

Endometrial cancer stage I

- Nicoletta Colombo
- Thomas Hogberg

Disclosure slide

- No relevant disclosures

Clinical case

- A 72 year-old woman with postmenopausal bleeding
- Weight: 95 Kg; Height: 160 cm; BMI: 37
- Endometrial biopsy: FIGO stage 3 endometroid endometrial carcinoma
- MRI: reveals a uterine mass of 3.5 cm with a focal myometrial invasion of more than 50%.
- CT scan: no distant metastases

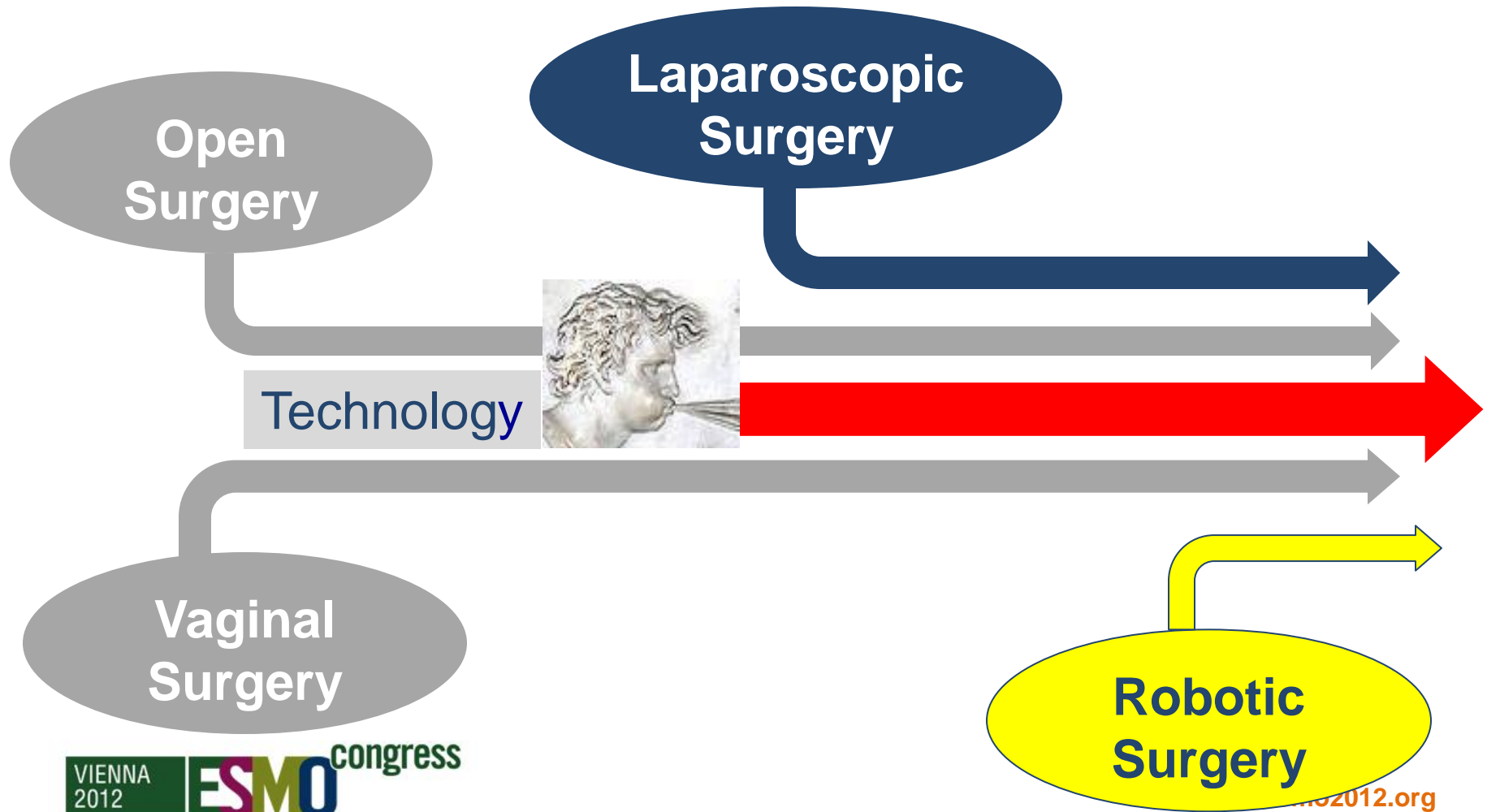
Which type of access do you prefer in this case?

1. Abdominal
2. Vaginal
3. Laparoscopic (eventually combined with vaginal)
4. Robot assisted
5. Other
6. No surgery

Discussion on type of access

- Nicoletta Colombo

Surgical Scenario in Gyn Oncology



Which type of access do you prefer in this case?

Vaginal

- Does not allow abdominal exploration, peritoneal washings and lymph node dissection
- Often the BSO is challenging

Therefore not the preferred mode

Vergote I, et al. *Lancet Oncol.* 2010;11(8):707-708.

