Fertility effects of ovarian tissue loss in endometrioma excision

Techniques to minimize the impact

Edgardo D. Rolla M.D.

Vice President – Sociedad Argentina de Endometriosis
Ambassador – World Endometriosis Society
Expert – The 2011 Montpellier Consensus on the Management of Endometriosis
Member of the Board – Sociedad Argentina de Cirugia Laparoscópica

Techniques to minimize the impact

Current known procedures

Cystectomy with careful disection of cyst wall

Incision % drainage

- & monopolar coag. of inner capsule
- & bipolar coag. of inner capsule
- & laser cauterization of inner caps.

Techniques to minimize the impact

New proposals

Partial excision and laser ablation (Donnez)

Incision, drainage, eversion and plasma ablation (Roman)

Techniques to minimize the impact

To keep in mind

Time has to be taken in order to identify the correct disection plane in order to avoid resection of surrounding follicular tissue

Coagulation of bleeding vessels after cystectomy should be done with care, one by one, with controlled bipolar coagulation or laser – specially at the hilus

Techniques to minimize the impact

To keep in mind

Electric coagulation of cyst wall is to be done only with controlled bipolar coagulator, superficially

Laser ablation must be done superficially

Evidence supporting IVF for endo patients

ESHRE GUIDELINES

Evidence level 1b

High quality

Laparoscopic ovarian cystectomy in patients with unilateral endometriomas between 3 and 6 cm in diameter before IVF/ICSI can decrease ovarian response without improving cycle outcome (Demirol et al., 2006).

Evidence supporting IVF for endo patients

ESHRE GUIDELINES

Laparoscopic ovarian cystectomy in patients with unilateral endometriomas between

3 and 6 cm in diameter

before IVF/ICSI can decrease ovarian response without improving cycle outcome

Evidence supporting IVF for endo patients

ESHRE GUIDELINES

GCP

Very low quality

Laparoscopic ovarian cystectomy is recommended if an ovarian endometrioma ≥ 4 cm in diameter is present to confirm the diagnosis histologically; reduce the risk of infection; improve access to follicles and possibly improve ovarian response. The woman should be counseled regarding the risks of reduced ovarian function after surgery and the loss of the ovary. The decision should be reconsidered if she has had previous ovarian surgery.

Evidence supporting IVF for endo patients

ESHRE GUIDELINES

Laparoscopic ovarian cystectomy is recommended if an ovarian endometrioma

≥ 4 cm in diameter

is present to:
- **confirm the diagnosis histologically**
- **reduce the risk of infection**
- **improve access to follicles**
- **possibly improve ovarian response**

The woman should be counseled regarding the risks of reduced ovarian function after surgery and the loss of the ovary

The decision should be reconsidered if she has had previous ovarian surgery.

Endometrioma Excision and Ovarian Reserve: A Dangerous Relation

·Mauro Busacca, MD Michele Vignali, MD
• Department of Obstetrics and Gynecology, University of Milano, Via Macedonio Melloni, 52, 20122 Milano, Italy.

Endometrioma is one of the most frequent pathologies in gynecologic surgery

Laparoscopic cyst excision is considered the best treatment in terms of lower recurrence and improved fertility

Question:

Is the ovarian tissue unintentionally removed functionally normal?

Endometrioma Excision and Ovarian Reserve: A Dangerous Relation

·Mauro Busacca, MD Michele Vignali, MD
• Department of Obstetrics and Gynecology, University of Milano, Via Macedonio Melloni, 52, 20122 Milano, Italy.

Endometrioma is one of the most frequent pathologies in gynecologic surgery

Laparoscopic cyst excision is considered the best treatment in terms of lower recurrence and improved fertility

Answer:

No. It does not show the follicular pattern observed in working ovaries

Endometrioma Excision and Ovarian Reserve: A Dangerous Relation

•Mauro Busacca, MD Michele Vignali, MD
• Department of Obstetrics and Gynecology, University of Milano, Via Macedonio Melloni, 52, 20122 Milano, Italy.

