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A Prospective, Single-blind, Randomized, Multi Centre, Study to Assess the Clinical Equivalence of Trutie® Ligating Clips to Ligaclip® Ligating Clips in Laparoscopic Cholecystectomy

Sanjay Kala [1], Seraj Ahmed [2], Prashant V Rahate [3], Srikant Kulkarni [4], Ramendra Kumar Jauhari [1], Anurag Singh [1], Abhishek Kumar Gond [1], Nabarun Manna [2], Ashok Kumar Moharana [5], Deepak TS *[5]

[1]Department of General Surgery, GSVM Medical college Kanpur, Uttar Pradesh, India.
[2]Department of General Surgery, Institute of Post Graduate Medical Education and Research and SSKM Hospital Kolkata, West Bengal, India.
[3]Department of General Surgery, Seven Star Hospital, Nagpur, Maharashtra, India.
[4]Department of General Surgery, BGS Global Institute of Medical Sciences Bengaluru, Karnataka, India.
[5]Department of Clinical Affairs, Healthium Medtech Limited Bengaluru, Karnataka, India.

*Corresponding author: Deepak TS; *deepak.ts@healthiummedtech.com*

Abstract

Introduction: Laparoscopic cholecystectomy, the gold standard for treating gallbladder diseases, requires reliable closure of the cystic duct and artery, typically using titanium ligating clips. This study aims to assess the clinical equivalence of Trutie® ligating clips compared to Ligaclip® ligating clips. ***Methods:*** A prospective, single-blind, randomized, multicenter study was carried out from May 2023 to April 2024 which included male and female subjects aged 18 to 60 years scheduled for elective laparoscopic cholecystectomy and were randomized to Trutie® Ligating clips (n=64) and Ligaclip® Ligating clips (n=62). Primary endpoints included the incidence of bile leakage and bleeding. Secondary endpoints assessed postoperative recovery, intraoperative handling of clips and clip applicator, number of clip breakage, failure to ligate, malformed/deformed clips, incidence of residual risks of ligating clips, quality of life, and adverse events. ***Results:*** There was no incidence of bile leakage and bleeding. Intraoperative and postoperative outcomes showed no significant differences. Quality of life improvements over six months were comparable between the two groups. No serious adverse events were reported. ***Conclusion:*** Trutie® ligating clips are clinically equivalent to Ligaclip® ligating clips in laparoscopic cholecystectomy.

Keywords: ***Bile leakage, Laparoscopic cholecystectomy, Ligaclip® ligating clips, Postoperative outcomes, Trutie® ligating clips.***

Introduction

Background: Laparoscopic cholecystectomy has become the gold standard for the treatment of gallbladder diseases such as cholelithiasis (gallstones) and cholecystitis (inflammation of the gallbladder) [1]. This minimally invasive technique involves the removal of the gallbladder using small incisions, a laparoscope, and various surgical instruments, offering benefits such as reduced postoperative pain, shorter hospital stays, and faster recovery times compared to open surgery [1,2].

A possible complication of laparoscopic cholecystectomy is bile leakage, which occurs in 0.5 to 1% of cases [3]. The cystic duct is the most common site for bile leakage after the procedure, responsible for up to 70% of all detected leaks [4,5]. Leakage from the cystic duct is more frequent, occurring in 0.5 to 3% of cases, which is higher than complicated gallstone disease and can lead to increased morbidity and mortality [6]. A critical component of this procedure is securely closing the cystic duct and artery [1,7]. Errors in cystic stump ligation can lead to complications such as major bleeding, infection, bile leakage, clip migration, and injury to the bile duct or bowel [8].

Various methods are used to secure the cystic artery and duct, including non-absorbable sutures, suture loops, absorbable and metallic clips, electrocautery, and harmonic scalpels [6,9]. Among these, the application of non-absorbable metal clips for vessels and cystic duct closure is widely practiced and accepted by surgeons due to its efficiency and reduced postoperative complications [6]. Titanium ligating clips are utilized in over 80% of laparoscopic cholecystectomies to close the cystic duct and artery, making it the most employed technique [4]. Titanium ligating clips are commonly

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employed due to their reliability, strength, and biocompatibility. These clips are small, non-reactive devices that provide hemostasis by mechanically constricting blood vessels and ducts, preventing bleeding and bile leakage [10,11].

Among the various ligating clips available, Ligaclip® titanium ligating clips are widely used. Due to widespread acceptance of ligating clips as an effective therapy choice for laparoscopic cholecystectomy procedure [6] the need for development of similar /alternative clips with comparable parameters were realized. Trutie® titanium ligating clips demonstrated potential equivalence in clinical outcomes and safety.

