Uterine Morcellation: Teasing Out the Issues

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Disclosures

• I have no industry conflicts of interest to report.

• I’m a fellowship trained minimally invasive gynecologist

• Have utilized morcellation throughout my career
Disclosures

“It is only about things that do not interest one that one can give really unbiased opinions, which is no doubt the reason why an unbiased opinion is always valueless.”

-Oscar Wilde
Objectives

• Describe contemporary data regarding the incidence of occult uterine malignancies in women undergoing presumed benign gynecologic surgery

• Discuss the implications, management and prognosis of leiomyosarcoma (LMS) and endometrial stromal sarcoma (ESS) in morcellated cases

• Review strategies to reduce the risk of encountering occult uterine malignancies during morcellation
April 17, 2014

FDA Warns Against Morcellation in Hysterectomy, Myomectomy

“If laparoscopic power morcellation is performed in women with unsuspected uterine sarcoma, there is a risk that the procedure will spread the cancerous tissue within the abdomen and pelvis, significantly worsening the patient’s likelihood of long-term survival. For this reason, and because there is no reliable method for predicting whether a woman with fibroids may have a uterine sarcoma, the FDA discourages the use of laparoscopic power morcellation during hysterectomy or myomectomy for uterine fibroids.”
Assumptions We Can Agree On…

- Morcellation has allowed hundreds of thousands of women to undergo MIS procedures.
- The rate of occult uterine malignancy in reproductive-aged women undergoing hysterectomy/myomectomy for presumed benign indications is exceptionally low.
- The prognosis of women diagnosed with a high grade sarcoma of any stage is poor.

AAGL J Minim Invasive Gynecol. 2011;18:1–3
Need cool heads and scientific reasoning to answer the question:

Is the status quo our best, or can we do better?
EPIDEMIOLOGY OF LMS AND ESS
Incidence of Occult Uterine Sarcoma at Benign GYN Surgery

- Rate of uterine sarcoma = 0.0 to 9.1%
- Few studies in which overall hysterectomy denominator is known and even fewer with in house patients only
- But many elderly patients included
Current Summary of Literature

2014 Meta-analysis¹

134 studies 30,193 women

• Prospective: 1 in 8,333 women (0.01%)
• Retrospective: 1 in 1,794 women (0.06%)
• Combined: 1 in 1,961 women (0.05%)

¹Pritts et al. JMIG 2015
Incidence of Occult Uterine Cancers Detected After Morcellation: *Age Matters*

- Incidence uterine malignancy 0.3%
- Significant correlation between occult cancer incidence and advancing age

Wright et al. *JAMA*. 2014 Jul 22
Hopkins Morcellation Data

- 2005-2014—All *in-house* hysterectomies and myomectomies performed for benign indications

- Two occult cancers detected in a cohort of 3081 pts over a 10-year period (*0.06% risk of malignancy in overall cohort; 0.11% in MIS cohort*)
  - 1 microscopic, early-stage cervical cancer in 2013
  - 1 myxoid leiomyosarcoma in 2009

- Morcellation cohort
  - No occult cancers identified in women <50 years (n=401)
  - 2 occult cancers in 23 patients >50 years

*Ricci et al, SGO, 2015*
Common Themes Among LMS and ESS Cases at Johns Hopkins (Unpublished)

- Clinical and consult (referral) service cases (n=47 cases in 2010-2014)
- 95% are post menopausal
  - 30% morcellated
- 50% underwent supracervical hysterectomy and did not undergo preoperative biopsy or MRI/CT
Summary Regarding Incidence of Occult Uterine Cancer During Fibroid Surgery

• It is simply **NOT** true that 1:350 reproductive aged women undergoing presumed benign fibroid surgery will have a uterine sarcoma diagnosed

• **Age, clinical presentation and appropriate patient selection matter!!!**

• Caution with morcellation in elderly, postmenopausal women or those with a higher risk of uterine cancer
Unanswered Questions

- Is the prognosis of women with LMS undergoing morcellation, supracervical hysterectomy or myomectomy worse than those with “intact” LMS?

- Does open myomectomy impact prognosis in cases of sarcoma?

