GLOBAL CONGRESS ON MIGS

SYLLABUS

604-FIBR:
Fibroids & Adenomyosis - Extirpative Non-Hysterectomy
Professional Education Information

Target Audience
This educational activity is developed to meet the needs of surgical gynecologists in practice and in training, as well as other healthcare professionals in the field of gynecology.

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AAGL is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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604-FIBR: Fibroids & Adenomyosis - Extirpative Non-Hysterectomy

**COURSE CO-CHAIRS:** Errico Zupi and Joerg Keckstein

**FACULTY:** Innie Chen, John C. Petrozza, Marco A. Pinho de Oliveira, Nikolai Rukhilada

The aim of this course is to provide all the most recent results in approaching two of the more common women’s pathologies, Adenomyosis and Uterine fibroids. The course will demonstrate, with high-quality evidence and video presentation, all of the modalities of minimally invasive approaches to the mentioned diseases in order to give the best possible up-to-date to the attendants.

**Learning Objectives:** *At the conclusion of this course, the participants will be able to:* 1) Describe all the actual opportunities, we have in approaching Adenomyosis and Uterine fibroids; 2) Describe the role of Minimally invasive approach to the mentioned pathologies; and 3) discuss among panelists and attendees.

**COURSE OUTLINE**

<table>
<thead>
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<th>Session Description</th>
<th>Speaker(s)</th>
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<tr>
<td>7:00 am</td>
<td>Welcome Introduction and Course Overview</td>
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<tr>
<td>7:05 am</td>
<td>Technical Aspects for Fertility Sparing Resection of Adenomyosis</td>
<td>J. Keckstein</td>
</tr>
<tr>
<td>7:20 am</td>
<td>When and How to Perform Conservative Surgery for Extensive Adenomyosis?</td>
<td>M. Pinho de Oliveira</td>
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<tr>
<td>7:35 am</td>
<td>Surgery for Adenomyosis: Is There a Limit?</td>
<td>M. Pinho de Oliveira</td>
</tr>
<tr>
<td>7:50 am</td>
<td>The Strategy of Adenomyosis Management and Reproductive Outcomes</td>
<td>N. Rukhilada</td>
</tr>
<tr>
<td>8:05 am</td>
<td>Preoperative and Intraoperative Medical Adjuncts for Fibroid Surgery</td>
<td>I. Chen</td>
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<td>Adenomyosis and Pain</td>
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<td>Fertility Conserving Surgery for Symptomatic Uterine Fibroids</td>
<td>J.C. Petrozza</td>
</tr>
<tr>
<td>9:05 am</td>
<td>Image Based Surgery for Uterine Fibroids</td>
<td>J.C. Petrozza</td>
</tr>
<tr>
<td>9:20 am</td>
<td>Questions &amp; Answers</td>
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<tr>
<td>9:30 am</td>
<td>Adjourn</td>
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PLANNER DISCLOSURE
The following members of AAGL have been involved in the educational planning of this workshop (listed in alphabetical order by last name).
Linda J. Bell, Admin Support, AAGL*
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Erin T. Carey, MD, MSCR
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Mark W. Dassel, MD
 Contracted Research: Myovant Sciences
Linda Michels, Executive Director, AAGL*
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 Speaker: AbbVie
Consultant: Medtronic, Lumenis
Erinn M. Myers, MD
Speakers Bureau: Laborie Medical Technologies, Teleflex Medical
Other: Unrestricted educational grant to support NC FPMRS Fellow Cadaver Lab: Boston Scientific Corp. Inc.
Amy Park, MD
Speaker: Allergan
Nancy Williams, COO, CME Consultants*
Harold Y. Wu, MD*
Errico Zupi, MD*
Joerg Keckstein, MD
Speaker: Storz Germany

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).
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Speaker: Storz Germany
John C. Petrozza
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Nikolai N. Rukhilada, MD*
Errico Zupi, MD*

Content Reviewers have nothing to disclose.

Asterisk (*) denotes no financial relationships to disclose.

All relevant financial relationships noted have been mitigated.
Technical Aspects For Fertility Sparing Resection Of Adenomyosis

Prof. Dr. Jörg Keckstein
apl. PROFESSOR, University Ulm, Germany
CONSULTANT, University Tübingen, Germany
CHAIR, SIG (Special Interest Group Endometriosis), ESGE
AMBASSADOR, WES (World Endometriosis Society)

Certified Endometriosis Centre - Dres. Keckstein Villach, Austria

Disclosure

Speaker: Fa. Karl Storz, Germany


Indication for fertility sparing surgery

- Pain
- Pain + bleeding disorder
- Pain + bleeding disorder + infertility
- Infertility

19 studies with a total of 1843 patient

Satisfactory:
- control of pain and bleeding
- reduction of uterine volume
- Long-term results
- Parameters related to the recurrence of adenomyosis
- Comparison of conservative surgical treatment of adenomyosis with other treatment options


Main issues of surgical intervention in adenomyosis:

- Identification of the entire pathology
- Complete removal of the disease
- Deterioration of the function of the uterus
- Adhesion formation
- Risks during pregnancy (delivery)
Hysteroscopy

Laparoscopy/laparotomy

Laparotomy


- 64 studies 1049 Pat
- 20 (488 Pat.) complete excision
- 11 (128 Pat.) partial excision
- 22 (38 Pat.) cystic adenomyosis
- 15 (395) “nonexcisional technique”


- Complete?
- Tactile feedback
- Closure of the uterus with flap technique
- Microsurgical techniques


<table>
<thead>
<tr>
<th>Classification of surgery</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extent of excision</td>
<td>focal</td>
<td>diffuse</td>
</tr>
<tr>
<td>Technique</td>
<td>easier</td>
<td>much more difficult</td>
</tr>
<tr>
<td>Risk for entering the cavity</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>Risk of destroying myometrium</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>Symptom control</td>
<td>good to excellent</td>
<td>fair</td>
</tr>
<tr>
<td>Fertility preservation</td>
<td>high</td>
<td>probably low</td>
</tr>
<tr>
<td>Risk of rupture</td>
<td>low</td>
<td>possible high</td>
</tr>
</tbody>
</table>


Conservative surgery is feasible and has promising results

- Pain and pregnancy rate sign. improved
- Risk of adhesion formation and rupture
- Individual indication for surgery is mandatory

- Limited data available
- Further controlled studies are necessary

References


When and How to Perform Conservative Surgery for Extensive Adenomyosis?