Despite their potential benefits, comprehensive clinical evaluations comparing Trutie® ligating clips to the established Ligaclip® in terms of safety, efficacy, and patient outcomes are limited. This study aims to fill this gap by rigorously assessing the clinical equivalence of Trutie® ligating clips to Ligaclip® ligating clips in the context of laparoscopic cholecystectomy. Through a prospective, single-blind, randomized, multicenter design, this research seeks to provide robust evidence on whether Trutie® can match the clinical efficacy and safety of Ligaclip®. The findings of this study could have significant implications for clinical practice, offering surgeons a reliable ligating clip option that maintains high standards of patient outcomes.

Objectives

The primary objective was to assess the efficacy of Trutie® ligating clips compared to Ligaclip® ligating clips in laparoscopic cholecystectomy. Secondary objectives included evaluating the safety of the ligating clips in both groups, the duration of surgery, the number of clips used, and the intraoperative handling of the clips and clip applicators, as well as any issues encountered during clip application. Additionally, the study aimed to assess the length of hospital stay, the residual risks of the ligating clips, the time to recovery, and the quality of life in both groups.

Methods

Trial Design

This prospective, single-blind, randomized (1:1), multi-center study was conducted from May 23, 2023, to April 4, 2024.

Participants

The study included male or female subjects aged between 18 to 60 years who were scheduled for elective laparoscopic cholecystectomy surgery and agreed to provide written informed consent and while adhering to all study protocols.

Subjects with history of pancreatitis, those suspected of having gallbladder carcinoma or other metastatic diseases, and those who were pregnant or lactating at the time of surgery, with coagulation disorder, intraoperatively found to have modified Nassar difficulty grading scale 3, 4 & 5 and whose surgical approach was converted from laparoscopic to open surgery were excluded from the study.

Study settings

This study took place at the department of general surgery of four distinct centres throughout India: 1) GSVM Medical College, Kanpur 2) IPGME and R and SSKM Hospital, Kolkata 3) Seven Star Hospital, Nagpur 4) BGS Global Institute of Medical Sciences, Bengaluru.

Ethical Approval and Compliance

Clinical Trials Registry of India (CTRI) registration was done on May 11, 2023, under the registration number CTRI/2023/05/052531. Approval was secured from the Institutional Ethics Committees of all participating sites, including:

1. GSVM Medical College, Kanpur, India [Approval number- EC/136/May/2023 Date- 10/May/2023]
2. IPGME and R Research Oversight Committee, Kolkata, India [Approval number- IPGME&R/IEC/2023/501 Date- 12/Jun/2023]
3. Rahate Surgical Hospital, Nagpur, India [Approval number- NA Date- 06/May/2023]
4. BGS Global Institute of Medical Sciences, Bangalore, India [Approval number- BGS GIMS IEC/APP/APR/01 Date- 21/Apr/2023]

Intervention

Trutie® Titanium Ligating clips (Healthium Medtech Limited, Bangalore, Karnataka, India) and Ligaclip® Titanium Ligating clips (Ethicon-Johnson & Johnson, Mumbai, Maharashtra, India) are sterile, single patient use clips produced from titanium, indicated in surgical procedures that requires ligation of tubular structures or vessels with metal clips.

Outcomes

Primary Endpoint

The primary endpoint of the study was to evaluate the incidence of bile leakage and bleeding following closure of cystic duct and cystic artery in both groups. Subjects presenting with post-operative symptoms suggestive of bile leakage or bleeding (fever, increasing upper abdominal pain, vomiting, jaundice, and/or bile leakage through the drain) were planned to be assessed clinically and subjected to additional blood and radiological testing basis investigator discretion to confirm the bile leakage and bleeding. This was recorded on the day of surgery, the day of discharge, and all the postoperative visits until day 180 post-surgery.

Secondary Endpoints

Secondary endpoints of the study were: Assessment of intra- and post-operative complications, adverse device reactions, and adverse events from day of surgery to 6 months post-operatively, Time taken from initial incision to closure of wound (day of surgery), Number of clips used to ligate cystic duct and artery (day of surgery), Assessment of intraoperative handling of clips in terms of Cartridge ergonomics, Clip applier compatibility, Ease of clip loading, Force required to fire the device, Occlusion provided by the formed clip, Overall ease of use of ligating clip and Overall ease of use of ligating clip applicator between the two groups using 5-point scale (5: Excellent, 4: very good, 3: good, 2: fair, 1: poor), Assessment of number of clip breakage, failure to ligate, and malformed/deformed clips (day of surgery), Postoperative length of hospital stay in both the groups (day of discharge), To assess the incidence of residual risks of ligating clips (infection, inflammatory reaction, injury during the procedure, foreign body reaction, and allergy) (day of surgery, day of discharge, all the post-discharge visits till day 180 post-surgery), To assess the time to recovery as measured by return to the normal day to day activities (all discharge visits until day 180 post-surgery), To evaluate the quality of life using the Otago gallstones condition specific questionnaire (baseline visit, day 30 post-surgery, day 180 post-surgery).

