Radiation Therapy Compared With Pelvic Node Resection for Node-Positive Vulvar Cancer

A Randomized Controlled Trial

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OBJECTIVES: To report long-term survival and toxicity of radiation compared with pelvic node resection for patients with groin node–positive vulvar cancer.

METHODS: A Gynecologic Oncology Group protocol enrolled 114 patients randomly allocated to postoperative pelvic and groin radiation (45–50 Gy, n=59) or to ipsilateral pelvic node resection (n=55) after radical vulvectomy and inguinal lymphadenectomy. Retrospective analyses for 114 enrolled patients included both risk of progression and death after treatment and assessment of toxicity.

RESULTS: Median age was 70 years. Median survivor follow-up was 74 months. The relative risk of progression was 39% in radiation patients (95% confidence interval [CI] 0.17–0.88, P=.02). Fourteen intercurrent deaths occurred after radiation as compared with only two after pelvic node resection, narrowing 6-year overall survival (51% compared with 41%, hazard ratio 0.61 [95% CI 0.30–1.3], P=.18). However, the cancer-related death rate was significantly higher for pelvic node resection compared with radiation (51% compared with 29% at 6 years, hazard ratio 0.49 [95% CI 0.28–0.87], P=.015). Six-year overall survival benefit for radiation in patients with clinically suspected or fixed ulcerated groin nodes (P=.004) and two or more positive groin nodes (P<.001) persisted. A ratio of more than 20% positive ipsilateral groin nodes (number positive/number resected) was significantly associated with contralateral lymph node metastasis, relapse, and cancer-related death. Late chronic lymphedema (16% compared with 22%) and cutaneous desquamation (19% compared with 15%) were balanced after radiation and pelvic node resection.

CONCLUSION: Radiation after radical vulvectomy and inguinal lymphadenectomy significantly reduces local relapses and decreases cancer-related deaths. Late toxicities remained similar after radiation or pelvic node resection.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, www.clinicaltrials.gov, NCT00898352.

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LEVEL OF EVIDENCE: I

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For a list of the other members of the Gynecologic Oncology Group member institutions who participated in this study, see the Appendix online at http://links.lww.com/AOG/A119.

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The extent of groin nodal disease at diagnosis consistently predicts vulvar cancer-related recurrence and death.[1–6] At 5 years, 80% of patients having no or a single unilateral nodal metastasis are estimated to be alive compared with 30% when having three or more unilateral nodal metastases.[2] With the goal of improving outcomes for patients with carcinoma of the vulva found to have groin nodal metastasis, the Gynecologic Oncology Group (GOG) conducted a prospective randomized study of radiation

therapy compared with pelvic node resection after radical vulvectomy and bilateral groin lymphadenectomy (GOG protocol #37).[1]

In 1986, the GOG reported preliminary survival estimates of the 114 patients randomized to groin and pelvic radiation (n=59) or to pelvic node resection (n=55) short of projected accrual goals because differences in 2-year overall survival were statistically significant, favoring radiation (68% compared with 54% [pelvic node resection], *P*=.03) at an interim analysis.[1] Survival advantages attributable to radiation were most evident for women with 1) clinically suspected or fixed ulcerated nodes or 2) two or more pathologic positive groin nodes. Acute surgical or radiation-related toxicities were similar for both regimens, and 2-year radiation-related morbidity was 16% (8 of 48 patients). The 2-year findings from this GOG study defined a new standard of care for patients found to have vulvar cancer with groin node metastasis.

Whether the survival benefit of groin and pelvic radiation in groin node–positive patients with vulvar carcinoma persists with extended follow-up is unknown. The purpose of this report is to confirm durable survival advantage and toxicities observed on GOG protocol #37.

MATERIALS AND METHODS

Detailed methodology of GOG protocol #37 has been published previously.[1] Briefly, 114 patients with primary invasive squamous cell carcinoma of the vulva whose primary lesions and groin nodes were amenable to radical vulvectomy and bilateral inguinal lymphadenectomy were entered into the clinical trial regardless of clinical 1969 International Federation of Gynecology and Oncology staging (Fig. 1). Patients with vulvar cancer recurrence, prior malignancies, those not candidates for radiation, or those with positive groin nodes not resected at surgery were ineligible. All patients determined at the time of surgery to have either unilateral or bilateral groin metastasis were intraoperatively randomly assigned by central telephone allocation to either ipsilateral pelvic node resection or pelvic radiation. Written informed consent consistent with institutional, state, and federal regulations and each treating institution's local institutional review board approval was obtained before conducting the study.