Marco Pinho Oliveira PhD
Associate Professor – State University of Rio de Janeiro - Brazil

Disclosure

“I have no financial relationships to disclose”

Objectives

• To point out difficulties in establishing the diagnosis of adenomyosis
• To review the main complaints related to adenomyosis
• To outline the medical options to treat adenomyosis
• To describe the available techniques for excisional and non-excisional conservative surgery in adenomyosis
• To demonstrate the main steps necessary to perform conservative surgery for adenomyosis
• To summarize the main results of conservative surgery for adenomyosis

Adenomyosis

• Adenomyosis lead to significant symptoms such as dysmenorrhea, pelvic pain, dyspareunia, heavy menstrual bleeding and infertility in up to one-third of the cases
  
  • Is reported to be associated with adverse fertility, pregnancy and neonatal outcomes in a recent systematic review
  
  • The prevalence of adenomyosis in women treated by hysterectomy: 20-30%
    
  • Histological diagnosis: ectopic endometrium 2.5mm (0.5 HPF) below the endometrial-myometrial junction

Pre-operative

• Finger-like invasion

• Image diagnosis: difficult even with MRI

JZ (>12mm)

Sens: 53%
Spec: 94%

Recurrence of adenomyosis: 53.7% - 2/3 HPF

Recurrent abortion (spontaneous and with ART)


Horton et al. Hum Reprod Update. 2019

Tellum et al. Eur Radiol. 2019


Sens: 74%

Adenomyosis

The role of cine MR imaging in the assessment of uterine function
Deborah Menezes Sousa1,2, Henan Wener Ludin1, Leonardo Kayal Bitencourt1,2, Flávia Paiva Pires Leite1,2, Ana Luísa de Oliveira1,2
Archives of Gynecology and Obstetrics 2019

Abnormal peristalsis in women with adenomyosis (cervical-fundal in periovulatory period).

Adenomyosis

Symptomatic patients?
(desire future pregnancy)

LNG-IUS

GnRH-a

Dienogest

Adenomyosis

Medical treatment failure
SURGERY!

Abnormal uterine bleeding
Dysmenorrhea

Dienogest

Adenomyosis

Infertility patients?

Infertility

IVF (+ GnRH-a?)

GnRH-a for spontaneous pregnancy?

GnRH-a therapy before IVF or Frozen Embryo Transfer may improve pregnancy outcome
Silva et al. Fertility and Sterility 1994

There is no published information on the impact of GnRH agonist therapy on the subsequent fertility improvement
Vercellini et al. Nat. Rev. Endocrinol 2014

Adenomyosis

Improve conception rate within 6 months of cessation of GnRH agonist therapy
She et al. Fertility and Sterility 1992

When to perform surgery?

• Medical failure for AUB and/or Dysmenorrhea (and desire future pregnancy)
• Infertility – mainly recurrent abortions (spontaneous and/or IVF)
  • Number of previous abortion should be individualized (depends on age and adenomyosis extension)

Similar indications as for myomectomy - especially for adenomyomas

Adenomyosis

Non-excisional techniques (ablative)

- MRRFUS (MR-guided focused ultrasound)
- HIFU (High Intensity Focused Ultrasound)
- PMWUA (Percutaneous MicroWave Ablation)
- RF (laparoscopic)

When to perform surgery?

1- Non-excisional techniques such as thermal coagulation of the diseased myometrium
2- Excisional techniques

Adenomyectomy – Type 1 (removal of the focal disease, usually adenomyoma)
Myomectomy – Type 2 (partial removal of the diseased myometrium, usually diffuse infiltration)

Adenomyosis

How to perform surgery?

2017

1- Non-excisional techniques such as thermal coagulation of the diseased myometrium
2- Excisional techniques

Metastasis

Meta-analysis with 38 studies involving 15,008 patients; significant results for symptomatic patients (AUB and dysmenorrhea), but not robust data for pregnancy rates after treatment
Liu et al. J Hyperthermia. 2021
Adenomyosis

Excisional techniques

- Adenomyomectomy
  - Hysteroscopic resection (not for extensive disease)
  - Laparoscopic / Robotic
  - Wedge resection
  - Flap techniques

- Excisional techniques
  - Step 1 – Preoperative GnRHa?
    - No evidence that it should be used, but may shrink the lesion and reduce blood loss
  - Step 2- Intraoperative procedures to reduce bleeding?
    - Vasopressin - we use 20u (1ml) diluted in 40ml of saline
    - Tourniquet
    - Uterine artery ligation
Adenomyosis

Excisional techniques

• Step 1 – Preoperative GnRHa?

• Step 2 – Intraoperative procedures to reduce bleeding?
  - Vasopressin
  - Tourniquet
  - Uterine artery ligation

Horizontal/oblique incision may cause less damage to muscular fibers and less bleeding.

Adenomyosis

Excisional techniques

• Step 3 – Incision

Adenomyosis

Excisional techniques

• Step 4 – Resection (wedge x flaps)

Adenomyosis

Conservative surgery

Adenomyosis

Excisional techniques

• Step 5 – Suture

<table>
<thead>
<tr>
<th>Study</th>
<th>B</th>
<th>Hb</th>
<th>Ht</th>
<th>C2</th>
<th>Hb</th>
<th>Ht</th>
<th>C2</th>
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<tbody>
<tr>
<td>Interval</td>
<td>179</td>
<td>13.9</td>
<td>44</td>
<td>0.88</td>
<td>132</td>
<td>10.9</td>
<td>46</td>
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<tr>
<td>Shaver</td>
<td>178</td>
<td>13.8</td>
<td>44</td>
<td>0.88</td>
<td>132</td>
<td>10.8</td>
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<tr>
<td>bipolar</td>
<td>173</td>
<td>14.0</td>
<td>43</td>
<td>0.86</td>
<td>130</td>
<td>10.8</td>
<td>44</td>
</tr>
<tr>
<td>Laser</td>
<td>173</td>
<td>14.0</td>
<td>43</td>
<td>0.86</td>
<td>130</td>
<td>10.8</td>
<td>44</td>
</tr>
<tr>
<td>36 months</td>
<td>173</td>
<td>14.0</td>
<td>43</td>
<td>0.86</td>
<td>130</td>
<td>10.8</td>
<td>44</td>
</tr>
</tbody>
</table>

36 months

Who will benefit from uterus-sparing surgery in adenomyosis-associated subfertility?