Otago Gallstones Condition-Specific Questionnaire: The Otago Gallstones Condition-Specific Questionnaire is designed to evaluate the quality of life in individuals suffering from gallstone disease. It includes a series of questions that focus on key areas affected by the condition, such as physical functioning (pain, dyspepsia and diet

changes), systemic functioning (fatigue), social functioning (daily duties, leisure, relationships) and emotional functioning (mood). The questionnaire contains 12 items, each with a 5-point Likert response scale. Subjects rate their experiences and symptoms on a Likert scale, providing quantifiable data. The total score is derived by summing up the responses, where higher scores indicate more significant impairment or more severe symptoms [12].

Sample Size

Laparoscopic cholecystectomy stands as the most performed gastrointestinal surgery. Despite identification of risk factors for challenging surgeries and post-operative complications, these complications still affect up to 10% of patients [13]. Considering 10% of post-operative complications with equivalence margin of 20%, level of significance as 5%, and power as 90%, total sample size is estimated to be 98. Considering 25% dropout the sample size comes up to 132. Sample size was calculated as follows (using R software version 4.2.2):

$$n = \frac{(z_\alpha + z_{\beta/2})^2}{(\delta - |\epsilon|)^2}\left[\frac{p_1(1-p_1)}{\kappa} + p_2(1-p_2)\right]$$

Where p1 and p2 are the percentages in the test and the comparator arms respectively

Zα and Zβ are scores for α=0.05 and β=0.1 respectively
k= randomization ratio between the two arms
δ= equivalence margin and
ε= true difference between the two arms

Randomization and Blinding

Eligible subjects were randomized in a 1:1 ratio using block randomization with a block size of 4 using cloud-based software PageOne version 1.0. Participants remained unaware of their assigned group. Post-operative assessments were conducted at each center by healthcare providers not involved in the study, ensuring they remained blind to the type of clips used. While the operating team could not be blinded due to the nature of the procedure, they were instructed not to reveal the allocation status of any participant.

Statistical Methods

Baseline and demographic continuous variables (e.g., age, height) will be summarized using the number of observations, mean, and standard deviation (SD) and P-value will be based on two sample t test. Categorical variables (e.g., gender, smoking status) will be summarized using counts and percentages for each category and P-value will be based on chi-square test. Time taken from initial incision to closure of wound, post-operative length of hospital stays and return to the normal day to day activities will be summarized descriptively for both the groups, P-value will be based on log-rank test. Number of clips used to ligate artery, and cystic duct will be summarized for both the groups and P-value will be based on two-sample t test. Intraoperative handling of clips between the two groups using 5-point scale will be summarized by group and P-value will be based on chi-square test. The quality of life using the Otago gallstones condition specific questionnaire will be summarized descriptively by visit and by group and P-value will be based on two-sample t test. All adverse events were summarized using counts and percentages for each treatment group based on frequency and percentages. All statistical analyses were conducted using the SAS (Statistical Analysis System) version 9.4. For hypothesis test, two-tailed P-values < 0.05 will be considered statistically significant.

Study procedure

Subjects were planned to be screened, recruited, and randomized over 3 months period. Subjects were admitted before the surgery and followed for up to 6 months after the surgery.

The surgical procedure routinely involved the use of titanium ligating clips for ligation of the cystic duct and artery. After dissecting the cystic duct from the gallbladder, titanium ligating clips were applied to securely seal it, preventing bile leakage [4]. Similarly, the cystic artery, responsible for blood supply to the gallbladder, was identified and ligated with titanium ligating clips to ensure hemostasis and facilitate safe gallbladder removal [1]. This method not only allowed for precise closure without sutures but also minimized tissue trauma and reduced operative time. The incisions were closed using sutures, and Theruptor NXT (Healthium Medtech Limited) sterile wound dressings were applied on the surgical wounds.

Study assessments included six visits: Pre-Surgery or Screening visits: Baseline visit (Visit 1) and Day of surgery (Visit 2). Post-Surgery Visits: Day of discharge (Visit 3), Day 10 post-surgery (Visit 4), Day 30 post surgery (Visit 5) and Day 180 post surgery (Visit 6).

Demographic and Other Pertinent Characteristics

Baseline demographics like age, gender, height, weight, body mass index, smoking and alcohol history and activity level were evaluated. [The activity level of the participants was assessed by considering less than 1 hour of physical activity per day as sedentary, 1 to 2 hours per day as moderate and more than 2 hours per day as high].

Results

132 subjects of both genders aged 18 years to 60 years who were scheduled for laparoscopic cholecystectomy surgery were randomized. Out of 132 subjects randomized, 126 subjects were included in this study and completed their 6-month follow-up visit. 6 subjects were excluded after randomization due to appearance of exclusion criteria (2 subjects due to surgical approach conversion from laparoscopic to open surgery; 2 subjects didn't receive clearance for surgery, 1 subject intraoperatively found to have Nassar difficulty grading scale 4, and 1 subject due to presence of a wide and short Cystic duct) [**Figure 1**].

