AGL 2022

51st GLOBAL CONGRESS ON MIGS

December 1–4, 2022 | Gaylord Rockies Resort and Convention Center | Aurora, Colorado

SYLLABUS

Panel 5: Fibroids and Adenomyosis - Surgical Management

SCIENTIFIC PROGRAM CHAIR
ANDREW I. SOKOL, MD

HONORARY CHAIR
CHARLES E. MILLER, MD

PRESIDENT
MAURICIO S. ABRÃO, MD, PHD

Table of Contents

Disclosure of Relevant Financial Relationships

As an ACCME accredited provider, AAGL must ensure balance, independence, and objectivity in all CME activities to promote improvements in health care and not proprietary interests of an ineligible company. AAGL controls all decisions related to identification of CME needs, determination of educational objectives, selection and presentation of content, selection of all persons in a position to control content, selection of educational methods, and evaluation of the activity. Course chairs, planning committee members, faculty, authors, moderators, and others in a position to control the content of this activity are required to disclose all financial relationships with ineligible companies. All relevant financial relationships are appropriately mitigated, and peer review is completed by reviewers who have nothing to disclose. Learners can assess the potential for commercial bias when disclosure, mitigation of conflicts of interest, and acknowledgment of commercial support are provided prior to the activity. Informed learners are the final safeguards in assuring that a CME activity is independent from commercial bias. We believe this mechanism contributes to the transparency and accountability of CME.

Asterisk (*) denotes no financial relationships to disclose.

PLANNER DISCLOSURE

The following members of AAGL have been involved in the educational planning and/or review of this course (listed in alphabetical order by last name).

Linda J. Bell, Admin Support, AAGL*
Linda D. Bradley, MD, Medical Director, AAGL*
Erin T. Carey, MD, MSCR
Honorarium: Med IQ
Research Funding: Eximis
Mark W. Dassel, MD*
Linda Michels, Executive Director, AAGL*
Vadim Morozov, MD
Speaker: AbbVie
Consultant: Medtronic, Lumenis
Erinn M. Myers, MD
Speakers Bureau: Intuitive Surgical
Amy J. Park, MD
Speaker: Allergan
Nancy Williams, COO, CME Consultants*
Harold Y. Wu, MD*
Ja Hyun Shin, MD*

SCIENTIFIC PROGRAM COMMITTEE

Andrew I. Sokol, MD - Medical Legal Defense: Johnson & Johnson
Angela Chaudhari, MD - Consultant: Johnson & Johnson
Cara R. King, DO*
Mario Malzoni, MD – Consultant: KARL STORZ
Jessica Opoku-Anane, MD, MS – Consultant: Boston Scientific; Myovant Sciences; AbbVie
Shailesh P. Puntambekar, MD, PHD*
Frank F. Tu, MD, MPH*
Jonathon M. Solnik, MD – Consultant: Olympus; Medtronic; Stockholder: Field Trip Health, Inc.; Felix Health
Linda D. Bradley, MD, Medical Director*
Linda Michels, Executive Director, AAGL*

FACULTY DISCLOSURE

The following have agreed to provide verbal disclosure of their relationships prior to their presentations. They have also agreed to support their presentations and clinical recommendations with the "best available evidence" from medical literature (in alphabetical order by last name).

Antonio R. Gargiulo, MD - Medicaroid Incorporated; Lumenis - Consultant
Ja Hyun Shin, MD*
Prakash H. Trivedi, MD*

PANEL 5: ***Fibroids and Adenomyosis - Surgical Management***

Chair: *Ja Hyun Shin*

Faculty: *Prakash H. Trivedi, Antonio R. Gargiulo*

Course Description

Participation in this course will provide gynecologic surgeons with an enhanced knowledge of how to tackle complex fibroid and adenomyosis conditions. This course will provide expert recommendations on surgical approaches for the most effective and safe outcomes from start to finish. Through case reviews and surgical videos, the faculty will discuss important considerations for a comprehensive evaluation, preoperative planning and intraoperative preparations, identifying when and what surgery is indicated, and technical pearls for challenging cases. We will also discuss fertility considerations and innovative approaches to treatment including multidisciplinary efforts.

Learning Objectives

At the conclusion of this activity, the participant will be able to: 1) Integrate advanced techniques into their surgical management of patients with complex fibroid and adenomyosis conditions; 2)Evaluate the different modes of minimally invasive surgical approaches for successful outcomes and 3) Recognize the benefits of a multidisciplinary approach to care with interventional radiologists and fertility specialists.

Course Outline

11:30 am	Welcome, Introduction and Course Overview	J.H. Shin
11:35 am	Multidisciplinary Approach to Fibroids and Adenomyosis	J.J. Shin
11:50 am	Surgical Management of Fibroids and Adenomyosis: Fertility Considerations and Implications of Treatment	A.R. Gargiulo
12:05 pm	Complex Fibroid and Adenomyosis Management: Challenges and Novel Approaches	P.H. Trivedi
12:20 pm	Questions & Answers	All Faculty
12:35 pm	Adjourn	

NewYork-Presbyterian Weill Cornell Medicine

A Multidisciplinary Approach to Fibroid and Adenomyosis Surgical Management

Ja Hyun Shin, MD
Associate Professor
Director, Minimally Invasive Gynecologic Surgery
Weill Cornell Medicine/NewYork Presbyterian Hospital

Disclosure

- None

Objectives

1. Discuss benefits of a multidisciplinary approach to fibroids and adenomyosis treatment.
2. Present development and implementation strategies for a comprehensive fibroid and adenomyosis care program.
3. Demonstrate examples of collaborative efforts and a combined case approach.
4. Describe alternative treatment options to hysterectomy in older patients

A paradigm shift: MIGS as a mode of surgery-> subspecialty with a disease-based focus

- **Fibroids**
  - Multiple non-surgical and surgical treatment options
  - Treatment considerations related to fertility and pregnancy outcomes
- **Endometriosis**
  - Medically challenging
  - No definitive cure and need for continued management after surgery
- **Chronic Pelvic Pain**
  - Multisystem involvement requires multidisciplinary approach

Fibroids: Multiple Treatment Options

- Medical management
- Uterine artery embolization
- MRI-guided focused ultrasound
- Hysteroscopy
- Transabdominal radiofrequency ablation
- Transcervical radiofrequency ablation
- Myomectomy
- Hysterectomy
- Combination treatments

➢ **70% of women with symptomatic fibroids undergo hysterectomy**
➢ **38% of women who undergo hysterectomy do not discuss alternative treatments**
➢ **12.5% have a myomectomy**

Keller E, et al. JVIR, 2017. Tan N, et al. Jultrasound, 2014. Corona L, et al. AJOG, 2015.