Currently, no definitive data clarify whether the damage to the ovarian reserve, observed in patient with endometrioma, is related to the surgical procedure, to the previous presence of the cyst, or both

Endometrioma Excision and Ovarian Reserve: A Dangerous Relation

·Mauro Busacca, MD Michele Vignali, MD
• Department of Obstetrics and Gynecology, University of Milano, Via Macedonio Melloni, 52, 20122 Milano, Italy.

Electrosurgial coagulation during hemostasis could play an important role in terms of damage to ovarian stroma and vascularization

Fertility and Sterility

The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis

Ioanna Tsoumpou, Maria Kyrgiou,, Tarek A. Gelbaya August 2008

Department of Reproductive Medicine, St. Mary's Hospital, Central Manchester and Manchester Children's University Hospitals, Manchester, United Kingdom

20 eligible publications between January 1985 and November 2007 yielded five studies admitted for a meta-analysis comparing

surgery vs. no treatment

of endometrioma previous to IVF

Fertility and Sterility®

The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis

Ioanna Tsoumpou, Maria Kyrgiou,, Tarek A. Gelbaya August 2008

Department of Reproductive Medicine, St. Mary's Hospital, Central Manchester and Manchester Children's University Hospitals, Manchester, United Kingdom

The following isues were considered →

Clinical pregnancy rate

Ovarian response to gonadotrophins: number of gonadotrophin ampoules
peak E_2 levels
number of oocytes retrieved

Number of embryos available for transfer

Fertility and Sterility

The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis

Ioanna Tsoumpou, Maria Kyrgiou,, Tarek A. Gelbaya August 2008

Department of Reproductive Medicine, St. Mary's Hospital, Central Manchester and Manchester Children's University Hospitals, Manchester, United Kingdom

There was no significant difference in clinical pregnancy rate between the treated and the untreated groups.

No significant difference was found between the two groups with regard to the outcome measures used to assess the response to controlled ovarian hyperstimulation with gonadotrophins.

Fertility and Sterility

Effects of ovarian endometrioma on the number of oocytes retrieved for in vitro fertilization

Benny Almog, Fady Shehata, Boaz Sheizaf, Seang Lin Tan, Togas Tulandi

April 2010

Department of Obstetrics and Gynecology, McGill Reproductive Center, McGill University Health Center, Montreal, Quebec, Canada

Retrospective cohort study

81 women with unilateral endometrion … first IVF cycle

There was no significant difference ir … follicles and oocytes retrieved

…..but there was a difference

	Ovary with endometrioma	Ovary with no endometrioma	*P* value	95% Confidence interval
No. of antral follicles	7.7 ± 1.0	8.5 ± 0.9	.3	−1.0 to 3.0
No. of retrieved oocytes	6.0 ± 0.4	6.1 ± 0.5	.8	−1.0 to 1.0
No. of retrieved oocytes when endometrioma size >25 mm	5.8 ± 1.4	6.6 ± 1.1	.5	−4.0 to 2.0

Table 1. Number of antral follicles and retrieved oocytes from endometrioma-containing ovaries and from the contralateral ovaries

Fertility and Sterility

Effects of ovarian endometrioma on the number of oocytes retrieved for in vitro fertilization

Benny Almog, Fady Shehata, Boaz Sheizaf, Seang Lin Tan, Togas Tulandi

April 2010

Department of Obstetrics and Gynecology, McGill Reproductive Center, McGill University Health Center, Montreal, Quebec, Canada

Whether an endometrioma should be removed before IVF is a frequently asked question

Several authors previously demonstrated that excision of ovarian endometrioma is associated with reduced ovarian reserve as expressed by a reduced number of retrieved oocytes

This could be due to inadvertent removal of healthy cortical tissue, thermal injury, local inflammation, or scarring

Donnez showed that treatment of ovarian endometrioma with fenestration and coagulation was less deleterious to the ovarian function. However, fenestration and coagulation is associated with a higher risk of recurrence than excision

Fertility and Sterility

Ovarian endometrioma ablation using plasma energy versus cystectomy: a step toward better preservation of the ovarian parenchyma in women wishing to conceive

October 2011

•Horace Roman, **Mathieu Auber, Cécile Martin, Alain Diguet, Loïc Marpeau, Nicolas Bourdel**