Surgical Scenario in Gyn Oncology

Laparoscopic
Surgery



Robotic
Surgery

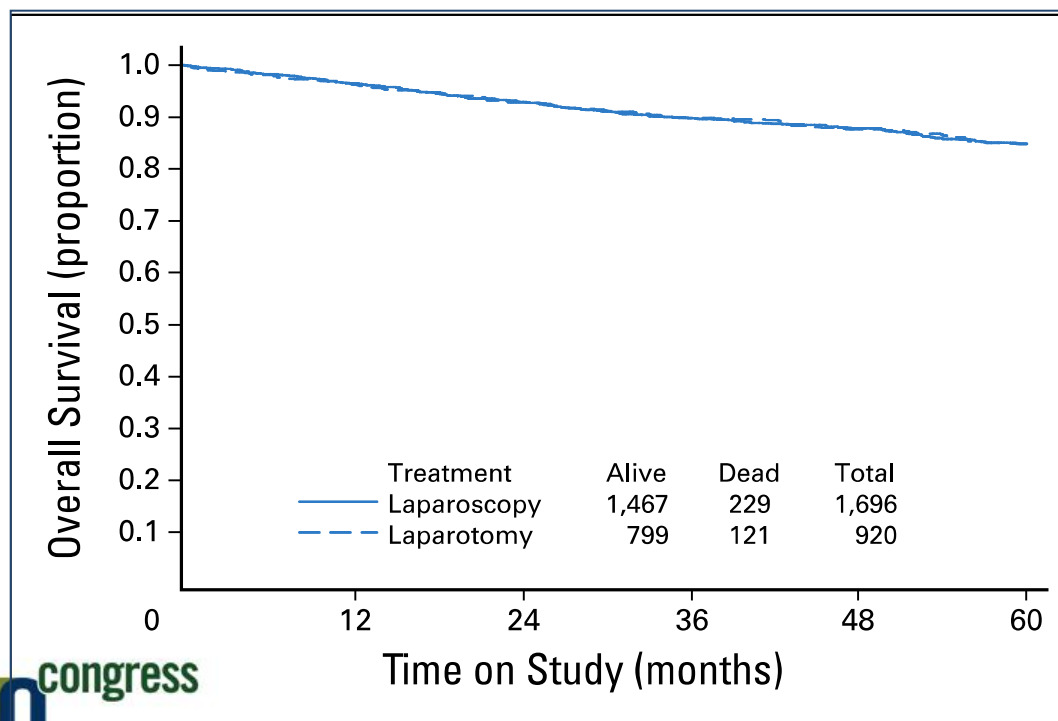


- ◆ **Expanded** applications
- ◆ **Faster learning** curve
- ◆ Easy transition from **Open** Surgery Experience to **Robotic**-Assisted LaparoscopySurgery

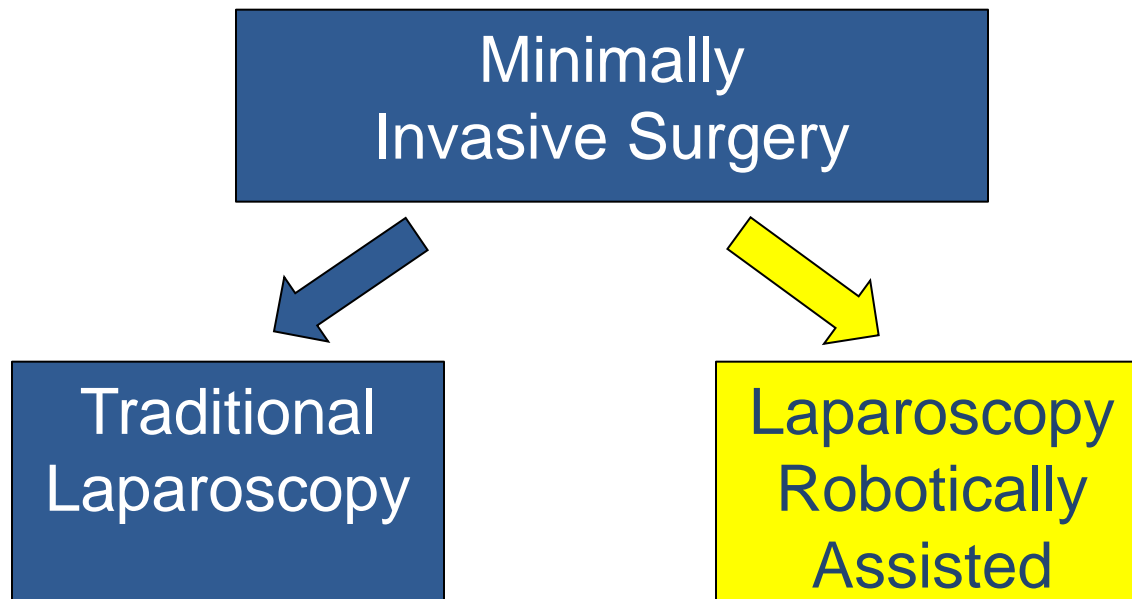
“Minimally invasive surgery is the optimal treatment in the management of Endometrial Cancer”

Recurrence and Survival After Random Assignment to Laparoscopy Versus Laparotomy for Comprehensive Surgical Staging of Uterine Cancer: Gynecologic Oncology Group LAP2 Study

Joan L. Walker, Marion R. Piedmonte, Nick M. Spirtos, Scott M. Eisenkop, John B. Schlaerth, Robert S. Mannel, Richard Barakat, Michael L. Pearl, and Sudarshan K. Sharma



Early Endometrial Cancer Surgical Treatment

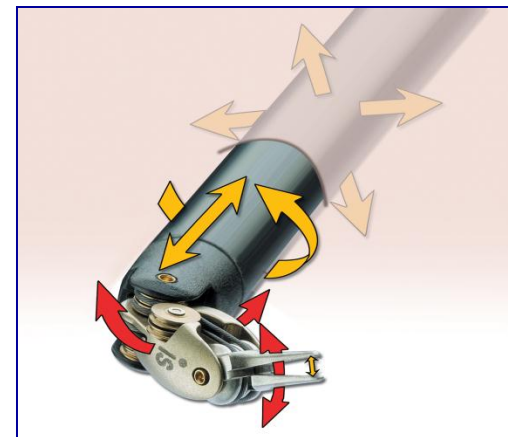


❖ Surgical robotics is defined as a **computer interface** between the surgeon and the patient

❖ Computer-assisted surgery **can enhance** human visualization , strength, precision and degrees of motion in performing surgical tasks .

What does robotic surgery offer ?