Pregnancy outcomes:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 50)</th>
<th>Adenomyosis (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical pregnancy rate (%)</td>
<td>98 (22)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Clinical abortion rate (%)</td>
<td>17 (4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Liveborn rate (%)</td>
<td>74 (18)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Preterm birth rate (%)</td>
<td>7 (18)</td>
<td>2 (2.6)</td>
</tr>
<tr>
<td>SGA rate (%)</td>
<td>2 (4.5)</td>
<td>1 (1.3)</td>
</tr>
</tbody>
</table>

References


References


Li Y, Qi H, Ma W, Wu C, Li X, Zhao D, Ye W, Yang Y, Temporarily blocking the uterine artery to Dig Out a Diffused Adenomyosis lesion Stipped Laparoscopy / Minim Invasive Sterilization 2017 Nov 14.(211)519-523.


Surgery for Adenomyosis: Is There a Limit?

Marco Pinho Oliveira PhD
Associate Professor – State University of Rio de Janeiro - Brazil

Disclosure

“I have no financial relationships to disclose”

Objectives

- To outline the conservative surgical options for diffuse adenomyosis
- To demonstrate the main steps necessary to perform conservative surgery for diffuse adenomyosis
- To summarize the main results of conservative surgery for diffuse adenomyosis
- To discuss the limits of conservative surgery for diffuse adenomyosis and complications of the procedure

Focal Adenomyosis

Diffuse Adenomyosis
Adenomyosis

Surgical procedure to conserve the uterus for future pregnancy in patients suffering from massive adenomyosis

Case

- 37 years-old woman; G 4 P 0
- Four abortions: 1st and 2nd after spontaneous pregnancies; 3rd after IUI and 4th after spontaneous pregnancy
- Previous treatments: two laparoscopic surgeries for deep endometriosis; Gossamerlin 3.5mg for 6 months and Dienogest for 12 months with no improvement of adenomyosis
- Patient refers moderate dysmenorrhea (VAS=7) and desire of a term pregnancy
Adenomyosis

- Total operative time was 255 minutes
- EBL was 250ml
- Moderate pain for 48 hours
- Discharge after 72 hours with no complaints
- 3 months after surgery (dysmenorrhea VAS=2)
- Planning to transfer frozen embryos 6 months after surgery

Adenomyosis

Is there a limit for conservative surgery?
Some uterine size that is not possible to be conservative?
There are extensive adenomyosis that is not amenable to resection?

OR

Should we (almost) always try it before indicate hysterectomy?

"I personally removed 112 myomas from a patient at one operation, but at the time I was unaware of the world record achieved by Bonney of 125 lesions during an individual myomectomy in 1930.
My patient became pregnant 3 months later and had three children born by cesarean section and two subsequent myomectomies."
In my early years as a gynaecological surgeon, a case occurred which profoundly affected my outlook. A lady, recently married, wishing above all things to have a child underwent a subtotal hysterectomy on account of a single submucous fibroid, and none but those who knew her well perceived the tragedy. I was among this number and the grief of it is still keen in me today.


Bonney’s clamp
>700 myomectomies
(only 5 deaths)

References


Thank you very much!
Marco Aurelio Pinto Oliveira
endometros@gmail.com
Surgical treatment of adenomyosis

Adenomyosis for reproduction

- Average in population 20-25%
- … after 35 y.o. 40%
- Coexist with myoma 40-50%, with endometrial hyperplasia – до 90%

A and repr problems

- A in infertility 15-20 %
- Recurrent abortion 30 %,
Is there a place for surgery?

Other approaches?

Drugs treatment:
- GnRH agonists
- COC
- Dienogest
- Ulipristal

Surgical alternatives:
- Embolisations
- Intrauterine surgery – ablation, myolysis

Surgical strategy

- Depends on AIMS!!! Do you need to save the uterus and fertility??
- Depends on adenomyotic total size
- Depends on ART plans (Cryotransfer? Stimulation?)

What should we do before surgery?

- MRI for surgery plan!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!
- Neoadjuvant medical hormones (GnRH agonists, Veni, Ulipristal, Mirena) ??????? – as most are anemic!
- If anemic – get at least 90 g/l hemoglobin
- Especially in big volume of adenomyotic tissue to be excised.
Clinical case

- 34 y.o., anemic 84 gl, heavy menstrual blood loss and pain, 3 sp.ab. Last 3 years – sec.infert. 2 art attempts – no implantation.
- Visanne 3 month before surgery – 105 gl, but no change in uterine size and pain (7-8 VAS)
- Adenomyomectomy by “roll-over tech”
- Visanne 6 month after surgery
- Immediately ART (cryotransfer)
- Now pregnant 21 week – no path clinical signs

“Roll-over” Surgical technique
By 2018 in literature are described 6565 adenomyomectomies performed in 29 hospitals. After surgery 875 (13.3%) pregnancies were confirmed and 728 (83.2%) led to interm birth, noted 8 cases of antenatal fetal death (1.2%). Total described 18 (2.0%) uterine ruptures.

