"A COMPARISON OF TITANIUM CLIPS V/S ROEDER'S KNOT TYING SUTURE IN LAPAROSCOPIC APPENDICEAL STUMP CLOSURE: A ONE YEAR RANDOMIZED CONTROLLED TRIAL STUDY IN KLE'S DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELGAUM"

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This is to certify that the dissertation entitled **"A COMPARISON OF TITANIUM CLIPS V/S ROEDER'S KNOT TYING SUTURE IN LAPAROSCOPIC APPENDICEAL STUMP CLOSURE: A ONE YEAR RANDOMIZED CONTROLLED TRIAL STUDY IN KLE'S DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELGAUM"** is a bonafide research work done by **CANDIDATE REG. NO. BH0113009**.

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LIST OF ABBREVIATIONS USED

^{0}F	-	Degree Fahrenheit
A	-	Acute
AnC	-	Acute on Chronic
AP	-	Abdominal Pain
BP	-	Blood pressure
C	-	Chronic
cm	-	Centimeters
CO2	-	Carbon dioxide
CRP	-	C-reactive protein
DS	-	Double Shank
gm	-	Gram
H2O	-	Water
Hb	-	Haemoglobin
HCG	-	Human chorionic gonadotropin
i.e.	-	That is
IP. No.	-	In patient number
Kgs	-	Kilograms
LA	-	Laparoscopic Appendectomy
Min	-	Minimum
mm Hg	-	Millimeter of mercury
mm	-	Millimeters
n	-	Total number
OA	-	Open appendectomy
OR	-	Odds Ratio

p	-	Probability
PG	-	Pressure gradient
PI	-	Pre Ileal
R	-	Retrocaecal
RCTs	-	Randomized controlled trials
RIF	-	Right iliac fossa
RR	-	Respiratory rate
SD	-	Standard deviation
SE	-	Subcutaneous Emphysema
SSI	-	Surgical Site Infection
US	-	United States
vs	-	Versus
WBC	-	White blood cell

ABSTRACT

Background and Objectives

Appendiceal stump closure during laparoscopic appendectomy is an important step. The present study was an attempt to evaluate the ease of use and safety of titanium clips compared to Roeder's knot in the appendiceal stump closure in patients undergoing laparoscopic appendectomy by comparing complications (intraoperative and post operative), hospital stay and follow up period.

Methodology

This one year randomized controlled trial was done in under the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014. A total of 60 patients were divided into two groups of 30 each that is, Group R (Roeder's Knot using Silk suture and Group T (Titanium clips).

Results

In the present study 53.33% of the patients in group R were females compared to 36.67% in group T ($p=0.795$). The mean age in group R was 29.77±11.24 years and in group T it was 29.53±8.96 ($p=0.929$). Other preoperative characteristics of the study population in group R and T were comparable ($p>0.050$). Significantly higher number of patients (60%) in group T required lower operative time (45 to 60 minutes) compared to group R. (83.33% patients required 61 to 75 minutes $p<0.001$). The pressure gradient was 1 in 23.33% of the patients in group R compared to 56.67% in group T ($p<0.001$).

The mean operative time, pressure gradient (the difference between the initial pneumoperitoneum pressure and the pressure during clip / knot application) and hospital stay were significantly high in group R compared to group T ($p<0.050$). However, the intra-operative complications ($p=0.177$), post operative complications ($p=0.303$) and follow up period in both the groups was comparable ($p>0.050$).

Conclusion and interpretation

Appendiceal stump closure with titanium clips is advantageous in terms of operative time, pressure gradient and offers early resumption of daily activities.

Keywords

Appendiceal stump closure; Roeder’s knot; Titanium clips;

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INTRODUCTION

One among the most common clinical presentations requiring emergent intervention is acute appendicitis. The lifetime incidence of this condition is about 8%.[1,2] People between 10 and 20 years of age are the most affected.[2] A male preponderance exists, with a male to female ratio of 1.4:1 and the overall lifetime risk is 8.6% for males and 6.7% for females.[1-3]

Obstruction of the lumen is the dominant factor for acute appendicitis and fecoliths are the usual cause of obstruction. Other causes of obstruction could be lymphoid hyperplasia, intestinal worms, tumors, or other conditions.[4,5]

Since its first description by Fitz in 1886, there have been lot of papers about acute appendicitis and the prompt intervention required to prevent many serious consequences including that of perforation.[6] Over the years, the surgical management of appendicitis has advanced from open techniques to minimal invasive ones. The gold standard for appendectomy, now, is Laparoscopic Appendectomy (LA), even for complicated appendicitis. Studies have shown that LA has significant advantages.[7,8]

Patients undergoing LA experience reduced wound infections, require less intra-operative and postoperative analgesia, require reduced hospital stay, have a quick return of normal bowel function, and good cosmetic tool, avoiding a large laparotomy scar.[8] Intra-abdominal abscesses, higher costs and lengthy procedure time are some of its disadvantages.[9,10] The technique of stump closure apparently influences chances of abscess formation.[11]

Although the surgical technique of laparoscopic appendectomy has been well established, concerns and controversy exists regarding the closure of appendiceal stump, which is a key point in the procedure.

During a laparoscopic appendectomy, an important step in the procedure is the closure of the appendiceal stump. Postoperative complications can occur from its inappropriate closure. The development of dangerous occurrences such as enterocutaneous fistulas, peritonitis, and sepsis is feared and undesirable.[12]

Several modifications to the original technique with new materials have been introduced for optimizing and controlling the appendiceal stump closure, such as endoloop, double endoloop, ultrasonically activated scalpel, instrument-assisted knotting, bipolar coagulation, slipknot tying, metal clip, Hem-o-lok clip and linear endostaplers. Currently, polymeric clips, pre-knotted loops and staplers are being used for stump closure. The finest method is not known and that topic is debatable.[13-15]

Roeder's knot tying is the most commonly used procedure for ligation of the appendiceal stump. However, controversies about the efficacy and safety of these novel materials still exist, and the need to evaluate this through new research has become important.[16]

An innovative appliance for appendicular stump closure is the Titanium Clip. It is a proven biocompatible implant material, made of pure titanium with a constant and high closing force. It allows good adaptation to tissue. The design is characterized by parallel shanks. The tissue is compressed, between the shanks during the closing process, providing safety against axial displacement. Scissoring is

also prevented by the shanks. The contact surface of tissue is increased by the pyramid shaped inner surface imprint, allowing the tissue to descend in between. This ensures a strong grip. The tip of the clip prevents slippage of tissue. Its clinical use has been approved.[17]

This study was designed to assess the ease of use and safety of titanium clips compared to Roeder's knot in the appendiceal stump closure and to compare intra operative complications, post operative complications, hospital stay and follow up period among the patients undergoing laparoscopic appendectomy.

OBJECTIVES

The objectives of the present were;

Primary

To assess the ease of use and safety of titanium clips compared to Roeder's knot in the appendiceal stump closure in laparoscopic appendectomy.

Secondary

To compare the following outcomes between titanium clips and Roeder's knot appendiceal stump closure groups;

1. Intraoperative complications
2. Post operative complications
3. Hospital stay
4. Follow up period

REVIEW OF LITERATURE

Historical review

Reginald J. Fitz of Harvard University was the first person to officially describe appendicitis. Since then, appendectomy ranks amongst the most common surgeries of our time. In 1980, the Laparoscopic Appendectomy was introduced which has led to a lessened infection risk, post-operative pain and hospital stay.[18]

Ancient Egyptians were the first ones to know about the appendix. They referred to it as "the worm of the intestine" as found in their Coptic jars. In 1492, Leonardo da Vinci published the first ever drawing of the appendix. Jacopo Berengaro Dan Carpi, an Anatomist, is credited with the first description of the appendix in 1521.[19] In his publication “De Humani Corporis Fabrica”, Andrea Vesalius gave a clear artwork of the appendix, in 1543.[18]

Jean Francois Fernel, a French doctor, is thought to have given the first description of appendicitis in the early 1500's in the "Universa Medicina". He described *"A girl of seven afflicted with diarrhoea passed for many days from the bowels a white putrid and foul material. She swelled up with increasingly severe pains and repeated loss of consciousness and vomiting of a fecal liquid. She died miserably two days later. On opening the body, the caecum intestinum was narrowed and constricted....and material opened up itself an unusual route by necrosis and perforation".*[18]

A definite description of a perforated appendix and abscess in post-mortem sections was first given by Lorenz Heister in the late 1600s.

The suggestion that appendix can be surgically removed was given by Francois Melier in his largely ignored paper in 1827. He was opposed by French surgeon, Guillaume Dupuytren who believed that the caecum was the primary cause of right lower quadrant inflammatory disease.[20] It was in 1840s that Thomas Hodgkin, Voltz, Addison and Bright all suggested that appendix was the source of the disease.[18]

After Melier's paper, for 50 years, there was no definitive treatment and the disease was called typhilitis, tuphloenteritis, perityphilitis, paratyphilitis, iliac passion and caecitis.[18]

Describing his paper "Perforating Inflammation of the Vermiform Appendix" to the Association of American Physicians, American anatomist Reginald. J. Fitz, was the first person to provide a clear account of the pathology, diagnosis and treatment of appendicitis in 1886. The term "Appendicitis" was used for the first time here.[18]

Claudius Amyand performed the first appendectomy at St. Georges Hospital in London, when a perforated appendix was found in a scrotal hernia sac. In his honor, a hernia containing appendix till date is known as Amyand’s hernia.[18]

The diagnosis and early operative intervention of appendicitis was pioneered by Charles McBurney.[21]

The McBurney’s point, which is one-third of the distance from the anterior superior iliac spine to the umbilicus in the right lower quadrant of the abdomen was described in 1889. In 1894, the appendectomy incision was named McBurney’s incision. A.J. Oschner advocated for a non-operative treatment of peritonitis, and

stated *"After my first operation I was completely disgusted because after cutting my patient lengthwise and crosswise, I found, behind the ascending colon, an inoffensive looking, shriveled up remains of what had been an appendix. I felt that I had subjected my patient to a very grave operation without a corresponding benefit".*[22]

Kurt Semm, a gynecologist, invented the Laparoscopic Appendectomy in 1983.[22]

Embryology and Physiology

Vermiform is Latin and means “in the shape of a worm”. The appendix vermiformis is an approximately 2- to 20-cm long (average 9 cm in adults) and 0.5- to 1-cm-wide blind-ended tubular sac, extending from the caecum, just distal to the ileocaecal junction, of the human large intestine.[23]

The caecum gives a protuberance at its end, that is the first visibility of the appendix, during eighth week of intrauterine development. The rate of growth of caecum surpasses that of the appendix and hence the appendix is pushed medially, during both antenatal and postnatal development. The association of the caecum with the base of the appendix is constant, whereas the tip can be found in a pelvic, retrocaecal, pre-ileal, subcaecal, or right pericolic position. There is significant clinical importance with respect to these anatomical factors in the setting of acute appendicitis. The appendix is identified by the convergence of three taenia coli at the junction of appendix with the caecum. This is a vital landmark. The absence of appendix, duplication, and diverticula have all been described.[24]

The appendix was viewed wrongly as a vestigial organ for many years without any function. But now, it is well known that the appendix has an immunological role. It takes part in the secretion of immunoglobulins, as an immunological organ, particularly immunoglobulin A. Recent studies have shown a relation between appendectomy and the development of inflammatory bowel disease, though there is no clear role in human disease development. There appears to be a negative age-related association between prior appendectomy and subsequent development of ulcerative colitis. In addition, comparative analysis clearly shows a delay in onset of disease and a benign nature in ulcerative colitis in people with prior appendectomy. The association between Crohn's disease and appendectomy is less clear. Although earlier studies suggested that appendectomy increases the risk of developing Crohn's disease, more recent studies that carefully assessed the timing of appendectomy in relation to the onset of Crohn's disease demonstrated a negative correlation. These data suggest that appendectomy may protect against the subsequent development of inflammatory bowel disease; however, the mechanism is unclear.[24]

Approximately 2 weeks after birth, lymphoid tissue first appears in the appendix. The tissue increases till puberty, remains steady and then begins to decrease with age. No lymphoid tissue remains within the appendix after 60 years of age, and commonly the lumen is completely obliterated.[24]

Anatomy

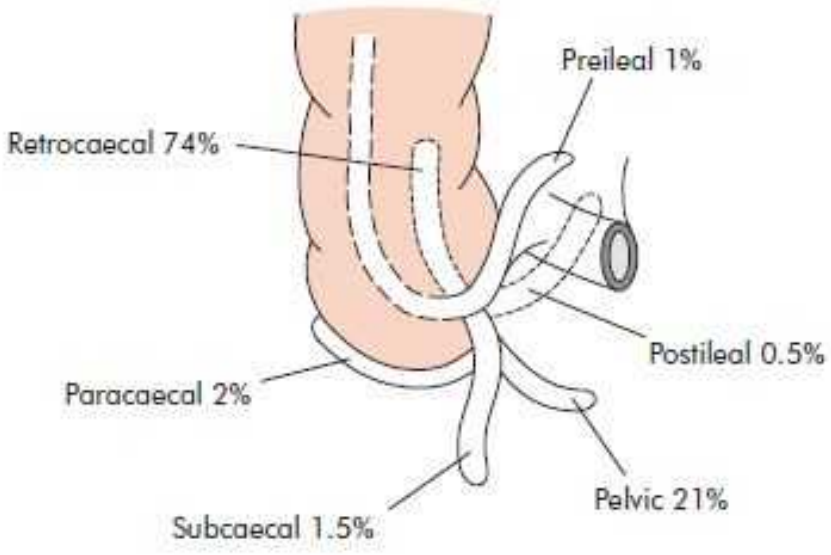


Figure 1. Different positions of appendix

The vermiform appendix is a narrow, vermian (worm shaped) tube, arising from posteromedial caecal wall, 2 cm or less below the end of the ileum. It can be found in any of the following position:[25]

1. Retrocaecal (12 O'clock) position – directed upwards in the retrocaecal recess. If the length is greater it may be retrocolic on hepatic.
2. Right Paracaecal (11 O'clock) position: lies on right side of caecum.
3. Left Paracaecal (10 O'clock) position: lies on left side of caecum. It may be preileal or postileal.
4. Splenic (2 O'clock) position: directed towards spleen.
5. Promontoric (3 O' clock) position: directed towards sacral promontory.
6. Pelvic (4 to 5 O'clock) position: Crosses the pelvic brim and lies in true pelvis.

7. 6 O'clock position: Appendix in mid inguinal position.

The location of appendix is as follows.[25]

Retrocaecal and retrocalic	:	74%
Pelvic	:	21%
Sub caecal	:	1.5%
Preileal	:	1%
Post ileal	:	0.5%

It is lengthier in children. 5 mm is the average diameter. The lumen is quite narrow.

The appendicular orifice is situated at posteromedial aspect of the caecum 2 cms below the ileocaecal orifice. The appendicular orifice is occasionally guarded by a semi lunar fold of mucous membrane known as valve of Gerlach.

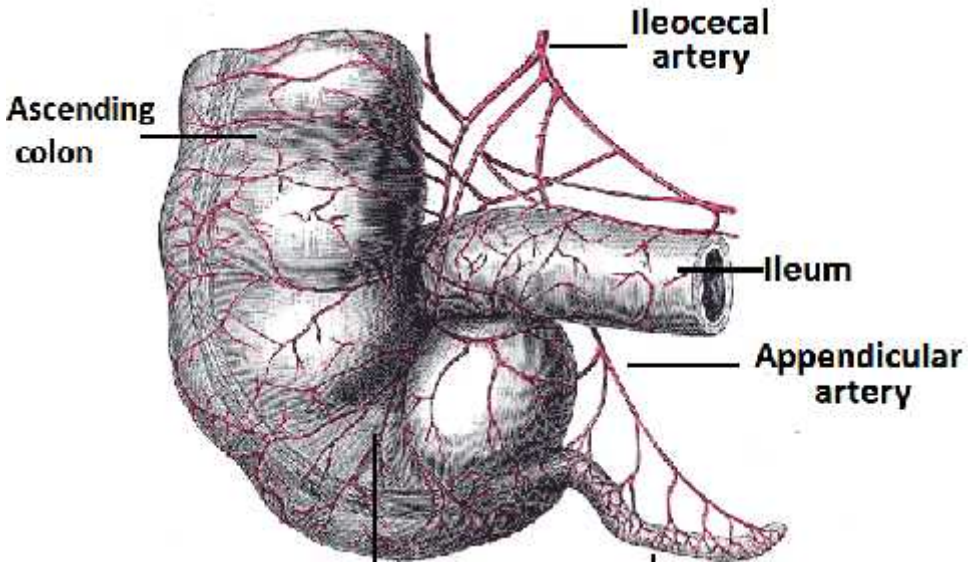


Figure 2. Blood supply and peritoneal relations of the appendix

Mesoappendix is the fold of peritoneum, triangular in shape, which suspends the appendix. The appendicular artery often runs in its free edge, but may run closer to the base of the appendix.[25]

Blood supply

The caecum is supplied by the anterior and posterior caecal branches of the ileocolic artery which is a branch of superior mesenteric artery.

