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Systematic Review

The Relationship Between Laparoscopic Cystectomy and Ovarian Reserve: A Systematic Review and Meta-Analysis

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Laparoscopic Cystectomy; Ovarian Reserve Marker

ABSTRACT

Introduction: Laparoscopic cystectomy is the first-line recommended treatment for different ovarian cysts. Several mechanisms have been proposed to explain the negative impact of laparoscopic cystectomy on ovarian reserves, including the loss of normal ovarian tissue during cyst stripping, heat damage from electrosurgery, inflammation, and edema. The purpose of this systematic review is to synthesize and quantify the currently available research on the effect of laparoscopic cystectomy on ovarian reserve using multiple indicators.

Material and Methods: The PubMed database was searched using the keywords "laparoscopic cystectomy" and "ovarian reserve," which yielded 23 papers for the final review. The Cochrane Risk of Bias tool was used to assess potential bias.

Results: AMH, FSH, reserve ovarian volume, and PSV all showed significant changes at different time points after surgery, although LH and estradiol did not. AMH is the most frequently utilized and sensitive method for evaluating ovarian reserve at various time periods.

Conclusion: Laparoscopic cystectomy reduces ovarian reserve across various indicators.

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INTRODUCTION

Laparoscopic cystectomy is the first-line therapy for different ovarian cysts [1]. Several mechanisms have been proposed to explain the negative impact of laparoscopic cystectomy on ovarian reserves, including the loss of normal ovarian tissue during cyst stripping, heat damage from electrosurgery, inflammation, and edema [2]. Ovarian reserve, defined as the reproductive potential at a certain time point, is notoriously difficult to measure. Markers used to measure ovarian reserve include anti-Mullerian hormone (AMH), follicle-stimulating hormone (FSH), antral follicle count (AFC), ovarian volume, and others [3]. This systematic review seeks to synthesize and quantify the current data on the influence of laparoscopic cystectomy and ovarian reserve through the assessment of several indicators.

MATERIAL AND METHODS

Search Strategy

This study adheres to PRISMA standards [4]. The literature search was done using the PubMed database. The keywords for the search were "laparoscopic cystectomy" and "ovarian reserve". The reviewer evaluated the results of the search to assess the study's eligibility.

Inclusion Criteria

1. Studies published in English.
2. Studies conducted using prospective designs (single-arm and cohort)
3. Studies comparing ovarian reserve markers before and after laparoscopic cystectomy, with mean ± SD values.

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Exclusion Criteria

1. Studies not published in English.
2. Studies comparing various laparoscopic cystectomy procedures, sutures, and treatments.
3. Studies without detailed data statements in mean ± SD.

Selection Process

The PubMed database yielded 92 publications, 23 of which were included in the final review. Studies were omitted for the reasons described in **Fig.1**.

Risk of Bias Assessment

The Cochrane Risk of Bias tool was used to identify potential biases [5].

Statistical Analysis

Statistical analysis was performed using the Review Manager 5 program.

RESULTS

This analysis includes 23 prospective studies that assessed the influence of laparoscopic cystectomy on several ovarian reserve indicators [6–28]. The Cochrane Risk of Bias tool revealed a significant risk of bias in random sequence generation, allocation concealment, participant and personnel blinding, and blinding of outcome assessment due to the nature of the studies included, which were single-arm and cohorts. Incomplete outcome data, selective reporting, and other forms of bias were not shown to pose a major risk.

Several studies studied the quantity of AMH at various time periods following the laparoscopic cystectomy technique. AMH was assessed at 1 week, 1 month, 6 weeks, 2 months, 3 months, 6 months, 9 months, and 12 months after surgery. The quantity of AMH tested at various time periods never returned to the preoperative level. A statistically significant decrease of AMH was found during 1 week (MD: -1.85, 95% CI -2.06, -1.33, $p < 0.00001$), 1 month (MD: -0.71, 95% CI -0.74, -0.69, $p < 0.00001$), 2 months (MD: -0.61, 95% CI -1.13, -0.09, p: 0.02), 3 months (MD: -0.63, 95% CI -0.67, -0.60, $p < 0.00001$), 6 months (MD: -1.05, 95% CI -1.34, -0.75, $p < 0.00001$), 9 months (MD: -1.72, 95% CI -1.87, -1.58, $p < 0.00001$), and 12 months (MD: -1.66, 95% CI -2.34, -0.98, $p < 0.00001$) postoperatively.

