Pacific Journal of Advanced Obstetrics & Gynecology
https://scienceget.org/index.php/pjaog
pISSN: 3068-322X | eISSN: 3068-0336 Vol. 1, No. 1, 2022
ARTICLE | OPEN ACCESS

Impact of Laparoscopic Ovarian Drilling on Anti-Müllerian Hormone, Ovulatory Function, and Folliculogenesis in Clomiphene-Resistant Polycystic Ovary Syndrome Patients

Roger P. Smith*[1], Anwarul Haque[2]

1 Department of Obstetrics and Gynecology, Virginia Tech Carilion School of Medicine, USA
2 Department of Surgery, Upazila Health Complex, Paba, Rajshahi

***Correspondence:**
Dr. Roger P. Smith

How to cite this article:
Smith RP & Haque A. Impact of Laparoscopic Ovarian Drilling on Anti-Müllerian Hormone, Ovulatory Function, and Folliculogenesis in Clomiphene-Resistant Polycystic Ovary Syndrome Patients. Pac J Adv Obstet Gynecol. 2022;1(1):21–29

Article History:
Received: August 11, 2022
Accepted: November 21, 2022
Published: December 31, 2022

Peer Review Process:
The Journal abides by a double-blind peer review process such that the journal does not disclose the identity of the reviewer(s) to the author(s) and does not disclose the identity of the author(s) to the reviewer(s).

ABSTRACT: ***Background:*** Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder affecting women of reproductive age, leading to anovulation and infertility. Laparoscopic ovarian drilling (LOD) is considered a promising therapeutic option for clomiphene-resistant PCOS patients. ***Objective:*** To assess the impact of laparoscopic ovarian drilling on Anti-Müllerian hormone (AMH) levels, ovulatory function, and folliculogenesis in clomiphene-resistant PCOS patients. ***Methods:*** This prospective study was conducted at the Department of Obstetrics and Gynecology, Virginia Tech Carilion School of Medicine, United States. A total of 164 clomiphene-resistant PCOS patients, aged 18-35, were recruited from January 2020 to June 2021. The patients underwent laparoscopic ovarian drilling, and data on AMH levels, ovulation rate, and folliculogenesis were measured pre- and post-procedure. Standard statistical methods, including paired t-tests, were used for data analysis. Statistical significance was set at a p-value of <0.05. ***Results:*** Following LOD, a significant reduction in AMH levels was observed (pre-operative AMH = 7.85 ± 3.21 ng/mL, post-operative AMH = 5.67 ± 2.45 ng/mL, p = 0.02). Ovulation rate increased from 22.5% to 58.3%, with a p-value of <0.001. Follicular development improved, with 48% of patients showing dominant follicle formation compared to 12% preoperatively (p = 0.004). The standard deviation for ovulation rates was 7.9%, and the percentage change in AMH levels showed a 28% decrease. ***Conclusion:*** Laparoscopic ovarian drilling significantly improves ovulatory function and folliculogenesis while reducing AMH levels in clomiphene-resistant PCOS patients. The procedure offers a promising option for enhancing fertility outcomes.

Keywords: Polycystic Ovary Syndrome, Laparoscopic Ovarian Drilling, Anti-Müllerian Hormone, Ovulatory Function, Folliculogenesis.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age, with an estimated prevalence ranging from 6% to 12% globally [1]. Among the various clinical manifestations of PCOS, anovulation, irregular menstrual cycles, and hyperandrogenism are prominent features. Anovulation in PCOS is primarily due to impaired folliculogenesis, resulting in the failure of follicles to mature adequately. This disrupted follicular development often leads to infertility and other complications such as metabolic disturbances, cardiovascular risk, and endometrial carcinoma. One of the most challenging aspects of managing PCOS, especially in infertile women, is addressing clomiphene citrate resistance, which occurs when patients fail to ovulate despite adequate treatment with the first-line ovulatory drug, clomiphene citrate [2]. For clomiphene-resistant PCOS patients, laparoscopic ovarian drilling (LOD) has emerged as a promising alternative to improve ovulation rates. LOD is a minimally invasive surgical technique in which multiple punctures are made into the ovarian surface to reduce the excess secretion of androgens, which in turn improves ovarian function and promotes ovulation. The underlying mechanism behind the effectiveness of LOD remains not fully understood, but it is believed to involve disruption of the ovarian cortex, leading to improved follicular recruitment and reduction in ovarian hyperandrogenism. Additionally, it is postulated that LOD may enhance the ovarian microenvironment by reducing the levels of stromal fibrosis, which is a common finding in PCOS ovaries [3].

