC. The warty and basaloid subtypes manifest at earlier ages and are linked to HPV, whereas the keratinized type appears at older ages and typically occurs independently of HPV.[3,6] The predominant symptom of the disease is pruritus; however, hemorrhage, discharge, dysuria, discomfort, and mass-related symptoms may also be present. In cases of suspected vulvar cancer, a pelvic examination, speculum examination, and colposcopy of the vulva and vagina should be performed; the definitive diagnostic procedure for the disease is biopsy.[3] The conventional management for vulvar squamous cell carcinoma is surgical excision, adjuvant radiotherapy and/or chemotherapy may be recommended if there are factors that increase the risk of recurrence as a result of surgical pathology.[2,3,7] This review aims to provide information about the indication, field, technique and doses of radiotherapy in vulvar SCC.

RADIOTHERAPY IN VULVAR SQUAMOUS CELL CARCINOMA

Once vulvar cancer is diagnosed, the disease should be staged. Staging can be done according to TNM system or FIGO system.[8,9] Tumor size, stromal invasion, involvement of adjacent pelvic structures, lymph node metastasis status and presence of distant metastasis are taken into account in disease staging. During staging, the assessment of neighboring pelvic structures (rectum, anus, urethra, vagina) is crucial. Ultrasound and pelvic MRI are proficient in assessing the local progression of the tumor and the inguinofemoral lymph nodes. The use of T2WI, DWI and DCE-MR modalities is recommended. FDG PET/CT may be used when there is a suspicion of distant metastases in advanced illness or involvement of inguinofemoral lymph nodes.[9,10]

The principal intervention for vulvar squamous cell carcinoma is radical local excision.[9,10]

While the objective in surgery for many years was to secure a minimum of 8 mm negative margin, new studies have diminished the significance of this threshold, emphasizing instead the necessity of obtaining tumor-negative surgical margins.[9–13] Treatment is indicated for inguinal lymph nodes with > T1a malignancies. Midline tumors necessitate bilateral inguinal surgical assessment. Sentinel lymph node assessment is advised for patients with tumors less than 4 cm, unifocal, and clinically negative lymph nodes. Inguinofemoral lymphadenectomy is advised for patients with tumors measuring ≥4 cm and/or exhibiting multifocality. During lymphadenectomy, both superficial and deep femoral lymph nodes must be removed. Should metastases be identified in the ipsilateral lymph nodes, contralateral lymphadenectomy may be conducted. Radiotherapy for vulvar squamous cell carcinoma will be analyzed in two categories: Primary and postoperative radiotherapy.

Primary Radiotherapy in Vulvar Squamous Cell Carcinoma

Neoadjuvant and definitive radiation are regarded as primary forms of radiotherapy. The GOG 101 and GOG 205 phase 2 studies are significant investigations assessing neoadjuvant radiation in locally advanced vulvar carcinoma. In these experiments, three-dimensional radiotherapy (3DRT) was employed as the radiation method. In GOG 101, 73 patients with stage 3–4 vulvar squamous cell carcinoma had split-course radiation in conjunction with simultaneous administration of cisplatin and 5-fluorouracil.[14] Following radiotherapy, patients received extensive tumor resection and inguinofemoral lymphadenectomy. Radiotherapy dose was 47.6 Gy/1.7 Gy. On chemotherapy administration days, 2 fractions were given daily. In clinical N2–3 patients, the radiation field encompasses the primary vulvar tumor, inguinofemoral lymph nodes, and lower pelvic nodes, whereas in other stages it just includes the primary vulvar tumor. Post-chemoradiotherapy, 48% of patients exhibited no detectable malignancy. Of these patients, 3 did not undergo surgery and it was determined that 70% of the patients who went to surgery had no residual microscopic disease. Urinary and/or gastrointestinal continence could not be maintained in only 3 patients. Cutaneous toxicity and problems related to surgical wounds were the predominant treatment toxicities. The study indicated that neoadjuvant chemoradiotherapy is an effective treatment that diminishes the necessity for pelvic exenteration in advanced vulvar squamous cell carcinoma. In the GOG 205 study, patients with locally ad-

vanced T3–4 vulvar squamous cell carcinoma, which was inoperable with routine radical vulvectomy, received chemoradiotherapy followed by excision of remaining tumor.[15] Cisplatin was administered weekly as concomitant chemotherapy. The dose of radiotherapy was 57.6 Gy/1.8 Gy. In contrast to GOG 101, a divided course regimen was not favored in radiotherapy. A radical vulvectomy was conducted 6 to 8 weeks post-chemoradiotherapy. The overall clinical response rate was 64%, whereas the pathological complete response rate was 50%. The predominant adverse effects included leukopenia, discomfort, and radiation dermatitis. The study concluded that concurrent radiation and cisplatin for locally advanced vulvar SCC is a treatment approach characterized by a good response rate and acceptable toxicity levels.

