# **Original Research**

# **Comparative analysis of Laparoscopic Surgery to Open Surgery**

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#### Abstract

**Background and Objective:** In the last 20 years, laparoscopic surgery for appendicitis has been introduced as a good alternative to open surgery. We aim to examine up to what extent laparoscopic surgery is practicable instead of open surgery in our setup. We examine the effect of shifting to laparoscopy surgery, comparing laparoscopic surgery to open surgery with quality indicators such as length of post operative stay, operating time, post operative pain, morbidity and follow up of each method during the period 2021 to 2022.

**Materials and method:** All adult patients presenting with appendicitis requiring operation were identified and randomised into two groups. One group underwent open surgery and the other one laparoscopic surgery for appendicitis. The time of surgery, duration of post operative stay, morbidity, mortality and VAS pain score were noted.

Result: A total of 90 patients underwent appendectomy either by open method or by laparoscopic method.

**Conclusion**: The standard surgical procedure for appendicitis can be easily done by laparoscopic surgery at the same time, the operating time was significantly more, the duration of stay is a bit less and has got lesser post operative complications on comparing with open surgery.

Keywords: Appendicitis, length of stay, laparoscopy and cohort studies

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#### Introduction

Appendicitis is the most frequent cause of abdominal pain in all ages, the only way to reduce the morbidity and to prevent complication of appendicitis, is to perform appendectomy before perforation or gangrene has occurred. <sup>1,2,3</sup>

The typical presentation of acute appendicitis begins with peri-umbilical pain, followed by anorexia and nausea. The pain then localizes to the lower right quadrant due to involvement of overlying parietal peritoneum. Fever ensues followed by development of leukocytosis. Recurrent appendicitis patients may have episodic bouts of right lower quadrant pain in the absence of acute febrile illness. <sup>3</sup> Patients with perforated appendix, generally very ill and require prior fluid resuscitation. Patients who present late in the course of disease, have mass and fever, may be subjected to non-operative management with close monitoring. Imaging studies are used to confirm the diagnosis and evaluate the size of abscess. Abscesses greater than 4 to 6 centimeters in size or with high fever require drainage.<sup>4,5,6,7</sup>Older patients are more likely to delay seeking treatments presenting with atypical findings and have higher rate of perforation.9 Treatment of appendicitis is essentially unchanged since its first description by Charles McBurney by his eponymous incision and has remained the procedure of choice for nearly a century. The appendicectomy can also be performed by Laparoscopic technique, as proposed by Kurt Semm in 1983. Though laparoscopic appendectomy has been shown to be both feasible and in randomized comparisons with open safe appendectomy, with advantage of increased diagnostic accuracy, quicker and less painful recovery, fewer postoperative complications and better cosmesis and allows better assessment of other intra-abdominal pathologies. 1-2. However, relative ease, wide feasibility and very few post of morbidities with Mc Burney's open surgery technique is a challenge to establishing role of laparoscopic surgery in appendicitis.

Laparoscopic appendectomy, though widely practiced, has not gained universal acceptance, as it is more time consuming and is associated with increased hospital costs and requirement of costly equipment which are a few reasons for its slow uptake in peripheral hospitals.

Overall advantages of laparoscopic appendectomy achieved by experienced laparoscopic surgeons are marginal compared with open appendectomy which can also be performed by surgeons in training. <sup>3,4,5,6</sup>

The debate which modality is better in dealing with appendicitis is still unsettled. The current study was undertaken to reassess the feasibility and compare outcome in case of open appendectomy and laparoscopic appendectomy.

Sample size calculated based on the results of a pilot study, a randomized trial was undertaken to compare the outcome of laparoscopic appendectomy with that of open appendectomy. This was based on the hypothesis that laparoscopic appendectomy would prove superior to open appendectomy in terms of hospital stay, post operative morbidity like pain, complication like wound infections, ileus, cosmesis, operating time, earlier return to normal activity and work. <sup>5,6,7-17</sup>

## **Materials and Methods**

Ethical clearance and permission from Institutional Review Board obtained to carry out the study before starting the work. Requisite informed consent from each participant obtained.

