



“COMBINED LAPAROSCOPIC UTERINE ARTERY LIGATION AND LAPAROSCOPIC MYOMECTOMY VERSUS LAPAROSCOPIC MYOMECTOMY ALONE - A COMPARISON”

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ABSTRACT **Objective:** To evaluate the surgical and reproductive outcome of laparoscopic occlusion of uterine artery (LUAL) done before laparoscopic myomectomy in comparison with laparoscopic myomectomy done alone in patients presenting with symptomatic fibroid uterus **Design:** Prospective controlled trial. **Setting:** Sunrise Hospital (Private), Delhi (India) from Jan 2014- June 2015 (18 months) and followed for 2 years. **Methods:** 102 patients with symptomatic uterine myomas necessitating surgical intervention were included in the study, out of which 57 underwent laparoscopic myomectomy alone and 45 patients underwent bilateral laparoscopic occlusion of uterine artery (LUAL) prior to the laparoscopic myomectomy. The two groups were compared in terms of operating time, blood loss, post-operative complications, symptomatic improvement, recurrence rate and reproductive outcome in terms of pregnancy rate, fetal growth restriction and development of morbidly adherent placenta, and fetal outcomes between the two groups. **Result (s):** The average operating time in LUAL was 108.6 ± 36.9 min as compared to 90.2 ± 56.94 min in the control group. However, average blood loss was found to be significantly lower ($p < 0.001$) in LUAL group (115.1 ± 37.9 ml) than the myomectomy group alone (269.4 ± 58.9 ml). Postoperative complication rate, symptomatic relief and reproductive outcomes were similar in both groups. 17 patients in the LUAL group had a term pregnancy with no maternal and fetal complications and were electively delivered by cesarean section between 37-38 weeks of gestation with average birth weight of 2.86 kg. There was no evidence of adherent placenta intraoperatively and none of the babies required neonatal intensive care later. The rate of recurrence was also lesser in LUAL group. **Conclusion:** This study demonstrated superiority of LUAL combined with laparoscopic myomectomy as surgical modality of treatment for symptomatic fibroid uterus.

KEYWORDS : Laparoscopic uterine artery ligation (LUAL), laparoscopic myomectomy , myomectomy , obstetric outcomes after laparoscopic myomectomy, Laparoscopic uterine artery ligation with myomectomy

INTRODUCTION

Uterine leiomyomas are benign, monoclonal tumor of smooth muscle of human uterus (1,2). The established treatment for a symptomatic large fibroid is myomectomy in women who wish to retain their fertility and hysterectomy in women who have completed their family. Over the last few decades, laparoscopic myomectomy has emerged as an excellent modality for treatment of fibroids.

The major concern of myomectomy either by open or laparoscopic means is intraoperative bleeding which increases the operating time and further the post-operative morbidity.(3,4).

Various methods have been tried to reduce this intraoperative blood loss. Impact of medical interventions on hemostasis during myomectomy have been studied and a study by Lisa Hickmann et al showed that drugs like tranexamic acid are ineffective in controlling bleeding during myomectomy(5). However, oxytocin which was previously thought to be effective only on the pregnant uterus has been found to decrease intraoperative blood loss during myomectomy. (6) Vasopressin is another drug which has been found to be extremely useful. When injected in a dilution of 0.05 to 0.03 units/ml in the area adjacent to the fibroid, it significantly decreases blood loss. Careful usage and administration is required to prevent complications like hypotension, bradycardia, cardiac arrest and pulmonary edema. Other useful interventions are use of tourniquets, vaginal misoprostol, preoperative administration of gonadotropin-releasing hormone (GnRH) agonist, and peri-operative injection of ascorbic acid.

Laparoscopic uterine artery ligation(LUAL) from origin bilaterally is a surgical technique which is extremely effective not only to control bleeding at the time of myomectomy but also has been postulated to prevent the recurrence of fibroids later in life. Several studies have shown that future fertility and pregnancy outcome (in terms of fetal growth restriction or placenta accreta) remain unaffected after LUAL compared to UAE (uterine artery embolization) wherein subsequent pregnancy is not advisable as the polyvinyl alcohol particles block the complete blood supply including the collateral circulation of the uterus.

