SCIENTIFIC SEMINARS
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Recent Developments in the Transmission of Human Life

Polyps and embryo implantation

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Faculty Disclosure

I have no potential conflict of interest to declare

Endometrial polyps

DEFINITION

HYPERPLASTIC OVERGROWTHS OF ENDOMETRIAL GLANDS AND STROMA AROUNDA VASCULA CORE

- FOCAL
- SESSILE
- PEDUNCOLATED PROJECTIONS
- MOSTLY BENIGN
- ATYPICAL HYPERPLASIA (3,8%)

MACROSCOPIC ASPECTS

- MOSTLY (80%), SINGLE
- MULTIPLE (20%)
- FEW MILLIMETERS TO CENTIMETERS
- THE MAJORITY ARISE FROM THE FUNDUS (55,8%); CORNUAL MUCOSA (29,4%)
- OCCASIONALLY. PEDUNCOLATED, BEYOND THE EXTERNAL CERVICAL ORIFICE

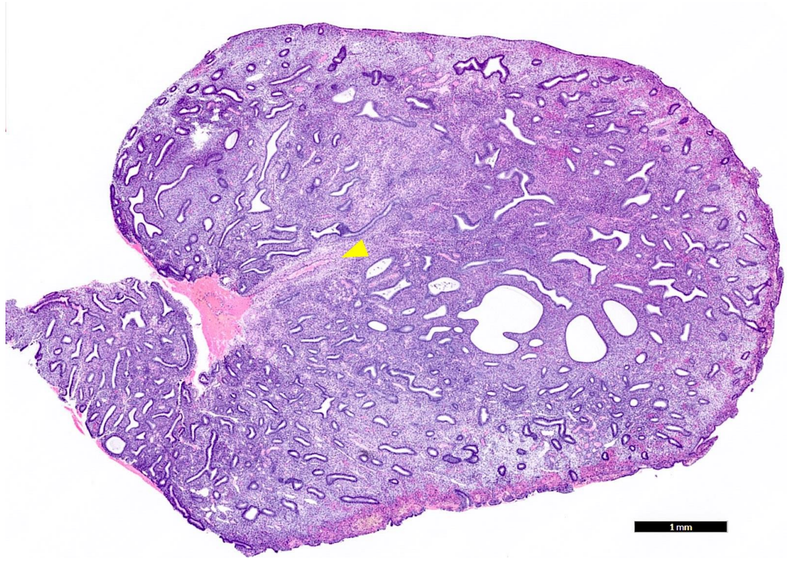
Endometrial polyps

HYSTOPATHOLOGY

- STROMA (DENSE, FIBROUS TISSUE) AND GLANDS
- VACULAR CORE
- SUPERFICIAL EPITHELIUM
- SMOOTH MUSCLE TISSUE (SOME CASES)

FIVE CATEGORIES

- HYPERPLASTIC
- ATROPHIC (postmenopausal)
- FUNCTIONAL
- ADENOMATOUS
- PSEUDOPOLYPS



https://www.pathologyoutlines.com/topic/uterusendopolyp.html

Endometrial polyps

EPIDEMIOLOGY

- THE ACTUAL PREVALENCE OF ENDOMETRIAL IN GENERALE POPULATION POLYPS IS UNKNOWN

- IT IS ESTIMATED THAT EP MAY AFFECT WOMEN FROM 7,8% TO 34,9% (Salim et al., 2011)
- IT IS HIGHER IN POSTMENOPAUSAL WOMEN (11,8%) THAN IN PREMENOPAUSAL (5,8%)
- IN SUBFERTILE WOMEN SEEMS TO BE HIGHER (UP TO 32%)

Endometrial polyps

1000 Office-Based Hysteroscopies Prior to In Vitro Fertilization: Feasibility and Findings

Mary D. Hinckley, MD, Amin A. Milki, MD

JSLS 2004; 8:103–107 ; 2004

Findings of 1000 Office Hysteroscopies Prior to IVF

FINDINGS	CASES
Normal Findings	618 (62%)
Endometrial Polyps	**323 (32%)**
Submucous Fibroids	27 (3%)
Intrauterine Adhesions	25 (3%)
Polypoid Endometrium	9 (0.9%)
Septum	5 (0.5%)
Bicornuate uterus	3 (0.3%)
Retained Products of conception	3 (0.3%)

Endometrial polyps

PATHOGENESIS

THE CAUSE OF ENDOMETRIAL POLYPS IS UNKNOWN

MULTIFACTORIAL (Nijkang et ., 2019)

- GENETIC (Chromosome 6 and 12; protein p53)
- INFLAMMATION (MMPs)
- HORMONAL FACTORS (Aromatase expression; ERs and PRs)
- IATROGENIC (?)