FSH levels were also studied at several time points: 1 week, 1 month, 6 weeks, 2 months, 3 months, 6 months, 9 months, and 12 months. A statistically significant change in FSH was found during 1 week (MD: 3.91, 95% CI 2.72, 5.10, $p < 0.00001$), 6 weeks (MD: 2.33, 95% CI 0.74, 3.92, p: 0.004), 3 months (MD:

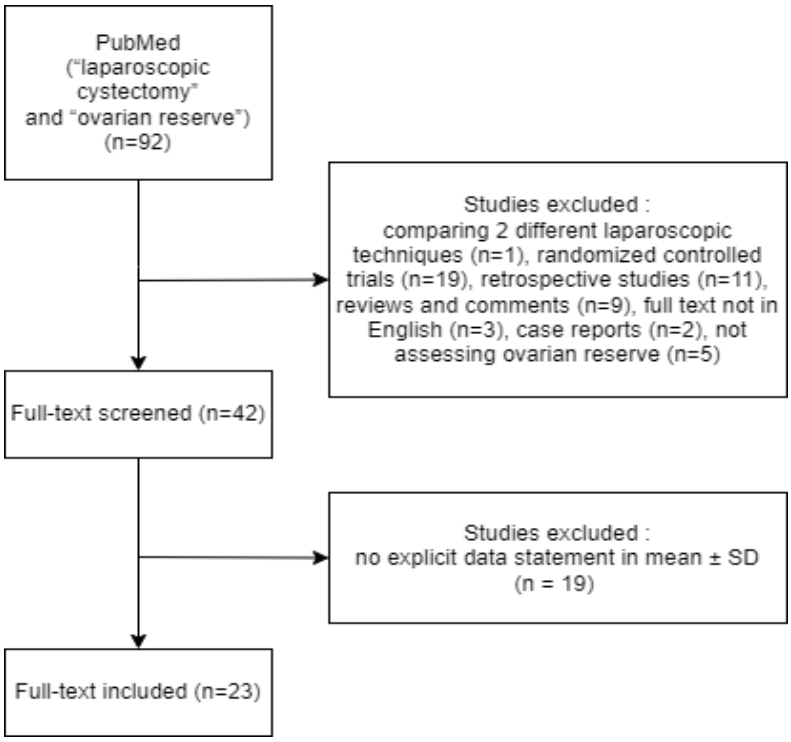

Fig. 1. Article screening process

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Table 1. Study Characteristics

First Author, Year	Sample Characteristics	n	Inclusion Criteria	Exclusion Criteria
Alborzi et al. (2014) [6]	Endometrioma	193	18-43 years old, regular menses, unilateral/bilateral/single/multiple endometrioma with pelvic pain or infertility	Previous adnexal surgery, hormone therapy, OC use for past 3 cycles, endocrine disorders, suspected/proven ovarian malignancy, previous ovarian failure/ premature menopause
Bhat et al. (2014) [7]	Endometrioma	73	Subfertile women undergoing laparoscopic cystectomy for the first time	Prior pelvic surgery
Biacchiardi et al. (2011) [8]	Endometrioma	43	Symptomatic endometrioma	PCOS, basal FSH > 15 IU/l, any hormonal treatment for ≥ 6 months, BMI > 30 kg/m2, concommitant ovarian pathology
Celik et l. (2012) [9]	Endometrioma	65	Endometrioma diameter ≥ 3 cm, no prior ovarian surgery, 18-45 years old, regular menses	Suspected malignant ovarian disease, OC use/hormone therapy during past 3 months, postmenopausal FSH levels, endocrine disorders
Chang et al. (2010) [10]	Endometrioma	13	Previous diagnostic procedures of benign ovarian tumors, 18-45 years old, regular menses	Postmenopausal status, PCOS, previous adnexal surgery, suspected malignant ovarian disease, OC use/hormone therapy during past 3 months, endocrine disorders
	Mature cystic teratoma	6		
	Mucinous cystadenoma	1		
Chen et al. (2014) [11]	Endometrioma	40	Previous diagnostic procedures of benign ovarian tumors, histologic confirmation of endometriomas/other benign ovarian cyst, 20-40 years old, regular menses	Postmenopausal status, previous adnexal surgery, suspected malignant ovarian disease, hormone therapy during past 3 months, endocrine disorders
	Tubal factor infertility	36		
	Other benign ovarian cyst	23		
Ding et al. (2015) [12]	Bilateral endometrioma	21	20-43 years old, regular menses, ovarian cysts > 3 cm	Previous adnexal surgery, OC use/hormone therapy for past 3 cycles, endocrine disorders, suspected/proven ovarian malignancy, premature ovarian failure/premature menopause
	Unilateral endometrioma	29		
	Unilateral other benign ovarian cyst	20		
Dubinskaya et al. (2019) [13]	Unilateral endometrioma	131	25-35 years old, unilateral endometrioma diameter : 3-5 cm, BMI < 30 km/m2, primary/secondary infertility >1 year, tubal factor of infertility screened by HSG	Any pelvic pathology, male infertility factor, general disease, on any medication that could reduce pelvic blood flow
Ercan et al. (2011) [14]	Unilateral endometrioma	36	20-39 years old, unilateral endometrioma diameter ≥ 4 cm, regular menses	Suspected malignant ovarian disease, hormone therapy during past 6 months, previous adnexal surgery, BMI > 30 kg/m2, positive beta-HCG, premature ovarian failure
Georgievska et al. (2014) [15]	Unilateral endometrioma	31	20-40 years old, unilateral endometrioma diagnosed by USG with mean diameter ≥ 4 cm	Previous adnexal surgery, OC use/hormone therapy for past 3 cycles, endocrine disorders, PCOS
Georgievska et al. (2015) [16]	Endometrioma	30	20-42 years old, endometrioma diagnosed by USG	PCOS, BMI > 35 kg/m2, endocrine disorders, previous adnexal surgery
Karadag et al. (2020) [17]	Endometrioma	36	18-35 years old, endometrioma/dermoid cyst diagnosed by USG ≥ 4 cm	Previous adnexal surgery, irregular menses, >1 unilateral cyst/bilateral cysts, PCOS, endocrine disorders, OC use/hormone therapy during past 6 months
	Dermoid cyst	32		
Kostrzewa et al. (2019) [18]	Unilateral endometrioma	35	18-40 years old, unilateral ovarian cyst,	Bilateral ovarian cysts, suspected malignant ovarian disease
	Simple cyst	10		
	Mature teratoma	16		
	Other	9		
Lee et al. (2011) [19]	Endometrioma	13	21-46 years old, endometrioma diagnosed by USG, regular menses	Bilateral ovarian lesions, menopausal symptoms, previous adnexal surgery, endocrine disorders, medications that could affect test results in the past 6 months