The NCDB review compared definitive chemoradiotherapy with radiation in 1352 unresectable patients.[16] The median dose of radiation administered was 59.4 Gy. In the chemoradiotherapy cohort, 65.2% underwent single-agent chemotherapy, whereas 30.6% received multiple-agent chemotherapy. The analysis revealed that the 5-year overall survival rate was considerably greater in the chemoradiotherapy group (49.9% compared to 27.4%). A prospective study by Montana involved surgery following preoperative chemoradiotherapy in individuals with vulvar cancer classified as N2–3.[17] The GOG 101 regimen was implemented in the chemotherapy and radiation procedure. Surgery was conducted 3 to 8 weeks following the chemoradiotherapy regimen. During the procedure, excision of the residual vulvar lesion and bilateral inguinofemoral dissection were conducted. Following chemoradiotherapy, the resectability rate of the lymph nodes was determined to be 95%, the local control rate for the lymph nodes was 97%, and the local control rate for the primary tumor was 76%. Preoperative chemoradiotherapy is an effective treatment approach that yields a high rate of resectability and local control in locally advanced vulvar cancer. In the phase 2 study, definitive chemoradiotherapy was administered to 52 patients with locally advanced vulvar carcinoma.[18] Capecitabine was administered in conjunction with chemotherapy. 64.8 Gy was designated for the tumor and 50.4 Gy for the elective lymph nodes. The predominant > G2 acute adverse events were skin/mucosal reactions (54%) and discomfort (37%). The predominant > G2 late adverse effect was skin/mucosal reaction (10%). Following 12 weeks of treatment, the local clinical complete response rate was 62%, while the regional control rate was 75%. The 5-year progression-free survival (PFS) rate was 45%, while the overall survival (OS) rate was 52%. The study highlighted that capecitabine-based chemoradiotherapy for vulvar cancer should be considered an alternative to major surgery, demonstrating satisfactory locoregional control and survival rates. In the prospective study conducted by Beriwal, preoperative chemoradiotherapy was applied to 18 vulvar cancer patients with the intensity modulated radiotherapy (IMRT) technique.[19] 5-FU and cisplatin were administered concurrently. A hybrid hyperfractionated regimen was employed in split-course radiotherapy. The median dose of radiation administered was 46.4 Gy. In the cohort of patients who underwent surgery following treatment, the rate of pathological complete response was 64%. The 2-year cause-specific survival rate was 75%, whereas the overall survival rate was 70%. A significant observation was that no patient experienced grade 3 or higher acute or late adverse effects attributable to radiation. It was concluded that preoperative chemoradiotherapy with IMRT technique is an effective and highly tolerable treatment modality in vulvar cancer. The retrospective study by Rishi assessed the outcomes of high-dose radiation administered to 26 vulvar cancer patients with the IMRT technique.[20] The majority of patients underwent platinum-based concomitant chemotherapy. The median dosage was 65.4 Gy. A complete response was achieved in 80.7% of patients. The one year local, regional, and distant control rates were 72.4%, 85.4%, and 86%, respectively. The overall survival rates at 1 and 2 years were established at 91% and 62%, respectively. Grade 3 late soft tissue toxicity/dermatitis was noted in 5 patients, 3 of whom had previously undergone radiotherapy to the pelvic area. Grade 4 dermatitis was not seen in any patient. A tumor dosage above 66 Gy and prior pelvic irradiation were identified as predictive variables for Grade 3–4 toxicity. It was emphasized that the high dose given with IMRT in vulvar cancer is a treatment with a successful control rate and acceptable toxicity. The retrospective study by Richman assessed the outcomes of dose escalation in patients undergoing neoadjuvant or definitive chemoradiotherapy with the IMRT technique.[21]

In the study, the median dose was 66 Gy for those receiving definitive treatment and 59.4 Gy for those receiving preoperative treatment. The study's results indicated that dose escalation using IMRT is a tolerated treatment associated with a high complete response rate. Mahantshetty's retrospective study assessed the

Table 1 Important studies on preoperative and definitive chemoradiotherapy in vulvar cancer and their findings