Abo Taleb Saremi, Homa Bahrami et al. (Reprod. Healthcare 2014) – n=103

Surgical procedure to conserve the uterus for future pregnancy in patients suffering from massive adenomyosis

** Affiliated University of Health Sciences, Department of Obstetrics and Gynecology, Tokyo Women's Medical University, Japan
* Department of Obstetrics and Gynecology, Graduate School of Medicine, Chiba University, Japan
** Department of Obstetrics and Gynecology, Graduate School of Medicine, Chiba University, Japan

Abo Taleb Saremi, Homa Bahrami et al. (Reprod. Healthcare 2014) – n=103
• 212 total surgeries - 92 made for reproduction restoration in recurrent SA and infertility; total pregnancies achieved 44 (47.8% or 20.7% of total surgeries number). In other cases the target of the surgery was normalization of mestrual blood loss or mestrual pain syndrome (if patient refused of suggested hysterectomy and in case of insufficient effect of hormonal therapy).

The reproductive outcomes were following: spontaneous abortion before 22 wg – 8 cases, 35 – birth cases, among them 12 – preterm (20.5%, 66.7% and 28.2%, respectively). Total successful percentage 39.1% - of all, interested in reproduction restoration. Only 2 pregnancies were spontaneous – other resulted from ART (as we almost always damage the tubal ostia in intramural part of the uterus)

How to prepare for the surgery?

• **Anemic:**
  - Agonists
  - Visanne
  - Gynestril or ulipristal
  - + iron medications
  - HB more 90
  - Or consider Mirena AND leave it during the surgery

• **Not anemic:**
  - Mirena just before surgery
  - Leave Mirena for 6 months or consider COC for reliable contraception

Contraception minimum for 6 month!!!
And better no menstruations for 3 month!

T-shape uterine rupture after metroplasty for placenta percreta
USG 18 wg, myomectomy 14 month ago

References


Preoperative and Intraoperative Medical Adjuncts for Fibroid Surgery

Innie Chen, MD, MPH, FRCSC
Associate Professor, University of Ottawa
604-FIBR: Fibroids & Adenomyosis - Extirpative Non-Hysterectomy

Disclosure

- I have no financial relationships to disclose

Objective

- Describe medical adjuncts to decrease surgical bleeding and need for transfusion in patients undergoing myomectomy.
  - Pre-operative adjuncts
  - Intra-operative adjuncts
  - Include abdominal laparoscopic/robotic, and laparotomic approaches

Surgical risks of fibroid surgery

- Hysterectomy vs.
- Hysteroscopic myomectomy vs.
- Laparoscopic myomectomy vs.
- Abdominal myomectomy
- Anesthesia
- Bleeding, transfusion
- Infection
- Injury to pelvic organs
- Laparotomy, reoperation
- VTE
- Death
- Injury to reproductive organs
- Hysterectomy
- Fluid overload
Medical adjuncts

**Pre-operative**
- Increase pre-operative hemoglobin
- Decrease menstrual bleeding
- Decrease fibroid size
- Provide symptomatic relief

**Intra-operative**
- Promote local vasoconstriction
- Promote local coagulation
- Decrease surgical blood loss

---

**Pre-operative: Fe supplementation**
- Pre-operative anemia (<12g/dL) is a known risk factor for transfusion
- Correction of pre-operative anemia, commence as soon as decision for surgery
- Target Hb >13g/dL
- Oral supplementation, IV iron
- Hematology consultation

---

**Pre-operative GnRH agonist**
- Reductions in uterine volume (MD -175 mL, 95% CI -219.0 to -131.7; 13 studies; 858 participants)
- Reduction in fibroid volume (heterogeneous studies, MD 5.7 mL to 155.4 mL)
- Increased preoperative haemoglobin (MD 0.88 g/dL, 95% CI 0.7 to 1.1; 10 studies; 834 participants)
Medical pretreatment - GnRHa

• Hysterectomy – decrease operative time, intraoperative blood loss (MD 25 mL to 148 mL), blood transfusion (OR 0.54, 95% CI 0.3 to 1.0), postoperative complications.
• Myomectomy - Reduce intraoperative blood loss (MD 22 mL to 157 mL)
• No clear evidence of a difference among groups for other primary outcomes after myomectomy: duration of surgery, blood transfusions, nor postoperative complications (OR 1.07, 95% CI 0.43 to 2.64; I² = 0%; 5 studies; 190 participants; low-quality evidence).

Preoperative: Other agents

• Tranexamic acid
  - reduces menstrual blood loss by 26 to 54 percent in patients with heavy menstrual bleeding
  - 1g po q8h x3-5d prn heavy menstrual bleeding
• GnRH antagonist
  - N=412, 300mg po bid
  - primary outcome: <80cc and >50% reduction in menstrual blood loss
  - 77%-84.1% elagolix alone; 68.5%-76.5% elagolix plus add-back therapy
  - 8.7%-10% placebo (P<0.001 for both trials).
• SPM
  - Ulipristal acetate – limited by drug-induced live injury

Preoperative and Intraoperative Medical Adjuncts for Myomectomy

Medical adjuncts – blood loss

• Vaginal misoprostol (2 RCTs, 89 women: MD -97.88 ml, 95% CI -125.52 to -70.24)
• Intramyometrial vasopressin (3 RCTs, 128 women: MD -245.87 ml, 95% CI -434.58 to -57.16)
• Intramyometrial bupivacaine plus epinephrine (1 RCT, 60 women: MD -68.60 ml, 95% CI -93.69 to -43.51)
• Intravenous tranexamic acid (1 RCT, 100 women: MD -243 ml, 95% CI -460.02 to -25.98)
• Gelatin thrombin matrix (1 RCT, 50 women: MD -554.00 ml, 95% CI -793.26 to -314.74)
• Intravenous ascorbic acid (1 RCT, 102 women: MD -411.46 ml, 95% CI -502.58 to -320.34)
• Vaginal dinoprostone (1 RCT, 108 women: MD -131.60 ml, 95% CI -253.42 to -9.78)
• Fibrin sealant patch (1 RCT, 70 women: MD -26.50 ml, 95% CI -44.47 to -8.53)

Intra-operative: Vasopressin

• Vasopressin acts by constricting the smooth muscle in the walls of capillaries, small arterioles, and venules.
  - MD -245.87 ml, 95% CI -434.58 to -57.16
  - 10-20 units in 100 mL of normal saline
  - Caution:
    • Avoid intravascular injection by aspirating and confirming the absence of blood prior to each injection
    • Intravascular injection or absorption has been associated with profound hypertension, bradycardia, and death.
    • May be contraindicated with patients with cardiovascular or renal disease.