Need for coordinated care for fibroid and adenomyosis management

- Patients can self-refer or be referred by a non-GYN provider to interventional radiologists for fibroid management without evaluation by a gynecologist
- Some gynecologist may not think a minimally invasive procedure is possible and default to referring for UAE vs a laparoscopic or robotic myomectomy
- Timing and decision for surgery has fertility and fertility treatment implications
- Biases in management practices by specialty

Specialty-Specific Values Affecting the Management of Symptomatic Uterine Fibroids

Keller E, et al. JVIR, 2017

Purpose: To better understand why interventional radiologists and gynecologists differ in their approaches to symptomatic uterine fibroids.

Methods: Interview transcript analysis of 13 IR and 13 Gyns

Table 4. Example Word/Concept Frequency Comparisons

Word/Concept	Gynecologists	Interventional Radiologists	*P* Value
Surgery/surgeon	22 (26, 8)	15 (19, 6)	.35
Right	20 (19, 9)	23 (34, 11)	.69
Procedure	11 (14, 6)	17 (23, 10)	.28
Options	11 (12, 7)	7 (9, 4)	.25
Hysterectomy	9 (10, 2)	6 (8, 0)	.38
Embolization	8 (10, 3)	7 (8, 4)	.71
Need for better system	2 (4, 0)	5 (7, 2)	.05
Turf wars vs collaboration	3 (5, 2)	6 (9, 4)	< .01
Ulterior motives	1 (1, 0)	3 (3, 1)	.04
Reimbursement/economic gain	2 (2, 1)	2 (3, 1)	.18

- IR- strongly prioritized UFE and myomectomies as less invasive treatment options
- Gynecologists- UFE for poor surgical candidates
- Inter-specialty tension was perceived more strongly by IRs

(Gynecologists motivated by economic incentives and felt devalued by Gyns as only "proceduralists")

Specialty-Specific Values Affecting the Management of Symptomatic Uterine Fibroids

Keller E et al. JVIR 2022.

The power of proximity: Effects of a multidisciplinary fibroid clinic on interspecialty perceptions and practice patterns

- UFE referrals by the clinic gynecologists significantly increased as did the number of combined fibroid procedures.
- Specialty-specific perceptions of fibroid treatments and interspecialty dynamics did not change.
- Clinicians unanimously perceived the clinic and post-clinic practice patterns as positive and distinct from their previous work and relationships between gynecology and IR elsewhere.

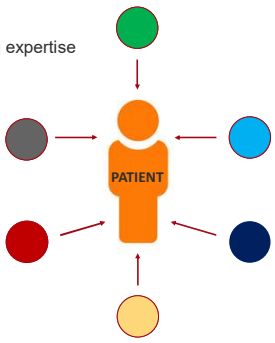
Weill Cornell Medicine Fibroid and Adenomyosis Center

MIGS
Dr. Cynthia Arvizo
Dr. Tamatha Fenster
Dr. Yelena Havyrluik
Dr. Kristen Pepin
Dr. Ja Hyun Shin

IR
Dr. Marc Schiffman
Dr. Nicole Lamparello
Dr. Bradley Pua
Dr. Kimberly Scherer

Benefits of a Multidisciplinary Team Approach

- Optimize collective knowledge and expertise
- Enhance coordination of care
- Decrease adverse events
- Improve patient outcomes
- Improve patient satisfaction



A collaborative multidisciplinary effort in action at WCM Fibroid and Adenomyosis Center

Dedicated time, place, staff, and resources for patients

Administration and providers work together to create a clear workflow

Shorter waiting times for appointments

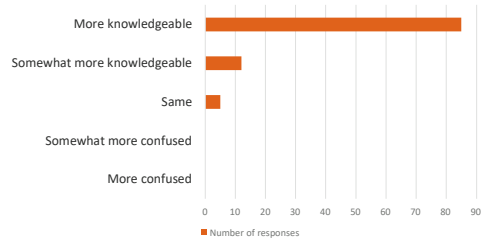
Same day consultations with both specialties offered

↓

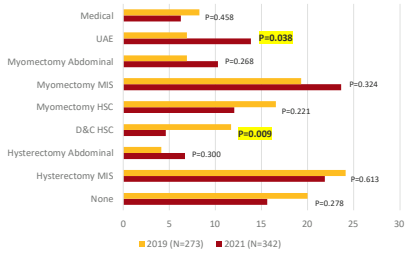
Increase in communication between IR and MIGS providers→ improved collaboration for patient care

Monthly "tumor board" style review of cases → a more unified approach to counseling

WCM Fibroid and Adenomyosis Center Survey - Patient experience with dual consultations

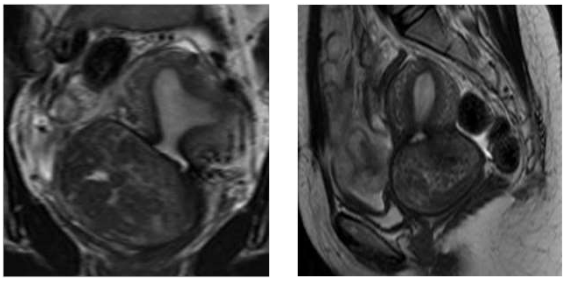


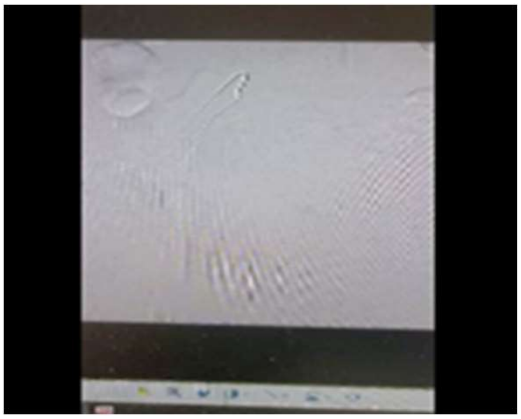
Management by MIGS pre/post implementation of a multidisciplinary fibroid center



Preop embolization and cervical myomectomy

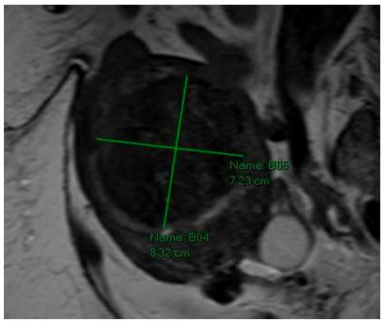
-- 40 yo with 7cm full thickness cervical fibroid

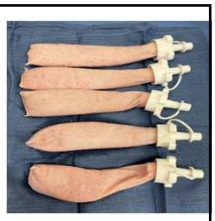




Preop embolization and hysteroscopic resection of 8cm submucosal fibroid

52 yo with HMB, managed on progesterone therapy for 2 years





Adenomyosis
-limited surgical options

UAE is a safe and effective alternative to hysterectomy for adenomyosis

Clinical investigation of fertility after uterine artery embolization
- Serres-Cousine et al. Am J Obstet Gynecol. 2021.