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First Author, Year	Sample Characteristics	n	Inclusion Criteria	Exclusion Criteria
Mansouri et al. (2022) [20]	Endometrioma	41	18-45 years old, BMI: 18.5-29.9 kg/m2, regular menses	Hormone therapy in the last 3 months and during the study period, previous adnexal surgery, chemotherapy, or pelvic radiotherapy, PCOS, endocrine disorders, premature ovarian failure/premature menopause, suspected/proven genital/ extragenital malignancy.
	Serous cystadenoma	9		
	Dermoid cyst	29		
	Other	34		
Kashi et al. (2017) [21]	Unilateral endometrioma	45	<40 years old, endometrioma diameter ≥ 3 cm/regardless of size if infertile/ dysmenorrhea/ dyspareunia/ dyschezia	History of unilateral oophorectomy, OC use/GnRH agonists/danazol use, endocrine disorders, PCOS
	Bilateral endometrioma	25		
Ozaki et al. (2016) [22]	Endometrioma	143	Symptomatic ovarian endometrioma diameter > 4 cm by USG, <45 years old, regular menses,	Pregnant, leiomyoma involving the cavity/intramural leiomyoma diameter >3 cm, bleeding disorders, endocrine disorders, previous abdominal surgery, malignant ovarian disease, hormone therapy in the last 3 months
Rasoul et al. (2021) [23]	Endometrioma	332	19-42 years old, chronic pelvic pain, dysmenorrhea, dyspareunia, endometrioma diagnosed by USG, normal AMH and FSH	Other ovarian cysts, PCOS, comorbidities that could affect fertility
Salihoglu et al. (2016) [24]	Endometrioma	34	18-40 years old, regular menses, largest endometrioma diameter > 4 cm with histopathological confirmation	Previous pelvic/adnexal surgery, hormone therapy in the last 3 months, metabolic/psychiatric disease, concomitant non-endometriotic cyst with endometrioma, suspicion of malignancy, radiotherapy/ chemotherapy
	Other	33		
Sarmadi et al. (2013) [25]	Teratoma	17	<40 years old, regular menses, benign cysts	Endocrine disease, previous adnexal surgery
	Mucinous cystadenoma	7		
	Simple cyst	11		
	Simple serous	10		
Shao et al. (2016) [26]	Endometrioma	80	21-35 years old, endometrioma ≥ 4 cm	PCOS, previous adnexal surgery, ovarian malignancy, hormone therapy in the last 3 months, endocrine disorders
Shi et al. (2011) [27]	Endometrioma	33	<45 years old, ovarian cyst	Malignant ovarian tumors
Sireesha et al. (2021) [28]	Endometrioma	29	25-39 years old, benign ovarian cysts sized 6-15 cm	Pregnant, PCOS, active PID, suspected genital/extragenital malignancy, premature ovarian failure, previous adnexal surgery, hormone therapy in the last 3 months
	Serous cystadenoma	14		
	Mucinous cystadenoma	8		
	Cystic teratoma	11		
	Corpus luteal cysts	10		

0.99, 95% CI 0.60, 1.37, p < 0.00001), 9 months (MD: 1.40, 95% CI 0.14, 2.66, p: 0.03), and 12 months (MD: -1.04, 95% CI -1.46, -0.63, p < 0.00001).

