# 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

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# 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*

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# 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."

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# 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 ***extremely 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*
*Rosero et al. Obstet Gynecol. 2013;122:778–786*

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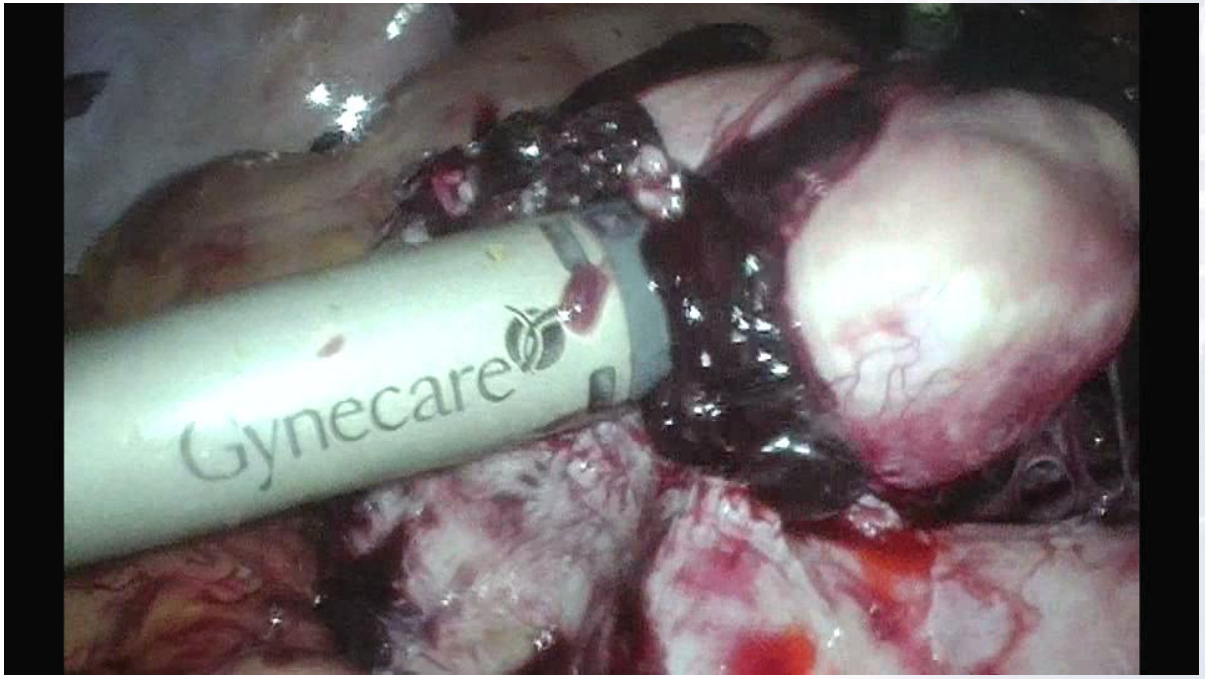
# Need cool heads and scientific reasoning to answer the question:

Is the status quo our best, or can we do better?

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# EPIDEMIOLOGY OF LMS AND ESS

# Incidence of Occult Uterine Sarcoma at Benign GYN Surgery

| Author | Year Published | Study Years | Procedure(s) | Indication(s) | Country | Total Patients | Number of Uterine Sarcomas | Rate of Uterine Sarcoma (95%CI) | Number of Leiomyosarcomas | Rate of Leiomyosarcoma (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| Primary Analysis | | | | | | | | | | |
| Leibsohn, et al.[1] | 1990 | 1983-1988 | Hysterectomy | Leiomyoma(s) | U.S. | 1429 | 7 | 4.9 (2.0-10.1) | 7 | 4.9 (2.0-10.1) |
| Reiter, et al.[2] | 1992 | 1986-1989 | Hysterectomy | Leiomyoma(s) | U.S. | 104 | 0 | 0.0 (0.0-34.9) | 0 | 0.0 (0.0-34.9) |
| Parker, et al.[3] | 1994 | 1988-1992 | Hysterectomy or Myomectomy | Leiomyoma(s) | U.S. | 1332 | 3 | 2.3 (0.5-6.6) | 1 | 0.8 (0.0-4.2) |
| Takamizawa, et al.[4] | 1999 | 1983-1997 | Hysterectomy | Leiomyoma(s) | Japan | 923 | 2 | 2.2 (0.3-7.8) | 1 | 1.1 (0.0-6.0) |
| Sinha, et al.[5] | | | | | | | | | | 4.0 (0.5-14.2) |
| Kamikabeya, et al.[6] | | | | | | | | | | 0.7 (0.0-4.1) |
| Rowland, et al.[7] | | | | | | | | | | 2.7 (0.6-7.8) |
| Leung, et al.[8] | | | | | | | | | | 2.3 (0.5-6.8) |
| Seidman, et al.[9] | | | | | | | | | | 0.9 (0.0-5.1) |
| | | | | | | | | | | |
| Frick, et al.[10] | | | | | | | | | | 0.0 (0.0-5.7) |
| Hageman, et al.[11] | | | | | | | | | | 0.0 (0.0-35.9) |
| Mahajan, et al.[12] | | | | | | | | | | 0.0 (0.0-14.5) |
| Ramm, et al.[13] | | | | | | | | | | 1.4 (0.0-7.8) |
| Wan, et al.[14] | | | | | | | | | | 1.6 (0.0-8.7) |
| Theben, et al.[15] | | | | | | | | | | 1.3 (0.2-4.6) |
| Ouldamer, et al.[16] | | | | | | | | | | 0.0 (0.0-1.7) |
| Durand-Réville, et al.[17]€ | 1996 | 1989-1994 | Hysterectomy | Leiomyoma(s) | France | 660 | 6 | 9.1 (3.3-19.7) | 6 | 9.1 (3.3-19.7) |
| Park, et al.[18]¥ | 2012 | n/a | Not specified | Leiomyoma(s) | South Korea | 22825 | 49 | 2.2 (1.6-2.8) | 49 | 2.2 (1.6-2.8) |