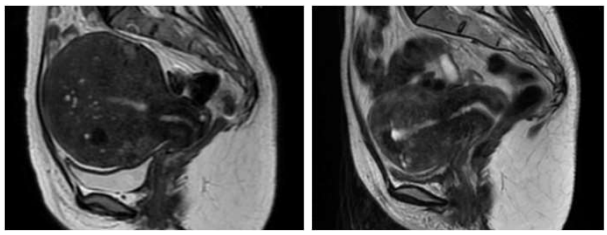
Long-term durability of uterine artery embolization for treatment of symptomatic adenomyosis.
- *Ma et al. Ayst N Z J Obstet Gynaecol. 2021.*

Uterine artery embolization: A review of current concepts.
- *Keung et al. Best Pract Res Clin Obstet Gynaecol. 2018.*

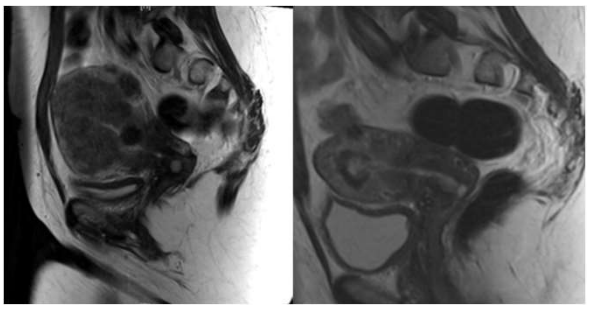
Uterine Artery Embolization for the Treatment of Adenomyosis: A systematic Review and Meta-Analysis.
- *de Brujin et al. J Vasc Interv. Radiol. 2017.*

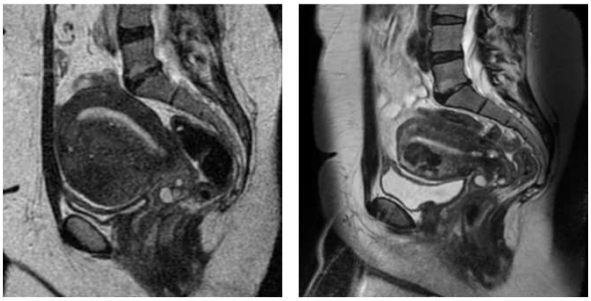
Uterine artery embolization for symptomatic adenomyosis: a new technical development of the 1-2-3 protocol and predictive factors of MR imaging affecting outcomes.
- *Kim et al. J Vasc Interv. Radiol. 2011.*

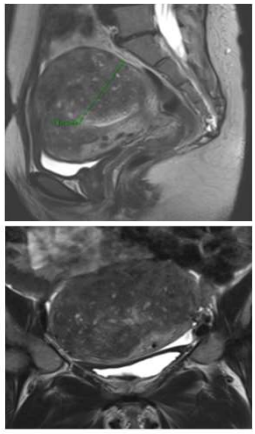
Diffuse adenomyosis
Pain and bleeding symptoms resolved



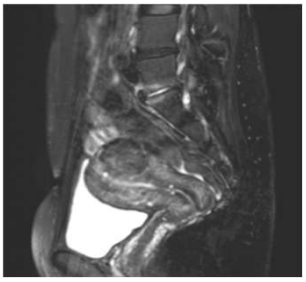
Complete resolution of adenomyosis and symptoms







64% volume reduction



WCM Fibroid and Adenomyosis Center Survey

- Average age = 43.6 years
- Desires future fertility?
  - Yes – 29.4%
  - No – 44.1%
  - Unsure – 26.5%
- ~60% previously underwent evaluation of their fibroids

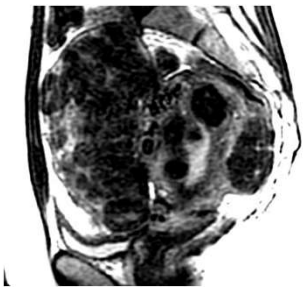
"I want to leave this world with what I came in with"

- 45 yr old patient

"If I have a 45 yr old patient who wants a myomectomy she can see someone else"

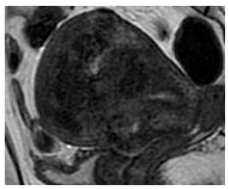
- GYN at a conference (not AAGL)

Tailoring your surgical approach Shared decision making



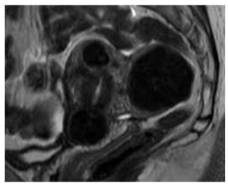
44 yo P0 with symptomatic fibroids, undesired future fertility

Plan: RA-myomectomy and Hysteroscopy with Transcervical RFA



44yo P2 with symptomatic fibroids, desires definitive management

Plan: RA-TLH, bilateral salpingectomy, cystoscopy



44yo P0 s/p 11 IVF cycles now planning for embryo transfer with donor egg

Plan: RA-myomectomy

Original Article

Comparison of 30-day Complication Rates between Laparoscopic Myomectomy and Total Laparoscopic Hysterectomy for the Treatment of Uterine Leiomyoma in Women Older Than Age 40

David Sheyn, MD, C. Emi Bretschnieder, MD, Sangeeta T. Mahajan, MD, Sherif El-Nashar, MD, Megan Billow, MD, and Cara S. Ninivaggio, MD

- ACS National Quality Surgical Improvement Program Database
- Women between 40-60 yrs old undergoing laparoscopic surgery for fibroid between 2010-2016
- 631 myomectomies and 1231 hysterectomies
- Propensity matched cohort

Myomectomy in Women Older Than Age 40

Table 2

Operative Characteristics Stratified by Type of Surgery

Operative Characteristics	Laparoscopic Myomectomy (n = 631)	Laparoscopic Hysterectomy (n = 1262)	p Value
Operating time (min), mean ± SD	166.8 ± 90.3	157.9 ± 70.9	.03
Adhesiolysis	34 (5.3)	69 (5.5)	.93
Adnexectomy	11 (1.7)	686 (54.3)	<.001
Wound class >3*	5 (0.8)	4 (0.3)	.04
Uterine weight > 250 g	—	510 (40.4)	—
Myomas ≥5 removed or ≥250 g	184 (29.2)	—	—
Conversion to hysterectomy	19 (3.0)	—	—
Conversion to laparotomy	2 (0.3)	5 (0.4)	.29

SD = standard deviation.
* Wound class >3 = contaminated, dirty, or infected wounds.