- Surgeon controls the robotic arms remotely
- 3-D image through stereoscopic viewer (high definition option)
- Seven degrees of movement mimic human wrist movement (eliminate fulcrum effect)
- Tremor filtration & motion scaling



What does robotic surgery offer?

- Intuitive motion
- Emulate “open” surgery
- Fast learning curve
- Ergonomic position for surgeon



Robotic vs Laparoscopic Hysterectomy & Staging: Endometrial Cancer

Robotic vs LPS	Bogges (2008) N= 103 vs 81	Bell (2008) N= 40 vs 30	Seamon (2009) N= 105 vs 76
BMI (Kg/m ²)	33 vs 29	33 vs 32	34 vs 29*
OP time (min)	191 vs 213*	184 vs 171	242 vs 287*
EBL (mL)	75 vs 146*	166 vs 253	100 vs 250*
LOS (day)	1.0 vs 1.2	2.0 vs 2.3	1 vs 2*
Nodes (n)	33 vs 23*	17 vs 17	21 vs 22
Conversion (%)	2.9 vs 4.9	NA	12 vs 26*
Complication (%)	5.8 vs 13.6	7.5 vs 20*	13 vs 14



Obese
patient



Comprehensive Surgical Staging for Endometrial Cancer in Obese Patients: **Comparing Robotics and Laparotomy**

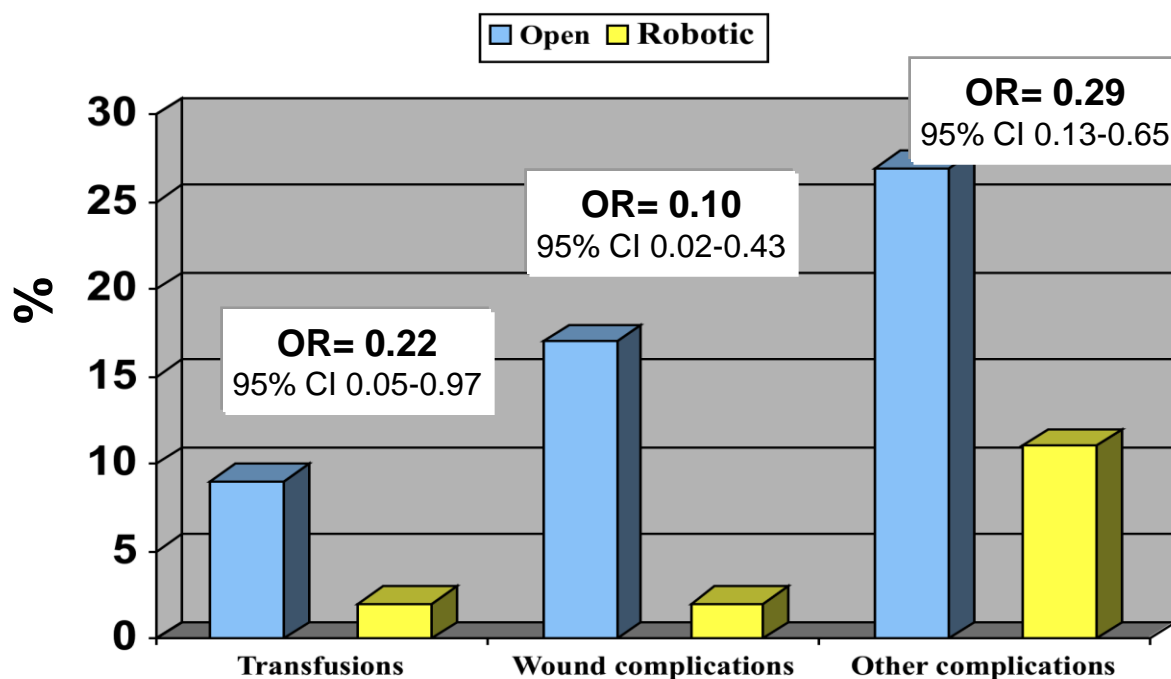
Seamon LG. et al. Obstet Gynecol. 2009.

TRH	TAH	P value
N= 109	n= 191	

Age (y)	58	65	.003
BMI (Kg/m2)	39.6	39.9	Matched
OR time (min)	228	143	<.001
EBL (mL)	109	394	<.001
Transfusion Rate	2%	9%	.046
Hospital Stay (day)	1	3	<.001
Total Nodes	24.7	23.9	NS
Pelvic Nodes	18.5	18.7	NS
Aortic Nodes	8.5	7.2	NS
Complication	11%	27%	.0

Comprehensive Surgical Staging for Endometrial Cancer in Obese Patients: **Comparing Robotics and Laparotomy**

Seamon LG. et al. Obstet Gynecol. 2009.



What is the **optimal minimally invasive** surgical procedure for endometrial cancer staging in the obese and morbidly obese woman?

Gehrig PA et al. Gynecol Oncol. 2008.

	TRH n: 49	TLH n: 32	P value
BMI (Kg/m2)	37.5	35	NS
Distribution BMI			NS
35-39.9	41%	28%	
≥ 40	26%	22%	
OR time (min)	189	215	<.001
EBL (mL)	50	150	<.001
Hospital Stay (day)	1.0	1.2	0.011
Total Nodes	33.7	21.7	0.001
Complication	6	7	NS
Conversion	1	3	NS



- In a world where we all drive a Ford Taurus...
- One day, a neighbor buys a Ferrari
 - It goes faster, it's sexier, it's smaller
- Do I need a randomized study to show it is faster on left handed turns, on right handed turns, the acceleration is faster, the leather is softer ...



Audience Question

- Has the issue of minimally invasive surgery in endometrial cancer been settled?
 - A. I need more data before I will integrate MIS into routine practice
 - B. I think comparative trials between Robotic and Laparoscopic and/or Open surgery are still needed
 - C. The dust has settled, a new moon has risen- MIS is here to stay- move on already!
 - D. There is no data set that will make me incorporate MIS- ever!