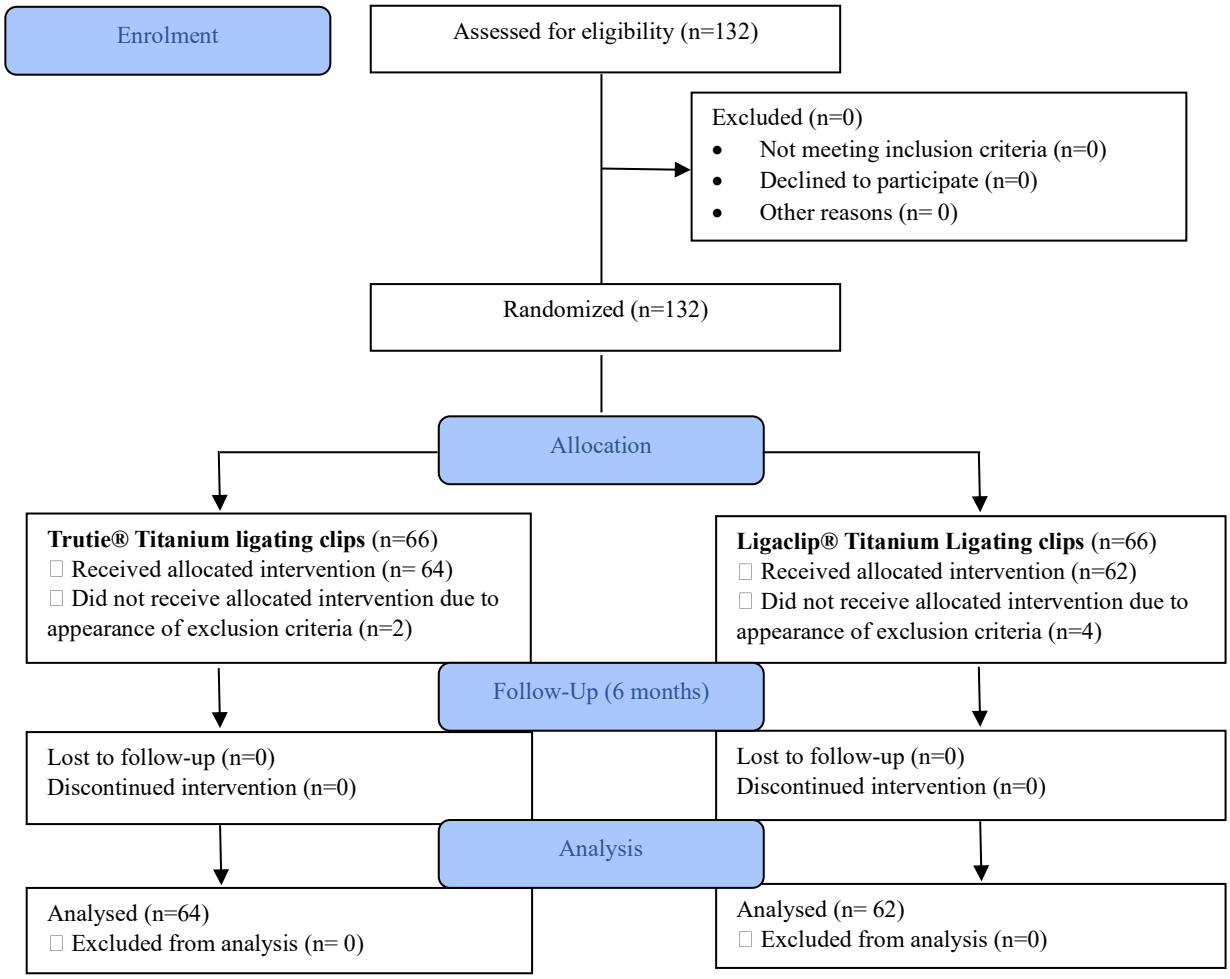


Figure 1: CONSORT flow chart of study design

Demographics and Baseline Characteristics

Table 1 compares the demographic and baseline characteristics between participants using Trutie® and Ligaclip® ligating clips. There were no significant differences between the two groups regarding age, gender distribution, height, weight, body mass index (BMI), smoking status, alcohol consumption, and activity levels. This suggests that the two groups were well-matched in terms of baseline characteristics, with P values indicating no statistically significant differences (P > 0.05).