All entered patients underwent standardized radical vulvectomy and bilateral groin resection. Surgical excision of bilateral groin nodes included both superficial and deep nodes relative to the inguinofemoral fascia, including nodal skeletonization of the femoral artery and vein. Nodal tissue medial to the femoral artery and vein was designated the Cloquet node and surgically excised. For patients randomized to pelvic node resection (n=55), pelvic node resection followed a standardized extraperitoneal approach, enabling excision of external iliac, internal iliac, obturator, and common iliac nodes.[1]

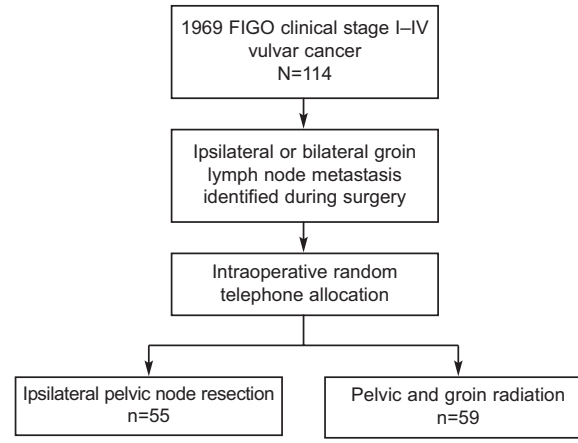

Fig. 1. Flow diagram of patient random allocation on Gynecologic Oncology Group study #37. FIGO, International Federation of Gynecology and Obstetrics.

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For patients randomized to pelvic radiation (n=59), radiation treatment fields encompassed both groins, obturator, and external and internal iliac nodal areas even if only a unilateral positive groin node was found. No central vulvar radiation was administered. Beginning within 6 weeks of vulvectomy, patients received 45 to 50 Gy to the pelvic midplane halfway between the superior border of the obturator foramina and L5-S1 vertebral body interspace at a daily fraction of 1.8 to 2 Gy. Dose calculations were made in the center of the inguinal and femoral node areas at a depth of 2 to 3 cm from the anterior body surface to deliver 45 to 50 Gy. Anterior–posterior and posterior–anterior fields were treated each day for 4.5 to 6 weeks of radiation therapy. Complete blood counts and platelet counts were obtained weekly.

Patient clinical and follow-up data were abstracted from patient charts maintained through November, 1990, at the GOG Statistical and Data Center (Buffalo, NY). In the original design of this study,[1] it was desired to detect a 20% or greater increase in survival after radiation as compared with the baseline 40% survival estimate. To achieve this sensitivity with a power of 0.80 and significance level of 0.05, 76 patients per treatment arm were required. Because of an observed statistical superiority of radiation (*P*=.03)

and after careful deliberation, the study was closed in July 1984, approximately 2 years short of projected accrual goals.[1]

In the previous report, median follow-up was 32 months.[1] In this report, median survivor follow-up was 74 months. For the current retrospective analysis, 114 patients were analyzed using an intent-to-treat method.[7] Three originally reported patients may not contribute to all statistical analyses owing to incomplete or missing data—one for primary disease not resected and two for wrong/no treatment after randomization. As such, this study retrospectively compared patient clinical, tumor, and treatment outcome variables by randomized treatment group: either postoperative pelvic and groin radiation (n=57) or operative ipsilateral pelvic node resection (n=54). For each group, survival was determined from date of study entry to date of all-cause death or date last seen. Cancer-related death was calculated from date of study entry to date of physical or radiographic evidence of cancer-specific death or date last seen. Recurrence-free survival was defined as date of study entry to date of physical or radiographic evidence of recurrent vulvar cancer. Median survivals were computed using the product-limit estimate of Kaplan and Meier method, and a log rank test was used to compare the group-difference in survival function.[8] Cox proportional hazards models adjusting for adverse tumor characteristics (tumor differentiation, exophytic tumor, depth of tumor invasion, largest dimension of primary tumor, lymphatic invasion, vascular invasion) were used in evaluation of treatment differences for recurrence-free survival, cancer-related death, and overall survival.[3,9] Cumulative incidence of cancer-specific death was estimated using the procedure proposed by Gray,[10] and the hazard ratio was estimated using a competing-risk proportional hazards model proposed by Fine and Gray.[11] This statistical procedure compares cumulative incidence for a statistical event among different groups using weighted averages of the hazards of the subdistribution for the event type of interest.[10–12]

A ratio of the number of positive nodes to the total number of nodes surgically resected was calculated and associated with treatment outcome; a ratio of 20% or greater was chosen based the association of a 20% nodal positivity rate and a high locoregional-relapse rate seen in breast cancer managment.[13,14] For right-sided or left-sided unilateral lesions, this ratio represents the number of ipsilateral positive lymph nodes divided by the number of ipsilateral lymph nodes retrieved. For midline lesions, this ratio represents the total number of positive lymph nodes from either groin divided by the total number of lymph nodes retrieved from both groins.

