

Ejection fraction of normal gall bladder by ultrasonography in patients with biliary colic: Is it a parameter for cholecystectomy?

Original Article

Abdallah B. Abdallah, Samir A. Ammar, Mohamed G. Ameen and Ahmed Yaseen

Department of General Surgery, Faculty of Medicine, Assiut University Hospitals, Assiut, Egypt.

ABSTRACT

Background: Functional biliary disorders such as gallbladder dyskinesia (GBD), biliary hyperkinesia, and sphincter of Oddi dysfunction are common causes of abdominal pain. Although hepatobiliary scintigraphy is the gold standard for diagnosing sphincter of Oddi dysfunction, there is still debate about the best way to establish diagnoses of GBD and whether gallbladder ejection fraction (GBEF) is a reliable predictor of treatment outcomes.

Aim: The purpose of this study is to evaluate GBEF as a predictor of GBD and an indicator of cholecystectomy.

Patients and Methods: This is a prospective study conducted between July 2021 and December 2023 on patients presented with biliary dyskinesia. All patients with an ejection fraction of less than 35% underwent laparoscopic cholecystectomy. The preoperative workup involved clinical assessment, laboratory tests, fasting and postprandial ultrasounds, and hepatobiliary scintigraphy to determine ejection fraction. Postoperative follow-up at 1, 3, and 6 months assessed pain relief, symptom improvement, and patient satisfaction.

Results: Eight patients were excluded due to a GBEF greater than 35%. The remaining 21 patients with an ejection fraction of less than 35% underwent laparoscopic cholecystectomy. The mean age was 31 ± 12 years, and the majority of patients (86%) were females. The preoperative visual analog scale pain score was 7.2 ± 1.4 , decreasing significantly to 1.2 ± 0.8 at 1-month follow-up ($P < 0.001$). The pain was fully resolved in all patients by 3 months. Medication usage, daily activity levels, and patient satisfaction also significantly improved. The mean ejection fraction was $27.1 \pm 3.3\%$. No postoperative complications occurred.

Conclusion: In patients with GBD, laparoscopic cholecystectomy provided excellent symptomatic relief when GBEF was less than 35%. The ejection fraction appears to be a useful diagnostic predictor of positive surgical outcomes in such functional biliary pain presentations. Larger, controlled clinical trials are needed to generalize the findings.

Key Words: Cholecystectomy, functional biliary colic, gallbladder dyskinesia, gallbladder ejection fraction.

Received: 14 July 2024, **Accepted:** 28 July 2024, **Published:** 4 October 2024

Corresponding Author: Ahmed Yaseen, MBCh, Department of General Surgery, Faculty of Medicine, Assiut University Hospitals, Assiut, Egypt. **Tel.:** 01151150507, **E-mail:** ahmedyaseenae1995@gmail.com

ISSN: 1110-1121, October 2024, Vol. 43, No. 4: 1597-1602, © The Egyptian Journal of Surgery

INTRODUCTION

Biliary dyskinesia (BD), according to Rome IV criteria, is a condition of some element of the digestive system's biliary portion in which bile cannot physically flow down the tubular biliary tract in the correct direction, resulting in biliary colic^[1,2].

Gallbladder dyskinesia (GBD), gallbladder hyperkinesia, and sphincter of Oddi dysfunction (SOD) are the functional reasons for BD^[2].

The exact pathology of functional biliary colic is still unknown. Although the current gold standard for the diagnosis of SOD is the sphincter of Oddi manometry, there is some debate about the best method to establish the diagnosis of GBD and whether or not ejection fraction is an accurate predictor of outcome^[3,4].

While the true pathogenesis often remains enigmatic without an identifiable gallbladder stone (GS), evaluating GB contractility holds significance. Impaired emptying demonstrated on GBEF assessment helps implicate dyskinesia as a potential etiology, aiding clinical decision-making regarding long-term management including the threshold for elective cholecystectomy^[5,6].

The flow of radioactive tracer expelled from the GB following a high-fat meal is used to determine GBEF. A GBEF of less than 35% is qualified as abnormal. Patients who present with functional biliary pain according to the Rome IV criteria are considered for a hepatobiliary iminodiacetic acid (HIDA) scan^[1,2,7].