Myomectomy in Women Older Than Age 40

Table 3

Complication Rates Stratified by Type of Surgery

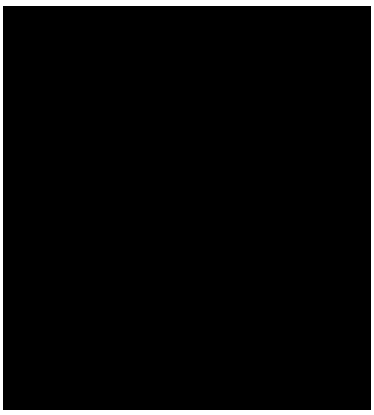
Complication	Laparoscopic Myomectomy (n = 631)	Laparoscopic Hysterectomy (n = 1262)	p Value
Any complication	37 (5.9)	83 (6.6)	.54
Perioperative transfusion	19 (3.0)	21 (2.2)	.29
Intraoperative cystotomy	1 (0.2)	5 (0.4)	.37
Superficial surgical site infection	5 (0.8)	5 (0.4)	.33
Deep/organ space surgical site infection	2 (0.3)	1 (0.1)	.42
Wound dehiscence	1 (0.2)	1 (0.1)	.76
Reoperation	5 (0.8)	18 (1.5)	.24
Pneumonia	1 (0.2)	1 (0.1)	.76
Urinary tract infection	4 (0.6)	28 (2.3)	.01
Sepsis	3 (0.5)	7 (0.5)	.91
Pulmonary embolism	1 (0.2)	4 (0.3)	.55
Deep venous thrombosis	1 (0.2)	1 (0.1)	.76

Key Points

- Consider structured collaboration with IR, radiology, and fertility specialists to implement a comprehensive Fibroid Center
- A multidisciplinary Center requires administrative support and a clearly defined workflow
- Consider combination treatment approaches especially in cases where hysterectomy is not the desired treatment.
  - Large submucosal fibroids
  - Myomectomy with concern for significant blood loss
  - Adenomyosis
- Practice shared-decision making with patients at every age
  - Older patients with symptomatic fibroids should have the same treatment options

Approach to myomectomy/adenomyosis resection

- **Preop planning**
  - MRI for fibroid mapping and presence of adenomyosis
  - Correct anemia
    - IV iron
    - Hormonal suppression
    - Consider preop embolization
- **Minimize intraop blood loss**
  - *Speed and efficiency of movements*
  - Hemostatic agents
    - Misoprostol 800mcg rectally
    - TXA 1gr bolus
    - Vasopressin 20U/100
    - Gelatin/thrombin matrix
- **Instrumentation setup**
  - 30 deg camera
  - Maryland bipolar, monopolar endoshears, tenaculum/prograsp
  - Insufflation to maintain stable pneumoperitoneum
  - Barbed suture
  - Manipulator depending on need/chromotubation/assistance(uterine positioning system)
  - Specimen containment
- **Incision considerations**
  - Access multiple fibroids
  - Identify important structures (extension into tubes, uterines, bladder, rectum?)
  - Consider ease of suturing



Weill Cornell Medicine NewYork-Presbyterian

Surgical Management Of Fibroids And Adenomyosis: Fertility Considerations And Implications Of Treatment

Antonio Gargiulo, MD

Center for Infertility and Reproductive Surgery
Brigham and Women's Hospital, Harvard Medical School

AAGL 2022 51st GLOBAL CONGRESS ON MIGS
December 1-4, 2022 | Aurora, CO | congress.aagl.org

Disclosure

I **have** the following financial relationships:

- Consultant:
  - Lumenis, Inc (now within Boston Scientific)
  - Medicaroid, Inc.

Objectives

- Define the impact of fibroids and adenomyosis - in their variable manifestations - on human reproduction
- Define the role of surgery in the management of fibroids and adenomyosis in the fertility patient

FIBROIDS IN FERTILITY PATIENTS

- There is convincing data to indicate that submucosal and intramural fibroids affect LBR in IVF.
- There will never be DEFINITIVE data to indicate that removal of submucosal and intramural fibroids improves LBR in IVF.
- In this scenario, choice of intervention is PERSONALIZED and depends on access to high quality myomectomy.

Do Fibroids Affect Fertility and Live Birth Rate?

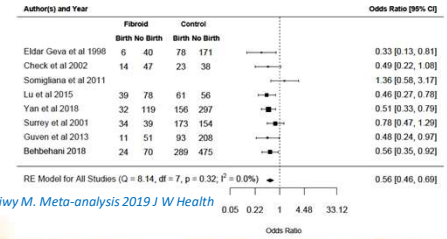
FIBROIDS AND IVF OUTCOMES

- **Submucosal fibroids:**
  - 50% reduction in ongoing pregnancy rates (OR 0.5, 0.3-0.8)[1]
  - Decreased implantation rates (RR 0.3, 0.1-0.6)[2]
- **Intramural fibroids:**
  - Cumulative pregnancy rates: 36.9% vs. 41.1%[1]
  - Decreased implantation rates: (RR 0.5, 0.4-0.8)[2]
- **Subserosal fibroids:** Not associated with fertility outcomes[1,2]

[1]Klatsky et al, AJOG, 2008; [2]Pritts et al, Fertil Steril 2009

FIBROIDS IN FERTILITY PATIENTS

Lower odds of live birth in women with non-cavity distorting fibroids

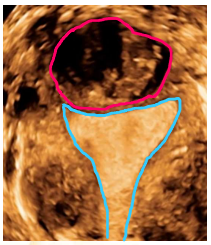


Rikraj K...Bedaiwy M. Meta-analysis 2019 J W Health

FIBROIDS IN FERTILITY PATIENTS

FIGO 3 FIBROID: SILENT KILLER

- Two large case-control studies show that intramural fibroids abutting but not distorting the uterine cavity significantly decrease LBR



Yan L. et al, Fertil Steril 2018 : Threshold **>2 cm**

Bai X. et al, Eur J Obstet Gynecol Reprod Biol 2020: Threshold **>3 cm**

FIBROIDS IN FERTILITY PATIENTS

There is insufficient evidence to conclude that myomas reduce the likelihood of achieving pregnancy with or without fertility treatment. (Grade C) [3]

Practice Committee of the ASRM, Fertil Steril, 2017

FIBROIDS and MISCARRIAGE : IMPACT

- Prospective database: 143 women with fibroids and 715 women without. Loss rate was double in women with fibroids, but ART rate was also double.[1]
  - Documented heart rate – selection bias towards women who can achieve pregnancy
- 8% prevalence in patients with RPL (n=966)[2]
  - Cavity distorting fibroid who underwent resection
    - Early loss- no change
    - Mid-trimester losses were reduced significantly

[1]Benson J et al, Clinical Medicine 2001, [2]Saravelos et al, Hum Reprod, 2011

FIBROIDS and MISCARRIAGE : NO IMPACT

- ***Right from the Start*** study found a 30% increase (1.02-1.64)[1]
  - But after adjusting for age alone or age, race, parity, alcohol use: no difference between groups (0.83, 0.63, 1.08)
  - Bias: the study excluded women who had been treated for infertility
- No evidence for a significant decrease in miscarriage rate after myomectomy[2]

[1]Hartmann KE et al, Am J Epidemiol, 2017; [2]Metwally M et al , Cochrane Database Syst Rev, 2012

Can Myomectomy Affect Live Birth Rate?

