Giovanni Scambia

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Università Cattolica del Sacro Cuore

VULVAR CANCER SURGERY: WHY, WHEN AND HOW
- 5% of all female genital tract malignancies
- 92% squamous cell carcinoma (SCC)
  - Melanoma
  - Adenocarcinoma
  - Basal cell carcinoma
  - Sarcoma
- In the United States in 2012
  - New cases: 4,490
  - Deaths: 950.
  - [Cancer facts and figures, ACS 2012]
- Highest estimated incidence in Malta: 3.5/100,000
- Increasing among young women

Age-standardised (World) incidence of vulval cancer by world region, 2002 estimates (CR-UK)
In the open scene of vulvar cancer treatments surgery plays a *central role* currently being the *first choice* and exerting a *great impact on prognosis.*

- An updated standard of care hasn’t yet been defined
- Most approaches to treatment are mainly based on the experience of small series
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

MAIN GOALS OF SURGERY

STAGING

TREATMENT
In 1988 (1) vulvar cancer staging system switched from clinical to surgical

In 2009 FIGO staging system (2) was revised on the base of the main emerging features affecting prognosis:

- tumor size
- number and size of groin lymphnode metastasis
- surrounding tissues involvement

(1) Meeting Report 1988
(2) FIGO 2009 Meeting Report, Pecorelli 2009
**TREATMENT**

**Improvement in OS:**
- Radical vulvectomy with en bloc bilateral inguinofemoral and pelvic lymphadenectomy - 5 year survival rate improved from 20-25% to 60-70%
- Removal of > 10 IFL for each side in patients with positive nodes (2)
- Removal of deep and superficial IFL (3)

**Reduction of local relapse:**
- Extent of surgical margins (4). Surgical margin is the most powerful predictor of local vulvar recurrence. Accounting for specimen preparation and fixation, a 1-cm tumor-free surgical margin on the vulva results in a high rate of local control

---

(1) FJ Taussig 1940
(2) Courtney-Brooks 2010
(3) Stehman 1992, Burke 1995
(4) JM Heaps 1990
In case of resectable disease, radical surgery should always be performed in early and locally advanced stages of disease.

In case of unresectable local advanced disease, surgery should be attempted after a neoadjuvant treatment.

In metastatic disease with local severe symptoms, surgery retains a palliative role.

to summarize… "always if possible!"
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

SURGICAL BURDEN

- Local and systemic morbidity
- Prolonged hospitalization
- Mortality

- Type of affected patients: advanced age and related systemic diseases
- Specific issues related to the anatomical area in question: contamination of wounds and humidity
- Frequent need for massive demolition
- Delayed feeding and consequential development of intestinal bacterial flora, potentially reaching a septic status
Short and long-term post-operative complications are frequent and sometimes severe

- wound_breakdown
- infection
- lymphocele
- lymphedema cellulitis
- erysipelas
- deep venous thrombosis

Possible delay on the start of adjuvant therapies sometimes up to lose the correct indication
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

CRITERIA FOR SURGERY

I. Restricted more than possible
II. Radical and oncologically safe
III. Supported by plastic surgical techniques
IV. Peri-operative management protocols
Minimizing demolition up to minimum required is mandatory, especially for early disease.

Over the years, many acquisitions allowed to resize the extent of surgery towards a more sparing vulvar and nodal surgery.
MAJOR STEPS IN THE HISTORY OF VULVAR SPARING SURGERY

- BUTTERFLY INCISION
- TRIPLE INCISION
  - NO NODAL STAGING IN MICRO-INVASIVE CANCER
  - MONOLATERAL LYMPHADENECTOMY
  - SAPHENOUS VEIN SPARING
  - SENTINEL NODE BIOPSY
  - CONSERVATIVE VULVAR SURGERY
    - WLE - EV
  - CLITORAL SPARING SURGERY

CRITERIA FOR SURGERY
Radical vulvectomy with en bloc inguinofemoral lymphadenectomy through butterfly incision