Mode of Access in This Patient

In this obese patient I would prefer the robot-assisted access because:

- Endoscopy results in the same **survival**
- **Less** complications, shorter hospital stay and better QOL with endoscopy
- Robot-assisted surgery is **easier** to perform than laparoscopy in obese patients. One of the advantages is that it is possible to operate at **lower pressure** (5-7 mmHg) than with traditional endoscopy, due to the improved dexterity

Which type of surgery do you recommend in this case?

1. Total abdominal hysterectomy bilateral salpingo-oophorectomy (TAH-BSO)
2. TAH-BSO + pelvic lymphadenectomy
3. TAH-BSO + pelvic and peri-aortic lymphadenectomy

Discussion on the role of lymphadenectomy

- Nicoletta Colombo

Religion vs Science

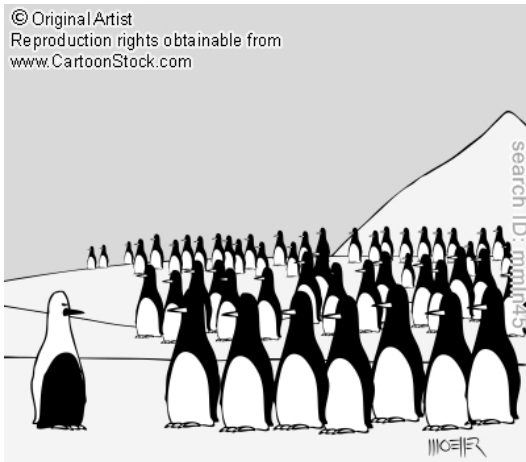
Why do we perform lymphadenectomy?

- Identify disease spread
 - Prognosis
 - Target postoperative treatment and potentially reduce the number of pts requiring postoperative treatment
- Therapeutic and debulking effect (node +)

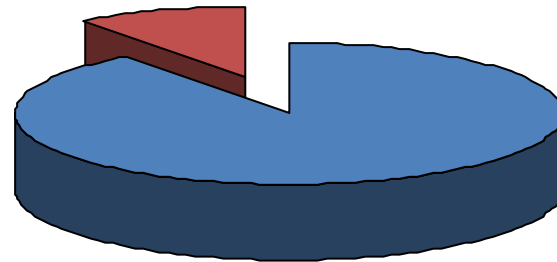
Who should undergo lymphadenectomy?

- Selective
- All
- None

Lymphatic Dissemination in Endometrial Cancer



4-15%



- Negative Lymph Nodes
- Positive Lymph Nodes

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SCHOOL



search ID: gjao083

"Here comes mine."