LUAL (Laparoscopic uterine artery ligation from origin bilaterally)

done in combination with laparoscopic myomectomy is one among them, introduced by Liu et al in 2000 (7). The mechanism of LUAL has not been well established, but necrosis and cell apoptosis of myoma due to reduced blood supply restricts growth and prevent the development of new uterine leiomyoma (8).

Recent research has reported reduction of intraoperative blood loss, improvement in symptoms and reduction of recurrence (9,10). Noting these reported benefits, laparoscopic ligation of uterine artery at origin (LUAL) which causes fewer complications is a better alternative, despite the higher technical skills required to perform this procedure (11).

Therefore our study was designed to study the surgical outcomes and complication in short term and reproductive complications and outcomes in long term in patients undergoing only laparoscopic myomectomy in comparison to patients undergoing laparoscopic uterine artery ligation along with laparoscopic myomectomy.

MATERIAL AND METHODS:

A Prospective Observational Case Control Study was carried out from 2014 to 2016 in the Department of Obstetrics and Gynaecology, Sunrise hospital, Delhi. 116 patients with symptomatic uterine myomas necessitating surgical intervention were included in the study. Informed consent was obtained from each patient after explaining the surgical procedure, risks, and benefits. All surgeries were performed by a single senior laparoscopic surgeon. The patients were divided into two groups: group 1 (n=57) included patients who underwent only laparoscopic myomectomy; and group 2 (n=45) which underwent laparoscopic uterine artery ligation bilaterally along with laparoscopic myomectomy.

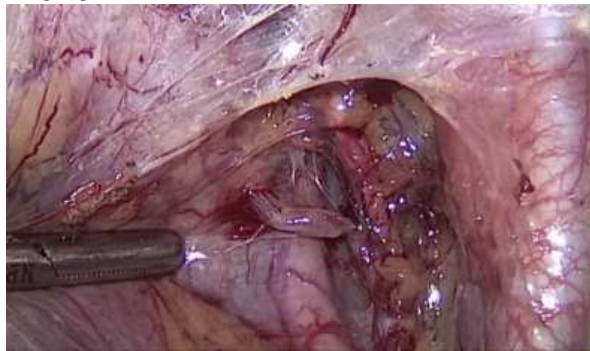
Baseline uterine leiomyoma size location were measured by ultrasonography, in some cases MRI was used.

Operative Procedure Details

The laparoscopic surgeries were performed under general anesthesia. The patients were placed in low lithotomy position, primary port was inserted at modified palmer's point(2 cm medial and inferior to the palmer's point) and three secondary ports were placed infra

umbilically. In the group undergoing laparoscopic myomectomy alone, the surgery was proceeded with directly. In the second group, peritoneum was opened in the ovarian fossa, after identification of the ureter and internal iliac artery, the uterine artery was ligated at its origin from the Internal Iliac Artery with either Ligamax (clips) or coagulated with the help of Ligasure. When both the uterine arteries had been successfully occluded, laparoscopic myomectomy was done. Myometrium was repaired in multiple layers with barbed vicryl 1-0(V-loc) and carefully approximated in both groups. The excised leiomyoma was removed through the right lateral port by an electromechanical morcellator (Karl Storz). The pelvic lavage was carried out with normal saline and adequate hemostasis was achieved. Immediate postoperative complication like fever, drain requirement, prolonged hospital stay was noted. Patients were followed up with ultrasound and complete blood count on day 10, 6 months, 12 months and lastly at 24 months after the surgery. The recurrence was defined as the recurrence of myoma of at least 2 cm in diameter and resolution of symptoms. Further the infertile patients who became pregnant after surgery and the outcome after pregnancies such as spontaneous abortions and live births were recorded. The patients who conceived were followed up antenatally and were planned for an elective cesarean section at 37 weeks after given steroid coverage for fetal lung maturation.