Table 1: Demographics and Baseline Characteristics

Patient Characteristics	Trutie® Ligating clips (N=64)	Ligaclip® ligating clips (N=62)	P value
Age (years)			
[Mean ± SD]	40.20±10.24	39.23±11.87	*0.6213
Gender n (%)			
Male	22 (34.4%)	17 (27.4%)	#0.3984
Female	42 (65.6%)	45 (72.6%)	
Height (cms)			
[Mean ± SD]	162.5± 6.04	162.4± 8.03	*0.9293
Weight (Kgs)			
[Mean ± SD]	62.26± 9.04	62.48± 8.14	*0.8839
Body Mass Index (kg/m2)			
[Mean ± SD]	23.64± 3.33	23.71± 2.73	*0.8979
Smoking Status n (%)			
Smoker	9 (14.1%)	7 (11.3%)	#0.6403
Non-Smoker	55 (85.9%)	55 (88.7%)	
Alcohol consumption n (%)			
Non-Alcoholic	56 (87.5%)	56 (90.3%)	#0.614
Alcoholic	8 (12.5%)	6 (9.7%)	
Activity Level n (%)			
Sedentary	7 (10.9%)	5 (8.1%)	#0.8599
Moderate	51 (79.7%)	51 (82.3%)	

High	6 (9.4%)	6 (9.7%)	
SD: Standard deviation, %: Percentage, *P-value based on two sample t test for continuous variables, # P-value based on chi-square test for categorical variables			

Primary endpoint analysis

Incidence of Bile Leakage and Bleeding after Closure of Cystic Duct and Cystic Artery

There was no incidence of bile leakage and bleeding after closure of cystic duct and cystic artery in the study.

Secondary endpoints analysis

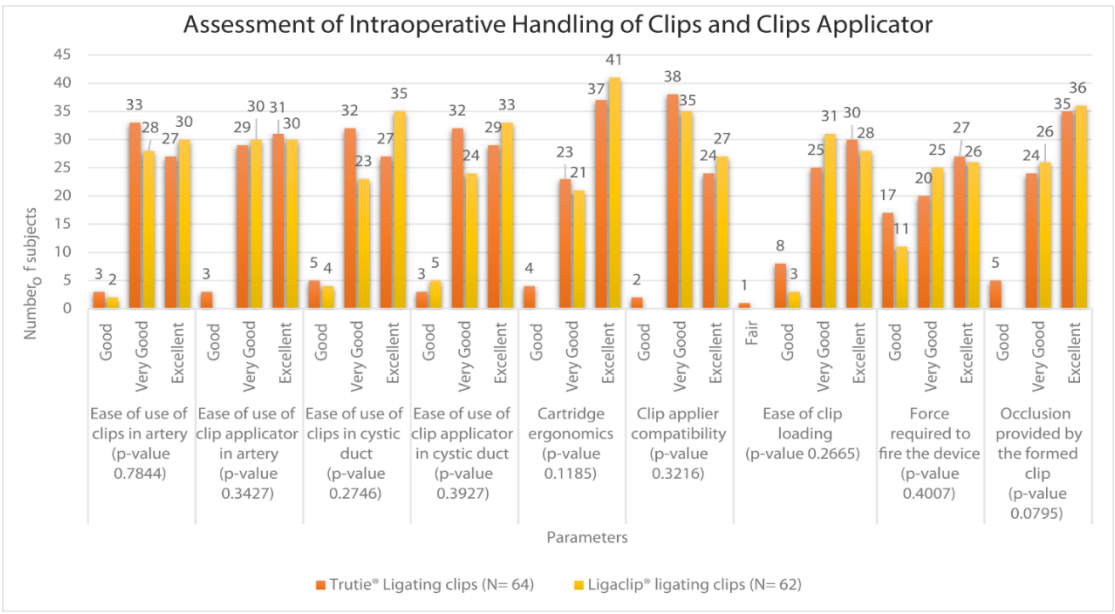
i) Intraoperative Characteristics

Table 2 presents the intraoperative characteristics of participants in the study. The mean time taken from the initial incision to wound closure was similar between the Trutie® ligating clips group (52.5 ± 20.6 minutes) and the Ligaclip® ligating clips group (51.3 ± 22.8 minutes), with no significant difference (P = 0.6933). The average number of clips used to ligate the artery was slightly higher in the Trutie® group (2.4 ± 0.6) compared to the Ligaclip® group (2.2 ± 0.6), but this difference was not statistically significant (P = 0.0757). Similarly, the number of clips used to ligate the cystic duct was comparable between the Trutie® group (2.3 ± 0.8) and the Ligaclip® group (2.2 ± 0.8), with no significant difference (P = 0.5915). These results suggest that both types of clips perform similarly in terms of intraoperative efficiency and resource use.

The study suggests that Trutie® and Ligaclip® ligating clips exhibit comparable performance. Figure 2 provides a detailed comparison across various parameters, highlighting user satisfaction percentages and p-values. Both clips generally perform similarly across most criteria, with slight statistically non-significant variations. For instance, 27 (42.2%) of users rated the force required to fire Trutie® clips as "Excellent," compared to 26 (41.9%) for Ligaclip® clips (p = 0.4007), and 30 (46.9%) rated the ease of clip loading for Trutie® clips as "Excellent," compared to 28 (45.2%) for Ligaclip® clips (p = 0.2665). Parameters such as ease of clip usage in artery, ease of clip usage in the cystic duct, ease of clip applicator usage in the cystic duct, cartridge ergonomics, and clip applier compatibility received better "Very Good" ratings for Trutie® clips, whereas ease of clip applicator usage in the artery and occlusion provided by the formed clip received better ratings for Ligaclip® clips. Overall, the comparison indicates that both types of clips are well-received, with no significant statistical differences in user satisfaction across the assessed parameters.