## **Study Area**

This prospective randomized controlled study was carried out in the department of General Surgery, at tertiary Teaching hospital and medical college, in western part of UP.

## **Study Population**

Patients with clinically diagnosed with Acute or recurrent appendicitis.

Inclusion Criteria-

Cases of Acute appendicitis admitted in the Surgery department.

Exclusion criteria-

1. Cases where general anesthesia is contraindicated

2. Cases where non-pathological appendix is found have been excluded.

3. Cases of perforated appendix, appendicular abscess

#### **Study Period**

The study was done over a period of one and half year.

### **Sample Size**

Sample size has been calculated using power analysis by taking alpha at 5% and power of the test at 80%. Accordingly, 45 samples in each of the two groups were selected. A p value < 0.05 has been considered

significant. All analysis has been done using SPSS software version.  $^{\rm 16}$ 

# Sample Design

Randomization based on pre-determined computergenerated randomization schedule in which patients were allocated to blocks of 10 comprising five patients of each group.

## Study Design

A single blind Parallel group randomized study.

## **Parameter Studied**

A. Intra-operative

Duration of operation

Intra-operative cardiovascular stability

B. Early postoperative

Pain intensity (after equivalent dosage with respect to body weight of non-steroidal anti-inflammatory analgesics).

Omission of drip and return to normal life.

Number of days of hospital stay.

Wound infection and wound dehiscence

C. Late postoperative

Scar tenderness.

Hernia

.

Ugly scar

D. Diagnostic advantage- for finding any other intraabdominal pathology in the intra- operative period.

#### Study tools:

1] Clinical examination

2] Questionnaires during operation and first and second postoperative days.

3] Visual analogue scale (VAS) was used to assess the severity of pain.

**Study Technique:** All cases of appendicitis presented to our facility were admitted through outdoor in general surgery ward of our hospital after evaluation from anesthesia point of view. Preoperative examination was done on the first post admission day. Patients are given adequate and relevant information regarding intra operative and post operative morbidity, advantages, and disadvantages of both the operative procedures. After taking informed consent patients were enrolled in the study. Randomization was done with the help of random number list. After written consent, operative procedure was performed.

During the intra operative period, the data was collected from multi-channel monitor regarding cardiovascular stability. After induction of anesthesia and before extubating maximum pulse rate and highest systolic blood pressure were recorded. Those patients who were known to be hypertensive were excluded from the study. Patients with compromised cardio-vascular system excluded from study. Operating time was calculated from time of incision till the last stitch for skin closure was done. Time taken by an anesthetist for induction of anesthesia at the beginning and recovery from anesthesia were recorded. During surgery the entire peritoneal cavity was inspected after passing a laparoscope. Appendectomy was done irrespective of any other pathology.

In the early post operative period, intensity of pain perception was assessed using visual analogue scale. Pain intensity was noted after standard dose of analgesics at one, twelve, twenty-four and after fortyeight hours. Non-steroidal anti-inflammatory drugs was (100-150 mg daily in divided doses) used according to body weight.

Sips of water (30 ml/hour) were allowed as soon as peristaltic sounds reappeared. If the patient tolerates water, drip was omitted after four hours and liquids were allowed. Soft diet was allowed gradually. Patient ambulation was encouraged. Any wound infection or wound discharge is taken care. Patients were discharged as soon as they were able to carry out normal day to day activity.

After discharge patients were followed on outdoor basis at weekly interval for next fifteen days and then monthly interval for next three months. Any ugly scar, scar tenderness and hernia noted and taken into account.

# **Statistical Analysis Of Data**

Numerical data was analyzed by using Student unpaired t - test, categorical data was analyzed by Fisher exact test or Chi square test which ever applicable. P value of <0.05 considered to be statistically significant.

# Observations

Total Ninety patients were included in the study who accepted to undergo randomization for appendectomy procedure. These patients were equally randomized to laparoscopic or open appendectomy group of forty each.

Baseline characteristics of both (laparoscopic or open appendectomy) groups were comparable.

Table-1: Sex distribution

This table shows that 44.5% were female and 55.5% were male in laparoscopic appendectomy group whereas in open appendectomy group 37.7% female and 62.3% were male. There were no differences between these two groups.

