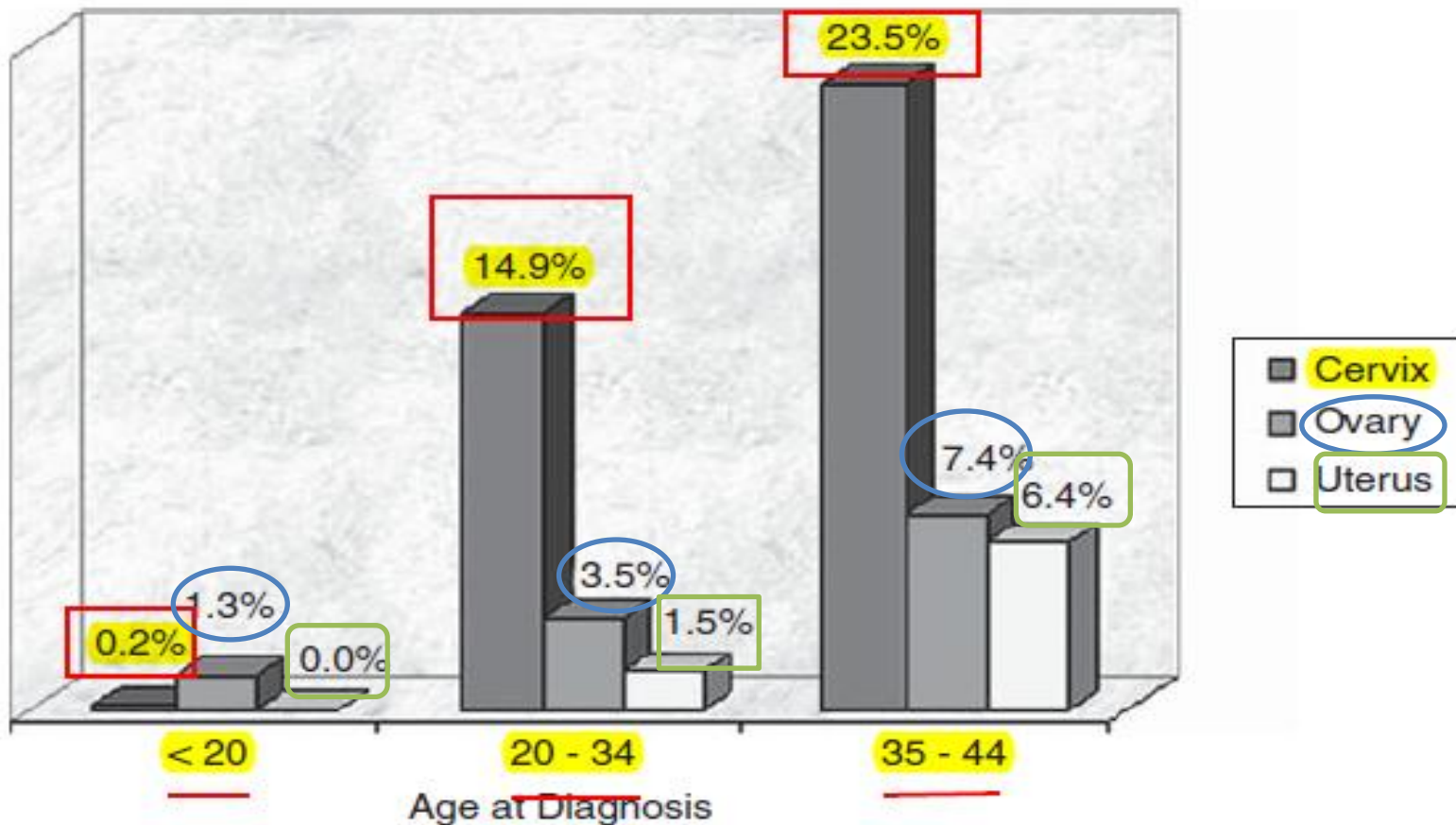


Fertility Preventive Management In Gynecologic Cancers

Ateş Karateke, M.D.
Professor of Obstetrics and Gynecology
Zeynep Kamil Hospital
ISTANBUL



| | | |
|------------------------------|------------|--------------------------|
| All Cervical cancer cases | 41% | } <u><45years old</u> |
| All Ovarian cancer cases | 12% | |
| All Endometrium cancer cases | 8% | |

American Society of Clinical Oncology Recommendations on Fertility Preservation in Cancer Patients

Stephanie J. Lee, Leslie R. Schover, Ann H. Partridge, Pasquale Patrizio, W. Hamish Wallace, Karen Hagerty, Lindsay N. Beck, Lawrence V. Brennan, and Kutluk Oktay

VOLUME 24 · NUMBER 18 · JUNE 20 2006

JOURNAL OF CLINICAL ONCOLOGY

Physicians should discuss with patients the risk of infertility and possible interventions to preserve fertility prior to initiating potentially gonadotoxic therapy. This discussion should occur soon after diagnosis since some interventions to preserve fertility take time and could delay the start of treatment. Early referral to a reproductive endocrinologist can be useful(ASCO, 2006).

Cervical cancer

- Cervical cancer continues to be an important gynecologic malignancy in women of reproductive age
- According to SEER data, approximately 41% of all cervical cancer patients will be diagnosed at an age younger than 45 years

Jemal A et al. Global cancer statistics. *CA Cancer J Clin* 2011;61:69–90.

Carter J, Sonoda Y, Baser RE, et al. A 2-year prospective study assessing the emotional, sexual, and quality of life concerns of women undergoing radical trachelectomy versus radical hysterectomy for treatment of early-stage cervical cancer. *Gynecol Oncol* 2010;119:358–65.

SEER Stat fact sheet: cervix uteri cancer. National Cancer Institute. <http://seer.cancer.gov/statfacts/html/cervix.html> Accessed September 27, 2011.

The incidence of invasive cervical cancer in young women

- The mean age of first intercourse has decreased
- The maternal age at first pregnancy has increased
- Increased cervical cancer screening detect earlier stages of the disease
- More women with a diagnosis of cervical cancer have not yet completed their families
- Fertility sparing surgery for early cervical carcinoma has become more desirable

Fertility-sparing procedures

- Oophoropexy

The rates of ovarian preservation

vaginal brachytherapy → % 90

pelvic radiation → %60

- Conservative gynecologic surgery

- Conization

- Stage 1A1 LVSI(-)

- Radical trachelectomy

- Stage 1A1 LVSI(+)
- Stage 1A2
- Stage 1B1

| | Number | 5-Year Survival |
|------------------------------|--------|-----------------|
| Hysterectomy | 841 | 98 (96–99) |
| Fertility-conserving surgery | 568 | 99 (97–99) |

Data are % (95% confidence interval).

Wright et al. Obstet Gynecol 2010

Daniel Dargent

- Daniel Dargent first introduced radical vaginal trachelectomy in 1994

Dargent D, Brun JL, Roy M, et al. Pregnancies following radical trachelectomy for invasive cervical cancer. *Gynecol Oncol* 1994;52:105.

Oncologic outcomes

- In the past 2 decades that early-stage cervical cancer can be appropriately managed with fertility preservation in mind without compromising oncologic outcomes

Plante M, Renaud MC, Harel F, Roy M. Vaginal radical trachelectomy: an oncologically safe fertility-preserving surgery. An updated series of 72 cases and review of the literature. *Gynecol Oncol* 2004;94:614.

Covens A, Shaw P, Murphy J, et al. Is radical trachelectomy a safe alternative to radical hysterectomy for patients with stage IA – B carcinoma of the cervix? *Cancer* 1999;86:2273–9.

Schlaerth JB, Spirtos NM, Schlaerth AC. Radical trachelectomy and pelvic lymphadenectomy with uterine preservation in the treatment of cervical cancer. *Am J Obstet Gynecol* 2003;188:29–34.

Burnett AF, Roman LD, O'Meara AT, Morrow CP. Radical vaginal trachelectomy and pelvic lymphadenectomy for preservation of fertility in early cervical carcinoma. *Gynecol Oncol* 2003;88:419–23.

Roman LD. Pregnancy after radical vaginal trachelectomy: maybe not such a risky undertaking after all. *Gynecol Oncol* 2005;98:1–2.

Ungar L, Palfalvi L, Hogg R, et al. Abdominal radical trachelectomy: a fertilitypreserving option for women with early stage cervical cancer. *Br J Obstet Gynaecol* 2005;112:366–9.

Obstetrical outcomes

- There have been additional studies demonstrating the favorable obstetrical outcomes of patients who underwent this procedure

Plante M, Gregoire J, Renaud MC, et al. The vaginal radical trachelectomy: an update of a series of 125 cases and 106 pregnancies. *Gynecol Oncol* 2008;111: S105–10.

Shepherd JH, Spencer C, Herod J, Ind TE. Radical vaginal trachelectomy as fertility-sparing procedure in women with early stage cervical cancer cumulative pregnancy rate in a series of 123 women. *Br J Obstet Gynaecol* 2006;4:353–61.

Plante M, Renaud MC, Hoskins IA, Roy M. Vaginal radical trachelectomy: A valuable fertility-preserving option in the management of early-stage cervical cancer. A series of 50 pregnancies and review of the literature. *Gynecol Oncol* 2005;98:3–10.

RT techniques

- After laparoscopic pelvic lymphadenectomy or by the abdominal route
- Vaginal RT is based on the vaginal radical hysterectomy technique according to Schauta-Stoeckel
- Abdominal RT is based on the abdominal radical hysterectomy according to Wertheim
- Reported in small case series
 - Total laparoscopic RT
 - Total robotic RT
 - Laparoscopic and robotic assisted RT
 - Nerve-sparing RT



Reproductive outcomes of patients undergoing radical trachelectomy for early-stage cervical cancer

C.H. Kim ^a, N.R. Abu-Rustum ^a, D.S. Chi ^a, G.J. Gardner ^a, M.M. Leitao Jr. ^a, J. Carter ^b,
R.R. Barakat ^a, Y. Sonoda ^{a,*}

^a Department of Surgery, Gynecology Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^b Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Patient and tumor characteristics.

| Characteristics | N = 105 (%) |
|-------------------------------|-----------------|
| Median age | 32 (6–45 years) |
| Stage | |
| IA1 | 14 (13%) |
| IA2 | 12 (11%) |
| IB1 | 79 (75%) |
| Histology | |
| Squamous | 45 (43%) |
| Adenocarcinoma | 50 (48%) |
| Adenosquamous | 8 (8%) |
| Other | 2 (2%) |
| Type of radical trachelectomy | |
| Abdominal | 49 (47%) |
| Vaginal | 51 (48%) |
| Robotic-assisted | 5 (5%) |



Reproductive outcomes of patients undergoing radical trachelectomy for early-stage cervical cancer

C.H. Kim ^a, N.R. Abu-Rustum ^a, D.S. Chi ^a, G.J. Gardner ^a, M.M. Leitao Jr. ^a, J. Carter ^b,
R.R. Barakat ^a, Y. Sonoda ^{a,*}

^a Department of Surgery, Gynecology Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^b Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Fertility characteristics of radical trachelectomy patients.

| | Total | RAT | RVT | RRT |
|-------------------------------|------------|-----|-----|-----|
| Planned | <u>105</u> | 49 | 51 | 5 |
| Fertility spared ^a | <u>77</u> | 31 | 42 | 4 |
| Nulliparous | 66 | 44 | 41 | 3 |
| Attempting conception | 35 | 12 | 23 | 0 |
| Parity 0 | 29 | 11 | 18 | n/a |
| 1 | 5 | 0 | 5 | n/a |
| ≥2 | 1 | 1 | 0 | n/a |
| Conceived – yes | <u>23</u> | 7 | 16 | n/a |
| Conceived – no | 12 | 6 | 6 | n/a |
| Conceptions | 27 | 8 | 19 | 0 |
| Live births | 20 | 5 | 15 | 0 |
| SAB | 4 | 3 | 1 | 0 |
| ETOP | 3 | 0 | 3 | 0 |

RAT: radical abdominal trachelectomy; RVT: radical vaginal trachelectomy; RRT: radical robotic trachelectomy.