THERE ARE RISK FACTORS

- GENETIC AND HEREDITARY (CHROMOSOME 6 AND 20) (Nijang et al., 2019)
- AGE (PREVALENCE) (AAGL, 2012)
- DIABETES & HYPERTENSION (Nappi et al., 2009)
- OBESITY & TAMOXIFEN (Kossaï et al., 2020)

Endometrial polyps

NATURAL HYSTORY

EP MAY REGRESS, PERSIST, ENLARGE, MALIGNANT TRANSFERMATION

REGRESSION RATE OF (Lienget al., 2009):

- 26,7% AFTER 1 YEAR FU WHEN MEAN DIAMETER WAS 10,7 mm
- 4,4 % AFTER 1 YEAR FU WHEN MEAN DIAMETER WAS 15,1 mm

MENOPAUSAL STATUS (Wong et al., 2017)

	Persisted	Regressed	P<0,0029
PREMENOPAUSAL (%)	39 (37)	6 (86)	0.016
POSTMENOPAUSAL (%)	66 (63)	1 (14)	

Endometrial polyps

CLINICAL PRESENTATION

- THE MAJORITY OF EP ARE ASYMPTOMATIC

WHEN SYMPTOMATIC

❑ BLEEDING

- In postmenopausal, EP can be identified as a cause of AUB in 30% of cases (Cohen et al., 1999)
- Intermenstrual bleeding is the most frequent complaint in 13% to 50% of women suffering from premenopausal bleeding (Tjarks and Van Voorhis, 2000);
- The bleeding may be due to stromal congestion within the polyp leading to venous stasis and apical necrosis (Jakab et al., 2005)

❑ INFERTILITY (15%-32%); (Hinckley et al., 2004; Taylor and Gomel, 2008; Afifi et al., 2010)

Endometrial polyps

CLINICAL PRESENTATION: INFERTILITY

NATURAL PREGNANCY

- 50%-78% AFTER REMOVAL OF EP IN APPARENT UNEXPLAINED INFERTITLITY

(Varasteh et al., 1999; Spiewankiewicz et al., 2003; Shokeir et al., 2004)

LOCATION RELEVANT (Yanaihara et al., 2008);

- Utero-tubal junction (57,4%);
- Posterior wall (28,5%);
- Lateral wall (18,8%).

- No difference after removal of small polyps (<10 mm) (Stamatellos et al., 2008)

Endometrial polyps

CLINICAL PRESENTATION: INFERTILITY

MAR IUI

1. RCT (Perez-Medina et al., 2005)

- Cumulative CPR after 4 IUI; similar EP size
- 101 infertile patients; US diagnosed EP and removed; Pregnancy rate 63,4
- 103 infertile patients; US diagnosed EP with biopsed; Pregnancy rate 28,2

} P<0,001

2. RETROSPETIVE STUDY (Kalampoks et al., 2012)

- Cumulative CPR after 3 IU similar EP size
- 86 infertile patients; US diagnosed EP and removed; Pregnancy rate 40,7
- 85 infertile patients; US diagnosed EP and not removed; Pregnancy rate 63,4

