

Diagnostic L/S: Is it ever indicated?

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Diagnostic Laparoscopy (DLS)

DLS is the gold standard in diagnosing tubal pathology and other intraabdominal causes of infertility.

DLS was the final diagnostic procedure of any infertility investigation, as outlined by the AFS in 1992 and by the WHO guidelines (1993) .

In 1997, 89% of all reproductive endocrinologists in the USA routinely performed a DLS in the diagnostic work-up of infertility.

Glatstein et al. 1997

Diagnostic Laparoscopy

Identified pathologies with DLS;

Intrinsic tubal disease	3–24%
Peritubal adhesions	18–43%
Endometriosis	up to 43%

DLS have a higher yield in secondary infertility (54%) compared primary infertility (22%) (level III).

Hovav, Y. Et al. J Assist Reprod Genet 1998
Komori, S et al. J Laparoendosc Adv Surg Tech A. 2003
Corson, S. L. Et al. J Am Assoc Gynecol Laparosc 2000
Mol, B. W., Swart, P., Bossuyt, P. M., and van der
Veen, F. J Reprod Med 1999

Diagnostic Laparoscopy

Depending on the severity of the laparoscopic findings, the initial treatment decision, can be changed into;

- ❖ Direct laparoscopic correction of the abnormality
- ❖ Fertility-improving surgery by laparotomy
- ❖ Referral to IVF

Diagnostic Laparoscopy (DLS)

Potential benefits

1. It is possible to avoid fertility treatments and their direct as well as indirect financial and social costs such as multiple gestation pregnancy.
2. Intraoperative findings can guide postsurgical management that are of low benefit and costly.
3. Surgically correcting endometriosis may enhance response to fertility treatments or mitigate the effects of comorbidities such as pelvic pain.

Diagnostic Laparoscopy (DLS)

“Laparoscopy should be seriously considered before applying aggressive empirical treatments involving significant cost and/or potential risks”

Practice Committee of the American Society of Reproductive Medicine.
Fertil Steril 2006

Diagnostic Laparoscopy

Disadvantages of DLS;

- The need for general anaesthesia
- Patient's anxiety
- The possibility of adhesion formation

In a large Finnish follow-up study, the complication rate of diagnostic laparoscopy was 0.6 per 1000 procedures.

Diagnostic Laparoscopy

DLS did not reveal any pathology or only minimal and mild endometriosis in 40–70% of all cases.

Forman et al., 1993, Collins et al., 1995

These findings convinced some authors to challenge the need for this procedure in the work-up of infertility.

Balasz 2000, Fatum et al 2002

The routine use of diagnostic laparoscopy for the evaluation of all cases of female infertility is currently under debate.

Diagnostic Laparoscopy

Recently, there has been a growing tendency to bypass DLS after a normal HSG and instead to start direct infertility treatment [IUI or IVF] in an effort to be cost-effective on the one hand and on the other hand, to protect patients from possible hazards of surgical complications and general anesthesia.

Diagnostic Laparoscopy

Alternative diagnostic methods

Available evidence for detecting tuboperitoneal infertility with respect to alternative diagnostic methods and the position of DLS is still lacking.

Tuboperitoneal Infertility work-up

Alternative diagnostic methods;

- » Medical history
- » Serum Chlamydia screening (CAT)
- » HSG

Tuboperitoneal Infertility work-up

Medical history; predicting tuboperitoneal infertility

	PPV
Based on symptoms suggestive for previous PID	56%
A history of abnormal vaginal discharge	59%
A previous diagnosis of a lower genital tract infection	35%

Tuboperitoneal Infertility work-up

Serum Chlamydia screening (CAT)

- CAT fails to provide information about the extent of tubal pathology which is of significance to further treatment decisions.
- CAT is unable to detect other causes of tubal pathology nor the presence of endometriosis.
- Since endometriosis is more frequently found at laparoscopy than tubal pathology, the use of CAT would be of limited additional value after normal HSG.

Tuboperitoneal Infertility work-up

HSG

The most common screening test for tubal pathology.