^a These patients did not require immediate radical hysterectomy or postoperative adjuvant treatment.



Reproductive outcomes of patients undergoing radical trachelectomy for early-stage cervical cancer

C.H. Kim ^a, N.R. Abu-Rustum ^a, D.S. Chi ^a, G.J. Gardner ^a, M.M. Leitao Jr. ^a, J. Carter ^b,
R.R. Barakat ^a, Y. Sonoda ^{a,*}

^a Department of Surgery, Gynecology Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^b Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Obstetrical outcomes of 23 women after radical trachelectomy.

| Total no. of conceptions | 27 | RAT | RVT | RRT |
|--------------------------------|----------------|-----|-----|-----|
| Total live births | | | | |
| C/S at 32–36 6/7 weeks | <u>7 (35%)</u> | 1 | 6 | 0 |
| C/S at ≥ 37 weeks ^a | 13 (65%) | 4 | 9 | 0 |
| Spontaneous abortions | | | | |
| 1st trimester | 1 (4%) | 0 | 1 | 0 |
| 2nd trimester | <u>3 (12%)</u> | 3 | 0 | 0 |
| Elective terminations | | | | |
| 1st trimester | 2 (8%) | 0 | 2 | 0 |
| 2nd trimester | 1 (4%) | 0 | 1 | 0 |

C/S: Cesarean section, RAT: radical abdominal trachelectomy, RVT: radical vaginal trachelectomy, RRT: radical robotic trachelectomy.

^a The 2 patients who were pregnant during the study time period have since delivered full term via C/S.



Reproductive outcomes of patients undergoing radical trachelectomy for early-stage cervical cancer

C.H. Kim ^a, N.R. Abu-Rustum ^a, D.S. Chi ^a, G.J. Gardner ^a, M.M. Leitao Jr. ^a, J. Carter ^b,
R.R. Barakat ^a, Y. Sonoda ^{a,*}

^a Department of Surgery, Gynecology Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^b Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Methods of conception in women attempting pregnancy.

| | |
|-------------------------------------|-----------------|
| Total women attempting conception | 35 |
| # successful | <u>23 (66%)</u> |
| Attempting conception spontaneously | <u>17</u> |
| # successful | 12 (71%) |
| Attempting conception with ART | <u>18</u> |
| # successful | 11 (61%) |

Obstetric outcome

- There is an increased risk in midtrimester losses and preterm birth
- There is also a higher incidence of infertility due to cervical abnormalities
 - require the use of assisted reproduction technologies

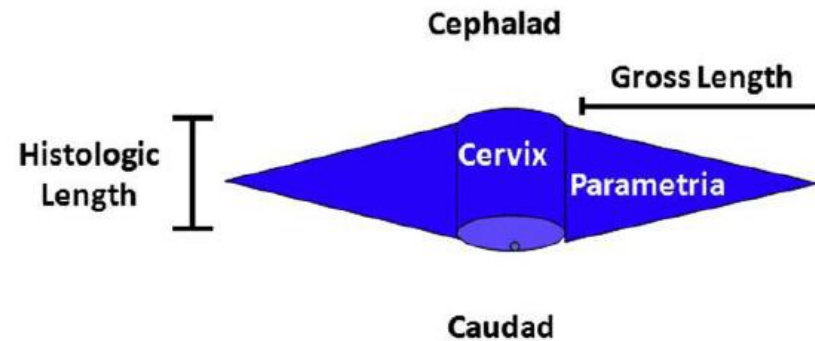
VRT/ART

- Surgical specimen of the cervix has at least 3 to 4 cm of parametrial tissue in ART
- Approximately 2 cm of parametrial tissue is resected in VRT

Radical vaginal versus abdominal trachelectomy for stage IB1 cervical cancer: A comparison of surgical and pathologic outcomes

Margaret H. Einstein^a, Kay J. Park^b, Yukio Sonoda^a, Jeanne Carter^c, Dennis S. Chi^a, Richard R. Barakat^a, Nadeem R. Abu-Rustum^{a,*}

Gynecologic Oncology 112 (2009) 73–77



Pathologic results of the unfixed trachelectomy specimens with bilateral parametrial measurements by the pathologist

| | VRT (<i>n</i> =28) | ART (<i>n</i> =15) | <i>P</i> value |
|--|---------------------|---------------------|----------------|
| Median gross length (cm) | 1.45 (0.73–1.63) | 3.97 (2.7–5.36) | 0.01 |
| Median histologic length (cm) | 1.07 (0.89–1.25) | 1.51 (1.36–1.77) | ≤0.0001 |
| Patients with parametrial lymph nodes detected | 0 (0%) | 8 (57.3%) | 0.0002 |

Results reported as *n* (%) or *n* (25%ile–75%ile). VRT, vaginal radical trachelectomy; ART, abdominal radical trachelectomy. 27 VRT and 11 ART patients had slides available. 5 VRT and 12 ART patients had gross parametrial measurements recorded in the pathology report.

ART/VRT

- Pregnancy rates after ART are lower than after VRT and simple trachelectomy/cone biopsy.
- Pregnancy rate has been reported to be 30% after VRT and 15% after ART

| | VRT (n=28) | ART (n=15) | P value |
|------------------------------------|------------------|-----------------|---------|
| Median age (years) | 30 (27–32) | 34 (32–36) | 0.0003 |
| Histology: | | | 0.53 |
| Adenocarcinoma | 13 (46.6%) | 9 (60%) | |
| Squamous cell carcinoma | 15 (53.6%) | 6 (40%) | |
| Residual disease in specimen | 14 (50%) | 9 (60%) | 0.74 |
| Lymph vascular space invasion | 10 (35.7%) | 7 (46.7%) | 0.53 |
| Median lymph nodes obtained | 31 (21–42) | 24 (18–30) | 0.14 |
| Conversion to hysterectomy | 2 (7.1%) | 2 (13.3%) | 0.6 |
| Median estimated blood loss (mL) | 100 (56–200) | 300 (100–350) | 0.001 |
| Median operating time (minutes) | 363 (310–398) | 319 (298–338) | 0.01 |
| Complications (# patients) | 12 | 2 | 0.09 |
| Median hospital stay (days) | 3 (3–5) | 4 (3–5) | 0.35 |
| Median follow up interval (months) | 24.9 (12.7–31.2) | 11.6 (2.7–18.2) | 0.006 |
| Radiation or chemoradiation | 5 (17.9%) | 7 (46.7%) | 0.07 |

Radical Abdominal Trachelectomy

Advantages

- Technically easier
- No learning curve for gyn oncologists
- Wider parametrium, operate on bigger tumours

Disadvantages

- May entail transection of uterine vessels
- Fertility rate may be decreased vs vaginal approach
- If done by laparotomy , ↑ blood loss,hosp stay

Criteria used to select candidates for radical vaginal hysterectomy

1. Confirmed invasive cervical cancer: squamous, adenocarcinoma, or adenosquamous
2. FIGO stage IA1 with lymphovascular space involvement, FIGO IA2 IB1
3. Desire to preserve fertility
4. Lesion size < 2cm
5. No previous history of infertility
6. Estimated length of remaining cervix ≥ 1 cm
7. Postconization adequate resolution of acute inflammation required (usually a 6-wk interval between conization and RT)
8. Negative pelvic lymph node status

Radical trachelectomy in late pregnancy: is it an option?

Karateke A, Cam C, Celik C, Baykal B, Tuq N, Ozbasli E, Tosun OA.

- Abdominal RT has been performed successfully in pregnant patients with FIGO stage IB1 cervical cancer in the first trimester and second trimester
 - preservation of uterine arteries
- This type of surgery is experimental

Volume XXXIII
Number 2, 2012

ISSN: 0953-2096

EJGO

European Journal of Gynaecological Oncology

www.ijog.net



Founded by
A. ONNIS

Radical abdominal trachelectomy is a safe and fertility preserving option for women with early stage cervical cancer

A. Karateke, C. Kabaca

Department of Gynecologic Oncology, Zeynep Kamil Women and Children Diseases Education and Research Hospital, Istanbul (Turkey)

Summary

Purpose of investigation: To present the surgical, oncological and obstetrical outcomes gained from patients who underwent radical abdominal trachelectomy (RAT) in Zeynep Kamil Women and Children Diseases Education and Research Hospital and radical Yeditepe University Hospital. *Methods:* A total of eight RATs were performed between 2003-2010. Data were obtained from medical and pathological records of the patients. *Results:* The mean age of the patients was 27.37 ± 6.39 years. The mean follow-up time of the patients was 33.62 ± 27.47 months. Three (37.5%) patients had a tumor size smaller than 2 cm, and five (62.5%) patients had a tumor size larger than 2 cm. Seven (87.5%) patients had Stage IB1 and one (12.5%) patient had Stage IIA tumor. Three (37.5%) patients had late post-operative complications: uterotubal abscess, severe lymphedema and lymphocyst. There were no recurrences. Three patients became pregnant which resulted in two live births and one abortus. The spontaneous pregnancy rate was 50%. *Conclusion:* We think that RAT is a reliable surgical option for a patient with early stage cervical cancer who wants to preserve fertility.

Key words: Radical abdominal trachelectomy; Early stage cervical cancer; Pregnancy; Fertility.

Table 1. — *Data of the patients.*

| Patients | Age, years | Follow-up time, months | Operation time minutes | Number of units of blood transfusion | Hospital stay, days | Post-operative complication | Recurrence | Pregnancy |
|----------|------------|------------------------|------------------------|--------------------------------------|---------------------|-----------------------------|------------|--|
| 1 | 19 | 92 | 210 | 0 | 12 | Late uterotubal abscess | No | Hysterectomized |
| 2 | 28 | 55 | 210 | 0 | 10 | No | No | No |
| 3 | 25 | 28 | 150 | 0 | 5 | No | No | Yes, delivered term baby |
| 4 | 28 | 25 | 150 | 0 | 5 | Left leg lymphedema | No | No |
| 5 | 35 | 26 | 160 | 0 | 5 | No | No | Yes, delivered a baby at 31 weeks of gestation |
| 6 | 33 | 21 | 180 | 2 | 7 | Lymphocyst | No | Yes, abortus at 21 weeks |
| 7 | 18 | 17 | 120 | 0 | 12 | No | No | No |
| 8 | 33 | 5 | 130 | 0 | 10 | No | No | No |

Table 2. — *Pathological results.*

| Patients | Histologic subtype | Tumor size, cm | Disease free upper surgical margin, mm | Vaginal invasion | LVSI | Number of lymph nodes removed | Lymph node positivity | Stage |
|----------|--------------------------------|-------------------|--|------------------|------|-------------------------------|-----------------------|-------|
| 1 | Clear cell | 1.2 × 1.8 × 1.1 | 12 | 0.1 mm | Yes | 19 | No | II a |
| 2 | Squamous cell | 2.9 × 2 × 1.7 | 7 | No | Yes | 36 | No | Ib1 |
| 3 | Squamous cell | 3 × 2.2 × 0.7 | 28 | No | No | 15 | No | Ib1 |
| 4 | Squamous cell | 0.6 × 0.8 × 1 | 6 | No | Yes | 35 | No | Ib1 |
| 5 | Squamous cell | 1.2 × 1 × 1 | 11 | No | No | 25 | No | Ib1 |
| 6 | Adenocarcinoma, villoglandular | 2.2 × 1.2 × 0.3 | 13 | No | No | 42 | No | Ib1 |
| 7 | Adenocarcinoma | 3 × 4, exophytic* | 40 mm, no residual tumor in material | No | No | 48 | No | Ib1 |
| 8 | Adenocarcinoma | 2.1 × 1 × 0.5* | 30 mm, no residual tumor in material | No | No | 37 | No | Ib1 |

* Tumor sizes within the conization specimen. Disease-free upper margin was deemed as the longitudinal length of the cervix in 2 patients in whom no residual tumor was present. LVSI: lymphovascular space invasion.