Preoperative and Intraoperative Medical Adjuncts for Myomectomy

Hormonal suppression

Decrease pre-operative menstrual/uterine bleeding

Decrease pre-operative hemoglobin

Decrease fibroid/uterine size

Decrease fibroid/uterine vascularitiy

Decrease surgical bleeding

Pre-operative adjuncts

Decrease pre-operative menstrual/uterine bleeding

Increase pre-operative hemoglobin

Decrease fibroid/uterine size

Decrease fibroid/uterine vascularitiy

Decrease surgical bleeding

Intra-operative adjuncts

Iron

Decrease pre-operative menstrual/uterine bleeding

Decrease fibroid/uterine size

Decrease surgical bleeding
Misoprostol

- Eight studies, 385 patients
- Lower blood loss by -170.32 ml (95% CI -201.53 to -139.10)
- Lower drop in haemoglobin by -0.48 g/dl (95% CI -0.65 to -0.31)
- Reduced need for blood transfusion (odds ratio [OR] 0.48, 95% CI -0.65 to -0.31)
- Reduction in operative time by -11.64 minutes (95% CI -15.73 to -7.54)
- There was no difference in postoperative pyrexia or length of postoperative stay.

Lalonde 2012

- N=67
- Placebo significantly higher EBL (217 +/- 74 vs 126 +/- 41)
- Larger decline of postoperative Hb, placebo (1.6 +/- 0.43) compared to misoprostol (1 +/- 0.33)
- The operative time and side-effects was comparable in both groups.

Intra-operative: Tranexamic acid

- Lower blood loss
- Increased recovery
- Reduced need for transfusion
- Reduced operative time
- No increase in fevers or length of stay

Figure 1. Coagulation cascade and the site of action for various local hemostatic agents. OR=ovoid, see legend. (ACOG 2018)

Intraoperative: Other

- Local anesthetics with epinephrine
  - 1 RCT, 60 women: MD -68.60 ml, 95% CI -93.69 to -43.51
- Oxytocin
  - Systematic review of 2 RCTS showed no benefit
- Topical agents

Preoperative and Intraoperative Medical Adjuncts for Myomectomy

- Increase pre-operative hemostasis
- Decrease fibroid/uterine vascular
- Increase pre-operative menstrual/ovarian bleeding
- Decrease fibroid/uterine size
- Increase pre-operative amenorrhea
- Decrease fibroid/uterine vascularity
- Decrease surgical bleeding

ACOG Committee Opinion

Topical Hemostatic Agents at Time of Obstetric and Gynecologic Surgery

ACOG 2020
References


Errico Zupi, MD
Full Professor Obstetrics and Gynaecology
Department of Molecular and Developmental Medicine, University of Siena

- Adenomyosis and Infertility
- Adenomyosis and Pain

I have no financial relationships to disclose

Learning Objectives
- Non invasive diagnosis
- Clinical management
- Medical and surgical approach

Adenomyosis
The true incidence of adenomyosis is unknown.
The prevalence has been reported to range from 1% to 70%
lack of standard diagnostic criteria both by imaging modalities and pathological analyses

Adenomyosis and clinical symptoms
- Abnormal uterine bleeding
- Dysmenorrhea
- Dyspareunia
- Infertility

65%

Adenomyosis and associated pathologies
- Endometriosis 40-70%
- Adenomyosis
- Leiomyomas 35-55%
Adenomyosis and endometriosis

Adenomyosis
- Hyperestrogenic state
- Progesterone receptors alteration
- Chronic inflammation
- Cytokines
- Growth factors

Endometriosis

Pathogenesis of adenomyosis: different mediators

- Pain
- Progesterone
- UCN
- Activin A
- CRH
- IL-1β
- VEGF
- TGF-β
- COX-1
- COX-2
- NGF
- SYN
- CRHR-2
- MMP-2
- MMP-9
- Myostatin
- Myostatin
- Activin A
- follistatin
- Desmin
- Collagen
- Vimentin
- TUN
- CRH
- IL-1β
- Follistatin
- Myostatin
- MMP-2
- MMP-9

Adenomyosis classification

- Musa Statement 2016
- Int J Gynaecol Obstet. 2018

Adenomyosis and endometriosis
- Similar pathogenesis

Imaging

TVS
- High diagnostic accuracy

Adenomyosis and risk factors

- Age between 35-50 years
- Short menstrual cycles (≤24 days in length)
- Multiparity

Adenomyosis features in young nulliparous women and adolescent

- Myometrial hyperechoic areas, uterine wall asymmetry, intramyometrial cystic areas and some types of junctional zone (JZ) alterations.
- Association with dysmenorrhea, dyspareunia and heavy menstrual bleeding.

Adenomyosis and endometriosis

- Young age <30 years
- Nulliparity
- Uterine women 18-40 years
- 33.9% of women showed diffuse adenomyosis features

Adenomyosis and endometriosis

- Young women with endoscopic features of adenomyosis
- Presence of different forms of adenomyosis
- Association with dysmenorrhea, dyspareunia and heavy menstrual bleeding

Adenomyosis classification

- Musa Statement 2016
- Int J Gynaecol Obstet. 2018
Diffuse adenomyoma

MILD, MODERATE or SEVERE disease?

Fertility and Sterility 2018

50 women with adenomyosis

Score 1-3 mild

Score 4-6 moderate

Score >7 severe

Score 4 for DIFFUSE adenomyosis is associated with higher level of dysmenorrhea and heavy menstrual bleeding

108 patients

FOCAL adenomyosis was found in younger women with high percentage of infertility

FOCAL JZ alteration is associated with heavy menstrual bleeding

No correlation to symptoms when classifying the extension of the diseases inside the uterus as mild, moderate, and severe.