This study aims to evaluate GBEF as a predictor of GBD and an indicator for cholecystectomy in patients presenting with chronic biliary colic but normal GB anatomy on ultrasound (US).

PATIENTS AND METHODS:***Study design and setting***

This is a prospective study conducted at the Department of General Surgery, Assiut University Hospital, a tertiary care referral center in Egypt, between July 2021 and December 2023. The study was done on patients complaining of biliary colic or pain with normal GB in the US. The study protocol was approved by the Institutional Ethics Committee, and each participant provided signed informed consent.

Patient selection***Inclusion criteria***

- (a) Patients who meet the Rome IV criteria for GBD^[1,2,8].
- (b) Patients who are older than 18 years.
- (c) Normal GB US.

Exclusion criteria

(a) Patients with chronic abdominal pain from a secondary diagnosis (such as Crohn's disease, peptic ulcer disease, or pain responsive to antacid/anti-secretory therapy).

(b) Patients with positive US GB findings, which can be defined as having polyps, sludge, pericholecystic fluid, GB wall thickening (>4 mm), or GS.

- (c) Patients with a history of acute cholecystitis
- (d) Patients with jaundice or elevated liver enzymes.
- (e) Patients with previous biliary surgery.
- (f) Pregnancy and systemic diseases preclude surgery.
- (g) GB was completely evacuated by the US after a fatty meal.

Ethical considerations

A written informed consent will be obtained from each patient after informing him or her about the steps of the procedure and the expected effects or possible complications.

The study protocol was approved by the Institution Review Board (IRB) at Assiut University Hospital.

Data collection

The study enrollment was carried out over 2 years between July 2021 and June 2023, followed by 6 months of follow-up for the last patients.

All patients were subjected to a complete history taking.

Medical history: including asking about a history of acute cholecystitis, jaundice, and other conditions he had been treated for, and all medications or supplements he had taken.

A physical and general examination was performed on every participant. Physical examination: to check for signs of acute cholecystitis, jaundice, and the overall health of the patient. Pain severity was assessed using a visual analogue scale (VAS).

Investigation

(a) Imaging: Abdominal US was performed by an experienced radiologist after fasting for 6 h. Only patients found to have normal GB without GS in the US were included in the study. Fasting and postprandial US were done on all included patients to measure GB size.

(b) Laboratory preoperative routine investigations are crucial components of the preanesthetic assessment that establish a patient's suitability for anesthesia and surgery, particularly liver function tests.

(c) Gallbladder Ejection Fraction Measurement

All study participants underwent a HIDA scan (cholescintigraphy), which is a nuclear medicine imaging procedure used to evaluate the function of the GB and bile ducts. The procedure involves intravenous administration of a radioactive tracer agent known as technetium-99m (99mTc) iminodiacetic acid (IDA), which is taken up by the liver and secreted into the bile. Scintigraphic images are then obtained at regular intervals using a specialized gamma camera to visualize the movement of radioactive tracer through the hepatobiliary system^[9].

Initially, static images of the abdomen are obtained immediately and 15–30 min after injection to visualize hepatic uptake and biliary excretion of the radiotracer respectively. This is followed by dynamic imaging at 1 frame/min for 30 min to assess the GB filling phase. Additional delayed static and/or dynamic images are acquired typically 1–2 h after a fatty meal to evaluate the GB emptying phase^[10].

Fasting GB volume was measured just before administration of a standard liquid formula meal (Ensure, 250 ml; providing 250 kcal, 12 g fat)^[11]. Postprandial volume was recorded 30 min after meal completion for 90 min^[12].

Surgical intervention

All patients underwent laparoscopic cholecystectomy as the sole intervention, as long as the GBEF value was less than 35%. The standard four-port technique was used under general anesthesia.

Postoperative care and follow-up

Patients received intravenous fluids and analgesics for 6 h, followed by oral intake as tolerated. Pain resolution, symptom improvement, medication usage, and the ability to perform daily activities were assessed using standardized questionnaires.