Table-1: Age distribution

Mean age in laparoscopic appendectomy group was 28.84 years and in open appendectomy group it was 31.0 yrs. There was statistically no significant difference between two groups.

Table-1: Operative time

\*Unpaired t- test

There was significantly shorter operating time in patients randomized to open appendectomy compared with laparoscopic appendectomy ( $62.96 \pm 16.49$  and  $38.5 \pm 12.82$ ).

Table-1: Inflamed appendix

\* Independent attribute: Chi-Square test

Appendix was assessed intra-operatively by the surgeon whether it was inflamed or not. Inflamed appendix was found in more number in laparoscopic than open appendectomy group (87.5% and 82.5%). P value >0.05.

	Open	Laparoscopic	Significant
Age	31.04 66-15	28.84062-10	No
Sex	28 17	25 20	No
Operative Time	38.5 75-15	62.95 100-23	Yes
Cardiovascular Stability	128.9 142-110	134.5 156-98	Yes
Pulse per minute	91.73 113-76	105 132-76	Yes
Wound Infection	6	1	Yes

 Table 1: Baseline indicators of open and laparoscopic surgery

\*Independent attribute: Chi-Square test

Table-1: Cardiovascular stability (Pulse/min& Systolic blood pressure) Intra-operative cardiovascular stability (pulse/min and systolic blood pressure) was compared between these two groups. Patients randomized to open appendectomy group were more stable than laparoscopic group (pulse=91.73  $\pm$  12.47 and 105.83  $\pm$  12.24; SBP=128.95  $\pm$  9.31 and 134.5  $\pm$  6.88). P<0.001.

Diagnosis of other pathology was done intra-operatively by proper inspection of adjacent gut and pelvic organs. More number of other pathologies were detected in patients who were randomized to laparoscopic group (35.0% and 12.5%).

Pain after 12 hrs.&24 hrs.

Judged based on VAS score, there was no statistically significant difference in pain perception 12 hours postoperatively. Mean value for laparoscopy appendectomy.  $(15.46 \pm 3.09)$  and mean value for open appendectomy was  $(14.95 \pm 2.22)$  (P > 0.05). There was statistically no significant difference in pain found 24 hours after operation  $(15.02 \pm 8.18 \text{ and } 14.36 \pm 5)$ . The number of NSAID required in the first 24 hours post-operative period did not differ between the two groups, but the number of doses of oral analgesics required was less in patients undergoing laparoscopic appendectomy.

	Open	Laparoscopic
Hospital Stay	5.59	3.2 6-2
Pain at 24 hours	14.36	15.02
Pain at 12 hours	14.95	15.46
Scar tenderness at 3 months	5	2
Intraoperative Findings	2	4
Return to full activity	13.18	10.12 15-6

Table 2: Pain, scar and intra operative findings and follow up

\*Independent attribute: Chi-Square test

Patients randomized to laparoscopy had significantly fewer wound infection than patients randomized to open appendectomy. In open Appendectomy, wound infection was present in 6 (17.5%) patients in the post operative period. There was one patient with wound infections in the laparoscopic group who had minor SSI in suprapubic port site.

Wound infection

Table-2: Return to full activity\*Unpaired t-test.

There was a significantly shorter period of convalescence in the laparoscopic group ( $10.12 \pm 2.37$  days and  $13.18 \pm 2.29$  days): than open appendectomy group.

Return to full activity.

The mean value for hospital stays in days after laparoscopic appendectomy was 3.2 days( $3.18 \pm 0.81$ ) as compared to hospital stay after open appendectomy was 5.59 days( $5.5 \pm 1.26$ ). Thus, reintroduction of normal diet and discharge from the hospital occurred earlier after laparoscopic than open surgery (P <0.001) Table-2: Scar tenderness after three months

\*Independent attribute: Chi-Square test

Scar tenderness after two weeks and three months was compared between these two groups. Result shows scar tenderness was more in patient randomized to open appendectomy group both at two weeks and at three months (5.0% and 22.5%) (0% and 12.5%).P<0.05. Hernia was not reported in any patient.