Studies	Study design/ phase	Radiotherapy modality	Concomitant chemotherapy	Number of Pts	Radiotherapy dose	Response rate	Survival data	Control rate	Pelvic toxicity
Moore [14]	Phase 2	Split course radiotherapy, 3DRT	5 FU+Cisplatin	73	47.6 Gy/1.7 Gy	Post CRT no detectable malignancy: 48%			3 patients had urinary and/ or gastrointestinal incontinence. Cutaneous toxicity and surgical wounds problems were the predominant treatment toxicities.
Moore [15]	Phase 2	3DRT	Cisplatin	58	57.6 Gy/1.8 Gy	Overall clinical response: 64%, pathological complete response: 50%.			Leukopenia, pain, radiation dermatitis were predominant toxicities.
Beriwal [19]	Phase 2	IMRT	5 FU+Cisplatin	18	46.4 Gy	Pathological complete response: 64%	2 y cause specific survival: 75, 2 y OS: 70%		No >G2 acute or late toxicity
Montana [17]	Phase 2	Split course radiotherapy, 3DRT	5 FU+Cisplatin	46	47.6 Gy/1.7 Gy			Local control rate for lymph nodes: %97, local control rate for primary tumor: %76	
van Triest [18]	Phase 2	3DRT and IMRT	Capesitabine	52	64.8 Gy		1, 2, 5 years PFS: 58%, 51%, 45%; OS: 76%, 66%, 52%	After 12 weeks of tx: Local clinical complete response rate: 62%, egional control rate: 75%	Predominant > G2 acute toxicities: Skin/mucosal reactions (54%) and discomfort (37%), predominant >G2 late toxicities: Skin/mucosal reactions (10%)
Rishi [20]	Retrospective	IMRT	Majority platinum based	26	65.4 Gy	Complete response: 80,7%	1, 2 years OS: 91%, 62%	1 y local, regional, distant control: 72.4%, 85.4%, 86%	Grade 3 late soft tissue toxicity/ dermatitis was noted in 5 patients
Richman [21]	Retrospective	IMRT	Majority platinum based	49	≥ 55Gy	Clinical complete response: 76%, pathologic complete response: 70%	2 years disease free survival: 65%		Grade 3 acute and late radiation toxicities: 29%, 6%
Gaudineau [22]	Retrospective	3DRT	Carboplatin+5FU or Paclitaxel	22	50 Gy/25 fr	Pathological complete response vulvar and nodal: 27%			Necrosis:14.3%, breakdown of groin wounds:14.3%, breakdown of vulvar wounds: 31.8%, lymphocele: 63.6%, chronic lymphedema: 63.6%
Han [23]	Retrospective	3DRT	5FU+Mitomycin C	54	40-54 Gy+ 6-17 Gy boost		5 years OS: CRT: 54%, RT: 10%, 5 years disease specific survival: CRT: 62%, RT: 14%		

3DRT: Three dimension radiotherapy; IMRT: Intensity modulated radiotherapy; CRT: Chemoradiotherapy; RT: Radiotherapy; PFS: Progression free survival; OS: Overall survival

Turk J Oncol 2025;40(3):233–241
doi: 10.5505/tjo.2025.4567

outcomes of high dose rate interstitial brachytherapy in vulvar cancer among 38 patients.[24] Among the 38 patients, 29 patients received definitive brachytherapy, 6 patients received postoperative brachytherapy and 3 patients received salvage brachytherapy. Brachytherapy boost was administered to 29 patients, whereas single brachytherapy was administered to 9 patients. The median EQD2 dose was 23,3 Gy10 for patients receiving a brachytherapy boost, compared to a median EQD2 dose of 38,4 Gy10 for those undergoing single brachytherapy. A clinical complete response was observed in 30 patients during the 3-month control evaluation following treatment. At a median follow-up of 30 months, 29 patients (76.3%) were disease-free. The overall survival rate at five years was 82%, with disease-free survival at 51% and local control at 77%. Interstitial brachytherapy for vulvar cancer is recognized as a tolerable treatment that provides effective control and survival rates.