Cranial extent of the tumor

- The main selection criteria for fertility-sparing procedure should be rather cranial extent of the tumor allowing for the preservation of at least 1 cm of endocervical canal than a maximal tumor diameter or a tumor volume

Cerclage

- There is no clear consensus if a cervicoisthmic cerclage should be done during RT or only after the patient became pregnant
- Primary cerclage might impair fertility by inducing subsequent cervical stenosis, erosions, and/or chronic discharges

10-mm negative endocervical margin

- 5-mm negative margin is sufficient, while others prefer a 10-mm negative endocervical margin
- Radical abdominal trachelectomy to some patients who have larger lesions (tumor size between 2 and 4 cm)
 - at least a 10 mm negative endocervical margin

IMPORTANCE OF THE PARAMETRIUM

Tableau 2

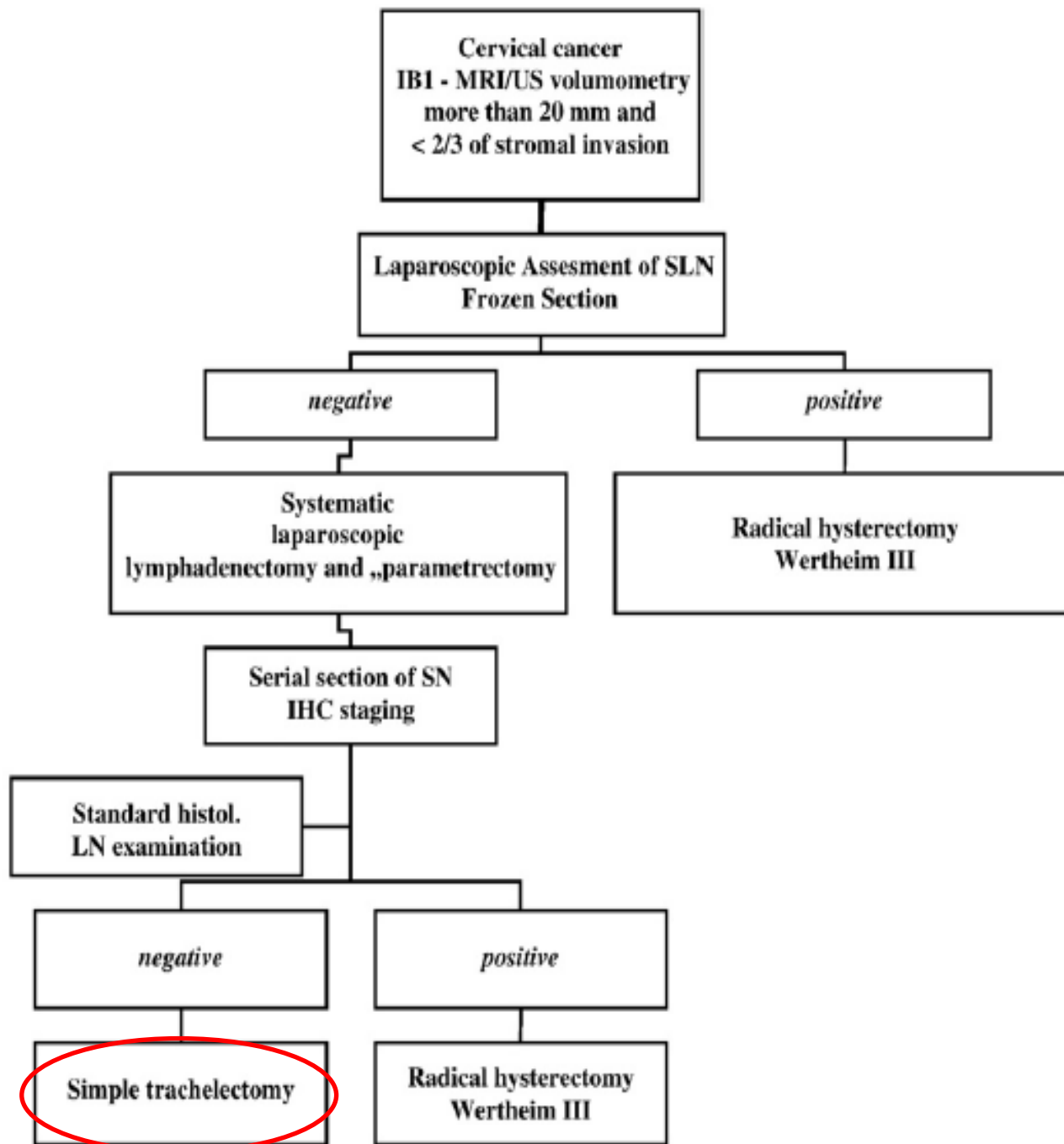
Revue de la littérature des cas de cancer du col à bas risque (tumeur de moins de 2 cm, pas d'atteinte ganglionnaire pelvienne, profondeur d'invasion de moins de 10 mm).

| | Stades | Nombre total de patientes | Nombre de patients avec T < 2 cm et N ⁻ ^a | Paramètre atteint (%) |
|----------------------------|-------------|---------------------------|---|-----------------------|
| Kinney, 1995 | IB | 83 | 83 | 0 |
| Covens et al., 2002 [18] | IA1-IA2-IB1 | 842 | 536 | 3 (0,6) |
| Sonoda, 2004 | IA1-IA2-IB1 | 89 | 77 | 0 |
| Stegeman et al., 2007 [18] | IA1-IA2-IB1 | 103 | 103 | 2 (1,9) |
| Total | | | 799 | 5 (0,62) |

^a N⁻ : absence d'atteinte ganglionnaire pelvienne.

Cone/Simple Trachelectomy

- < 2cm tumours
 - Laparoscopic PLN and parametrial node dissections. If positive Rad. Hyst.
 - If negative nodes 7 days later cone (stage 1A2), or simple trachelectomy (stage 1B1)
- >2cm or >50% stromal invasion
 - Cisplatin/ifos or cisplatin/adr, Then above schema.



Cone/Simple Trachelectomy

| | Stage 1A1/1A2 | Stage IB1 | NAC |
|---------------------|------------------|-----------|-----|
| N | 13 | 27 | 9 |
| + nodes | 3 | 3 | |
| Cone | 10 | | |
| Simple trach | | 24 | 7 |
| Median fup | 47 mos | | |
| Recurrence | 1 (central) | | |

Cone/Simple Trachelectomy

Pregnancy Outcomes

Attempted preg 24 of 32 women

preg 23 in 17 women

TAB/ectopic 2

SA T1 2

T2 loss 3

24-34 1

34-35 2

37-39 9

What is new

Early –Stage low –risk Cervical Cancer

Simple Vaginal Trachelectomy / Conization might
be suitable for

**stage IB 1 lesions, smaller than 20 mm, with
negative Pelvic lymph nodes, Grade 1**

Stage IB1, <20 mm

| No. of patients | Procedure | No. of patients with recurrence |
|-----------------|--|---------------------------------|
| 16 | Conization + pelvic laparoscopic lymphadenectomy | 0 |
| 36 | Conization + pelvic laparoscopic lymphadenectomy | 1 (pelvic lymph-nodal relapse) |
| 10 | Conization + pelvic laparoscopic lymphadenectomy | 0 |

**The incidence of parametrial involvement is only 0.6%, if
tumor size<2 cm
negative pelvic lymph nodes
depth of invasion<10 mm**

Fanfani F, J Reprod Infertil. 2014
Maneo A, Gynecol Oncol, 2011
Ditto A, Gynecol Surg, 2009

Neoadjuvant chemotherapy

- Neoadjuvant chemotherapy is evaluated for tumors greater than 2 cm in diameter to allow treatment by RT, simple trachelectomy, or conization NACT can decrease the tumor volume before the surgery
- The complete removal of the tumor with negative margins, while preserving the adequate amount of cervical tissue, which improves the chance for a successful pregnancy



Neoadjuvant chemotherapy and vaginal radical trachelectomy for fertility-sparing treatment in women affected by cervical cancer (FIGO stage IB–IIA1)

Pierangelo Marchiole ^{a,*}, Jean-Dominique Tigaud ^b, Sergio Costantini ^c, Serafina Mammoliti ^d, Annie Buenerd ^b, Eva Moran ^e, Patrice Mathevet ^b

^a Department of Obstetrics and Gynaecology, Ospedale Villa Scassi-ASL 3 Genovese, Corso O.Scassi 1, 16149 Genoa, Italy

^b Service de Gynécologie, Hôpital Femme-Mère-Enfant, 69677 Bron cedex, France

^c Department of Obstetrics and Gynaecology, San Martino Hospital, University of Genoa, Largo Rosanna Benzi 1, 16132, Genoa, Italy

^d Medical Oncology Unit, San Martino Hospital, Largo Rosanna Benzi 1, 16132, Genoa, Italy

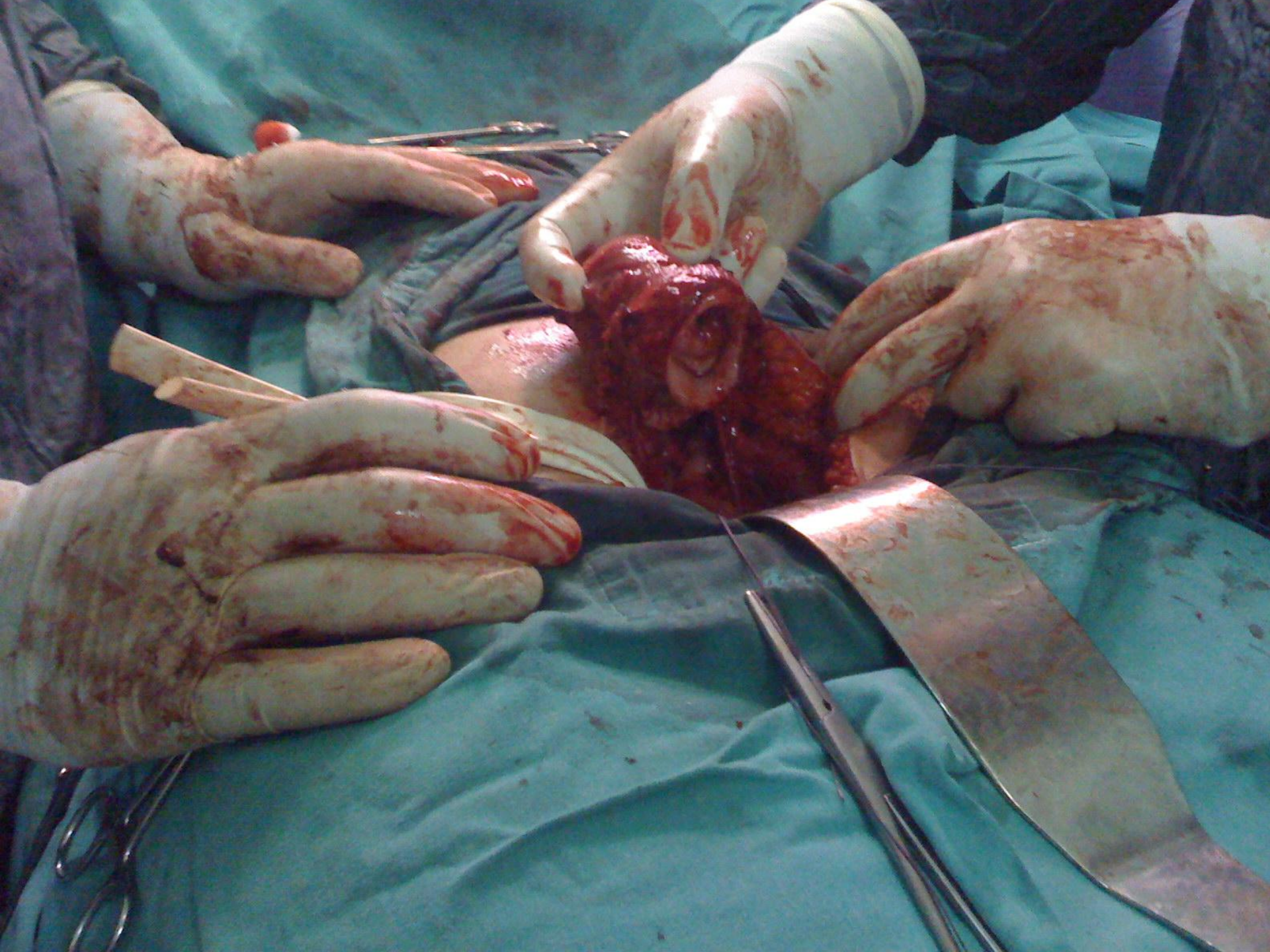
^e Laboratory of Cellular Therapy: Oncology, Department of Internal Medicine, University of Genova, Genova, Italy