## Discussion

In Significant variation in operating times was noted in various controlled studies. The difference in mean (or median) operating time ranged from 8.3 to 29 minutes and was longer for laparoscopic appendectomy in all studies. In five of seven studies the difference was statistically significant <sup>6,7,31,32</sup>. Some studies revealed no difference in the operating time <sup>1</sup>. Similarly in this study increased operating time (mean) was noted for laparoscopic appendectomy.

Cardiovascular stability was more in patients randomized to open surgery group.

The present study revealed a significantly shorter hospital stay for patients undergoing laparoscopic appendectomy. The results of our study are in keeping with several previous studies.

Some randomized controlled trials associated laparoscopic appendectomy with decreased hospital stay. However, others report no significant difference between laparoscopic appendectomy and open appendectomy. Even meta-analysis reports had many controversial findings. The current literature describes that the differences may be affected by hospital factors or social habits rather than reflecting difference resulting from the operative technique itself. Moreover, further discrepancies may arise from diverse health care policies in different institutions.

In accordance with other studies there were significantly fewer wound infections in the laparoscopy group. Theoretically, a reduction in wound infection rate can be achieved by extraction of the specimen through a port or retrieval of appendix in endobag. This has been confirmed in the present intention to treat analysis on large number of patients have shown that wound infection is lower in case of laparoscopic appendectomy.<sup>6,30,32</sup>

In this study, post – operative pain was assessed, in the immediate post – operative period non-opiate analgesics were used in both groups after 12 hours and 24 hours visual analogue scale was used to assess the post – operative pain, which found to be less in the laparoscopic group with the same dose of parenteral analgesics per kg body weight as compared to open appendectomy. Variable analgesic requirement and pain control reported by various authors. Analgesics requirement was significantly less after laparoscopic appendectomy reported in three different studies.<sup>6,31,32</sup> In the study by Ortega et al, linear analogue pain scores were recorded in a subgroup of 135 patients. Pain scores were significantly lower after 24 hours and 48

hours. A similar retrospective study of assessment of post – operative pain by visual analogue scale.  $^{6.35}$ 

REIERTSEN and coll study showed no significant difference in pain scores both for open appendectomy and laparoscopic appendectomy.

In another retrospective study showed that the number of pethidine doses (1mg/kg body weight) required in the immediate post – operative period did not differ between the two groups but the mean number of doses of oral analgesics required was less in patients undergoing laparoscopic appendectomy<sup>5</sup>.

In the present study, patients were equally informed to resume normal activity and work as soon as possible at their discretion. The results show that time to return to normal work was significantly reduced by the laparoscopic approach. Less pain in the post operative period was the major contributing factor. Kald el al found that laparoscopic cholecystectomy was not cost effective on accounting for long term basis whereasLin et al and Heikkinen et al not only found laparoscopic appendicectomy to be cost effective but also associated with less abscess and complication formation.<sup>10,23</sup>

In 11 of 13 controlled trials that have studied postoperative convalescence, was found to be shorter in patients treated by a laparoscopic approach <sup>5, 6, 14, 25</sup>. In a retrospective study, Minne L and coll 1997 postoperative convalescence was found to be similar in both groups. Similar result was found by Ignacio and others. <sup>19,22,27,34</sup>

In this study, laparoscopic appendectomy was associated with less scar tenderness when compared with open appendectomy. According to Pedersen and Coll 2001, laparoscopy was associated with improved cosmesis which was recorded on a visual analogue scale by the patient from excellent (0) to poor (10). According to Mustafa Kamal in Pakistan J. Med laparoscopy procedure gives us a small scar which is more cosmetic and acceptable. <sup>4,13,22</sup>

More number of other pathologies were detected in patients who had laparoscopic procedure.

This study is validated externally.

We found an overall advantage of laparoscopic appendectomy. It is worthy of note that further studies should be conducted to evaluated diverse outcomes that were analyzed in our study and in other controlled trials to elucidate whether there is advantage in using either technique.

## Summary

From the present study, we concluded that laparoscopic appendectomy has been shown to be both feasible and safe in comparison with open appendectomy.