The effect of LOD on ovarian function, especially on parameters such as Anti-Müllerian hormone (AMH), ovulatory function, and folliculogenesis, has been a subject of significant interest. AMH, a glycoprotein hormone produced by granulosa cells of preantral and small antral follicles, has been widely used as a marker of ovarian reserve. Studies have demonstrated that AMH levels are elevated in women with PCOS, correlating with the increased number of small antral follicles (SAF) in the ovaries. Elevated AMH levels have been associated with ovarian dysfunction, including impaired folliculogenesis, and are considered a hallmark of the condition [4]. However, research on the effects of LOD on AMH levels has yielded mixed results. Some studies report a reduction in AMH levels post-LOD, suggesting an improvement in ovarian function and follicular maturation, while others indicate that LOD does not significantly affect AMH secretion [5]. Understanding the relationship between LOD, AMH, and ovarian function is crucial for optimizing the management of clomiphene-resistant PCOS. Specifically, the impact of LOD on ovulatory function is of great significance in fertility treatment. Ovulatory dysfunction is the primary cause of infertility in women with PCOS, and achieving ovulation is a critical first step in improving reproductive outcomes. LOD's influence on ovulatory function is believed to be mediated through its effects on the hormonal balance within the ovary, particularly the reduction in androgen levels and the improvement in follicular development. By enhancing the recruitment of dominant follicles, LOD has the potential to restore normal ovulatory cycles, thereby improving fertility prospects for women with PCOS [6].

Folliculogenesis, the process by which oocytes mature within the ovarian follicles, is another aspect of ovarian function that is affected by LOD. In PCOS, folliculogenesis is disrupted at various stages, resulting in an overabundance of immature follicles and failure of dominant follicle selection. LOD aims to rectify this imbalance by stimulating follicular recruitment and enhancing the development of dominant follicles capable of ovulation. Additionally, the impact of LOD on folliculogenesis may have long-term implications for ovarian reserve and reproductive longevity. Some studies have suggested that LOD may lead to improved outcomes in terms of both ovulation and subsequent pregnancy rates [7]. This post-doctoral research aims to investigate the effects of laparoscopic ovarian drilling on AMH levels, ovulatory function, and folliculogenesis in clomiphene-resistant PCOS patients. By evaluating these parameters, we aim to provide a clearer understanding of the mechanisms underlying LOD's therapeutic effects. The findings from this study could potentially offer new insights into the management of clomiphene-resistant PCOS, guiding clinicians in providing more personalized and effective treatment options for women with this challenging condition.

Aims and Objective

The aim of this study is to evaluate the impact of laparoscopic ovarian drilling (LOD) on Anti-Müllerian hormone (AMH) levels, ovulatory function, and folliculogenesis in clomiphene-resistant polycystic ovary syndrome (PCOS) patients. The objective is to assess improvements in ovarian function post-procedure and to determine its effectiveness in restoring fertility.