* Myomectomy was included in search terms. Cases of hysterectomy may have been included, but were not specified in search terms in the Methods section of the article.
€ Article in French. Primary analysis included only English language articles
¥ This was a reply to a reply of an article. Insufficient information was provided in the reply to include in the primary analysis.

- **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**

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# Current Summary of Literature

## 2014 Meta-analysis[1]

**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%)**

[1]Pritts et al. JMIG 2015

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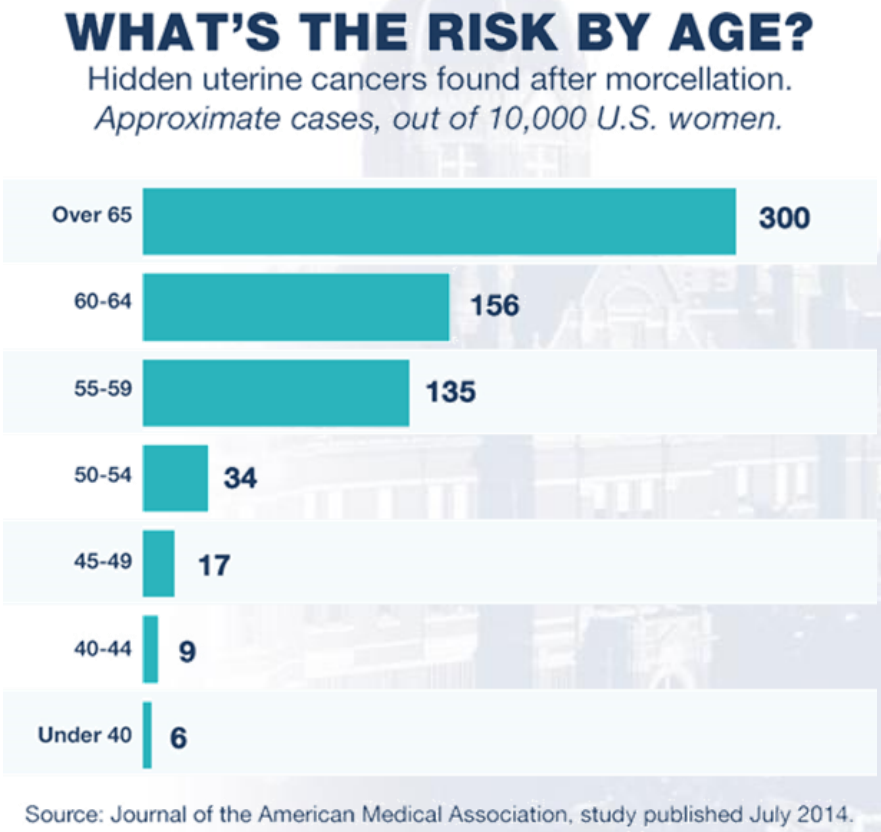
# Incidence of Occult Uterine Cancers Detected After Morcellation: *Age Matters*

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




Wright et al. *JAMA*. 2014 Jul 22

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# 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*

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# 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