The appendicular artery, a branch of ileocolic artery reaches the appendix through the mesoappendix. There may be an accessory appendicular artery (artery of Seshachalam) arising from the posterior caecal artery. If the mesentery is incomplete, the artery lies on the wall of appendix in its distal part and may be thrombosed in acute appendicitis.[26]

Venous drainage

Venous drainage is brought about by the appendicular, ileocolic and superior mesenteric veins and is to the portal vein.[27]

Lymphatic drainage

The lymph vessels from caecum and appendix terminate in ileocolic nodes situated close to the ileocolic artery. Small appendicular nodes usually lie close to the mesoappendix.[27]

Nerve supply

A plexus of nerves consisting of both sympathetic and parasympathetic fibres accompany the arteries to reach the caecum and appendix. The plexus is an

offshoot from the superior mesenteric plexus. The sympathetic fibres are derived from T10 – T11 segment of the cord and the parasympathetic fibres are derived from vagi.[27]

Epidemiology

250,000 cases of appendicitis, in the United States, are reported annually. Since 1940, it has been steadily declining. The annual incidence is 10 per 100,000 population, currently.[28] In the United States and European countries, the incidence is 7% of the population.[29]

Its incidence steadily rises from the time of birth, hits a peak in the late 10 years and declines with age. It is most prevalent between 10-19 years of age.[30] But in recent years, the number of patients aged 30-69 has increased to 6.3%.[31]

In Asia and Africa, due to the diet, there is a lower incidence of appendicitis. Decreased faecal viscosity, decreased bowel transit time and reduced faecolith formation is seen in people consuming dietary fibre. These factors predispose to the obstruction of the appendiceal lumen.[32]

Recently a retrospective study by Lohar HP. et al.[28] in Pune during 2010 to 2011, over 3 years excluding negative appendectomy cases, diagnosed a total of 130 cases with acute appendicitis based on clinical suspicion and investigations. In the 1st year, the incidence was 3.1 per 1000, 2nd year was 4.17 and 3rd year was 3.85. It remained almost stable during the study period of 3 years. The incidence of appendicitis was found to be the highest between 11-20 years of age which constituted 44.6%. 21-30 years age group constituted 36.1%, 31-40 years age group constituted 11.5% and 0-10 years age group was 3%. 41-50 years and 51-75 years of

age group was 2.3% each. Occurrence of appendicitis in both sexes was nearly equal. Non vegetarians were affected more. Seasonal variation was seen as the incidence hit a peak in spring and found to be low in the summer.

Etiology and Pathogenesis

The dominant etiological factor in acute appendicitis is obstruction of the lumen. The most common cause of appendiceal obstruction are faecoliths. Other causes are inspissated barium from x-ray studies, lymphoid hypertrophy, tumours, intestinal parasites and vegetable and fruit seeds. More severe the inflammatory process, higher the chances of obstruction. In 40% of cases of simple acute appendicitis, faecoliths are found. Gangrenous appendicitis without rupture is around 65%, and with rupture is nearly 90%.[24]

Traditionally the belief has been that there is a predictable sequence of events leading to eventual appendiceal rupture. A closed loop obstruction is produced in the proximal obstruction of the appendiceal lumen. Distension is rapidly produces due to the appendiceal mucosal secretion. 0.1 mL is the normal capacity of the appendiceal lumen. The intraluminal pressure is increased to 60 cm H_2O due to continuous secretion. Appendiceal distension stimulates the nerves. Visceral afferent fibers are stimulated to produce vague, dull, diffuse pain in the umbilical region. Early in the course of appendicitis, some cramping may be superimposed on the visceral pain due to distension leading to peristalsis.[24]

Due to multiplication of the dwelling bacteria of the appendix and continuous mucosal secretion, the distention within appendix increases, which in turn causes reflex nausea and vomiting, and the severity of diffuse abdominal pain

increases. As the appendiceal pressure increases, the venous pressure increases. There is occlusion of capillaries and venules, but the arteriolar inflow continues, which results in engorgement and congestion. The inflammation then involves the appendiceal serosa and parietal peritoneum in the region, which produces a characteristic shift in pain to the right lower quadrant.[24]

Bacterial invasion is allowed due to the early compromised integrity of the appendiceal mucosa as it is susceptible for impaired blood supply like the rest of the GI tract. As the venous and arterial supply is hampered due to progressive distension, the poorest vascular area is the most affected: the antimesenteric border develop ellipsoidal infarcts. As bacterial invasion, distension, compromise of vascular supply, and infarction progresses, there is occurrence of perforation through one of the infarcted areas. Due to the effect of diameter on intraluminal tension, perforation generally occurs beyond the point of obstruction rather than at the tip.[24]

Spontaneous reduction of acute episodes of appendicitis can occur. Previous history of similar complaints, but lesser in severity can be elicited from patients who are found to have acute appendicitis. Old, healed acute inflammation is correlated with thickening and scarring in the histopathological examination of removed appendices. It is now established that appendiceal perforation is the advanced stage of acute appendicitis and there is a link between delay in patient presentation and perforation. But recent studies indicate it to be different diseases. (Non perforated and perforated).[24]

Bacteriology

Normal appendiceal bacterial flora is similar to that of the colon. Except Porphyromonas gingivalis, the flora remain constant lifelong. This bacteria is seen in adults only. Colonic infections such as diverticulitis hence have the same bacterial cultures as appendicitis. Escherichia coli and Bacteroides fragilis are the most common organisms found in appendicitis. Other bacteria present in this condition are other anaerobic and facultative bacteria along with mycobacteria. Appendicitis is a polymicrobial infection, with some series reporting the culture of up to 14 different organisms in patients with perforation.[24]

Common Organisms Seen in Patients with Acute Appendicitis

Aerobic and Facultative	Anaerobic
Gram-negative bacilli	*Gram-negative bacilli*
Escherichia coli	Bacteroides fragilis
Pseudomonas aeruginosa	Other Bacteroides species
Klebsiella species	Fusobacterium species
Gram-positive cocci	*Gram-positive cocci*
Streptococcus anginosus	Peptostreptococcus species
Other Streptococcus species	Gram-positive bacilli
Enterococcus species	*Clostridium species*

In patients with either perforated or nonperforated appendicitis, routine culture tests from samples is debatable. As discussed earlier, the flora is known, and therefore broad-spectrum antibiotics are indicated. The patient often recovers from the illness by the time results are documented. In addition, the number of organisms cultured and the ability of a specific laboratory to culture anaerobic organisms vary greatly. Peritoneal culture should be reserved for patients who are immunosuppressed, as a result of either illness or medication, and for patients who develop an abscess after the treatment of appendicitis.[24]

Postoperative wound infection and intra-abdominal abscess are prevented as antibiotics are effective in this regard. In cases of nonperforated appendicitis, the coverage of antibiotics is limited to 24-48 hours. It is recommended to give 7-10 days of antibiotics in perforated cases. Intravenous antibiotics are usually given until the total count is normal and the patient has no fever for 24 hours. Antibiotic irrigation of the peritoneal cavity and the use of transperitoneal drainage through the wound are controversial.[24]

Clinical features

The clinical diagnosis of acute appendicitis relies upon a detailed history and a thorough physical examination. The differential diagnosis is that of the acute abdomen as it can mimic the presentation of most abdominal emergencies.

History

The principal presenting complaint of patients with acute appendicitis is abdominal pain. Murphy was the first to describe colicky pain abdomen which is central which is followed by migration of the pain to the right iliac fossa and

vomiting.[33] This classical presentation is only seen in approximately 50% of patients. The history of pain is usually 24 hours of colicky peri-umbilical pain followed by movement of the pain to the right iliac fossa with a progression to a more constant severe pain.[34] This progression results from the initial pain being referred from the visceral innervation of the midgut followed by more defined localization of the pain when the parietal peritoneum is involved by the inflammatory process. Associated symptoms include loss of appetite and nausea but profuse vomiting is rarely a feature of simple appendicitis and may well represent the development of diffuse peritonitis following perforation. Patients will often have a low grade fever. It is common for patients to report no change in bowel habit but a range of bowel habit disturbances may be associated with the onset of pain.[33]

Cope reported that patients may feel constipated and anticipate relief of pain with defecation but this does not occur.[35] The appendix can take a variety of anatomical positions and as a result the clinical presentation is influenced by the surrounding structures that become involved in the inflammatory process.[33]

Those at the extremes of age often present a significant diagnostic challenge as they present with atypical signs and symptoms.[36] Infants may appear listless whilst the elderly may present with confusion. A high index of suspicion is therefore required to make the diagnosis in such cases.

Examination

The patient presents with systemic features of an inflammatory response. They usually have a low grade fever with associated tachycardia, and appear flushed and a fetor oris may be present. The patient will often lie still as movement and

coughing exacerbate the pain. In children the hop test has been advocated as a test to confirm appendicitis. The child is asked to hop but refuses as this causes pain. On abdominal palpation, the maximal site of tenderness is said to lie over McBurney's point, which lies two thirds of a way along a line drawn from the anterior superior iliac spine to the umbilicus.[33] The patient will be tender and may display signs of peritoneal irritation with localized guarding and muscular rigidity. Patient's distress is further avoided by not eliciting Rebound tenderness. The signs found on clinical examination which are associated with a high positive likelihood ratio are signs of peritoneal irritation (rebound and percussion tenderness, guarding and rigidity).[37]

Findings on rectal or vaginal examination may be normal although pain on the right on rectal examination may indicate a pelvic appendix. A rectal examination is part of a thorough assessment of the patient with acute abdominal pain, however, the value of rectal examination in the diagnosis of appendicitis is debatable. In the presence of tenderness and guarding in the right iliac fossa in a study of 1,204 patients admitted to hospital with right lower quadrant pain little extra information was gained. The presence of right sided pain on rectal examination was more common in those with appendicitis (Odds Ratio [OR] 1.3) but this gave little diagnostic information.[38]

These findings were confirmed in a further study of 477 patients with acute appendicitis and a systematic review and meta-analysis which concluded that the opinion that rectal examination is indispensible in the diagnosis of appendicitis cannot be supported.[38,39]

It has been suggested that opiate analgesia should be withheld from patients with suspected acute appendicitis as its administration masks clinical signs.[40]

Two small randomized controlled studies in adult and paediatric cohorts have concluded that analgesia does not alter the clinician's ability to accurately diagnose acute appendicitis, and therefore, appropriate analgesia should be given to all patients on admission.[41]

Further examination findings have been suggested to aid in the diagnosis of appendicitis. Rovsing's sign is named after Danish surgeon Niels Rovsing and is said to be present when palpation in the left iliac fossa results in pain in the right iliac fossa. The psoas muscle can be irritated by an inflamed appendix and movement of the muscle can result in pain. The patient may lie in the supine position with the hip flexed. This can be tested by asking the supine patient to lift the thigh whilst applying pressure just above the knee or by extending the right leg at the hip with the patient in the left lateral decubitus position. Pain with either maneuver confirms psoas irritation and is regarded as a positive PSOAS sign.[34]

Lastly the OBTURATOR sign results from irritation of the obturator muscle. This can be elicited by passively flexing the right hip and knee and internally rotating the leg at the hip which stretches the obturator muscle and causes pain in the right side of the abdomen.[34]

Laboratory Investigations

Specialist investigations are not required to make the diagnosis of appendicitis because the diagnosis is predominantly clinical. The judicious use of simple bedside tests and laboratory markers of inflammation can provide additional

evidence to support the diagnosis of acute appendicitis and exclude important differentials. The majority of patients presenting with abdominal pain will have blood drawn for a full blood count and urea and electrolyte analysis. Urine analysis and microscopy can exclude urinary tract infection but may be deranged in around 48% of patients undergoing appendectomy.[42]

The cause for abnormalities often leukocytosis and microscopic hematuria is the underlying inflammatory process irritating the renal tract along the line of the inflamed appendix.[42]

The most commonly used serological markers of inflammation in the diagnosis of acute appendicitis are the leukocyte count and C-reactive protein (CRP), neither is diagnostic of acute appendicitis. Studies have attempted to define potential thresholds values which are predictive of a diagnosis and disease severity.[33,43] Repeated tests may also be useful in the context of patients in whom the diagnosis is unclear initially and are observed clinically with two studies suggesting other diagnoses or further tests should be considered if repeat measures are normal.[33,44]

In the presence of normal inflammatory markers CRP, WBC and neutrophil count the diagnosis of acute appendicitis is unlikely.[37,45]

The performance of these tests is clearly related to the population under study and a meta-analysis of studies of reporting results on patients admitted to hospital with acute abdominal pain and those selected for appendectomy demonstrated that CRP performed better as a diagnostic test in those with an acute abdomen than in those selected already for surgery.[33]

A further meta-analysis of studies reporting on patients with a clinical suspicion of appendicitis concluded that the diagnosis of acute appendicitis was more likely when two or more inflammatory variables [granulocyte count, proportion of polymorphonuclear blood cells, white blood cell count (WBC) and CRP] were elevated.[37]

Studies of inflammatory markers in children notably of CRP and WBC count have concluded that an elevation of both parameters can support the diagnosis of acute appendicitis.[46,47] These studies have all used different cut off levels to determine abnormal results and have generally been small single centre studies. The authors, therefore, suggest that the use of inflammatory variables should be used to support a clinical diagnosis of acute appendicitis and to exclude other pathologies. All women of child bearing age should have a serum or urine beta HCG requested to confirm pregnancy status. Given the differential diagnosis of acute appendicitis other blood tests including amylase, lipase, liver function tests, and clotting studies may be required to confirm or exclude other diagnoses. Given the limitations of the current inflammatory markers there has been considerable research interest in identifying other potential biomarkers for the diagnosis of acute appendicitis and for predicting perforation. Hyper-bilirubinemia has been shown to correlate with a diagnosis of perforated appendicitis[48] but a stronger correlation has been recently reported for CRP.[49]

Interleukin-6 serum levels have not been shown to aid the diagnosis of appendicitis or reduce negative laparotomy rates.[50] The use of plasma D-lactate levels in the diagnosis of appendicitis is unclear with some studies suggesting it may[51] or may not be a useful adjunct.[52]

A recent study of 51 patients with appendicitis suggested plasma concentration of lactoferrin and calprotectin are elevated in those with appendicitis but their role in diagnosis is unclear.[53]

Clearly the use of these markers in routine clinical practice will require much larger validation studies in defined cohorts of patients. Laboratory tests have also been used to try and determine the need for further investigation in patients presenting with abdominal pain. Due to the non specific nature of most inflammatory variables, however, no single specific test has been able to predict the need for further radiological investigation.[54]

Scoring Systems

The diagnosis of acute appendicitis can be difficult and any delay in definitive treatment with surgery can lead to an increase in mortality and morbidity as the disease progresses to appendiceal perforation. This increase in morbidity and mortality has been used to justify the high rates of negative appendectomy which range from 14 to 75%.[55] A drive, therefore, has been to improve the diagnosis of appendicitis using clinical scoring systems. These systems have been based on symptoms, signs and laboratory findings. In some instances they have been part of a computer-aided diagnostic algorithm.[33]

The most widely cited score in the diagnosis of adults with acute appendicitis is the Alvarado score.[55] Whereas, in children the pediatric appendicitis score or Samuel score is most widely used.[56] The scores have now been validated in a wide variety of populations, however, they have not made it into routine clinical practice in all settings.[33]

A number of studies have also used computer aided diagnosis in patients with acute abdominal pain in an attempt to improve the management of patients presenting with acute abdominal pain. These systems have reported a diagnostic accuracy of 97.2% in acute appendicitis, improvement in time to surgery, with a reduction in the number of perforations over a 2 year period. They have, however, not been introduced into routine clinical practice. In an aid to further improve diagnosis artificial neural networks have been suggested as adjuncts to diagnosis but this remains an area of research with only a small number of patients having had diagnoses made in this way.[57,58]

Diagnosis

As the diagnosis is largely a clinical one, special investigations are not necessary to confirm the diagnosis of appendicitis. Simple tests like blood and urine examination can allow to differentiate with other conditions and also support the diagnosis, as no specific test exists for appendicitis. To help or aid the clinician to diagnose appendicitis, various scoring systems and algorithms have been introduced but hardly are being used.[2]

Radiology can help with the diagnosis of appendicitis. Computed Tomography and ultrasonography are helpful in this context.