Follow-up was scheduled at 1, 3, and 6 months to assess symptom resolution using structured questionnaires administered by study coordinators either through clinic visits or telephone interviews. Persistent pain was defined as recurrent biliary type pain in the prior month in response to fatty meals.

Histopathological examination

Resected GB specimens were formalin-fixed and blindly evaluated by a pathologist for evidence of inflammation, ischemia, or other abnormalities. The findings were correlated with preoperative GBEF and clinical outcome measures.

Outcomes

The primary outcome measure was the persistence of biliary type pain at a 3-month follow-up. The presence of recurrent colicky pain at least once in the 3-month follow-up consistent with the initial symptomatology was considered treatment failure.

Secondary outcomes included medication usage and the need for analgesics for refractory pain at follow-up, daily activity level improvement, and patient satisfaction, which is a subjective scale from 1 to 10 points.

Statistical analysis

The sample size calculation was based on the assumption that GBEF would predict treatment failure rate at 3 months with 80% power and 5% level of significance. Assuming a symptomatic recurrence rate of 20% (15), a minimum of 20 patients was required. SPSS is a statistical software package that was originally developed by SPSS Inc., which was acquired by IBM in 2009. So the current manufacturer and owner of SPSS is IBM, which is headquartered in Armonk, New York, United States.

Descriptive analyses were performed. Preoperative and 1-month postoperative parameters were compared using paired t-test/Wilcoxon signed-rank test. Descriptive statistics included mean, standard deviation, and percentages. Associations between categorical variables were assessed using χ^2 or Fisher's exact test as appropriate. Independent samples t-test was applied to compare continuous variables. Logistic regression analysis determined independent predictors of symptomatic outcomes. *P* less than 0.05 was considered statistically significant.

RESULTS:

Patient characteristics

A total of 29 patients with biliary colic but normal GB in the US were assessed for eligibility from July 2021 to June 2023. Age varied between 18 and 54 years, and 24 of them were females.

Eight patients were excluded based on GBEF greater than or equal to 35% and managed conservatively.

The remaining 21 patients with GBEF less than 35% comprised the study who underwent laparoscopic cholecystectomy and consisted of the participants in this study.

Baseline demographics and clinical characteristics

The mean age was 31±12 years (range 18–54). The majority of patients 18 (85.7%) were females, and three (14.3%) were males. The average symptom duration before enrollment was 8.2±4.3 months (range 3–24 months).

Abdominal US findings

All patients demonstrated normal GB morphology and caliber bile ducts in the US with no evidence of GS, sludge, masses, or structural abnormalities.

All included patients showed a partial decrease in size and volume of GB after fatty meals compared with fasting for 6 h US. Fasting GB diameter averaged 8±1.2 * 3.4±0.5 cm, while postprandial diameter was 7.1±0.9 * 1.2±0.3 cm.

Gallbladder ejection fraction

The mean GBEF was 27.1±3.3% (range 18.9–31.5%). GBEF result in one of the patients is illustrated in (Fig. 1).

Surgical details

Laparoscopic cholecystectomy was successfully completed in all 21 patients with a median operative duration of 46±8 min. Intra-operative findings and operative details are summarized in (Table 1).

Post-operative course

The post-op hospital stay was one day. All patients recovered well without major complications and were discharged in stable condition.

Primary outcome: pain relief

At 1, 3, and 6 months follow-up; pain resolution and improvement in symptoms, medication usage, daily activities, and patient satisfaction were assessed.

The pre-operative mean VAS pain score was 7.2 ± 1.4 , which decreased significantly to 1.2 ± 0.8 ($P < 0.001$) at 1 month (Table 2). Persistent pain was resolved completely by 3 months of follow-up in all patients. Persistent pain was resolved completely in 20 (95.2%) patients by 1 month and the remaining 1 by 3 months. These findings validated symptomatic relief conferred by cholecystectomy in this study.

Secondary outcomes

Medication usage decreased significantly from preoperative 20 (95.2%) patients to one (4.8%) patient at 1 month ($P < 0.001$).

Daily activity levels improved from a mean of 3.8 ± 0.7 to 7.2 ± 0.4 on a scale of 1–10 ($P < 0.001$).