LH was tested after one month, six weeks, three months, six months, and nine months after surgery. There was no statistically significant change at any time point, or between time points. Estradiol levels were assessed at six weeks, three months, six months, and nine months after surgery. There was no statistically significant change at any time point, or between time points. AFC was measured one month, six weeks, three months, six months, nine months, and twelve months after surgery. The statistically significant difference was found during 1 month (MD: 0.60, 95% CI 0.25, 0.94, p: 0.0007), 3 months (MD: 0.54, 95% CI 0.33, 0.75, p < 0.00001), and 9 months (MD: 1.80, 95% CI 0.16, 3.44, p: 0.03) postoperatively.

Residual ovarian volume was assessed at one, three, nine, and twelve months after surgery. The statistically significant difference was found d uring 1 month (MD: -2.12, 95% CI -3.90, -0.34, p: 0.02), 3 months (MD: -1.84, 95% CI -2.31, -1.49, p < 0.00001), and 9 months (MD: -1.90, 95% CI -2.31, -1.49, p < 0.00001). A statistically significant difference was found between time points (p: 0.01).

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PSV levels were assessed at 2 days, 1 month, and 3 months postoperatively, with statistically significant results at 2 days (MD: -4.80, 95% CI -6.49, -3.11, $p < 0.00001$) and 3 months (MD: -2.40, 95% CI 3.86, -0.94, p: 0.001). A statistically significant change was seen between time points ($p < 0.0001$).

DISCUSSION

The lowest AMH level assessed at various time periods occurred one week after surgery, which might be attributed to the effects of inflammation, ischemia, vascular damage, and edema [6]. The highest points in AMH measurement were achieved six weeks, two months, and three months after surgery. Few studies are exploring AMH measurement throughout the 6-week and 2 month time points, but there is a wealth of data testing AMH during the 3 month time point, which shows a considerable reduction in AMH levels but is significantly higher than 1 week time point. The recovery at three months postoperatively indicates a continuous healing process following the initial trauma encountered during surgery and adnexal reperfusion [6]. AMH levels are decreasing after reaching a peak at 3 months postoperatively, according to measurements taken at 6 months, 9 months, and 12 months. This observation suggests permanent injury to the adnexa [26].

The measurement of FSH at various time periods results in a largely consistent rise postoperatively, with the exception of the 2-month time point. In the Salihoglu et al. research, the group that had bilateral laparoscopic cystectomy showed greater FSH levels at 2 months postoperatively than the unilateral group. This may have an impact on the results in the two months following surgery. In all other time periods, FSH levels rise after surgery before dropping after a year.

The measurement of AFC yields a mixed outcome with significant variation in the data given. The aggregated results of all time points show a rise in AFC relative to preoperative values. The results of LH and estradiol measurements were not explored as extensively as other ovarian reserve indicators, yielding an inconsequential result. The PSV measurement was also not frequently explored across research, with only one study investigating it at various time periods. Overall, the measurement of PSV implies a decline with time.

The assessment of reserve ovarian volume yielded consistent and constant levels from 1 month to 9 months postoperatively, followed by an increase at 12 months. Only one research looked at reserve ovarian volume 12 months after surgery and found a significant increase; further data is needed to corroborate this conclusion. Based on the data gathered from numerous research, we propose using AMH as the primary way of evaluating ovarian reserve due to its sensitivity to changes at various time periods.