The surgical outcome was measured in terms of operating time, blood loss, need of blood transfusion, drain output, hospital stay, febrile morbidity, symptomatic improvement, recurrence rate and reproductive outcome was measured in terms of pregnancy rate, fetal growth restriction and development of morbidly adherent placenta (placenta accreta), need of hospitalisation of the babies between the two groups.



Statistical Analysis

The collected data was transformed into variables, coded and entered in Microsoft Excel. Data was analyzed and statistically evaluated using SPSS-PC-19 version.

Quantitative data was expressed in mean±standard deviation difference between two comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test while qualitative data were expressed in percentage. Statistical differences between the proportions were tested by chi square test or Fisher's exact test. 'P' value less than 0.05 was considered statistically significant.

RESULTS:

In total, 102 patients in both the groups completed the follow up for 24 months (at post op day 10, 6 months, 12 months and 24 months). No difference existed between the two groups in term of demographic and clinical characteristics of the patients in the two groups.(table 1)

Table 1 – Clinical And Demographic Details Of The Patients In The Two Groups

		Group 1 (n=57) (Laparoscopic myomectomy alone)	Group 2 (n=45) (Laparoscopic myomectomy + LUAL)	P value
Mean Age (in years)		32.95	33.22	0.82
Size of fibroid (in cm)	5-10 cm	22	13	0.30
	10-15cm	29	27	0.35
	>15cm	6	5	0.92

Primary complaint	Mass per abdomen	4	3	0.99
	Primary infertility	22	27	0.40
	Secondary infertility	13	6	0.22
	Bad obstetric history	2	0	0.50
	Heavy menstrual bleeding	16	9	0.34

Though the operative time in myomectomy +LUAL group was significantly more than the only myomectomy group which can be attributed to a technically difficult procedure, but at the same time, the intraoperative blood loss was significantly less in the myomectomy +LUAL group.

Table 1- Surgical outcomes

	Group 1 (n=57) (Laparoscopic myomectomy alone)	Group 2 (n=45) (Laparoscopic myomectomy + LUAL)	P value
Mean operative time (minutes)	90.21	108.67	.01
Mean Blood loss (ml)	126.32	116.67	.05
Drain requirement for 2 days(number)	18	15	.85
Febrile morbidity (number of patients)	6	0	.06
Average hospital stay(days)	1.65	1.49	.89
No recurrence(number) till 24 months	40	41	.01
Single fibroid <5cm till 24 months	16	3	.01
Multiple fibroid on MRI at 24 months	1	1	.99
Symptomatic relief	45	42	0.05

There was no significant difference between the two groups with respect to drain output, febrile morbidity and average hospital stay.

The recurrence was lesser when LUAL was done.no recurrence was reported for 40 patients in only myomectomy group and 41 patients in the LUAL+myomectomy group after 2 years. 16 patients in the only myomectomy group and 3 patients from the LUAL+myomectomy group had a recurrence with at least one single fibroid less than 5 cm after 2 years. One patient each from both the groups had a recurrence of multiple fibroids as reported on MRI. The histopathology of the patient who had recurrence of multiple fibroids in the LUAL+myomectomy group was suggestive of cellular leiomyoma.

The symptomatic relief was measured in terms of resolution of abnormal uterine bleeding. Significant symptomatic resolution was observed in patients in LUAL+myomectomy group rather than myomectomy alone.(p=0.05)

Table 2- Obstetric outcomes

	Group 1 (n=57)	Group 2 (n=45)	P value
Number of viable pregnancies	16	19	0.19
Number of FGR babies	0	0	-
Adherent placenta/ uterine rupture	0	0	-
Neonatal icu stay	0	0	-