According to a meta-analysis;

HSG has a reasonable specificity (83%) but a low sensitivity (65%) to document patency of the Fallopian tubes.

Swart et al., 1995

DLS after Normal HSG

In infertile couples laparoscopy reveals abnormal findings in 21% - 68% of the cases after normal HSG (level III).

Hovav, Y. Et al. J Assist Reprod Genet 1998

Tanahatue, S. Et al. Fertil Steril 2003

Corson SL J Am Assoc Gynecol Laparosc 2000

DLS after Normal HSG

The changed treatment decisions;

- (i) Direct laparoscopic surgery of minimal/mild endometriosis and periadnexal adhesions (20.8%)
- (ii) Open surgery of double sided adhesions, moderate/severe endometriosis and double sided phimosi (2.6%)
- (iii) Referral to IVF due to severe periadnexal adhesions, hydrosalpinx and bilateral tubal occlusions (1.6%)

Should diagnostic laparoscopy be performed after unilateral pathology with HSG

In cases of unilateral pathology diagnosed by HSG;

IVF	13%
Normal or at least one patent tube	57%
Minimal abnormality (endometriosis)	30%

Tanahatoc et al. RBM Online 2008

Should laparoscopy be a mandatory component of the infertility evaluation in infertile women with normal hysterosalpingogram or suspected unilateral distal tubal pathology?☆

Yuval Lavy*, Ahinoam Lev-Sagie, Hananel Holtzer, Ariel Revel, Arye Hurwitz

Laparoscopic findings in relation to HSG results

Laparoscopic findings	HSG findings			
	Normal	Unilateral occlusion	Bilateral occlusion	Total
Normal	34	19	1	54
Unilateral occlusion	4	1	6	11
Bilateral occlusion	1	2	16	19
Pelvic adhesions	2	0	0	2
Total	41	22	23	86

91%

Should laparoscopy be a mandatory component of the infertility evaluation in infertile women with normal hysterosalpingogram or suspected unilateral distal tubal pathology?☆

Yuval Lavy*, Ahinoam Lev-Sagie, Hananel Holtzer, Ariel Revel, Arye Hurwitz

Comparison between HSG results and laparoscopic findings in regard to treatment plan based on HSG

Laparoscopic findings	HSG results		
	Combined normal ^a	Bilateral occlusion	Total
Normal	53	1	54
Unilateral occlusion	5	6	11
Bilateral occlusion	3	16	19
Pelvic adhesions	2	0	2
Total	63	23	86

^a Patients with normal HSG or suspected unilateral occlusion which were assigned to ovulation induction and IUI.

DLS after normal or unilateral occlusion on HSG

Taking into consideration the high financial costs and intra-operative risks, L/S is not indicated in women with normal HSG or suspected unilateral tubal pathology on HSG, since the information obtained by L/S in these patients would change the treatment protocol only in a small percentage.

Should laparoscopy be a mandatory component of the infertility evaluation in infertile women with normal hysterosalpingogram or suspected unilateral distal tubal pathology?★

Yuval Lavy*, Ahinoam Lev-Sagie, Hananel Holtzer, Ariel Revel, Arye Hurwitz

Table 1

Laparoscopic findings in relation to HSG results

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Diagnostic laparoscopy is needed after abnormal hysterosalpingography to prevent over-treatment with IVF

Table 3. Laparoscopic findings and treatment versus findings revealed by hysterosalpingography (HSG).

<i>HSG finding</i>	<i>Laparoscopic finding and treatment</i>			
	<i>No abnormality and IUI</i>	<i>Unilateral abnormality and IUI</i>	<i>Intervention and IUI</i>	<i>IVF</i>
Unilateral pathology	52 (41)	20 (16)	38 (30)	16 (13)
Bilateral pathology	36 (29)	13 (10)	19 (15)	58 (46)
Total	88 (35)	33 (13)	57 (23)	74 (29)

Values are expressed as number (percentage).

DLS after bilateral tubal occlusion on HSG

DLS should be recommended in cases with bilateral tubal occlusion on HSG, since it altered the original treatment plan in;

30% Lavy et al 2004

42%..... Bosteels et al 2007

46% Tanahatoc et al 2008

DLS could avoid IVF treatment in these cases.