Table 2: Intraoperative Characteristics of Participants

Characteristics	Trutie® Ligating clips (N=64)	Ligaclip® ligating clips (N=62)	P value
Time (Min) Taken from Initial Incision to Closure of Wound [Mean ± SD]	52.5 ± 20.6	51.3 ± 22.8	*0.6933
Number of clips used to ligate artery [Mean ± SD]	2.4 ± 0.6	2.2 ± 0.6	#0.0757
Number of clips used to ligate cystic duct [Mean ± SD]	2.3 ± 0.8	2.2 ± 0.8	#0.5915
SD: Standard deviation, Min: Minutes, *: P-value based on log-rank test, # P-value is based on two-sample t test			



P-value based on chi-square test

Figure 2: Assessment of Intraoperative Handling of Clips and Clips applicator

ii) Postoperative outcomes

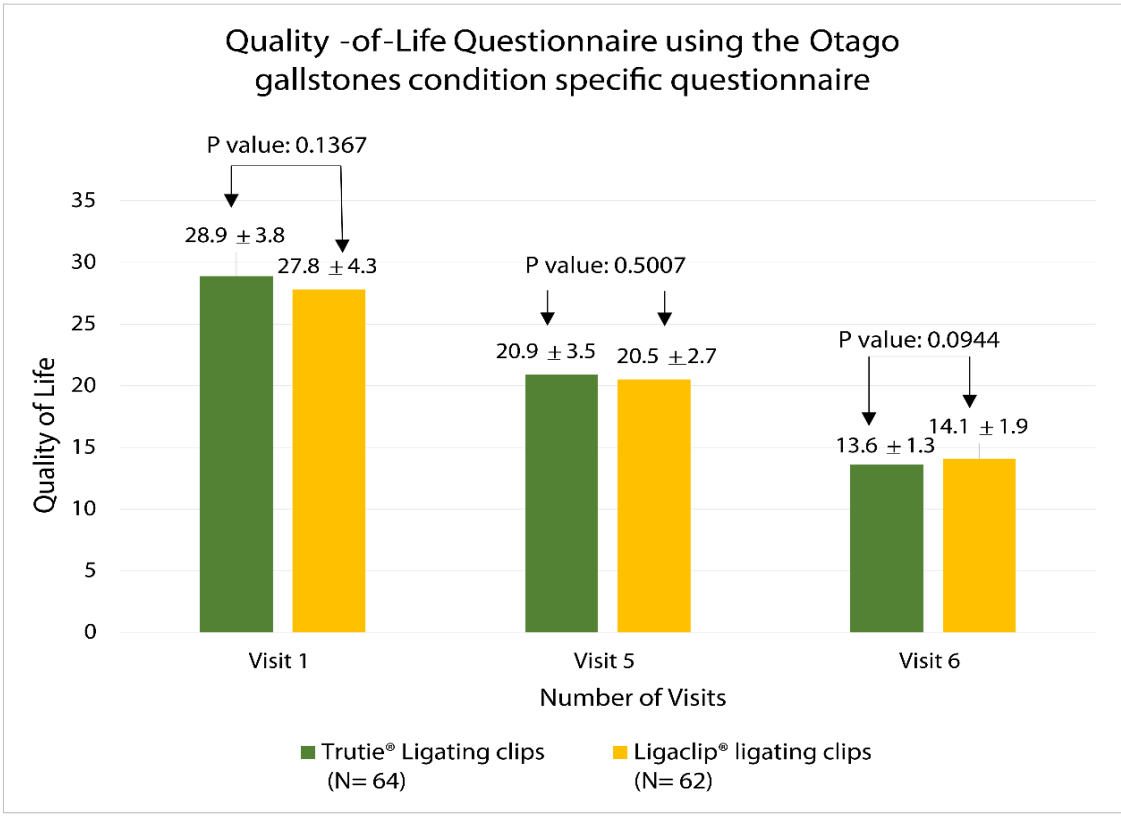
The postoperative outcomes for participants using Trutie® and Ligaclip® ligating clips are summarized in Table 3. The mean postoperative length of hospital stay was similar between the Trutie® group (2.5 ± 0.9 days) and the Ligaclip® group (2.4 ± 0.8 days), with no statistically significant difference (P = 0.4629). Additionally, the meantime taken for participants to return to their normal day-to-day activities was 7.4 ± 2.2 days for the Trutie® group and 7.2 ± 2.3 days for the Ligaclip® group, also showed no significant difference (P = 0.7620). There was no clip breakage, failure to ligate, malformed/deformed clips and incidence of residual risks of ligating clips (infection, inflammatory reaction, injury during the procedure, foreign body reaction, and allergy) (day of surgery, day of discharge, all the post-discharge visits till day 180 post-surgery). These results indicate that both types of ligating clips result in comparable postoperative recovery times.