•Department of Gynecology and Obstetrics, Rouen University Hospital-Charles Nicolle, Rouen, France
•Research Group 4308 Spermatogenesis and Gamete Quality, IHU Rouen Normandy, IFRMP23,
•Reproductive Biology Laboratory, Rouen University Hospital, Rouen, France

Retrospective study including 30 patients with endometriomas >30 mm

	Plasma energy (15)	Cystectomy (15)	
Volume of nonoperated ovary (mL)	7 ± 2.7	8.8 ± 4.2	.15
Volume of operated ovary (mL)	5.2 ± 2.5	3 ± 1.6	.007
Ratio of the volume operated/nonoperated ovary	0.79 ± 0.26	0.35 ± 0.17	<.001
AFC of nonoperated ovary	6.8 ± 3.5	8 ± 5.3	.47
AFC of operated ovary	5.5 ± 3.9	2.9 ± 2.4	.03
Ratio of the AFC of operated/nonoperated ovary	0.83 ± 0.31	0.33 ± 0.25	<.001

Table 1. Patient characteristics and results of three-dimensional ultrasound examination

Fertility and Sterility

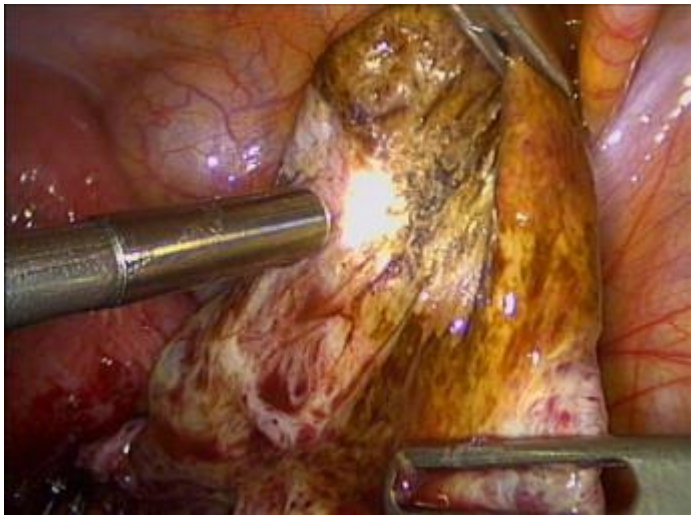
Ovarian endometrioma ablation using plasma energy versus cystectomy: a step toward better preservation of the ovarian parenchyma in women wishing to conceive

October 2011

•Horace Roman,**Mathieu Auber, Cécile Martin, Alain Diguet, Loïc Marpeau, Nicolas Bourdel**

•Department of Gynecology and Obstetrics, Rouen University Hospital-Charles Nicolle, Rouen, France
•Research Group 4308 Spermatogenesis and Gamete Quality, IHU Rouen Normandy, IFRMP23,
•Reproductive Biology Laboratory, Rouen University Hospital, Rouen, France

Retrospective study including 30 patients with endometriomas >30 mm



Fertility and Sterility.

Ovarian cystectomy versus laser vaporization in the treatment of ovarian endometriomas: a randomized clinical trial with a five-year follow-up

May 2011

Francisco Carmona•M. Angeles Martínez-Zamora, Aintzane Rabanal, Sergio Martínez-Román, Juan Balasch,

Institut Clínic de Ginecologia, Obstetrícia i Neonatologia, Hospital Clínic de Barcelona, Villarroel

Prospective randomized clinical trial

Five year follow up

	Cystectomy (36)	Drainage and laser (38)	
Recurrence at 12 mo			
Per patient	4/36 (11)	12 (31)	.04
Per endometrioma	4/44 (9)	4/50 (8)	.1
Recurrence at 60 mo			
Per patient	8 /36 (22)	14/38 (37)	.2
Per endometrioma	8/44 (18)	14/50 (28)	.4
Time of recurrence (mo)	18.1 ± 10.1	7.5 ± 4.3	<.003

Larger recurrence

Shorter time

Table 2. Surgical characteristics, follow-up, and sonographic recurrence rate of the two groups of patients ovarian endometriomas

Laparoscopic stripping of endometriomas: a randomized trial on different surgical techniques. Part II: pathological results