It is concluded that in patients who cannot be clinically or laboratorial confirmed of appendicitis, computed tomography scanning and ultrasonography should be carried out, according to one meta-analysis and systematic review. As ultrasonography studies need careful examination and are hugely operator dependent, it is recommended by some authors that a greater diagnostic accuracy is by the use

of computed tomography when compared to ultrasonography in this select group of patients.[2,59]

The status of rates of negative appendectomy with the introduction of radiological scanning is debatable. It has been suggested in a longitudinal study that in spite of the advent of radiological tests, the rate of negative appendectomy have been the same.[60] A possible reason for this maybe is because of the ultrasonography having moderate accuracy in diagnosis.[61] According to two prospective studies there is a decrease in the number of unnecessary admissions and appendectomies when the use of computed tomography is evaluated. Some authors have raised their opinion that there is a risk of ionizing radiation exposure in computed tomography scannings, and hence low or lower dose protocols have been encouraged.[2]

Differential diagnosis

Acute abdomen causes form the differential diagnosis for appendicitis.[2]

Differential diagnosis of acute appendicitis

Surgical

- Perforated peptic ulcer
- Meckel's diverticulitis
- Mesenteric adenitis
- Intestinal obstruction
- Intussusception
- Acute cholecystitis
- Colonic/appendicular diverticulitis

- Rectus sheath haematoma
- Pancreatitis

Urological

- Right ureteric colic
- Right pyelonephritis
- Urinary tract infection

Gynaecological

- Ectopic pregnancy
- Ruptured ovarian follicle
- Torted ovarian cyst
- Salpingitis/pelvic inflammatory disease

Medical

- Gastroenteritis
- Pneumonia
- Terminal ileitis
- Diabetic ketoacidosis
- Preherpetic pain on the right 10th and 11^{th} dorsal nerves
- Porphyria

Treatment

The fact that, acute appendicitis needs early diagnosis and treatment/ surgery was first published by Herbert Fitz.[6] Appendectomy is the treatment of choice after resuscitation. There is no proof that, to get a proper clinical diagnosis, analgesia

should be withheld. Antibiotics(1-3 doses) should be given perioperatively, usually broad spectrum, to prevent abscess and post-operative wound infection.[2,62]

Timing of surgery

No significant differences were found between early or late appendectomy in a retrospective study recently. Early being less than 12 hours after presentation and late being 12-24 hours.[63] But the rate of perforation can have a bearing effect if the actual time of symptom onset is taken into consideration, which wasn't. The rate of perforation on an average, is between 16% and 36% after 36 hours from symptom onset, and for every 12 hour thereafter, perforation risk is 5%. Appendectomy should be done without any delay, after confirmation of diagnosis.[1,16]

Operative procedure

The open procedure has been done by a Gridiron incision or through a Lanz's incision. The former is taken at right angle to a line joining anterior superior iliac spine and umbilicus at the McBurney's point. The Lanz's incision is beneficial cosmetically. With the advancement of laparoscopic surgeries, the amount of open appendectomies have fallen.

Open appendectomy

From the past 120 years, the approach to appendectomy has not changed and the person who described the technique for open appendectomy (OA) was McBurney.[65,66]

At the midpoint between the right anterior-superior iliac spine and the umbilicus, just lateral of the right rectus muscle, an incision of around 5cm is taken,

according to the conventional approach. The muscle layers and the fascia are dissected by using blunt dissection and, along with that, electrocautery. After this, the peritoneum is opened. The appendix is revealed after mobilization of the caecum post visualization. The caecum is held with a Babcock's forceps and along with the appendix it is brought out of the peritoneal cavity and the ligation of mesoappendix is carried out. A stump is left after dividing the base of the appendix.[66]

There is still debate about the continued practice of OA. In complicated appendicitis (gangrenous and perforated appendices), OA is considered the gold standard due to lesser complications in the postoperative period like abscess or infection. If laparoscopic dissection is not possible or difficult (inflammation or adhesions], OA is used as a backup plan. Conversion from LA to OA is found to be 8.6%, but this number too is steadily decreasing as surgeons gain more experience with LA.[66]

Laparoscopic Appendectomy

With the introduction of the first described minimally invasive laparoscopic appendectomy (LA) by Kurt Semm in 1983, surgery slowly shifted away from the era of OA.[67]

In the laparoscopic procedure, ports are placed to facilitate working space within the abdomen. A 10 mm port is placed at the umbilicus and two 5 mm ports in suprapubic and left iliac fossa. The appendix is visualized and manipulated using a Grasper. Endoscopic stapler or harmonic scalpel is used to divide the mesoappendix. The appendiceal base is ligated with either an endoscopic stapler or Endoloop. An Endobag is used to retrieve the appendix through the 10 mm port.[66]

LA approach is advantageous, some studies have shown. It reduces chances of wound infections, require less intraoperative and postoperative analgesia, lesser hospital stay, quickened return of normal bowel function, and improved cosmetic outcome. This avoids a large scar.[66] This is proved in a meta-analysis by Sauerland et al.[68] Lap patients returned to work 5 days earlier, stayed in hospital 1.1 fewer days, had reduced pains by 8 mm on a 100 mm visual analogue scale, and approximately had 1/2 the number of wound infections.

Laparoscopy also has an added advantage, that of being diagnostic. This is beneficial in gynecological conditions. It was found out in a study, which looked at unnecessary appendectomies in females, that if a simultaneous gynecological pathology was present, it was diagnosed 73% in laparoscopic group compared to 17% in the open group.[66]

A controversial area is what steps should be taken in a patient without a clear diagnosis and an uninflamed appendix. 60% surgeons in an Italian Consensus Conference, felt that the normal appendices should be removed.[66] When examined histologically, 1/3rd of all “normal looking appendices” will actually be inflamed, was found out by Phillips et al..[69] Recently, potential dangerous consequences of “negative appendectomy, was published in a study by M. N. Anderson and R. E. Anderson.[70] They stated that the morbidity and mortality nearly paralleled that of a perforated appendicitis. It remains to be seen whether this changes the opinions and practices of majority of the surgeons.[66]

In most minimally invasive institutions, LA is the standard procedure in uncomplicated appendectomies. There is an increase in the rate of LA to

approximately 58% of all appendectomies. It is surprising that in spite of LA encompassing majority of appendectomies, OAs are still performed, at a high amount.[66] A German study in 2009 questioned whether LA is the standard procedure in German hospitals as it reported that nearly half of all appendectomies were open procedures (46%).[67] This can be explained due to the fact that the conventional open approach hasn't yet been shown to be inferior to LA, and in an affordable way, it provides reliable clinical results compared to LA.[66]

Special considerations

Pregnancy

With an incidence of 0.15 to 2.10 per 1000 pregnancies, appendicitis is the most frequent non-obstetric emergency needing intervention/surgery in pregnancy.[71] There is a reduced incidence in appendicitis during pregnancy, particularly during the third trimester, in contrast to earlier studies which suggested an equal incidence, according to a recent study.[2]

Presentation is often atypical and may be mistaken for labour. This can be explained by the gravid uterus pushing or displacing the appendix. Tenderness along anywhere over the right side of the abdomen with an associated symptoms of nausea and vomiting are present. Maternal mortality rises to 4% with advanced gestation and perforation in appendicitis whereas fetal mortality ranges from 20-35% in cases of perforation compared to 0.5-1% in simple cases.[71]

Appendicular mass

A tender mass may be felt in the right iliac fossa with muscle rigidity, in patients with a delay in presentation. It is confirmed on radiological scans like ultrasonography or computed tomography scan but in elderly population, underlying neoplasia must be excluded. With appropriate resuscitation and intravenous broad spectrum antibiotics, the initial management of this condition is conservative. As the inflammation resolves, the mass decreases in size, although patients need careful monitoring to detect early signs of progression. Interval appendectomy is carried out after resolution of the mass, as appendicitis can occur in the future. No definitive evidence exists to support conservative management with Out Patient follow up.[2]

Appendicular abscess

Patients presenting with pyrexia, tachycardia, and leukocytosis and an associated mass are said to have an appendicular abscess. Most commonly it is situated in the right iliac fossa on the lateral aspect, but sometimes it can be pelvic which is confirmed by a rectal examination. On ultrasonography or computed tomography, it can be confirmed. A percutaneous drainage under radiological guidance can be done. Appendectomy can be done if open drainage is planned. That is the added advantage.[2]

Chronic (recurrent) appendicitis

Neuroimmune appendicitis is a new concept which has evolved after the introduction of neurogastroenterology. Altered visceral perception from the gut is resulted by subtle alterations in enteric neurotransmitters after bouts of intestinal

inflammation; this has been implicated in a wide range of gastrointestinal conditions. It remains an interesting area but further work is required.[2]

Inflammatory bowel disease

Delayed disease onset and a benign type of ulcerative colitis is associated with patients having a history of appendectomy.[2,72] The same association with Crohn's disease is not clear, but some studies suggest a delayed disease onset.[2] There is contradictory evidence also which suggests an increased risk of developing this disease depending on the patient's age, sex, and diagnosis at the time of operation.[73]

Complications

Appendectomy is a safe procedure. 0.8 per 1000 is the mortality rate associated with appendectomy (uncomplicated).[74] The mortality in complicated cases like perforation is 5.1 per 1000. 30% is the average rate of perforation at presentation, but this is increased in young children and elderly people, with the rate up to 97%, due to delay in diagnosis.[2]

The increased mortality and morbidity associated with perforation has been used as justification for high rates of negative appendectomy, quoted as between 20% and 25%.[74] Despite this, complications can occur after removal of a normal appendix, and the surgical community continues to strive to reduce the numbers of negative procedures.[2]

A perforated appendix during childhood does not have a long term effect on subsequent female fertility, according to a large cohort study.[75] Low incidences of

intraoperative and postoperative complications have been reported in association with laparoscopic appendectomy.[2]

Bleeding

Most conversions to open procedure is due to this complication. It is usually overestimated due to the camera magnification. Bleeding can occur from the mesoappendix secondary to aggressive dissection or through the retroperitoneum in a retrocaecal appendix which is inflamed. Careful dissection can prevent this complication. It isn't difficult to recognize. Suction, pressure of the site of bleeding with an instrument or gauze and an additional trocar facilitate identification and control of the site of bleeding. Coagulation, clips, or by an endoloop, the bleeding can be controlled. Very rarely, conversion to open procedure is needed.

Faecolith

This is a frustrating but rare complication. During dissection of a distended, gangrenous appendix, a faecolith may drop into the peritoneal cavity. Retained faecoliths may cause an intrabdominal abscess. Therefore, faecoliths should be avoided being lost between the loops of the intestine and the pelvis and should be carefully dealt with. Faecoliths should be thrown into an endobag and a peritoneal lavage should be done. As laparoscopic appendectomy becomes a more common method of treatment, this complication will be found more often.[74]

In order to treat faecolith adequately, surgeons should be aware of this, when recognized intra or postoperatively. This complication can be prevented by the gentle treatment of an inflamed, gangrenous appendix and the use of an endobag. Since in all described cases of a dropped faecolith after open appendectomy, an

abscess develops, it is recommended to remove the faecolith when it is established that one has dropped intraoperatively. Removal by relaparoscopy is possible in cases if the presence of a faecolith is confirmed postoperatively.[76] A retained faecolith which is manifested as an intraabdominal abscess is treated like any other abscess.[74]

Incomplete appendectomy

After an incomplete appendectomy, delayed obstruction and inflammation of the residual tissue is called stump appendicitis.[75] This is a rare but serious complication. However, it leads to recurrent appendicitis. Most reports published are for open appendectomy, though theoretically it is increased in laparoscopic cases.[2]

When the appendix is excised from a point far away from the base, this stump appendicitis occurs. An important point is the clear visualization of the junction between the caecum and the appendix. Identification is carried out by tracing the taenia coli up to the appendix. The base of the appendix can be alternatively marked by dissecting and ligating of recurrent branches of the appendicular artery.[71] The base of the appendix should be dissected to avoid injury to the caecum. If a patient with history of appendectomy complains of similar pain, this condition should be considered.[2]

Postoperative abscesses

A good lavage and clear cleaning of the operative field with the help of a good camera, is shown to prevent this complication. It is rarely seen after laparoscopic appendectomy. There is also a significant decrease in the incidence of post-operative abscess after laparoscopic appendectomy. An unproven theory is that

infected fluid in the abdominal cavity causes subhepatic and subphrenic abscesses when the patient is in Trendelenburg's position. They are treated by radiologically guided drainage along with antibiotics.[62]

Stump leak

When there is excessive coagulation of the stump or an inadequately placed endoloop, the tissue goes into necrosis. This is a rare complication and is characterized by an enterocutaneous fistula.

Wound infection

Even in gangrenous appendicitis, wound infection is rare after laparoscopic appendectomy when compared to open technique. The incidence of wound infection is reduced by the advent of the endobag and the maneuver of retrieving the appendix through a port.

Intra-abdominal abscess

In cases with gross contamination of the abdominal cavity, this complication may occur. The patient has fever and abdominal pain. It is confirmed by a computed tomography or ultrasonography. With a pigtail catheter, the abscess can be drained under radiological guidance. But occasionally, open or rectal drainage is to be carried out. The incidence of these abscesses are reduced by administering perioperative antibiotics.[62]

On a whole, laparoscopic appendectomy has advantages, which are proven, over the open technique. There are lower risks of wound infection, lesser post-operative pain and shorter hospital stay. The most common reasons for unsuccessful

procedures are the position of the appendix, bleeding and abscess. Surgeon's inexperience may contribute to these factors. The procedure becomes difficult especially in cases of retrocaecal appendix and abscess. In these cases, approach is easier by laparoscopy which indicates the site of the incision. The abdominal cavity is cleansed completely, by laparoscopy in cases of generalized peritonitis. Important characteristics of laparoscopy are less irritation of the bowel, less trauma to tissues, lesser postoperative pain, short hospital stay, a faster recovery and return to everyday activities. The economic importance and its implications favoring this approach cannot be ignored.[77]

Appendiceal Stump Closure during Laparoscopy

During a laparoscopic appendectomy, the closure of the appendiceal stump is an important step for the potentially serious postoperative complications which arise from inappropriate management. The development of dangerous events such as postoperative peritonitis, enterocutaneous fistulas, and sepsis are feared and unwanted. When Kurt Semm published his laparoscopic technique, he described and illustrated in detail all the steps taken in the operation. He opted for the endoligature with a surgical knot, for stump, followed by a purse-string suture, in addition to a Z-suture.[78] Endoligature and double surgical knotting requires high skill and experience from the surgeon. There are chances of developing a mucocele and some anatomic alterations in the caecum, which may confuse future diagnosis.[79]

In 1985, Engstrom and Fenyo[80] published a study, which was randomized prospective, with 735 patients who underwent an appendectomy within 5 years. There were 2 groups in the study. In the first group, endoligation and invagination

through purse string suture followed by Z suture was carried out at the base of the appendix, in 357 patients. In group 2, endocoagulation of the extraverted mucosa was done after ligating the base with absorbable endoligature in 361 patients. Both groups were comparable in terms of sex, percent forms of complication, and antimicrobial treatment. In accordance to infectious complication rate, postoperative fever and hospital stay, there was no significant difference found. It was concluded that the procedure of choice is single appendiceal stump endoligature during appendectomy and that the destruction of the mucosa, after an appendix section, may avoid mucocele.

