Difficulties in laparoscopic treatment of deep infiltrating endometriosis

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Objectives

- Overview of endometriosis
- Laparoscopic and robotic treatment of endometriosis
- Results
Suggested Reading

Nezhat’s Video-Assisted and Robotic-Assisted Laparoscopy and Hysteroscopy
EDITED BY: Camran Nezhat, Farr Nezhat, and Ceana Nezhat

ENDOMETRIOSIS
ADVANCED MANAGEMENT AND SURGICAL TECHNIQUES
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Gary S. Berger
Farr R. Nezhat
Veasy C. Buttram, Jr.
Ceana H. Nezhat

Springer-Verlag
Endometriosis Defined

- Endometriosis is the presence of endometrial glands and stroma in ectopic positions
Endometriosis Characteristics

- Chronic
- Inflammatory
- Estrogen-Dependent
- Typically Recurrent/Progressive
Endometriosis Concerns

• Pain
• Infertility
• Abnormal Uterine Bleeding
• Organ Dysfunction
• Malignant Potential
Endometriosis Pelvic Exam

- Pelvic tenderness ( Majority of cases: 70% )
- Posterior cul-de-sac nodularity
- Tender nodules along uterosacral ligaments
- Retroverted and fixed uterus
- Lateral displacement of cervix
- Adnexal mass ( ovarian endometrioma )
- Adnexal fixation
Endometriosis Ultrasound

- Homogeneous appearance of ovarian cyst(s), no solid components, consistent with old blood
• Look for the presence of adenomyosis,
• endometriosis in ectopic locations,
• or genital tract abnormalities
Endometriosis Diagnosis

- Laparoscopy
- Biopsy
Endometriosis Lesions
Translucent endometriosis lesions may be better visualized with irrigation
Atypical and Infiltrative Endo
Normal Pelvis

Cul-de-Sac Obliteration

Ovarian Endometrioma

Cul-de-Sac Obliteration
Extragenital Endometriosis

• Most Common Sites
  – GI Tract
  – Urinary Tract

• Remote Sites
  – Diaphragm and Lungs
  – Skin
  – Nervous System
  – Retina
  – Adrenal Gland
Infiltrative Bladder Endo

- Most common site of genitourinary tract endo
- Pathological confirmation is crucial: 1 out of 15 cases of deeply infiltrating bladder endometriosis is adenosarcoma

Ureteral Endometriosis
Ureteral Endometriosis
Bowel Endometriosis
Incidence: Bowel Endo

- Rectum and Sigmoid: 76%
- Appendix: 18%
- Cecum: 5%
Extragenital Endometriosis

• Occurs in 1-12% of patients with endometriosis
• Can occur in the absence of visible pelvic disease
• Endometriosis has been reported in almost all body structures

Transverse Colon Endo
Diaphragmatic Endometriosis
Diaphragmatic Defect (Endo)
Liver Endometriosis

- First 15 cases reported in the literature were treated by laparotomy
- Report of 2 cases treated laparoscopically

Umbilical Endometriosis
Management: Diagnosis

• Medical
• Surgical
Management: Medical

- NSAID
- OCP
- Progesterone
- Androgen (Testosterone, Danazol)
- GnRH Agonist and Antagonist
- Aromatase Inhibitors
Management: Surgical

• Destruction of endometriosis implants
  – Coagulation
  – Ablation
  – Resection
• Restoration of normal anatomy and function
• Hysterectomy and bilateral salpingo-oophorectomy
Videolaparoscopy
Introduced to Literature

Surgical treatment of endometriosis via laser laparoscopy

• Fertil Steril 1985 as an abstract
• 1986 as a publication;25(6):778-83
  Nezhat C, Crowgey S, Garrison C

Even advanced (stage IV) endometriosis was treated by this technique
Advantages of Laparoscopy

- Smaller incisions
- Less complications (blood loss, ileus, infection, etc.)
- Shorter interval to chemotherapy
- Better visualization
"Wherever in the body a cavity exists or cavity can be created, operative laparoscopy is indicated and probably preferable. The limiting factors are: skill and experience of the surgeon and the availability of proper instrumentation”