Separate triple incisions sparing the inguino-crural skin bridge

CRITERIA FOR SURGERY
Radical wide local excision instead of radical vulvectomy

- small lesions (< 2cm)
- tumor/vulvar size ratio is favorable
CLITORAL SPARING SURGERY

Available online at www.sciencedirect.com

Gynecologic Oncology 95 (2004) 152–156

Conservative clitoral preservation surgery in the treatment of vulvar squamous cell carcinoma

John K. Chan, Valerie Sugiyama, Tania R. Tajalli, Huyen Pham, Mai Gu, Joanne Rutgers, Bradley J. Monk

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, CA 94305-5317, United States
Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Chico Family Comprehensive Cancer Center, University of California, Irvine Medical Center, Orange, CA 92866, United States
Department of Pathology, Long Beach Memorial Medical Center, Long Beach, CA 90806, United States

Received 19 February 2004
Available online 28 August 2004

Safety and efficacy of clitoral-sparing surgery when tumor doesn’t involve the very anterior vulva

CRITERIA FOR SURGERY
Omission of nodal surgical staging if T stromal invasion < 1 mm
Risk of groin metastasis is negligible

CRITERIA FOR SURGERY
Mono-ipsilateral inguinofemoral lymphadenectomy

- unilateral tumors distant > 1 cm from the median line
- clinically negative groin lymph nodes risk of contralateral metastasis 0.4 %

CRITERIA FOR SURGERY
Routinary sparing of the saphenous vein

Estimated benefit: 30% of reduction in legs lymphedema and thrombosis

Preservation of the Saphenous Vein during Inguinal Lymphadenectomy Decreases Morbidity in Patients with Carcinoma of the Vulva

Sunny H. Zhang M.D., Ph.D.
Anil K. Sood, M.D.
Joel I. Sorosky, M.D.
Barrie Anderson, M.D.
Richard E. Buller, M.D., Ph.D.

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Iowa Hospitals and Clinics, Iowa City, Iowa.

BACKGROUND. Traditional inguinal lymphadenectomy includes the removal of a portion of the saphenous vein. The authors hypothesized that preserving the saphenous vein would decrease morbidity without affecting treatment outcome.

METHODS. A retrospective review of 83 patients with carcinoma of the vulva who underwent inguinal lymphadenectomy between 1990–1998 was performed. Postoperative short term and long term complications were evaluated.

RESULTS. A total of 139 inguinal dissections were performed in 83 patients. The saphenous vein was preserved in 62 patients and ligated in 77 patients. The clinical characteristics of the patients, the operating time, and the estimated blood loss were not significantly different between the two groups. The incidence rate of short term complications including fever, seroma, phlebitis, lymphocyst, and deep venous thrombosis also was similar. Cellulitis occurred in 39% of the patients who underwent vein ligation compared with 18% of the patients who underwent a vein-sparing procedure ($P = 0.006$). Short term (< 6 months) lower extremity lymphedema occurred in 70% of the vein-ligated group compared with 32% of the vein-spared group ($P < 0.001$). Chronic edema ($\geq$ 2 years) was present in only 3% of the patients who underwent saphenous vein preservation compared with 32% of those who underwent vein ligation ($P = 0.003$). Chronic lymphedema in the vein-spared group was observed in only one patient who received postoperative radiation. Overall, individuals with preservation of the saphenous vein were less likely to develop complications (56% vs. 23%; $P < 0.001$). There was no difference in the rate of incidence of recurrent disease between the two groups.