A Cochrane systematic review evaluated the effectiveness of preoperative chemoradiotherapy in patients with advanced vulvar SCC.[25] Skin toxicity was observed in all patients. Common side effects include wound infection, lymphedema, and lymphocele. The operability rate ranged from 63% to 92%. Preoperative chemoradiotherapy is recognized for its role in reducing tumor size and enhancing operability. However, the efficacy of neoadjuvant chemotherapy in patients eligible for radical vulvectomy and bilateral inguinal lymph node dissection remains unproven. The studies included in the review comprised patients who received treatment with older radiotherapy techniques. In the review by Tagliaferi, it was mentioned that there was no survival advantage in the patient group receiving chemoradiotherapy in locally advanced vulvar cancer compared to the primary surgery group, but the risk of incomplete data and bias in the literature was expressed.[26] Furthermore, it was noted that the existing literature primarily comprises retrospective studies and those utilizing outdated radiotherapy techniques. Modern radiotherapy techniques, such as IMRT, enable treatments characterized by low toxicity and high complete response rates. The studies indicate that definitive/neoadjuvant radiotherapy, administered concurrently with cisplatin or capecitabine-based chemotherapy in patients with advanced vulvar cancer who are inoperable due to tumor or patient-related factors, demonstrates a high locoregional control rate and acceptable long-term side effects. According to the European Society of Gynaecological Oncology (ESGO) guideline, primary chemoradiotherapy is the main treatment option for unresectable disease and should be considered if morbid surgery requiring stoma insertion is necessary. The guideline recommends that treatment response evaluation after chemoradiotherapy should be performed 12 weeks after the end of treatment.[9] The National Comprehensive Cancer Network (NCCN) guideline also indicates to primary chemoradiotherapy as the main treatment option for unresectable disease.[27] Radiotherapy may be administered as external radiotherapy alone, brachytherapy alone, or a combination of both modalities, contingent upon the clinic's available facilities.[2,3,9,14–28] Important studies on preoperative and definitive chemoradiotherapy in vulvar cancer and their findings are shown in Table 1.

Adjuvant Radiotherapy in Vulvar Squamous Cell Carcinoma

Adjuvant treatments have been brought to the agenda due to the high rate of locoregional recurrence after surgery in vulvar cancer.[9,29] Adjuvant treatments aim to minimize the risk of local and regional recurrence. Bhatla's review indicates that margin status and lymph node status are the primary factors influencing the decision regarding adjuvant treatment in vulvar cancer.[30] In a retrospective study conducted by Parthasarathy on 208 patients, the effectiveness of adjuvant radiotherapy was evaluated in patients with postoperative single inguinal node positivity.[31] The analysis revealed that 5-year disease-specific survival was significantly greater with adjuvant radiotherapy, at 77% compared to 61.2%. Survival rates have been observed to improve with the use of adjuvant radiotherapy in patients who have undergone excision of 12 or fewer lymph nodes. Kunos conducted a randomized controlled trial involving 114 patients, categorizing those with operated lymph nodes into two groups: Radiotherapy and ipsilateral pelvic node resection.[32] Radiotherapy included the pelvic and inguinal nodes, with a prescribed dose of 45–50 Gy. The study found that adjuvant radiotherapy significantly reduced local recurrences and cancer-related deaths, with late toxicities remaining comparable. The multicenter retrospective AGO-CaRE-1 study demonstrated that adjuvant radiotherapy was associated with an increase in 3-year progression-free survival (PFS) and overall survival (OS) in patients with pathological lymph node positivity.[33] In the subgroup analysis of the patient group in the AGO-CaRE-1 study, 360 patients with positive pathological lymph nodes were evaluated.[34] Vulvar recurrence was significantly lower in the group that received radiotherapy to the vulva and groin/pelvis compared to the group that received radiotherapy to the groin/pelvis alone and the group that received no radiotherapy. The recurrence-reducing ef-