Abstracted acute or late (more than 60 days after protocol treatment) toxicity data were scored retrospectively according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 3, http://ctep.cancer.gov/reporting/ctc.html). Charted patient comorbid conditions of heart disease, lung disease, and diabetes were abstracted. Charted patient height and weight were used to calculate body mass index using the formula advocated by the Centers for Disease Control and Prevention and associated with treatment outcome and treatment-related late toxicity.[15] In addition, time between study entry and date of first radiation treatment, coined radiation lead time, was associated with treatment outcome. Fisher exact tests were calculated among adverse tumor characteristics, clinical nodal status, treatment-related toxicities and treatment groups.[16] All P values reported were two-sided, and $P<.05$ was interpreted as statistically significant. Analyses were done using SPSS 12.0 (SPSS, Inc., Chicago, IL) and R 2.7.2 (The R Foundation for Statistical Computing, www.r-project.org).

RESULTS

For the 114 evaluated patients in this study, median age was 70 years (range 23–89 years). Median survivor follow-up from date of study entry was 74 months, with a maximum follow-up of 143 months. Two non-white patients were enrolled, one in each treatment arm. The numbers of positive groin nodes, histopathological grade, depth of invasion, maximum tumor dimension, and tumor lymphovascular invasion were similar among the radiation and pelvic node resection arms. Clinical groin status based on 1969 International Federation of Gynecology and Oncology staging appears in Table 1. Among all 114 patients, the median number of groin lymph nodes surgically retrieved was 22 (25–75% quartile 17 to 29, range 1 to 65). Single, pathologically confirmed groin lymph node metastases were observed in 39 (35%) patients. The number with two and three or more pathologically confirmed groin lymph nodes was 23 (21%) and 49 (44%) patients, respectively (Table 1). There was no significant difference in the distribution of clinical groin node status between the two arms.

In the previous report of 114 patients, there were 19 patients treated by radiation whose disease had recurred and 22 who had died. After pelvic node resection, 25 patients had a recurrence and 29 died. At the time of this report and in 111 evaluable patients, there are 21 radiation and 27 pelvic node resection patients whose disease has recurred. There

Table 1. Clinical Stage and Nodal Positivity by Treatment Group

FIGO (1969) Clinical Groin Node Status	Treatment Group: Radical Vulvectomy, Bilateral Groin Dissection, Pelvic Radiation Therapy*	Treatment Group: Radical Vulvectomy, Bilateral Groin Dissection, Pelvic Node Dissection*	Total
N0/N1 (no nodes palpable/nodes palpable, and normal)	28 (47)	19 (35)	47 (41)
N2 (nodes palpable, enlarged, firm, and suspicious)	22 (37)	25 (45)	47 (41)
N3 (fixed and ulcerated nodes)	9 (15)	11 (20)	20 (18)
Single groin lymph node metastasis	19 (32)	21 (38)	40 (35)
Two groin lymph node metastases	16 (27)	9 (16)	25 (22)
Three or more groin lymph node metastases	24 (41)	25 (45)	49 (43)
Total	59 (100)	55 (100)	114 (100)

FIGO, International Federation of Gynecology and Obstetrics.
Data are number of patients (%).
* Percentages may not total 100% because of rounding.

have been 18 compared with 28 cancer-related deaths and 32 compared with 30 all-cause deaths on the radiation and pelvic node resection treatment arms, respectively. Forty percent (13 of 32) of observed deaths in the radiation arm occurred after 2 years compared with 20% (6 of 30) in the pelvic node resection arm.

When adjusting for age and adverse tumor characteristics, the adjusted hazard ratio for relapse was 0.39 (95% confidence interval [CI] 0.17–0.88, P=.02), favoring radiation. With long-term follow-up, recurrence-free survival at 6 years was estimated to be 48% after pelvic node resection compared with 59% after radiation (Fig. 2A). All 27 vulvar cancer recurrences recorded after pelvic node resection occurred within 24 months; 4 of 21 recurrences after radiation occurred after 24 months. The recurrence pattern is shown in Table 2. Thirteen groin recurrences (13 of 27 [48%]) were observed in the pelvic node resection arm compared with only three groin recurrences (3 of 21 [14%]) in the radiation therapy arm.