Table 3: Postoperative outcomes

Characteristics	Trutie® Ligating clips (N=64)	Ligaclip® ligating clips (N=62)	*P value
Postoperative length of hospital stays (days) [Mean ± SD]	2.5 ± 0.9	2.4 ± 0.8	0.4629
Return to the normal day-to-day activities (days) [Mean ± SD]	7.4 ± 2.2	7.2 ± 2.3	0.7620
SD: Standard deviation, *: P-value based on log-rank test			

iii) Assessment of Quality of Life

The figure 3 illustrates the quality-of-life scores for subjects using Trutie® and Ligaclip® ligating clips, as measured by the Otago Gallstones Condition-Specific Questionnaire, across three visits: Baseline (Visit 1), 30 days post-surgery (Visit 5), and 180 days post-surgery (Visit 6). At baseline, the mean QoL scores were 28.9 ± 3.8 for Trutie® and 27.8 ± 4.3 for Ligaclip®, with a non-significant P value of 0.1367. By Visit 5, the scores decreased to 20.9 ± 3.5 and 20.5 ± 2.7, respectively, with a P value of 0.5007, indicating no significant difference. At Visit 6, the QoL scores further improved to 13.6 ± 1.3 for Trutie® and 14.1 ± 1.9 for Ligaclip®, with a P value of 0.0944. Overall, both groups showed significant improvement in QoL over time, with no statistically significant differences between the two groups at any visit, indicating an increase in perceived quality of life, as lower scores represent improved quality of life according to the Otago Gallstones Condition-Specific Questionnaire. This suggests that both types of ligating clips have a comparable impact on patients' quality of life over the course of the study.



P-value is based on two-sample t test

Figure 3: Quality-of-Life Questionnaire using the Otago gallstones condition specific questionnaire

iv) Adverse events

Adverse events and serious adverse events

A total of 6 adverse events reported in the study, 3 (4.7%) in Trutie Ligating clip group [fever (1), serous discharge at port site (1) and cough (1)] and 3 (4.8%) in Ligaclip ligating clip group which were [fever (2), sore throat (1)] These adverse events were not related to the ligating clips. There were no serious adverse events and unexpected serious adverse device effects in both the groups.

Discussion

This prospective, single-blind, randomized, multicenter study assessed the clinical equivalence of Trutie® ligating clips compared to Ligaclip® ligating clips in laparoscopic cholecystectomy. The study findings offer valuable insights into the safety, efficacy, and patient outcomes associated with these two types of ligating clips.

Primary and Secondary Outcomes

The primary outcome of this study focused on the incidence of bile leakage and bleeding post-surgery. Our results demonstrated that both Trutie® and Ligaclip® ligating clips were effective in achieving secure occlusion of the cystic duct and artery, with no incidence of these complications in both the groups. A study by Singal R et al., involving 70 patients in whom the cystic duct and artery were ligated using Ligaclips, reported no bile leakage [14]. This corroborates our finding, suggesting that Trutie® clips are clinically equivalent to Ligaclip® clips in terms of safety and efficacy in preventing bile leakage and bleeding. These results indicate that the use of rigorous surgical techniques played a vital role in the procedures. The meticulous closure of the cystic duct and artery helped ensure a secure outcome. The surgeons' expertise, combined with careful preoperative and postoperative care, further minimized

risks. These factors collectively ensured a favorable outcome and the absence of bile leakage and bleeding in the study group.

Secondary outcomes, including intraoperative and postoperative parameters, further support the equivalence of Trutie® and Ligaclip® clips. Intraoperatively, both types of clips performed similarly regarding the time taken from the initial incision to wound closure. Our study reported an average time of 52.5 ± 20.6 minutes in Trutie® group and 51.3 + 22.8 minutes in Ligaclip® group, comparable to times reported in other studies: Teja HV et al. (61.83 ± 10.55 minutes), Naikoo GM et al. (41.2 minutes), and Emmi SM et al. (56.50 ± 12.9 minutes) [15-17]. Postoperative outcomes, such as the length of hospital stay 2.5 ± 0.9 days in Trutie® group and 2.4 + 0.8 in Ligaclip® group, align with findings by Emmi SM et al., who reported an average stay of 2.93 ± 0.75 days [16]. Additionally, the time to return to normal activities showed no significant differences between the two groups. These results indicate that Trutie® clips can be used interchangeably with Ligaclip® clips without compromising the efficiency of the surgical procedure or extending the patient's recovery period.