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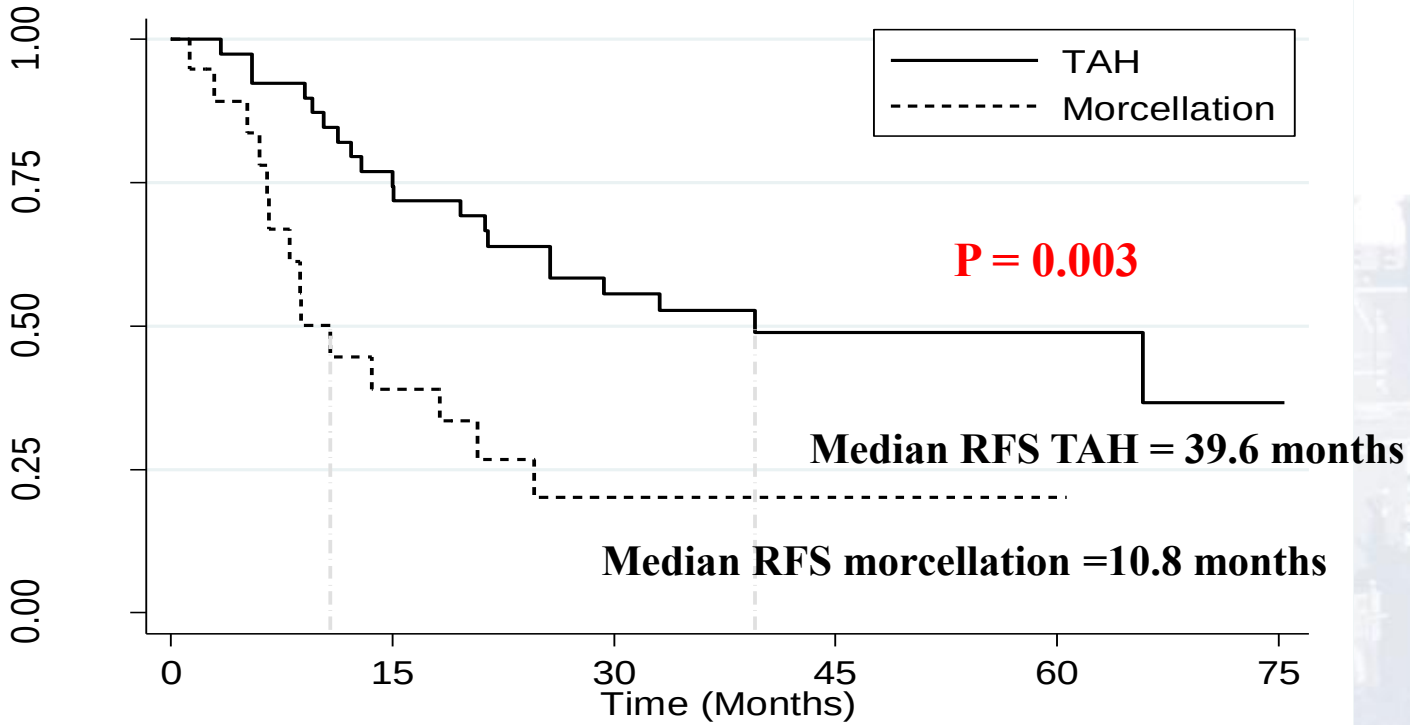
# Unanswered Questions

- 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 | | | | | | |
|---|---|---|---|---|---|---|
| TAH | 39 | 29 | 20 | 13 | 6 | 1 |
| Morcellation | 19 | 7 | 3 | 1 | 1 | 0 |

*George et al, Cancer, 2014*

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# Does Morcellation, Myomectomy or Supracervical Hysterectomy Worsen Outcomes for LMS?

| Study | Year | Study Period | Open vs Lsc Hysteroscopic | Endpoint | Outcome |
|---|---|---|---|---|---|
| Perri et al | 2009 | 1969-2005 | 21/16 | "Tumor injury" | Increased recurrence /Decreased survival |
| Park et al | 2011 | 1989-2010 | 31/25 | Morcellation of any kind | 2.59 recur 3.07 death |
| George et al | 2014 | 2007-2012 | 39/19 | Intraperiton. morcellation | 3.18 recur increased |

*Perri et al, Int J Gyn Canc, 2009*
*Park et al, Gynecol Oncol, 2011*
*George at al, Cancer Oct 2014*

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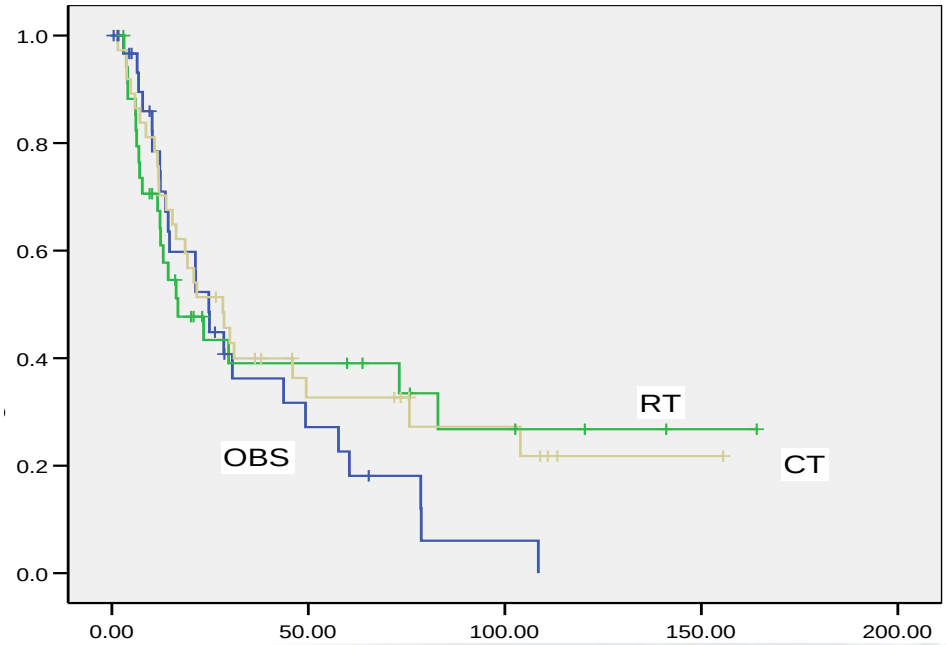
# Prognosis for Intact LMS