For long-term follow-up, the adjusted hazard ratio of all-cause death for radiation compared with pelvic node resection was 0.61 (95% CI 0.30–1.3, P=.18), with 51% of patients receiving radiation and 41% of patients receiving pelvic node resection estimated to be alive at 6 years (Fig. 2B). On the radiation treatment arm, 14 of 32 (44%) observed deaths occurred as a result of other causes (cardiovascular disease n=7, natural causes n=5, liver cirrhosis n=1, small cell lung cancer n=1). Only 2 of 30 (7%) deaths observed in the pelvic node resection treatment arm were attributable to other causes (pneumonia n=1, non–small cell lung cancer n=1). At 6 years, the cumulative incidence of cancer-related death was 29% for radiation compared with 51% for pelvic node resection (hazard ratio 0.49, 95% CI 0.28–0.87, P=.015, Fig. 2C).

After adjusting for age, treatment, and adverse tumor characteristics, factors such as body mass index, preradiation hematocrit, and medical comorbidities (diabetes, hypertension, and pulmonary disease) did not significantly affect survival (P>.05 for all). Although postsurgical complications may have delayed the start of radiation in those randomized to radiation treatment, perhaps leading to a higher number of recurrences, radiation lead time (time between date of study entry and date of first radiation treatment) did not associate with vulvar cancer recurrence, vulvar cancer-related death, or overall survival (P>.05 for all).

In the previous report of GOG protocol #37, radiation significantly improved 2-year estimated survival in patients with 1) clinically suspected (N2) or fixed ulcerated (N3) groin nodes and 2) two or more positive groin nodes. The long-term follow-up data still supported that those patients with N2/N3 groin nodes (Fig. 2, P=.004) or two or more positive groin nodes (Fig. 3, P<.001) significantly benefited from radiation treatment.

Detection of clinically suspicious N2/N3 groin metastases has been inaccurate.[1,5,17] In the current study, a ratio of positive groin nodes to sampled groin nodes (unilateral–number of ipsilateral positive groin nodes:number ipsilateral groin nodes retrieved; midline–total positive nodes from both groins:total nodes retrieved from both groins) was associated with regional nodal metastases and treatment outcomes. Table 3 shows the significant univariable association between greater than 20% positive ipsilateral groin