Camran Nezhat
Fertility and Sterility 1986
Limiting Factors of Surgery

Excision / Vaporization

- Type of treatment is dependent on depth of lesion, location, and experience of surgeon
Bladder Endometriosis
Ureterolysis
Ureteral Endometriosis
Bowel Endo: Management

- Shaving
- Disc Excision
- Segmental Resection
Bowel Endo: Shaving

SHAVING USING CO 2 LASER AND HYDRODISSECTION
Bowel Endometriosis
Multi-Organ Endometriosis
Small Bowel Endometriosis
Diaphragm Endometriosis
Thoracic Endometriosis
Endometriosis Surgery: Summary

- Different stages of endometriosis can be managed by operative laparoscopy
- Knowledge of anatomy and surgical skill are essential
- Multidisciplinary
- In experienced hands, the benefits outweigh the risks
Thank You
Clinical Implications

Cancer Arising from Endometriosis
Publications


Endometriosis and Epithelial Ovarian Cancer

- The malignant transformation of endometriosis was first suggested by Sampson in 1925
- Common characteristics
  - Metastatic – locally and distant
  - Loss of control of cell proliferation
  - Invade and damage
  - But does not cause catabolic and metabolic disturbances

Sampson JA

*Endometrial carcinoma of ovary arising in endometrial tissue in that organ*

Arch Surg 1925;10:1-72
Ovarian Cancer in Women with Endometriosis

- Epidemiological, Histological, and Molecular studies suggest a link between endometriosis and invasive epithelial ovarian cancer
  - based on frequent co-occurrence in surgical specimens
  - particularly the histological subgroups:
    - endometrioid
    - clear cell
    - low grade serous ovarian carcinoma


Nezhat F, Pejoivc T, Reis FM, Guo SW. *The Link Between Endometriosis and Ovarian Cancer: Clinical Implications.* Int J Gynecol Cancer 2014.
Endometriosis-Associated Ovarian Cancer

- Pathogenesis
  - Somatic Genetic Mutation
  - Inflammation
  - Hormonal
Clinical Implications
Ovarian Cancer Statistics

• “Average” life-time risk = 1.3%
  – High-risk populations
    • BRCA mutations: 20-40%
    • Lynch Syndrome: 9%
• *Endometriosis* = 2-3%
• Median age at diagnosis is 63 years old
• Most lethal gynecologic malignancy
  – 21,980 newly diagnosed cases
  – 14,720 deaths

Prevalence of histologic types of epithelial ovarian cancer and their associated molecular genetic changes

Kurman RJ, Shih LM. Molecular Pathogenesis and Extraovarian Origin of Epithelial Ovarian Cancer. Shifting the Paradigm. Hum Pathol. 2011; 42(7):918-931
Stage I Ovarian Carcinoma: Different Clinical Pathologic Patterns

• 76 patients with Stage I ovarian carcinoma underwent surgical staging and cytoreduction


Fertil Steril 2007;88(4):906-10
Results

• **Non-Serous** ovarian carcinomas comprised over 2/3 of the Stage I ovarian carcinomas

• Most patients with **Serous** carcinoma presented with **asymptomatic pelvic masses**

• **Non-Serous** carcinomas presented with **pelvic pain, abnormal vaginal bleeding**, with or without a pelvic mass
  – Majority had pelvic or ovarian endometriosis

• Endometrial abnormalities 36%
  – Hyperplasia and carcinoma
Screening
Prevention
Diagnosis
Treatment
Epithelial Ovarian Cancer

- Screening
- **Prevention**
- Diagnosis
- Treatment
What preventative measures can be offered for endometrioma?

- Most endometriomas are composed of endometrial implants, which invade a functional cyst


What preventive measures can be offered for endometrioma?

- Most endometriomas are composed of endometrial implants, which invade a functional cyst.
- Hormonal therapy that suppresses ovulation decreases the rate of Ovarian endometrioma formation.