- 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]

**Progression Free Survival of uterine-confined LMS by adjuvant therapy**




[1]Ricci, Fader. Gynecol Oncol, 2013
[2]George et al. Cancer 2014

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# 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*

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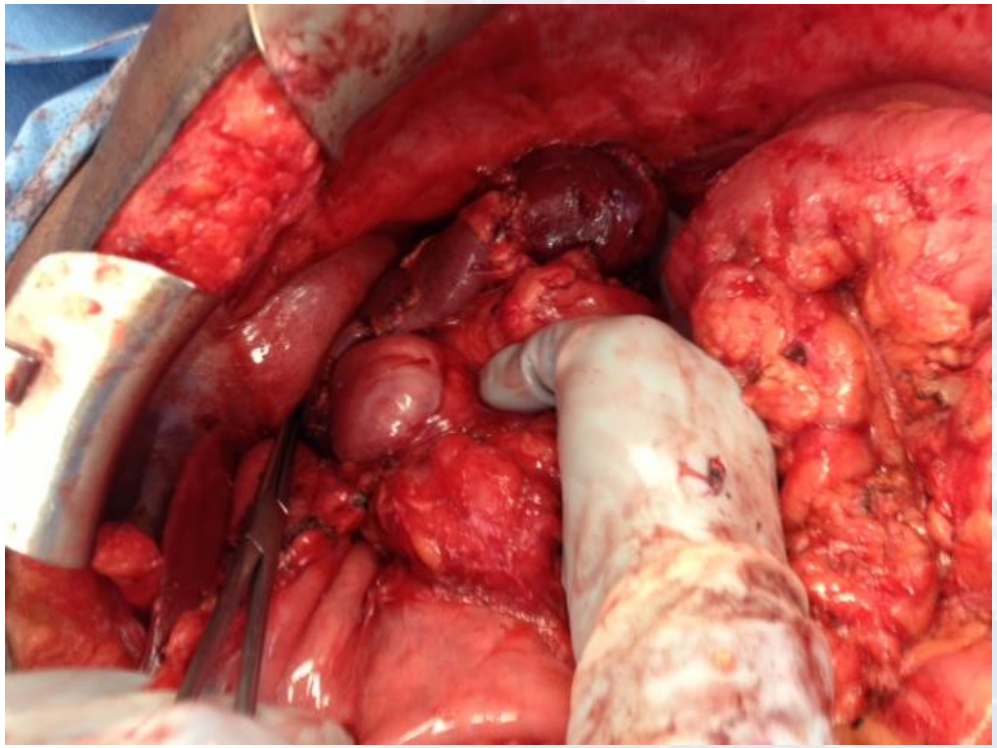
# Being Intellectually Honest…

- 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*

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# 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 w/ morcellation, stage will not be changed
- Perhaps a Stage IC addition in the future…

| | Stage definition |
|---|---|
| **Leiomyosarcomas and endometrial stromal sarcomas*** | |
| I | Tumor limited to uterus |
| IA | Less than or equal to 5 cm |
| IB | More than 5 cm |
| II | Tumor extends beyond the uterus, within the pelvis |
| IIA | Adnexal involvement |
| IIB | Involvement of other pelvic tissues |
| III | Tumor invades abdominal tissues (not just protruding into the abdomen) |
| IIIA | One site |
| IIIB1 | More than one site |
| IIIC | Metastasis to pelvic and/or para-aortic lymph nodes |
| IV | |
| IVA | Tumor invades bladder and/or rectum |
| IVB | Distant metastasis |
| **Adenosarcomas** | |
| I | Tumor limited to uterus |
| IA | Tumor limited to endometrium and endocervix with no myometrial invasion |
| IB | Less than or equal to half myometrial invasion |
| IC | More than half myometrial invasion |
| II | Tumor extends beyond the uterus, within the pelvis |
| IIA | Adnexal involvement |
| IIB | Tumor extends to extrauterine pelvic tissue |
| III | Tumor invades abdominal tissues (not just protruding into the abdomen) |
| IIIA | One site |
| IIIB | More than one site |
| IIIC | Metastasis to pelvic andor para-aortic lymph nodes |
| IV | |
| IVA | Tumor invades bladder andor rectum |
| IVB | Distant metastasis |
| **Carcinosarcomas** | |
| | Carcinosarcomas should be staged as carcinoma of the endometrium |