} P<0,001

Endometrial polyps

CLINICAL PRESENTATION: INFERTILITY

MAR IVF/ICSI

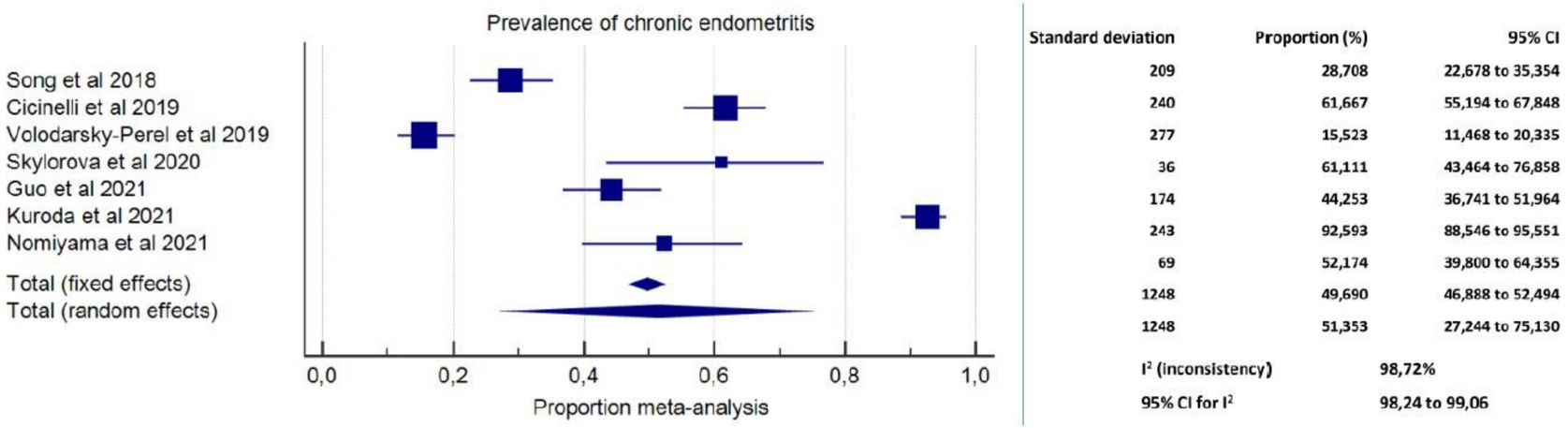
FIVE, ONLY RETROSPETIVE STUDIES

- Lass et al., 1999
- Isikoglu et al., 2006
- Check et al., 2011
- Tiras et al., 2012
- Elias et al., 2015

No statistical difference in clinical pregnancy rates in any study

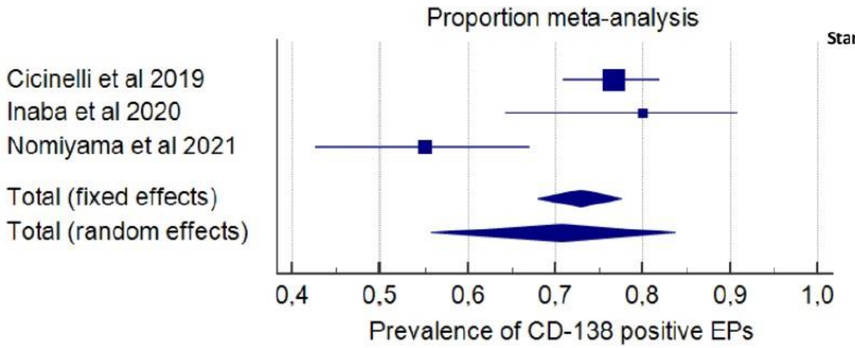
Association between Endometrial Polyps and Chronic Endometritis: Is It Time for a Paradigm Shift in the Pathophysiology of Endometrial Polyps in Pre-Menopausal Women? Results of a Systematic Review and Meta-Analysis

(Vitagliano, A, et al., Diagnostics **2021**, 11, 2182)



Standard deviation	Proportion (%)	95% CI
209	28,708	22,678 to 35,354
240	61,667	55,194 to 67,848
277	15,523	11,468 to 20,335
36	61,111	43,464 to 76,858
174	44,253	36,741 to 51,964
243	92,593	88,546 to 95,551
69	52,174	39,800 to 64,355
1248	49,690	46,888 to 52,494
1248	51,353	27,244 to 75,130
I^2 (inconsistency)		98,72%
95% CI for I^2		98,24 to 99,06

Forest plot. Prevalence of chronic endometritis in pre-menopausal women with endometrial polyps.