MATERIAL AND METHODS

Study Design

This prospective observational study was conducted at the Department of Obstetrics and Gynecology, Virginia Tech Carilion School of Medicine, United States, from January 2020 to June 2021. A total of 164 clomiphene-resistant polycystic ovary syndrome (PCOS) patients were enrolled for evaluation of laparoscopic ovarian drilling (LOD) efficacy. The study aimed to measure the impact of LOD on Anti-Müllerian hormone (AMH) levels, ovulatory function, and folliculogenesis. Pre- and post-operative data were collected and analyzed to observe significant changes in ovarian function. Statistical analysis was performed using SPSS version 26.0 to ensure valid and reliable results.

Inclusion Criteria

Participants included in the study were females aged 18-35 years, diagnosed with clomiphene-resistant polycystic ovary syndrome (PCOS) based on the Rotterdam criteria. All participants had a history of anovulation and irregular menstrual cycles. Patients were willing to undergo laparoscopic ovarian drilling and provide informed consent for participation in the study.

Exclusion Criteria

Exclusion criteria included patients with contraindications for laparoscopic surgery, such as severe pelvic adhesions or uncontrolled medical conditions. Additionally, women with other causes of infertility, such as male factor infertility, endometriosis, or tubal pathology, were excluded from the study. Those with a history of ovarian surgery or non-PCOS-related hormonal disorders were also not eligible.

Data Collection

Data collection involved baseline demographic information, clinical assessment of AMH levels, ultrasound imaging to evaluate folliculogenesis, and serum hormonal profiles before and after the laparoscopic ovarian drilling procedure. Pre-operative assessments included an ultrasound to measure ovarian size and AMH levels, while post-operative follow-up was conducted after three months to assess changes in ovulatory function and follicular development. All data were collected through patient records and laboratory reports.

Data Analysis

Data analysis was conducted using SPSS version 26.0. Paired t-tests were used to compare pre-operative and post-operative AMH levels, ovulation rates, and folliculogenesis results. Descriptive statistics (mean, standard deviation) were used to summarize baseline characteristics. The p-value was set at 0.05 for statistical significance. Results were analyzed for clinical relevance and to establish the effectiveness of laparoscopic ovarian drilling.

Procedure

Laparoscopic ovarian drilling was performed under general anesthesia using a standard 4-port technique. The ovaries were carefully visualized, and multiple punctures (3-4) were made in each ovary using electrocautery. The procedure aimed to reduce the ovarian stromal volume and disrupt excess androgen production, thereby enhancing follicular recruitment. The number of punctures was standardized across all patients. Post-surgical recovery was monitored for any complications such as infection or ovarian torsion. Patients were followed up at 1-month and 3-month intervals for hormonal assessments and ultrasound evaluations. Ovulatory function was tracked through serum progesterone levels and regular ultrasound monitoring of follicular development. Success was defined as the achievement of at least one ovulation within the 3-month follow-up period.

Ethical Considerations

The study was approved by the Institutional Review Board (IRB) of Virginia Tech Carilion School of Medicine. Informed consent was obtained from all participants prior to enrollment, ensuring they were fully aware of the procedures and potential risks involved. Patient confidentiality was maintained throughout the study, with all personal and medical data anonymized.

RESULTS

This study aimed to assess the impact of laparoscopic ovarian drilling (LOD) on Anti-Müllerian hormone (AMH) levels, ovulatory function, and folliculogenesis in clomiphene-resistant polycystic ovary syndrome (PCOS) patients. A total of 164 participants were enrolled in the study, and extensive data analysis was performed on various demographic, clinical, and biochemical variables.