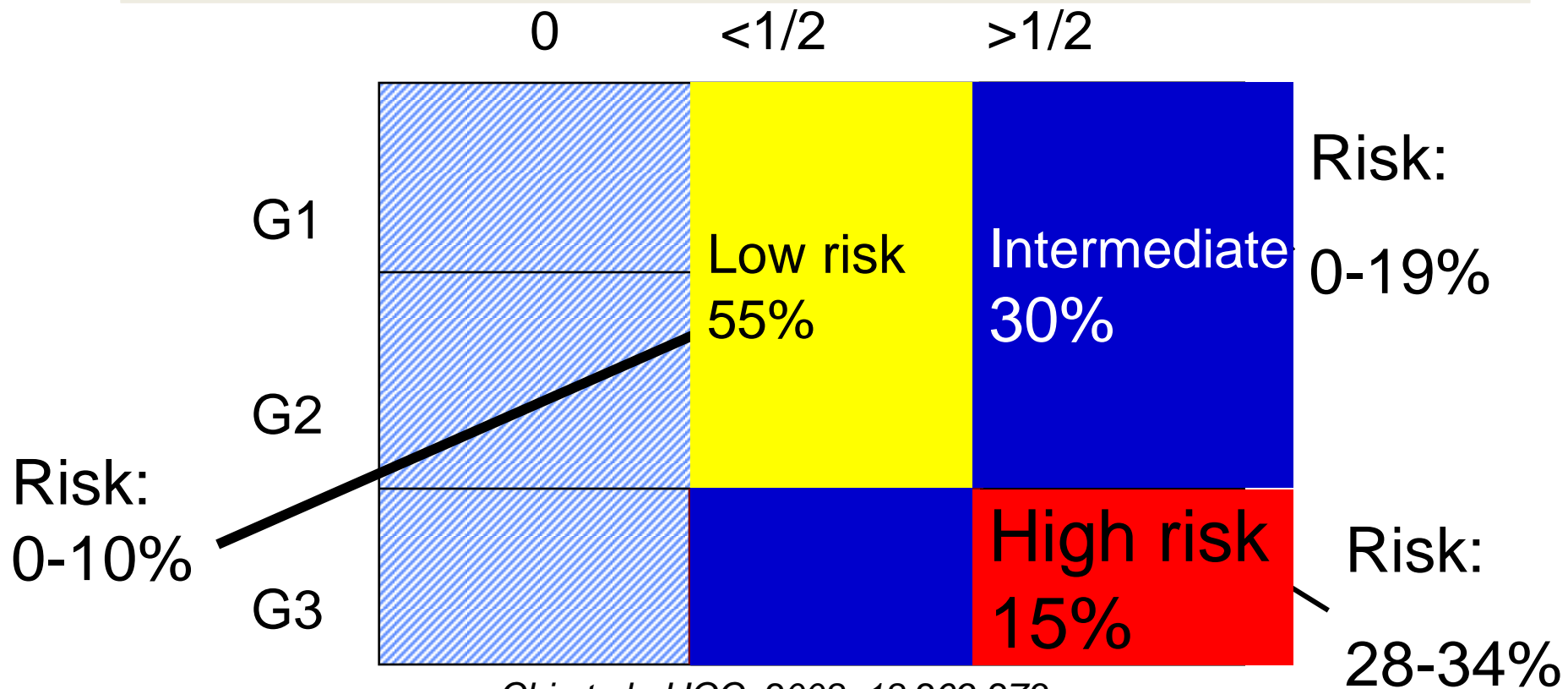
JARTOS

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www.esmo2012.org

Fraction of patients in each substage and percentage of node metastases



Chi et al., IJGC, 2008, 18:269-273

Creasman et al., Cancer, 1987, 60:2035-41

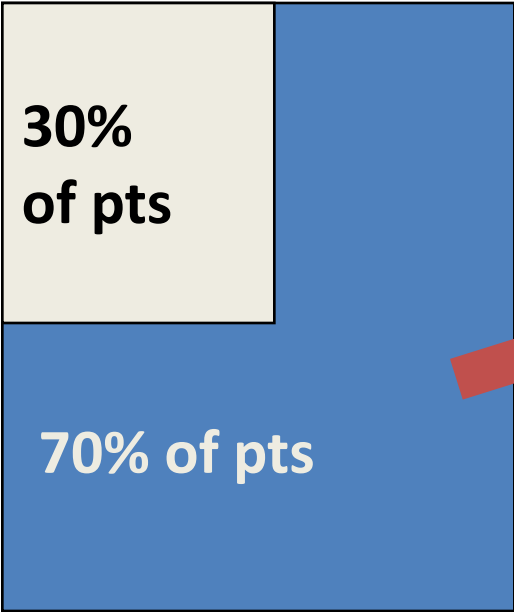
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Preliminary Findings* on Patients from the Prospective Study (n=494) Pelvic Lymph Node Invasion

Endometrioid
G1-2
Myo≤50%
TD ≤ 2 cm

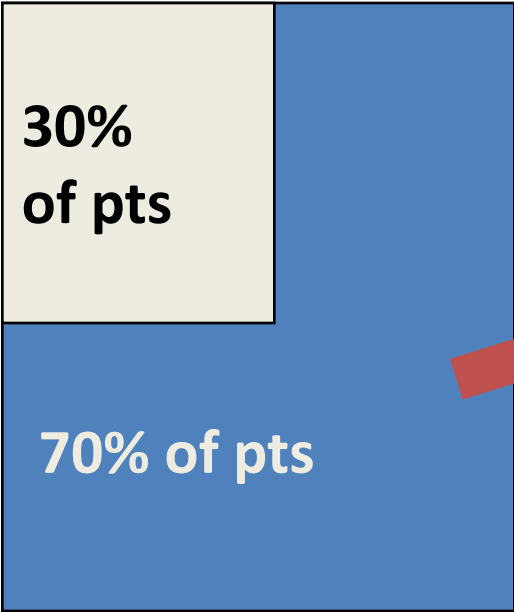


	Myo≤50%	Myo>50%
G1		14%
G2	7%	28%
G3	15%	53%

Preliminary Findings* on Patients from the Prospective Study (n=463)

Paraaortic Lymph Node Invasion

Endometrioid
G1-2
Myo≤50%
TD ≤ 2 cm



	Myo≤50%	Myo>50%
G1		11%
G2	6%	25%
G3	10%	41%

Our patient....

Has a 30-50% probability of having positive pelvic node

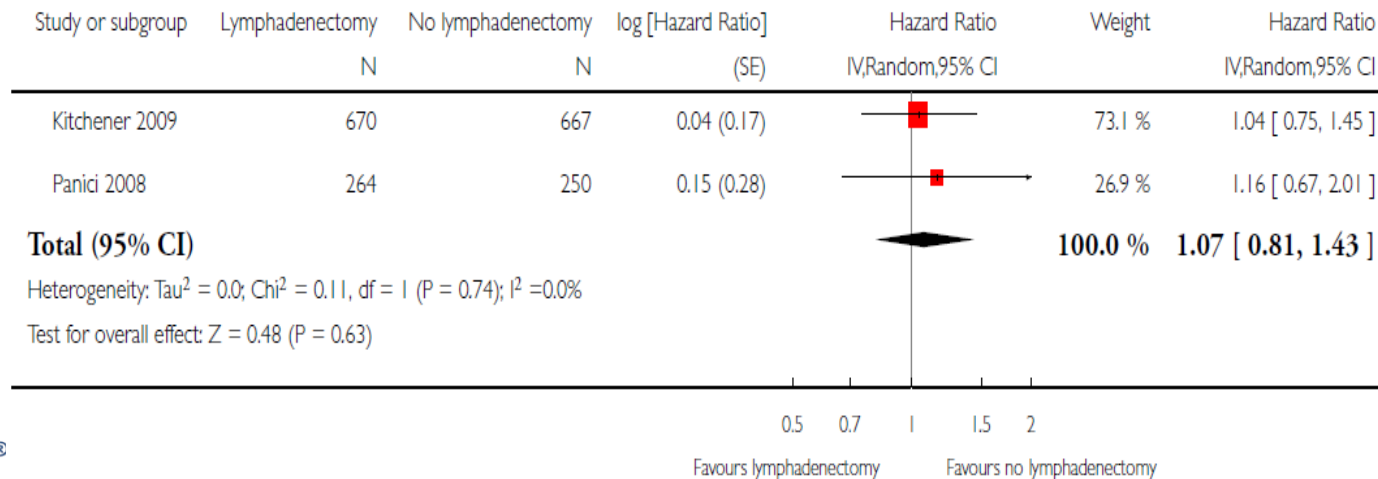
Has a 40% probability of having positive para-aortic nodes

However....is there a level 1 evidence ?