Standard deviation	Proportion (%)	95% CI
240	76,667	70,795 to 81,867
40	80,000	64,352 to 90,948
69	55,072	42,619 to 67,077
349	72,918	67,954 to 77,493
349	70,735	55,792 to 83,683
I^2 (inconsistency)		84,00%
95% CI for I^2		51,99 to 94,67

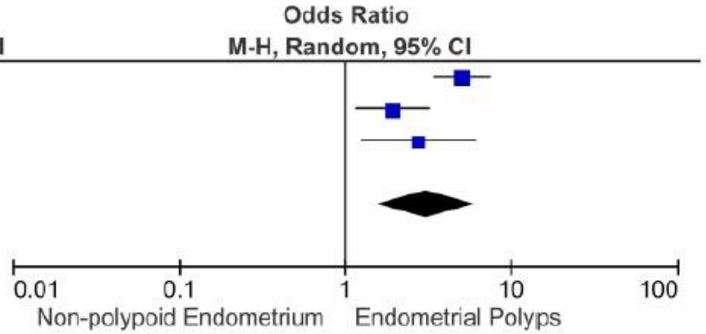
Association between Endometrial Polyps and Chronic Endometritis: Is It Time for a Paradigm Shift in the Pathophysiology of Endometrial Polyps in Pre-Menopausal Women? Results of a Systematic Review and Meta-Analysis

(Vitagliano, A, et al., Diagnostics **2021**, 11, 2182)

	Endometrial Polyps		Non-polypoid Endometrium			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Cicinelli et al 2019	148	240	58	240	38.3%	5.05 [3.40, 7.48]
Guo et al 2021	77	174	30	103	34.8%	1.93 [1.15, 3.25]
Nomiyama et al 2021	36	69	13	46	26.9%	2.77 [1.25, 6.14]
Total (95% CI)		**483**		**389**	**100.0%**	**3.07 [1.59, 5.95]**
Total events	261		101			

Heterogeneity: Tau² = 0.26; Chi² = 8.67, df = 2 (P = 0.01); I² = 77%

Test for overall effect: Z = 3.34 (P = 0.0008)



Forest plot. Women with endometrial polyps versus women with a non-polypoid endometrium: prevalence of chronic endometritis.

From a molecular point of view, chronic inflammation may promote EPs development by distorting the signaling pathways that control endometrial tissue proliferation

Endometrial polyps

CLINICAL PRESENTATION: INFERTILITY

Cochrane Library

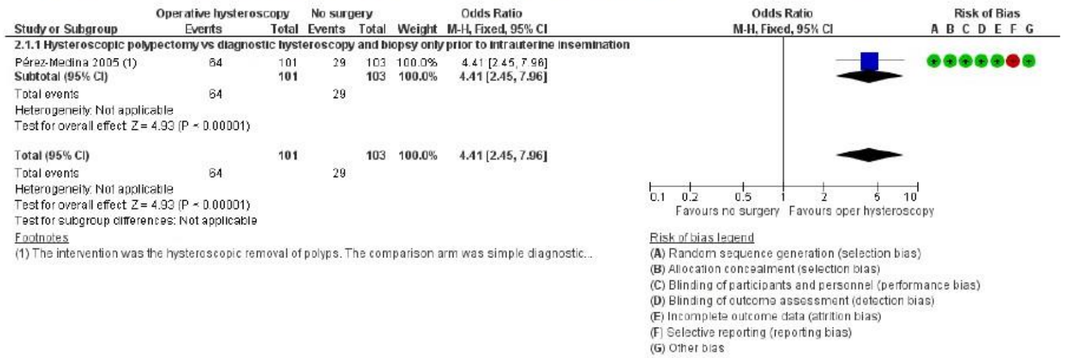
Cochrane Database of Systematic Reviews

2018

Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities (Review)

Bosteels J, van Wessel S, Weyers S, Broekmans FJ, D'Hooghe TM, Bongers MY, Mol BWJ

Figure 6. Forest plot of comparison: 2 Hysteroscopic removal of polyps vs diagnostic hysteroscopy and biopsy only prior to intrauterine insemination. Outcome: 2.1 Clinical pregnancy per woman randomised.