This modification is simple, requires less operative time, and less anatomic deformities at the caecum, and has been well adjusted to laparoscopic appendectomy in the following years. It is performed by various alternatives and ligature is the preferred intervention for the stump. The alternatives are mechanical endostapler, endoligature (endo-loop), metal clips, bipolar endocoagulation, polymeric clips, and intracorporeal suture.[79]

Various methods of the appendiceal closure haven't been fully assessed in randomized studies.[81] Different studies with endoligature (endo-loop) and metal clips with their end points are given in Table.

Author	Method	Operative time (min)	SSI (%)	Iatrogenic injury (n)
Beldi et al.[82]	Endoloop	53.4	2.1	4 (2465)
Brosseuk and Bathe[83]	Endoloop	36	4	0
McAnena et al.[84]	Endoloop	48	4	0
Cristalli et al.[85]	Metallic clip	36.5	0	0
Gomes and Nunes[86]	Metallic clip	31.4	6.7	0
Khanna et al.[87]	Endocoagulation	25	3.4	0

Mechanical endostaplers and simple endoligature, according to literature, is most used to manage the stump. There are many advantages of a mechanical endostapler include decreased enterocutaneous fistula rates and possible treatment of complicated forms of appendicitis. Costs, technical problems, rare cases of obstruction in adherence to the suture line are the disadvantages. Partial obstruction of the ileocecal valve can be produced when stapling the caecal-appendiceal transition, and the surgeon should be careful in this regard.[82]

Benefits of the endoligature include 6- to 12-fold decreased costs and an easier procedure. When patient comes back with necrosis at the insertion of the appendix into the caecum, this ligatured stump does not allow treatment. This is the disadvantage. Approximately only 3% of the cases have been observed but this has been discussed much in literature.[86] Intracorporeal caecorrhaphy can be carried out in this scenario or a video-assisted laparotomy as published by Browne.[88] Both require surgeons with experience in the laparoscopic treatment of complicated forms of the acute appendicitis. If endostapler is available, it can be definitely used.

A meta-analysis to compare the use of the endostapler with the endoligature in the appendiceal stump closure was done by Kazemier et al.[13] Data from 427 patients enrolled in 4 prospective randomized studies were included. The variables were operative time, complication rate and in-hospital stay. After analyzing these details, it was concluded that endostapler was preferred.

A systematic review by comparing endostapler and endo-loop was carried out by Sajid et al.[14] They included 622 patients from 5 randomized studies. In the endo-loop group, it was observed that it had a longer operative time, compared to

the endostapler and no significant difference between groups regarding hospital stay and intra-abdominal abscess. But perioperative rate of complication was higher in the endoloop group. It was concluded that endoloops are safe to use.

Cristalli et al.[85] described the use of a metal clip (Ethnor T1300) to treat an uncomplicated appendiceal stump in appendicitis. In 20 patients who underwent laparoscopic appendectomy, the advantages and disadvantages were analyzed. Mean time for the procedure was found to be 36.5 minutes, conversion not required, and there were zero postoperative complications. This procedure is fast, feasible and indicated in patients with a right inferior quadrant pain bearing an uncomplicated acute appendicitis.

In 105 patients, metal clip (Ethicon T400) was used for the appendiceal stump closure by Gomes and Nunes[86] Mean operative time was found to be 31.4 minutes, complications of infection around 6.7%, and laparotomy was needed to complement the laparoscopic procedure in 1.9% cases. There were no complications directly related to the clip. The presence of necrosis at the junction of the appendix into the caecum and considerable appendiceal diameter were the main flaws. Laparoscopic knot using 3-0 polygalactin, caecorrhaphy, and video-assisted laparotomy were the alternatives.

Bipolar endocoagulation was the treatment of choice in 60 patients for the appendiceal stump by Khanna et al.[87] Located 3 to 5mm from the caecal wall, the appendix was subjected to endocoagulation. The time needed was between 60 to 180 seconds, with an average of 90 seconds, until bubbling of the tissue was no longer seen and a ring formed at the said point. The appendix is then sectioned with the

help of a magnified image provided by laparoscopy. The basic principle is that in the presence of less intense heat (45 to 601C) for longer periods, the tissue protein denatures and determines the loss of its quaternary structure and solidification. This is widely used for hemostasis in laparoscopic procedures. 3 patients had complications but they were not described, and 1 case needed laparotomy. It was concluded that bipolar endocoagulation was simple and cost effective and makes unnecessary to use any material that is foreign to the body. Two studies compared nonabsorbable polymeric clip (Hem-o-lok MLX) and the treatment with an endostapler and evaluated the advantages and disadvantages.[89,90]

The Hanssen trial[89] was comprised of 2 stages. 28 patients were divided into 2 groups of 14 patients in the first stage. One group used the clip and the other used the laparoscopic stapler. Variables such as operative time, hospital stay, complications, and costs were studied. Following the same pattern, 250 patients were evaluated in stage 2. The use of polymeric clip is safe, feasible and a cost-effective alternative to treat the appendiceal stump, it was found.

A single nonabsorbable polymeric clip was compared to the endostapler and evaluated for feasibility, morbidity, and cost effectiveness of the same in appendiceal stump closure in the Partecke et al.[22] study. It was a prospective nonrandomized study with 56 patients closed by endostaplers, and in 26 patients, a single Hem-o-lok MLX polymeric clip was used. The time of surgery, costs, time of hospitalization and complications were analyzed. It was noticed that the length of surgery was longer in the clip group because of the introductory phase. Morbidity was comparable and acceptable in both groups. The costs of 1 set of Hem-o-lok clips were negligible compared with endostaplers (19.94 vs. 356.43 Euros). It was

concluded that the use of a single nonabsorbable polymeric clip is easy to use, safe and cost effective. Therefore it is suggested that a tactical modification of the appendiceal stump closure with a single appendiceal endoligature, replacing the invaginating suture, is the procedure of choice during an appendectomy whenever possible.

In selected cases only, the management of the appendiceal stump by an invaginating suture should be used. Studies suggest the use endostapler, endoligature (endoloop), metal clips, bipolar endocoagulation, and polymeric clips, which don't require an invaginating suture. All are having advantages and disadvantages up against the different clinical stages of appendicitis, and there are no prospective studies available that assess all of them. For a safe and more cost-effective procedure, knowledge about and appropriate use of the different forms of appendiceal stump closure are important.[79]

Roeders knot in appendiceal stump closure

Appendiceal stump closure is the most controversial issue in the laparoscopic appendectomy procedure. Despite the fact that many authors have described several modifications with new materials for appendiceal stump closure, an optimal closure material has not yet been determined. Moreover, most of these materials may prolong the operation time or increase cost, which may limit the popularity of laparoscopic appendectomy.[16]

Knot tying is challenging when performed during laparoscopy. A new horizon for laparoscopy has opened up by laparoscopic vessel ligation, suturing and performing anastomosis. Laparoscopic knots can be done extracorporally or

intracorporally. The tumble square, Dundee, Aberdeen, Midship and blood knots are the most common intracorporeal knots. Decreased sensation of the tension applied to the tissues and the knot and difficulty in knotting because of technical requirements and limited space are the disadvantages. Duncan, Roeder, modified 4-S Roeder, Tayside, Yanni and Gea knots are the most common extracorporeal knots. It is much easier to tie than intracorporeal knot, but they can cause tissue trauma from pulling long lengths of suture through the needle tract, excessive tension on the tissue while pushing the knot into position, and loss of focus on the operative field during knotting. One kind of knot-pusher would not fit for all and hence use of different knot-pushers for different suture materials are suggested.[16]

In routine cases, the intracorporeal knot-tying procedure requires 4 trocars. One holds the camera, 2 are for working to tie the suture, and the last is for holding and manipulating the appendix to be tied. If the fourth port is not used, the dissected appendix remains unsupported, and placing the knot precisely at the base becomes difficult. The percutaneous hanging technique was first introduced by Joshi et al.[91] for laparoscopic appendectomy. This technique removed the need for the fourth trocar and reduced the operating time. This model is with a minor modification, that is, without the use of an epidural, and thus we do not need a fourth trocar for stabilization. Although this hanging method is ergonomic and useful for intracorporeal knot-tying, the operation time is still longer than that for the endoclip procedure.

The titanium endoclip is made of a nonabsorbable metal material used routinely in surgery. Various studies, especially in laparoscopic cholecystectomy, have demonstrated that titanium endoclips can be used safely and efficiently. With

the widespread use of the titanium endoclip in surgery, endoscopic procedures have been greatly facilitated, and operation times have been considerably shortened. Moreover, it can be applied easily and does not require advanced surgical skills on the part of surgeons.[16]

The use of metal clips to close the appendicular stump was first described by Cristalli et al.[85] in 1991. However, it has not gained general acceptance despite the increased popularity of laparoscopic appendectomy. Nonabsorbable polymeric clips have lock systems that resemble the titanium endoclip, but they are expensive. Recently, some studies have compared the polymeric clip with the endoloop and stapler in appendiceal stump closure during laparoscopy and reported that the polymeric clip is safe, easy to use, and more cost effective.[89,90,92]

The recent studies suggest that titanium endoclips are safe and they shorten the operation time and simplify the procedure. Thus, the endoclip can be a useful alternative to intracorporeal knot-tying for appendiceal stump closure. Knot-tying techniques, in contrast to the endoclip, require hanging the appendix, which entails an added intervention and increases the operation time significantly.[16]

One concern is that a drawback of titanium endoclips may be abscess formation in the later period. There are no reports about abscess formation after appendectomy with endoclips; however, a few case reports of abscess formation associated with dropped metallic surgical clips after laparoscopic cholecystectomy have been reported, none of which has specified whether the clip was titanium.[93,94]

Singh et al.[95] reported an important study of 26 cases in which surgical metal clips were dropped during cholecystectomy, and none was associated with increased

risk of abscess. They pointed out that dropped gallstones, rather than dropped metal clips, was the main cause of abscess formation in their study.

A second drawback of titanium endoclips is the question of migration, as some studies have presented case reports showing that metal clips used in cholecystectomy may migrate into the common bile duct. No prospective study or case report has discussed the migration of titanium endoclips used in laparoscopic appendectomy into the intestines, although some case reports have indicated the migration of the clip into the bile duct after cholecystectomy.[16]

Despite the increasing number of cholecystectomies being performed annually, clip migration cases are still rare. The exact pathophysiology underlying the migration of endoclips into the bile duct is unknown. However post cholecystectomy clip migration into the bile duct has also been reported for absorbable clips. The most likely reason for migration is improper or erratic application of the clips, resulting in bile leakage. Secure and correct placement of the clips could help prevent this complication.[16]

Beldi et al.[96] reported that 1 endoloop used in appendiceal stump closure is sufficient and safe.

Ates M. et al.[16] used double intracorporeal knot-tying sutures and double titanium endoclips, and there were no differences in the complication rate or length of hospital stay between these groups. Their experience in all 61 cases revealed no increased risk of complications and leakage in laparoscopic appendiceal stump closure with intracorporeal knot-tying, but the operation time is significantly longer

than that with endoclip closure because the intracorporeal knot-tying is not as easy as endoclip application and requires extensive laparoscopic training.

The Double Shank (DS) Clip is an effective and safe device for closing the appendiceal base in laparoscopic appendectomy. In university and country hospitals the clip was applied in large number of patients. The complications are comparable to other methods. It is suitable as a standard tool for laparoscopic appendectomy in hospitals of different supply levels. There are limitations for the clip application in cases of severely inflamed or wide appendix base. When these conditions were met, a group of patients were excluded but nevertheless in a group of patients the clip was applied, even when the appendix base was estimated severely inflamed or extremely enlarged.[16]

No significant difference was found in the incidence of intra-abdominal abscesses in some randomized and prospective clinical trials when staplers are compared to endoloops for appendiceal stump closure. Endoloop was an easy, safe, and cost-effective procedure.[97]

Among 4489 patients with acute appendicitis, in a non-concurrent cohort study, it was found that the endoloop group had a significantly higher rate of intra-abdominal surgical-site infection and readmission compared with stapling.[82]

The routine use of endoscopic staplers was favoured in a meta-analysis of 427 patients in four randomized controlled trials on appendix stump closure. When the appendix stump was secured with staplers, superficial wound infections and postoperative ileus were obviously less frequent but there was no significant difference in relation to intra-abdominal abscess.[13]

One or two proximal ligatures and one distal ligature are applied around the base of the appendix, which results in extraversion of the appendiceal stump mucosa in endoloops, as opposed to the inversion of the mucosa with stapling devices. Insufficient closure of the stump or exposure of the remaining contaminated mucosa to the abdominal cavity may be the cause of abscess formation after endoloop. Mucosal necrosis with loosening of the ligature could be postulated as another mechanism of leakage.[13]

METHODOLOGY

The present study was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014.

Study design

The study design was a randomized controlled trial.

Study period and duration

The present study was conducted for one year from January 2014 to December 2014.

Place

The present study was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum a tertiary care teaching hospital attached to KLE University's Jawaharlal Nehru Medical College, Belgaum.

Source of Data

Patients diagnosed with appendicitis (Acute, chronic or recurrent) and undergoing laparoscopic appendectomy were included in the study.

Sample size

A total of 60 patients divided into two groups of 30 each undergoing laparoscopic appendectomy were studied.

Sampling procedure

Due to the lack of proven data on prevalence, the effect size could not be calculated. Hence based on the rule of thumb a sample size of 60 divided into two groups of 30 each was planned.

Randomization

Patients were divided into two groups of 30 each as group T and R by Sequential Numbered Opaque Envelope Method

Selection criteria

Inclusion

- Patients diagnosed with appendicitis and willing for laparoscopic appendectomy.
- Clinically diagnosed as appendicitis
- Patients aged between 18 to 60 years.

Exclusion

Patients with

- Bleeding disorders
- Immunocompromised state

- Pregnancy
- Patients who refused to participate.

Ethical clearance

Prior to the commencement, the study was approved from the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed Consent

The patients fulfilling selection criteria were informed in detail about the nature of the study and a written informed consent was obtained before enrollment (Annexure I).

Method of collection of data

Patients were interviewed and demographic data such as age, sex and the presenting symptoms were noted. These patients were subjected to clinical examination and evaluated for vitals and clinical signs. These findings were recorded on a predesigned proforma (Annexure II).

Investigations

The following investigations were done

- Routine blood investigations including:
    - Complete blood count.
    - Urine examination (routine and microscopy)
- Serum Urea
- Serum Creatinine

- Liver function test
- Ultrasound

Procedure

Diagnosis of appendicitis

Diagnosis of appendicitis was based on disease history (Right Iliac Fossa pain, vomiting, nausea, anorexia, fever) and clinical signs (McBurney's point tenderness, Rebound Tenderness), and laboratory tests (elevated leukocyte count). The preoperative diagnosis of appendicitis was confirmed by ultrasound abdomen and pelvis revealing either probe tenderness in the right Iliac fossa or an aperistaltic, tubular appendix.

Patient positioning

The patient was placed in a supine position, combined with the Trendelenburg position and left lateral position (10–15^{o}, inclined towards the surgeon). The surgeon and an assistant stood on the left side, and the monitor was placed on the right side of the patient.

Anaesthesia

All the surgeries were performed under general anesthesia.

Surgical technique

All the laparoscopic appendectomies were performed by the same surgeon.

The bladder was decompressed with a Foley catheter to avoid injury during insertion of the supra-pubic ports. Through the umbilicus, a 10 mm port was inserted by Hasson's open technique and pneumoperitoneum was created and another 10 mm port was inserted in the midline lower pelvic (suprapubic) region. One 5 mm trocar was inserted in the left lower quadrant forming a triangle with the previous two ports. An additional 5 mm port was inserted at the right lower quadrant if necessary. After that, diagnostic laparoscopy was done.

The mesoappendix was skeletonized from the top to the base using cautery or at occasion using clips through the 10 mm umbilical port. The base of the appendix was then isolated.