Laparoscopy before ovulation induction treatment

Anovulatory infertility

Should a DLS systematically be performed before the onset of any OI treatment?

Can a DLS, performed after several failed OI treatment cycles, reveal significant pathology amenable to surgical treatment with a positive effect on the overall ongoing pregnancy rate?

Laparoscopy before ovulation induction treatment

Anovulatory infertility

The routine use of DLS cannot be advocated, but DLS can offer;

1. The opportunity to assess tuboperitoneal status
2. To treat pelvic pathology that may limit conception
(endometriosis, adhesions)
3. To perform LOD

Laparoscopy before ovulation induction treatment

LOD in CC-resistant PCOS is at least as effective as Gn treatment, and results in a lower multiple pregnancy rate.

There is however a lack of knowledge regarding the long-term outcome of this procedure on the reproductive function of the ovary.

Laparoscopy before ovulation induction treatment

DLS in 92 patients after 4 failed cycles of OI with CC

Normal	36%
Endometriosis	50%
Pelvic adhesions	33%

Authors did not present any pregnancy rates following LS surgery.

Laparoscopy before ovulation induction treatment

Laparoscopic adhesiolysis

Only one non-randomized controlled study;

CPRs in 12 and 24 months;

After operative laparoscopy 32% and 45%

Non-treated control group 11% and 16%

DLS and the treatment of endometriosis

Table 1: Laparoscopic treatment of minimal/mild endometriosis

	Laparoscopic surgery	Diagnostic laparoscopy	RR
	(n = 172)	(n = 169)	
Pregnancies carried beyond 20 weeks	50	29	
36 weeks cumulative probability (Marcoux <i>et al.</i> 1997)	30.7	17.7	1.7 (1.2–2.6)
	(n = 54)	(n = 47)	
Pregnancy (Parazzini, 1999)	12	13	NS
	(n = 437)		
Ongoing pregnancy at 20 weeks or live birth (Jacobson <i>et al.</i> 2002)		Peto OR (95% CI) 1.64 (1.05–2.57)	

DLS and the treatment of endometriosis

- The monthly fecundity rate among women who underwent laparoscopic surgery (6.1%), albeit double as high as in the diagnostic laparoscopy group, was still much lower than the fecundity rate expected in fertile women (20%).

Marcoux S, N Engl J Med 1997;337:217–222.

DLS and the treatment of endometriosis

ESHRE guideline for the diagnosis and treatment of endometriosis

- Ablation of endometriotic lesions plus adhesiolysis to improve fertility in minimal–mild endometriosis is effective compared to diagnostic laparoscopy alone (Jacobson *et al.*,2004b).

Kennedy F et al. Hum Reprod 2005

DLS and the treatment of endometriosis

ESHRE guideline for the diagnosis and treatment of endometriosis

- There is insufficient evidence available to determine whether surgical excision of moderate–severe endometriosis enhances pregnancy rates.

Kennedy F et al. Hum Reprod 2005

Extensive Excision of Deep Infiltrative Endometriosis before In Vitro Fertilization Significantly Improves Pregnancy Rates

Paulo H. M. Bianchi, MD*, Ricardo M. A. Pereira, MD, Alysson Zanatta, MD, Jose Roberto Alegretti, BSc, Eduardo L. A. Motta, PhD, and Paulo C. Serafini, PhD

From the Huntington Medicina Reprodutiva, São Paulo, Brazil (all authors).

