

Surgical Innovations in Gynecologic Cancers

Moderators: Kara Long Roche, MD, and Jamie Bakkum-Gamez, MD

May 12, 6:00 p.m. CST

Validation of sentinel lymph biopsy in patients with early stage vulvar cancer: A prospective trial of 1552 women (GROINSS-V II/GOG270)

B. Slomovitz^a, M. Oonk^b, B.J. Monk^c, W.J. Van Driel^d, D. Cibula^e, P.A. DiSilvestro^f, A.L. Covens^g, D.M. O'Malley^h, R.S. Mannel^b and A. van Der Zeeⁱ. ^aSylvester Comprehensive Cancer Center, University of Miami Health Center, Miami, FL, USA, ^bUniversity Medical Center Groningen, Groningen, Netherlands, ^cUniversity of Arizona College of Medicine Phoenix, Phoenix, AZ, USA, ^dDGOG (Dutch Gynecologic Oncology Group), Amsterdam, Netherlands, ^eCharles University and General Faculty Hospital, Prague, Czech Republic, ^fWomen & Infants Hospital, Brown University, Providence, RI, USA, ^gUniversity of Toronto, Toronto, ON, Canada, ^hThe Ohio State University, James Cancer Hospital, Columbus, OH, USA

Objective: The sentinel lymph node (SLN) procedure in vulvar cancer has become standard of care since our first GROINSS-V study reported a groin recurrence rate of 2.3%. In GROINSS-V II/GOG270, a study that investigated the safety of radiotherapy in patients with metastases in their SLN, all SLN-negative patients were registered in order to confirm our previous findings. Here we present the analysis of the patients with a negative SLN.

Method: A prospective observational trial was performed in patients with early-stage squamous cell carcinoma of the vulva (diameter <4 cm), without suspicious lymph nodes at palpation or imaging, and planned for surgery (radical local excision in combination with an SLN procedure). In case of a metastatic SLN (metastasis of any size), radiotherapy was given to the groin(s) to a total dose of 50 Gy. In case of a negative SLN, patients were followed up for 2 years. Stopping rules were formulated in order to monitor the groin recurrence rate.

Results: From December 2005 until October 2016, 1,708 patients were included in GROINSS-V II/GOG270. After exclusion of 156 ineligible patients, 1,552 patients were available for analysis. The SLN was negative in 1,222 patients (78.7%). During follow-up, 144/1,222 (11.8%) patients were diagnosed with local recurrence, of whom 16/144 (11%) also had groin metastasis. Isolated groin recurrences were diagnosed in 38/1,222 patients (3.1%). In 6/38 patients, clear protocol violations were observed: incomplete treatment of groin ($n = 3$); primary tumor >4 cm ($n = 1$); not all SNs visualized on the lymphoscintigram were removed ($n = 2$). Prognostic factors related to groin recurrences will be presented.

Conclusion: In the largest prospective series of SLN-negative vulvar cancer patients ever reported, the safety of omitting inguinofemoral lymphadenectomy after a negative SLN could be confirmed with a groin recurrence rate of 3.1% (after exclusion of the protocol violations 2.7%), comparable to the data of our first GROINSS-V study.

Radiotherapy as an alternative treatment for inguinofemoral lymphadenectomy in vulvar cancer patients with a metastatic sentinel node: Results of GROINSS-V II.

A.G. van Der Zee^a, B. Slomovitz^b, A.L. Covens^c, J. van Der Velden^d, J.A. de Hullu^e, B. Slangen^f, E. van Dorst^g, W.J. Van Driel^h, R. Hermansⁱ, I.B. Vergote^j, D. Nunns^k, C. Holland^l, D. Cibula^m, R.S. Mannelⁿ, P.A. DiSilvestro^o, D. Provencher^p, B.J. Monk^q and M. Oonk^a. ^aUniversity Medical Center Groningen, Groningen, Netherlands, ^bMemorial Sloan Kettering Cancer Center, New York, NY, USA, ^cSunnybrook Odette Cancer Centre, Toronto, ON, Canada, ^dAcademic Medical Centre, Amsterdam, Netherlands, ^eRadboud University Medical Center, Nijmegen, Netherlands, ^fCancer Center, Maastricht, Netherlands, ^gCancer Center, Utrecht, Netherlands, ^hDGOG (Dutch Gynecologic Oncology Group), Amsterdam, Netherlands, ⁱCatharina Hospital, Catharina, Netherlands, ^jUniversity Hospital Leuven, Leuven, Belgium, ^kCancer Center, Nottingham, United Kingdom, ^lManchester University NHS Trust, Manchester, United Kingdom, ^m2nd Medical Faculty Charles University Prague, Faculty Hospital Motol, 150 06 Praha 5, Czech Republic, ⁿThe University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, ^oWomen & Infants Hospital, Brown University, Providence, RI, USA, ^pUniversite de Montreal, Montréal, QC, Canada, ^qArizona Oncology (US Oncology Network), University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA

Objective: In order to reduce treatment-related morbidity, the GROINSS-V II trial investigated whether radiotherapy is a safe alternative for inguinofemoral lymphadenectomy (IFL) in vulvar cancer patients with a metastatic sentinel node.