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doi: 10.5505/tjo.2025.4567

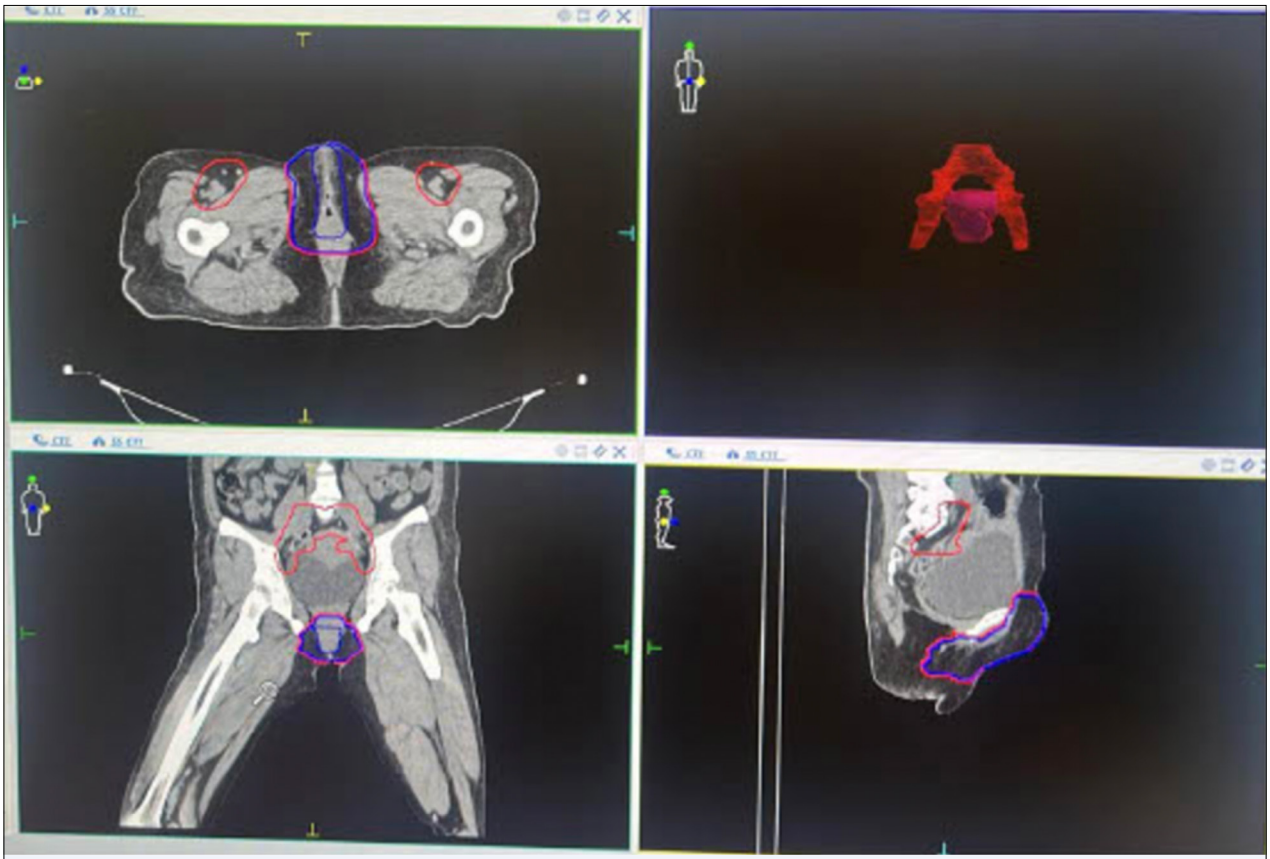

Fig. 1. Radiotherapy field image of a vulvar cancer patient who applied postoperative radiotherapy.

fect of local radiotherapy is independent of the status of the resection margin. The effect of radiotherapy on the vulva in reducing local recurrence was significantly greater in HPV-positive tumors compared to HPV-negative tumors. In the multicentric phase 2 GROINSS-V 2 study involving 1535 patients, local excision combined with sentinel node biopsy was conducted on early-stage vulvar cancer patients who were clinically lymph node-negative.[35] Inguinofemoral radiotherapy was administered to patients exhibiting sentinel node positivity. During the study, the protocol was amended to include inguinofemoral lymphadenectomy (IFL) when macrometastasis (>2 mm) was detected in the sentinel lymph node. In patients receiving radiotherapy with micrometastases (≤ 2 mm) in the sentinel tumor, the isolated groin recurrence rate at 2 years was 1.6%. The presence of macrometastasis in sentinel tumors resulted in a 2-year isolated groin recurrence rate of 22% for patients receiving radiotherapy, compared to 6.9% for those undergoing IFL. Radiotherapy is associated with lower morbidity compared to IFL. Radiotherapy is acknowledged as a minimally invasive and safe treatment modality for IFL in the presence of sentinel micrometastases.

In a database-based retrospective study, the effectiveness of adjuvant treatment in 2779 inguinal node-positive vulvar cancer cases was evaluated.[36] Patients were categorized into two groups: Those with one positive lymph node and those with more than one positive lymph node. Adjuvant radiotherapy was shown to enhance survival in both groups. The incorporation of chemotherapy into adjuvant radiotherapy demonstrated a survival benefit for patients with two or more positive lymph nodes; however, this benefit was not observed in patients with a single positive lymph node. A database analysis involving 1,797 patients assessed the effectiveness of adjuvant chemotherapy in those who received adjuvant radiotherapy due to node positivity.[36] The study concluded that adjuvant chemotherapy significantly decreased mortality risk in this patient population.

Postoperative radiotherapy is advised for cases with close surgical margins, tumor invasion depth exceeding 5 mm, lymphovascular invasion positivity, single lymph node metastasis with size under 2 mm, as indicated by the data from the studies. Postoperative chemoradiotherapy is indicated for patients with positive surgical margins, single lymph node metastasis greater than 2 mm, two or

more lymph node metastases, or extracapsular extension in lymph node metastases. It is stated that postoperative radiotherapy should start within 6–8 weeks as soon as the wound healing process is completed.[9,24,27] According to ESGO guideline, radiotherapy should be performed with intensity-modulated radiotherapy techniques.[9] The radiotherapy field image of a vulvar cancer patient who applied postoperative radiotherapy was shown in Figure 1.