Ludovico Muzii, Filippo Bellati, Antonella Bianchi, Innocenza Palaia, Natalina Manci, Marzio Angelo Zullo, Roberto Angioli, Pierluigi Benedetti Panici

February, 2005

Department of Obstetrics and Gynaecology, University Campus Bio-Medico of Rome

Prospective randomized trial comparing different surgical approaches:

Two techniques were used at the adhesion site:

- Circular excision and subsequent stripping
- Immediate stripping

Two techniques at the ovarian hilus:

- stripping
- Coagulation and cutting

Laparoscopic stripping of endometriomas: a randomized trial on different surgical techniques. Part II: pathological results

Ludovico Muzii, Filippo Bellati, Antonella Bianchi, Innocenza Palaia, Natalina Manci, Marzio Angelo Zullo, Roberto Angioli, Pierluigi Benedetti Panici

Department of Obstetrics and Gynaecology, University Campus Bio-Medico of Rome

February, 2005

Prospective randomized trial comparing different surgical approaches:

Pathological data		Direct stripping (24 patients)		Circular excision (24 patients)		*P*
Tissue thickness Specimen 1 (mean±SD) [mm]		1.0±0.4		1.4±0.4		<0.05
Presence of ovarian tissue Specimen 1		12 (50%)		19 (79%)		N.S.
Ovarian tissue Specimen 1(G)						
Ovarian tissue quality	0	5	21%	9	37%	N.S.
	1	6	25%	9	37%	
	2	0	0	0	0	
	3	0	0	1	4%	
	4	1	4%	0	0	

Thicker tissue removed

Few cases with normal ovarian tissue

G=Grade 0, complete absence of follicles; 1, primordial follicles only; 2, primordial and primary follicles; 3, some secondary follicles; 4, pattern of primary and secondary follicles as seen in the normal ovary (Maneschi *et al.*, 1993).

Laparoscopic stripping of endometriomas: a randomized trial on different surgical techniques. Part II: pathological results

Ludovico Muzii, Filippo Bellati, Antonella Bianchi, Innocenza Palaia, Natalina Manci, Marzio Angelo Zullo, Roberto Angioli, Pierluigi Benedetti Panici

Department of Obstetrics and Gynaecology, University Campus Bio-Medico of Rome

February, 2005

Prospective randomized trial comparing different surgical approaches:

No difference at the hilus

Pathological data **(Hilus)**	Completion with stripping (*n*=24)	Bipolar coagulation and subsequent cutting (*n*=24)	*P*
Tissue thickness Specimen 3 (mean±SD) [mm]	1.6±0.5	1.5±0.6	NS
Presence of ovarian tissue	18 (75%)	16 (67%)	NS
Ovarian tissue thickness (mean±SD) [mm]	0.72±0.29	0.82±0.42	NS

The Vasopressin Injection Technique for Laparoscopic Excision of Ovarian Endometrioma: A Technique to Reduce the Use of Coagulation

Ai Saeki, MD, Takashi Matsumoto, MD, Kenichiro Ikuma, MD, Yasuhito Tanase, MD, Fujiyuki Inaba, MD, Hisato Oku, MD, Atsushi Kuno, MD

Department of Gynecology, Osaka central hospital, Japan

November, 2009

Prospective randomized study

(1) ordinary laparoscopic cystectomy without injection

(2) laparoscopic cystectomy with the injection of saline solution

(3) laparoscopic cystectomy with the vasopressin injection technique.

The Vasopressin Injection Technique for Laparoscopic Excision of Ovarian Endometrioma: A Technique to Reduce the Use of Coagulation

Ai Saeki, MD, Takashi Matsumoto, MD, Kenichiro Ikuma, MD, Yasuhito Tanase, MD, Fujiyuki Inaba, MD, Hisato Oku, MD, Atsushi Kuno, MD
Department of Gynecology, Osaka central hospital, Japan

November, 2009

Prospective randomized study

The vasopressin injection technique reduces the use of coagulation, in such a way as to suggest the possibility to protect ovarian reserves

Laparoscopic ovarian cystectomy of endometriomas does not affect the ovarian response to gonadotropin stimulation

Marconi G, Vilela M, Quintana R, Sueldo C.
Instituto de Ginecología y Fertilidad, Buenos Aires, Argentina.

