

**The role of  
lymphadenectomy in  
gynecologic oncology (GO)**

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# The role of lymphadenectomy in GO

- \* **General considerations**
- \* **Vulvar cancer**
- \* **Vaginal cancer**
- \* **Cervical cancer**
- \* **Endometrial cancer**
- \* **Cancer of the fallopian tube (PCFT)**
- \* **Ovarian cancer**

# General considerations (1)

- \* **Conclusions according to EBM, if possible**
  - **meta-analysis/syst. review of RCTs** **A**
  - **RCTs**
  - **nRCTs (present, historical)**
  - **CCS**
  - **cross sectional studies**
  - **follow-up studies**
  - **case series / reports**
  - **expert opinion** **D**

## **General considerations (2)**

- \* In all (almost) cancers**
  - lymph node status is included to the staging system (TNM, FIGO)**
  - lymphadenectomy is a basic procedure in primary surgery**
  - the presence of lymph node metastases (LNMs) is a highly significant prognostic factor**

## **General considerations (3)**

- \* The presence of LNMs can not be profoundly judged by**
  - ultrasound, CT or MRI**
  - inspection or palpation**
  - sampling of "suspicious" or enlarged nodes**

## General considerations (4)

- \* **More the 50 % of the pelvic nodes are < 1 cm in size (endometrial cancer)**

**Girardi 1993, Benedetti 1998**

## **General considerations (5)**

- \* The size and shape of LNs do not correlate with the presence of LNMs**
  - only 10 % of the metastatic LNs are enlarged**

**Wu et al. 1984, Petru et al. 1994**

## General considerations (6)

- \* **Lymphadenectomies in gyn ca**
  - N=126, LNMs were found in 5 %
  - in 64 % palpation = histology
  - in 34 % palp normal, histo = LNMs
  - in 3 % palp = LNMs, histo normal
  - sens 72 %, spec 81 %, PPV 56 %, NPV 89 %

**Arango et al. Gynecol Oncol 2000;95:553-**



# General considerations (7)

- \* **Quality control of LND**
  - what is that - is there any ?
  - different handling of specimens, pathologist-dependent (?)
  - groin: 5-10 LNs per side
  - pelvis: biopsy < 10 , sampling 10-15, LND > 20 LNs
  - para-aortic: 10-15 LNs

# General considerations (8)

- \* **We can not base our decisions on RCTs**
  - **mainly because there are not any**
  - **some is going on, some are planned to begin**
    - vulvar cancer /sentinel node**
    - endometrial cancer / LND (MRC-ASTEC-trial)**

# General considerations (9)

- \* **Decision maker's burden**
  - enormous amount of data / studies / opinions with limited value
  - still you have to make a decision how to perform surgery
  - "on the other hand on the other hand" is not enough
  - decision's validity = benefit of the patient

# **General considerations (10)**

## **Slogans to remember**

- 1. There is no cure for the bad surgery - especially in primary phase**
- 2. There are many roads to Rome**
- 3. Seeking the truth is endless, but not hopeless**
- 4. The bigger head, the bigger headache !**

# Vulvar cancer (1)

- \* Staging is based on surgical findings (FIGO)
- \* Groin LNMs are frequent: 21-59 %
- \* Clinical examination overestimates the presence of LNMs by 15 %