Lymphadenectomy for the management of endometrial cancer

May K, Bryant A, Dickinson HO, Kehoe S, Morrison J

Overall Survival



Meta-analysis indicated:

➤ **no significant difference in overall and recurrence-free survival between women who received lymphadenectomy and those who received no lymphadenectomy** (pooled HR = 1.07, 95% CI: 0.81 to 1.43 and HR = 1.23, 95% CI: 0.96 to 1.58 for overall and recurrence-free survival respectively).

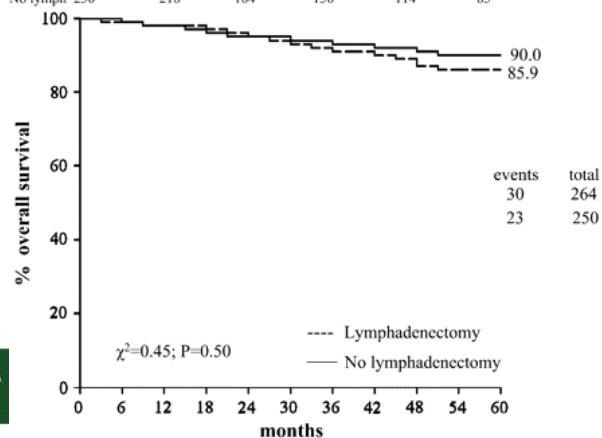
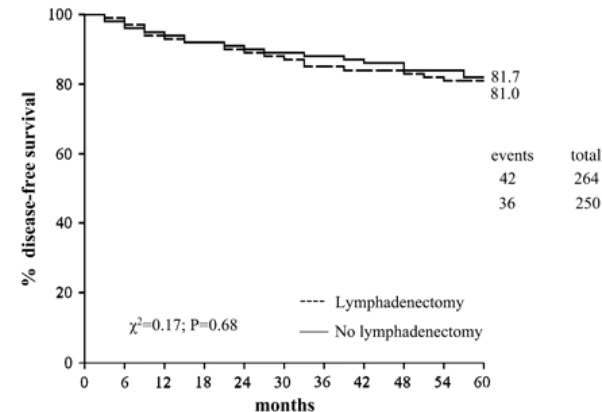
NO SURVIVAL BENEFIT

JNCI Journal of the National Cancer Institute Advance Access published November 25, 2008

ARTICLE

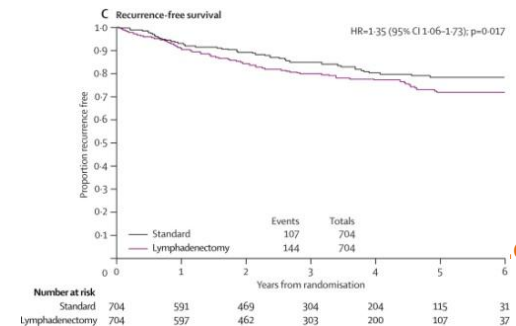
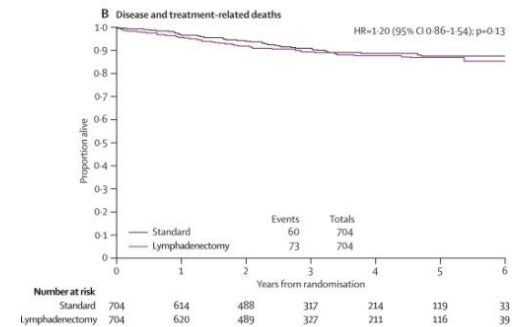
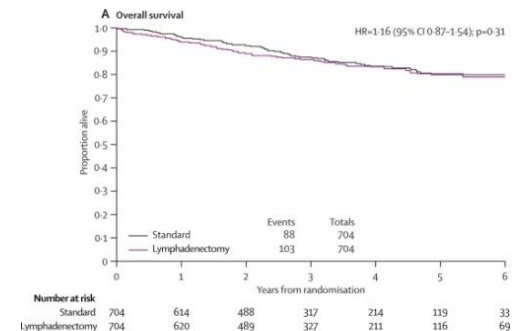
Systematic Pelvic Lymphadenectomy vs No Lymphadenectomy in Early-Stage Endometrial Carcinoma: Randomized Clinical Trial

Pierluigi Benedetti Panici, Stefano Basile, Francesco Maneschi, Andrea Alberto Lissori, Mauro Signorelli, Giovanni Scambia, Roberto Angioli, Saverio Tateo, Giorgia Mangili, Dionyssios Katsaros, Gaetano Garozzo, Elio Campagnutta, Nicoletta Donadello, Stefano Greggi, Mauro Melpignano, Francesco Raspagliesi, Nicola Ragni, Gennaro Cormio, Roberto Grassi, Massimo Franchi, Diana Giannarelli, Roldano Fossati, Valter Torri, Mariangela Amoroso, Clara Crocè, Costantino Mangioni



Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study

The writing committee on behalf of the ASTEC study group*



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Low Risk Populations Included in the 2 Prospective Endometrial Cancer Studies

JNCI Journal of the National Cancer Institute Advance Access published November 25, 2008