MYOMECTOMY FOR CAVITY-DISTORTING FIBROIDS

- Prospective, RCT n=181 seeking fertility <35 years
  - Pregnancy rates higher in women with surgery in SM/SM-IM[1]
    - submucosal 27% → 43%
    - submucosal-Intramural 15%→36%
  - No major differences in women with subserosal fibroids
- Retrospective Case-Control study using donor oocyte or IVF: myomectomy vs. controls
  - No difference in on-going pregnancy or implantation rates[2]
  - In well selected cases, myomectomy was appropriate

[1]Casini ML et al, Gynecol Endocrinol, 2006; [2]Surrey E et al, Fertil Steril, 2005

MYOMECTOMY FOR NON-CAVITY-DISTORTING FIBROIDS

- Cohort (n=163)[1]
  - no difference in myomectomy vs. in situ vs. no fibroids
- Prospective (n=212)[2]
  - Higher pregnancy rates in myomectomy (42%) vs. no surgery (11%) vs. infertility controls (25%)
  - No discussion of differences in age & patients chose treatment

[1]Aboulghar et al, Mid East Fertil Soc J, 2004; [2]Bulletti C et al, J Am Assoc Gynecol Laparoscopists, 1999

MYOMECTOMY: CURRENT ASRM GUIDELINES

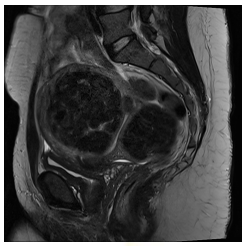
- *Fair evidence that hysteroscopic myomectomy improves clinical pregnancy rates & does not impair reproductive outcomes after ART*
- *In women with asymptomatic cavity-distorting myomas, myomectomy may be considered to optimize pregnancy outcomes.*
  - Generally not advised to improve pregnancy rates if non-cavity distorting

Practice Committee of the ASRM, Fertil Steril, 2017

OBSTETRICAL CONSDERATIONS

EFFECT OF FIBROIDS ON PREGNANCY: SYSTEMATIC REVIEW

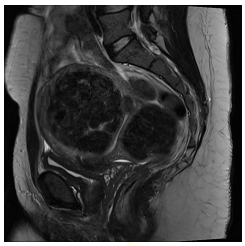
- Summary:
  - Most common findings:
    - higher c-section rates,
    - malpresentation,
    - preterm labor
  - Abruption may be related to retroplacental fibroids
  - Postpartum hemorrhage risk elevated



Klatsky, AJOG, 2008

EFFECT OF MYOMECTOMY ON PREGNANCY: SYSTEMATIC REVIEW

- Uterine Rupture in Viability Range
- Uterine Rupture during Terminations
- Abnormal Placentation
- Preterm Delivery
- Intrapartum bleeding and PPH
- Cesarean Section



Milazzo GN et al, J Obstet Gynecol Res, 2017

ARE THERE SAFE AND PRACTICAL ALTERNATVES TO MYOMECTOMY ?

ALTERNATIVES TO MYOMECTOMY

ULIPRISTAL and IVF

- 1 small case-control study + 2 single case reports on PubMed
- European Commission RESTRICTS USE (November 2020): remains available to treat premenopausal women who could not have surgery (or for whom surgery had not worked).
- Never available in USA
- Voluntary (temporary?) withdrawal in Canada, 2020

ALTERNATIVES TO MYOMECTOMY

UTERINE ARTERY EMBOLIZATION and IVF

- 1 case report
- Miscarriage 64%, 56% and 34% in 1 RCT and 2 cohort studies (on spontaneous pregnancy)
- Most updated review: Ludwig et al. Br J Radiol 2020
  - pregnancy is attainable
  - fertility rate remains uncertain
  - increased risk of PTD and spontaneous abortion (vs. Myomectomy)

ALTERNATIVES TO MYOMECTOMY

MR guided-FOCUSED ULTRASOUND and IVF

- 1 case report

RF THERMAL ABLATION and IVF (Accessa/Sonata)

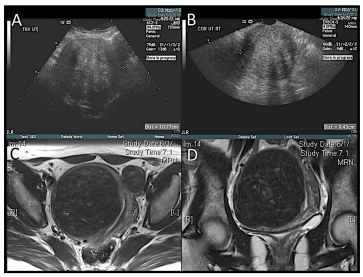
- 1 case report

Level 1 Evidence for A Myomectomy Role in IVF may never become available.

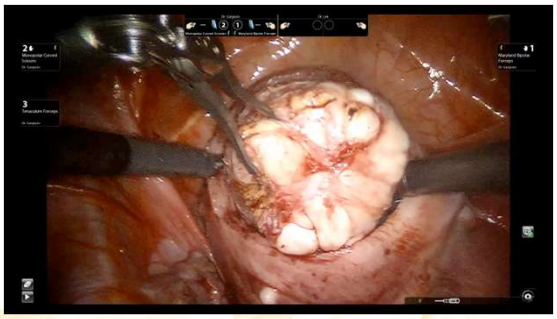
We must offer personalized treatment based on the evidence we have.

BASIC TOOLBOX FOR PERSONALIZED MYOMECTOMY

- Optimize IMAGING
- Optimize PATIENT COUNSELING (empowering/patient-centered)
- Optimize TECHNIQUE (microsurgical/least impact)



Gargiulo 2022 Mass General Brigham



Gargiulo 2022 Mass General Brigham

ADENOMYOSIS IN FERTILITY PATIENTS

Gargiulo 2022 Mass General Brigham

No longer a "condition of the MULTIPARA"

PREVALENCE of ADENOMYOSIS in INFERTILE WOMEN:

- 24.4% in women 40 years and above
- 7.5–22% in women < 40 years

Abu Hashim H, et al. Reprod Biomed Online 2020
Puente JM, et al. Reprod Biol Endocrinol 2016

Gargiulo 2022 Mass General Brigham

Does Adenomyosis Affect Fertility and Live Birth Rate?

IMPACT of ADENOMYOSIS on ASSISTED REPRODUCTION:

- Meta-analysis 1: *Vercellini P, et al. Hum Reprod 2014*
  - 28% lower IVF clinical pregnancy rate (CPR) in patients with adenomyosis vs controls.
  - 56% higher miscarriage rate in patients with adenomyosis vs controls.
- Meta-analysis 2: *Younes G and Tulandi T, et al. Fertil Steril 2017*
  - 41% lower IVF live birth rate (LBR) in patients with adenomyosis vs controls.
  - Miscarriage OR 2.2 in patients with adenomyosis vs controls.
- Meta-analysis 3: Miscarriage OR 3.4 in patients with adenomyosis vs controls. *Horton J, et al. Hum Reprod Update 2019*
- Meta-analysis 4: Miscarriage OR 2.8 in patients with adenomyosis vs controls. *Huang Y, et al. Biomed Res Int 2020*

Gargiulo 2022 Mass General Brigham

IMPACT of ADENOMYOSIS on ASSISTED REPRODUCTION:

- Prospective observational study on IVF patients diagnosed with adenomyosis by ultrasound. First evidence of effect on CPR based on severity of disease.
- Overall CPR: 29% with adenomyosis vs 43% without; "adenomyosis score" was correlated to CPR.