CRITERIA FOR SURGERY
Adoption of SNB as a reliable nodal staging system avoid bilateral IFL in almost 70% of cases
Results
- SNB is a very safe procedure in selected early vulvar cancer:
  - T < 4 cm
  - Unifocal disease
  - Midline disease with bilateral drainage in lymphoscintigram
  - Using the radiotracer procedure instead of blu-dye

Pros
- Less morbidity
- Ultrastaging with serial sections and IHC (micrometa and ITC detection)
- Possible localization on nodes in atypical positions (radioisotope)
- Overall minor costs

Cons
- Experienced dedicated surgeons
- Nuclear medicine unite
- Specific devices (gamma probe)

Sentinel Node Dissection Is Safe in the Treatment of Early-Stage Vulvar Cancer
Arie G.J. Van der Zee, Maaike H. Oonk, Joanne A. De Hullu, Anca C. Assink, Ignace Vergeot, René H. Verheijen, Angelo Maggioni, Katja N. Goorhuis, Peter J. Baldwin, Eleonore B. Van Dors, Jacobus Van der Velden, Ralph H. Hermans, Hans van der Putten, Pierre Drouin, Achim Schneider, and Wim J. Sluiter

The largest observational multicentric study
- 403 pts and 623 groins
- T1-T2 clinically and radiologically N0
- SNB Tc99-labeled nanocolloid and/or blu dye

127 pts complete IFL
259 unifocal + 17 multifocal no IFL

CRITERIA FOR SURGERY
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

SENTINEL NODE BIOPSY

For reprint orders, please contact reprints@expert-reviews.com

Update on the sentinel lymph node procedure in vulvar cancer

Expert Rev Anticancer Ther. 10(1), 61-69 (2010)

Key issues

- The sentinel lymph node (SLN) procedure is safe in the treatment of early-stage vulvar cancer with clinically negative lymph nodes.
- Application of the SLN procedure should be centralized in oncology centers to keep the experience of surgeons at a sufficient level and to ensure quality control at every step of the multidisciplinary procedure.
- All SLN metastases require adjuvant treatment, independent of their size.
- Treatment-related morbidity is much lower when only a SLN is removed compared with inguinofemoral lymphadenectomy.
- A standard protocol for pathologic examination of SLNs in vulvar cancer should be formulated.
- The Groningen International Study on Sentinel Nodes in Vulvar Cancer (GROINSS-V-II) trial will answer the question of whether radiotherapy alone is sufficient in the treatment of patients with a positive SLN.
I. Restricted more than possible

II. *Radical and oncologically safe*

III. Supported by plastic surgical techniques

IV. Peri-operative management protocols
SOME RECOMMENDATIONS FROM LITERATURE

VULVAR SURGERY

- Obtain microscopical tumor free margins measuring > 8 mm, observing about 2 cm of macroscopic resection margins (1)
- Avoid conservative surgery when tumor is bilateral or multifocal, in favor of a radical vulvectomy (2)
- Remove the skin bridge between inguinal regions and perineal area in cases of massive metastatic involvement of the groin lymph nodes (3)

CRITERIA FOR SURGERY

(1) Boonstra 1983  
(2) Dittmer 2012  
(3) De Hullu 2002
SOME RECOMMENDATIONS FROM LITERATURE

INGUINOFEMORAL SURGERY

- IFL should always include the removal of deep LN, located below the cribriform fascia and medial from the femoral vein (1)
- Bilateral radical IFL should be performed in case of positive SN or when the tracer does not reach inguinal regions (2)
- In case of a midline tumor a SLN should be identified in both groins, if not, the SNB procedure should be abandoned and lymphadenectomy performed (3)

1) Hacker 2000
2) Van der Zee 2008
3) Recommendation by a panel of International Lymph Node Society - ISNS - 2008
CRITERIA FOR SURGERY

I. Restricted more than possible
II. Radical and oncologically safe
III. Supported by oncoplastic surgical techniques
IV. Peri-operative management protocols
When disease is locally advanced and surgery is still indicated, oncoplastic and reconstructive surgical techniques are necessary, allowing:

- ultraradical extended surgery
- tension free closures
- rehabilitation of the basic functions otherwise compromised (as walking and sitting)
- sometimes the preservation of sensitive facilities
- good long-term results