Radiotherapy Technique, Field, Dose/Fraction Regimes in Vulvar Cancer

In the context of vulvar cancer radiotherapy, the prescribed dose to the primary surgical bed (with clear margins) and uninvolved lymph nodes is 45–50.4 Gy delivered in 25–28 fractions.

In case of a close or positive margin, a dose of 54–60 Gy is defined to the primary site. In case of positive and gross residual disease with ECE negative lymph nodes, a radiation dose of 50–55 Gy may be administered to the affected lymph node. A dose of 54–64 Gy is recommended for lymph nodes with extracapsular extension (ECE) positivity. In the presence of gross residual or unresectable lymph node, a dose of 60–70 Gy is defined for the relevant lymph node. In the presence of gross primary disease, a dose of 60–70 Gy should be defined for the primary region.[9,37] The primary tumor, the vulva, and the bilateral inguinofemoral region are all included in the classical radiotherapy field. Depending on the primary tumor and lymph node involvement, pelvic lymph nodes may be included. The lymph node that is one level above the most involved cranial lymph node should be treated if the pelvic lymph nodes are involved. The response rate is high and the toxicity rate is tolerable in the studies, which is why it is recommended to use modern planning methods such as IMRT as an external radiotherapy technique.[19–21,38]

Chemotherapy Regimens in Chemoradiotherapy

Chemoradiotherapy is a critical treatment option for vulvar cancer, particularly in cases of locally advanced disease and high-risk early-stage disease. The initial treatment option for chemotherapy that is administered concurrently with radiotherapy is cisplatin-based regimens.

The protocol that is most frequently recommended is to administer cisplatin at a weekly dose of 40 mg/m2 during radiotherapy.[15,39] Carboplatin (AUC 2 weekly) is recommended as an alternative option for patients who are intolerant to cisplatin. The efficacy of the cisplatin-gemcitabine combination has been demonstrated in recent studies, particularly in locally advanced disease, and it has since assumed its place among the current treatment options.[40]

During chemoradiotherapy, it is crucial to manage toxicity. Weekly complete blood count monitoring, close monitoring of liver and renal functions and appropriate hydration support should be provided for the monitoring and management of hematologic toxicity. Dose modifications may be necessary in patients with Grade 3–4 toxicity. Close follow-up and supportive treatment should be applied especially for mucositis and skin reactions. The treatment process must be completed as planned and interruptions should be avoided, as the local control rates are adversely affected as the treatment period extends.[14]

CONCLUSION

Radiotherapy and chemoradiotherapy stand out as effective and safe treatment modalities in both definitive and adjuvant treatment of vulvar cancer, which accounts for approximately 5% of malignancies in the female genital system.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: No AI technologies utilized.

Author Contributions: Concept – S.U.A., G.G., E.Ş., M.S.; Design – S.U.A., G.G., E.Ş., M.S.; Supervision – S.U.A.; Funding – S.U.A., G.G., E.Ş., M.S.; Materials – S.U.A., G.G., E.Ş., M.S.; Data collection and/or processing – S.U.A., G.G., E.Ş., M.S.; Data analysis and/or interpretation – S.U.A.; Literature search – S.U.A.; Writing – S.U.A., G.G., E.Ş., M.S.; Critical review – S.U.A., G.G., E.Ş., M.S.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Wohlmuth C, Wohlmuth-Wieser I. Vulvar malignancies: An interdisciplinary perspective. J Dtsch Dermatol Ges 2019;17(12):1257–76.
2. Alkatout I, Schubert M, Garbrecht N, Weigel MT, Jonat W, Mudhenke C, et al. Vulvar cancer: Epidemiology, clinical presentation, and management options. Int J Womens Health 2015;7:305–13.
3. Capria A, Tahir N, Fatehi M. Vulvar cancer. Treasure Island: StatPearls Publishing; 2025.
4. Faber MT, Sand FL, Albieri V, Norrild B, Kjaer SK, Verdoodt F. Prevalence and type distribution of human papillomavirus in squamous cell carcinoma and