*Note: Simultaneous endometrial stromal sarcomas of the uterine corpus and ovary'pelvis in association with ovarian/pelvic endometriosisshould be classified as independent primary tumors

# HOW DOES ONE MANAGE A CASE OF MORCELLATED ESS OR LMS?

# Management of Morcellated LMS and ESS

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

NCCN National Comprehensive Cancer Network®

- Surgery is the only potentially curative treatment for LMS and ESS of any anatomic site

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# CAN MOST CASES OF OCCULT UTERINE CANCER BE AVOIDED WITH CAREFUL PREOPERATIVE ASSESSMENT AND APPROPRIATE PATIENT SELECTION?

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# 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*

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# 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

*Sato et al. Am J Obstet Gynecol. 2014;210(4):368.e1-8.*

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# 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

*Goto A et al.* Int J Gynecol Cancer, 2002. 12(4):354–361.

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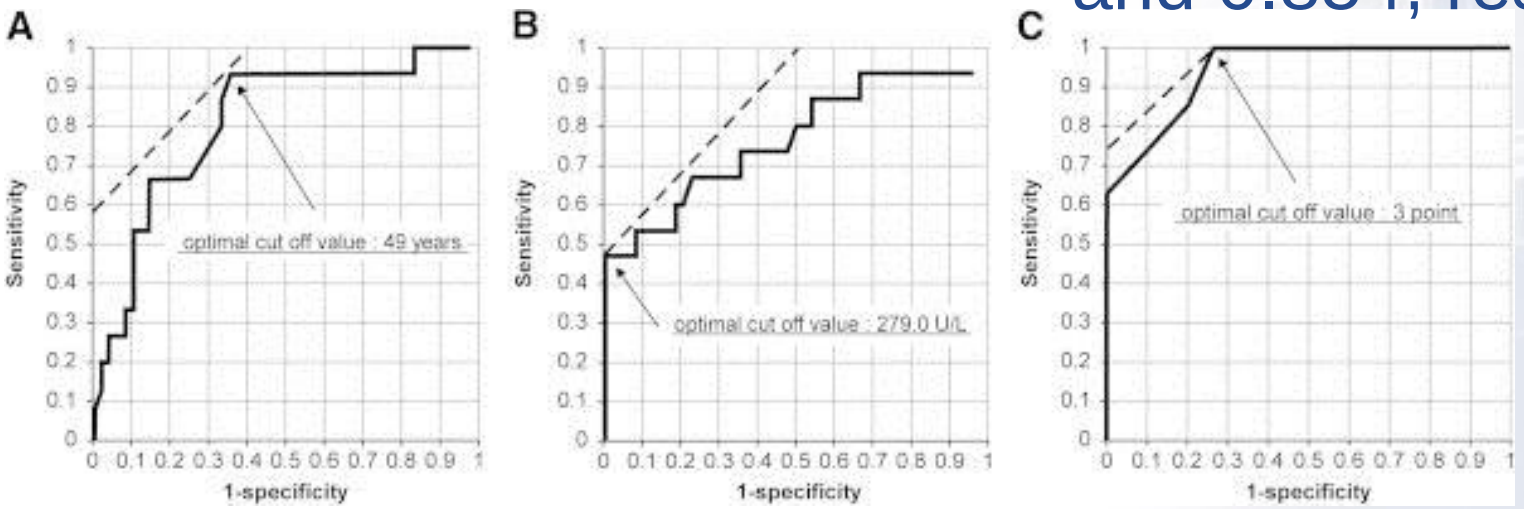
# PREoperative Sarcoma Score (PRESS)

| Points | 0 | 1 | 2 |
|---|---|---|---|
| Age | <49 | | ≥49 |
| Serum LDH | <279 | | ≥279 |
| Cytologic Findings | Negative | | Positive |
| MRI Findings | Negative | Positive | |

- Positive score ≥ 3 points
- PPV, NPV, sensitivity and specificity were 63.2%, 93.2%, 0.800 and 0.854, respectively.