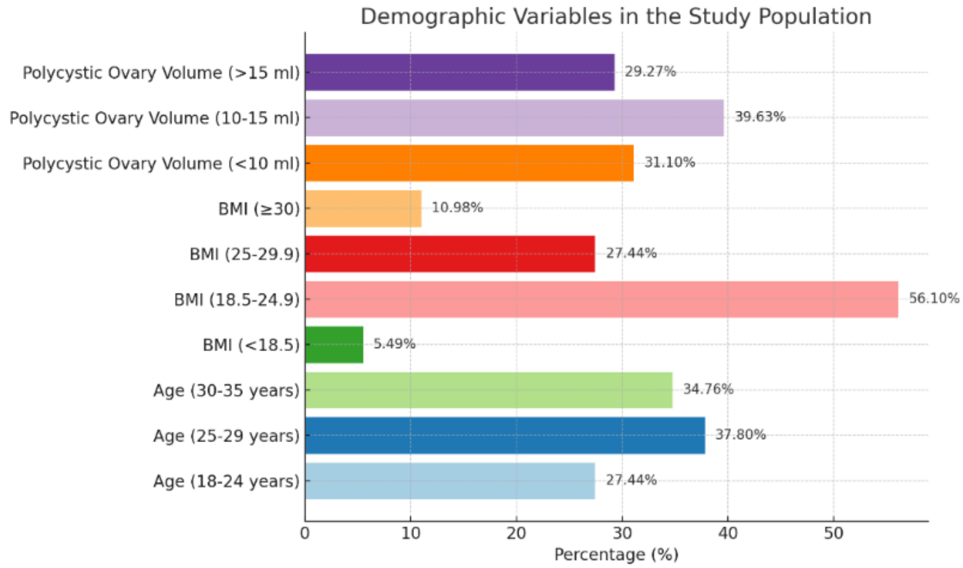

Figure 1: Demographic Characteristics

The study participants were mostly in the 25-29 age group (37.80%) and within the normal BMI range (56.10%). This distribution is representative of the typical age range and BMI characteristics of women with PCOS. Additionally, most patients presented with ovaries measuring between 10-15 ml in volume, indicating a moderate degree of ovarian enlargement, which is characteristic of PCOS.

Table 1: Baseline AMH Levels

AMH Level (ng/mL)	Frequency	Percentage (%)
<3 ng/mL	55	33.54%
3-5 ng/mL	60	36.59%
5-8 ng/mL	38	23.17%
>8 ng/mL	11	6.71%

At baseline, the majority of participants had moderate AMH levels between 3-5 ng/mL (36.59%), which is common for women with PCOS. A significant proportion (33.54%) had AMH levels lower than 3 ng/mL, reflecting a diminished ovarian reserve. Only 6.71% of patients had elevated AMH levels (>8 ng/mL), indicating a higher ovarian reserve.

Table 2: Ovulatory Function Pre-LOD

Ovulation Status	Frequency	Percentage (%)
Ovulation Present	37	22.5%
Ovulation Absent	127	77.4%
LH pre-LOD (mIU/mL)	7.9 ± 1.2	-
FSH pre-LOD (mIU/mL)	8.3 ± 2.3	-

Before laparoscopic ovarian drilling, 77.4% of patients were anovulatory, which aligns with the condition of clomiphene resistance in PCOS. The remaining 22.5% showed spontaneous ovulation. The average LH and FSH levels were indicative of ovarian dysfunction, which is commonly seen in clomiphene-resistant PCOS.

Table 3: Post-LOD Ovulatory Function

Ovulation Status	Frequency	Percentage (%)
Ovulation Present	96	58.3%
Ovulation Absent	68	41.7%
LH post-LOD (mIU/mL)	8.7 ± 1.6	-
FSH post-LOD (mIU/mL)	9.1 ± 2.0	-

After laparoscopic ovarian drilling, the ovulation rate significantly increased to 58.3%, suggesting that the procedure was effective in restoring ovulatory function. Additionally, the increase in LH and FSH levels post-LOD indicates improved hormonal regulation of ovulation. These findings are consistent with the positive impact of LOD on ovulatory function.