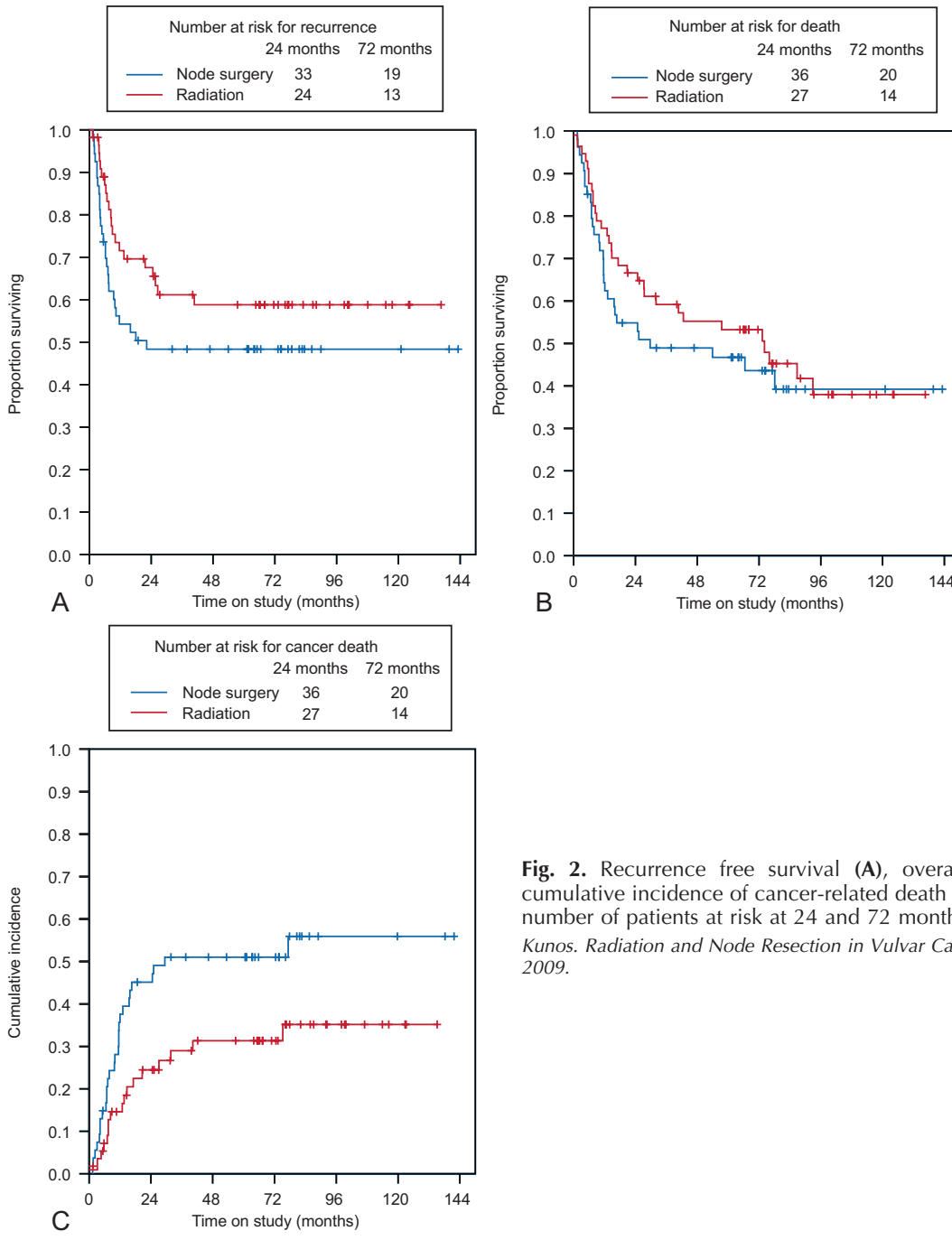

Fig. 2. Recurrence free survival **(A)**, overall survival **(B)**, and cumulative incidence of cancer-related death **(C)** by treatment and number of patients at risk at 24 and 72 months.

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nodes and 1) the number of contralateral lymph node metastases (P=.02), 2) pelvic node metastasis (P=.06), 3) recurrence (P=.03), 4) cancer-related deaths (P=.02), and 5) all-cause deaths (P=.01). Figure 4 illustrates the marked treatment benefit for radiation among patients showing 20% or more positive ipsilateral groin nodes. However, this advantage was not evident for those patients defined as having less than 20% positive ipsilateral groin nodes. After adjusting for age, treatment, and tumor characteristics, the hazard ratio of overall death in patients with 20% positive groin nodes was 3.9 (95% CI 2.1–7.4, P<.001), favoring radiation. At 6 years, estimated overall survival in patients treated by radiation was 36% as compared with 13% in patients treated by pelvic node resection (Fig. 5).

Table 2. Recurrence Pattern and Cancer-Related Deaths by Treatment Arm

Site of Recurrence	Treatment Arm*	
	Radical Vulvectomy, Bilateral Groin Dissection, Radiation Therapy (n=57)	Radical Vulvectomy, Bilateral Groin Dissection, Pelvic Node Resection (n=54)
None	36 (63.2)	27 (50.0)
Any	21 (36.8)	27 (50.0)
Local (vulva)	5 (8.8)	4 (7.4)
Regional (groin)	3 (5.3)	13 (24.1)
Regional (pelvis)	3 (5.3)	1 (1.8)
Distant only	7 (12.3)	6 (11.1)
Distant+local (vulva)	2 (3.5)	2 (3.7)
Unknown	1 (1.7)	1 (1.8)
Cancer-related death	18 (31.6)	28 (51.9)

Data are number of patients (%).
* Percentages may not total 100% because of rounding.

Acute toxicities occurring postoperatively or within 60 days of protocol treatment are shown in Table 4. The proportion of patients developing postoperative wound infections, urinary tract infection, and other adverse sequelae were similar between treatment groups.

There were 39 patients in the radiation arm and 28 patients in the pelvic node resection arm alive after 2 years who could be reassessed for long-term adverse sequelae. Delayed or late toxicities, defined as occurring more than 60 days after protocol treatment, are presented in Table 4. Adverse events as recorded reflect maximum grade observed during study follow-