October, 2002

Fertility and Sterility.

Retrospective study with prospective selection of participants and controls

39 pts. underwent *atraumatic* cyst removal / minimal bipolar cauterization

39 controls (tubal factor infertility)

Both groups had similar:
- Estradiol levels
- Number of mature follicles
- Number of oocytes retrieved
- Number & quality of embryos
- Clinical pregnancy rate

Laparoscopic ovarian cystectomy of endometriomas does not affect the ovarian response to gonadotropin stimulation

Marconi G, Vilela M, Quintana R, Sueldo C.
Instituto de Ginecología y Fertilidad, Buenos Aires, Argentina.

October, 2002

Fertility and Sterility.

Retrospective study with prospective selection of participants and controls

39 pts. underwent *atraumatic* cyst removal / minimal bipolar cauterization

39 controls (tubal factor infertility)

The only difference was the number of FSH ampoules needed:

Significantly higher in the endometrioma group

Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery

•Jacques Donnez, Jean-Christophe Lousse, Pascale Jadoul, Olivier Donnez, Jean Squifflet

Department of Gynecology, Université Catholique de Louvain, Brussels, Belgium

Fertility and Sterility.

April 2009

Descriptive and prospective study

Combined surgical technique proposed:

A large part of the endometrioma wall was excised according to the cystectomy technique.

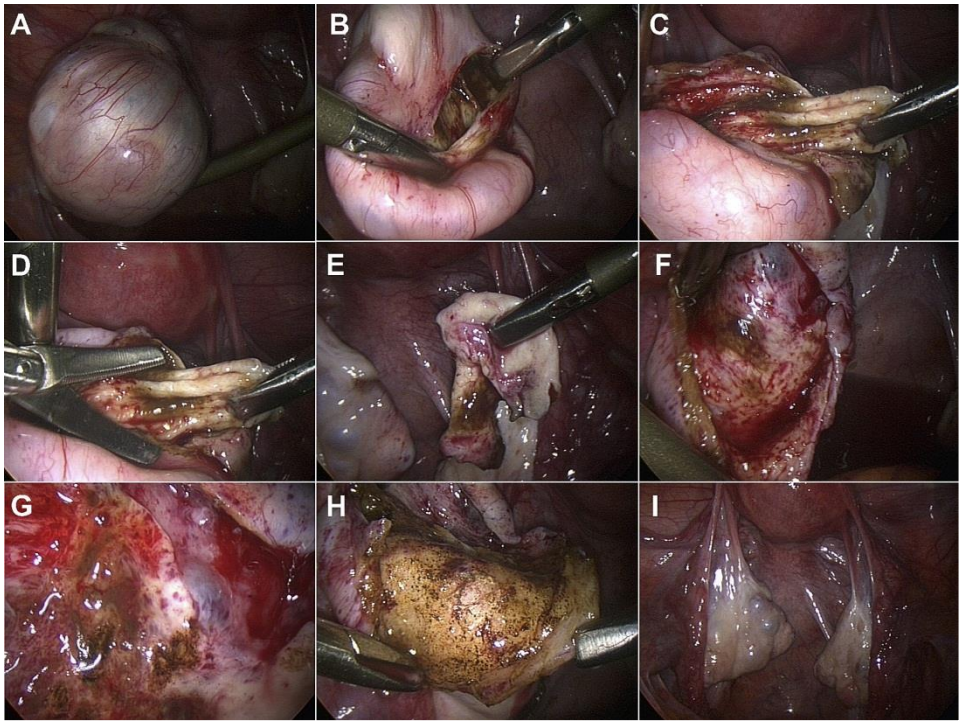
Afterwards CO_2 laser was used to vaporize the remaining 10%–20% of the endometrioma wall close to the hilus.

Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery

•Jacques Donnez, Jean-Christophe Lousse, Pascale Jadoul, Olivier Donnez, Jean Squifflet

Department of Gynecology, Université Catholique de Louvain, Brussels, Belgium

April 2009



Source: Fertility and Sterility 2010; 94:28-32 (DOI:10.1016/j.fertnstert.2009.02.065

Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery

•Jacques Donnez, Jean-Christophe Lousse, Pascale Jadoul, Olivier Donnez, Jean Squifflet

Department of Gynecology, Université Catholique de Louvain, Brussels, Belgium

Fertility and Sterility.