Intervention

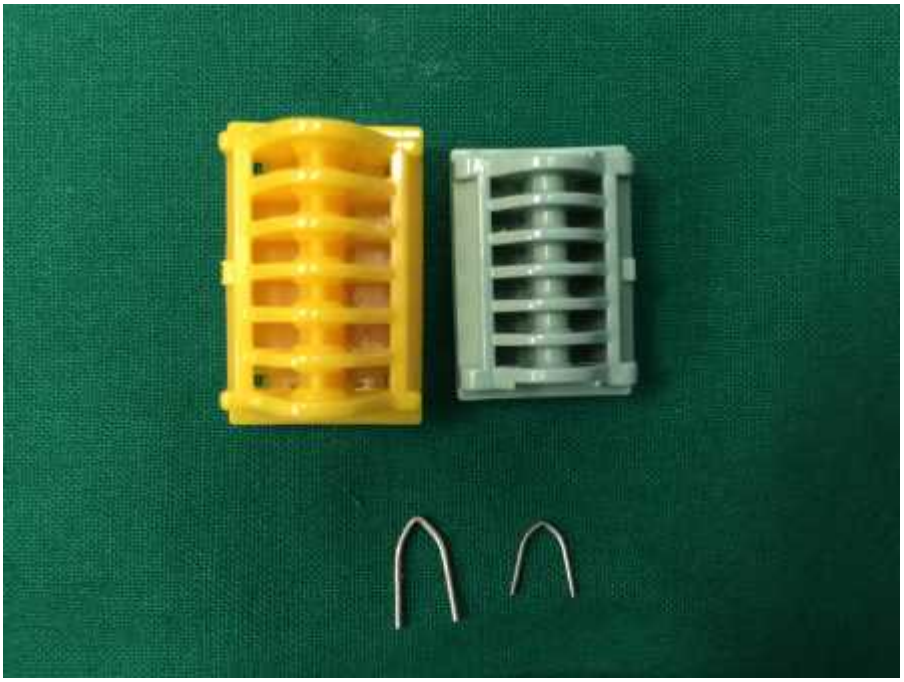
Group T

Titanium clips were passed through the 10 mm port and secured at the base of the appendix. Two clips were placed at the base and a 3rd clip placed distally. Using a grasper, the base of the appendix was measured and if < 10mm, Titanium clips were applied.

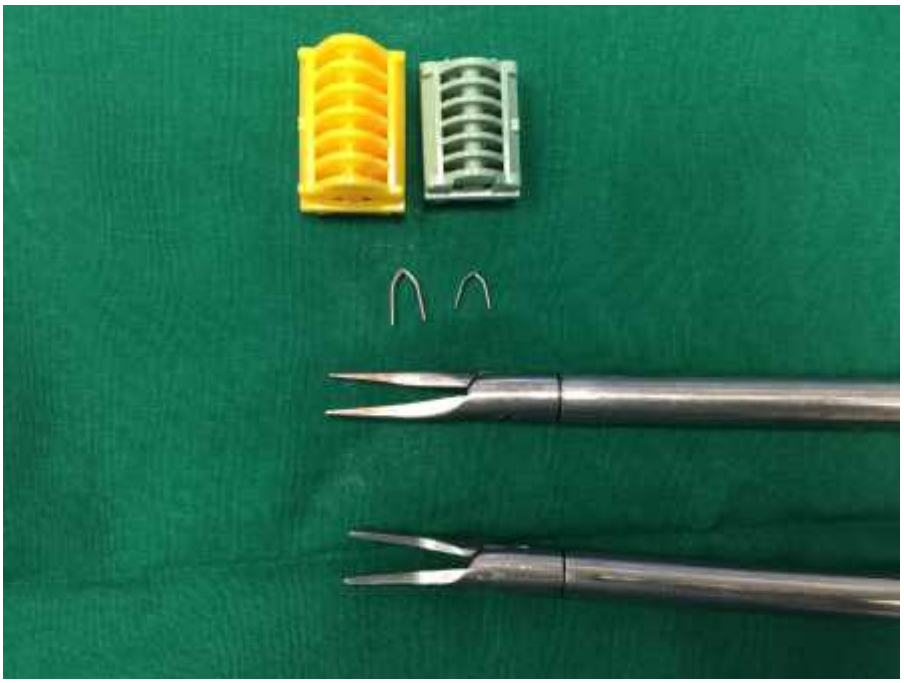
Group R

Through the same port a Roeder's Knot (Silk suture) is introduced in the same way. Two knots were applied and the appendix is transected between the ties. After resection of the appendix, it was retrieved through a 10 mm trocar. Silk suture was used to carry out Roeder's knot.

Diagnosis was correlated with Histopathology report.

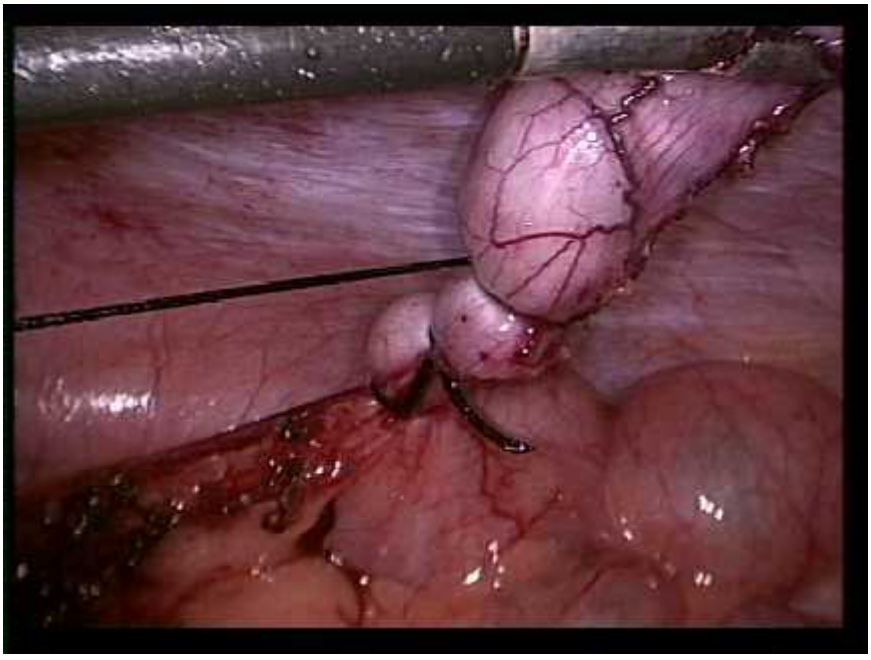


Photograph 1. Different sizes of the titanium clip

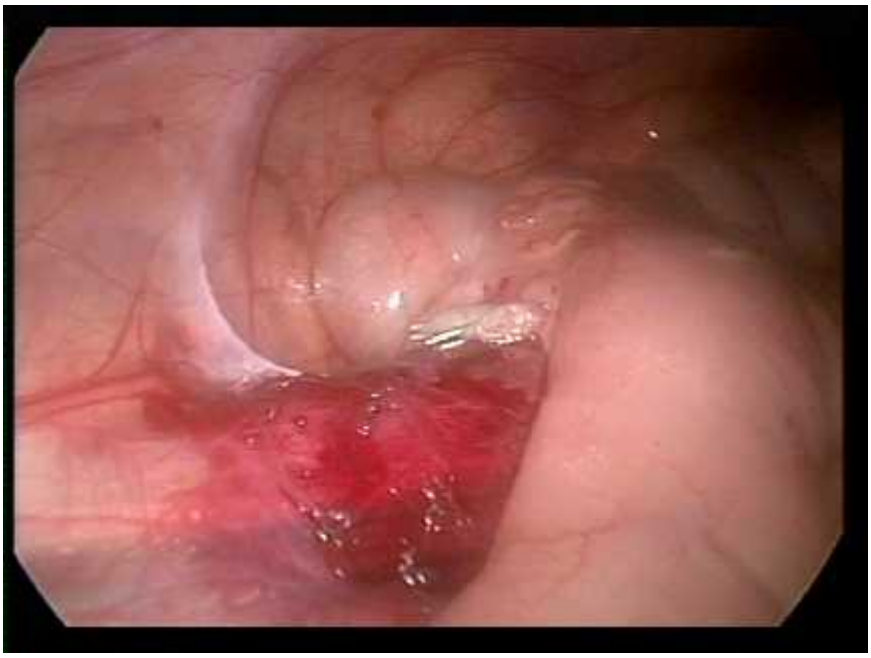


Photograph 2. Clip along with applicator

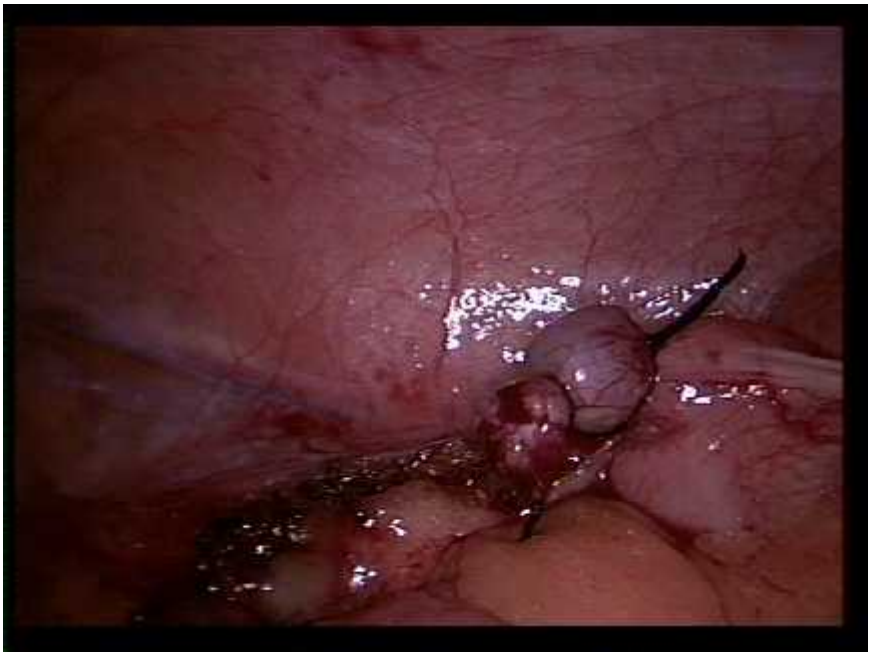
Photograph 3. Titanium clip ligation



Photograph 4. Roeder's knot ligation



Photograph 5. Post operative stump picture (Clip)



Photograph 6. Post operative stump picture (Knot)

Post operative care

Post operative management was the same for both the groups. Both groups were monitored for any complications till discharge from the hospital. The skin sutures were removed between postoperative day seven to ten. Routine follow up examinations were ordered for all patients for first two months after surgery.

Outcome variables

The following variables were evaluated intra operatively and post operatively.

- Ease of use and safety of titanium clips compared to Roeder's knot by operative time and pressure gradient respectively
- Intraoperative complications
- Post operative complications
- Hospital stay
- Follow up period

Statistical analysis

The data was entered into the Microsoft Excel Spreadsheet (Annexure III). The data was analyzed using SPSS statistical software version 20.0. The categorical data was expressed as rates, ratios and percentages and comparison was done using Fishers exact test and chi-square test. Continuous data was expressed as mean ± standard deviation and the comparison was done using independent sample t test. A probability ('p' value) of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant.

RESULTS

The present one year randomized controlled trial was done in the the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 60 patients diagnosed with appendicitis (Acute, chronic or recurrent) and undergoing laparoscopic appendectomy from January 2014 to December 2014 were enrolled. Based on the intervention, these patients were divided into two groups of 30 each based according to the opaque envelope method as below.

Group R

The appendiceal stump closure during laparoscopic appendectomy in this group was done using Roeder's Knot (Silk suture).

Group T

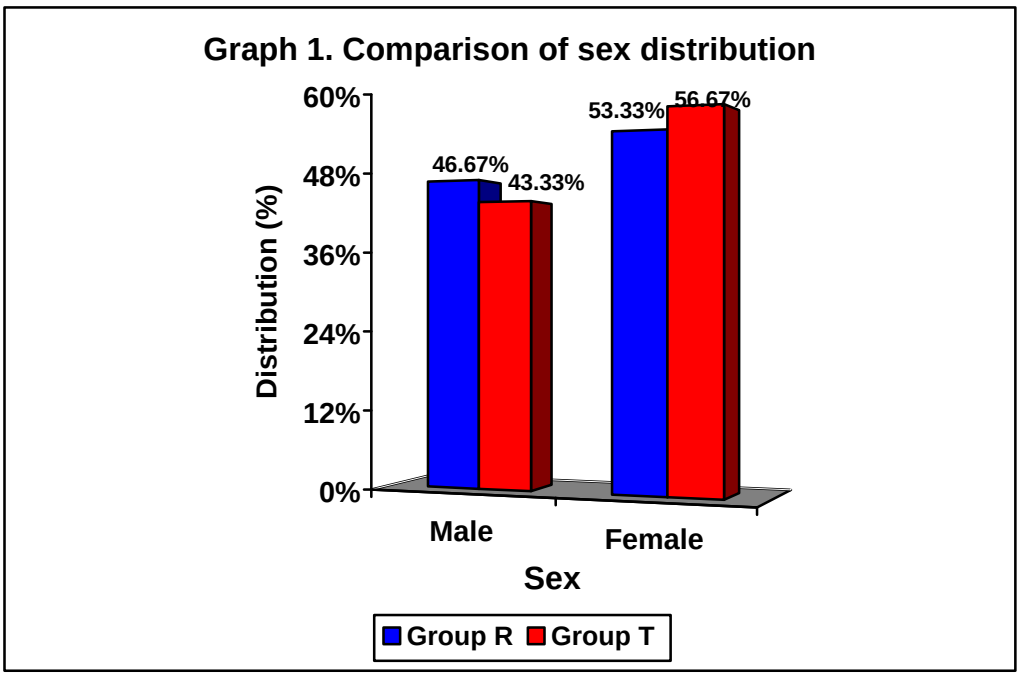
Patients in this group underwent the appendiceal stump closure during laparoscopic appendectomy using Titanium clips.

The data obtained was analyzed and the final results and observations were tabulated and interpreted as below.

Table 1. Comparison of sex distribution

Sex	Group R (n=30)		Group T (n=30)	
	No.	**%**	**No.**	**%**
Male	14	46.67	13	43.33
Female	16	53.33	17	56.67
Total	**30**	**100.00**	**30**	**100.00**

p = 0.795

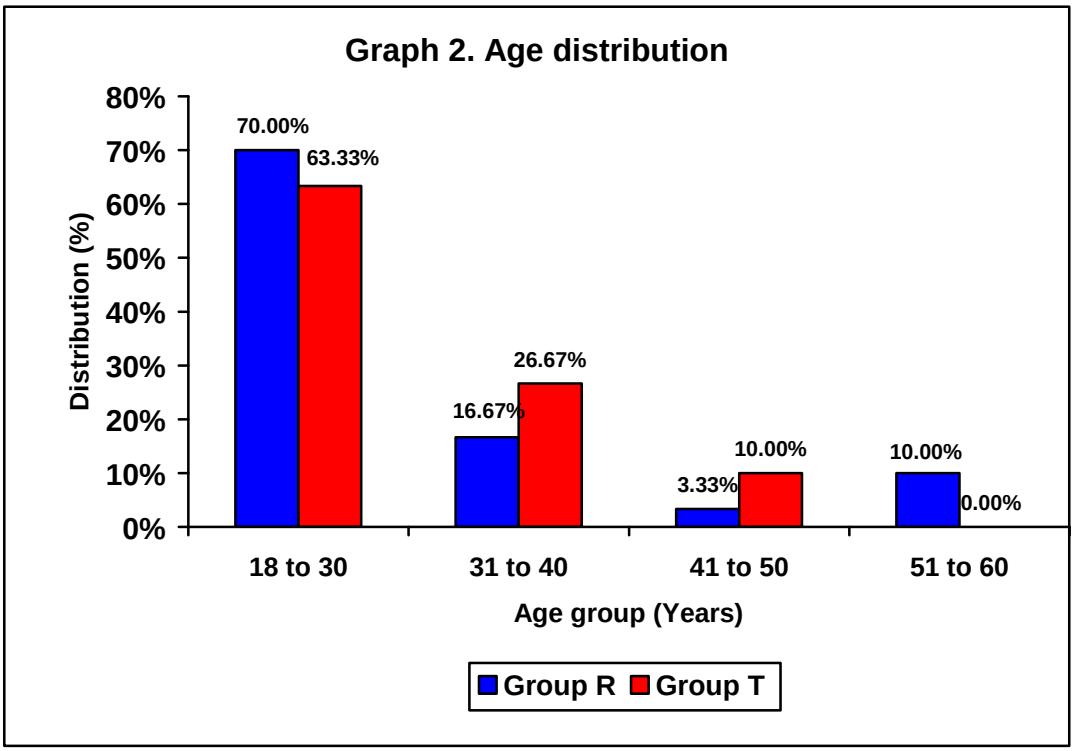


In the present study 53.33% of the patients in group R were females compared to 56.67% in group T. The female to male ratio in group R was 1.14:1 compared to 1.30:1 in group T. However, this difference was statistically not significant (p=0.795).