Mavrelos D, et al. Reprod Biomed Online 2021

Mavrelos D, et al. Reprod Biomed Online 2021

Table 4 – Logistic regression results with all ultrasonic features of adenomyosis score as independent variables and clinical pregnancy as dependent variable.

Ultrasonic feature (n)	Odds ratio of clinical pregnancy (95% CI)
Endometrial striae (38)	3.80 (0.84–13.60)
Myometrial cysts (59)	0.81 (0.27–2.40)
Asymmetric thickening (46)	0.63 (0.22–1.80)
Parallel shadowing (28)	0.63 (0.13–3.10)
Adenomyoma (6)	2.70 (0.29–24.50)
Irregular EMJ (44)	0.13 (0.02–1.00)
Endometrial islands (47)	1.90 (0.37–10.60)

CI = confidence interval; EMJ = endometrial myometrial junction.

Table 2 – Logistic regression results with each level of adenomyosis score as independent variable and clinical pregnancy as dependent variable. Reference category is no adenomyosis features and all variables are entered in the model.

Number of ultrasonic adenomyosis features [score] (n)	Odds ratio of clinical pregnancy (95% CI)
Single adenomyosis feature (1) (10)	0.85 (0.23–3.20)
Two features (2) (15)	0.95 (0.31–2.80)
Three features (3) (8)	1.00 (0.23–4.60)
Four features (4) (8)	0.22 (0.26–1.80)
Five features (5) (17)	0.39 (0.12–1.30)
Six features (6) (11)	0.30 (0.07–1.60)
Seven features (7) (3)	0.24 (0.09–6.40)

Mavrelos D, et al. Reprod Biomed Online 2021

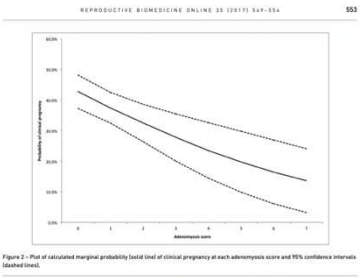
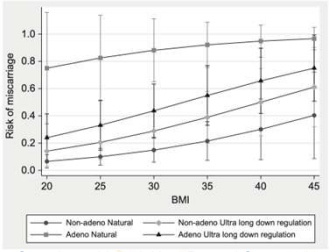


Figure 2 – Plot of calculated marginal probability (solid line) of clinical pregnancy at each adenomyosis score and 95% confidence intervals (dashed lines).

IMPACT of ADENOMYOSIS on ASSISTED REPRODUCTION:

EUPLOID MISCARRIAGE



Stanekova, V et al. Hum Reprod Open 2018

IMPACT of ADENOMYOSIS on OBSTETRICAL OUTCOMES:

- Meta-analysis: Higher odds of PTD (OR=3.09) and SGA (OR=3.23) in patients with adenomyosis vs. controls.
- Meta-analysis: Higher odds of PTD (OR=3.05), SGA (OR=3.22) and preeclampsia (OR=4.35) in patients with adenomyosis vs. controls.

Bruun MR, et al. Acta Obstet Gynecol Scand 2018
Rizavi M, et a. Int J Gynaecol Obstet 2019

REAL PROBLEM, NO CLEAR SOLUTION

- No accepted classification, no staging system: WE CANNOT DESIGN MEANINGFUL STUDIES (PROSPECTIVE OR RETROSPECTIVE) WITHOUT A STAGING SYSTEM
- We need studies that take in account ASSOCIATED ENDOMETRIOSIS
- We need studies that use EUPLOID EMBRYOS, because we are dealing with patients who are mostly in advanced maternal age (> 35yo)
- We need to understand MEDICAL OPTIONS and consider SURGICAL TECHNIQUES THAT MAKE ANATOMICAL SENSE !

Can Treatment of Adenomyosis Affect Live Birth Rate?

ADENOMYOSIS: CONSERVATIVE OPTIONS

- MEDICAL TREATMENT
- ADENO-MYOMECTOMY FOR FOCAL ADENOMYOSIS
- CYTOREDUCTION FOR DIFFUSE ADENOMYOSIS
- NON-EXCISIONAL PROCEDURES

ADENOMYOSIS: CONSERVATIVE OPTIONS

- MEDICAL TREATMENT
  - Adenomyosis: sex steroid hormone-dependent disorder, characterized by
    a) increased inflammation
    b) impaired apoptosis
    c) neuroangiogenesis
    Vannuccini S, et al. Reprod Biomed Online 2017
  - Adenomyosis: **hyperestrogenism** (↑ ER expression, ↑ ARO, ↓ Estrogen Catabolism), and **progesterone resistance** (↓ PR expression)
  - NO FDA-LABELED MEDICTION EXISTS FOR ADENOMYOSIS

ADENOMYOSIS: CONSERVATIVE OPTIONS

- COMMONLY USED MEDICAL TREATMENTS
  - GnRH-AGONISTS (with and without progestin add back) reduce the inflammatory reaction and angiogenesis and to significantly induce apoptosis
  - PROGESTINS antagonize progesterone-resistance: oral NETA and DIENOGEST (endometrial decidualization and mild hypo-estrogenism), vaginal DANAZOL (androgenic/hypoestrogenic milieu), LNG-IUS (endometrial atrophy) for uteri <150 cc volume
  - COMBINATION CONTRACEPTIVES (widely used, no studies available)
  - NSAIDs (widely used, no studies available)
  - TRANEXAMIC ACID (widely used, no studies available)

ADENOMYOSIS: CONSERVATIVE OPTIONS

- PROMISING NOVEL MEDICAL TREATMENTS
  - AROMATASE INHIBITORS: Aromatase cytochrome P450 present in endometrium of adenomyosis, fibroids and endometriosis patients (only). RCT VS GnRHa shows comparable effect. *Badawy AM, et al. Acta Obstet Gynecol Scand 2012*
  - SELECTIVE PROGESTERONE RECEPTOR MODULATORS: progesterone agonist and antagonist activities in the endometrium. Clinical use limited by regulatory restrictions in place. Recently published RCT VS placebo shows high efficacy in adenomyosis. *Capmas P et al. J Gynecol Obster Hum Reprod 2021*
  - GnRH ANTAGONISTS: act competitively preventing GnRH from binding to the pituitary receptor. Thus, allow dose-dependent modulation. Most promising option, with progestin add back. *Muneyyirci-Delale O et al. Fertil Steril Reports 2021*