Though the number of pregnancies in the LUAL+myomectomy group was more than that in only myomectomy group,(21 and 17 respectively, of which viable pregnancies were 19 and 16 respectively), the difference was not statistically significant. All pregnancies continued till term. Elective cesarean section was planned for all patients at 37 weeks gestation in view of myomectomy after giving steroid coverage for fetal lung maturity. However, owing to various obstetric complications and logistics, all patients could not be delivered at 37 weeks. In the only laparoscopic myomectomy group, 7 patients underwent cesarean section at 37 weeks, 4 at 36 weeks, 2 at 37 weeks and one each at 32,34 and 35 weeks and one patient had spontaneous abortion at 12 weeks.In the lual+myomectomy group, one patients each had spontaneous abortion at 12 and 14 weeks respectively, while the others had delivery by cesarean section at the following gestation – 8 at 37 weeks, 4 at 36 weeks, 3 at 34 weeks, 2 at 35 weeks and one each at 33 and 38 weeks. Intraoperatively there was

no evidence of placenta accreta in both the groups.

The average weight of the baby was 2.875 kg in the LUAL+ myomectomy group and 2.88 kg in the only myomectomy group.

DISCUSSION

Over recent years laparoscopic myomectomy has gained acceptance and done more frequently, with excellent results. This procedure has several advantages including faster recovery, shorter hospital stays, decreased operative time, less postoperative pain, reduced adhesion formation and superior cosmetic results. At the same time, it may be related to increased intra and postoperative bleeding. Until now, different methods have been designed to decrease intraoperative bleeding during myomectomy one of them was laparoscopic bipolar coagulation of uterine vessels (LBCUV) described in 2000 by Liu et al [7]. In that method both uterine arteries and the anastomosis zone of uterine and ovarian arteries were occluded to achieve hemostasis.

Our study demonstrated the efficacy of combined LUAL and laparoscopic myomectomy to alleviate intraoperative morbidity, to decrease the recurrence of fibroid, improvement in myoma-related symptoms and the effect of LUAL on pregnancy outcome. Though successful pregnancies have been reported in the literature following occlusion of both internal iliac and ovarian arteries (12) but the pregnancy outcome in terms of continuation of pregnancy till term, effect on fetus growth, risk of development of placenta accreta is not clearly known.

Our technique involved bilateral ligation of uterine artery at origin with Ligamax or Ligasure. Mean operative time in LUAL + LM was 108 min and average blood loss was 116 ml as compared to 90 min the mean operative time and 126 ml blood loss in case of only laparoscopic myomectomy. Longer operating time in the LUAL+ myomectomy group could be attributed to LUAL being a relatively technically demanding procedure. Also, since the study was not randomized, LUAL was more commonly done in patients having larger fibroids and those who had higher chances of intraoperative bleed which could have resulted in longer average operative time in patients undergoing LUAL at the time of myomectomy. However, the patients undergoing LUAL+ myomectomy had significantly decreased intraoperative blood loss. Similar study was done by Alborzi et al in 2008 which had similar results. The average operating time and blood loss were 112 minutes and 173 mL in the experimental group and 95 minutes and 402 mL in the control group. Extra time taken to perform bilateral uterine artery ligation was 18 minutes in our study which was similar to 17 minutes in the study conducted by Alborzi et al and 13 minutes in the previous studies(13).

Postoperative drain requirement and hospital stay was similar in the both groups. 6 patients in the only laparoscopic myomectomy group and none in the LUAL + myomectomy group developed fever in the postpartum period. Hematoma formation in the myometrium is the most common cause of febrile morbidity in the postoperative period. LUAL decreases ooze at myomectomy site and decreases hematoma formation, which might explain the postoperative fever in the patients in the only myomectomy group. However, these results were not statistically significant in our study probably because of smaller sample size.

42 (93.33%) patients in LUAL+ LM were relieved of their symptoms (viz menorrhagia) in comparison with 45 (78.94%) patients in LM only group ($p=0.05$). Thus our results were similar to those reported by previous studies. This resolution of menorrhagia may be attributed to partial uterine ischemia and necrosis of small myomas which might be instrumental in causing symptoms(10,11).