Table 2. Age distribution

Age group (Years)	Group R (n=30)		Group T (n=30)	
	No.	**%**	**No.**	**%**
18 to 30	21	70.00	19	63.33
31 to 40	5	16.67	8	26.67
41 to 50	1	3.33	3	10.00
51 to 60	3	10.00	0	0.00
Total	**30**	**100.00**	**30**	**100.00**

p = 0.253



In this study most of the patients in group R (70%) and T (63.33%) were aged between 18 to 30 years (p=0.253).

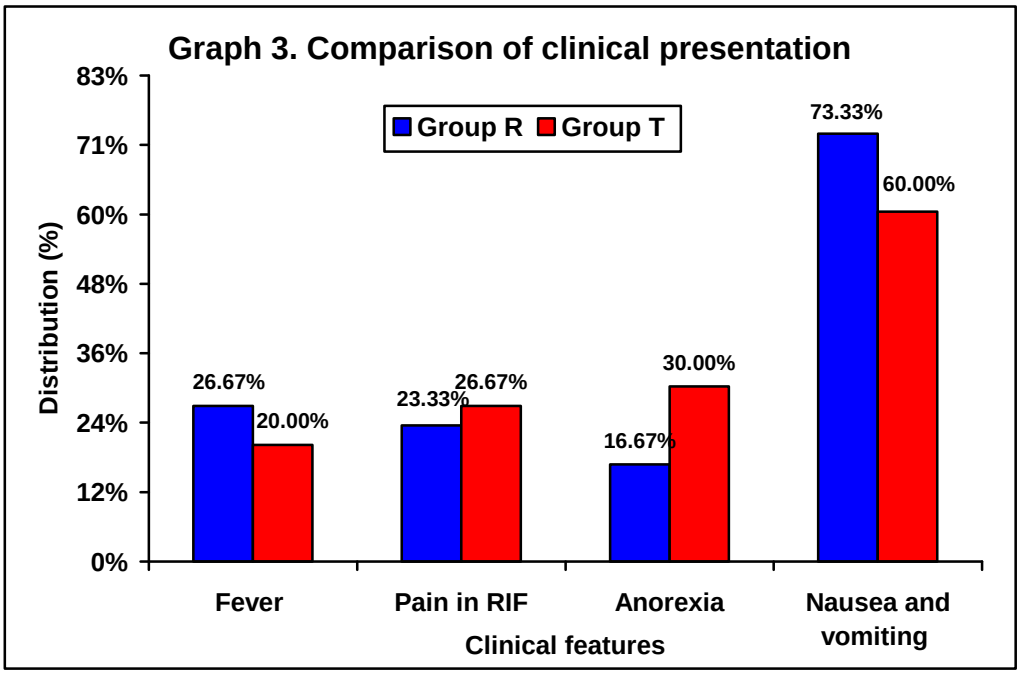
Table 3. Mean age

Variables	Group R (n=30)		Group T (n=30)		p value
	Mean	**SD**	**Mean**	**SD**	
Age (Years)	29.77	11.24	29.53	8.96	0.929

In the present study the mean age in group R (29.77 ± 11.24 years) and group T (29.53 ± 8.96 years) were comparable (p=0.929).

Table 4. Comparison of clinical presentation

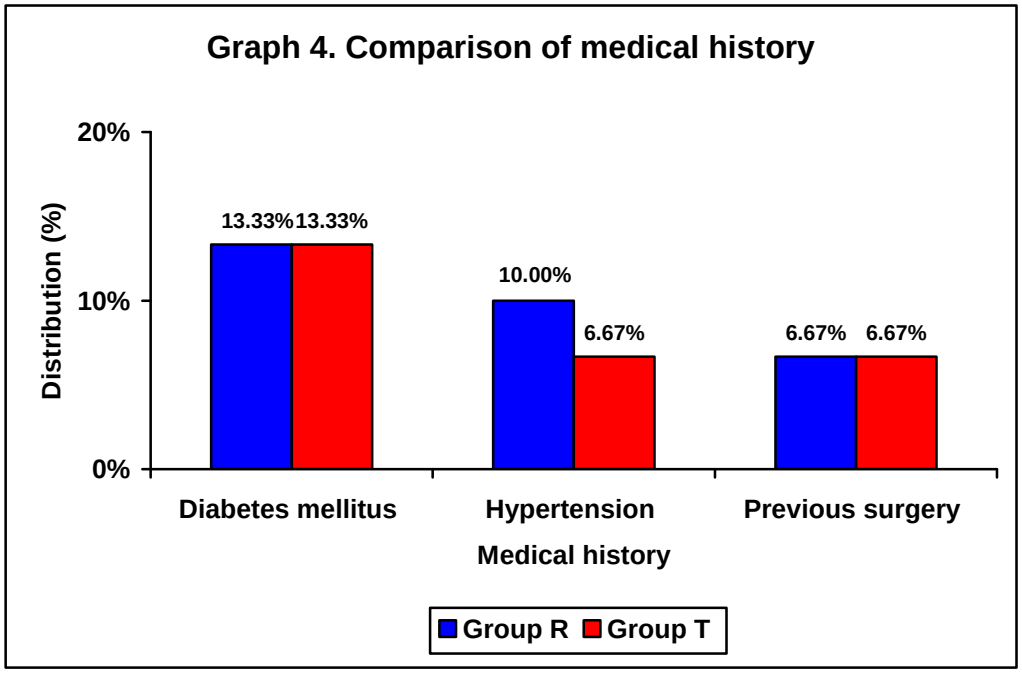
Presentation	Findings	Group R (n=30)		Group T (n=30)		p value
		No.	%	No.	%	
Fever	Present	8	26.67	6	20.00	0.542
	Absent	22	73.33	24	80.00	
	Total	**30**	**100.00**	**30**	**100.00**	
Pain in RIF	Present	7	23.33	8	26.67	0.766
	Absent	23	76.67	22	73.33	
	Total	**30**	**100.00**	**30**	**100.00**	
Anorexia	Present	5	16.67	9	30.00	0.222
	Absent	25	83.33	21	70.00	
	Total	**30**	**100.00**	**30**	**100.00**	
Nausea and	Present	22	73.33	18	60.00	0.273
Vomiting	Absent	8	26.67	12	40.00	
	Total	**30**	**100.00**	**30**	**100.00**	



In the present study at presentation clinical symptoms including fever (p=0.542), pain in RIF (p=0.766), anorexia (p=0.222) and nausea and vomiting (p=0.273) did not differ significantly in both the groups.

Table 5. Comparison of medical history

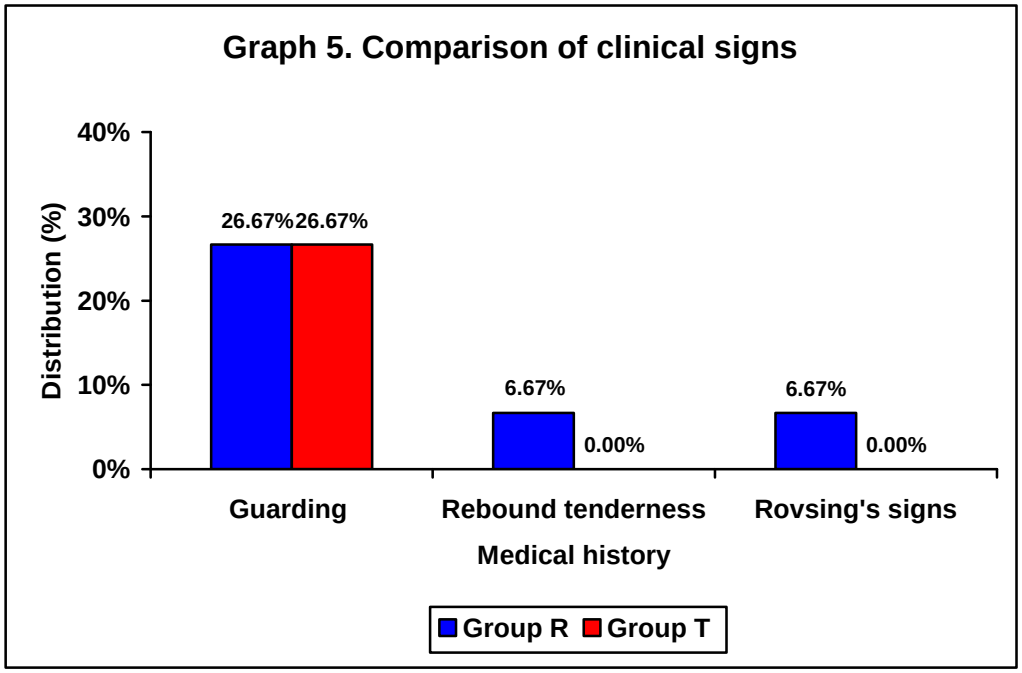
Presentation	Findings	Group R (n=30)		Group T (n=30)		p value
		No.	%	No.	%	
Diabetes mellitus	Present	4	13.33	4	13.33	0.647
	Absent	26	86.67	26	86.67	
	Total	**30**	**100.00**	**30**	**100.00**	
Hypertension	Present	3	10.00	2	6.67	0.500
	Absent	27	90.00	28	93.33	
	Total	**30**	**100.00**	**30**	**100.00**	
Previous surgery	Present	2	6.67	2	6.67	0.694
	Absent	28	93.33	28	93.33	
	Total	**30**	**100.00**	**30**	**100.00**	



In this study medical history including diabetes mellitus, hypertension and previous surgery were comparable in group R and T (p>0.050).

Table 6. Comparison of clinical signs

Clinical signs	Findings	Group R (n=30)		Group T (n=30)		p value
		No.	%	No.	%	
Guarding	Present	8	26.67	8	26.67	1.000
	Absent	22	73.33	22	73.33	
	Total	**30**	**100.00**	**30**	**100.00**	
Rebound tenderness	Present	2	6.67	0	0.00	0.246
	Absent	28	93.33	30	100.00	
	Total	**30**	**100.00**	**30**	**100.00**	
Rovsing's sign	Present	2	6.67	0	0.00	0.246
	Absent	28	93.33	30	100.00	
	Total	**30**	**100.00**	**30**	**100.00**	



In the present study, on examination, the distribution of patients according to the clinical signs that is, guarding (p=1.000), rebound tenderness and Rovsing's sign (p=0.246) was equal.

Table 7. Comparison of anthropometric, vitals and haemoglobin levels

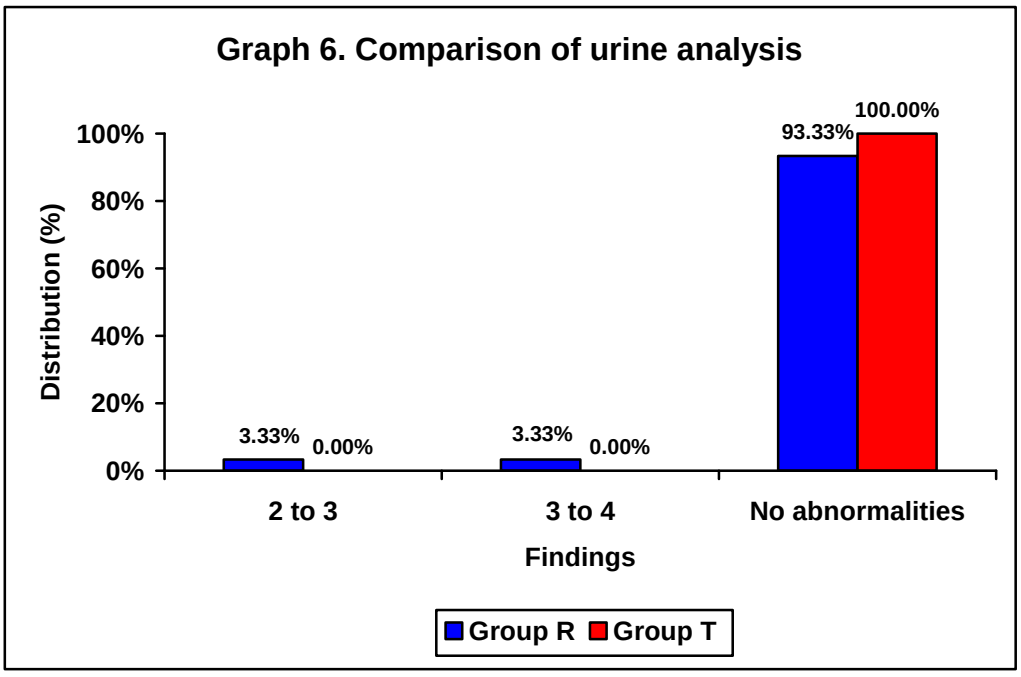
Parameters	Group R (n=30)		Group T (n=30)		p value
	Mean	SD	Mean	SD	
Weight (Kgs)	79.47	115.78	60.23	10.71	0.372
Height (Cms)	163.10	9.22	161.77	7.38	0.539
Pulse rate (/Minute)	84.50	8.59	83.80	6.94	0.730
Respiratory rate (/Min)	19.27	24.17	15.33	2.26	0.382
Systolic BP (mm Hg)	122.33	17.75	121.33	11.67	0.798
Diastolic BP (mm Hg)	73.00	9.15	74.67	8.19	0.322
Temperature (0F)	98.53	0.63	98.40	0.50	0.367
Haemoglobin (gm %)	12.35	1.29	12.19	1.08	0.603

Table 7 shows comparison of anthropometric, vitals and haemoglobin levels. However both the groups were comparable for weight (p=0.372), height (p=0.539), pulse rate (p=0.730), respiratory rate (p=0.382), systolic BP (p=0.798), diastolic BP (p=0.322), temperature (p=0.367) and haemoglobin (p=0.603).

Table 8. Comparison of urine analysis

Findings	Group R (n=30)		Group T (n=30)	
	No.	%	No.	%
2 to 3 Pus cells	1	3.33	0	0.00
3 to 4 Pus cells	1	3.33	0	0.00
No abnormalities	28	93.33	30	100.00
Total	**30**	**100.00**	**30**	**100.00**

p = 0.492

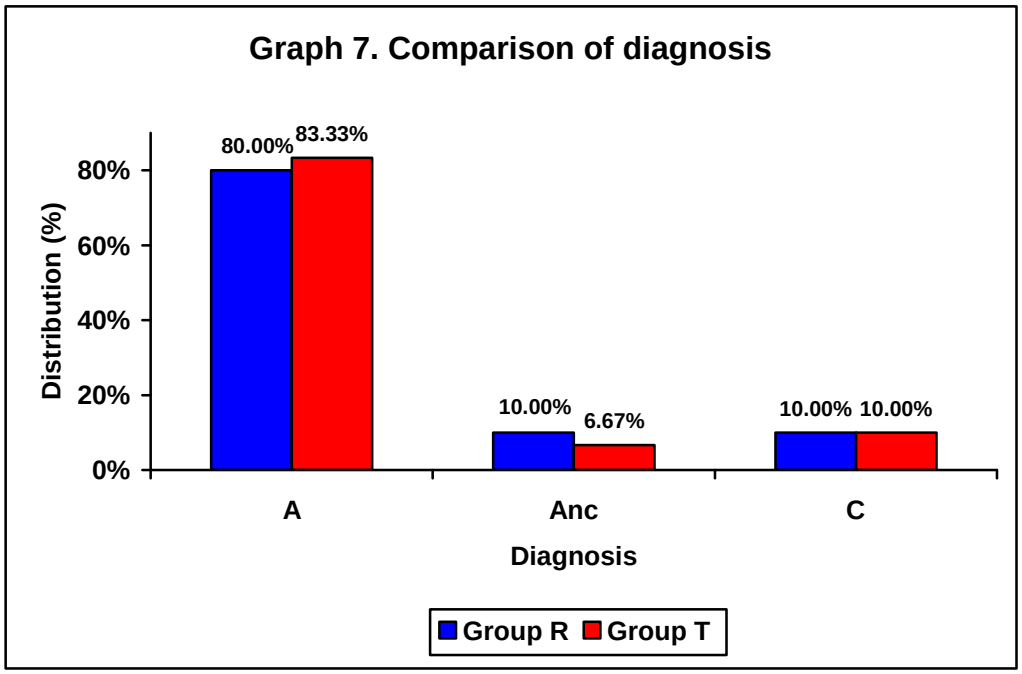


In the present study urine analysis in majority of the patients in group R was normal and all the patients (100%) in group T had normal urine analysis (p=0.492).