April 2009

Table 1. Ovarian volume and AFC 6 months after surgery in women treated for endometriomas by the combined technique and in women of similar age with normal ovaries and regular ovulatory cycles presenting for IVF because of male factor infertility.

	Ovarian volume (cm^3)	AFC
Combined technique (n = 31)	7.64 ± 2.95	6.1 ± 3.2
Women without endometriosis (n = 20)	7.99 ± 5.33	6.2 ± 4.8

Treated and "normal" patients: no difference

Laparoscopic management of endometriomas using a combined technique of excisional (cystectomy) and ablative surgery

•Jacques Donnez, Jean-Christophe Lousse, Pascale Jadoul, Olivier Donnez, Jean Squifflet

Department of Gynecology, Université Catholique de Louvain, Brussels, Belgium

Fertility and Sterility.

April 2009

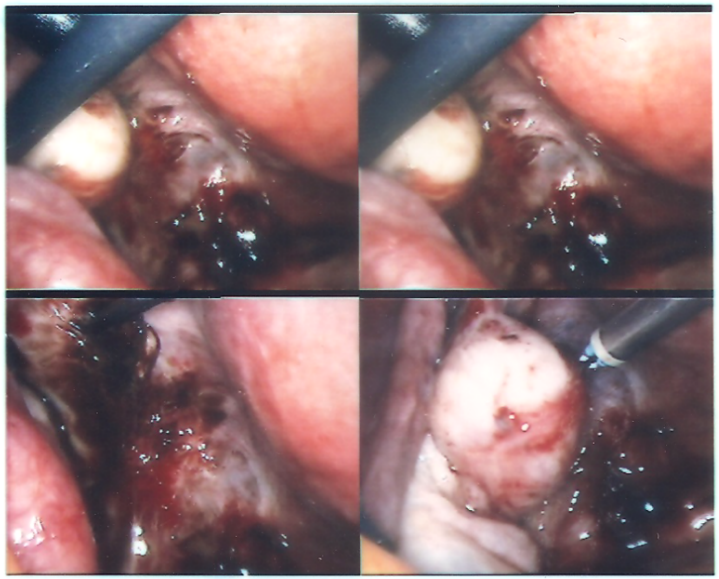
Table 2. Ovarian volume and AFC 6 months after surgery in women with unilateral endometriomas and contralateral normal ovaries serving as controls.

	Ovarian volume (cm^3)	AFC
Combined technique (n = 20)	7.45 ± 2.93	5.5 ± 2.4
Contralateral normal ovaries (n = 20)	7.82 ± 3.91	5.7 ± 1.6

Treated and "normal" ovaries: no difference

But, what are we talking about?

Spontaneous breakage of a severely adherent endometrioma at the time of adhesiolysis previous to cystectomy

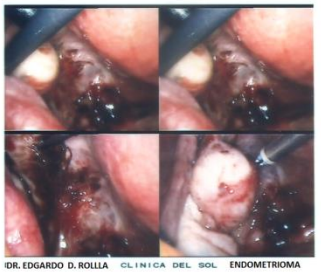


But, what are we talking about?

When the ovary is severely damaged prior to surgery, if done with care and expertise, will the technique make a difference?

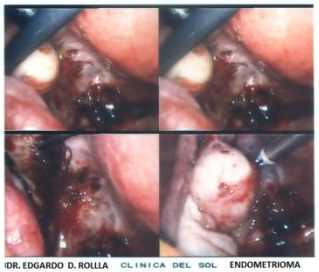
How could we firmly state that the damage was post-op and not pre-op with

EVIDENCE OF HIGH LEVEL?