In our study more operating time was required for laparoscopic appendectomy.

Patients randomized to open appendectomy group had more cardiovascular stability in the intra-operative period.

Less post – operative pain was found in the laparoscopic group patients and same dose of parenteral analgesics per kg body weight was required as compared to open appendectomy (statistically non-significant).

There were significantly fewer wound infections in the laparoscopic group.

Time to return to normal work was significantly short laparoscopic group. Less pain in the post operative period was the major contributing factor.

The present study revealed a significantly shorter hospital stay for patients undergoing laparoscopic appendectomy.

Laparoscopic appendectomy group had less scar tenderness when compared with open appendectomy. Hernia was absent in either group.

More number of other pathologies were detected in patients who were randomized to laparoscopic group.

## Conclusion

Laparoscopic appendectomy and open appendectomy were comparable for complications, post operative pain control, length of hospitalization, recovery time and wound infection.

Laparoscopic appendectomy was associated with increased operating time. Faster recovery and earlier return to work was also seen after laparoscopic appendectomy. Less post operative pain and improved cosmesis was seen after laparoscopic appendectomy than open appendectomy. In addition, a greater number of other pathologies were detected in laparoscopic procedure.

Hence, we concluded that laparoscopic appendectomy has been shown to be both feasible and safe in comparison with open appendectomy.

## References

- 1. Pleser JG Greenberg D. Isr Med Assoc J. 2002 Feb 4 (2); 91-4.
- 2. Salam IM. Early patient discharge following appendicectomy: Safety and feasibility. JR CollsurgEdinb 1995. Oct; 40(5): 300-2.
- Humes DJ, Simpson J. Acute appendicitis. BMJ. 2006 Sep 9;333(7567):530-4. doi: 10.1136/bmj.38940.664363.AE. PMID: 16960208; PMCID: PMC1562475.
- 4. Pederson AG. Randomized clinical trial of laparoscopic versus open appendicectomy. BJS 2001; 88:200 –
- Kum CK, NgoiSS. Goh PMY, Tekant Y, Isaac JR. Randomized controlled trial comparing. Laparoscopic and open appendicectomyBirtish Journal of Surgery 1993;80: 1599 – 1600.
- 6. Ortega AE, Hunter JG, Peters JH, Swanstom LL, Schirmer B, The laparoscopic appendicectomy study

group. A prospective randomized comparison of laparoscopic appendicectomy with open appendicectomy. American Journal of Surgery 169;208 -13.

- Tate JJT, Dawson JW, Chung SCS, Lau WY, LI AKC. Laparoscopic versus open appendicectomy: prospective randomized trial. Lancet 1993; 342:633–7.
- Nazir A, Farooqi SA, Chaudhary NA, Bhatti HW, Waqar M, Sadiq A. Comparison of Open Appendectomy and Laparoscopic Appendectomy in Perforated Appendicitis. Cureus. 2019 Jul 9;11(7): e5105. doi: 10.7759/cureus.5105. PMID: 31523536; PMCID: PMC6728774.
- 9. Gürleyik, Günaya; Gürleyik, Eminb. Age-related clinical features in older patients with acute appendicitis. European Journal of Emergency Medicine 10(3):p 200-203, September 2003.
- Heikkinen TJ, Haukipuro K, Hulkko A. Cost effective appendicectomy open or laparoscopic? A prospective randomized study Surgery Endosc 1998; 1204–8.
- 11. Tate JJT. Laparoscopic appendicectomy BJS 1996; 83:1169–70.
- Mc Call JI. Sharples K, Jadallah T. Systematic review of randomized controlled trials comparing laparoscopic with open appendicectomy 1997;84:1045–50.
- 13. Kamal M., Qureshi KH. Laparoscopic versus open appendicectomy Pakistan J. Med Res 2003;42(1).
- Villazon DO, Espinosa JA, Cardenas. Co, Valdez CA. Hospital. Angeles de laslomas. Laparoscopic appendicectomy [pud. Med. Com.].
- De Utpal .Laparoscopic versus open appendicectomy. An Indian perspective Journal of minimal Access Surgery March 2005;1(1):15-20.
- Resutra R, Gupta R. Comparative Study of Laparoscopic Appendectomy versus Open Appendectomy for the Treatment of Acute Appendicitis. Int J Minim Access Surg. 2020;1(1):1005.
- 17. Citone G, Perri S, Pugno V, Lotti R, Amendolara M, Gola P, Nardi M, Trunfio A, Gabbrielli F. Appendicectomialaparoscopica: esperienzaclinica di 8 anni [Laparoscopicappendicectomy: an 8-year clinical experience]. Minerva Chir. 2001 Feb;56(1):13-21. Italian. PMID: 11283477.
- 18. Cariati A, Brignole E. Laparoscopic or open appendicectomy. Critical review of the literature and personal experienxe. G. Chir2001;22(10):353 7.
- 19. Long KH, Bannon MP, Zietlow SP, Helgeson ER, Harmsen WS, Smith CD, Ilstrup DM, Baerga-Varela Y, Sarr MG; Laparoscopic Appendectomy Interest Group. A prospective randomized comparison of laparoscopic appendectomy with open appendectomy: Clinical and economic analyses. Surgery. 2001 Apr;129(4):390-400. doi: 10.1067/msy.2001.114216. PMID: 11283528.
- 20. Benett J, Boddy A. Choice of approach for appendicectomy: meta analysis of open versus laparoscopic appendicectomy.