Table 9. Comparison of diagnosis

Diagnosis	Group R (n=30)		Group T (n=30)	
	No.	**%**	**No.**	**%**
(A)Acute	24	80.00	25	83.33
AnC(Acute on Chronic)	3	10.00	2	6.67
(C)Chronic	3	10.00	3	10.00
Total	**30**	**100.00**	**30**	**100.00**

p = 1.000

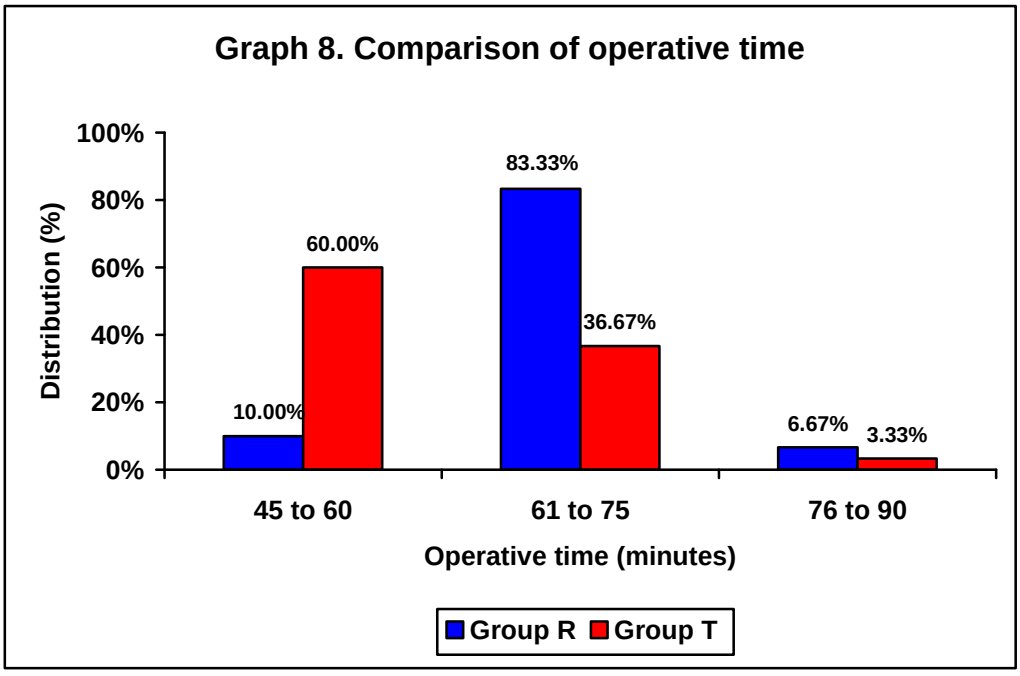


In this study majority of the patients in group R (80%) and group T (83.33%) were diagnosed to have acute appendicitis.

Table 10. Comparison of operative time

Operative time (minutes)	Group R (n=30)		Group T (n=30)	
	No.	%	No.	%
45 to 60	3	10.00	18	60.00
61 to 75	25	83.33	11	36.67
76 to 90	2	6.67	1	3.33
Total	**30**	**100.00**	**30**	**100.00**

p<0.001

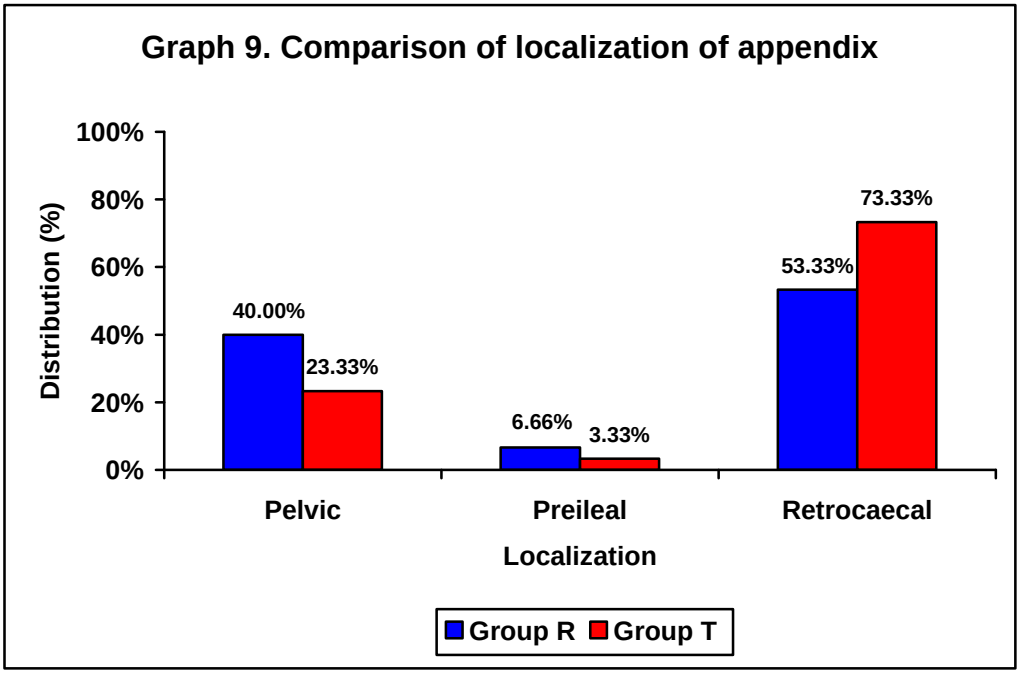


In the present study the 60% of the patients in group T the duration of operation ranged between 45 to 60 minutes while in group R, 83.33% of the required operative time between 61 to 75 minutes. This difference was statistically significant (p<0.001).

Table 11. Comparison of localization of appendix

Localization	Group R (n=30)		Group T (n=30)	
	No.	%	No.	%
P(Pelvic)	12	40.00	7	23.33
PI(Pre Ileal)	2	6.66	1	3.33
R(Retrocaecal)	16	53.33	22	73.33
Total	**30**	**100.00**	**30**	**100.00**

p=0.273

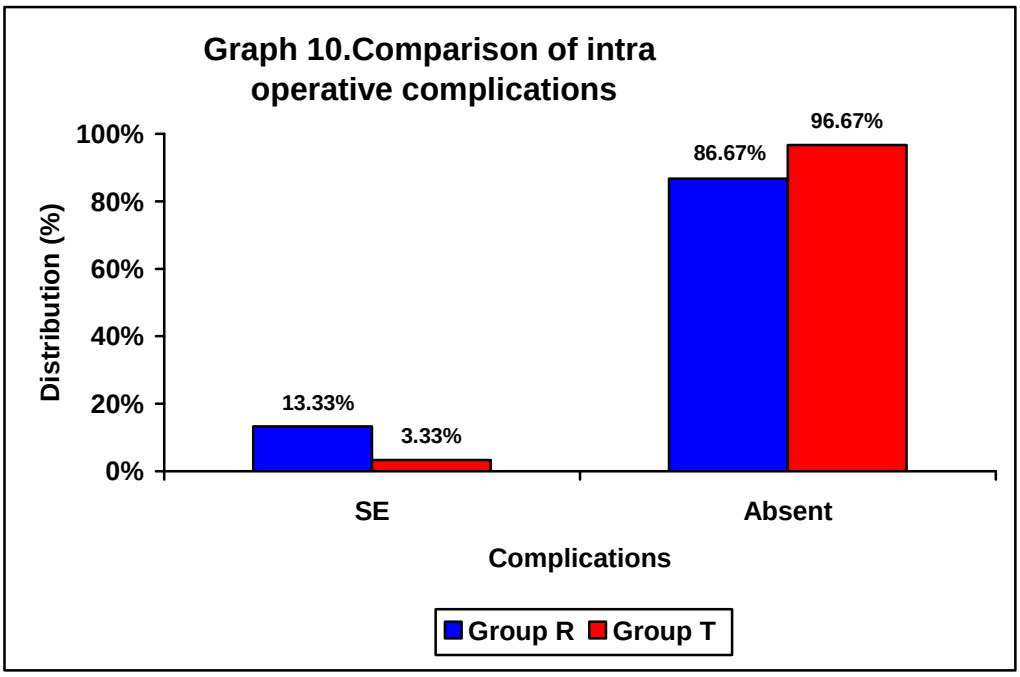


In this study retrocaecal position of appendix was noted in 73.33% of the patients in group T compared to 53.33% in group R. However this difference was statistically not significant (p=0.273).

Table 12. Comparison of intra operative complications

Complications	Group R (n=30)		Group T (n=30)	
	No.	**%**	**No.**	**%**
SE(Subcutaneous Emphysema)	4	13.33	1	3.33
Absent	26	86.67	29	96.67
Total	**30**	**100.00**	**30**	**100.00**

p=0.177

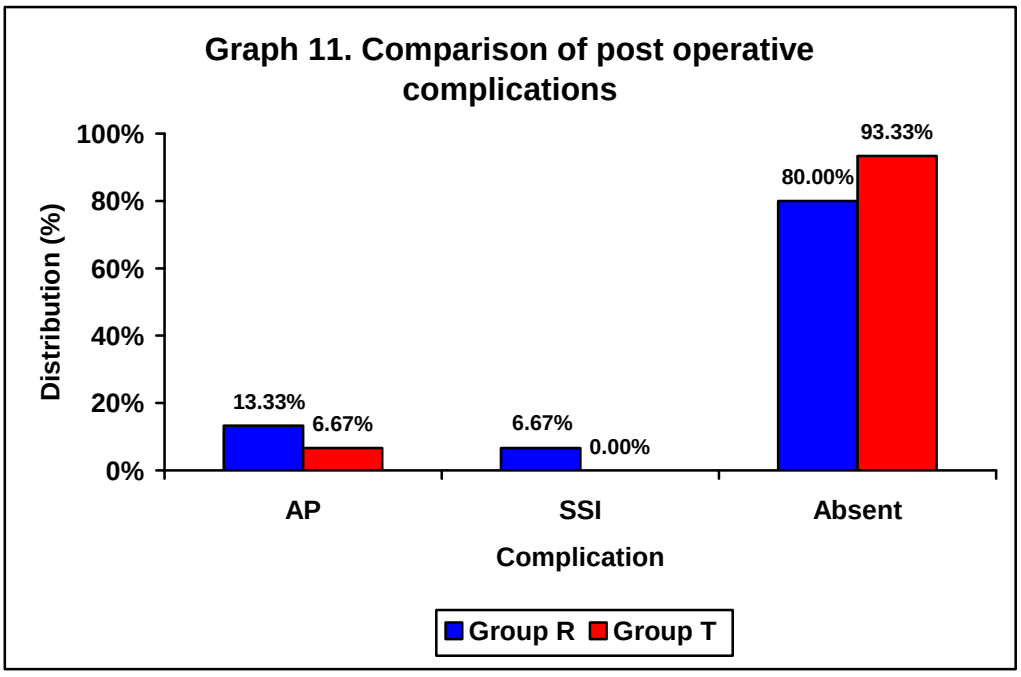


In the present study intraoperative complications of Subcutaneous Emphysema were noted in 13.33% of the patients in group R compared to 3.33% of the patients in group T but statistically, the difference was not significant (p=0.177).

Table 13. Comparison of post operative complications

Complications	Group R (n=30)		Group T (n=30)	
	No.	%	No.	%
AP(Abdominal Pain)	4	13.33	2	6.67
SSI(Surgical Site Infection)	2	6.67	0	0.00
Absent	24	80.00	28	93.33
Total	**30**	**100.00**	**30**	**100.00**

p=0.303

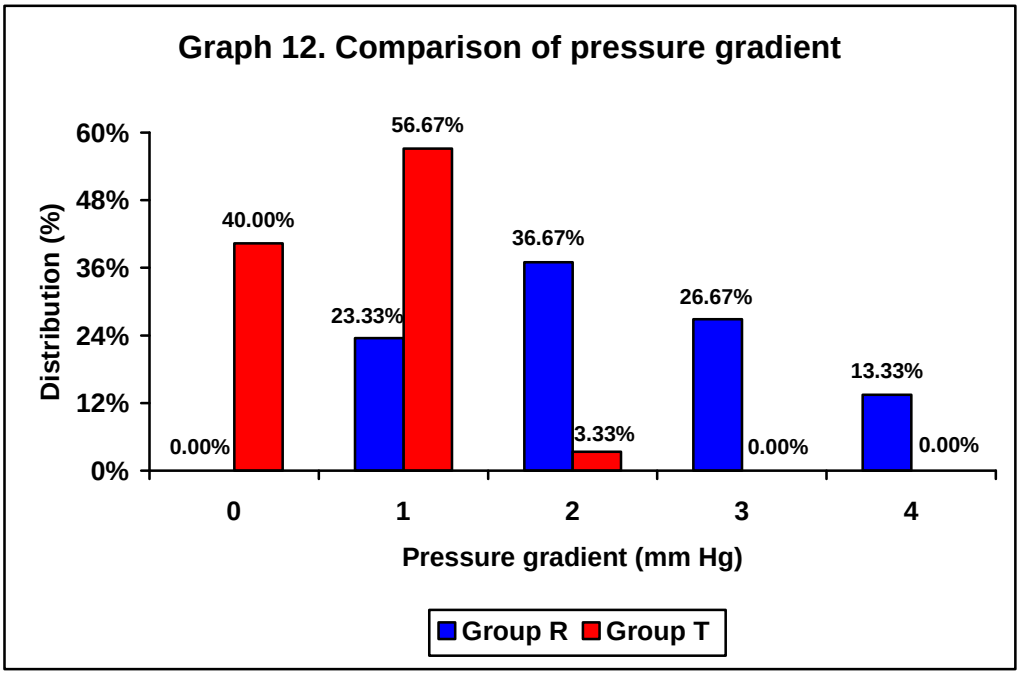


In this study, post operatively, Abdominal Pain and Surgical Site Infection were present in 13.33% and 6.67% of the patients in group R compared to 6.67% and nil in group T respectively. However, this difference was statistically not significant (p=0.303).

Table 14. Comparison of pressure gradient

Pressure gradient (mm Hg)	Group R (n=30)		Group T (n=30)	
	No.	%	No.	%
0	0	0.00	12	40.00
1	7	23.33	17	56.67
2	11	36.67	1	3.33
3	8	26.67	0	0.00
4	4	13.33	0	0.00
Total	**30**	**100.00**	**30**	**100.00**

p<0.001



In the present study, pressure gradient (i.e., the difference between the initial pneumoperitoneum pressure and the pressure during clip/knot application) was found to be 0 mm Hg in 0% of Group R & 40% of Group T, 1 mm Hg in 23.33% in group R & 56.67% in group T, 2 mm Hg in 36.67% in group R & 3.33% in group T, 3 mm Hg in 26.67% in Group R, 4 mm Hg in 13.33% in group R. This difference was statistically significant (p<0.001).

Table 15. Comparison of mean operative time

Variables	Group R (n=30)		Group T (n=30)		p value
	Mean	**SD**	**Mean**	**SD**	
Operative time (Minutes)	68.47	6.30	59.20	10.33	<0.001
Pressure gradient	2.30	0.99	0.63	0.56	<0.001
Hospital stay (Days)	3.70	1.02	3.16	0.53	0.015
Follow up period (Months)	2	-	2	-	-

In the present study the mean operative time, pressure gradient and hospital stay was significantly high in group R compared to group T ($p<0.050$) but follow up period in both the groups was comparable.