Turk J Oncol 2025;40(3):233–241
doi: 10.5505/tjo.2025.4567

intraepithelial neoplasia of the vulva. Int J Cancer 2017;141(6):1161–9.
5. Chokoeva AA, Tchernev G, Castelli E, Orlando E, Verma SB, Grebe M, et al. Vulvar cancer: A review for dermatologists. Wien Med Wochenschr 2015;165(7-8):164–77.
6. Horn LC, Klostermann K, Hautmann S, Höhn AK, Beckmann MW, Mehlhorn G, et al. HPV-associated alterations of the vulva and vagina. Morphology and molecular pathology. Pathologe 2011;32(6):467–75.
7. Michalski BM, Pfeifer JD, Mutch D, Council ML. Cancer of the vulva: A review. Dermatol Surg 2021;47(2):174–83.
8. Matsuo K, Klar M, Nishio S, Mikami M, Romand LD, Wright J. Validation of the 2021 FIGO staging schema for advanced vulvar cancer. Int J Gynecol Cancer 2022;32:474–9.
9. Oonk MHM, Planchamp F, Baldwin P, Mahner S, Mirza MR, Fischerová D, et al. European Society of Gynaecological Oncology Guidelines for the Management of Patients with Vulvar Cancer - Update 2023. Int J Gynecol Cancer 2023;33(7):1023–43.
10. Nikolić O, Sousa FAE, Cunha TM, Nikolić MB, Otero-García MM, Gui B, et al. Vulvar cancer staging: Guidelines of the European Society of Urogenital Radiology (ESUR). Insights Imaging 2021;12:131.
11. Nooij LS, van der Slot MA, Dekkers OM, Stijnen T, Gaarenstroom KN, Creutzberg CL, et al. Tumour-free margins in vulvar squamous cell carcinoma: Does distance really matter. Eur J Cancer 2016;65:139–49.
12. Te Grootenhuis NC, Pouwer AW, de Bock GH, Hollema H, Bulten J, van der Zee AGJ, et al. Margin status revisited in vulvar squamous cell carcinoma. Gynecol Oncol 2019;154:266–75.
13. Woelber L, Griebel LF, Eulenburg C, Sehouli J, Jueckstock J, Hilpert F, et al. Role of tumour-free margin distance for loco-regional control in vulvar cancer—a subset analysis of the Arbeitsgemeinschaft Gynäkologische Onkologie CaRE-1 multicenter study. Eur J Cancer 2016;69:180–8.
14. Moore DH, Thomas GM, Montana GS, Saxer A, Gallup DG, Olt G. Preoperative chemoradiation for advanced vulvar cancer: A phase II study of the Gynecologic Oncology Group. Int J Radiat Oncol Biol Phys 1998;42:79–85.
15. Moore DH, Ali S, Koh WJ, Michael H, Barnes MN, McCourt CK, et al. A phase II trial of radiation therapy and weekly cisplatin chemotherapy for the treatment of locally-advanced squamous cell carcinoma of the vulva: A Gynecologic Oncology Group study. Gynecol Oncol 2012;124:529–33.
16. Rao YJ, Chin RI, Hui C, Mutch DG, Powell MA, Schwarz JK, et al. Improved survival with definitive chemoradiation compared to definitive radiation alone in squamous cell carcinoma of the vulva: A review of the National Cancer Database. Gynecol Oncol 2017;146:572–9.
17. Montana GS, Thomas GM, Moore DH, Saxer A, Mangan CE, Lentz SS, et al. Preoperative chemo-radiation for carcinoma of the vulva with N2/N3 nodes: A gynecologic oncology group study. Int J Radiat Oncol Biol Phys 2000;48(4):1007–13.
18. van Triest B, Rasing M, van der Velden J, de Hullu J, Witteveen PO, Beukema JC, et al. Phase II study of definitive chemoradiation for locally advanced squamous cell cancer of the vulva: An efficacy study. Gynecol Oncol 2021;163:117–24.
19. Beriwal S, Coon D, Heron DE, Kelley JL, Edwards RP, Sukumvanich P, et al. Preoperative intensity-modulated radiotherapy and chemotherapy for locally advanced vulvar carcinoma. Gynecol Oncol 2008;109:291–5.
20. Rishi A, Rollins M, Ahmed KA, Hunt DC, Sarkar P, Fernandez DC, et al. High-dose intensity-modulated chemoradiotherapy in vulvar squamous cell carcinoma: Outcome and toxicity. Gynecol Oncol 2020;156:349–56.
21. Richman AH, Vargo JA, Ling DC, Sukumvanich P, Berger JL, Boisen MM, et al. Dose-escalated intensity modulated radiation therapy in patients with locally-advanced vulvar cancer—does it increase response rate. Gynecol Oncol 2020;159:657–62.
22. Gaudineau A, Weitbruch D, Quetin P, Heymann S, Petit T, Volkmar P, et al. Neoadjuvant chemoradiotherapy followed by surgery in locally advanced squamous cell carcinoma of the vulva. Oncol Lett 2012;4:719–22.
23. Han SC, Kim DH, Higgins SA, Carcangiu ML, Kacinski BM. Chemoradiation as primary or adjuvant treatment for locally advanced carcinoma of the vulva. Int J Radiat Oncol 2000;47:1235–44.
24. Mahantshetty U, Naga P, Engineer R, Sastri S, Ghadi Y, Upreti U, et al. Clinical outcome of high-dose-rate interstitial brachytherapy in vulvar cancer: a single institutional experience. Brachytherapy 2017;16:153–60.
25. van Doorn HC, Ansink A, Verhaar-Langereis M, Stalpers L. Neoadjuvant chemoradiation for advanced primary vulvar cancer. Cochrane Database Syst Rev 2006;3:CD003752.
26. Tagliaferri L, Lancellotta V, Casà C, Fragomeni SM, Ferioli M, Gentileschi S, et al. The radiotherapy role in the multidisciplinary management of locally advanced vulvar cancer: A multidisciplinary VulCan team review. Cancers (Basel) 2021;13:5747.
27. Abu-Rustum NR, Yashar CM, Arend R, Barber E, Bradley K, Brooks R, et al. NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2024;22(2):117–13.