*Nagai T et al. Springerplus, 2014. 18;3:678.*

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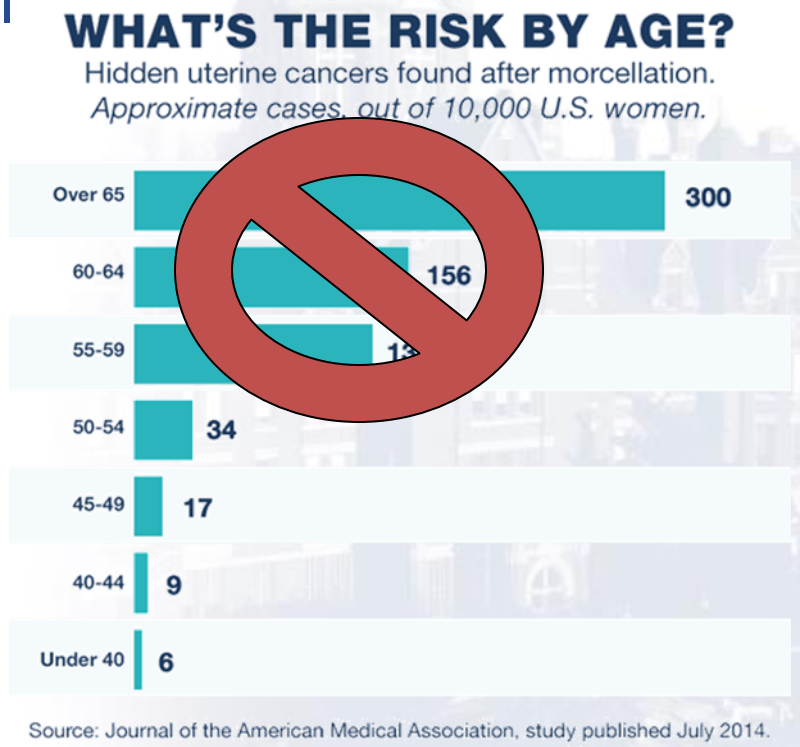
# An Impossible Standard

- 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

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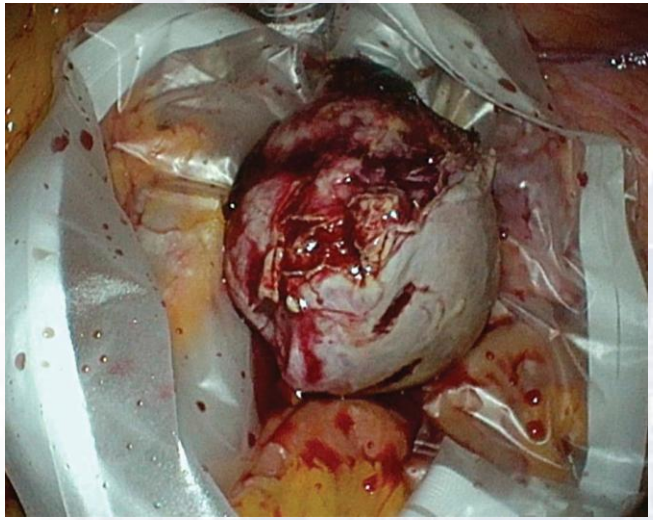
# Hopkins Morcellation Protocol

- 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



[1]Cohen et al. *Obstet Gynecol* 2014;124:491–7

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# 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***
-

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# Methods of Contained Morcellation

- Vaginal
- Minilaparotomy
- Power morcellation in a bag

# Vaginal Morcellation

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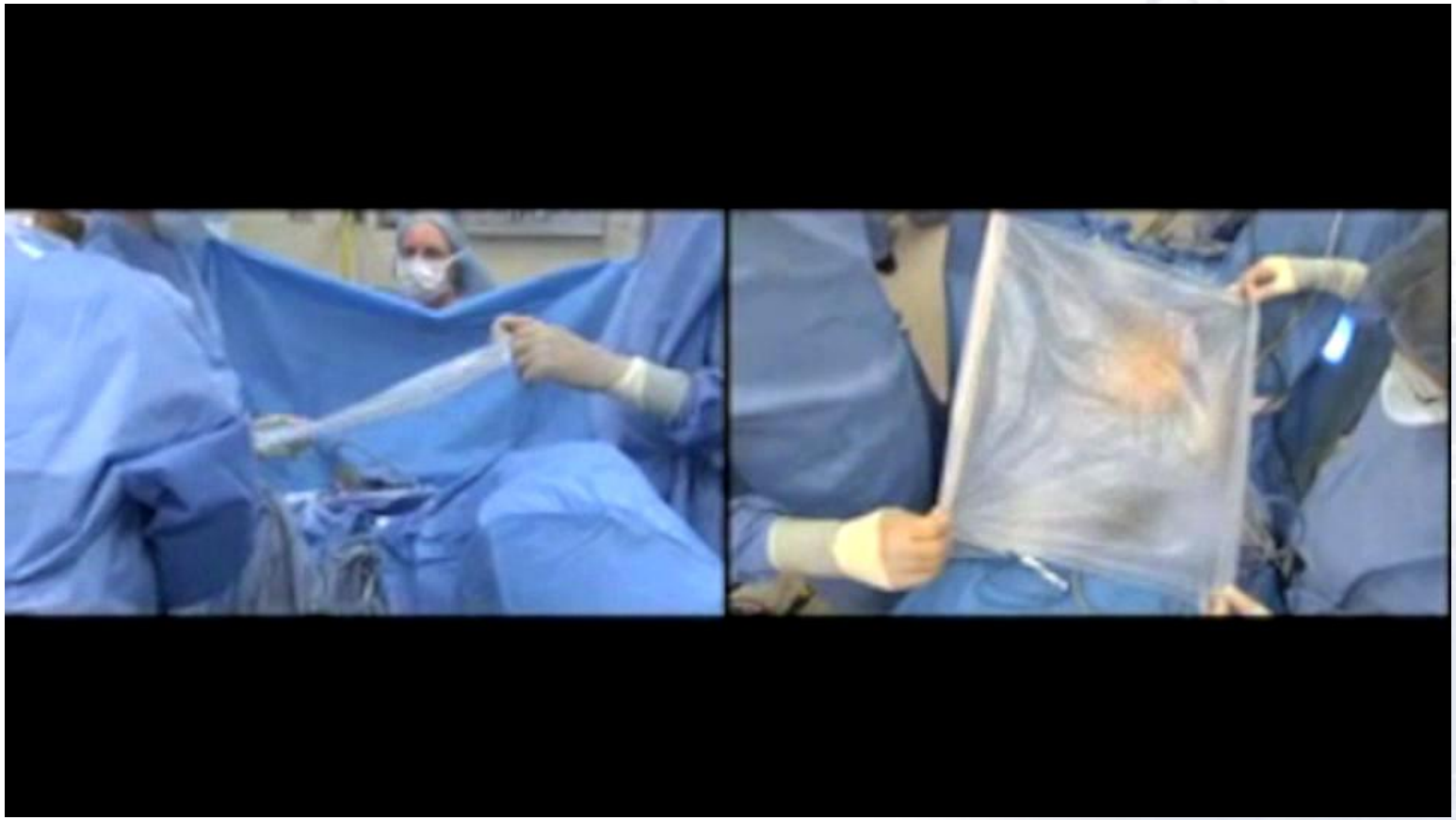
# Power Morcellation in a Bag