Method: GROINSS-V II was a prospective multicenter phase II trial, including patients with early-stage squamous cell carcinoma of the vulva (diameter <4 cm) without suspicious lymph nodes at imaging, who had primary surgical treatment with sentinel node procedure. In case of a metastatic sentinel node (metastasis of any size), radiotherapy was given to the groin (50 Gy). Stopping rules were defined to monitor groin recurrence rate.

Results: From December 2005 until October 2016, 1,708 patients were registered. Overall 1,552 patients were eligible, of whom 324 (21%) had a metastatic sentinel node. After 54 months of inclusion, the stopping rule was activated; interim analysis showed an increased risk for groin recurrence in case of sentinel node metastasis >2 mm and/or with extranodal extension (ENE). The protocol was amended, with patients only with micrometastasis ≤2 mm receiving radiotherapy from then on, and those >2 mm undergoing IFL (with radiotherapy if >1 metastasis or ENE). Final analysis after ≥2 years revealed 6 isolated groin recurrences in 157 patients with a sentinel node micrometastasis (3.2%). Four could not be considered radiotherapy failures: 2 developed recurrence in the contralateral (sentinel node-negative) groin; 2 refused radiotherapy. Twenty-eight patients did not undergo radiotherapy. Among 129 patients who received radiotherapy to the groin, 2 isolated groin recurrences were diagnosed (1.6%). Radiotherapy to the groin after sentinel node procedure showed only minimal toxicity: 5/118(4.2%) had grade 3 toxicity, while no grade 4 or 5 toxicity was observed.

Conclusion: Radiotherapy to the groin is a safe alternative for IFL in patients with sentinel node metastasis ≤2 mm, with minimal toxicity. For patients with sentinel node metastasis >2 mm, radiotherapy with a total dose of 50Gy was no safe alternative for IFL; dose escalation and/or chemoradiation should be investigated in these patients.

Sentinel lymph node biopsy versus lymphadenectomy for high-grade endometrial cancer staging (SENTOR trial): A prospective multicenter cohort study

M.C. Cusimano^a, D. Vicus^b, K. Pulman^c, M.Q. Bernardini^d, S. Laframboise^d, T. May^d, G. Bouchard-Fortier^d, L. Hogen^d, L.T. Gien^b, A.L. Covens^b, R. Kupets^e, B.A. Clarke^a, M. Cesari^c, M. Rouzbahman^d, J. Mirkovic^b, G. Turashvili^d, M. Maganti^d, A. Zia^d, G.E.V. Ene^d and S.E. Ferguson^d. ^aUniversity of Toronto, Toronto, ON, Canada, ^bSunnybrook Odette Cancer Centre, Toronto, ON, Canada, ^cTrillium Health Partners, Credit Valley Hospital/University of Toronto, Mississauga, ON, Canada, ^dPrincess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, ^eSunnybrook Cancer Centre/University of Toronto, Toronto, ON, Canada

Objective: It is unclear whether sentinel lymph node biopsy (SLNB) can replace complete lymphadenectomy in women with high-grade endometrial cancer (EC). We performed a prospective multicenter cohort study (the SENTOR trial) to evaluate the performance characteristics of SLNB using indocyanine green (ICG) in stage I high-grade EC (ClinicalTrials.gov ID: NCT01886066).

Method: Patients with clinical stage I grade 2 endometrioid or high-grade EC (grade 3 endometrioid, serous, clear cell, carcinosarcoma, undifferentiated, or mixed tumors) undergoing laparoscopic or robotic surgery at 3 cancer centers in Toronto, Canada, were prospectively recruited for SLNB with ICG. After SLNB, high-grade EC patients underwent pelvic and paraaortic lymphadenectomy (PLND/PALND), and grade 2 endometrioid EC patients underwent PLND only. All SLNs were submitted for standardized ultrastaging. The study was powered using a Fleming 2-stage design to accurately determine patient-specific sensitivity of the SLNB algorithm as the primary outcome; secondary outcomes were the negative predictive value (NPV), false negative rate (FNR), and bilateral detection rate.