Management of adenomyosis

Medical treatment

Non surgical alternatives

Surgery

Adenomyosis and progestin

MPA

100 mg medroxyprogesterone (MPA) daily

Reduced symptoms up to 12 months of follow-up compared with placebo

Significantly more cases of side effect, such as acne and edema

Vaginal 2.5 mg per day

Pain relief and satisfaction with treatment after 1 year

The efficacy seems to be more gradual, but progressively better with a longer duration of use

Effective and long-term method in alleviating dysmenorrhea and bleeding

Sheng J et al, Contraception 2009


Ferrero S, Remorgida V, Venturini PL. Endometriosis. Clin Evid (Online) 2010
Adenomyosis and Medical Treatment

LNG-IUS reduced dysmenorrhea and bleeding, and overall satisfaction was high.

Dueholm / Best Practice & Research Clinical Obstetrics and Gynaecology 51 (2018)

After 6 months NETA treatment

Before treatment

After 18 months treatment

Recurrence of menorrhagia

Laparoscopic hysterectomy

Diagnosis: Medical treatment

3 months Ulipristal

Ulipristal acetate therapy increases ultrasound features of adenomyosis: a good treatment given in an erroneous diagnosis of uterine fibroids.

Treatment was performed by ultrasound-guided aspiration of adenomyotic uterine lesions.

Desire of pregnancy...
Infertility

- Altered uterine receptivity
- Reduced fertility
- Increased oxidative stress
- Abnormal endometrial function

Adenomyosis and infertility

- Adenomyosis was associated with a 28% reduction in the likelihood of clinical pregnancy in infertile women who underwent IVF/ICSI with autologous oocytes.
- Adenomyosis was associated with a more than doubled risk of miscarriage.

Pre-operative diagnosis

- Leiomyoma
- Adenomyoma

Adenomyosis and infertility

- Increasing frequency in women attending infertility clinics for patients who wish to preserve their fertility, conservative surgery has been proposed.

Adenomyosis and infertility

- The treatment for severe adenomyosis has usually been because there is no line of demarcation between diseased and normal tissue.
The adenomyotic tissues are radically excised and the uterine wall is reconstructed to prevent uterine rupture in subsequent pregnancies. The procedure resulted in a dramatic reduction in symptoms and allowed to conceive without uterine rupture.

- Nishida M et al, Fertil Steril 2010
- Kinoshita K et al, J Minim Invasive Gynecol. 2006

The pregnancy rates after conservative surgical treatment vary widely. Case–control study including 104 case (MRI or TVS) and 208 control women with adenomyosis were associated with significantly increased risk of preterm delivery and PPROM.

- BJOG 2007

Adenomyosis and preterm birth:
- women with adenomyosis were associated with significantly increased risk of spontaneous preterm delivery and PPROM
- myometrial contractility increased uterine pressure inflammatory biochemical pathways

Adenomyosis and preterm delivery:
- women with adenomyosis were associated with significantly increased risk of preterm delivery than control group

Who will benefit from uterus-sparing surgery in adenomyosis-associated subfertility?
- age as a determinant in fertility outcomes. Surgery could be a beneficial treatment for women who experienced HF treatment failures, especially at age ≤ 39 years. We could not show a clear benefit of the surgery on fertility outcomes of the group aged 40 years.
case–control study including 38 case (MRI or TVS) and 144 control nulliparity, pregnancy achieved by fertility treatments, painful menstruation and menorrhagia were significantly higher in the adenomyosis group as compared with the control group. The rates of preterm delivery, SGA, and fetal malpresentation were higher in the adenomyosis than in the control group, showing uterine adenomyosis to be associated with poor pregnancy outcomes.

Pathophysiologic mechanism by which adenomyosis predisposes to postpartum haemorrhage and other obstetric complications

The possible role of paracervical zone infiltration

The possible role of micrometastasis

The possible role of inflammatory mediators on FMH in adenomyosis

The possible role of extraprostatic contusion

References

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Adverse pregnancy outcomes associated with adenomyosis with uterine enlargement

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Image Based Surgery for Uterine Fibroids

John C. Petrozza, M.D.
Chief, Division of Reproductive Medicine & IVF
Co-Director, MGH Integrated Fibroid Program
Massachusetts General Hospital
Harvard Medical School
Immediate Past President, Society of Reproductive Surgeons

Objectives

• Understand 2-Dimensional MRI
• Appreciate 3-Dimensional MRI
• Describe 3-Dimensional printing
• Evaluate Laparoscopic ultrasonography
• Understand Transrectal ultrasonography
• Appreciate artificial intelligence based imaging

Pre-Operative Evaluation

• Mapping fibroids is key to deciding surgical approach
• Fibroid "recurrence" is 51% – 62%
  • Higher in patients with multiple fibroids
  • Small or undetected myomas not removed

Pre-Operative Imaging

• Ultrasound
  • Accuracy decreases with large uteri and multiple myomas
  • Accuracy decreases with increased BMI
  • Operator dependent
  • High interobserver variability
• CT Scan
  • Poor soft tissue mass discrimination
• MRI
  • Excellent for large masses
  • Excellent contrast between different tissue types

Disclosure

• Hologic, Inc. (Consultant)
3-Dimensional MRI


- Korean survey (2019):
  - 61% use MRI for infertile patients
  - 19% use MRI for non-infertile patients
  - 100% have experienced inadvertent entry into uterine cavity
  - 89% have found (post-op imaging) fibroids they missed during surgery
  - 78% preferred 3D-MRI compared to conventional MRI

3-Dimensional Printing


Photo courtesy of GyneSim
Laparoscopic Ultrasound

- Used in liver tumor resection, bile duct detection, pelvic lymphadenectomy, TOAs
- Inserted through 10mm trocar
- Uses higher frequency transducer (7.5 – 10.0MHz)
- Excellent potential for detecting non-visible myomas