- How is surgical stage affected by morcellation?
Recurrence Free Survival: George Report

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>TAH</th>
<th>Morcellation</th>
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<tbody>
<tr>
<td>0</td>
<td>39</td>
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<td>15</td>
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P = 0.003
Median RFS TAH = 39.6 months
Median RFS morcellation = 10.8 months

George et al, Cancer, 2014
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Study Period</th>
<th>Open vs Lsc Hysteroscopic</th>
<th>Endpoint</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Perri et al</td>
<td>2009</td>
<td>1969-2005</td>
<td>21/16</td>
<td>“Tumor injury”</td>
<td>Increased recurrence/Decreased survival</td>
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<tr>
<td>Park et al</td>
<td>2011</td>
<td>1989-2010</td>
<td>31/25</td>
<td>Morcellation of any kind</td>
<td>2.59 recur 3.07 death</td>
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<tr>
<td>George et al</td>
<td>2014</td>
<td>2007-2012</td>
<td>39/19</td>
<td>Intraperiton. morcellation</td>
<td>3.18 recur increased</td>
</tr>
</tbody>
</table>

Perri et al, Int J Gyn Canc, 2009
Park et al, Gynecol Oncol, 2011
George et al, Cancer Oct 2014
Prognosis for Intact LMS

- Leiomyosarcoma; notoriously poor prognosis
- High recurrence rate when diagnosed at an early stage (69%)\(^1\)
- 65% dead at 5 years\(^1\)
- Morcellation: Are we affecting prognosis?\(^2\)

\(^1\)Ricci, Fader. Gynecol Oncol, 2013
\(^2\)George et al. Cancer 2014
Does Type of Tissue Extraction Matter?

- Tissue disruption DOES increase the risk of dissemination.
- Open power morcellation does not appear to increase risks of dissemination any more so than open myomectomy, hysteroscopic myomectomy or scalpel-based abdominal or vaginal morcellation.

- BOTTOM LINE: Risks of disseminated occult cancer exceptionally small in appropriate morcellation candidates. But must not falsely reassure ourselves that open scalpel-based morcellation is safer.

Perri et al, 2005, Park et al Gynecol Oncol, 2011
Being Intellectually Honest…

- Jury out on whether morcellation truly worsens survival for LMS or ESS
  - Retrospective data with major flaws
- Empirically, we must acknowledge the (strong) possibility that “cut through” procedures of the uterus may worsen outcome due to disruption of margins and residual disease status
- GYN surgical community must take the lead to reduce the risks associated with occult cancer morcellation
Dissemination of Benign Disease After Morcellation

• It happens!

• Three referred cases to Hopkins in 2012-2013 mimicking cancer (elevated tumor markers and carcinomatosis) requiring debulking surgery and multi-organ resection

• Endometriosis & adenomyomas

• Tissue extraction techniques critical

Ramos A, Fader AN, Long KC, Obstet Gynecol, In press
The Remaining Dilemmas: How Do We Stage a Morcellated Cancer?

- Traditional staging systems for uterine sarcomas are not ideal

- Until we have better data suggesting definitively worse survival outcomes with morcellation, stage will not be changed

- Perhaps a Stage IC addition in the future...

<table>
<thead>
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<th>Stage definition</th>
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<tr>
<td><strong>Leiomyosarcomas and endometrial stromal sarcomas</strong></td>
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<tr>
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<td>IB</td>
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<tr>
<td>IVA</td>
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<tr>
<td>IVB</td>
</tr>
<tr>
<td>Carcinosarcomas</td>
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*Note: Simultaneous endometrial stromal sarcomas of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumors*
HOW DOES ONE MANAGE A CASE OF MORCELLLATED ESS OR LMS?
Management of Morcellated LMS and ESS

• Hopkins Protocol: Use of National Comprehensive Cancer Network (NCCN) Guidelines

• Surgery is the only potentially curative treatment for LMS and ESS of any anatomic site
CAN MOST CASES OF OCCULT UTERINE CANCER BE AVOIDED WITH CAREFUL PREOPERATIVE ASSESSMENT AND APPROPRIATE PATIENT SELECTION?
Detecting Sarcomas Preoperatively

• True or false: A uterine sarcoma cannot be detected by endometrial biopsy.

• Among 72 women with sarcomas, preop sampling suggested an invasive tumor in 86% and predicted the correct histologic diagnosis in 64%.