1. Operative hysteroscopy versus control in women with otherwise unexplained subfertility and suspected major uterine cavity abnormalities

See: Summary of findings for the main comparison.

Endometrial polyps

The search identified no studies on endometrial polyps.

Submucous fibroids

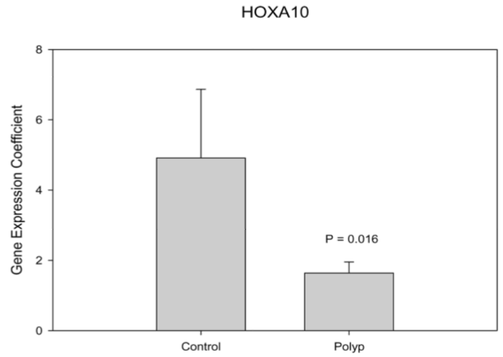
One study compared hysteroscopic myomectomy versus no surgery in women with unexplained subfertility and submucous fibroids only or combined with intramural fibroids (Casini 2006).

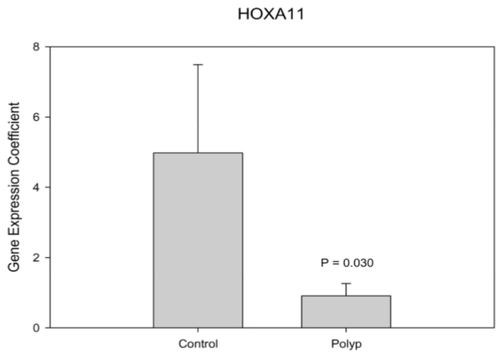
We graded the evidence of the trial on hysteroscopic polypectomy as low (Pérez-Medina 2005): we downgraded by one level for serious risk of bias related to a high risk of selective outcome reporting (see Assessment of risk of bias in included studies). We downgraded by one level for serious imprecision given the wide CIs of the point estimate of the treatment effect.

ENDOMETRIAL POLYPS AFFECT UTERINE RECEPTIVITY

Beth W. Rackow, MD, Elisa Jorgensen, BS, and Hugh S. Taylor, MD

Fertil Steril. 2011 June 30; 95(8): 2690–2692





Uteri with endometrial polyps demonstrated a marked decrease in *HOXA10* and *HOXA11*mRNA levels that may impair implantation; these findings suggest a molecular mechanism to support clinical findings of diminished pregnancy rates in women with endometrial polyps.

Endometrial polyps

CLINICAL PRESENTATION: INFERTILITY

NEVERTHELESS:

REMOVAL OF ENDOMETRIAL POLYPS WAS RECOMENDED IF THEY ARE IDENTIFIED IN INFERTILE WOMEN

- Taylor and Gomel 2008
- Afifi et al., 2010
- Pereira et., 2015

Endometrial polyps

Endometrial polyps. An evidence-based diagnosis and management guide

S.G.Vitale, S. Haimovich A.S.Laganà L. Alonso, A. Di Spiezio, J. Carugno
From the Global Community of Hysteroscopy Guidelines Committee

EJOG VOLUME 260, P 70-77, MAY 01, 20211

Reccomandations	LE
TVUS in infertile patients	B
In office hysteroscopy highest accuracy	B
Hysteroscopic polipectomy feasible and safe with no adesion formation	B
Polypectomy does not compromise reproductive outcome with subsequent MAR	B
Remove of EP < 2 cm in premenopausal women with risk factors of endometrial cancer	B
Hystopathology is mandatory	B
EP might alter endometrial receptivity	C
Avoid blind D&C	A