Summary: Combined oral contraceptive (COC) use and risk of cancer

<table>
<thead>
<tr>
<th>Studied relation</th>
<th>Reference</th>
<th>Type</th>
<th>Level of evidence</th>
<th>Material</th>
<th>Main findings</th>
<th>Relative risk (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of COC in relation to risk of epithelial ovarian cancer</td>
<td>Beral et al. [2008]</td>
<td>Meta-analysis</td>
<td>2</td>
<td>23,257 cases 87,303 controls</td>
<td>• Decreased risk in COC ever users&lt;br&gt;• A more pronounced effect by duration of use&lt;br&gt;• The protective effect lasts at least 30 years after use</td>
<td>0.73 (0.70–0.76)</td>
</tr>
<tr>
<td></td>
<td>Havrilesky et al.</td>
<td>Systematic review/</td>
<td></td>
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<tr>
<td></td>
<td>[2013]</td>
<td>meta-analysis</td>
<td></td>
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<tr>
<td></td>
<td>Hannaford et al.</td>
<td>Prospective cohort</td>
<td>2</td>
<td>657,055 women, 3,981,072 women years</td>
<td>• Decreased risk in COC ever-users&lt;br&gt;• A more pronounced effect by duration of use&lt;br&gt;• The protective effect lasts at least 15–20 years</td>
<td>0.73 (0.66–0.81)</td>
</tr>
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<td></td>
<td>[2007]</td>
<td></td>
<td></td>
<td>46,000 women 744,000 women years 17,032 women, 540,000 women years</td>
<td></td>
<td>0.54 (0.40–0.71)</td>
</tr>
<tr>
<td></td>
<td>Vessey and Painter</td>
<td>Prospective cohort</td>
<td></td>
<td></td>
<td></td>
<td>0.5 (0.3–0.7)</td>
</tr>
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<td></td>
<td>[2006]</td>
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</table>

• 2 prospective cohort studies
  – Nurses’ Health Study (121,700 US RNs, aged 30-55)
  – Nurses’ Health Study II (116,430 US RNs, aged 25-42)

• Hazard ratios (HR) and 95% CI adjusted for known and suspected ovarian cancer risk factors
• Tubal Ligation

- ↓ 24% risk of ovarian CA (HR, 0.76; 95%CI 0.64-0.90)
- Non-Serous >> Serous tumors p = 0.03
- Age < 35 p = 0.06

Fertility & Sterility. July 2014
• **Hysterectomy**
  – ↓ 20% risk of ovarian CA (95% CI 0.66-0.97)
  – Non-Serous >> Serous tumors \[ p = 0.15 \]

• **Oophorectomy (unilateral)**
  – ↓ 30% risk of ovarian CA (95% CI 0.53-0.91)
  – Non-Serous ≡ Serous histology \[ p = 0.60 \]
Subtype-specific risk of *invasive* and *borderline* ovarian tumors associated with Tubal Ligation

<table>
<thead>
<tr>
<th>Tumour behaviour, histology</th>
<th>Cases ( N )</th>
<th>Prior tubal ligation ( N (%) )</th>
<th>OR(^a) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Invasive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>4777</td>
<td>893 (18.7)</td>
<td>0.81 (0.74-0.89)</td>
</tr>
<tr>
<td>High-grade(^b)</td>
<td>3791</td>
<td>729 (19.2)</td>
<td>0.80 (0.73-0.89)</td>
</tr>
<tr>
<td>Low-grade(^b)</td>
<td>361</td>
<td>58 (16.1)</td>
<td>0.89 (0.65-1.22)</td>
</tr>
<tr>
<td>Mucinous</td>
<td>574</td>
<td>77 (13.4)</td>
<td>0.68 (0.52-0.89)</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>1273</td>
<td>138 (10.8)</td>
<td>0.48 (0.40-0.59)</td>
</tr>
<tr>
<td>Clear cell</td>
<td>737</td>
<td>81 (11.0)</td>
<td><strong>0.52 (0.40-0.67)</strong></td>
</tr>
<tr>
<td><strong>Borderline(^c)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>1309</td>
<td>233 (17.8)</td>
<td>0.98 (0.83-1.16)</td>
</tr>
<tr>
<td>Mucinous</td>
<td>906</td>
<td>161 (17.8)</td>
<td>1.01 (0.83-1.23)</td>
</tr>
<tr>
<td>Serous/mucinous</td>
<td>2215</td>
<td>394 (17.8)</td>
<td>0.98 (0.86-1.12)</td>
</tr>
</tbody>
</table>