Bianchi et al. Laparoscopic Resection Improves IVF Pregnancy Rates

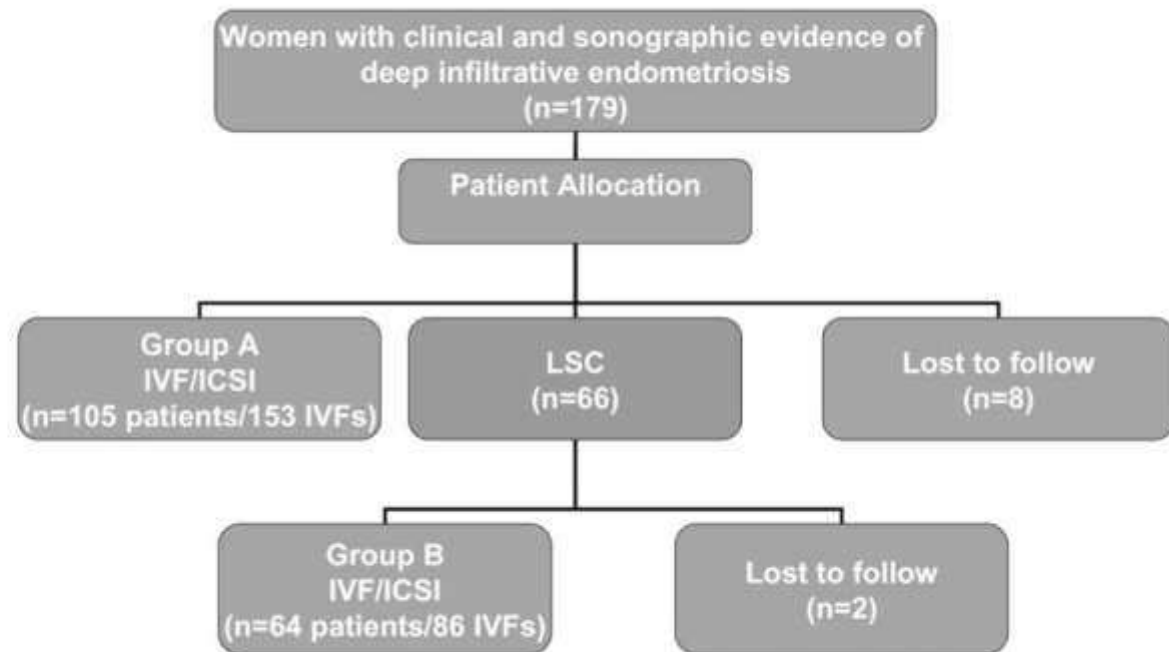


Fig. 1. Study flowchart and patient allocations. LSC = Laparoscopy with complete excision of DIE lesions.

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	Laparoscopy (n = 35)	No laparoscopy (n = 56)	p
Age (yrs)	32.6 ± 3	32.9 ± 3	.63
Infertility duration (mo)	35 ± 16	28 ± 18	.06
No. of previous IVF attempts	2 ± 2	2 ± 1	.87
Basal FSH (IU/L)	5.7 ± 1.9	5.6 ± 2.5	.85
Basal estradiol (pg/mL)	36.3 ± 21.1	40.7 ± 34	.49
Total dose of FSH (IU)	2611 ± 963	2471 ± 939	.39
No. of oocytes retrieved	10 ± 5	10 ± 5	.74
Fertilization rate (%)	86.5 ± 21	78.5 ± 17.8	.01
No. of top-quality embryos/patient	.67 ± 1	.53 ± 1	.46
Implantation rate (%)	21.7 ± 30	11.7 ± 23.7	.05

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In vitro fertilization outcomes in groups A and B

	Group A	Group B	p
Total dose of FSH (IU)	2380 ± 911	2542 ± 1012	.01
No. of oocytes retrieved	10 ± 5	9 ± 5	.04
Fertilization rate (%)	77.9	78	.76
No. of top-quality embryos/patient	.59 ± 1	.57 ± 1	.48
No. of embryos transferred	3 ± 1	3 ± 1	1
Implantation rate (%)	19 ± 25.1	32.1 ± 30.6	.03
Pregnancy rate (%)	24	41	.004

Laparoscopy before IUI

The position of operative laparoscopy for endometriosis and peritubal adhesions prior to IUI treatment or after several failed IUI cycles seems a matter of debate.

Should diagnostic laparoscopy be performed in the infertility work up programme in patients undergoing intrauterine insemination?