• Rate of detection of an invasive cancer by preoperative sampling was not statistically different among sarcomas and epithelial tumors (86% vs. 84%, p=0.76).

• Preoperative sampling was significantly less reliable in predicting the correct histology for uterine sarcomas (64% vs. 81%, p<0.0001).

Bansal et al, Gynecol Oncol, 2008
MRI assessment of LMS

- Diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC)
  - High or intermediate signal intensity on DWI and an ADC <1.1 – associated with an increased risk of LMS

Adding Serum LDH to DWI

- Increased LDH and high intensity DWI showed a specificity, accuracy and PPV of 99.2%, 99.3%, and 90.9% respectively of predicting LMS.

## PREoperative Sarcoma Score (PRESS)

<table>
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<tr>
<th>Points</th>
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<th>2</th>
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<tbody>
<tr>
<td>Age</td>
<td>&lt;49</td>
<td></td>
<td>≥49</td>
</tr>
<tr>
<td>Serum LDH</td>
<td>&lt;279</td>
<td></td>
<td>≥279</td>
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<tr>
<td>Cytologic Findings</td>
<td>Negative</td>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>MRI Findings</td>
<td>Negative</td>
<td>Positive</td>
<td></td>
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- Positive score ≥ 3 points
- PPV, NPV, sensitivity and specificity were 63.2%, 93.2%, 0.800 and 0.854, respectively.

An Impossible Standard

• The expectation that the only way power morcellation will survive is to ensure no women will be at risk for a disseminated occult cancer is untenable
  – A Lose:Lose situation for surgeons and their patients

• For the FDA or other regulatory agencies to eliminate or strongly curtail power morcellation in its current form would hurt far more women than it will help
Can We Do Better? ABSOLUTELY YES!!!!

- Most cases of occult cancer can be avoided with meticulous, thoughtful preoperative planning and patient risk stratification

- Cannot think in absolutes (ie, ban ALL morcellation or use MIS techniques in ALL women)

- Individualized, patient-centered care plans with rigorous informed consent
Hopkins Morcellation Protocol

- Preoperative peer-review
- Imaging (MRI for fibroids)
- Endometrial evaluation
- Exclusion criteria for morcellation
  - Caution in Postmenopausal Women
  - History of tamoxifen use
  - Pelvic radiation
  - BRCA mutation carrier status
  - Hereditary cancer syndromes (hereditary non-polyposis colorectal cancer (HNPCC) hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome or hereditary childhood retinoblastoma)
- Enhanced surgical consent
- High volume surgeons only
- Contained morcellation only

1Cohen et al. Obstet Gynecol 2014;124:491–7
Consent, Consent, Consent!

- **ALL** procedures, medications, interventions in medicine carry a risk:benefit ratio
  - Must individualize those risks and benefits based on patient age, demographic factors, clinical presentation and patient goals
Avoid Being Too Reactionary… But Keep Patient’s Informed and Safe

- Historically, pendulum has swung wildly when issues like the morcellation debate arise

- WHI Study and Impact on HRT administration
  - Stroke and cardiovascular disease are rare and affect elderly, comorbid women
  - HRT benefits thousands of women who are appropriate candidates for this therapy
Methods of Contained Morcellation

• Vaginal
• Minilaparotomy
• Power morcellation in a bag
Vaginal Morcellation
Power Morcellation in a Bag
Minilaparotomy
Umbilical Closure
Unanswered Questions and Future Directions

• Will morcellation in a bag or other containment system prevent dissemination of occult uterine cancers?¹

• How can we improve the preoperative detection of occult sarcoma?

• New instrumentation
  – FDA approved bags

• How do we educate and credential providers?

Conclusions

- Broad applications of MIS—including use of uterine morcellation—have significantly improved outcomes for women with benign and cancerous GYN conditions.
- Occult uterine cancers are RARE in reproductive-aged women and occur FAR more commonly in postmenopausal/elderly women.
- The outcome of women with either intact or morcellated sarcoma are poor.
Conclusions

• Contained morcellation should be considered and studied further
• Reducing or eliminating the use of open morcellation technique or supracervical hyst in symptomatic high-risk or elderly women
  – Exceptions: women undergoing prolapse surgery
• Meticulous preoperative planning
QUESTIONS?