



Right technique and sufficient dose equal effective radiation to the groins in vulvar cancer

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The management of vulvar cancer has significantly evolved from radical en bloc vulvectomy and bilateral inguinal lymphadenectomy to a more nuanced approach. Current management, for example, can involve radical local excision and sentinel lymph node biopsy. These advances have significantly reduced the morbidity associated with the surgical management of this disease. However, there remain unanswered questions regarding the treatment of vulvar cancer, including the ideal management of gross groin lymphadenopathy. Surgery remains the standard of care, but a risk of chronic lymphedema and poor wound healing are potential complications. These can have long term impacts on quality of life and so efforts are warranted to explore ways to minimize these risks.

The place of radiation in managing groin disease has been in question, since the results of the only prospective study investigating radiation versus surgery for the management of clinically node negative patients (1). The results showed an excessive number of groin recurrences in the radiation only arm. In the 27 patients managed with radiation alone, there were 5 groin recurrences that all occurred within the treatment field. These 5 patients subsequently died, leading to a progression free survival and overall survival benefit in the surgery group. This trial has been criticized for prescribing the radiation to a depth of 3 cm, which when reviewing the patient's CT scans showed an average vessel to skin distance of 6.1 cm (2). This demonstrates the intended dose to the actual inguinal lymph node target was significantly underdosed. Unfortunately, the results of this trial are interpreted as surgery being a

more effective treatment for controlling the groin but really just shows, unsurprisingly, that a subtherapeutic dose of radiation is not effective in controlling disease.

Stecklein *et al.* (3) provided a rare glimpse into managing gross groin nodes with definitive radiation using modern day, appropriately dosed, radiation. The patients were treated at a major high-volume academic facility and, despite this, only 33 patients were available for analysis over a 22-year time period. In the 31 patients who actually completed their full course of radiation, a median dose of 66 Gy (range, 60–70 Gy) was delivered with the median long-axis radiographic diameter of the largest inguinal lymph node being 2.5 cm (range, 1.4–8.7 cm). After a median follow-up of 28 months (range, 2–196 months), in the patients who completed their prescribed course of radiation, only 3/31 patients, developed a groin recurrence and only 3 patients were noted to have major late complications. This demonstrates that radiation can be highly effective in controlling gross nodes with limited major long-term side effects.

Questions remain, however, regarding the optimal dose to control nodal disease, and it appears that size alone is not a sufficient predictive marker. Stecklein *et al.* identified 3 patients who failed in the groin and their nodes were relatively small, measuring between 1.7–2.1 cm, and were treated with relatively high doses between 64–69.6 Gy. Other patients with much larger nodes and treated with similar doses did achieve local control. One possible explanation is the emerging vulvar cancer data (4-6) showing correlations between HPV positivity with lower in-field recurrence rates after radiation and improved

pathologic complete response rates after neoadjuvant chemoradiation when compared to HPV negative patients. It certainly would be insightful if Stecklein *et al.* were able to stratify their data by HPV status to help us better understand the relationship between tumor size, dose, and local control.

Ultimately, the optimal definitive dose of radiation for both the primary and nodes remains unanswered. As we've escalated the dose from 47.6 Gy (split course) in GOG 101 (7) to 57.6 Gy in GOG 205 (8) the pathologic complete response rates have improved. Results with further dose escalation >60 Gy are pending completion of the currently ongoing GOG 279 trial. Additionally, it is unclear if the dose required to control the primary disease is the same for gross nodal disease. We've seen in cervical cancer, for example, that the dose needed to control the primary is much higher than that of the nodes (9).

There are some limitations to the paper by Stecklein *et al.* These include limited radiation treatment details, the long time period over which patients were treated, the likely underreporting of more subtle late term toxicities, and the heterogeneity of their treatments. These limitations are inherent in a retrospective study but certainly don't meaningfully detract from the significance of the findings.

In summary, Stecklein *et al.* have provided an excellent retrospective series on a contemporary experience demonstrating appropriately delivered radiation is an effective treatment option in vulvar cancer.

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