28. Woelber L, Trillsch F, Kock L, Grimm D, Petersen C, Choschzick M, et al. Management of patients with vulvar cancer: A perspective review according to tumour stage. Ther Adv Med Oncol 2013;5(3):183–92.
29. Lukovic J, Han K. Postoperative management of vulvar cancer. Int J Gynecol Cancer 2022;32:338–43.
30. Bhatla N, Tomar S, Meena J, Sharma DN, Kumar L. Adjuvant treatment in cervical, vaginal and vulvar cancer. Best Pract Res Clin Obstet Gynaecol 2022;78:36–51.
31. Parthasarathy A, Cheung MK, Osann K, Husain A, Teng NN, Berek JS, et al. The benefit of adjuvant radiation therapy in single-node-positive squamous cell vulvar carcinoma. Gynecol Oncol 2006;103:1095–9.
32. Kunos C, Simpkins F, Gibbons H, Tian C, Homesley H. Radiation therapy compared with pelvic node resection for node-positive vulvar cancer: A randomized controlled trial. Obstet Gynecol 2009;114:537–46.
33. Mahner S, Jueckstock J, Hilpert F, Neuser P, Harter P, de Gregorio N, et al. Adjuvant therapy in lymph node–positive vulvar cancer: The AGO-CaRE-1 study. J Natl Cancer Inst 2015;107:dju426.
34. Woelber L, Prieske K, Eulenburg CZ, Corradini S, Petersen C, Bommert M, et al. Adjuvant radiotherapy and local recurrence in vulvar cancer—a subset analysis of the AGO-CaRE-1 study. Gynecol Oncol 2022;164:68–75.
35. Oonk MHM, Slomovitz B, Baldwin PJW, van Doorn HC, van der Velden J, de Hullu JA, et al. Radiotherapy versus inguinofemoral lymphadenectomy as treatment for vulvar cancer patients with micrometastases in the sentinel node: Results of GROINSS-V II. J Clin Oncol 2021;39:3623–32.
36. Rydzewski NR, Kanis MJ, Donnelly ED, Lurain JR, Strauss JB. Role of adjuvant external beam radiotherapy and chemotherapy in one versus two or more node-positive vulvar cancer: A National Cancer Database study. Radiother Oncol 2018;129:534–9.
37. Gill BS, Bernard ME, Lin JF, Balasubramani GK, Rajagopalan MS, Sukumvanich P, et al. Impact of adjuvant chemotherapy with radiation for node-positive vulvar cancer: A National Cancer Data Base (NCDB) analysis. Gynecol Oncol 2015;137:365–72.
38. Rao YJ, Chundury A, Schwarz JK, Hassanzadeh C, DeWees T, Mullen D, et al. Intensity modulated radiation therapy for squamous cell carcinoma of the vulva: Treatment technique and outcomes. Adv Radiat Oncol 2017;2:148–58.
39. Gaffney DK, King B, Viswanathan AN, Barkati M, Beriwal S, Eifel P, et al. Consensus recommendations for radiation therapy concomitant with cisplatin and for salvage radiation therapy in vulvar cancer. Int J Radiat Oncol Biol Phys 2016;95:1191–200.
40. Horowitz NS, Deng W, Peterson I, Mannel RS, Thompson S, Lokich E, et al. Phase II trial of cisplatin, gemcitabine, and intensity-modulated radiation therapy for locally advanced vulvar squamous cell carcinoma: NRG Oncology/GOG Study 279. J Clin Oncol 2024;42:1914–21.