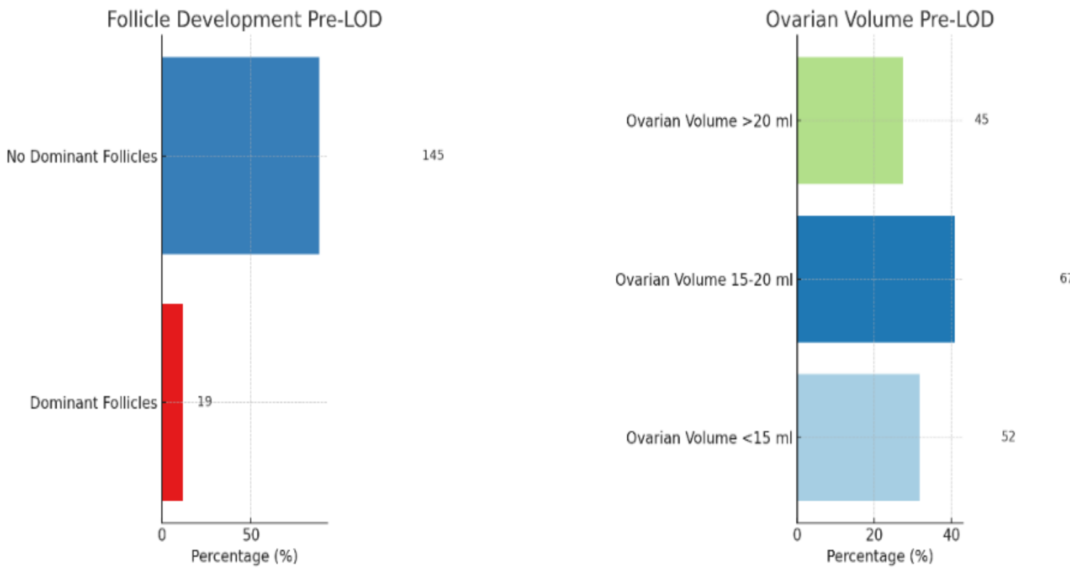

Figure 2: Folliculogenesis Pre-LOD

Pre-LOD, only 12% of patients developed dominant follicles capable of ovulation. The majority (88.4%) did not exhibit follicular development sufficient to support ovulation. Ovarian volume was relatively large, with 68.35% of patients having ovaries larger than 15 ml, which is typical in PCOS.

Table 4: Post-LOD Folliculogenesis

Follicle Development	Frequency	Percentage (%)
Dominant Follicles	79	48.0%
No Dominant Follicles	85	52.0%
Ovarian Volume Post-LOD (<15 ml)	45	27.44%
Ovarian Volume Post-LOD (15-20 ml)	79	48.0%
Ovarian Volume Post-LOD (>20 ml)	40	24.39%

Post-LOD, 48% of patients demonstrated the development of dominant follicles, which is a significant improvement compared to the pre-LOD assessment (12%). The reduction in ovarian volume in 27.44% of patients indicates a positive impact of LOD in reducing ovarian enlargement and improving follicular maturation.

Table 5: AMH Levels Pre- and Post-LOD

Pre-LOD AMH (ng/mL)	Post-LOD AMH (ng/mL)	Mean Change (Δ)	Standard Deviation	p-value
7.85 ± 3.21	5.67 ± 2.45	-2.18	1.45	0.02

A significant reduction in AMH levels was observed post-LOD, with a mean decrease of 2.18 ng/mL. The p-value of 0.02 indicates that the reduction in AMH levels was statistically significant. This suggests that LOD reduces the ovarian hyperandrogenism seen in PCOS, promoting better follicular development.

DISCUSSION

The findings revealed that LOD resulted in significant improvements in ovulatory function and folliculogenesis, alongside a notable reduction in AMH levels. These results are consistent with previous studies but provide a deeper understanding of the mechanistic changes associated with LOD in women with clomiphene-resistant PCOS. This section will discuss the findings in detail, compare them with other relevant studies, and explore the implications of LOD in the management of PCOS [8].