CONCLUSION

Laparoscopic cystectomy reduces ovarian reserve across various indicators. According to the data collected in this study, AMH testing is the most extensively used way of evaluating ovarian reserve, as well as the most sensitive and responsive marker.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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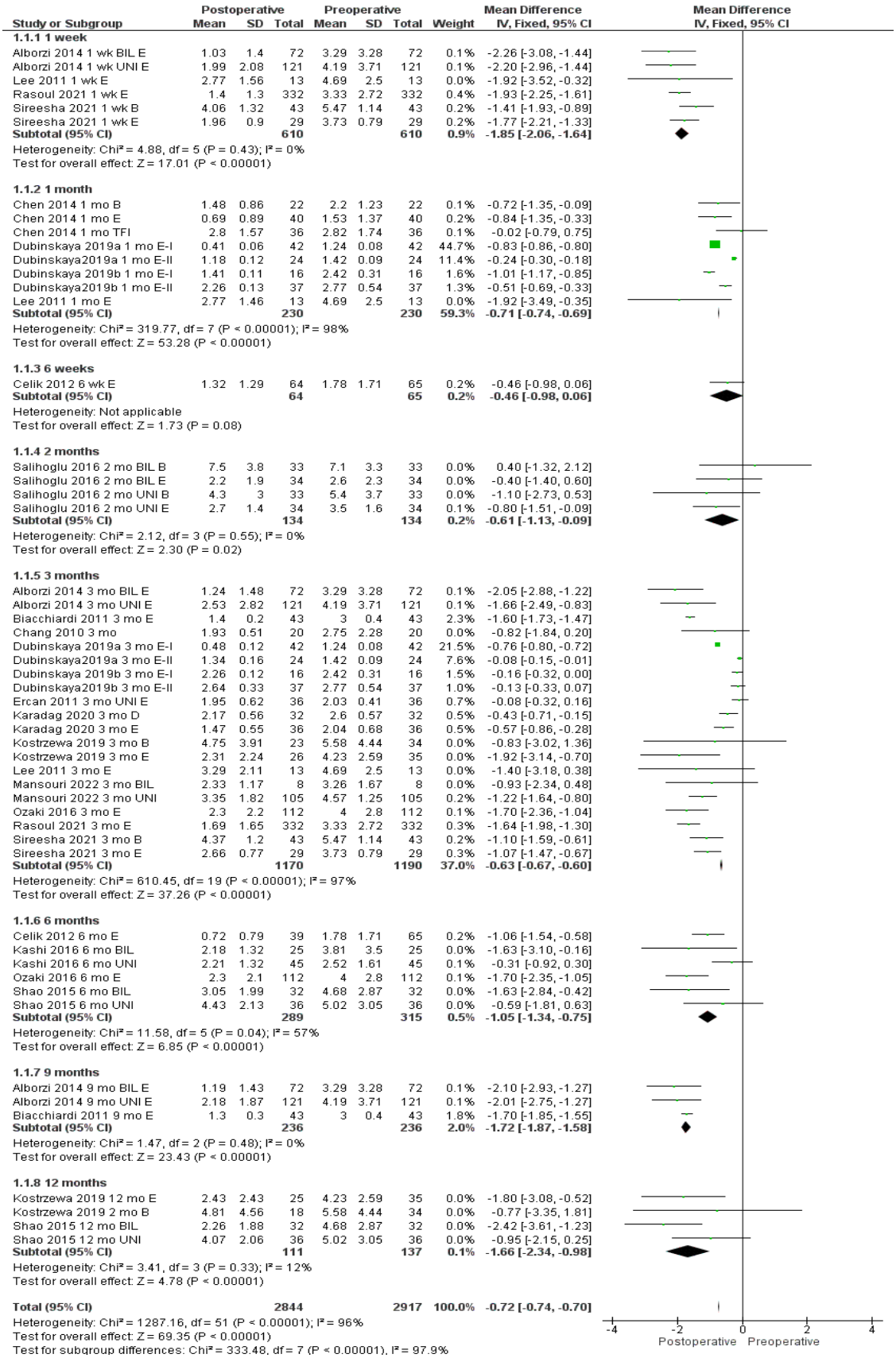

Fig. 2. Forest plot for AMH (ng/mL)