ARTICLE

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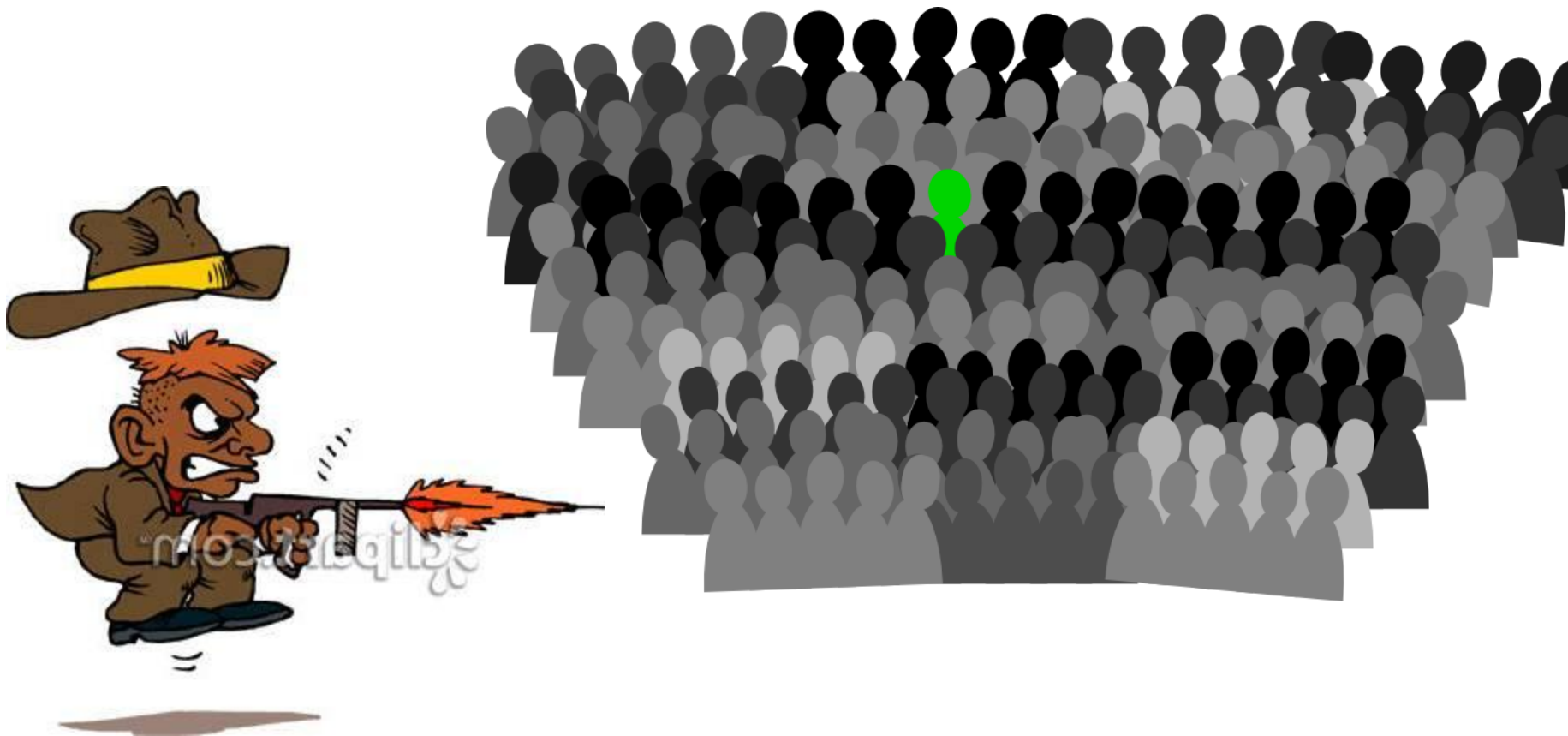
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Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study

*The writing committee on behalf of the ASTEC study group**

- Overall **13%** of positive lymph nodes

- **IA-IB G1 (45% of all cases)**
- Overall **9%** positive lymph nodes



Limited Extent of Lymphadenectomy in the 2 Prospective Endometrial Cancer Studies

JNCI Journal of the National Cancer Institute Advance Access published November 25, 2008

ARTICLE

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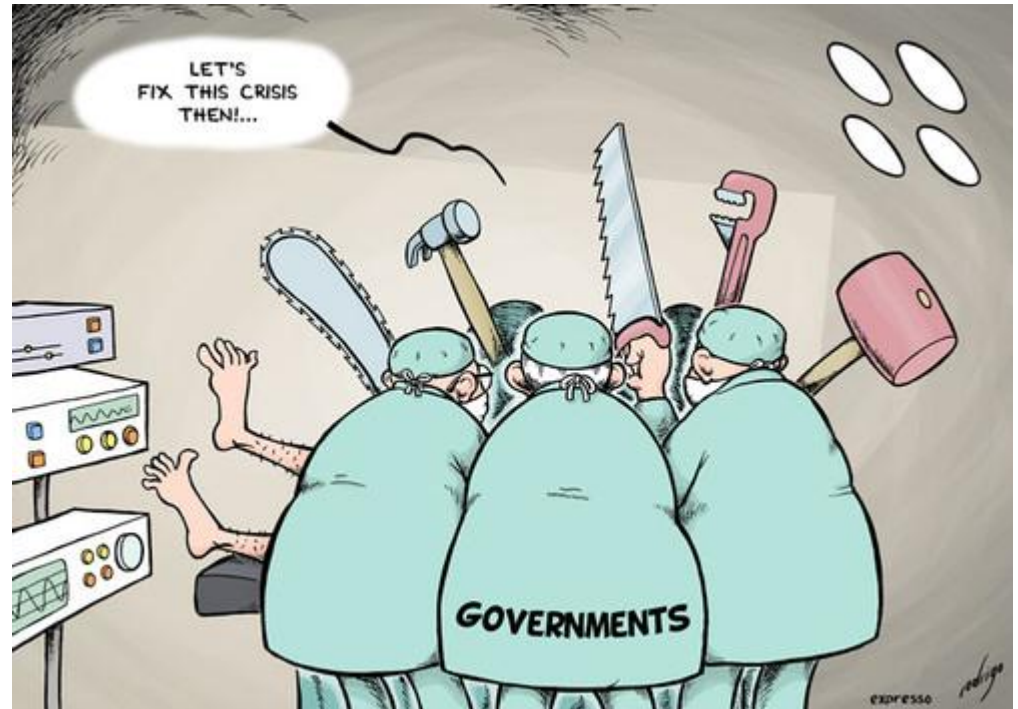
- **Pelvic LND: at least 20 nodes required**
- **Median Number of pelvic nodes = 26**
- **Paraortic LND at the discretion of the physician (performed in 26%)**

Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study

*The writing committee on behalf of the ASTEC study group**

- **“Iliac and obturator nodes”**
- **Median Number of Nodes = 12**
- **35% less than 10 nodes**
- **Paraortic LND at the discretion of the physician**

Results of including all different risk patients...