- L/S revealed abnormalities that resulted in changed treatment decisions in 25% of the patients.
- Because the effect of such interventions on the success rate of IUI has never been described, it still remains unclear whether laparoscopy is usefully performed in these cases.

DLS and IUI

Table 4: Pregnancy rate per patient and presence of pelvic pathology in patients treated with either diagnostic laparoscopy first (DLSF) or IUI first (IUIF)

	DLSF <i>n</i>	IUIF <i>n</i>	OR (CI)
No abnormalities	33/64	10/23	
Treated pathology			1.4 (0.5–3.6)
Adhesiolysis	3/64	0/23	
Treatment of endometriosis	28/64	12/23	
Fimbriolysis	0/64	1/23	
Pregnancy rate/patient	34/77	38/77	1.2 (0.7–2.3)

L/S performed after 6 cycles of unsuccessful IUI did not detect more abnormalities with clinical consequences compared with those performed prior to IUI treatment.

DLS and IUI

- To assess the value of COH and IUI in women with unilateral tubal occlusion diagnosed by HSG.
- 62 patients with isolated unilateral tubal occlusion by HSG
- Control group 115 patients with unexplained infertility
- CPRs of COH and IUI;
 - 30.9% study group
 - 42.6% control group
 - 19% mid-distal or distal tubal occlusion
 - 38.2% proximal tubal occlusion versus

unilateral proximal tubal occlusion	COH+IUI
mid-distal or distal tubal occlusion on HSG	IVF

DLS and IUI

Further studies should assess whether DLS is effective prior to IUI in terms of pregnancy rates and additional costs, and whether delayed performance of DLS after a few unsuccessful cycles of IUI instead of prior to IUI treatment is more effective.

DLS and unexplained infertility

With the current success rates of ART and relatively low contribution of DLS to the decision-making process of treating patients with a normal HSG, L/S should be omitted in couples with unexplained infertility.

Proceed directly to 3-6 cycles of IUI and if unsuccessful immediately switched to IVF instead of finalizing the infertility work up by DLS.

DLS in unexplained infertility

51 unexplained infertile patients with normal HSG

15/51 (29.4%) Minimal endometriosis and peritubal adhesions

14/51 (27.4%) Operative surgery

10 patients (14.0%) referred to ART

DLS changed our treatment strategy in 14/51 (27.4%)

24 pregnancies (47%) (6 ART-6 after operative surgery)

Patients with unexplained infertility and normal HSG findings should undergo DLS prior to ART.

DLS in unexplained infertility with normal HSG

57 infertile patients with normal HSG

46 (80.7%) pathologic abnormalities;

36 (63.2%) Endometriosis and peritubal adhesions

5 (8.8%) Perifimbrial adhesions

8 patients (14.0%) Referred to ART

29 pregnancies (50.9%) (6 ART-mediated pregnancies)

Patients with unexplained infertility and normal HSG findings should undergo DLS prior to ART.

Should diagnostic laparoscopy be performed initially or not, during infertility management of primary and secondary infertile women? A cross-sectional study

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Table 3 Ratios of pelvic pathologies and postoperative treatment strategy alterations among primary and secondary infertile patients with and without infertility-related risk factors (n: 191)

Main outcome	Primary infertile women				Secondary infertile women			
	With risk factors n: 67	Without risk factors n: 39	Total n: 106	P-value†	With risk factors n: 55	Without risk factors n: 30	Total n: 85	P-value†
Pathology on DLS	41 (61%)	23 (59%)	64 (60%)	0.82	41 (74%)	18 (60%)	59 (69%)	0.16
Change in treatment strategy after DLS	29 (43%)	3 (9%)	32 (30%)	<0.0001*	27 (49%)	4 (13%)	31 (36%)	0.001*

†Pearson χ^2 test result. *Statistically significant. DLS, diagnostic laparoscopy.