DISCUSSION

Since its report by Charles McBurney to the New York Surgical society, in 1889, the treatment of appendicitis had remained unchanged.[65] An alternative approach was put forward by Kurt Semm who described 'laparoscopic appendectomy' prior to the description of Laparoscopic Cholecystectomy, in 1983.[78] The first large series of laparoscopic appendectomies was reported Pier et al. in 1990.[98]

With respect to post operative pain or use of analgesia, hospital stay, number of post-operative complications and return to normal activities, laparoscopic appendectomy has been shown to be superior to open appendectomy in several randomized controlled trials. Yet, technical aspects still need to be evaluated and standardized.[91]

Regarding closure of the appendiceal stump, controversy exists, in spite of a good establishment of the surgical technique for laparoscopic appendectomy. Pre-knotted loops (Roeder loops or endoloops) were initially applied to the stump in Laparoscopic appendectomy. The application of linear staplers was "en vogue", after their introduction, in laparoscopic appendectomy, particularly for perforation at the base of appendix. Post-operative infections can be due to slippage of loops. If the inflammation of the appendix has involved the caecum or base of appendix is perforated, loops are not safe. Stump leakage can be caused by tissue necrosis and can cut through tissues if loops are tight.[91]

Titanium clips are the most commonly used clips in minimally invasive surgery because they are easy to use, safe and inexpensive; however, they have not been regularly used for appendiceal stump closure in laparoscopic appendectomy.[91] To date, few randomized clinical studies have been conducted to compare Roeder's knot and titanium clips. This study was designed to assess the ease of use and safety of titanium clips compared to Roeder's knot in the appendiceal stump closure among the patient undergoing laparoscopic appendectomy.

The present one year randomized controlled trial was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014. A total of 60 patients diagnosed with acute appendicitis or chronic appendicitis or recurrent appendicitis scheduled for laparoscopic appendectomy were studied. Based on the method of appendiceal stump closure, these patients were divided into two groups of 30 each by opaque envelope method as Group R (Patient underwent appendiceal stump closure with Roeder's Knot) and Group T (Patients underwent appendiceal stump closure using Titanium clips). The patients were evaluated for operative time, intra-operative and post operative complications, hospital stay, and follow up period.

In the present study frequency of females was slightly high in both the groups. In group R, 53.33% of the patients were females and in group T females constituted 56.67%. The female to male ratio in group R was 1.14:1 compared to 1.30:1 in group T. Though appendicitis was common among females in both the groups, the difference was statistically not significant (p=0.795). A study by Rickert A. et al.[11] to investigate the results after application of titanium clip for appendiceal stump closure also reported 59% of the females. In contrast Ates M. et al.[16] which

compared intracorporeal (polyglactin) knot-tying suture with titanium endoclips in appendiceal stump closure during laparoscopic appendectomy reported male preponderance.

The incidence of appendicitis gradually rises from birth, peaks in the late teen years, and gradually declines in the geriatric years.[28,31] In this study, the commonest age group was 18 to 30 years in group R (70%) and group T (63.33%) (p=0.253). The mean age in group R was 29.77 ± 11.24 years and in group T the mean age was 29.53 ± 8.96 years (p=0.929). These findings suggest that, most of the patients who presented with appendicitis were young. Most of the earlier studies[28,31] in the literature have observed that appendicitis is common in the younger age group.

Overall the demographic characteristics of the study population were comparable in group R and group T (p>0.050). Further, the history of associated illness (including diabetes mellitus, hypertension and previous surgery) clinical signs (guarding, rebound tenderness and Rovsing's sign) and symptoms (including fever, pain migration to RIF, anorexia, nausea and vomiting) did not differ significantly in groups R and group T (p>0.050). The comparison of anthropometric variables (Height and weight) vitals (pulse rate, respiratory rate, systolic and diastolic blood pressure, temperature) and haemoglobin levels and urine analysis were also comparable. Majority of the patients in group R (80%) and group T (83.33%) were diagnosed to have acute appendicitis (p>0.050).

An important step to avoid post-operative infectious complications is the appendiceal stump closure. Endoloops, endoclips and endostaplers are used for this

procedure. With each method having its advantages and disadvantages, various methods are being studied and tried for the same.

Any one of the methods cannot be preferred as the literature is mixed in this context. There are many studies where staplers are compared to endoloops. Routine use of endostaplers is preferred, in two reviews,[15,88] especially in case of an inflamed appendix base, because complications were lesser compared to endoloops. In contrast, endoloops were considered superior because of similar complication rates compared to staplers but much lower costs in another review, consisting of five RCTs having 622 patients.[13] Longer operation time associated with endoloops led to higher costs in these studies. Also for the placement and tightening of the loop around the appendiceal base experience is required. This can be counted as a disadvantage.[82]

More than 20 years ago, the use of endoclips for appendicular stump closure was described. In spite of this, it is less investigated and less commonly used. The diameter of the appendix base and severity of inflammation limits the use of the endoclips. Clips can be used safely for closure of the appendiceal base in selected cases have been shown in small studies.[11]

In the present study significantly higher number of patients in group T (60%) had lower operative time that is, 45 to 60 minutes compared to group R as majority of the patients i.e., 83.33% had operative time between 61 to 75 minutes ($p<0.001$). The mean operative time in group T was significantly low compared group R (59.20 ± 10.33 vs 68.47 ± 6.30 minutes; $p<0.001$). These findings suggest that, appendiceal stump closure during laparoscopic appendectomy requires significantly lower

operative time using titanium clips compared to Roeder's knot. When endostaplers were used (51.7-58 min) compared to endoloops (53.4-60 min), large cohort studies reported shorter operation times. The operation time in this study was 59.20 min, which is comparable to other studies that used endoclips for stump closure (46.3-64.9 min).[82,90,99,100] Findings of the present study were also comparable when metal clips were used instead of intracorporal knotting techniques in two recent small randomised trials with shorter operation time.[16,101] Comparison studies of metal endoclips to staplers or endoloops have not yet been published. In several studies, polymeric nonmetal clips have been used which resulted in reduced costs, shorter operation times and comparable complication rates.[89,90,92,101]

The optimal device for appendiceal stump closure should offer maximum safety for the patients and result in a safe stump closure with a low rate of complications. In this study 3.33% of the patients in group T had intra operative complications of SE (Subcutaneous Emphysema) compared to 13.33% in group R. However this difference was statistically not significant (p=0.177). Post operatively, in group T, complications of AP (Abdominal Pain) were noted in 6.67% while in group R, 13.33% of the patients had surgical site infections and AP in 6.67%. Though the frequency of post operative complications in group high, the difference not statistically not significant (p=0.303). These findings suggest that, the frequency of intra operative and post complications is less likely using titanium clips but comparable with appendiceal stump closure with Roeder's Knot. Only few studies are available, for the use of metal clips for appendix stump closure. The rate of Intra-Abdominal Abscess in these studies ranges from 1% to 1.6%.[11,99] The wound infection rate ranges also from 1% to 1.6%. Recently two randomised trials found

comparable complication rates when metal clips were used instead of intracorporal knotting techniques.[16,99]

In the present study, pressure gradient (i.e., the difference between the initial pneumoperitoneum pressure and the pressure during clip/knot application) between 0 to 1 was noted in significantly higher number of patients in group T (96.67%) whereas in group R, only 23.33% of the patients had pressure gradient between 0 to 1 ($p<0.001$). These findings show that Titanium clips were safe to use and maintain the pneumoperitoneum without causing much change in CO2 pressure.

In the present study the mean hospital stay in group T was significantly low compared to group R (3.16 ± 0.53 days vs 3.70 ± 1.02 days; $p=0.015$) however the mean follow period in both the groups was two months. Hence it may postulated that use of titanium clips significantly favours early discharge and resumption of normal daily activities compared to appendiceal stump closure with Roeder's Knot. 2 to 5.9 days was the median hospital stay found in recent studies with no significant differences between the different methods of appendix stump closure.[68,82,100]

Overall the results of this study suggest that titanium endoclips are safe and they shorten the operation time and simplify the procedure. Thus, the Titanium clip can be a useful alternative to Roeders knot-tying for appendiceal stump closure. However, there is a limitation of this study in that the follow-up period was not enough to discuss long-term side effects of titanium clips.

CONCLUSION

Overall the present study of titanium clips versus Roeder's knot in appendiceal stump closure showed that the clips had several advantages. Among them, less operative time, lower pressure gradient (maintenance of pneumoperitoneum), ease of application of clip and early discharge enabling daily routine activities were distinct. Though the intra operative and post operative complications were less with titanium clips, these findings need further evaluation.

SUMMARY

Appendiceal stump closure during laparoscopic appendectomy is an important step as it may result in postoperative complications. The present study was an attempt to evaluate the ease of use and safety of titanium clips compared to Roeder's knot in the appendiceal stump closure in patients undergoing laparoscopic appendectomy by comparing complications (perioperative and post operative), hospital stay and follow up period.

This one year randomized controlled trial was done in under the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014. A total of 60 patients undergoing laparoscopic appendectomy were enrolled. Based on the intervention, patients were divided into two groups of 30 each that is, Group R (Roeder's Knot using Silk suture and Group T (Titanium clips).

In the present study 53.33% of the patients in group R were females compared to 36.67% in group T ($p=0.795$). The mean age in group R was 29.77±11.24 years and in group T it was 29.53±8.96 ($p=0.929$). Other variables including clinical presentation, medical history, anthropometry, vitals, clinical signs, diagnosis, haemoglobin and urine analysis were comparable ($p>0.050$). The duration of surgery in 60% of the patients in group T was between 45 to 60 minutes while majority of the patients in group R (83.33%) required 61 to 75 minutes ($p<0.001$). Retrocaecal localization was done in 73.33% of the patients in group T compared to 53.33% of the patients in group R ($p=0.005$). The pressure gradient was 1 in 23.33% of the patients in group R compared to 56.67% in group T ($p<0.001$). The mean

operative time, pressure gradient (the difference between the initial pneumoperitoneum pressure and the pressure during clip / knot application) and hospital stay were significantly high in group R compared to group T ($p<0.050$). The mean operative time, pressure gradient and hospital stay were significantly high in group R compared to group T ($p<0.050$). However, the intra operative complications and post operative complications including abdominal pain and surgical site infections were comparable ($p=0.177$ and $p=0.303$ respectively). Also follow up period in both the groups was comparable ($p>0.050$).

Based on the results of this study it may be concluded that, appendiceal stump closure with titanium clips is advantageous in terms of less operative time, requires lower pressure gradient (maintenance of penumoperitoneum) and early discharge and resumption of daily activities.

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ANNEXURE I – CONSENT FORM

TITLE OF RESEARCH STUDY: A COMPARISON OF TITANIUM CLIPS V/S ROEDER'S KNOT TYING SUTURE IN LAPAROSCOPIC APPENDICEAL STUMP CLOSURE: A ONE YEAR RANDOMIZED CONTROLLED TRIAL STUDY IN KLE'S DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELGAUM

Principal Investigator

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Professor,
Department Of General Surgery,
Nehru Medical College,
Belgaum.

Co-investigator

DR. *** ******
Post Graduate Student,
Department of General Jawaharlal Surgery,
Jawaharlal Nehru Medical College, Belagaum.

Introduction and purpose

You are requested to participate in a study that is an attempt to find out the effectiveness of Titanium clips in comparison to Roeder's knot suturing in Appendiceal closure in Laparoscopic Appendectomy.

Although the surgical technique of laparoscopic appendectomy has been well established, concerns & controversy exists regarding the closure of appendiceal stump, which is a key point in the procedure. Therefore, several modifications to the original technique with new materials have been introduced for optimizing and controlling the appendiceal stump closure. Controversies about the efficacy and safety of the materials still exist, and the need to evaluate this through new research has become important.

In an effort to solve the above mentioned problems, this study has been undertaken to evaluate the efficacy of a alternate technique of Appendiceal stump closure in comparison to Roeder's Knot suturing.. About 60 patients with appendicitis will be enrolled in this study.

This study will be conducted by Dr. ***** *******, Post Graduate in Department of Surgery, under the direct supervision and guidance of Dr. ***** ******, Professor, Department of Surgery, J. N. Medical College, Belgaum.

You need to be eligible, meeting all the selection criteria to participate in this study. You should be willing to provide information about yourself. 60 subjects will be enrolled in this study who will then be randomized in either of 2 groups (details below).

Procedure

If you agree to participate in this study, you will be randomly allotted into a group (A or B) and accordingly receive either the standard treatment (Roeder's knot suturing) or the newer treatment (Titanium Clips). Intra operatively, the operative time, position of the appendix & complications will be noted along with any other problems faced during surgery. Postoperative complications will be noted until you are discharged.

Benefits

The benefits of the procedure under study are early recovery time, better cosmesis & minimum complications.

Risks

There is no additional risk compared to the standard treatment.

Compensation

Taking part in the study will not affect the cost of treatment i.e. it will be similar to the cost of standard procedure. In the event that you become injured as a result of taking part in this study, treatment will be offered to you or you will be given information about where to receive medical care: but you/your insurance company will be responsible for the costs. However, no reimbursement, compensation or free medical care will be given.

Confidentiality

Every effort will be made to protect the confidentiality of the information you provide. This means that the researchers will not let anyone, not a part of the study, see the information you provide. Only Dr. ***** ***** and Dr. ***** ***** will have access to the information collected. Results of this study may be published but your name will not be revealed.

Voluntary participation / withdrawal

Taking part in this study is voluntary; you may choose not to enroll in this study. Your decision will not change the present or future health care services offered to you at KLES Dr. Prabhakar Hospital, Belgaum. The alternative that you have is to undergo the traditional procedure that is carried out in KLES Hospital.

If you have any queries about the study, you may contact Dr. **** ***** (Mobile No. **** *****); or Dr. ***** ****** (Mobile No. ***** *****). If you need any further information regarding your rights as a study participant, you may also contact Dr. **** ***** (Mobile no. ***** *****), Chairman of Institutional Ethics Committee, JNMC, Belgaum.

CONSENT FOR PARTICIPATION IN RESEARCH TRIAL

I, Mr. /Ms/ Mrs. _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject: _____

Date:

Witness Name : _____

Signature: _____

Date:

Investigators Name: _____

Signature: _____

Date:

Place:

ANNEXURE II – PROFORMA

"A COMPARISON OF TITANIUM CLIPS V/S ROEDER'S KNOT TYING SUTURE IN LAPAROSCOPIC APPENDICEAL STUMP CLOSURE: A ONE YEAR RANDOMIZED CONTROLLED TRIAL STUDY IN KLE'S DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELGAUM."

Name & Address of the patient: _____

Age of the Patient: _____ IP. No. _____

Weight of Patient: _____ Sex.

Anaesthesiologist: _____ Surgeon: _____

Pre operative evaluation

Chief Complaints

Past History

- History of Diabetes Mellitus yes/no
- Hypertension yes/no
- Asthma yes/no
- Previous surgeries yes/no
- Drug therapy yes/no

Family History

General Physical Examination

Weight: Temperature: Pallor: Height

Cyanosis: Pedal Oedema:

Clubbing: Pulse : Blood Pressure: RR:

Systemic examination

Cardiovascular System:

Respiratory System:

Per Abdomen:

Central Nervous system:

Spine assessment:

Investigations

Hb%: Urine Routine:

Any Other:

USG Abdomen &Pelvis

Diagnosis

Inclusion Criteria

1. Diagnosed Appendicitis cases, willing for Laparoscopic Appendectomy
2. Age between 18 to 60 years.
3. Clinically diagnosed as Uncomplicated Appendicitis

Exclusion Criteria

1. Patients not willing to give consent
2. Complicated Appendicitis like perforated appendicitis AND local or diffuse peritonitis
3. Patients unfit/contraindicated for Laparoscopic Surgeries

Observations

Readings were recorded in the following manner

Group:

Age:

Sex:

Operative time:

Localization of Appendix:

Perioperative Complications:

Post operative Complications:

Other findings:

Any other problems faced

Signature of staff in charge:

ANNEXURE III – KEY TO MASTER CHART

-	-	Absent
+	-	Present
^{0}F	-	Degree Fahrenheit
A	-	Acute appendicitis
AnC	-	Acute on chronic appendicitis
AP	-	Abdominal pain
BP	-	Blood pressure
C	-	Chronic appendicitis
Cms	-	Centimeters
F	-	Female
gm	-	Gram
Kgs	-	Kilo grams
L	-	Laparoscopic appendectomy
M	-	Male
mm Hg	-	Millimeters of mercury
NAD	-	No abnormality detected
P	-	Pelvic
PI	-	Preileal
PR	-	Pulse rate
r	-	Retrocaecal
RIF	-	Right iliac fossa
RR	-	Respiratory rate
SE	-	Subcutaneous Emphysema
SSI	-	Surgical site infection
USG	-	Ultrasound