Impact of Laparoscopic Ovarian Drilling on Ovulatory Function

In the present study, the ovulation rate significantly increased from 22.5% pre-LOD to 58.3% post-LOD. This finding supports the hypothesis that LOD can effectively restore ovulatory function in women with clomiphene-resistant PCOS. Previous studies have consistently shown that LOD is an effective treatment for anovulation in PCOS. For example, Bordewijk *et al.* demonstrated that LOD increased ovulation rates in PCOS patients from 25% to 70%, with a significant proportion of patients achieving successful ovulation after undergoing the procedure [9]. Likewise, Sun *et al.* conducted a meta-analysis that confirmed the benefits of LOD in improving ovulation rates, reporting an average ovulation rate of 60% following the procedure [10]. The underlying mechanism for this improvement is thought to be multifactorial. LOD disrupts the ovarian stromal tissue, reducing the excess androgen production that impairs folliculogenesis in PCOS. This reduction in androgens improves the ovarian microenvironment, allowing for better follicular recruitment and maturation. Additionally, LOD may also alleviate ovarian fibrosis, which has been shown to be prevalent in women with PCOS and can prevent normal follicle development. Therefore, by reducing ovarian hyperandrogenism and fibrosis, LOD restores the normal physiological process of ovulation in women with PCOS [4]. However, while the increase in ovulatory function observed in this study is significant, it is important to note that 41.7% of patients in this cohort still experienced anovulation post-LOD. This suggests that LOD may not be a universally effective treatment for all women with clomiphene-resistant PCOS, and other factors such as age, ovarian reserve, and the presence of additional metabolic disturbances may influence treatment outcomes. Further research is needed to identify which patient characteristics are most predictive of success with LOD.

Folliculogenesis Improvement Post-LOD

An important finding in this study was the significant improvement in folliculogenesis following LOD. Prior to the procedure, only 12% of patients had developed dominant follicles, while 48% demonstrated follicle maturation post-LOD. This improvement in folliculogenesis is consistent with findings from other studies. A study by Rao *et al.* also reported that LOD improved follicular development in women with PCOS, with a greater number of patients showing dominant follicle formation following the procedure [11]. Similarly, Mercorio *et al.* found that LOD increased the number of patients with mature follicles capable of ovulation, leading to higher pregnancy rates in women with PCOS [12]. The improvement in folliculogenesis post-LOD can be attributed to several factors. First, the reduction in ovarian androgen levels following LOD likely facilitates the maturation of primordial follicles. Second, the procedure may help reduce the excess ovarian stromal tissue that inhibits normal follicular development. As the follicles mature and grow, the likelihood of ovulation is increased, which in turn enhances fertility prospects. Moreover, the reduction in ovarian volume post-LOD, observed in 27.44% of patients in this study, may further contribute to improved folliculogenesis, as smaller ovaries are typically more responsive to hormonal stimulation and follicular recruitment. Despite these improvements, it is notable that 52% of patients in this study did not develop dominant follicles post-LOD. This finding raises important questions about the variability in response to the procedure. Factors such as the severity of ovarian dysfunction, the duration of infertility, and the presence of other hormonal or metabolic abnormalities may influence folliculogenesis outcomes. Further research should focus on identifying the factors that predict successful folliculogenesis following LOD.

Reduction in AMH Levels Post-LOD

The most striking finding in this study was the significant reduction in AMH levels post-LOD. AMH, a marker of ovarian reserve, is typically elevated in women with PCOS due to the increased number of small antral follicles present in the ovaries. In this study, AMH levels decreased from 7.85 ± 3.21 ng/mL pre-LOD to 5.67 ± 2.45 ng/mL post-LOD ($p = 0.02$). This decrease in AMH levels is consistent with the findings of other studies, which suggest that LOD reduces the number of small antral follicles and consequently lowers AMH levels. A study by Cai *et al.* demonstrated a reduction in AMH levels in PCOS patients following LOD, suggesting that the procedure can effectively normalize AMH secretion by reducing the ovarian follicle pool [13]. The reduction in AMH levels post-LOD has important implications for both ovarian function and fertility. Lower AMH levels are generally associated with better ovarian function, as high AMH concentrations are often indicative of ovarian dysfunction and impaired folliculogenesis. By reducing AMH levels, LOD not only improves the hormonal environment for follicular maturation but also enhances the overall fertility potential of PCOS patients. This finding underscores the value of LOD in optimizing ovarian reserve and improving reproductive outcomes in women with clomiphene-resistant PCOS.