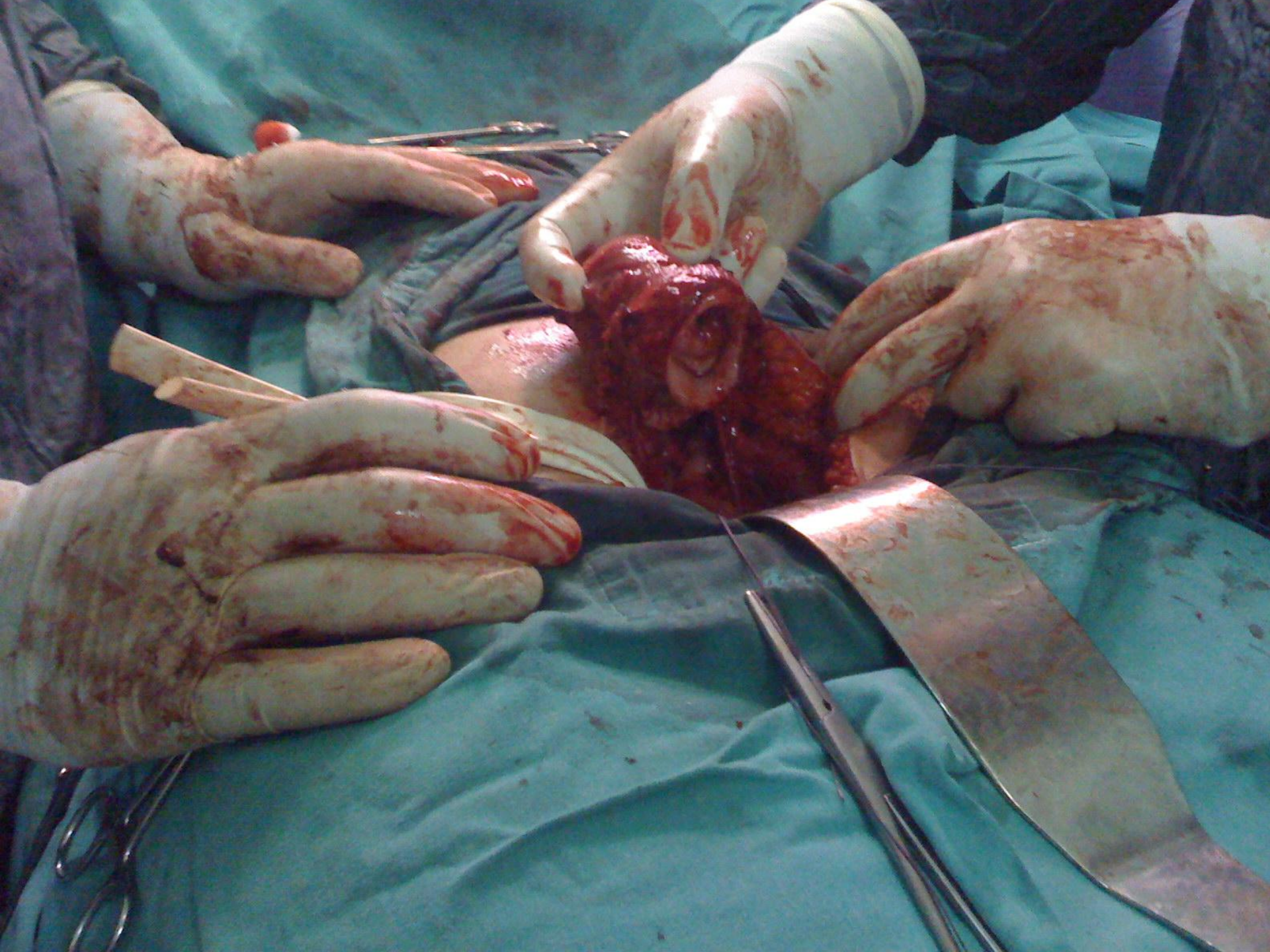
Clinical and tumor recurrence data in four studies after neoadjuvant chemotherapy and different techniques of fertility sparing surgery. NACT: neoadjuvant chemotherapy; T: paclitaxel; I: ifosfamide; P: cisplatin; E: epirubicin; BOMP: cisplatin, bleomycin, vincristine and mitomycin; Adk: adenocarcinoma; VRT: vaginal radical trachelectomy; ST: simple trachelectomy; PL: pelvic lymphadenectomy; CR: complete disappearance of tumor in the cervix with negative nodes; PR1: residual disease with <3 mm stromal invasion including in situ carcinoma.

| | Tumor size ≥ 2 cm (cases no.) | Fertility spared (cases no.) | NACT protocol | Conservative surgery | Rate of optimal pathologic response (CR + PR1) | Recurrences | Pregnancy |
|----------------------|---------------------------------------|---------------------------------|----------------------|-------------------------|---|-------------|-----------|
| Maneo et al. [8] | 8 | 6 | TIP (or TEP for Adk) | Conisation + PL | 6/6 (100%) | 0/6 | NR |
| Kobayashi et al. [9] | 1 | 1 | BOMP | Conisation | 1/1 (100%) | 0/1 | 1/1 |
| Plante et al. [10] | 3 | 3 | TIP | VRT + PL | 3/3 (100%) | 0/3 | 3/3 |
| Robova et al. [13] | 15 | 12 | IP (+ D for Adk) | ST + PL | 9/12 (75%) | 3/12 | 7/12 |
| Palaia et al. [26] | 1 | 1 | TIP | ST + PL | 1/1 (100%) | 0/1 | 0/1 |
| Present report | 7 | 7 | TIP (or TEP for Adk) | VRT + PL | 4/7 (57%) | 0/7 | 1/7 |

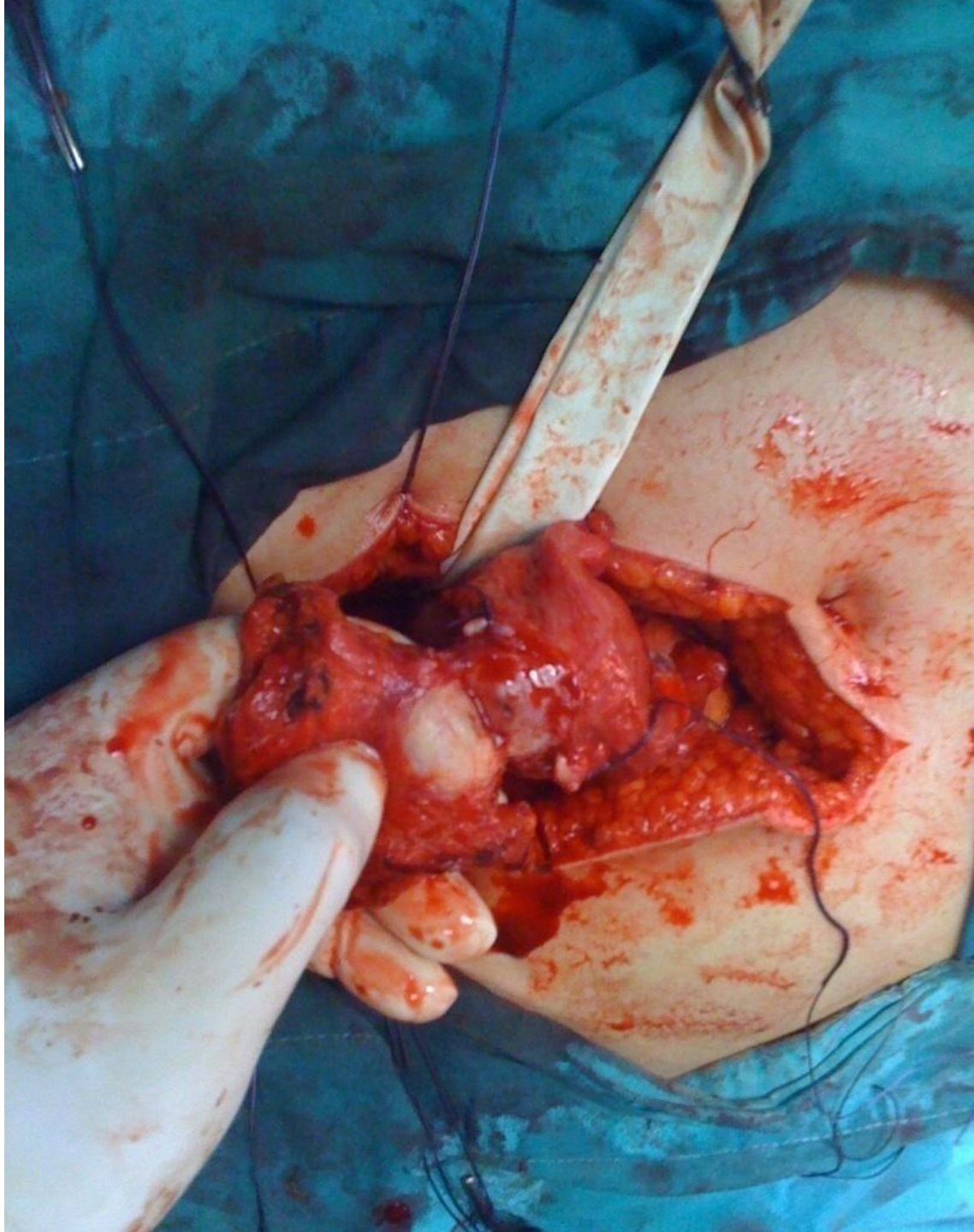
Neoadjuvant chemotherapy followed by conservative surgery

- The oncological safety of neoadjuvant chemotherapy and more conservative surgery must be investigated further