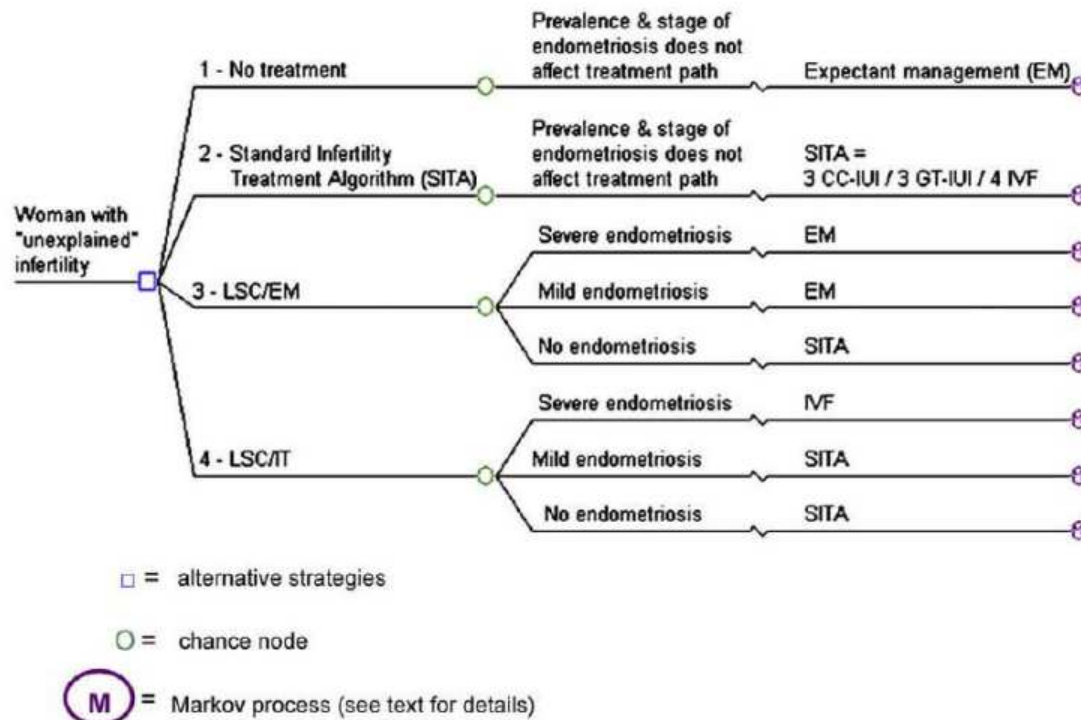
Conclusion: Diagnostic laparoscopy in preparation for operative procedures (especially for secondary infertile women) should be performed initially in all unexplained infertile patients with or without risk factors related to pelvic pathologies.

Laparoscopy in women with unexplained infertility: a cost-effectiveness analysis

Sharon E. Moayeri, M.D., M.P.H., M.S.,^{a,b} Henry C. Lee, M.D, M.S.,^c Ruth B. Lathi, M.D.,^a Lynn M. Westphal, M.D.,^a Amin A. Milki, M.D.,^a and Alan M. Garber, M.D., Ph.D.^{b,d}

FIGURE 1

Decision tree model (simplified).