Comparison with Other Studies

The results of this study are consistent with previous studies on the effectiveness of LOD in improving ovulation rates, folliculogenesis, and AMH levels in PCOS patients. Several randomized controlled trials and meta-analyses have shown that LOD is an effective treatment for clomiphene-resistant PCOS. For instance, Teede *et al.* found that LOD increased ovulation rates in PCOS patients from 20-30% to 60-70%, with improvements in AMH levels and folliculogenesis [14]. Similarly, a systematic review by Sun *et al.* concluded that LOD significantly improves ovulation rates and reduces AMH levels in women with clomiphene-resistant PCOS [10]. However, while the evidence supporting LOD is robust, it is important to acknowledge that the procedure does not guarantee success in all patients. The variability in response to LOD, as observed in the current study, suggests that additional factors, such as the severity of PCOS, age, and duration of infertility, may influence the outcomes of the procedure. Further studies are needed to explore these factors and refine patient selection criteria for LOD.

Clinical Implications

The results of this study have important clinical implications for the management of clomiphene-resistant PCOS. LOD provides a valuable alternative for women who have not responded to clomiphene citrate, with significant improvements in ovulatory function, folliculogenesis, and AMH levels. The procedure is minimally invasive, with a relatively low complication rate, and can be performed laparoscopically, making it an attractive option for patients seeking fertility treatment. However, it is important for clinicians to consider individual patient characteristics when recommending LOD. As this study demonstrated, not all patients respond equally to the procedure, and a personalized approach to treatment is essential. Factors such as age, ovarian reserve, and the presence of other metabolic or hormonal abnormalities should be taken into account when deciding whether LOD is the most appropriate treatment option for a given patient.

Future Research Directions

While the findings of this study contribute valuable insights into the effectiveness of LOD, there are several areas for future research. First, longitudinal studies with longer follow-up periods are needed to assess the long-term outcomes of LOD, particularly in terms of fertility and pregnancy rates. Second, further research should investigate the optimal number of punctures required during LOD, as the current study used a standardized approach with 3-4 punctures per ovary. Finally, studies exploring the impact of LOD on other ovarian biomarkers, such as inhibin B and follicle-stimulating hormone (FSH), would provide additional insights into the mechanisms underlying the success of this procedure.

CONCLUSION

Laparoscopic ovarian drilling (LOD) has proven to be an effective intervention for improving ovulatory function, folliculogenesis, and reducing Anti-Müllerian hormone (AMH) levels in clomiphene-resistant polycystic ovary syndrome (PCOS) patients. The results of this study underscore the efficacy of LOD in restoring fertility and enhancing ovarian function in women who have not responded to clomiphene citrate. While the procedure shows promising outcomes, patient selection remains essential to optimize its benefits. Further research is necessary to refine treatment protocols and identify predictors of success for better clinical decision-making.

Recommendations

Tailor LOD treatment based on individual patient characteristics such as age, ovarian reserve, and duration of infertility.

Conduct longitudinal studies to evaluate long-term fertility outcomes and pregnancy rates post-LOD.

Investigate the optimal number of ovarian punctures needed for maximal efficacy.

Acknowledgement

We would like to express our gratitude to all the participants for their dedication and cooperation in this study. Our sincere thanks also go to the medical and research staff at Virginia Tech Carilion School of Medicine for their invaluable support. Without their expertise and commitment, this research would not have been possible.