SurgLaparoscEndoscPercuta Tech 2007;17(4): 245 – 55.

- 21. Udwadia TE, Udwadia RT. Laparoscopic appendicectomy. Natl Med J India. 1999 Nov-Dec;12(6):281-4. PMID: 10732431.
- 22. Ignacio RL, Burlee R. Laparoscopic versus open appendicectomy. What is the real difference Results of a prospective randomized double blinded trial. Surg Enclose 2004; 18(2): 334–7.
- Lin HF, Lai HS, Lai IR. Laparoscopic treatment of perforated appendicitis. World J Gastroenterol. 2014 Oct 21;20(39):14338-47. doi: 10.3748/wjg.v20.i39.14338. PMID: 25339821; PMCID: PMC4202363.
- J. A. LUJAN MOMPEAN. Laparoscopic versus open appendicectomy: a prospective assessment. BJS 1994; 81:133–5.
- 25. Lord RV, Shane DR. Early discharge open appendicectomy. AustNZJ Surg 1996;66 (6):361–5.
- 26. Shah RC. Keyhole appendicectomy. J Indian Med Assoc 2004;102(10):565–7.
- Hellberg A, Rudberg C. Conversion from laparoscopic to open appendicectomy. A possible drawback of the laparoscopic technique? Eur J Surg 2001;167(3):209– 13.
- Kald A, Kullman E, Anderberg B, Wirén M, Carlsson P, Ringqvist I, Rudberg C. Cost-minimisation analysis of laparoscopic and open appendicectomy. Eur J Surg. 1999 Jun;165(6):579-82. doi: 10.1080/110241599750006497. PMID: 10433143.
- 29. Khalili TM. Perforated Appendicitis is not a contraindication to laparoscopy. Am Surg 1999;65(10):965–7. Yau KK Sul WT. laparoscopic versus open appendicectomy for complicated appendicitis, JAM CollSurg, 2007;205(1):60-5.
- Frazee RC, Roberts JW, Symmonds RE, Syndes SK, Hendricks JC, Smith RW et al. A prospective randomized trial comparing open versus laparoscopic appendicectomy Annals of surgery 1994;219:725-31.
- Attwood SEA, Hill ADK, Murphy PG, Thornton, J, Stephens RB. A prospective randomized trial of laparoscopic versus open appendicectomy. BJS 1992; 112:497–501.
- 32. Martin LC., Puente I., Sosa JL, et al. Annals of surgery. 1995;222(3):256-62.
- Hansen JB., Smithers BM., Schache D. World J. Surg. 1196;20:17–21.
- 34. Sauerland S, Jaschinski T, Neugebauer EAM. Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD001546. DOI: 10.1002/14651858.CD001546.pub3.