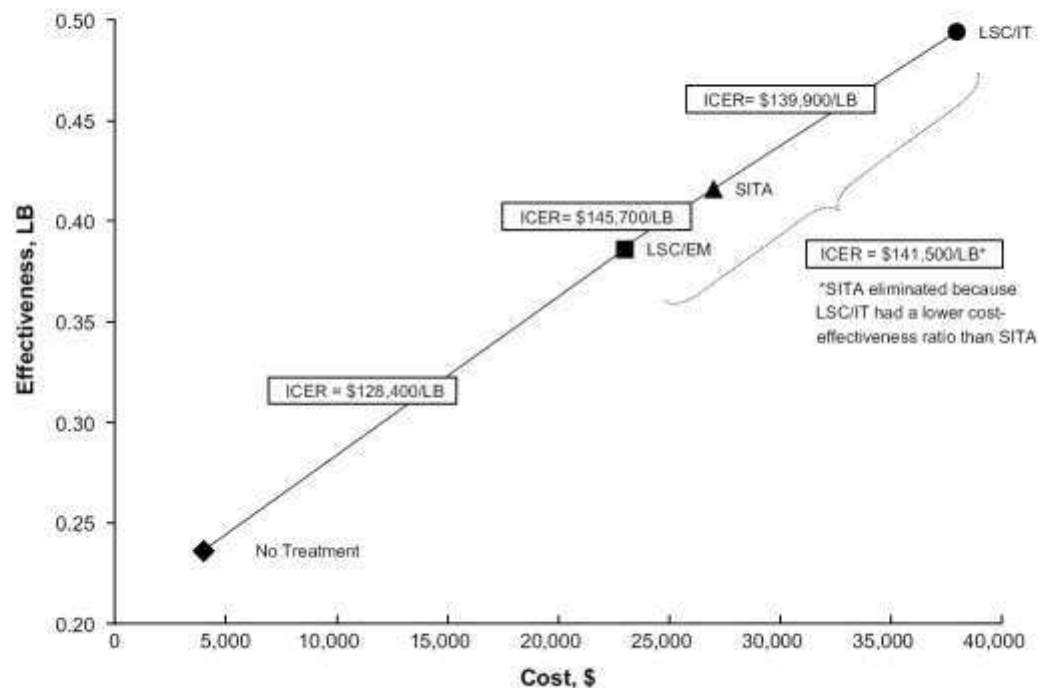


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Base-case scenario: Summary

Base-case scenario: base-case cost, effectiveness, and incremental cost-effectiveness ratio. See Table 3. (EM, expectant management; ICER, incremental cost-effectiveness ratio; IT, infertility treatment; LB, live birth; LSC, laparoscopy; SITA, standard infertility treatment algorithm.)



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Summary of base-case scenario: base-case cost, effectiveness, and incremental cost-effectiveness ratio.

Strategy	Cost (\$US)	Effect (LB)	ICER (\$/LB)
No treatment	4000	0.236	Baseline
LSC/EM	23,000	0.386	128,399 ^a
SITA	27,000	0.416	Eliminated ^b
LSC/IT	38,000	0.494	141,512 ^c

LSC/IT to a higher ICER, but it is an appropriate choice if the patient is willing to pay at least this amount for a successful pregnancy.

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TABLE 4

Sensitivity analyses: summary of variables whereby changes in base case estimates led to SITA as the preferred treatment strategy.

Variable	Base-case values	Critical point in base-case assumptions where SITA dominates LSC/EM	ICER where SITA becomes the preferred strategy (\$/LB)
Infertility dropout per cycle	10%	<9%	123,980
Cost of laparoscopy	\$10,000	>\$10,700	131,293
Preference weight, twins	0.8	>0.925	125,006
Reduced fecundity from endometriosis	40%–55%	<35%	128,242

Abbreviations: HOM, high-order multiple gestation; ICER, incremental cost effectiveness ratio; LB, live birth; LSC/EM, laparoscopy/expectant management; SITA, standard infertility treatment algorithm.

Moayeri. Cost effectiveness of laparoscopy for infertility. Fertil Steril 2009.

- SITA was preferred when dropout was less than 9% per cycle.
- L/S is cost effective in the initial management of young women when infertility treatment dropout rates exceed 9% per cycle.

CONCLUSION

- In women without a previous history suggestive of tubal disease and who have a normal HSG, the probability of clinically relevant tubal disease or endometriosis is very low and DLS does not seem justified or cost effective.
- Whether DLS in cases of unilateral obstruction should always be performed prior to IUI, or whether it should be delayed after a few cycles of IUI is still questionable.

CONCLUSION

- In a considerable number of patients DLS after abnormal HSG reveals normal findings or abnormalities not requiring IVF, even when the results of HSG suggest bilateral pathology.
- Abnormal HSG in the work-up prior to IUI should not immediately lead to IVF.

CONCLUSION

- The position of operative laparoscopy for endometriosis and peritubal adhesions prior to IUI treatment or after several failed IUI cycles seems a matter of debate.
- Although RCTs which have studied the benefit of laparoscopic surgery in moderate or severe endometriosis are still lacking, its value has generally been accepted.