Quality of Life

The quality-of-life assessment using the Otago Gallstones Condition-Specific Questionnaire revealed a similar trend of improvement over time for both Trutie® and Ligaclip® groups. At six months post-surgery, QoL scores converged, suggesting that both clip types positively impacted long-term patient well-being. These results are consistent with prior studies showing improved QoL post-laparoscopic cholecystectomy, affirming that Trutie® clips impact on patient's quality of life. In our study, the Trutie® groups, overall QoL scores were 28.9 ± 3.8 at Visit 1 (Screening), 20.9 ± 3.5 at Visit 5 (Day 30), and 13.6 ± 1.3 at Visit 6 (Day 180) and Ligaclip® groups, overall QoL scores were 27.8 + 4.3 at Visit 1 (Screening), 20.5 + 2.7 at Visit 5 (Day 30), and 14.1 + 1.9 at Visit 6 (Day 180). These findings are similar with the study by Daliya P et al., which reported overall QoL scores of 75.4 (23.3) preoperatively, 19.3 (26.0) at 30 days, and 16.4 (29.2) at 6 months [18].

Handling and User Satisfaction

Intraoperative handling and user satisfaction scores provided additional insights into the usability of the ligating clips. While there were minor differences in user ratings for various handling parameters, these differences were not statistically significant. Both Trutie® and Ligaclip® clips received high ratings for overall ease of use, clip applier compatibility, ease of clip loading, and the force required to fire the device. The statistically non-significant variations in scores did not translate into practical differences in the surgical outcome or user experience, reinforcing the practical equivalence of the two products.

Limitations

The limitations of the present study includes a single-blind design which may introduce bias, as the operating staff was aware of the allocation status, which could potentially influence their intraoperative handling and subjective assessments of the clips, and the follow-up period of six months, although adequate for assessing immediate postoperative outcomes and recovery, may not be long enough to detect late-onset complications or differences in long-term outcomes such as clip migration or chronic inflammation.

Generalisability of the trial findings

The results of this study are based on a sample of 126 male or female subjects aged 18 to 60 years scheduled for elective laparoscopic cholecystectomy across 4 different locations in India, which is a broad population in terms of age, sex and geographical location. The findings contribute valuable insights into usage of titanium ligating clips in laparoscopic cholecystectomy. Considering the statistically calculated sample size, broader population in a multicentre setting, and equivalence established to a current standard of care titanium ligating clips of Ethicon, the study findings can be generalized to a broader population of different ages and ethnic backgrounds.

Conclusion

In conclusion, Trutie® ligating clips are clinically equivalent to Ligaclip® ligating clips in terms of safety, efficacy, and patient outcomes in laparoscopic cholecystectomy. Both types of clips demonstrated similar performance in preventing bile leakage and bleeding, comparable intraoperative handling, and postoperative recovery times, as well as equivalent impact on patients' quality of life.

Declarations

Registration Number

This trial is registered prospectively at Clinical Trial Registry of India (CTRI Reg. No: CTRI/2023/05/052531; Registered on: 11/05/2023).

Ethical Approval

Approval was secured from the Institutional Ethics Committees of all participating sites, including: (1) GSVM Medical College, Kanpur, India [Approval number- EC/136/May/2023 Date- 10/May/2023] (2) IPGME and R Research Oversight Committee, Kolkata, India [Approval number- IPGME&R/IEC/2023/501 Date- 12/Jun/2023] (3) Rahate Surgical Hospital, Nagpur, India [Approval number- NA Date- 06/May/2023] (4) BGS Global Institute of Medical Sciences, Bangalore, India [Approval number- BGS GIMS IEC/APP/APR/01 Date- 21/Apr/2023]

All procedures performed in this study involving human subjects were in accordance with the ethical standards of the institutional ethics committee and principles of the declaration of Helsinki. This article does not contain any study with animals performed by any of the authors.

Data Availability

The data generated and analyzed during the study are available from the corresponding author upon request to qualified researchers, subject to appropriate ethical and legal considerations.

Funding

The study was funded by Healthium Medtech Limited, Bangalore, India. The funders role in addition to provide funding to the study was involvement towards conceptualization of the study design, literature search, finalization of the objectives and endpoints, manuscript writing and review. The funder didn't have an influence on the interpretation of the data.

Authors' Contributions

Concept: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS
Design: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS
Definition of intellectual content: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS

Literature search: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS
Clinical studies: SK, SA, PVR, SK, RKJ, AS, AKG, NM
Experimental studies: SK, SA, PVR, SK, RKJ, AS, AKG, NM
Data acquisition: SK, SA, PVR, SK, RKJ, AS, AKG, NM
Data analysis: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS
Statistical analysis: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS
Manuscript preparation: SK, SA, PVR, SK, RKJ, AS, AKG, NM, AKM, DTS
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Statement

The manuscript has been read and approved by all the authors, and the requirements for authorship have been met. Each author believes that the manuscript represents honest work.

Informed Consent

Informed consent was obtained from all subjects before their participation in the study.

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Conflicts of Interest/ Competing Interests

AKM and DTS work for Healthium Medtech Limited, which manufactures Trutie® Ligating clips. Authors SK, SA, PVR, SK, RKJ, AS, AKG and NM report no conflicts of interest in this work.

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