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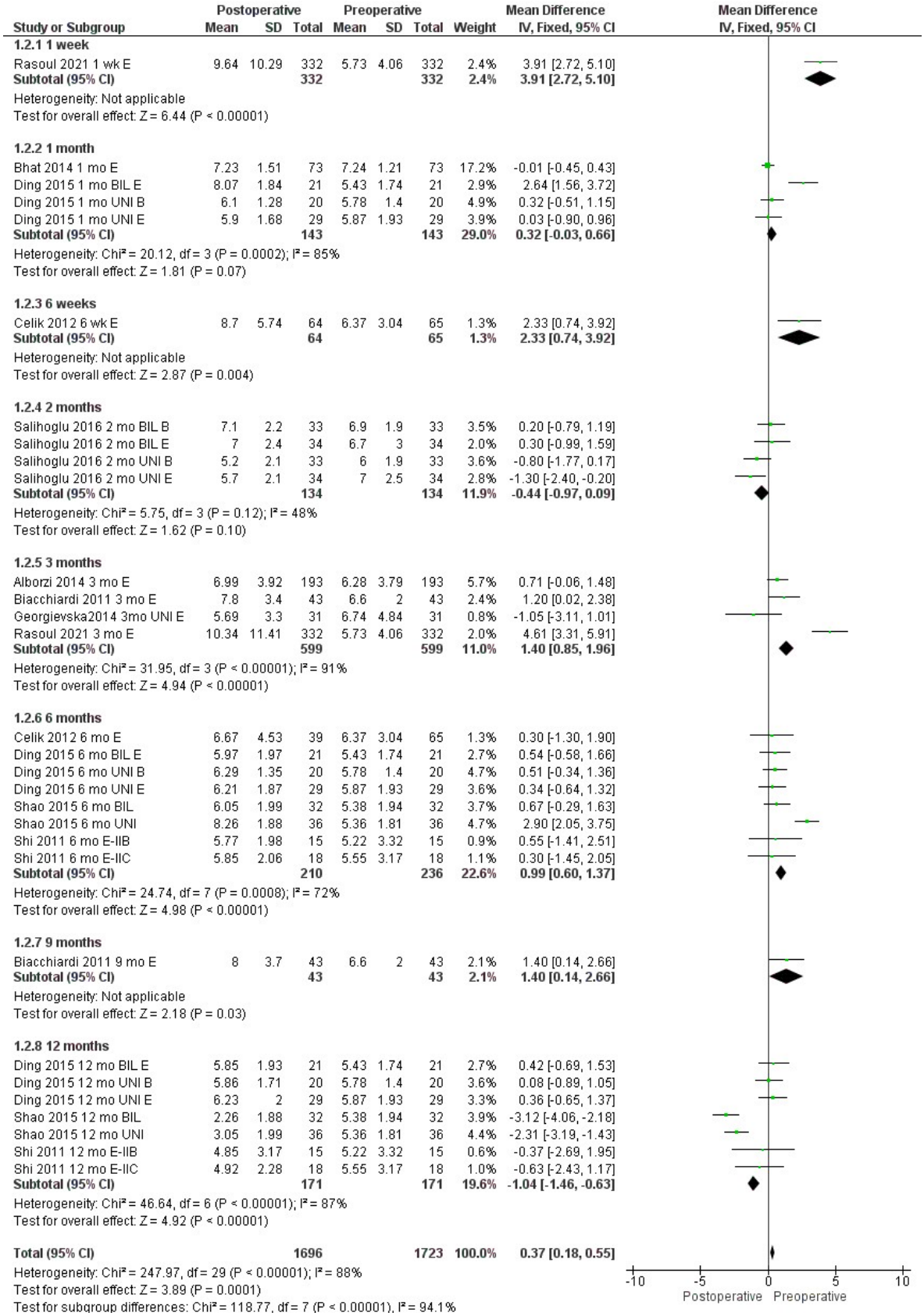

Fig. 3. Forest plot for FSH (mIU/mL)

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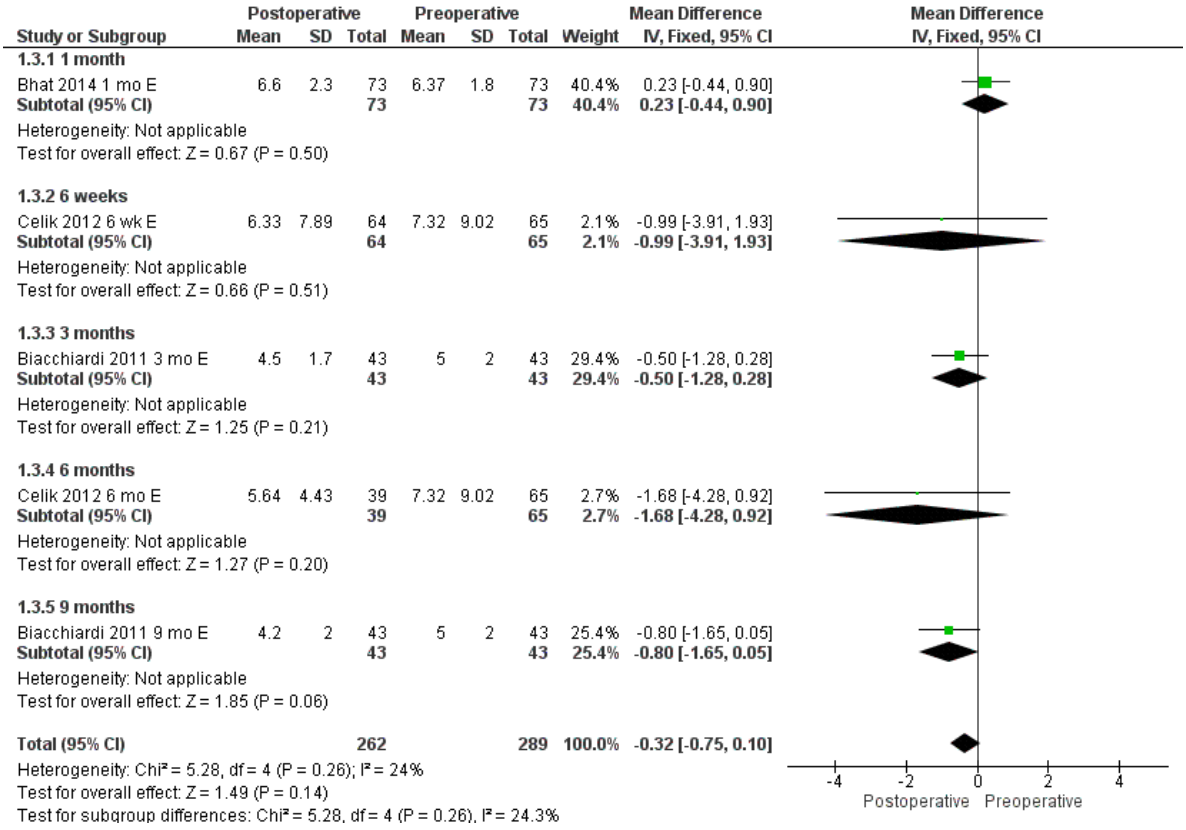