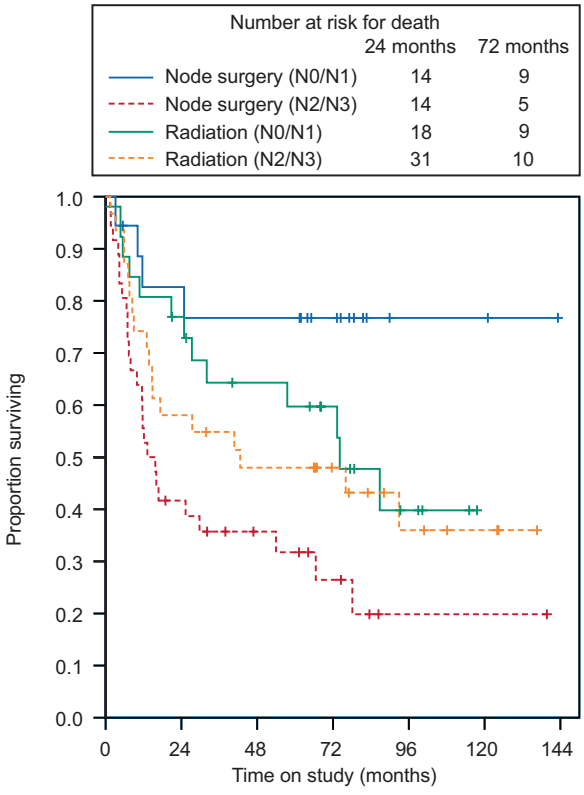

Fig. 3. Overall survival related to clinical groin node status by treatment and number of patients at risk for death at 24 and 72 months.

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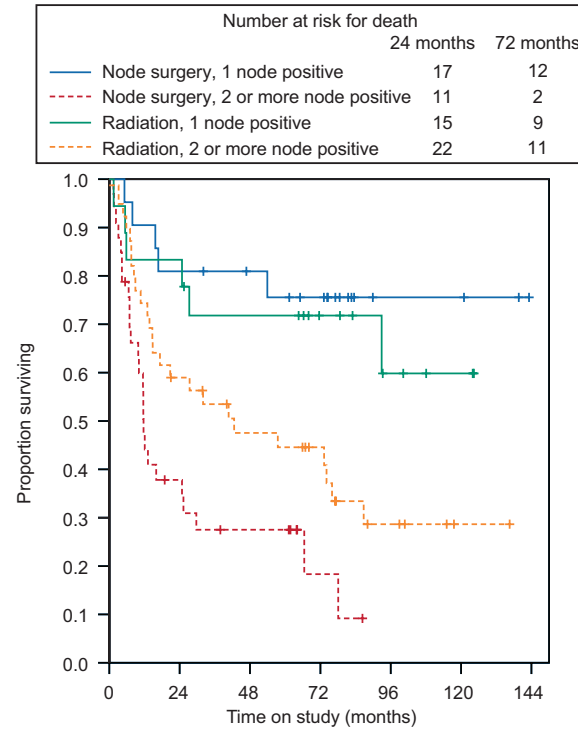

Fig. 4. Overall survival related to number of positive groin nodes by treatment and number of patients at risk for death at 24 and 72 months.

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Table 3. Association of Ratio of Positive Groin Nodes/Sampled Groin Nodes,* Nodal Metastasis, and Treatment Outcome

	Contralateral Groin Lymph Node–Positive	Ipsilateral Pelvic Lymph Node–Positive	Recurrence	Cancer-Related Death
20% or fewer positive (n=73)	21 (29)	5 (7)	26 (36)	24 (33)
More than 20% positive (n=38)	20 (53)	8 (21)	22 (58)	22 (58)
P	.02	.06	.03	.02

Data are number of patients (%) unless otherwise specified.
* Unilateral lesion–ipsilateral positive groin nodes:ipsilateral retrieved nodes; midline lesion–positive nodes from both groins:total number retrieved nodes from both groins.

up. Cutaneous toxicity rate was 19% after radiation and 15% after pelvic node resection (*P*=.62). Median time to late persistent grade 2 or higher cutaneous toxicity was 60 days (range 9 to 499 days) after radiation and 80 days (range 29 to 202 days) after pelvic node resection. Chronic lymphedema rate was 16% after radiation and 22% after pelvic node resection (*P*=.47). Median time to late persistent grade 2 or higher lymphedema was 202 days (range 15 to 715 days) after radiation and 192 days (range 86 to 799 days) after pelvic node resection. Chronic lymphedema was observed slightly more often in patients with comorbid diabetes and cardiovascular disease, but this was not statistically significant (*P*=.11, each). Body mass index correlated with radiation-related cutaneous toxicity (odds ratio: 0.82, 95% CI 0.69–0.98, *P*=.03) but not chronic lymphedema (*P*=.46).