ASTEC/Italian Trials

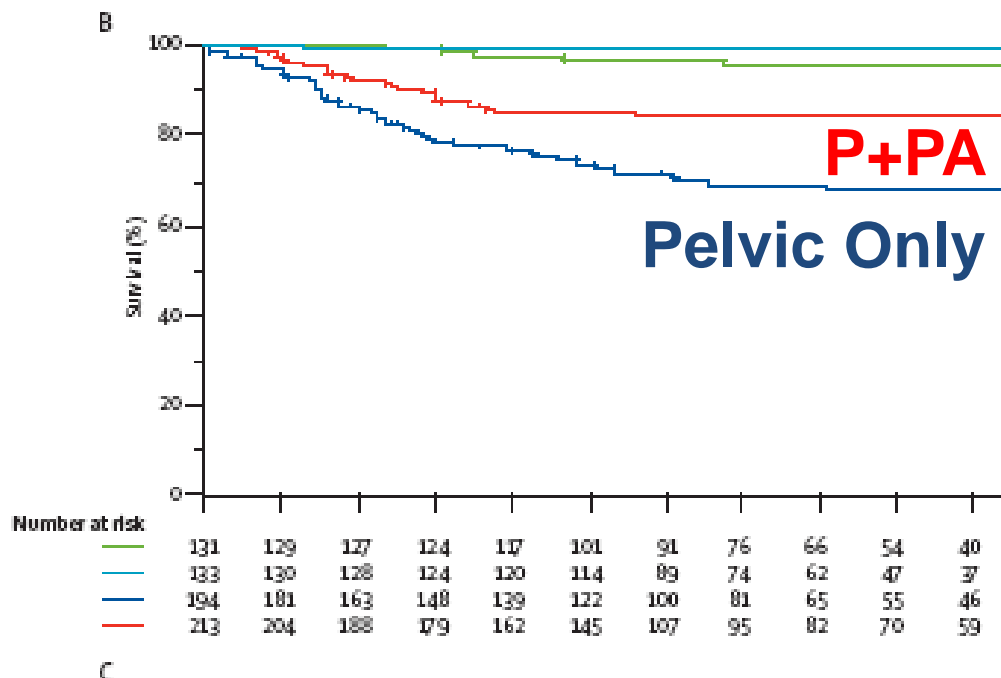
Unanswered questions

- Pelvic Lymphadenectomy (or sampling), if performed in every patient (including low risk patients) does not improve survival
- However, no significant conclusion can be drawn regarding the role of complete surgical staging (i.e. systematic pelvic and paraaortic lymphadenectomy) in high risk endometrial cancer

Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis

Yukiharu Todo, Hidenori Kato, Masanori Kaneuchi, Hidemichi Watanji, Mahito Takeda, Noriaki Sakuragi

Retrospective



Intermediate/High Risk

Significant Improvement
RFS
DRS
OS

Disease-Related Survival

*** At least one variable**

The Lancet 2010

VIENNA
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Question

- My interpretation of ASTEC + Benedetti LND studies is:
 - A. Well conducted RCT → consistent information
→ Very limited role for routine LND today
 - B. Interesting data → but not convincing due to design flaws
 - C. The overwhelming evidence outside of these 2 studies favors routine LND

Conclusions

- Low Risk patients do NOT need LND
- High Risk patients (G3, DMI, non endometrioid histo) *may* benefit from PPALND
 - Assess prognosis
 - Determine adjuvant treatment
 - Potentially reduce patients who need adjuvant treatment (morbidity)

Clinical case

- She is treated with robot assisted total abdominal hysterectomy (TAH) and bilateral salpingo- oophorectomy (BSO), including pelvic and peri-aortic lymph node resection and pelvic washings.
- Pathology confirms a grade 3 tumor with invasion of the deep 1/3 of the uterine wall (within 2mm of serosa)
- Lymphonodes are negative

What to do next?

- Nothing
- Pelvic radiotherapy
- Pelvic+para-aortic radiotherapy
- Chemotherapy
- Concomitant Chemo-radiotherapy
- Chemotherapy followed by radiotherapy

In case lymphanectomy was not performed

What to do next?

- Nothing
- Pelvic radiotherapy
- Pelvic+para-aortic radiotherapy
- Chemotherapy
- Concomitant Chemo-radiotherapy
- Chemotherapy followed by radiotherapy

Discussion

- Thomas Hogberg

Question

A 72 yo with Stage IC, gr 3

- Presents for consultation
- 0/27 PPALN, cytology (-)

The real question today is?

- A. What ???- she needs radiation!
- B. We need better models to predict risk of recurrence
- C. The question is cuff vs pelvic XRT
- D. Would this patient benefit from chemotherapy?

Clinical case

- She is treated with pelvic radiotherapy and 18 months later returns for follow-up with complaints of persistent non-productive cough.
- Chest x-ray reveals small bilateral pulmonary nodules (largest 1.8cm).
- Fine needle aspiration under CT guidance confirms grade 2 adenocarcinoma.
- CT scan of abdomen and pelvis shows no other evidence of recurrent disease.

What would you recommend now?

1. Megestrol acetate (Megace)
2. Megestrol acetate alternating with tamoxifen
3. An aromatase inhibitor
4. Doxorubicin + cisplatin
5. Doxorubicin + cisplatin + paclitaxel (Taxol)
6. Carboplatin+paclitaxel

Discussion

- Thomas Hogberg