CRITERIA FOR SURGERY
THE MOST IMPORTANT FEATURES OF AN ADEQUATE FLAP

• same thickness of the wound
• preservation of sensitive facilities
• require a single-stage operation
• minimal donor-site effects

Various reconstructive techniques can be performed to repair the different size and site skin defects
**VULVAR CANCER SURGERY: WHY, WHEN AND HOW**

- local dermo-hypodermal rotation and transposition flaps
- mio-cutaneous flaps

<table>
<thead>
<tr>
<th>CRITERIA FOR SURGERY</th>
<th>PUDENDAL TIGHT FLAP.</th>
<th>GLUTEAL FOLD FLAP.</th>
<th>V-Y FASCIOCUTANEOUS FLAP</th>
<th>VRAM FLAP.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertically oriented small to medium-size defects. It is not suitable if inguinal crural crease is involved.</td>
<td>Vertically oriented small to medium-size defects and narrow defects along the inguinal–crural fold.</td>
<td>Small, medium-size, and extensive defects, especially if they are located posteriorly.</td>
<td>Every kind of defect deeper ones extending adjoining areas.</td>
<td></td>
</tr>
<tr>
<td>Flaps</td>
<td>Donor site</td>
<td>Blood supply</td>
<td>Sensory innervation</td>
<td>Ref</td>
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<td>-----------------------------</td>
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<tr>
<td><strong>Grafts</strong></td>
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<tr>
<td>Split-thickness skin graft</td>
<td>Distant</td>
<td>NA</td>
<td>Recipient site</td>
<td>14, 15</td>
</tr>
<tr>
<td>Full-thickness skin graft</td>
<td>Distant</td>
<td>NA</td>
<td>Recipient site</td>
<td>16</td>
</tr>
<tr>
<td>Buccal mucosa graft</td>
<td>Distant</td>
<td>NA</td>
<td>Recipient site</td>
<td>17</td>
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<tr>
<td><strong>Random skin flaps</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limberg flaps*</td>
<td>Local</td>
<td>Random</td>
<td>53–4 dermatomes</td>
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</tr>
<tr>
<td>Pubococcygeal V-Y advancement flap†</td>
<td>Local</td>
<td>Random</td>
<td>53–4 dermatomes</td>
<td>19</td>
</tr>
<tr>
<td>Medial thigh V-Y advancement flap, with or without gracilis muscle</td>
<td>Local</td>
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<td>53–4 dermatomes</td>
<td>20, 21</td>
</tr>
<tr>
<td>Gluteal V-Y advancement flap, with or without obturator externus muscle</td>
<td>Local</td>
<td>Random</td>
<td>53–4 dermatomes</td>
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<tr>
<td><strong>Axial pattern skin flaps</strong></td>
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<td></td>
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<td>Anterior labial flap†</td>
<td>Local</td>
<td>Descending branch of superficial external pudendal artery</td>
<td>NA</td>
<td>24</td>
</tr>
<tr>
<td>Posterior labial flap</td>
<td>Local</td>
<td>Posterior labial artery (terminal branch of internal pudendal artery)</td>
<td>NA</td>
<td>25</td>
</tr>
<tr>
<td>Mons pubis flap²</td>
<td>Local</td>
<td>Superficial external pudendal artery</td>
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<td>26</td>
</tr>
<tr>
<td>Gracilis flap</td>
<td>Local</td>
<td>Superficial circumflex iliac artery</td>
<td>NA</td>
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<tr>
<td><strong>Fasciocutaneous flaps</strong></td>
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<td></td>
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<tr>
<td>Pubococcygeal thigh flap⊥‡</td>
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<td>Perineal terminal branches of internal pudendal artery</td>
<td>Superficial perineal branches of pudendal nerve; perineal branches of posterior cutaneous nerve of thigh</td>
<td>26, 20</td>
</tr>
<tr>
<td>Anterolateral thigh flap</td>
<td>Distant</td>
<td>Lateral circumflex femoral artery</td>
<td>Lateral femoral cutaneous nerve</td>
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<tr>
<td>Medial thigh flap</td>
<td>Distant</td>
<td>Branch of superficial femoral artery</td>
<td>Anterior cutaneous branches of femoral nerve</td>
<td>32</td>
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<tr>
<td><strong>Musculocutaneous flaps</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Rectus femoris flap</td>
<td>Distant</td>
<td>Lateral circumflex femoral artery</td>
<td>Anterior cutaneous branches of femoral nerve</td>
<td>33</td>
</tr>
<tr>
<td>Tensor fasciae lattice flap</td>
<td>Distant</td>
<td>Lateral circumflex femoral artery</td>
<td>Lateral femoral cutaneous nerve</td>
<td>34</td>
</tr>
<tr>
<td>Vastus lateralis flap</td>
<td>Distant</td>
<td>Lateral circumflex femoral artery</td>
<td>Lateral femoral cutaneous nerve</td>
<td>35</td>
</tr>
<tr>
<td>gracilis thgiip†</td>
<td>Distant</td>
<td>Terminal branches of inferior gluteal artery</td>
<td>Posterior cutaneous nerve of thigh</td>
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<tr>
<td>Gracilis flap</td>
<td>Distant</td>
<td>Medial circumflex femoral artery</td>
<td>Anterior cutaneous branches of femoral nerve; cutaneous branch of obturator nerve</td>
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<td>Sartorius flap</td>
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<td>Terminal branches of obturator artery</td>
<td>Cutaneous branch of obturator nerve</td>
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<td>Rectus abdominis flap**</td>
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<td>Deep inferior epigastric artery</td>
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<tr>
<td>Deep inferior epigastric perforator flap</td>
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<td>Deep inferior epigastric artery</td>
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<td><strong>Bowel flaps</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Ileum flap</td>
<td>Distant</td>
<td>Ileal artery</td>
<td>NA</td>
<td>42</td>
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<tr>
<td>(Jejunum flap</td>
<td>Distant</td>
<td>Ileocolic artery</td>
<td>NA</td>
<td>43</td>
</tr>
<tr>
<td>Sigmoid-colon flap</td>
<td>Distant</td>
<td>Sigmoid-colon artery</td>
<td>NA</td>
<td>44</td>
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</table>
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