Fig. 4. Forest plot for LH (mIU/mL)

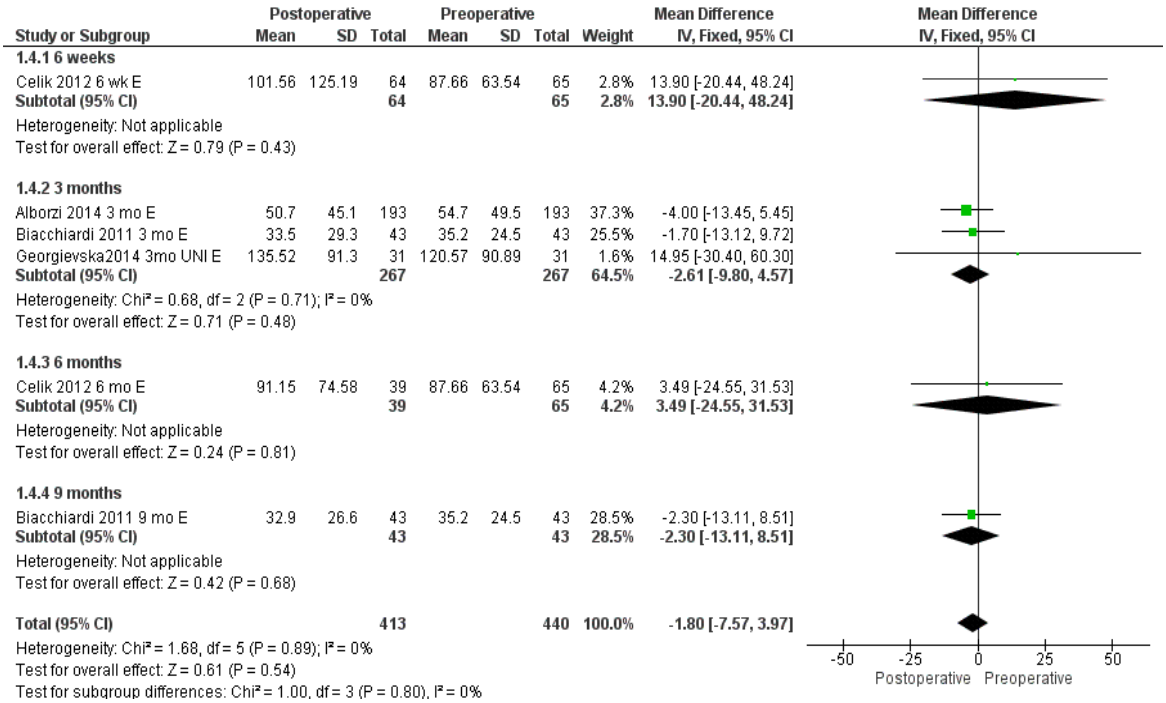

Fig. 5. Forest plot for estradiol (pg/mL)