The diminution of recurrence was statistically significant in the LUAL + myomectomy group. 41 (91%) patients did not have a recurrence in the LUAL + myomectomy group in comparison to 40 (70.17%) patients in the only myomectomy group. 16 (28%) patients in the only myomectomy group had recurrence of single fibroid < 5cm in size in comparison to 3(6.67%) patients in the LUAL + myomectomy group. Multiple fibroids were seen in one patient in each group on MRI within 2 years. Thus we can conclude that there is a definite decrease in the recurrence of myomas in patients where LUAL was done at the time of myomectomy in our study. According to the 'transient uterine ischemia' hypothesis' by Burbank and colleagues, uterine artery occlusion causes occlusion of both myometrial and myoma vessels

which results in organ ischemia and necrosis(14). This organ ischemia and necrosis causes shrinkage of very small fibroids which being very small generally cannot be removed during surgery. This ischemic necrosis is responsible for the prevention of recurrences.

Uterine artery embolization (UAE) has been introduced as an effective method for treatment of symptomatic uterine leiomyomas in 1995(15). This method, however, is associated with complications which can be clubbed as the post embolization syndrome and is characterized by nausea, vomiting, pain, fever and leukocytosis, and affects up to 26% patients undergoing this procedure. Symptomatic relief afforded by UAE is however good. Clinical outcomes similar to UAE can be replicated by LUAL+ myomectomy and thus the postembolization syndrome can be avoided. Thus, a clear differential here which differentiates the clinical outcomes and is responsible for obviation of the postembolization syndrome is doing a simultaneous myomectomy with uterine artery occlusion. According to a study conducted by Hui et al (16), myomectomy with uterine artery occlusion is better than uterine artery occlusion alone. This leads us to conclude that LUAL + myomectomy has better clinical outcomes than UAE as we can avoid the postembolization syndrome and achieve similar clinical outcomes. Another major concern with UAE is the loss of ovarian reserve with the procedure. The small embolic particles used for UAE can embolise ovarian arteries as well in 60% cases and this has been proven on histopathology(17). This complication, however can be avoided by laparoscopic uterine artery ligation, since here the uterine artery is dissected out and isolated before ligation.

A study was conducted by Qu X et al., (18) where concentrations of the follicle-stimulating hormone, leuteinizing hormone, and estradiol and serum inhibin B concentration were evaluated using an immunoassays at one, three, and six months postoperatively. No significant effect was found on ovarian reserve on short term follow up. Another argument which is given against uterine artery ligation is that sabotaging uterine circulation may result in endometrial insufficiency. Due to lack of long term evidence and randomized trials, many clinicians still have their reservations about the effect of LUAL on future pregnancy rate.

We recorded our data on pregnancy rates and outcomes of pregnancy in both arms of the study to understand the effect of laparoscopic uterine artery ligation on future fertility. 16 (28%) patients in the laparoscopic myomectomy only group and 19 (42.22%) patients in LUAL + myomectomy group had viable pregnancies during the 2 years follow up. Elective cesarean section for all patients was planned at 37 weeks after giving them steroids for fetal lung maturation. Few patients however had preterm labor and had to undergo cesarean sections at earlier gestations. No evidence of placenta accreta was found in any of the patients in either group. Birth weights of babies in both groups were comparable and none of the babies required intensive care. Thus, from the above results one can safely conclude that fertility outcome of patients undergoing LUAL + myomectomy is not inferior to those undergoing laparoscopic myomectomy alone.

CONCLUSION

Doing LUAL prior to laparoscopic myomectomy though is a technically demanding procedure, but in expert hands, it results in decreased intraoperative blood loss, less postoperative morbidity, and lesser recurrence rate than myomectomy alone. The pregnancy outcomes of the patients undergoing this procedure are similar to those undergoing laparoscopic myomectomy alone.

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