**Iversen et al. 1981**

- \* Ultrasound: sens 82 %, spec 87 %

**Mäkela, Leminen, Kärkkäinen, Lehtovirta 1993**

# Vulvar cancer (2)

## \* Groin LNMs (%) by size of the tumor

< 1 cm	18,0
1-2	19,4
2-3	31,4
3-4	54,3
4-5	39,6
> 5	51,8

**Homesley et al. Gynecol Oncol 1993**

# Vulvar cancer (3)

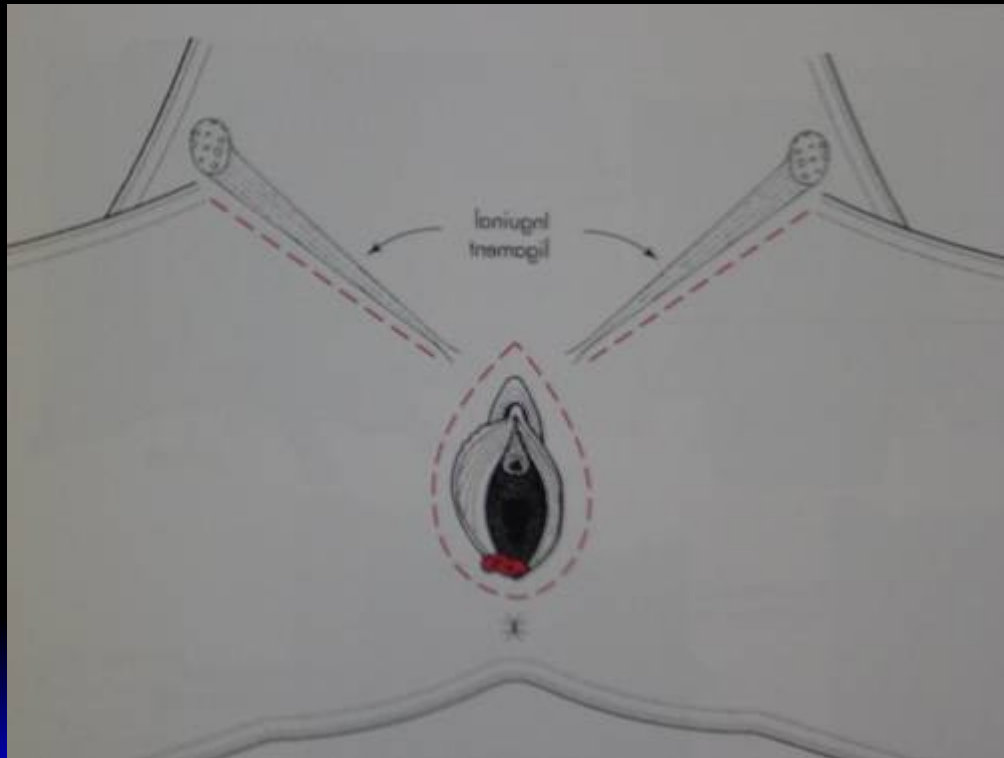
## \* Groin LNMs (%) by tumor thickness

	Ipsilat	Contralat	Bilat
< 2 mm	6,8	0	0
3-5	20,4	1,9	2,8
6-10	28,8	3,8	11,3
11-	36,7	6,7	6,7

Homesley et al. 1993

# Vulvar cancer (4)

**Lymph node dissection (LND); three-incision technique; modified vulvectomy**





# Vulvar cancer (5)

- \* **Ipsilateral groin LND in all stages when resectable except**
  - **stage 0 - Ia (size < 2 cm, inv < 1 mm)**
- \* **Bilateral groin LND when central lesion**
- \* **Pelvic LND when groin LNMs found (frozen section)**

# Vulvar cancer (6)

- \* **Sentinel lymph node technique (SND)**
- \* **Published studies over 250, ongoing RCTs**
- \* **Accreditation / learning curve**
  - **”30 procedures, 27 successful, 1 FN allowed”**
- \* **” Gyn oncologist who perform SND procedure in vulvar cancer patients should perform the technique by following strict protocol and within the protection of a clinical trial”**

**de Hullu JA et al. Gynecol Oncol 2004;94:10-**

# Vulvar cancer (7)

- \* **Sentinel lymph node technique (SND)**
  - systemic review, 29 studies 1979-2004
  - **SND by Tc is the best: sensitivity 97 %**
  - studies were small, often poor design
  - efficacy (reducing the radicality and patient morbidity without reducing survival demands RCT to be done

**Selman et al. Gynecol Oncol 2005 Aug**

# Vulvar cancer (8)

## \* Vulvectomy (modified) + LNDs complications (%)

<b>Wound infection</b>	<b>39 - 47</b>
<b>Wound breakdown</b>	<b>17 - 20</b>
<b>Lymphocysts</b>	<b>7 - 40</b>
<b>Lymphedema</b>	<b>12 - 28</b>

**Leminen et al. EJOG 2000: N=149**

**Vergote et al. IJGC 2003: N=172**

# Vaginal cancer

- \* Staging is based on *clinical findings* (FIGO)
- \* All pelvic lymph nodes are prone to LNMs; frequency ?
- \* Treatment is highly individualized
  - RT, CRT, surgery, combination
  - the role of LND ?

# Cervical cancer (1)

- \* Staging is based on *clinical* findings (FIGO); TNM if operation +
- \* Pelvic +/- para-aortic LNMs are frequent:  
st I 2-43 %, st II 40-71 %
- \* Pelvic LND is a crucial part of the primary surgery of stage Ib-IIa patients
  - Wertheim, Schauta, Meigs, Rutledge II-IV, LRH, trachelectomy
  - para-aortic - mostly when pelv LNMs

# Cervical cancer (2)

- \* **Pelvic LND is not needed**
  - **stage 0 (carcinoma in situ)**
  - **stage Ia1 (small microinvasive cancer)**
- \* **Trachelectomy**
  - **st. Ia2-b1, no fertility problems**
  - **size < 20-25 mm, G1-2, no LNMs**
    - ⊗ **prior pelvic LND (laparoscopy)**
    - ⊗ **if LNMs -> radical operation**