Transrectal Ultrasound

Summary

- Pre-Operative MRI has several advantages:
  - Maps fibroids
  - Best tool to date to screen for abnormal uterine fibroids
  - 3D MRI is easy to implement and provides unique imaging that may enhance surgical mapping
  - 3D printing is a rapidly developing technology that will improve education, training, and pre-operative surgical training
- Laparoscopic and transrectal ultrasound are 2 modalities that can improve myomectomy outcomes and enhance removal of all fibroids

Artificial Intelligence

References

- Sun S, et al. Diag Interv Radiol 2019; ePub
Fertility Conserving Surgery for Symptomatic Fibroids

John C. Petrozza, MD
Chief, Division of Reproductive Medicine & IVF
Co-Director, MGH Integrated Fibroid Program
Massachusetts General Hospital
Harvard Medical School
Immediate Past President, Society of Reproductive Surgeons

Objectives

- Understand the current recommendations for managing fibroids in the infertile woman
- Review the data that supports these recommendations
- Discuss surgical techniques
- Reinforce the need for maintain surgical skills

Pathogenesis

- Increased uterine contractility
- Increased endometrial cytokines
- Lower levels of E-cadherin
- No differences in endometrial expression markers and gene expression
  - > 4.0 cm
  - FIGO 3 >= 2.0 cm
  - Abnormal vascularization
  - Chronic endometritis
- Wingless type (WNT)/ß-catenin pathway via MED12, associated with TGF-ß3 and cellular proliferation and BMP-2 mediation of HOXA-10 expression
  - Reduced HOXA-10 associated with defective decidualization

Current Recommendations:

Remove fibroids if they are symptomatic
What are symptoms (ACOG, 2019):
- Changes in menstruation
- Pain
- Pelvic pressure causing bowel and bladder symptoms
- Enlarged uterus and symptoms
- Miscarriages
- Infertility
But wait….is infertility not a symptom?

- American Society of Reproductive Practice Committee (2017):
  - In asymptomatic (infertile) women with fibroids distorting the cavity, myomectomy should be considered.
  - Myomectomy is not advised in asymptomatic infertile women with other fibroids except in special circumstances.

Fertility and Sterility 2017; 108(3): 416-425

Limitations of Prior Studies

- Different diagnostic modalities
- No consistency with fibroid location, size or number
- No mention if fibroids left behind
- Too homogenous of a population
- No control group (infertile with fibroids)
- Too few patients
- Inconsistencies with surgical techniques
- Surgeries done by skilled physician – not generalizable

Randomized Controlled Trials

**Myomectomy Outcomes**


<table>
<thead>
<tr>
<th>Location</th>
<th>Treatment</th>
<th>No. of Patients</th>
<th>No. of Preg</th>
<th>Preg Rate (%)</th>
<th>P Value</th>
<th>SAB Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM</td>
<td>Surgery</td>
<td>30</td>
<td>22</td>
<td>33.3</td>
<td>&lt;0.05</td>
<td>38.5</td>
</tr>
<tr>
<td></td>
<td>No surgery</td>
<td>22</td>
<td>6</td>
<td>27.2</td>
<td></td>
<td>50.0</td>
</tr>
<tr>
<td>IM</td>
<td>Surgery</td>
<td>23</td>
<td>13</td>
<td>56.5</td>
<td>NS</td>
<td>30.8</td>
</tr>
<tr>
<td></td>
<td>No surgery</td>
<td>22</td>
<td>9</td>
<td>40.9</td>
<td></td>
<td>33.3</td>
</tr>
<tr>
<td>SS</td>
<td>No surgery</td>
<td>11</td>
<td>7</td>
<td>63.6</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>IM-SS</td>
<td>Surgery</td>
<td>17</td>
<td>6</td>
<td>35.3</td>
<td>NS</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>No surgery</td>
<td>14</td>
<td>3</td>
<td>21.4</td>
<td></td>
<td>66.6</td>
</tr>
<tr>
<td>IM-SM</td>
<td>Surgery</td>
<td>22</td>
<td>8</td>
<td>36.4</td>
<td>&lt;0.05</td>
<td>50.0</td>
</tr>
<tr>
<td></td>
<td>No surgery</td>
<td>20</td>
<td>3</td>
<td>15.0</td>
<td></td>
<td>66.6</td>
</tr>
</tbody>
</table>

**Intramural Fibroids Effect on Fertility**


<table>
<thead>
<tr>
<th>Outcome</th>
<th># Studies</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clin Preg Rate</td>
<td>12</td>
<td>0.810</td>
<td>0.696-0.941</td>
<td>P = 0.06</td>
</tr>
<tr>
<td>Ongoing/LBR</td>
<td>3</td>
<td>0.705</td>
<td>0.505-0.946</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>SAB Rate</td>
<td>8</td>
<td>1.747</td>
<td>1.236-2.489</td>
<td>P = 0.006</td>
</tr>
<tr>
<td>Prospective studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clin Preg Rate</td>
<td>3</td>
<td>0.708</td>
<td>0.417-1.246</td>
<td>NS</td>
</tr>
<tr>
<td>Ongoing/LBR</td>
<td>2</td>
<td>0.465</td>
<td>0.290-0.764</td>
<td>P = 0.019</td>
</tr>
<tr>
<td>SAB Rate</td>
<td>2</td>
<td>2.384</td>
<td>1.110-5.222</td>
<td>P = 0.002</td>
</tr>
</tbody>
</table>

Insufficient Evidence or Lack of RCTs

- "Absence of evidence is not evidence of absence."
- RCTs are perceived to yield causal inferences and estimates of average treatment effects with limited bias – the "Gold Standard."
- RCTs do not equate every study other than treatments in control and treatment groups.
- Often it is not generalizable.
- Too many are underpowered.
- Often not validated.
- Often not "intention-to-treat."
- Prior knowledge should be built upon to not only understand "what works," but "why things work."
Intramural Fibroids
Effect of Myomectomy on Fertility (fibroids in situ controls)