The Role of the Fallopian Tube

Endometrioid/clear cell

High grade serous cancer

Originates in distal fallopian tube (fimbria) : unique environment

Genetic Association
BCA1,BRCA2,p53
≥ 70 % detected in non-hereditary cases
~ 20 HGSC are + for BRCA1/2
Hormonal and surgical treatments for endometriosis and risk of epithelial ovarian cancer

ANNA-SOFIA MELIN¹,², CECILIA LUNDHOLM¹, NINOA MALKI¹, MARJA-LIISA SWAHN², PÄR SPARÈN¹ & AGNETA BERGQVIST¹,³

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• All women with a 1st time discharge Dx of endometriosis between 1969 – 2007 in Sweden [National Swedish Patient Register]
• Identified all women Dx with epithelial ovarian cancer [National Swedish Cancer Register] at least 1 year after the endometriosis Dx

Acta Obstet Gynecol Scand. 2013
Hormonal and surgical treatments for endometriosis and risk of epithelial ovarian cancer

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• Strong reduction in risk of epithelial ovarian CA:
  – One-sided oophorectomy involved with Endometriosis, multivariate analysis (OR 0.19, 95%CI 0.28-0.62) \textbf{81\%} reduction.
  – Complete extirpation of endometriotic tissue (OR 0.30, 95%CI 0.25-0.55) \textbf{70\%} reduction

Acta Obstet Gynecol Scand. 2013
What preventative measures can be offered to women with endometriosis?

• When endometriosis and endometrioma are diagnosed, surgical resection remains the most effective treatment
Epithelial Ovarian Cancer

• Screening
• Prevention
• **Diagnosis**
• Treatment
What Diagnostic Opportunities are Available to Practitioners for Women with Endometriosis?

- **Pelvic US**
  - Useful in the identification of ovarian endometrioma with homogeneous hypoechogenic cystic features and those with mural malignant changes
  - **Hyperdense mural nodules** within the ovary and **rapid growth** of an endometrioma can be visualized on MRI – associated with malignant transformation
  - Difficult to detect relatively small endocystic echogenic components with this modality

Endometrioma with diffuse, homogenous hypoechogenic features

Endometrioma with mural malignant features
What Diagnostic Opportunities are Available to Practitioners for Women with Endometriosis?

- **MRI**
  - More useful to both visualize endometriomas and possibly detect malignant transformation
  - **Hyperdense mural nodules** within the ovary and rapid growth of an endometrioma can be visualized on MRI – associated with malignant transformation
  - In a cohort study comparing MRI findings of 10 patients with ovarian adenocarcinoma to 10 patients with benign endometriomas, Tanaka and colleagues found mural nodules in all 10 malignancies but in only 3 of the benign cases


Summary

• There is now an unprecedented opportunity to develop a comprehensive plan for women with endometriosis for early detection and prevention of specific types of ovarian cancer
How should we approach treatment options for women with endometriosis who are determined to be at an increased risk for ovarian cancer?

- Identification of all women with endometriosis, either surgically documented or self-reported by symptoms
  - **Hormonal treatment/pregnancy** aimed at reducing the risk of recurrent endometriosis and endometriomas
  - Careful follow up of ovarian endometriomas with imaging studies, particularly MRI when US is suspicious, to detect any characteristics changes such as mural formation
  - Fertility preservation; embryo, egg or tissue preservation should be considered
How should we approach treatment options for women with endometriosis who are determined to be at an increased risk for ovarian cancer?

• Treatment planning:
  – **Complete surgical resection** of all endometriotic foci in women undergoing surgical treatment, with tissue evaluation of ovarian endometriomas to rule out malignancy
  – **Oophorectomy and Salpingectomy** should be individualized and offered based on the patient’s risks and desires
Thank You

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