LE= level of evidence

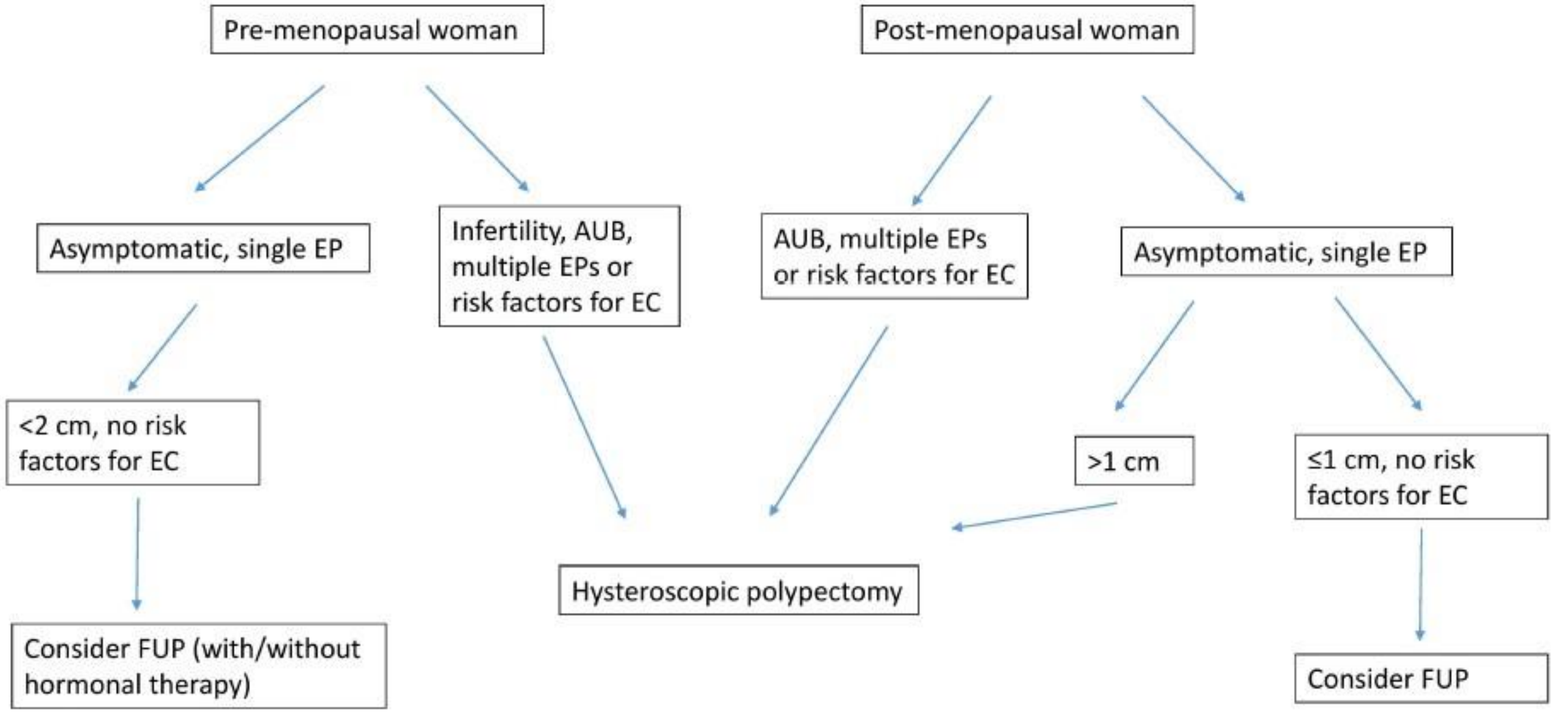
Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2022**; 49(10): 232
https://doi.org/10.31083/j.ceog4910232

Review

Endometrial Polyps: Update Overview on Etiology, Diagnosis, Natural History and Treatment

Mariana De Cunha Vieira[1], Amerigo Vitagliano[2,*], Mariana Costa Rossette[3], Luiz Cavalcanti de Albuquerque Neto[3], Alessandra Gallo[4], Attilio Di Spiezio Sardo[4]



Title of your presentation

Take-home messages

- ✓ EP may interfere with natural conception
- ✓ The mechanism(s) is (are) unknown
- ✓ Women with unexplained infertility may benefit from EP removal
- ✓ Women planning IUI may benefit from EP removal
- ✓ More prospective clinical studies are needed
- ✓There is non consensus about proper management
- ✓Management of EP should be individualized according the patient situation and balancing benefit with risks

THANK YOU

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