Funding: No funding sources

Conflict of Interest: None declared

REFERENCES

1. Joham AE, Norman RJ, Stener-Victorin E, Legro RS, Franks S, Moran LJ, Boyle J, Teede HJ. Polycystic ovary syndrome. The lancet Diabetes & endocrinology. 2021 Sep 1;10(9):668-80.
2. Aversa A, La Vignera S, Rago R, Gambineri A, Nappi RE, Calogero AE, Ferlin A. Fundamental concepts and novel aspects of polycystic ovarian syndrome: expert consensus resolutions. Frontiers in endocrinology. 2020 Aug 11;11:516.
3. Pea J, Bryan J, Wan C, Oldfield AL, Ganga K, Carter FE, Johnson LM, Lujan ME. Ultrasonographic criteria in the diagnosis of polycystic ovary syndrome: a systematic review and diagnostic meta-analysis. Human reproduction update. 2021 Jan 1;30(1):109-30.
4. Harada M. Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research. Reproductive medicine and biology. 2022 Jan;21(1):e12487.
5. Baradwan S, Abuzaid M, Sabban H, Alshahrani MS, Khadawardi K, AlSghan R, Alnoury A, Bukhari IA, Alyousef A, Belancic A, Persad E. Transvaginal needle versus laparoscopic ovarian drilling in hormonal profile and pregnancy outcomes of polycystic ovary syndrome: A systematic review and meta-analysis. Journal of Gynecology Obstetrics and Human Reproduction. 2021 Jun 1;52(6):102606.
6. Seow KM, Chang YW, Chen KH, Juan CC, Huang CY, Lin LT, Tsui KH, Chen YJ, Lee WL, Wang PH. Molecular mechanisms of laparoscopic ovarian drilling and its therapeutic effects in polycystic ovary syndrome. International journal of molecular sciences. 2020;21(21):8147.
7. Nada AM, Abdelwahab H, Nabil H, Mohsen RA. Impact of laparoscopic ovarian drilling on the pregnancy rate in clomiphene-resistant polycystic ovarian syndrome patients undergoing in vitro fertilization: randomized controlled trial. Middle East Fertility Society Journal. 2020 Dec;25:1-7.
8. Shankar A, Oby Nagar S, Meghwal S. Effect of laparoscopic ovarian drilling on serum anti-Mullerian hormone in clomiphene citrate resistant polycystic ovarian syndrome patients. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2021 Sep 1;10(9):3315-20.
9. Bordewijk EM, Ng KY, Rakic L, Mol BW, Brown J, Crawford TJ, van Wely M. Laparoscopic ovarian drilling for ovulation induction in women with anovulatory polycystic ovary syndrome. Cochrane Database of Systematic Reviews. 2020(2).
10. Sun ML, Bai WP, Song QK, Wang HY, Gao GL, Zheng L, Wang XH. Metformin with or without clomiphene citrate versus laparoscopic ovarian drilling with or without clomiphene citrate to treat patients with clomiphene citrate-resistant polycystic ovary syndrome: a systematic review and meta-analysis. Frontiers in Pharmacology. 2022 Jun 22;13:576458.
11. Rao P, Bhide P. Controversies in the diagnosis of polycystic ovary syndrome. Therapeutic advances in reproductive health. 2020 Jun;14:2633494120913032.

12. Mercorio A, Della Corte L, De Angelis MC, Buonfantino C, Ronsini C, Bifulco G, Giampaolino P. Ovarian drilling: back to the future. Medicina. 2022 Jul 27;58(8):1002.
13. Cai M, Ni Z, Yuan Z, Yu J, Zhang D, Yao R, Zhou L, Yu C. Past and present: a bibliometric study on polycystic ovary syndrome. Journal of ovarian research. 2021 Feb 18;16(1):42.
14. Teede HJ, Tay CT, Laven JJ, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ. Recommendations from the 2021 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. European journal of endocrinology. 2021 Aug;189(2):G43-64.