DISCUSSION

Previous studies of locally advanced vulvar cancer have revealed that 20–40% of patients with superficially invasive (more than 3 mm) or large (2 cm or more) primary tumors and 60–80% of stage III patients regardless of primary tumor size have groin lymph node metastases and suffer recurrence most often within 24 months after completion of primary treatment.[1,16] After radical vulvectomy, inguinal nodal recurrences are associated with high morbidity and early cancer-related death.[4,18,19] Early results of GOG protocol #37, showing a significant 2-year survival

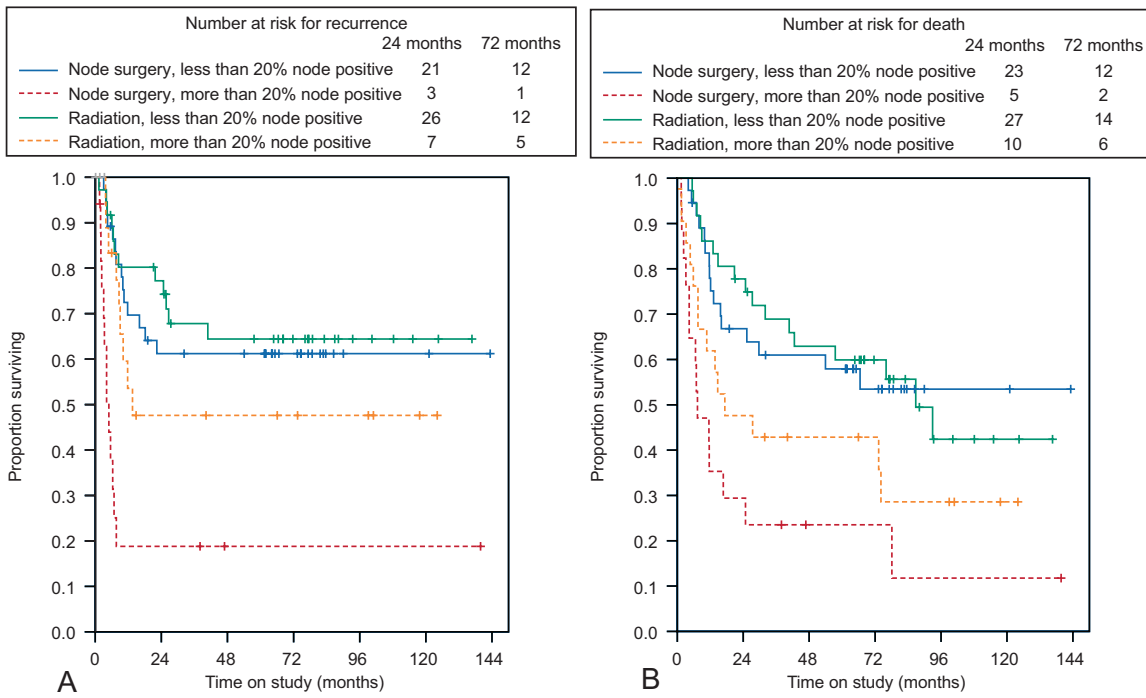

Fig. 5. Recurrence-free survival **(A)** and overall survival **(B)** related to ratio of positive groin nodes/sampled groin nodes by treatment and number of patients at risk at 24 and 72 months.
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Table 4. Acute and Late Toxicity by Treatment

	Pelvic Node Dissection (n=54)	Radiation (n=57)	*P*
Acute			
Wound infection	33 (61)	32 (56)	.70
Urinary tract infection	6 (11)	6 (11)	1.00
Pulmonary embolism	0 (0)	1 (2)	1.00
Stroke	1 (2)	0 (0)	.49
Sepsis	6 (11)	3 (5)	.31
Acute lymphedema	16 (30)	14 (25)	.67
Other	7 (13)	4 (7)	.35
Late			
Cutaneous (grade 2 or higher)	8 (15)	11 (19)	.62
Lymphedema (grade 2 or higher)	12 (22)	9 (16)	.47

Data are n (%).

benefit and recurrence-free interval advantage with adjuvant groin radiation with low morbidity, prompted rapid acceptance of radiation treatment in patients with clinically suspected or fixed ulcerated nodes (N2/N3) or more than one positive groin node.[1] The authors concluded that the improvement in survival from radiation was primarily because of a marked decrease in the rate of inguinal node recurrence (24% compared with 5%). Consistent with other reports, in this updated study of GOG protocol #37, inguinal groin node recurrences often resulted in death.[1] Despite acceptance, the lack of long-term study of efficacy and toxicity from GOG #37 has led some to question whether less radical or omission of groin nodal resection should be considered in favor of radiation alone to lower postoperative radiation-related morbidity.[20–22]