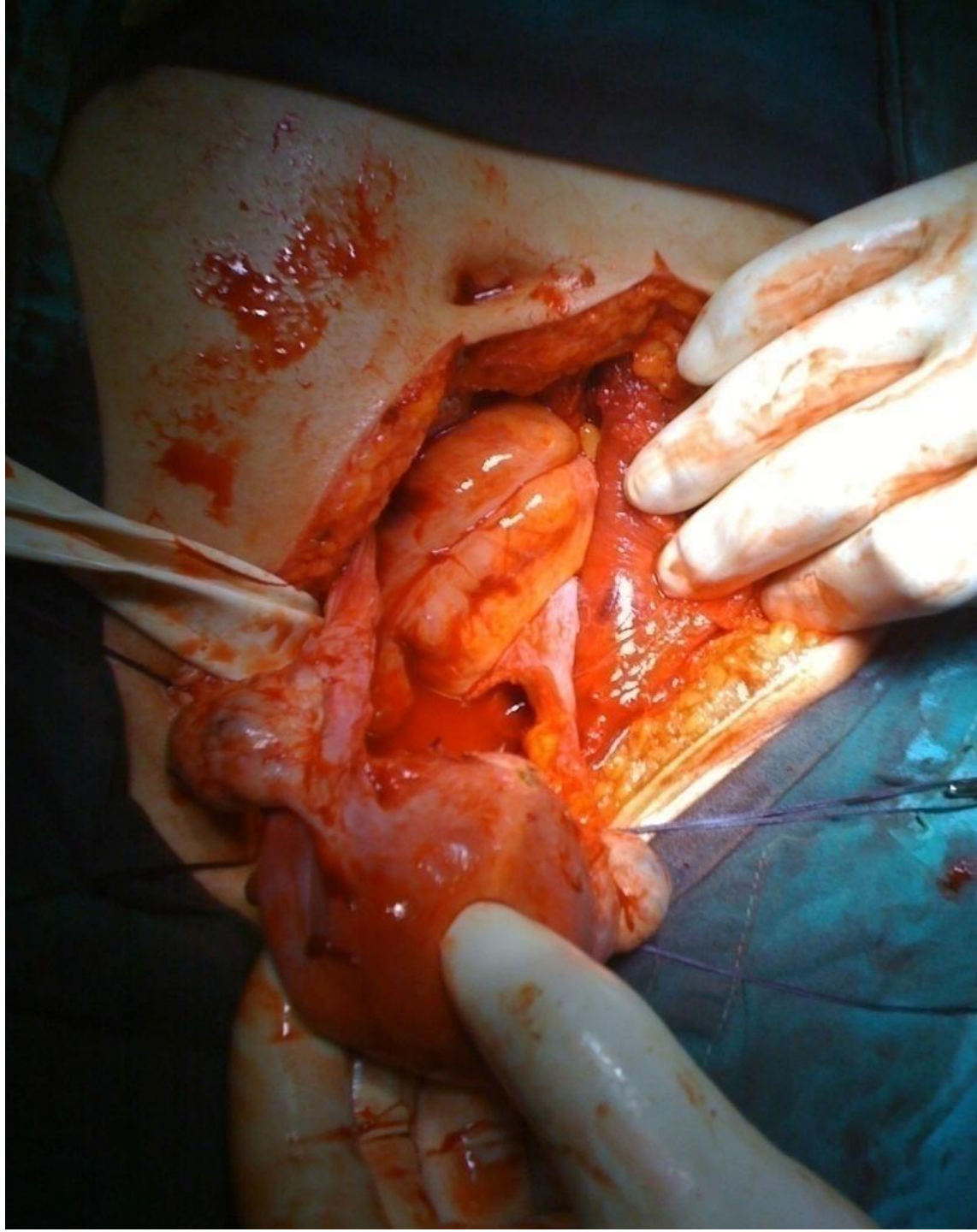
















Endometrial Adenocarcinoma

- 2–14% of endometrial adenocarcinoma occurs in women 40 years of age, who very often still desire pregnancy

Duska LR, Garrett A, Rueda BR, Haas J, Chang Y, Fuller AF. Endometrial cancer in women 40 years old or younger. *Gynecol Oncol* 2001;83:388–93.

Fertility-sparing treatment for endometrial carcinoma

- Two main points of medical treatment of end Ca:
 - the safety of this option
 - the risk of occult ovarian tumor
- The risk of occult ovarian tumor in the case of grade 1, stage 1A is **1 %**
- However, laparoscopic evaluation of ovaries are recommended

Martinez A. et al, Best Prac&Research Clin Obstet Gynecol, 2012

Lee TS. Et al., Gynecol Oncol, 2012

Indication for medical treatment

- Although histologic grade is probably the most important prognostic factor for endometrial carcinoma, grade 1 lesions are not so rarely associated with
 - pelvic lymph-node involvement 3%
 - paraaortic lymph node involvement 1.7%
 - deep myometrial invasion 9%
 - spread of tumor to the adnexa 6%
 - coexisting ovarian neoplasms 19%

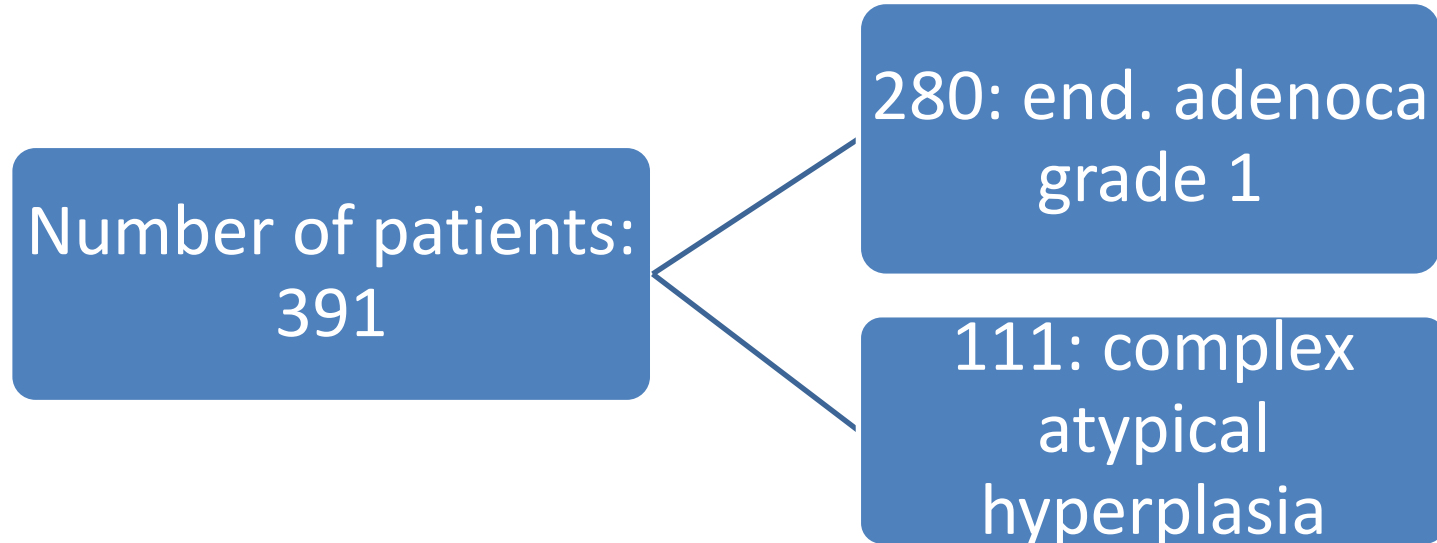
Indication for medical treatment

- age <40 years
- nulliparous
- grade 1 endometrial adenoCa
- presence of P receptor
- absence of myometrial invasion by MRI or tvUSG
- histologic findings other than clear cell and serous papillary

Oncologic and Reproductive outcomes with progestin therapy in women with endometrial hyperplasia and grade 1 Adenocarcinoma: A systematic review

Gynecologic Oncology 125 (2012)

Camille C. Gunderson^{a,*}, Amanda Nickles Fader^{a,b}, Kathryn A. Carson^c, Robert E. Bristow^d



- **Progestin agents administered**
 - MPA, megestrol acetate, Mirena, OCP, norethisterone, 17-OH progesterone

Oncologic and Reproductive outcomes with progestin therapy in women with endometrial hyperplasia and grade 1 Adenocarcinoma: A systematic review

Gynecologic Oncology 125 (2012)

Camille C. Gunderson ^{a,*}, Amanda Nickles Fader ^{a,b}, Kathryn A. Carson ^c, Robert E. Bristow ^d

- The rate of complete response **78%**
 - median time to response of 6 months
- The pregnancy rate **36%**
- The rate of recurrence **25%**
 - median time to recurrence of 24 months

| | Initial response | Complete response | Complete response with recurrence | Persistent/ progressive disease | Proportion achieving pregnancy | Number of live births |
|---------|------------------|-------------------|-----------------------------------|---------------------------------|--------------------------------|-----------------------|
| CAH | 85.6% | 65.8% | 23.2% | 14.4% | 28/111 (41%) | 28 |
| EC | 74.6% | 48.2% | 35.4% | 25.4% | 86/280 (34.8%) | 89 |
| p-value | 0.03 | 0.002 | 0.03 | 0.02 | 0.39 | n/a |

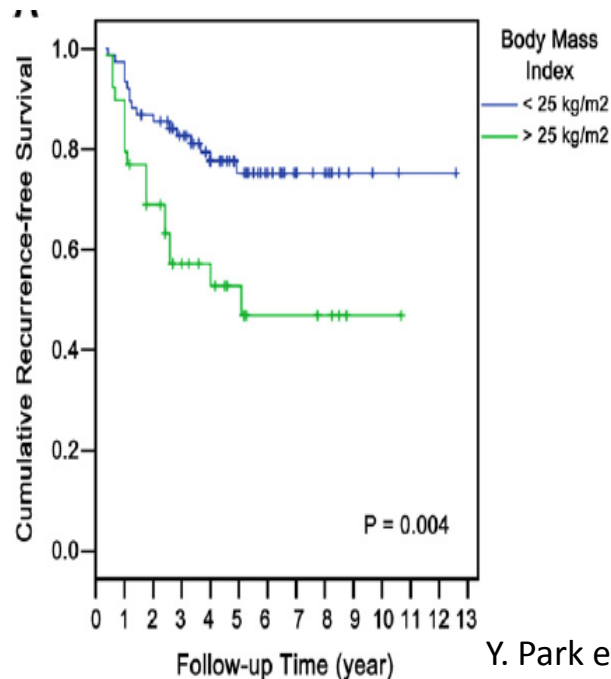
CAH: complex atypical hyperplasia.

EC: endometrial carcinoma.

Fertility sparing treatment is more successful for CAH than EC

| Characteristics | | Total, <i>n</i> | Complete response, <i>n</i> (%) | <i>p</i> -Value |
|---------------------------|-----------------------------|-----------------|---------------------------------|-----------------|
| Age | ≤30 years | 68 | 52 (76.5) | 0.740 |
| | >30 years | 80 | 63 (78.8) | |
| Body mass index | <25 kg/m ² | 89 | 79 (85.4) | 0.006 |
| | ≥25 kg/m ² | 59 | 39 (66.1) | |
| Medical co-morbidity* | No | 128 | 101 (78.9) | 0.374 |
| | Yes | 20 | 14 (70) | |
| Parity | 0 | 139 | 108 (77.7) | 0.999 |
| | 1-2 | 9 | 7 (77.8) | |
| Polycystic ovary syndrome | No | 125 | 98 (78.4) | 0.635 |
| | Yes | 23 | 17 (73.9) | |
| Progestin type | Medroxyprogesterone acetate | 57 | 45 (78.9) | 0.773 |
| | Megestrol acetate | 91 | 70 (76.9) | |
| Progestin dose | <500 mg/day | 73 | 56 (76.7) | 0.775 |
| | ≥500 mg/day | 75 | 59 (78.7) | |

The only factor predicting complete response to MPA is **BMI**



Selection of progestin agent

- **Megestrol acetate** 160 mg/day x minimum duration of 3 months is recommended

Mazzon I. et al, Fertil Steril, 2010

- In a long-term study, **MPA** (40-1000mg/day) was found to be superior than megestrol acetat

Y. Park et al, European Journal of Cancer, 2012

- No sufficient data is availabe for Mirena and GnRH α .