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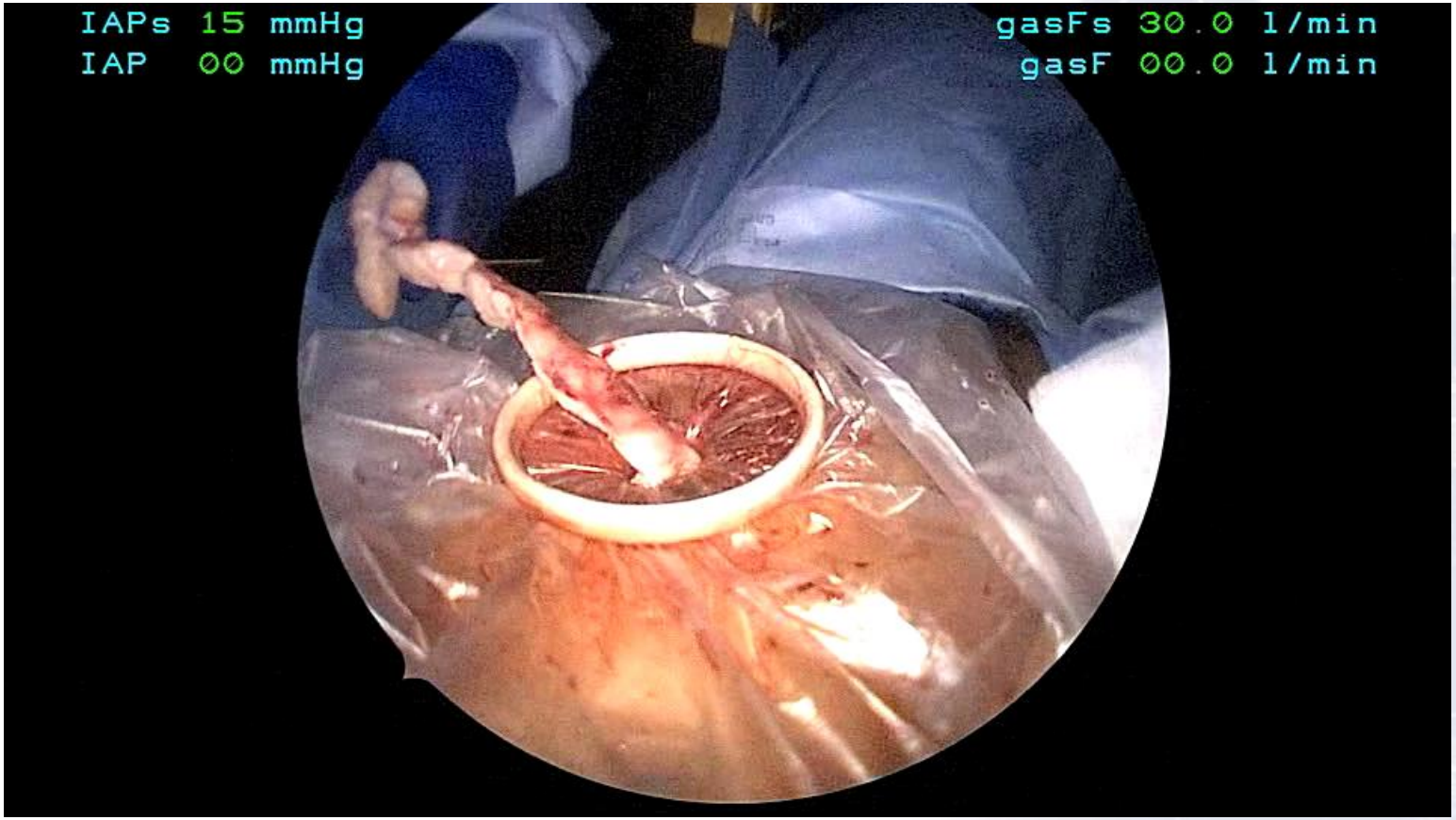
# Minilaparotomy