# Endometrial cancer (1)

- \* Staging is based on surgical findings (FIGO)
- \* Presence of LNM is associated with  
- stage, grade, invasion, histology
- \* LN status most powerful prognostic factor  
**Morrow et al. 1991**
- \* Still -the role of LND is not yet defined,  
no consensus has been found



# Endometrial cancer (2)

\* LNMs (%) by st Ia-b and grade

		Pelvic	Para-aortic
Ia	G 1	0-2	0
	G 2	2,7-4	2,7-4
	G 3	11-15	7-15
Ib	G 1	3,6-4	0-4
	G 2	8,1-10	2,7-7
	G 3	26-40	16-26,7

**Boronow et al. 1984, Creasman et al. Cancer 1987**

# Endometrial cancer (3)

\* LNMs (%) by G1-3 and stage I

		Pelvic	Para-aortic
G 1	Ia	3,4	1,5
	Ib	7,4	1,6
	Ic	7,8	2,1
G 3	Ia	11,4	-
	Ib	10,2	6,1
	Ic	21,7	8,9

FIGO 1993-95

# Endometrial cancer (4)

## ▼ Low risk (< 4 %)

- st Ia G1-2
- inv. < 1/3 + G 1-2
- inv. 1/3-2/3 + G 1
- LVI -
- histology = pure adeno

## ▼ High risk (20-45 %)

- G 3
- inv. 1/3-2/3 + G 2
- inv. > 2/3 + G 1-3
- LVI +
- histology = other than pure adeno

**Boronow 1984, -87, -97**

# Endometrial cancer (5)

- \* **Problems of risk evaluation**
  - 81-88 % of the cases represent st I-II (**FIGO statistics, Faught et al. 1994**)
  - reliable method (besides histologic specimen) to evaluate invasion is missing
    - ⊗ ultrasound, peroperative inspection or frozen section; accuracy 80-85 %

# Endometrial cancer (6)

- \* **The effect of LND on survival**
- \* **Improves**
  - **Kilgore et al. Gynecol Oncol 1995, Barnes and Kilgore. Semin Radiol Oncol 2000, Fanning et al. Gynecol Oncol 2001**
- \* **No effect**
  - **Trimle, Kosary and Park. Gynecol Oncol 1998**
    - ⊗ **N=9185; st Ia G 3 better, st I-II improved**

# Endometrial cancer (7)

- \* **The effect of para-aortic LND on survival (Mariani et al. Gynecol Oncol 2000;76:348-)**
- \* **Criteria: at least 5 removed LNs**
- \* **N=188**
  - 1) N=137: high risk, not st IV
    - ⊗ 5-YSR **85 %** P-ALND +, **71 %** P-ALND -
  - 2) N=51: pelvic LNMs, not st IV
    - ⊗ 5-YSR **77 %** P-ALND +, **42 %** P-ALND -

# Endometrial cancer (8)

\* The effect of LND on survival

\* **FIGO 1993-95** (N=5694); 5-YSR (%)

		Clinical	Surgical
Stage	I	53,8	87,4 (+ 33,6)
	II	41,4	76,3 (+ 34,9)
	III	23,1	56,6 (+ 33,5)
	IV	12,0	17,8 (+ 5,8)

# Endometrial cancer (9)

- \* Complete surgical procedure gives significant information considering postoperative treatment modalities
  - brachy instead of pelvic RT
  - CT instead of RT
  - less complications, better survival (?)

**Goudge et al. Gynecol Oncol 2004**



# Endometrial cancer (5)

## \* Impact of proper surgical staging

Perfor- mer	PSS in St I-II G 2-3 (%)	The use of adj. RT (%)	Adj. RT St I (%)
Gynecol. oncol.	96	8.6	0
General gynecol.	19	21.7	18

# Endometrial cancer (10)

## \* AH + BSO +/- LND complications (%)

	LND -	LND +	p
BTFs (%)	6	14	0.01
Febr. morb (%)	20	26	ns
Op. time (min)	117	139	<0.001
Blood loss (ml)	322	442	0.03
1. bowel mov.	4,8	6,6	<0.001
Hosp.stay	6,0	7,6	ns

**Mariana et al. AJOG 2000**

# Endometrial cancer (11)

## \* AH + BSO + LND complications

	%	Related to LND
Lymphocysts	1,2 - 3	+
Bladder damage	0,45	+ -
Bowel damage	1,9	+ -
PE	1,1	+ -
Haemorrhage	2,3	+ -
Wound abcess	3,2	-
All	18-19,4	<b>Morrow et al. Gynecol Oncol 1991</b> <b>Mohan et al. Gynecol Oncol 1998</b>