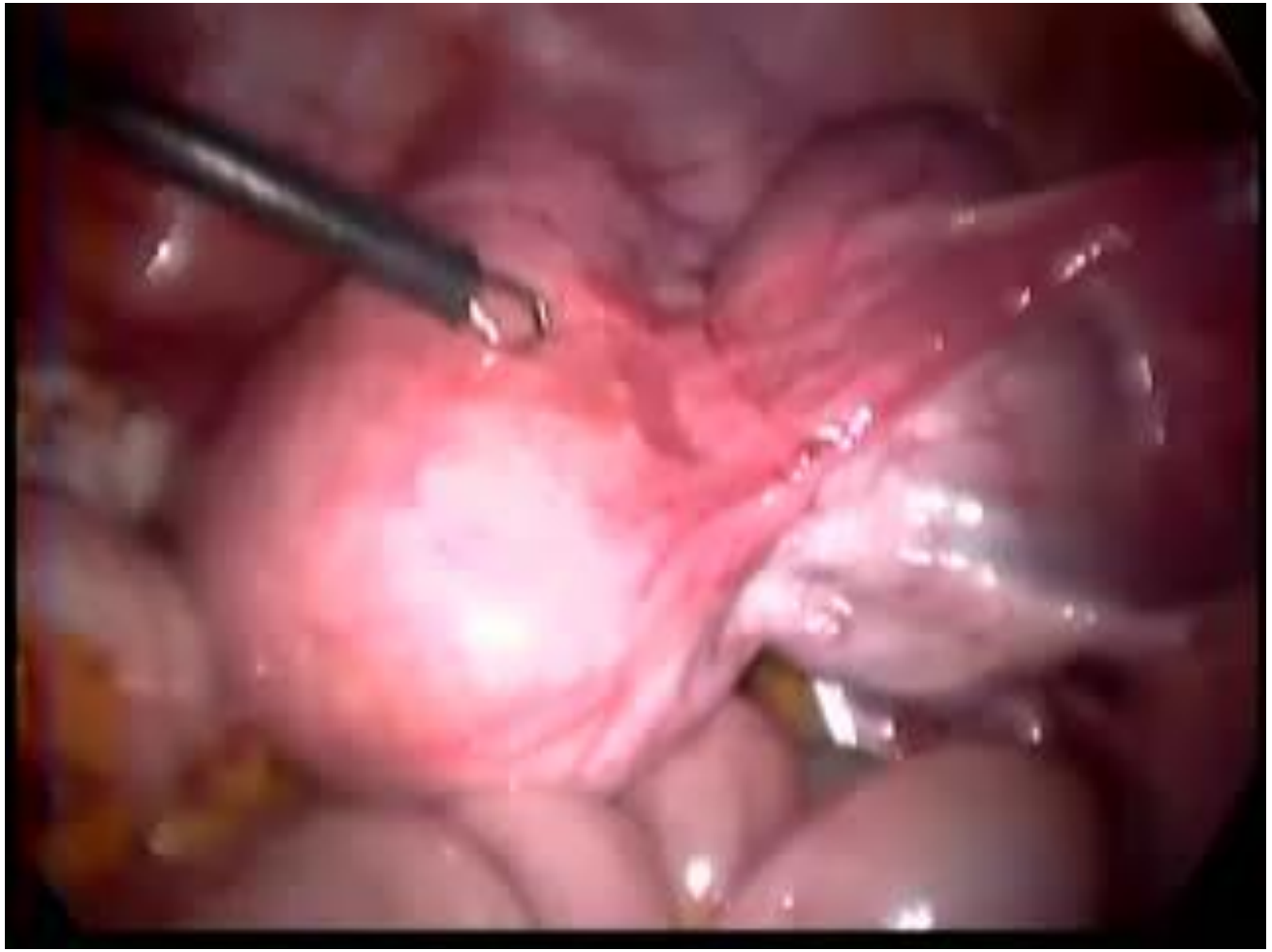


But, what are we talking about?

Shouldn't we classify endometriomas according NOT ONLY *to the size,* BUT ALSO *to the extension of their adhesions in order to make better comparisons before proposing new techniques or evaluate one against others?*



But, what are we talking about?



Is the damage caused by the disease or the surgeon?

That is the question

Othello, the movie

Director:
Oliver Parker
Writers:
William Shakespeare (play), Oliver Parker (adaptation)
Stars:
Laurence Fishburne, Kenneth Branagh and Irène Jacob

Today, I yet cannot tell