Dhar K., Gynecol Oncol, 2005

Conservative surgical management of stage IA endometrial carcinoma for fertility preservation

Ivan Mazzon, M.D.,^a Giacomo Corrado, M.D., Ph.D.,^b Valeria Masciullo, M.D., Ph.D.,^c Daniela Morricone, M.D.,^a Gabriella Ferrandina, M.D.,^b and Giovanni Scambia, M.D.^c

Fertil Steril® 2010

- A three-step technique is used:
 1. The removal of the tumor
 2. The removal of the endometrium adjacent to the tumor
 3. The removal of the myometrium underlying the tumor
- Megestrol acetate (160 mg/day) is continued for 6 months
- Follow-up:
 - first year, tvUSG + diagnostic hysteroscopy, every 3 months
 - second year, tvUSG + diagnostic hysteroscopy, every 6 months

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 |
|---|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Histology after operative hysteroscopy | EEA G1 | EEA G1 | EEA G1 | EEA G1 | EEA G1 | EEA G1 |
| Therapy: MA 160 mg (mo) | 6 | 6 | 6 | 6 | 6 | 6 |
| Diagnostic hysteroscopy with biopsy after 3 mo | Typical hyperplasia | Atypical hyperplasia | Proliferative endometrium | Typical hyperplasia | Typical hyperplasia | Proliferative endometrium |
| Diagnostic hysteroscopy with biopsy after 6 mo | Typical hyperplasia | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium |
| Diagnostic hysteroscopy with biopsy after 9 and 12 mo | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium | Proliferative endometrium |
| Follow-up (mo) | 82 | 59 | 49 | 46 | 46 | 21 |

Note: MA = megestrol acetate; EEA = endometrioid endometrial adenocarcinoma; G1= grading 1.

- All patients responded to 3 months of hormonal therapy
- None had recurrent disease
- 4 patients(%66) have given birth without ART

Mazzon et. al, Fertil Steril, 2010

Progestins side effects

- progestins are associated with risks of phlebitis of 5%–10%
- high doses of P change lipid metabolism,
 - leading to a greater risk of atherogenesis
 - diabetes
 - hypertension
 - hyperlipoproteinemia
- loss of libido
- weight gain
- mood changes
- breast cancer ?

Follow-up

- Repeat **USG** with **endometrial biopsy** every **three months**
 - Max 9-12 months
- Following completion of childbearing, **surgery** is recommended

Comparison of dilatation & curettage and endometrial aspiration biopsy accuracy in patients treated with high-dose oral progestin plus levonorgestrel intrauterine system for early-stage endometrial cancer

Mi Kyoung Kim ^a, Seok Ju Seong ^{a,*}, Taejong Song ^a, Mi-La Kim ^a, Bo Sung Yoon ^a, Hye Sun Jun ^a,
 Gun Ho Lee ^b, Yoon Hee Lee ^c *Gynecologic Oncology* 130 (2013) 470-473

The diagnostic accuracy of aspiration biopsy with LNG-IUS in place is very poor

High prevalence of insufficient tissue for pathologic evaluation was noted with endometrial aspiration

| D&C | N (%) | Endometrial aspiration biopsy | N |
|---------------------------------|-----------|---------------------------------|----|
| Normal | 10 (35.7) | Normal | 3 |
| | | Material insufficiency | 7 |
| Cancer | 9 (32.1) | Cancer | 3 |
| | | Normal | 3 |
| | | Material insufficiency | 3 |
| Complex endometrial hyperplasia | 7 (25) | Complex endometrial hyperplasia | 1 |
| | | Normal | 1 |
| | | Material insufficiency | 5 |
| Material insufficiency | 2 (7.1) | Material insufficiency | 2 |
| Total | 28 (100) | Total | 28 |



www.igo.org

Contents lists available at SciVerse ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo



CLINICAL ARTICLE

A Turkish Gynecologic Oncology Group study of fertility-sparing treatment for early-stage endometrial cancer[☆]

Polat Dursun^{a,*}, Serkan Erkanli^a, Ahmet Barış Güzel^b, Murat Gültekin^a, Nefise Çağla Tarhan^a, Ozden Altundag^a, Fuat Demirkiran^c, Tugan Beşe^c, Yusuf Yildirim^d, Gurkan Bozdağ^e, Hakan Yaralı^e, Tayyup Simsek^f, Bulent Özcelik^g, Firat Ortaç^h, Salih Taskin^h, Tevfik Guvenalⁱ, Nejat Özgül^j, Ali Haberal^a, M. Ali Vardar^b, Murat Dede^{j,k}, Mufit Yenen^{j,k}, Aytekin Altıntaş^b, Macit Arvas^c, Ali Ayhan^a

^a Department of Obstetrics and Gynecology, Baskent University School of Medicine, Ankara, Turkey

^b Department of Obstetrics and Gynecology, Çukurova University School of Medicine, Adana, Turkey

^c Department of Obstetrics and Gynecology, Istanbul University Cerrahpaşa School of Medicine, Istanbul, Turkey

^d Ege Maternity Hospital, İzmir, Turkey

^e Department of Obstetrics and Gynecology, Hacettepe University School of Medicine, Ankara, Turkey

^f Department of Obstetrics and Gynecology, Antalya University School of Medicine, Antalya, Turkey

^g Department of Obstetrics and Gynecology, Erciyes University School of Medicine, Kayseri, Turkey

^h Department of Obstetrics and Gynecology, Ankara University School of Medicine, Ankara, Turkey

ⁱ Department of Obstetrics and Gynecology, Celal Bayar University School of Medicine, Manisa, Turkey

^j Ankara Etilik Zübeyde Hanım Maternity Hospital, Ankara, Turkey

^k Department of Obstetrics & Gynecology, Gülhane Military School (GATA), Ankara, Turkey

A retrospective, multicenter designed study

43 endometrium cancer patients

treated with most commonly megestrol acetate, following MPA

| Response rate | Persistence rate | Pregnancy rate | Recurrence rate |
|---------------|------------------|----------------|-----------------|
| 81 % | 19 % | 42 % | 5 % |

mean duration of treatment **5 months**

mean follow up **49 months**

What if endometrial Ca recurs after progestin treatment

Progestin re-treatment in patients with recurrent endometrial adenocarcinoma after successful fertility-sparing management using progestin

Jeong-Yeol Park ^a, Sang-Hun Lee ^b, Seok Ju Seong ^c, Dae-Yeon Kim ^a, Tae-Jin Kim ^d, Jae Weon Kim ^e, Jong-Hyeok Kim ^a, Yong-Man Kim ^a, Young-Tak Kim ^a, Duk-Soo Bae ^f, Joo-Hyun Nam ^{a,*}

Gynecologic Oncology 129 (2013) 7–11

- 33 patients who had recurrence after complete remission by progestin
 - 13 patients: atypical hyperplasia
 - 20 patients: grade 1 end adenocarcinoma

Progestin re-treatment can be recommended for young women with recurrent endometrial cancer

- 30 patients received MPA 80-500 mg/day (29, received 500 mg/day)
3 patients received megestrol acetate (80-160 mg/day)
 - Median duration of treatment was 6 months
 - 5 patients failed to respond to re-treatment
 - 28 patients completed progestin treatment with complete remission
- median follow-up was 51 months

Borderline ovarian tumors(BOT)

- Serous BOT (SBOT)
- Mucinous BOT (MBOT)

Behavior of Borderline Tumors With Particular Interest to Persistence, Recurrence, and Progression to Invasive Carcinoma: A Prospective Study

J Clin Oncol 19:2658-2664. © 2001 by American Society of Clinical Oncology.

- 339 patients with serous and mucinous BOT;
 - group A: 150 patients → radical surgery
 - group B: 189 patients → fertility-sparing surgery
- The recurrence rate in group B (35/189) is more than group A (7/150)

| Stage | No. of Patients | Median Age (years) | Surgery | |
|-------|-----------------|--------------------|-------------------|---------|
| | | | Fertility-Sparing | Radical |
| IA | 171 | 39 | 95 | 76 |
| IB | 28 | 41 | 14 | 14 |
| IC | 84 | 37 | 55 | 29 |
| II | 27 | 38 | 13 | 14 |
| III | 29 | 39 | 12 | 17 |

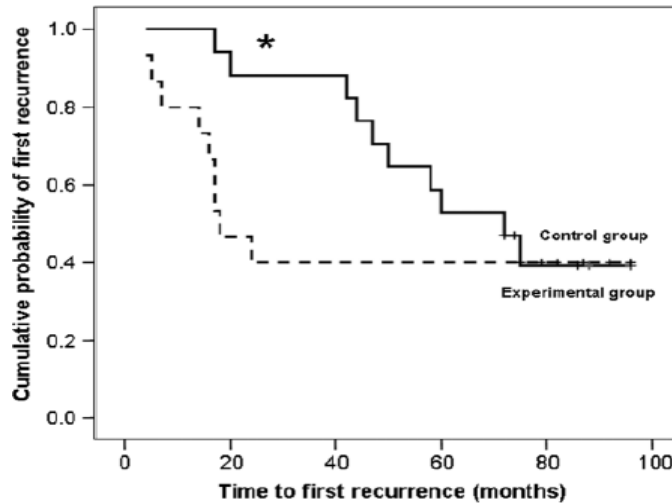
Bilateral early-stage BOTs

- **Bilateral cystectomy?** (15 patients)

OR

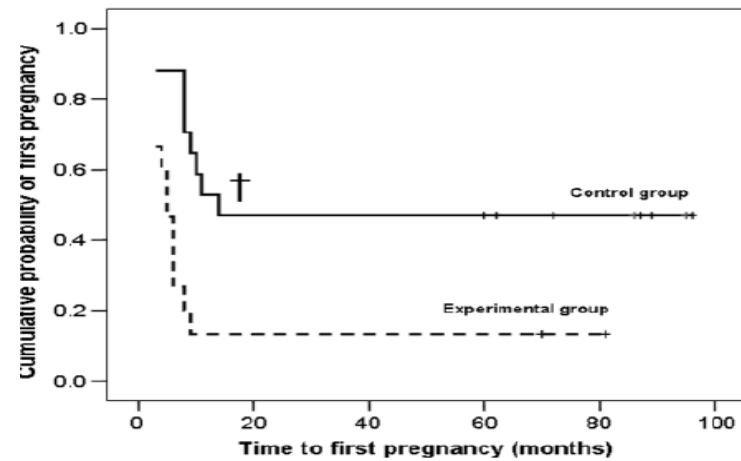
- **Unilateral cystectomy + USO?** (17 patients)

* $P = 0.358$



The probability of first recurrence do not differ significantly ($p=0.35$)

† $P = 0.003$



The probability of first pregnancy is higher for bilateral cystectomy group ($p=0.003$)

Advanced-stage serous BOTs

The most important criteria for success of conservative management
‘absence of invasive peritoneal implants’

| | No. | No. Recurrences | No. of Deaths | No. of Invasive Implants | Recurrence in Patients With Invasive Implants | Death in Patients With Invasive Implants |
|------------------------------------|-----|-----------------|---------------|--------------------------|---|--|
| Zanetta et al ¹⁹ | 25 | 10 | 0 | 7 | 5 | 0 |
| Prat and De Nictolis ³⁹ | 10 | 3 | 1 | 1 | 1 | 1 |
| Longacre et al ⁴⁰ | 21 | 5 | 0 | — | — | — |
| De Iaco et al ²⁶ | 21* | 4 | ? | ? | ? | ? |
| Uzan et al ⁴¹ | 41 | 22 | 1 | 3 | 2 | 0 |
| Total | 97 | 40 (41.2%) | 2 (2%) | 11 | 8 | 1 |

Morice P. et al., Int J

Mucinous BOT

- Management is same as serous BOT
- Oophorectomy should be performed instead of cystectomy

Ovarian cancer

- The leading cause of death from gynecologic malignancies

Makar AP., Endocr-Relat Cancer 2000

- Up to 90 % of ovarian tumors are **epithelial**, while 10 % are **germ-cell** and **sex-cord stromal tumors**