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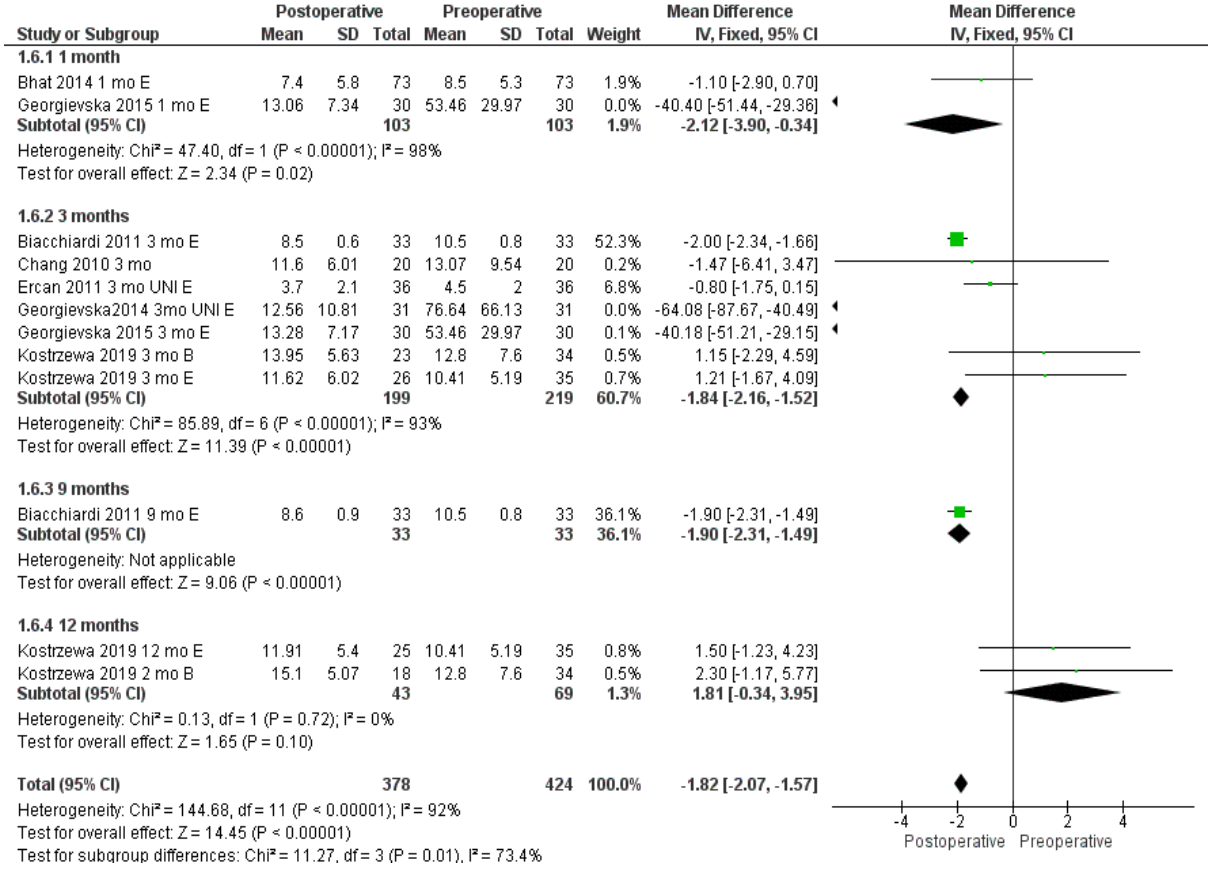

Fig. 6. Forest plot for residual ovarian volume (cm^3)

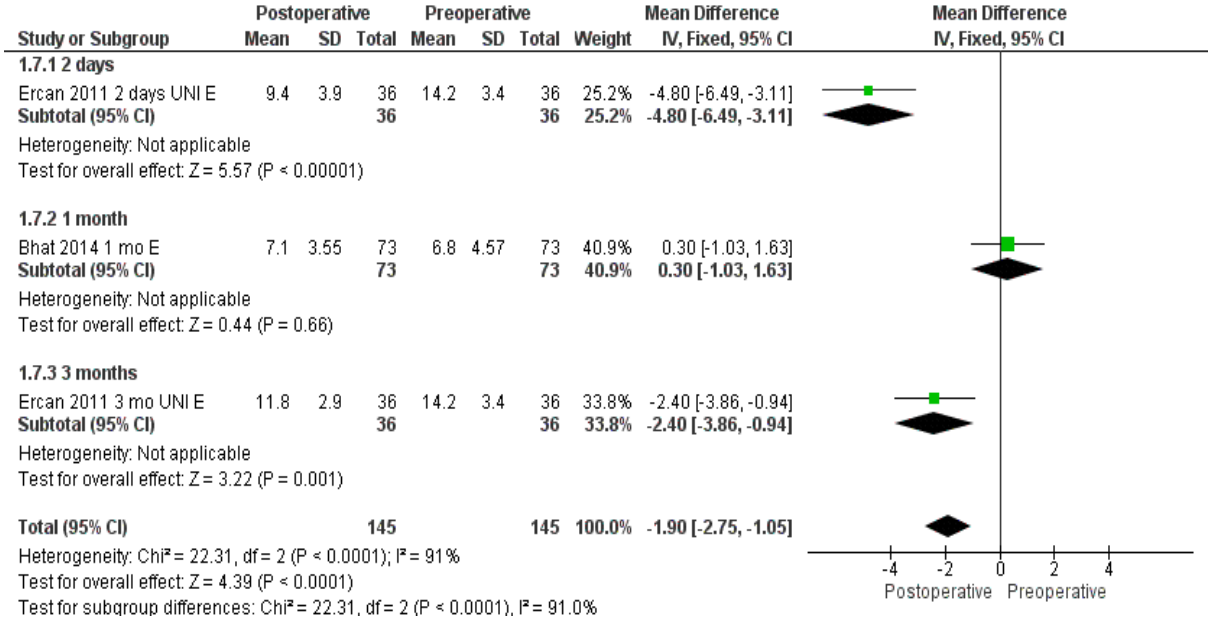

Fig. 7. Forest plot for PSV (cm/second)

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