Results: We accrued 156 patients (high-grade EC, $n = 126$) with mean age 64 years (range 40–86 years) and BMI 28 (range 18–47). All patients had SLNB and PLND, and 106/126 patients (84%) with high-grade EC had PALND. Median numbers of SLNs, PLNs, and PALNs removed per patient were 3 (IQR 2–5), 16 (IQR 12–20), and 6 (IQR 4–10), respectively. SLN detection rates were 99% per patient (95% CI 95–100), 88% per hemipelvis (95% CI 83–91), and 77% bilaterally (95% CI 70–83). Of 26 patients (17%) with nodal metastases, 25 were identified by the SLNB algorithm, for a patient-specific sensitivity of 96% (95% CI 80–100), FNR of 3.9% (95% CI 0–19), and NPV of 99% (95% CI 96–100). Only one patient (0.6%) would have been misclassified by the SLNB algorithm.

Conclusion: SLNB has excellent performance characteristics and the potential to replace lymphadenectomy in high-grade EC patients with an increased risk of lymph node metastases. Randomized trials comparing oncologic outcomes and morbidity between SLNB alone and complete lymphadenectomy are needed.

Characterization of patients with isolated tumor cells and micrometastasis on sentinel lymph node biopsy performed for endometrial cancer staging

K.A. Underkofler^a, M.N. Towner^a, A. Urh^b, P.J. Meacham^a, K.M. Robison^b and R.G. Moore^a. ^aUniversity of Rochester Medical Center, Rochester, NY, USA, ^bWomen & Infants Hospital, Brown University, Providence, RI, USA

Objective: Isolated tumor cells (ITC) are tumor deposits measuring ≤ 0.2 mm, whereas micrometastasis (MM) is defined as a metastatic deposit measuring >0.2 to ≤ 2 mm. While the characterization of these findings and their significance have been discussed in breast cancer literature, less is known about these results in endometrial cancer. We sought to determine whether patient and disease characteristics correlate with the finding of ITC or MM on sentinel lymph node (SLN) biopsy for endometrial cancer.

Method: We carried out an Institutional Review Board-approved retrospective chart review of all women with endometrial cancer who underwent SLN mapping and biopsy during surgical staging at two academic medical centers between 2013 and 2018. When available, follow-up data were included in the analysis. Statistical analysis was performed using a multiple logistic regression model.

Results: A total of 573 patient charts were identified and reviewed. Unilateral or bilateral SLNs were detected successfully in 92.7% ($n = 531$). Among women with identified SLN, 6% ($n = 31$) were found to have ITC or MM. Characteristics of women with ITC or MM can be found in **Table 1**. The median age of women with positive ITC or MM was 63 years (range 46–92 years), and median BMI was 33.8 (range 21–53). Neither was found to be related to the presence of ITC or MM. Tumors were most commonly FIGO grade 2 (45%, $n = 13$). Lymphovascular space invasion (LVSI) was present in 70% ($n = 21$). A small majority (55%, $n = 17$) had uterine disease confined to the inner 2/3 of the myometrium. ITC or MM was more likely to be seen in patients with LVSI (OR = 11.56, 95% CI 4.74–28.2) and with increasing tumor grade (OR = 1.93, 95% CI 1.13–3.31). In addition, the absolute depth of myometrial invasion had a weak effect on the presence of ITC or MM (OR = 1.13, 95% CI 1.07–1.19), as did percentage of myometrial invasion (OR = 1.03, 95% CI 1.02–1.04). Follow-up information was available for 272 patients in the cohort, including 14 patients with positive ITC or micrometastasis. Of these 14 patients, 1 had disease recurrence (7%). In patients with a negative SLN biopsy, the recurrent rate was 6.4%.

Conclusion: ITC or MM is a relatively rare diagnosis in women undergoing SLN biopsy for endometrial cancer staging. Additional data are needed to clarify risk factors for this finding and associated patient outcomes.

Table 1. Characteristics of patients with ITC or micrometastasis on SLN biopsy ($n=31$).

	n (%)
Age	
< 50	11 (35)
50-69	13 (42)
≥ 70	7 (23)
BMI	
≤ 25	2 (7)
25-30	9 (29)
30-40	15 (48)
≥ 40	5 (16)
FIGO Grade^a	
1	9 (31)
2	13 (45)
3	7 (24)
Lymphovascular space invasion^b	
Present	21 (70)
Absent	9 (30)
Depth of myometrial invasion^c	
Inner 1/3	6 (19)
Inner 2/3	17 (55)
Outer 1/3	14 (45)
Follow-up ($n = 14$)	
No evidence of disease	13
Recurrence	1

^a Information not available for 2 patients, $n = 29$

^b Information not available for 1 patient, $n = 30$

^c Percentage does not total 100, because 'inner 2/3' also includes all patients with 1/3 myometrial depth of invasion

Does the presence of nodal micrometastases or isolated tumor cells increase the risk of recurrent endometrioid adenocarcinoma? A case control study.