CRITERIA FOR SURGERY

I. Restricted more than possible

II. Radical and oncologically safe

III. Supported by plastic surgical techniques

IV. Peri-operative management protocols
Advanced vulvar carcinoma: Is it worth operating? A perioperative management protocol for radical and reconstructive surgery

Francesco Fanfani a, Giorgia Garganese a, Anna Fagotti a, Domenica Lorusso a, Maria Lucia Gagliardi a, Marco Rossi b, Marzia Salgarello c, Giovanni Scambia a,*

a Department of Oncology, Division of Gynecologic Oncology, Catholic University of Sacred Heart, Campobasso, Italy
b Department of Anesthesiology and Intensive Care, Catholic University of Sacred Heart, Campobasso, Italy
c Department of Plastic Surgery, Catholic University of Sacred Heart, Rome, Italy

Received 6 December 2005
Available online 2 May 2006

It is cautiously to combine perioperative protocols for local and systemic care and management
## VULVAR CANCER SURGERY: WHY, WHEN AND HOW

<table>
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<tr>
<th>Pre-operative</th>
<th>Intra-operative</th>
<th>Post-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>• improve preoperative caloric supply</td>
<td>• use of dynamic legs compression</td>
<td>• fasting /parenteral nutrition</td>
</tr>
<tr>
<td>• administration of probiotics</td>
<td></td>
<td>• antibiotics and anti-diarrhoic drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• prophylaxis for thromboembolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• inflatable mattress and immobilization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• careful management of the wound</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• blood oxygenation by ventimask</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• prolonging transurethral catheter</td>
</tr>
</tbody>
</table>
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

NEXT TARGETS

- Identification of new biologic factors
  - Uptake of natural history
  - Identification of prognosis predictors
  - Identification of response predictors to drug or physical treatments