Low JJ et al., Cancer 2000

Epithelial tumors

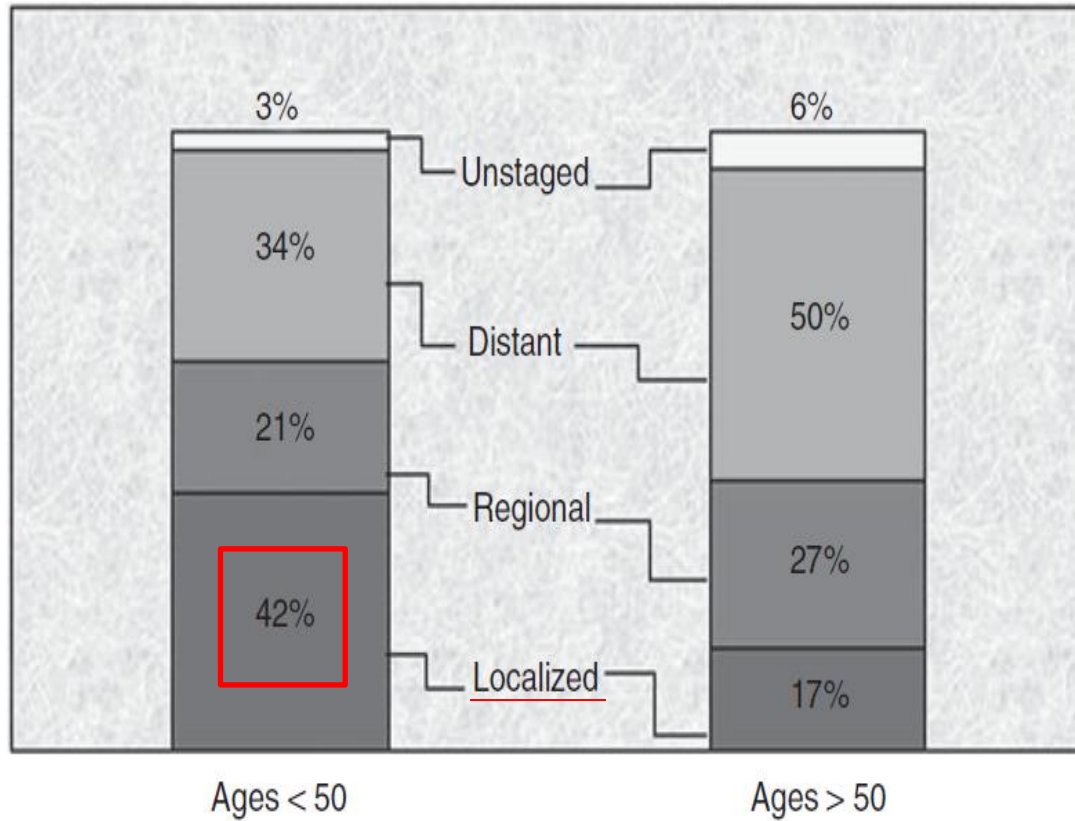
- **3-17 % of cases are <40 years old**

Duska LR et al., Cancer 1999

- **8 % of cases with stage 1 epithelial tumors are <35 years old**

Trimbos JB. et al., Curr Opin Obstet Gynecol 2004

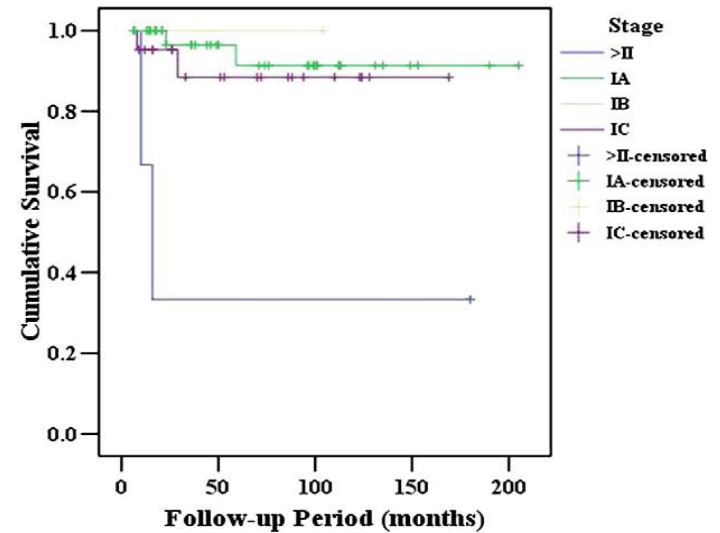
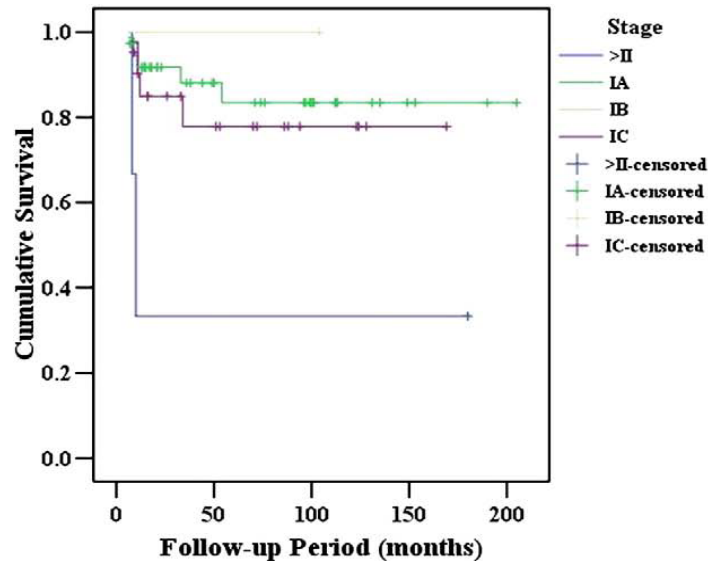
Ovarian Cancer Staging by Age



Younger patients are more likely to have a locally confined disease

Conservative surgery

- Unilateral salpingo-oophorectomy
- Full surgical staging, including
 - washings,
 - omentectomy,
 - appendectomy,
 - PPLN dissection should be done and should be negative
- Endometrial biopsy should be performed to exclude endometrial cancer



5-year disease-free survival rates of

-stage 1A: 83 %

-stage 1C: 78 %

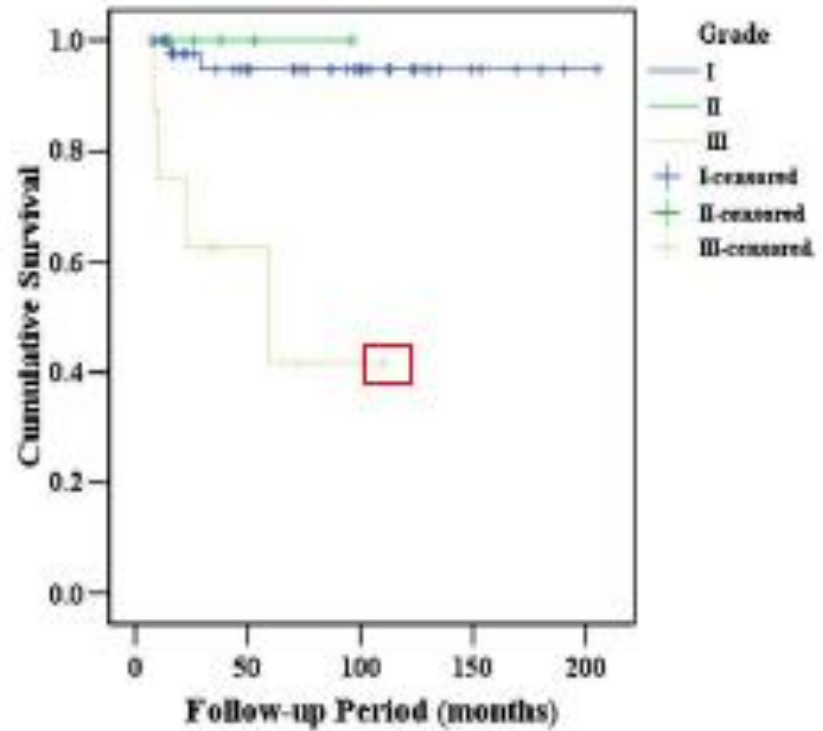
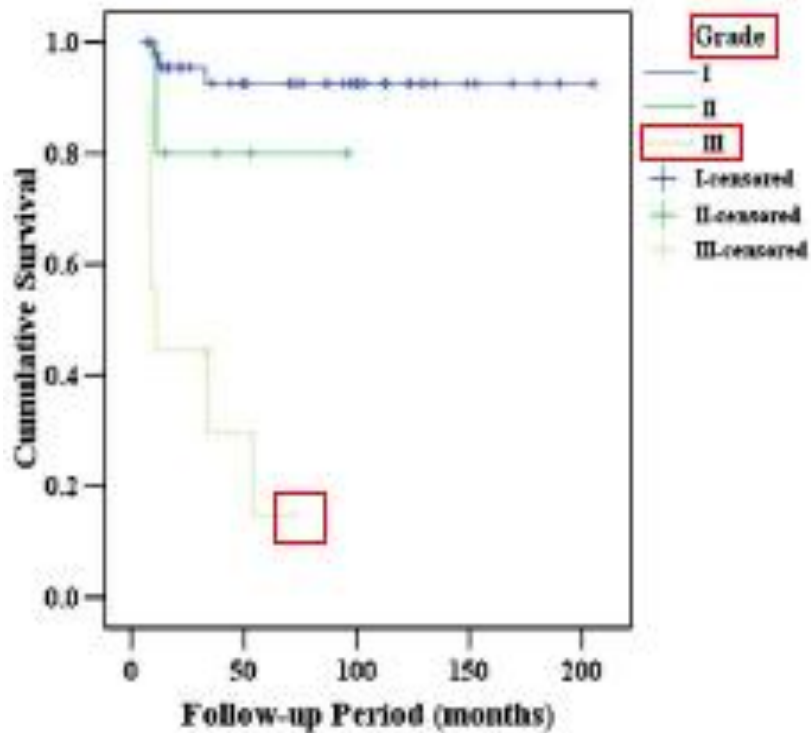
-stage 2 : 33 % (p=0.03)

J.Y. Park et al.,
Gynecol Oncol,
2008

Fertility-sparing surgery is a safe option for
stages 1A-1C and **grade 1-2** invasive EOC

| | | Number of patients | Patients with recurrence |
|-----------------|--------------|--------------------|--------------------------|
| FIGO stage | IA | 36 | 5 (13.9%) |
| | IB | 2 | 0 |
| | IC | 21 | 4 (19%) |
| | IIB | 1 | 0 |
| | IIIA | 1 | 1 (100%) |
| | IIIC | 1 | 1 (100%) |
| | Total | 62 | 11 |
| Histologic type | Serous | 7 | 0 |
| | Mucinous | 41 | 7 (17%) |
| | Endometrioid | 8 | 1 (12.5%) |
| | Clear cell | 4 | 2 (50%) |
| | Mixed | 2 | 1 (50%) |
| | Total | 62 | 11 |
| Grade of tumor | I | 48 | 3 (6.3%) |
| | II | 5 | 1 (20%) |
| | III | 9 | 6 (66.7%) |
| | Total | 62 | 11 |

- Median follow-up: 56 months
 - 62 patients with EOC treated conservatively
 - 11 had tumor recurrence
 - 6 died of disease
 - **Stage >1C** (p=0.0014) survival
 - **Grade 3** (p=0.0002)
- } significantly poorer



Even in patients with stage 1A disease, grade 3 shows significantly poorer disease-free survival (p=0.001)

| | Stage IA Grade 1 | Stage IA Grade 2 | Stage IA Grade 3 | Stage IC Grade 1 | Stage IC Grade 2 | Stage IC Grade 3 |
|--|---|--|--|--|--|--|
| Italian series Zanetta et al ⁵⁵ / Colombo et al ⁵⁶ | 1 recurrence among 24 patients | 3 recurrences among 8 patients | 1 recurrence among 4 patients | No recurrence among 10 patients | 1 recurrence among 6 patients | No recurrence among 3 patients |
| American series Schilder et al ⁵⁷ | 2 recurrences among 33 patients | 2 recurrences among 6 patients | No recurrence among 3 patients | No recurrence among 5 patients | 1 recurrence among 3 patients | No recurrence among 2 patients |
| French series Morice et al ⁵⁸ | 1 recurrence among 13 patients | 4 recurrences among 14 patients | 1 recurrence among 3 patients | 2 recurrences in 2 patients | No patient | 1 recurrence in 1 patient |
| Borgfeldt et al ⁵⁹ | No recurrence among 8 patients | No recurrence in 1 patient | No patient | No patient | No patient | 1 recurrence in 1 patient |
| Park et al ⁶⁰ | 1 recurrence among 29 patients | No recurrence in 3 patients | 4 recurrences in 4 patients | 1 recurrence in 15 patients | 1 recurrence in 2 patients | 2 recurrences in 4 patients |
| Anchezar et al ⁶¹ | 1 recurrence among 10 patients | No patient | 1 recurrence in 1 patient† | No recurrence in 3 patients | No recurrence in 1 patient | No recurrence in 1 patient |
| Satoh et al ⁶² | 5 recurrences among 95 patients | No recurrence in 13 patients | 2 recurrences in 3 patients | 5 recurrences among 65 patients | No recurrence in 2 patients | 1 recurrence in 3 patients |
| Total | 11 (5%) recurrences among 207 patients | 9 (20%) recurrences among 45 patients | 8 (45%) recurrences among 18 patients | 8 (8%) recurrences among 100 patients | 4 (29%) recurrences among 14 patients | 5 (33%) recurrences among 15 patients |

- Conservative management of **stage 1A, grade 1 and 2** seems to be **safe**
- However, in 18 patients with stage 1A **grade 3, 8 recurrences** were observed

Conservative management of stage 1C ?