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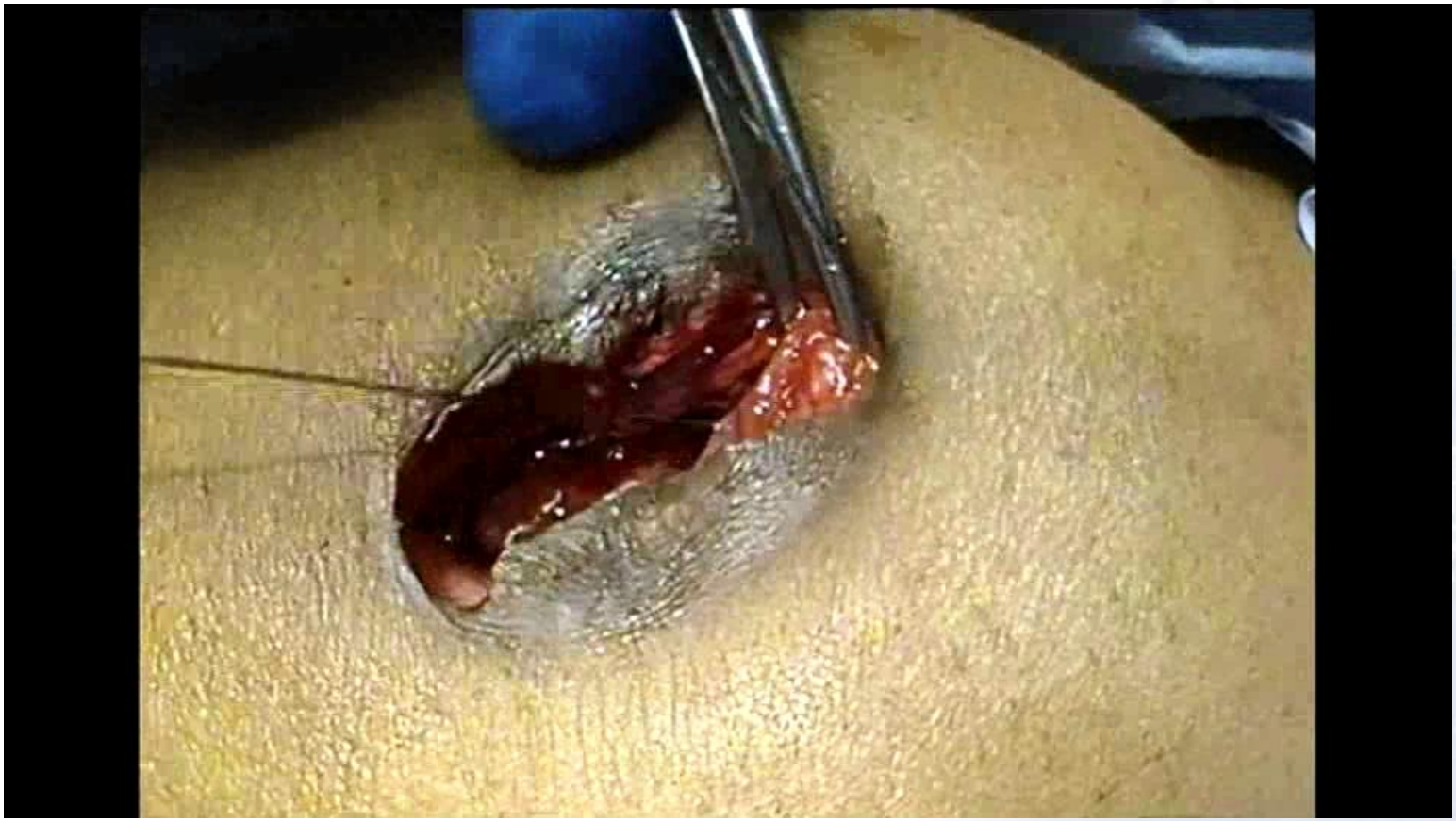
# Umbilical Closure



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# 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?

1. *Cohen S et al. J Minim Invasive Gynecol. 2014 ;21(5):935-9*

# 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

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# QUESTIONS?

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