Modulation of surgical extent

Scheduling of the non surgical neoadjuvant treatment

A shared and approved standard of care
The significant progressive decrease of pRB2/p130 expression from non-neoplastic epithelial alterations to invasive vulvar carcinomas suggests a role for this tumor suppressor gene in vulvar carcinogenesis.

biologic factors
Results showed that changes in both ERa and ERb expression characterize the transition from normal epithelium to cancer in patients with vulvar SCC.
The assessment of cytoplasmic Erb expression could be helpful to identify poor prognosis in elderly patients with non-HPV-related vulvar squamous cell carcinoma (SCC).
COX-2 overexpression may contribute to vulvar tumorigenesis and progression.

Tumor/stroma COX-2 IDV ratio could have a prognostic role in vulvar cancer

biologic factors
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

COX-2 expression is down-regulated in vulvar tumor cells invading the regional lymph nodes with respect to primary tumors need for deeper insight into the tissue specific relation between tumor cells and node microenvironment
NEXT TARGETS

Identification of new biologic factors for the

- Uptake of natural history
- Identification of prognosis predictors
- Identification of response predictors to drug or physical treatments

Modulation of surgical extent

Scheduling of the non surgical neoadjuvant treatment

A shared and approved standard of care
Almost all existing guidelines were published before 2009 and do not take into account

› revised FIGO staging system (2009)
› new technical tools (e.g. SNB)

January 2006
Royal College Of Obstetricians And Gynaecologists
“Management of vulval cancer”

July 2006
Society of Obstetricians and Gynaecologists of Canada
“Management of Squamous Cell Cancer of the Vulva”

Principal Author: John Jeffrey, Chair, MD, FRCSC, Kingston ON
VULVAR CANCER SURGERY: WHY, WHEN AND HOW

Clinical Stage and characteristics

<table>
<thead>
<tr>
<th>Stage IA</th>
<th>Stage IB</th>
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</thead>
<tbody>
<tr>
<td>T ≤ 2 cm and SI ≤ 1 mm cN0</td>
<td>T &gt; 2 cm or SI &gt; 1 mm cN0</td>
</tr>
</tbody>
</table>

Unilateral unifocal lesion

- < 4 cm: RLE or LEV or RV
- > 4 cm: LEV or RV ev PLS

Central unifocal lesion

- < 1 cm from midline: AEV/PEV or RV
- > 4 cm: RV ev PLS

Bilateral/multifocal lesion

Surgical treatment

- RLE or LEV or RV
- LEV or RV ev PLS
- AEV/PEV or RV
- RV ev PLS
- SNB*
- MID*

Adjuvant treatment

1. If LN is negative: Follow up
2. T > 4 cm or Close margins and unfit for re-excision (< 8 mm): "Consider" Adj RT of the VULVA
3. 1 LN, with intracapsular metastasis: Adj RT of the GROINS + PELVIS
   - Lympho-vascular space invasion
4. > 1 positive LN or extracapsular invasion or ≥ 10 mm metastasis size: Adj RT of the GROINS + PELVIS and "Consider" Adj RT of the VULVA
Chemo-radiation therapy

- CRT is mainly used in advanced vulvar cancer involving neighboring structures, where exenteration and/or bone or muscle resection would be necessary to obtain clear margins (1)
- More in general, CRT is an option to reduce tumor volume and the extent of surgery

Chemotherapy

- CT is not a common approach
- It is mainly used in the primary metastatic setting or in pts with recurrence after RT1

(1) Hoffman 2003
PBM NACT did not seem to add any substantial benefit to the surgery in patients with extremely advanced disease.
Weekly administration of paclitaxel-carboplatin has limited clinical benefit in the treatment of vulvar squamous cell carcinoma.

25 patients included in NACT protocols:
10 with bleomicine, 5 with paclitaxel and 10 with 5-fluorouracil/cisplatin
The best response and overall survival rates were achieved with the NACT scheme of bleomicine.