# Endometrial cancer (12)

- \* **LH + LND as good as AH + LND**
- \* **Certain limitations exists**
  - **severely obese patient**
  - **complicated heart or lung disease**
  - **previous surgery -> adhesions**
  - **if para-aortic procedure is not possible**
    - ⊗ **G 3, st. Ic, pelvic LNMs, serous ca**

**Malur et al. Gynecol Oncol 2001**

# Ovarian cancer and PCFT (1)

- \* Staging is based on surgical findings (FIGO)
- \* Presence of LNMs is associated with
  - stage, grade, histology (ser and clear cell)
  - stage I-II: 12-45 %, III-IV: 55-75 %

**di Re and Baiocchi. IJGC 2000**
- \* LN status is a prognostic factor
- \* Still -the role of LND is not yet defined, no consensus has been found

# Ovarian cancer and PCFT (2)

- \* **Macroscopic st Ia - b**
  - **LNMs are limited to ipsilateral side in 73 %**
  - **still in 15 % contralateral and in 11 % bilateral LNMs are found**
  - **when LND -> 10-18 % up-staging**

**Petru et al. AJOG 1994, Ferraris et al EJGO 1888**

**Gershenson ASCO 2000, Di Re et al. Gynecol Oncol 1996**

# Ovarian cancer and PCFT (3)

- \* **Primary surgery - recommendations for lymph node sampling (LNS) or LND**
  - **no residual tumor (RT) despite of stage**
  - **RT limited to the pelvis**
  - **RT outside the pelvis < 1 cm**

**Hoskins. Gynecol Oncol 1994**

**Trimbos and Bolis. Obstet Gynecol 1994**

# Ovarian cancer and PCFT (4)

## \* Restaging

- operation after incomplete prim. surgery

- in 30 % up-staging

**Young et al. JAMA 1983**

**Trimbos, Schueler, van der Burg. Cancer 1991**

**van der Burg et al. NEJM 1995**



# Ovarian cancer and PCFT (5)

- \* **Cytoreduction; interval or secondary**
  - if optimal result (RT < 1 cm, LND included) -> survival is better

**van der Burg et al. NEJM 1995**

**Williams et al. 1997**

**Vergote et al. 2001**

# Ovarian cancer and PCFT (6)

- \* **Second look operation**
  - after primary CT LNMs to be found in 25 - 77 %
  - false -ve CPR in 17 - 40 % if retroperitoneum is not assessed in second look

**di Re and Baiocchi. IJGC 2000**

# Ovarian cancer and PCFT (7)

\* **Systemic LND - effect on survival : no RCTs (and will not be)**

- historic series: 5-YSR 13 vs. 53 %

- comparative series: 4-YSR 0 vs 22%

and 5-YSR 30 vs 46 %

**Burhardt et al. AJOG 1986, Scarabelli et al. GO 1995, Kigawa et al. AJOG 1994, Spiritos et al. GO 1995, Di Re et al. GO 1996**

# Ovarian cancer and PCFT (8)

## \* LND complications (%)

Vessel damage	3,9
Lymphocysts	13,5
DVT	5,0
PE	2,8
Paresthesia	2,7

**Di Re and Baiocchi. IJGC 2000**

# Summary - role of LND

- \* **Vulvar and cervical cancers**
  - well defined and accepted
  - no major arguments
  - **SND** to be confirmed
- \* **Endometrial and ovarian cancers**
  - lots of suggestive data for the benefit
  - major arguments, no consensus

# Why systemic LND (1)

- \* **There is no other accurate method for proper staging and evidence of LNMs**
- \* **Doctors should not be "wrong" in such a amount of cancers cases**
  - **wrong stage -> wrong treatment -> wrong results -> non-comparable studies**
- \* **Optimal cytoreduction is more often reached, courages to "action"**

## **Why systemic LND (2)**

- \* Right stage - adjuvant treatment not needed**
  - early (macroscopic) stage - precise staging**
  - reducing the use of radiotherapy**
- \* Data for survival benefit exists**
- \* Complication rate acceptable**
  - intention to curative treatment in serious disease**
  - doing accomplish learning**

# How in HUCH ?

\*

## Systemic LND

- ovarian cancer since 1986/87

☒ when restrictions - LNS

☒ NOT if RT is carcinosis or far more than 1 (2) cm

- endometrial cancer since 1990

☒ LNS or AH/LH + BSO if serious medical conditions, age "enough", high BMI