ADENOMYOSIS: CONSERVATIVE OPTIONS

- BEST EVIDENCE FOR MEDICAL TREATMENT IN INFERTILITY : GnRHa
  - Retrospective. Long GnRHa suppression (>3 months) before FRESH IVF ET in 74 endometriosis patients, no LBR difference in high-stage endometriosis-only (n=50) vs high-stage endometriosis plus adenomyosis (n=24). *Mijatovic V, et al. Eur J Obstet Gynecol Reprod Biol 2010*
  - Retrospective. 339 patients planning FROZEN ET. Long GnRHa suppression (2 months) before ET. Ongoing Pregnancy Rate in treated group 49% vs untreated group 21%. *Niu Z et al. Gynecol Endocrinol 2013*
  - Retrospective. 295 patients. Groups: A) FRESH IVF, B) FRESH IVF after GnRHa (2-3 months), C) FROZEN ET after GnRHa (2-3 months). CPR higher in group C, but not significant. *Park CW, et al, Clin Exp Reprod Med 2016*

ADENOMYOSIS: CONSERVATIVE OPTIONS

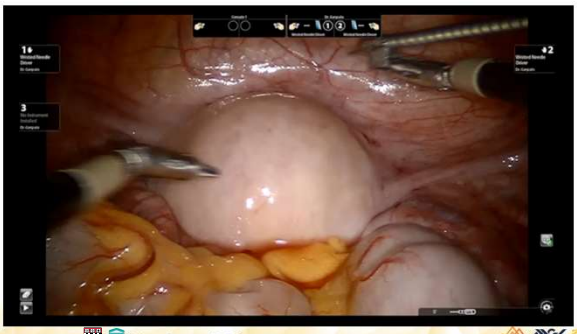
- MEDICAL TREATMENT
- ADENO-MYOMECTOMY FOR FOCAL ADENOMYOSIS
- CYTOREDUCTION FOR DIFFUSE ADENOMYOSIS
- NON-EXCISIONAL PROCEDURES

Gargiulo 2022 Mass General Brigham

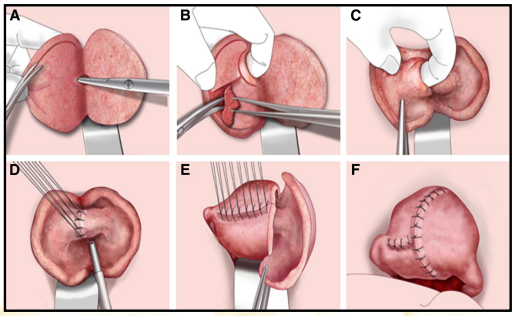
FERTILITY OUTCOMES AFTER SURGERY FOR ADENOMYOSIS

Authors	Follow-up (mo)	Desired pregnancy	Pregnancy rate (%)	Live birth rate (%)	Miscarriage rate (%)	Ectopic (%)	Still birth (%)	Complications
Saremi et al 2014 [24]	24	70 (49 IVF, 21 natural)	21/70 (30%) 14 IVF, 7 natural	16/21 (76%)	4/21 (19%)	0	1/16 (6%)	2 cases of uterine rupture at 37 and 32 wk
Osada et al 2011 [28]	24	26	16/26 (61%) 12 IVF, 4 natural	14/16 (87.5%)	2/16 (12.5%)	0	0	None
Al Juma 2011 [29]	36	18	8/18 (44.4%) 8 natural	6/8 (75%)	2/8 (25%)	0	0	None
Sun et al 2011 [30]		24	8/24 (33.3%) 5 IVF, 3 natural	3/8 (37.5%)	5/8 (62.5%)	0	0	None
Wang et al 2009 [32]	24	27 surgical, 44 surgical and medical	20/27 (74%) All natural: 35/44 (79.5%)	17/20 (85%) 32/35 (91%)	3/20 (15%) 3/35 (8.5%)	0 0	0 0	None
Wang et al 2009 [33]	24	28	13/28 (46.4%) All natural	9/13 (32.1%)	4/13 (14.3%)	0	0	None
Fedele et al 1993 [19]	52.7 ± 22.2	28	18/28 (64.2%) 1 IVF, 7 natural	9/18 (50%)	7/18 (38.8%)	1/18 (5.5%)	0	None
Fujishita et al 2004 [38]	36	4	2/4 (50%) All natural	2/2 (100%)				None
Takeuchi et al 2006 [35]	NA	8	2/8 (25%) All natural	2/2 (100%)	0			
Takeuchi et al 2010 [7]	35	3	3/3 (100%) All natural	3/3 (100%)				
Nishida et al 2010 [37]	12	NA	2 1 IVF, 1 natural			1/2 (50%)		

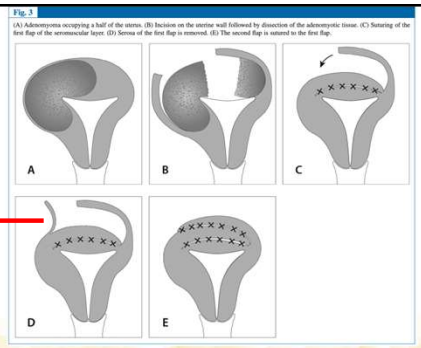
Younes G and Tulandi T, J Minim Invasive Gynecol 2017



Gargiulo 2022 Mass General Brigham

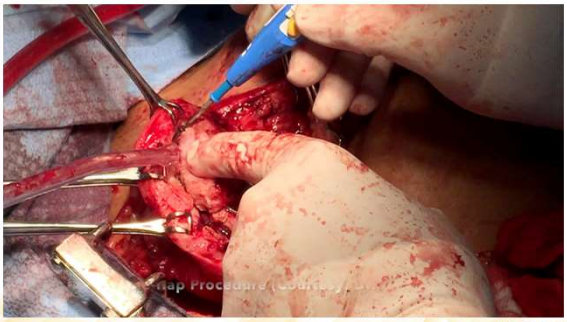


Osada H, Fertil Steril 2018



Deserosalization of the First Flap

Younes G and Tulandi T, J Minim Invasive Gynecol 2017



Gargiulo 2022 Mass General Brigham

ADENOMYOSIS: HANDLE WITH CARE

- MEDICAL TREATMENT REMAINS FIRST-LINE
- ADENO-MYOMECTOMY and CYTOREDUCTION CAN BE CONSIDERED IN SELECT CASES
- THIS FIELD IS RIPE FOR HIGH-QUALITY REPRODUCTIVE SURGERY INVESTIGATION OPPORTUNITY

THANK YOU !

AAGL 2022 51st GLOBAL CONGRESS ON MIGS
December 1–4, 2022 | Aurora, CO | congress.aagl.org

Complex fibroid & Adenomyosis~ Challenges & Novel approaches

Prakash Trivedi
Mumbai, India

No financial disclosure

Fibroids presents with multiple variants & overlap by adenomyosis adds different approach for accurate management. Out of thousands of cases we will focus on few of the subject allotted.

There can be multiple very large fibroids with ureteral compression, Rare unusual degeneration, mimicking like pelvic kidney, myxomucinous or aqueous fatty degeneration, low large cervical fibroid or Leiomyomatosis.

Case 1

Large multiple fibroids in 37year female with left nephrostomy, AMH 1.3 from Melbourne, diagnosis not classified.

After proper counselling 3D Laparoscopic Myomectomy done with contained bag morcellation & removal of nephrostomy. On returning back in 15 months patient conceived spontaneously delivered by CS.