Recent studies point to the use of \textbf{target} therapy.
Given the rarity of disease and technical skills required

- Address every single vulvar cancer to oncology cancer centers
  - collect experience
  - implement prospective and randomized clinical trials and allow an auditing practice
  - obtaining also a more favorable outcome.

- Multidisciplinary team including dedicated healthcare professionals
  - gynecological oncologist
  - plastic surgeon
  - Radiologist
  - nuclear medicine physician
  - radiotherapist
  - gynecological pathologist
  - Psychologist
  - specialist nurse
  - Physiotherapist
  - palliative care team
"Well done is better than well said."

Ben Franklin
<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Stage and characteristics</th>
<th>Neoadjuvant/Primary treatment</th>
<th>Surgical treatment</th>
<th>Following treatment</th>
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</thead>
<tbody>
<tr>
<td>II</td>
<td>Resectable disease</td>
<td>After pathological vulvar mapping</td>
<td>CR</td>
<td>BID</td>
</tr>
<tr>
<td></td>
<td>Extension to anus or to 1/3 lower urethra or vagina</td>
<td>Reconstruct before CR</td>
<td>If T&lt;4cm consider Bilat SNB*</td>
<td>If N+ or SN not found bilaterally See number 1, 2, 3 and 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If prior RT-CT: consider close PD If prior CT: adjuvant RT</td>
</tr>
<tr>
<td>III</td>
<td>Heavy surgical burden for resection</td>
<td>Primary CT or Primary RT-CT</td>
<td>PR SD</td>
<td>BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>According to surgical burden age and comorbidities</td>
<td>According to age and comorbidities * If LNs are negative Follow-up</td>
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<td>T&gt;4cm or Close margins and unfit for re-excision (&lt;8mm) “Consider” Adj RT of the VULVA</td>
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<td>1+LN, with intracapsular metastasis “Consider” Adj RT of the GROINS and PELVIS</td>
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<td>&gt;1 positive LNs or extracapsular invasion or ≥10 mm metastasis size Adj RT of the GROINS and PELVIS and “Consider” Adj RT of the VULVA</td>
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<td>Shift to alternative therapies (CT/RT-CT) See number 2, 3 and 4</td>
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<td>PD</td>
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<td>According to perineal disease</td>
<td>If bulky nodes consider PND</td>
</tr>
</tbody>
</table>

* If LNs are negative Follow-up

“Consider” Adj RT of the VULVA

Adj RT of the GROINS and PELVIS and “Consider” Adj RT of the VULVA

Shift to alternative therapies (CT/RT-CT)
CT-RT compared with PRIMARY SURGERY

No significant difference in OS or adverse events

high risk of bias in existing retrospective studies:

1. Entry criteria for primary CT-RT was based on inoperability or tumour requiring exenteration but no standard terminology exist for 'operative and inoperable vulval cancer'

2. The radiochemotherapy regimens widely varied

3. No standard terminology for 'primary and neoadjuvant chemoradiation'.

4. Need of stratification according to unresectability of the primary tumour and lymph nodes is needed

5. No data on QoL

Parameters determining adjuvant radiotherapy after groin dissection are still controversial

- The benefit of adjuvant RT was clearly demonstrated in patients with \( \geq 2 \) LN metastasis (1)
- The role of RT in pts with a single intracapsular LN metastasis is still under discussion (2)
- Adjuvant RT of pelvic LN is recommended in pts with metastatic inguino-femoral LN (3)

Criteria for the application of adjuvant radiotherapy to the vulva are not clearly defined

- Lymphangio invasion and large primary tumors are associated with an increased risk of local recurrence but no clear recommendation to RT is drown (4)
- Close margins should be considered a possible indication when surgical enlargement is not feasible

Chemoradiation in pts with LN metastasis has not yet been systematically addressed (5)

1. Homesley 1986
2. Oonk 2010
3. Kunos 2009
5. Moore 2005