- The definition of stage 1C disease:
 - a) tumor spread on the surface of the ovary and/or
 - b) capsular rupture and/or
 - c) ascites containing malignant cells or (+) cytology after peritoneal washing

1988, FIGO
- Conservative management of 59 patients with stage 1 EOC
 - stage 1A: 30 patients → 2 recurrence
 - stage 1C: 29 patients → 5 recurrence
 - *a: 1(3); b:0(17); c:4(9).

Kajiyama H. et al., EJSO, 2010
- FSS may be selected for stage 1C(b) patients as safely as for IA patients

| First author (ref) | Year | Patients (n) | Pregnancies (n) | Term deliveries (n) | No relapses (n) | Disease-related deaths (n) |
|--------------------|------|--------------|-----------------|---------------------|-----------------|----------------------------|
| Colombo [32] | 1994 | 56 | 25 | 16 | 3 | 2 |
| Zanetta [33] | 1997 | 84 | 33 | 22 | 5 | 3 |
| Duska [34] | 1999 | 6 | 2 | 2 | 1 | 1 |
| Morice [35] | 2001 | 34 | 10 | 7 | 10 | 4 |
| Schilder [36] | 2002 | 52 | 17 | 26 | 5 | 2 |
| Brown [37] | 1998 | 16 | 16 | 5 | 2 | 2 |
| Raspagliesi [38] | 1997 | 10 | 3 | 3 | 0 | 0 |
| Colombo [39] | 2005 | 24 | 7 | 6 | 7 | 2 |
| Total | | 282 | 113 | 87 | 33 | 16 |

- Of a total of **282 patients with EOC** who were treated **conservatively**
 - 113 pregnancy
 - 33 relapses
 - 16 death occurred
- Conservative management of early invasive EOC is acceptable with good obstetric and oncological outcomes

When counseling women on conservative surgery for EOC

| Study | Study Size | Recurrences (%) | Deaths (%) | Deliveries |
|----------------------------------|------------|-----------------|------------|------------|
| Colombo et al ¹⁴³ | 152 | 18 (11.8%) | 9 (5.9%) | 38 |
| Morice et al ¹⁴⁵ | 25 | 7 (28%) | 3 (12%) | 4 |
| Park et al ¹⁴⁶ | 62 | 11 (17.7%) | 6 (9.7%) | 22 |
| Schilder et al ¹⁴⁷ | 52 | 5 (9.6%) | 2 (3.8%) | 26 |
| Raspagliesi et al ¹⁴⁸ | 10 | 0 (0%) | 0 (0%) | 3 |
| Total | 301 | 41 (13.6%) | 20 (6.6%) | 93 |

It is important to counsel that
risk of recurrence is 14 %,
death rates approach 7 %

Contraindications of fertility-sparing surgery in EOC

- > stage 1
- A synchronous endometrial cancer
- Grade 3 disease
- Bilateral involvement of the ovaries
- BRCA mutations
- A histologically aggressive tumor variant
 - anaplastic tumor
 - small cell ca/neuroendocrine tumor

Anchezar JP. et al., J Surg Oncol. 2009

Morice P. et al., Int J Gynecol Cancer 2011

Biopsy of the contralateral ovary?

- Occult bilateral ovarian involvement is noted in only 2.5 % of women
- If it appears normal, biopsy of the contralateral ovary is not recommended

Benjamin I, Gynecol Oncol, 1999

According to suggestion of European Society of Gynecologic Oncology (2011)

- For these stages, conservative surgery may be performed safely
 - stage 1A,1C grade 1
 - stage 1A grade 2
- Conservative surgery is controversial for these cases
 - stage 1C grade 2
 - stage 1A, clear cell tumor

Germ-cell tumors

- These tumors most often occur in young women
- The current standard for treatment is
 - unilateral salpingoo-oophorectomy
 - omentectomy
 - cytologic washing
 - peritoneal biopsies
 - pelvic ve para-aortic lymph node sampling

Postoperative chemotherapy for germ-cell tumors

- Recommended for all patients except those with stage 1A dysgerminoma and immature teratom 1A G1
- The most widely used regimen
 - bleomycin, etoposid, cisplatin**
 - cure rates 95 % for early-stage disease, 75 % for advanced stages

| First author (ref) | Year | Patients (n) | Pregnancies (n) | Term deliveries (n) | Recurrences (n) | Deaths (n) |
|--------------------|------|--------------|-----------------|---------------------|-----------------|------------|
| Gershenson [63] | 1988 | 40 | 22 in 11 | 22 | n/a | n/a |
| Kanazawa [64] | 2000 | 21 | 11 in 8 | 9 | 1 | 1 |
| Low [24] | 2000 | 74 | 19 in 14 | 14 | 7 | 2 |
| Gershenson [65] | 2002 | 133 | 37 in 35 | n/a | n/a | n/a |
| Zanetta [66] | 2001 | 138 | 41 in 16 | 28 | 16 | 3 |
| Perin [67] | 1999 | 45 | 8 | 7 | 4 | 2 |
| Tangir [59] | 2003 | 64 | 47 in 29 | 38 | n/a | n/a |
| Total | | 515 | 185 | 118 | 28 | 8 |

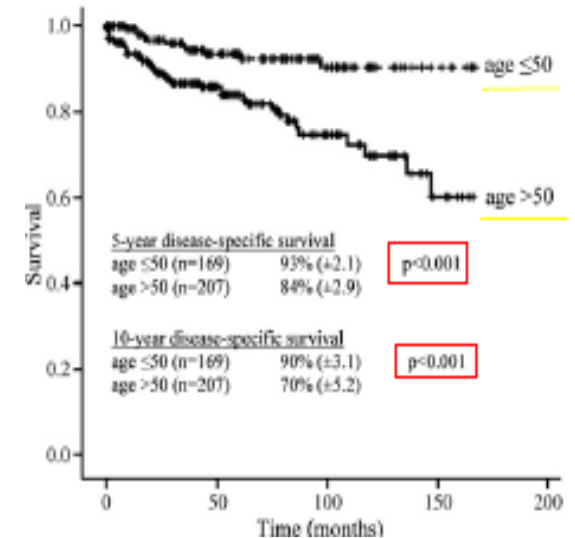
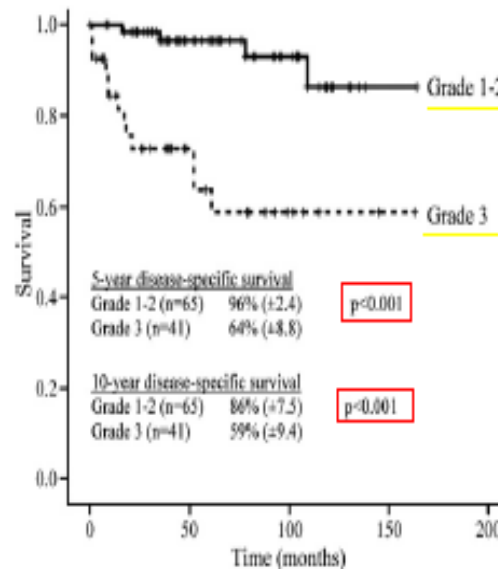
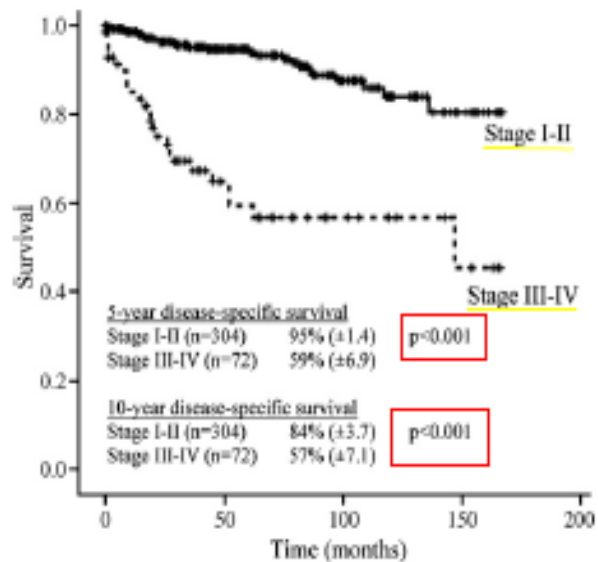
- In a total of 515 patients with germ-cell tumors
 - 185 pregnancies,
 - 118 livebirths,
 - 8 deaths

Although these tumors are highly malignant, conservative surgery with or without chemotherapy can achieve an equally good survival rate

Prognostic factors responsible for survival in sex cord stromal tumors of the ovary—An analysis of 376 women

Gynecologic Oncology 104 (2007)

The survival of patients treated conservatively did no differ from those treated radically



Sex-Cord Stromal Tumor

- Conservative surgery is acceptable for stage 1A, granulosa cell or Sertoli-Leydig cell tumors

Reed N. et al., Ann Oncol., 2010

- Biopsy of contralateral ovary is unnecessary for granulosa cell tumors

-endometrial sampling is needed because of hormonal activity

Schumer ST. et al., J Clin Oncol, 2003

Ovarian Cancer

Fertility preservation is an option for young women with

Borderline ovarian tumors (for any stage)

Ovarian germ-cell tumor (for any stage)

Stage 1A G1-2 –1C G1 epithelial ovarian cancer

Cervical Cancer

- The surgical, oncological and fertility outcomes suggested radical abdominal/vaginal trachelectomy an appropriate treatment option for young women with cervical malignancies

Cervical Cancer

Conization

1a1 LVSI (-)

Radical Trachelectomy +Pelvic LND

1a1 LVSI (+)

1a2

1b1 Depth<1cm

Endoscopy/Robotic/ vaginal /abdominal

Sentinel Node

Early –Stage Low –Risk Cervical Cancer

Simple Vaginal Trachelectomy / Conization might
be suitable for

**stage IB 1 lesions, smaller than 20 mm, with
negative Pelvic lymph nodes, Grade 1**

Endometrial Adenocarcinoma

- Conservative treatments are based on the hormonal sensitivity of endometrial adenocarcinomas.
 - grade 1 endometrioid type endometrium adenoCa
 - absence of myometrial invasion by MRI or tvUSG
- Hysterectomy is indicated, once the family has been completed.

Thank You