<table>
<thead>
<tr>
<th>Outcome</th>
<th># Studies</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clin Preg Rate</td>
<td>2</td>
<td>3.765</td>
<td>0.470-30.136</td>
<td>NS</td>
</tr>
<tr>
<td>Ongoing Preg/LBR</td>
<td>1</td>
<td>1.671</td>
<td>0.750-3.723</td>
<td>NS</td>
</tr>
<tr>
<td>SAB Rate</td>
<td>1</td>
<td>0.758</td>
<td>0.296-1.943</td>
<td>NS</td>
</tr>
</tbody>
</table>


FIGO 3 Fibroids

• >= 2.0 cm
• Retrospective cohort study
• 151 pts / 453 matched controls
• IVF/ICSI
• Results (all significant):
  • Biochemical preg 29% vs 51%
  • Implantation 23% vs 34%
  • Clinical preg 28% vs 44%
  • LBR 21% vs 34%

Yan et al, Fertil Steril, 2018

Sonohysterogram
Submucosal Fibroid & Polyp

Fibroid Management
Asymptomatic, Infertile Patient
  • Subserosal (FIGO 6-7) – leave alone
  • Submucosal (FIGO 0-2) – myomectomy
  • Intramural (FIGO 3-5) - ?
    • Treat them before ART
    • Treat them after pre-determined number of failed cycles
    • Treat them after a miscarriage
    • Treat them after an adverse obstetrical outcome
    • Treat them if patient is >35 years of age
    • Treat if > 4.0 cm
    • Treat if FIGO 3 >= 2.0 cm

Laparoscopic Radiofrequency Ablation

MRI
Hysteroscopic Radiofrequency Ablation

- End-point is blood loss

<table>
<thead>
<tr>
<th>Month Post-Treatment</th>
<th>Mean Pictoral Blood Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39%</td>
</tr>
<tr>
<td>6</td>
<td>48%</td>
</tr>
<tr>
<td>12</td>
<td>51%</td>
</tr>
</tbody>
</table>

Mean maximal fibroid volume reduction 62%


Laparoscopic Myomectomy

Laparoscopic Myomectomy

Uterine Scars
1 Week Post-Myomectomy

Post-Myomectomy Isthmocele Repair

Hysteroscopic Morcellation

Myoma bud closure - 2 layers of interrupted absorbable suture

BAD!!

GOOD!!
Hysteroscopic Myomectomy

References

- Oliveira et al, Fertil Steril 2004
- Horcajada et al, JCEM 2008
- Aghajanova et al, Biol Reprod 2017
- Horcajada JA et al, JCEM 2008; 93:3490-3498
- Levens ED, Fertil Steril 2008;89(A):1025-7
Assembly Bill 1195 was signed into law on July 1, 2006 requiring local CME providers, such as the AAGL, to assist in enhancing the cultural and linguistic competency of California’s physicians (researchers and doctors without patient contact are exempt). This mandate follows the federal Civil Rights Act of 1964, Executive Order 13166 (2000) and the Dymally-Alatorre Bilingual Services Act (1973), all of which recognize, as confirmed by the US Census Bureau, that substantial numbers of patients possess limited English proficiency (LEP). It is the intent of the Legislature to encourage physicians and surgeons, continuing medical education providers located in California, and the Accreditation Council for Continuing Medical Education to meet the cultural and linguistic concerns of a diverse patient population through appropriate professional development.

Linguistic Competence: Providing readily available, culturally appropriate oral and written language services to limited English proficiency (LEP) members through such means as bilingual/bicultural staff, trained medical interpreters, and qualified translators.

Cultural Competence: A set of congruent behaviors, attitudes, and policies that come together in a system or agency or among professionals that enables effective interactions in a cross-cultural framework.1

Cultural and Linguistic Competence: The ability of health care providers and health care organizations to understand and respond effectively to the cultural and linguistic needs brought by the patient to the health care encounter.

Cultural competence requires organizations and their personnel to:
• Value diversity.
• Assess themselves.
• Manage the dynamics of difference.
• Acquire and institutionalize cultural knowledge.
• Adapt to diversity and the cultural contexts of individuals and communities served.

California Business & Professions Code §2190.1(c)(3) states that associations that accredit continuing medical education courses shall develop standards before July 1, 2006, for compliance with the cultural competency requirements. The associations may update these standards, as needed, in conjunction with an advisory group that has expertise in cultural and linguistic competency issues. Cultural competency means a set of integrated attitudes, knowledge, and skills that enables a health care professional or organization to care effectively for patients from diverse cultures, groups, and communities. At a minimum, cultural competency is recommended to include the following: (A) Applying linguistic skills to communicate effectively with the target population. (B) Utilizing cultural information to establish therapeutic relationships. (C) Eliciting and incorporating pertinent cultural data in diagnosis and treatment. (D) Understanding and applying cultural and ethnic data to the process of clinical care, including, as appropriate, information pertinent to the appropriate treatment of, and provision of care to, the lesbian, gay, bisexual, transgender, and intersex communities.

Title VI of the Civil Rights Act of 1964 prohibits recipients of federal financial assistance from discriminating against or otherwise excluding individuals on the basis of race, color, or national origin in any of their activities. In 1974, the US Supreme Court recognized LEP individuals as potential victims of national origin discrimination. In all situations, federal agencies are required to assess the number or proportion of LEP individuals in the eligible service population, the frequency with which they come into contact with the program, the importance of the services, and the resources available to the recipient, including the mix of oral and written language services. Additional details may be found in the Department of Justice Policy Guidance Document: Enforcement of Title VI of the Civil Rights Act of 1964 http://www.usdoj.gov/crt/cor/pubs.htm.

Executive Order 13166, "Improving Access to Services for Persons with Limited English Proficiency", signed by the President on August 11, 2000 http://www.usdoj.gov/crt/cor/13166.htm was the genesis of the Guidance Document mentioned above. The Executive Order requires all federal agencies, including those which provide federal financial assistance, to examine the services they provide, identify any need for services to LEP individuals, and develop and implement a system to provide those services so LEP persons can have meaningful access.

Dymally-Alatorre Bilingual Services Act (Assembly Bill 305) requires that state agencies that serve a substantial number of non-English-speaking people employ a sufficient amount of bilingual persons in order to provide certain information and render certain services in a language other than English.