VIDEO ~DIFFICULT LOCATIONS, SIZE & NO.

Case 2

33 years lady had one child & now 20 cm fibroid from News Zealand come for Laparoscopic surgery. Investigative parameters were normal, right ureter at brim was 15 mm dilated.

After thorough counselling & options, she preferred Laparoscopic surgery which was undertaken, care was taken of right IP ligament vessels to avoid avulsion. Three layers closure for dead space was done with v loc sutures.

Visual contaitoned bag morcellation was done. A1 & SP took place after a year

Case 3

A 34 year lady with 12 years of infertility had two bizarre masses on anterior & posterior uterine wall 5 cms each vascular.

After explaining in a Live Workshop Laparoscopic surgery was done.

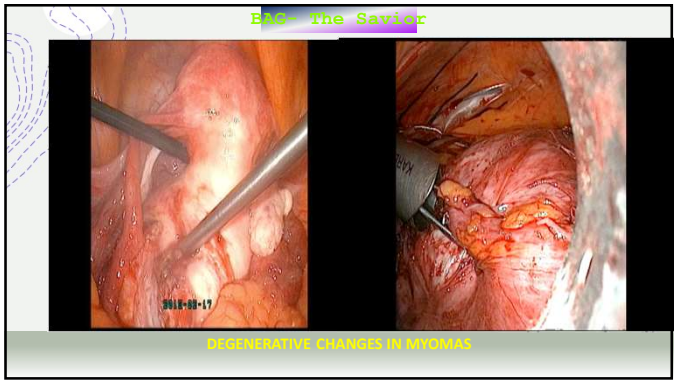
On injecting dilute vasopressin, on incision soft vascular mass came out with no possibility of using myoma screw or tenaculum, hence atraumatic bowel grasper was used to dissect. Both specimens were removed in bag & were reported as Angiolipoma. She conceived in 3 months of surgery

Case 4

These cases are of two very large fibroids with aqueous, fatty, mucinous degeneration & impossible to do morcellation.

Fortunately as both had contained bag morcellation, wherein conventional morcellation was not possible as tissues were soft.

Removal was done with ovum forceps & suction tubing passed through morcellation port. No spillage occurred in the peritoneal cavity.



Case 5

Lantern over Saint Paul's Cathedral is not uncommon & after thousands of cases in 5 figures of Laparoscopic myomectomy such cases do come.This case looked like yet another but was a surprise.

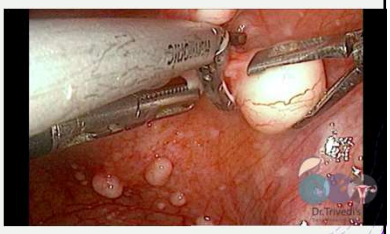
She wanted the uterus & we took a low vertical incision on posterior aspect of uterus. Surgery went perfect but surprisingly the gap between uterus & vagina was empty.

We had to pass dilators so that we can suture the lower ends of uterus to vagina actually at six places for security

Case 7

- Surprises in surgery are greatest challenge to an expert who defines the statement " Surgical genius are not born in crisis, but are borne to exhibit in crisis "
- Watch this last case to finalize

+VIDEO
Leiomyomatosis



Case 6

Patient with large uterus had 15 cm left posterior large mass crossing IP ligaments. Almost mimicking pelvic kidney.

All the suitable steps like on the table sonography & even left ureteral catheter was passed for adequate length.

Uterus & mass were remove vaginally a patient was for Hysterectomy. The mass was reported as degenerated fibroid & no malignancy was found.

CLOSING VIDEO ~ MYOMAS ? PELVIC KIDNEY

CULTURAL AND LINGUISTIC COMPETENCY & IMPLICIT BIAS

The California Medical Association (CMA) announced new standards for Cultural Linguistic Competency and Implicit Bias in CME. The goal of the standards is to support the role of accredited CME in advancing diversity, health equity, and inclusion in healthcare. These standards are relevant to ACCME-accredited, CMA-accredited, and jointly accredited providers located in California. AAGL is ACCME-accredited and headquartered in California.

CMA developed the standards in response to California legislation (Business and Professions (B&P) Code Section 2190.1), which directs CMA to draft a set of standards for the inclusion of cultural and linguistic competency (CLC) and implicit bias (IB) in accredited CME.

The standards are intended to support CME providers in meeting the expectations of the legislation. CME provider organizations physically located in California and accredited by CMA CME or ACCME, as well as jointly accredited providers whose target audience includes physicians, are expected to meet these expectations beginning January 1, 2022. AAGL has been proactively adopting processes that meet and often exceed the required expectations of the legislation.

CMA CME offers a variety of resources and tools to help providers meet the standards and successfully incorporate CLC & IB into their CME activities, including FAQ, definitions, a planning worksheet, and best practices. These resources are available on the CLC and IB standards page on the CMA website.

Important Definitions:

Cultural and Linguistic Competency (CLC) – The ability and readiness of health care providers and organizations to humbly and respectfully demonstrate, effectively communicate, and tailor delivery of care to patients with diverse values, beliefs, identities and behaviors, in order to meet social, cultural and linguistic needs as they relate to patient health.

Implicit Bias (IB) – The attitudes, stereotypes and feelings, either positive or negative, that affect our understanding, actions and decisions without conscious knowledge or control. Implicit bias is a universal phenomenon. When negative, implicit bias often contributes to unequal treatment and disparities in diagnosis, treatment decisions, levels of care and health care outcomes of people based on race, ethnicity, gender identity, sexual orientation, age, disability and other characteristics.

Diversity – Having many different forms, types or ideas; showing variety. Demographic diversity can mean a group composed of people of different genders, races/ethnicities, cultures, religions, physical abilities, sexual orientations or preferences, ages, etc.

Direct links to AB1195 (CLC), AB241 (IB), and the B&P Code 2190.1:

Bill Text – AB-1195 Continuing education: cultural and linguistic competency.
Bill Text – AB-241 Implicit bias: continuing education: requirements.
Business and Professions (B&P) Code Section 2190.1

CLC & IB Online Resources:

Diversity-Wheel-as-used-at-Johns-Hopkins-University-12.png (850×839) (researchgate.net)
Cultural Competence In Health and Human Services | NPIN (cdc.gov)
Cultural Competency – The Office of Minority Health (hhs.gov)
Implicit Bias, Microaggressions, and Stereotypes Resources | NEA
Unconscious Bias Resources | diversity.ucsf.edu
Act, Communicating, Implicit Bias (racialequitytools.org)
https://kirwaninstitute.osu.edu/implicit-bias-training
https://www.uptodate.com/contents/racial-and-ethnic-disparities-in-obstetric-and-gynecologic-care-and-role-of-implicitbiases
https://www.contemporaryobgyn.net/view/overcoming-racism-and-unconscious-bias-in-ob-gyn
https://pubmed.ncbi.nlm.nih.gov/34016820/