In the current update of GOG #37, a significant improvement in 6-year cancer-related death was seen among patients who received adjuvant radiation as compared with pelvic node resection. Survival benefit in patients with clinically suspected or fixed ulcerated nodes (N2/N3) or more than one positive groin node also persisted through 6 years. However, unlike the overall survival benefit of 14% reported in the original publication of GOG #37, the overall survival benefit narrowed with long-term follow-up such that the 10% survival advantage after radiation was no longer significant (*P*=.53). This observation is most attributable to a high number of non–cancer-related deaths occurring in the radiation group after 2 years. The proportion of patients alive and disease-free remained higher in the radiation group as compared with the pelvic node resection group and, after adjusting for age and tumor factors, was found to be statistically significant. Groin and lower pelvic radiation significantly lowered the number of groin relapses; however, as regional therapies, radiation and pelvic node resection were not able to mitigate distant disease recurrences, suggesting a role for cytotoxic and biologic chemotherapies.

Vulvar cancer–related death is critically linked to the number of positive groin nodes at initial surgery. Subgroup analyses of patients with clinically suspected or fixed ulcerated nodes (N2/N3) or more than one positive groin node showed a benefit with adjuvant radiation.[1] In this study, single pathologically confirmed groin lymph node metastases were observed in 39 (35%) patients, resulting in an inadequate statistical power to estimate clinical benefit of radiation or pelvic node resection reliably in this subgroup of patients. Because cancer-related death often associates with inguinal node recurrence, and radiation markedly decreases nodal recurrence, the debatable but often recommended therapy to sterilize occult groin disease in patients with pathologically confirmed single groin lymph node metastases remains adjuvant radiation.[1,23] A prospective randomized clinical trial of radiation compared with surgical resection in the single lymph node–positive patient population would need to confirm these findings; however, clinical trial accrual would be arduous given the propensity for sentinel lymph node assessment for vulvar cancer and the rarity of vulvar cancer disease itself.

Unfortunately, clinical suspicion of groin node metastases is unreliable and often complicated by the observation that nearly 16–24% of patients with clinically negative groin nodes have occult nodal metastases.[3,24] Moreover, sentinel node procedures or less radical groin node resections with low nodal yields are being performed more routinely, raising the important question as to whether adequate nodal sampling is being done to detect groin nodal metastases. In this update of GOG #37, a ratio of positive groin nodes detected to number of groin nodes excised was investigated to determine the association of this objective measure of nodal positivity and treatment outcome. A 20% nodal positivity rate was selected as the cut-point because of the high association of 20% ipsilateral axillary nodal positivity and high locoregional-relapse rate (approaching 40% at 8 years) observed after mastectomy and doxorubicin-based chemotherapy for breast cancer treatment.[13,14] Based on these data and in addition to traditional indications, a ratio of 20% nodal positivity serves as an additional criterion for postmastectomy radiation. We are not aware of this metric being applied to vulvar

cancer management. When applied, 20% nodal positivity was significantly associated with contralateral groin and pelvic nodal metastasis, vulvar cancer recurrence, and cancer-related death. Significant improvement in patient survival was seen with adjuvant radiation. In multivariable analyses, including known vulvar cancer prognostic factors, 20% nodal positivity remained highly statistically significant for recurrence-free survival, cancer-related death, and overall survival. The findings of the current GOG #37 update support the routine use of 20% nodal positivity rate as a tool for the clinician, indicating (or recommending) adjuvant groin and low pelvic radiation.

We found that radiation after radical vulvectomy and inguinal lymphadenectomy significantly reduces local relapses and decreases cancer-related deaths. Late toxicities remained similar after radiation or pelvic node resection. Excessive postoperative radiation-related morbidity for vulvar cancer has been used to argue for less aggressive surgical groin node resection or even radiation to the intact groin instead of groin lymphadenectomy.[20,21,25] Although the number of acute complications from surgery appears quite high in this study, with longer follow-up, chronic skin and lymphedema toxicities are in accord with or better than reported rates in patients treated in other institutional studies.[2,22,25] These findings are encouraging and provide further evidence that late complication rates should not be a barrier to aggressive groin resection.

In conclusion, long-term follow-up confirms significant recurrence-free and cancer-related death benefit of radiation as compared with pelvic node resection in vulvar cancer with positive groin node metastasis. This benefit appears most beneficial in those with clinically suspicious or more than one positive groin node. This update of GOG #37 provides a new objective indication for groin and pelvic radiation when greater than 20% ipsilateral groin nodes are present because radiation significantly benefits treatment-related survival. Long-term analysis of treatment-related toxicities shows similar rates of chronic skin and lymphedema complications after radiation or pelvic node resection.

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