T. Castellano^a, R. Conrad^a, C. Davey^a, S. Husain^a, J.D. Dvorak^a, K. Ding^b and C.C. Gunderson^a. ^aThe University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, ^bThe University of Oklahoma, Oklahoma City, OK, USA

Objective: The purpose of this case control study was to explore whether the presence of micrometastases (MMs) or isolated tumor cells (ITCs) is associated with an increased the risk for recurrence in women with fully staged, stage I–II endometrioid endometrial cancer.

Method: From 2008 to 2018, women with recurrent stage I or II endometrioid endometrial cancer who also had a full staging lymphadenectomy were identified. The outcome of interest was the presence of recurrence. A control group of women without recurrence within 2 years was selected based on the frequency-matching approach, with group size double that of the case group. The exposure of interest was the presence of previously unseen MMs (>0.2 mm) or ITCs (≤0.2 mm) on original surgical pathology. Original nodal surgical slides were re-reviewed for both cases and controls by a gynecologic pathologist; both pankeratin and H&E stained slides were evaluated to determine the presence of MMs or ITCs in nodal tissue. The effect of ITCs on recurrence was modeled by using logistic regression.

Result: A total of 153 participants were included for analysis, 50 with recurrence and 103 without, at a minimum of 24 months. There was no significant difference in age ($P = 0.46$), race ($P = 0.24$), stage ($P = 0.50$), FIGO grade ($P = 0.64$), lymphovascular space invasion (LVSI) ($P = 0.85$), or meeting GOG 99 high-intermediate risk criteria ($P = 0.43$). Patients with recurrence had a significantly higher mean number of lymph nodes removed (21.9 vs 18.9, $P = 0.03$). At time of analysis, 120 pathologic cases were reviewed with the identification of 10 ITCs (8.3%) and no MMs. Finding of ITCs was not associated with higher number of lymph nodes removed ($P = 0.33$) or tumor grade ($P = 0.55$) but was marginally associated with the presence of LVSI ($P = 0.07$). After adjusting for total lymph nodes removed, the presence of ITCs was not significantly associated with recurrence ($P = 0.93$). See **Figure 1**.

Conclusion: In an early-stage, appropriately treated, endometrioid endometrial carcinoma population, the finding of previously undiagnosed MMs and ITCs is a rare occurrence and is most closely associated with the finding of LVSI. The presence of ITCs was not significantly associated with recurrence-free survival or overall survival in this population. Thus, adjusting staging or treatment planning should be avoided with the finding of ITCs in otherwise negative LNs.

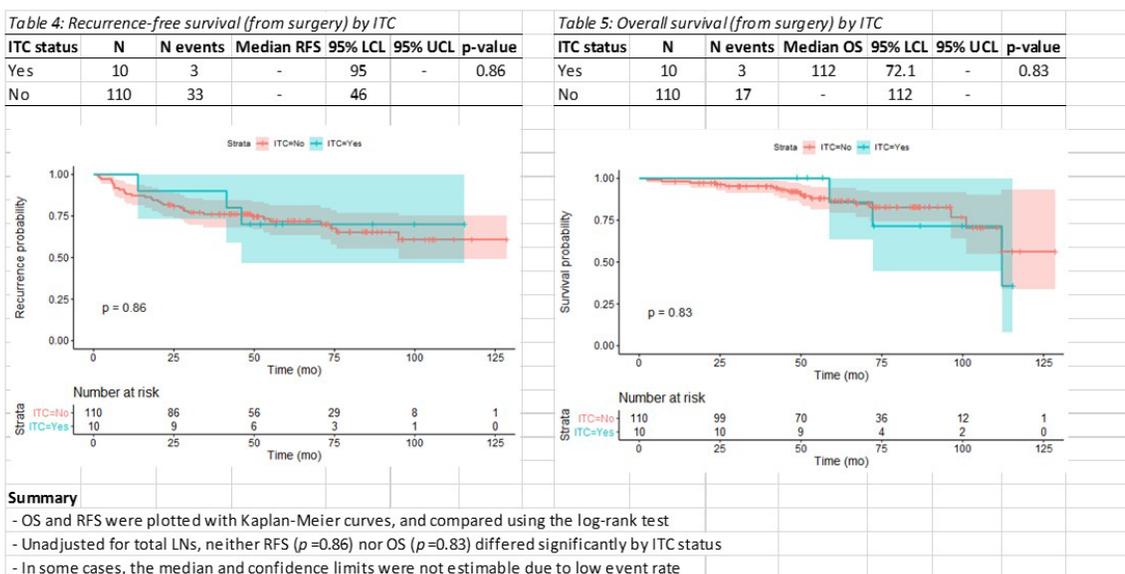


Fig. 1.