Patient satisfaction with outcome was high (mean 8.8 ± 0.6 on a scale of 1–10).

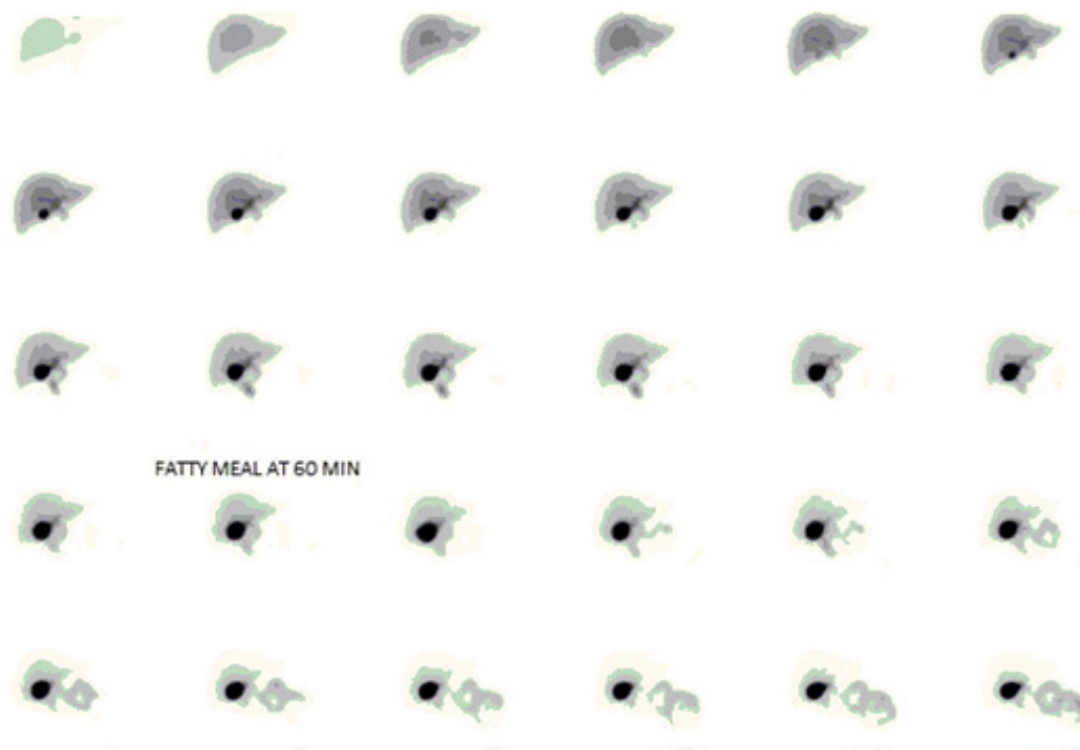


Fig. 1: GBEF in one patient=29%.

Table 1: Intraoperative findings (n=21)

Parameter	Results
Operative time (min)	Mean±SD: 46±8 Range: 30–65
GB appearance, n (%)	
Normal	21 (100)
Edematous	0
Operative findings, n (%)	
No abnormalities	18 (85.7)
Adhesions	3 (14.3)

Table 2: Pain resolution and symptom improvement

Parameter	Preoperative	1-month	P value
VAS score (mean±SD)	7.2 ± 1.4	1.2 ± 0.8	<0.001
Patients with pain No. (%)	21 (100)	1 (4.8)	<0.001
Medication usage No. (%)	21 (100)	1 (4.8)	<0.001
Daily activity levels (mean±SD)	3.2 ± 0.7	7.8 ± 0.4	<0.001

Histopathological findings

Mild nonspecific inflammatory cells were seen in the GB mucosa of one (4.8%) of the three patients who had intraoperative adhesions. The remaining 20 (95.2%) specimens showed no inflammation or abnormalities.

Adverse events

No patients experienced postoperative complications, re-admissions, or mortality during the 6-month follow-up.

DISCUSSION

BD occurs when bile cannot properly drain from the GB or sphincter of Oddi due to functional blockages. While sphincter of Oddi manometry is the gold standard diagnosis for SOD, there is a debate around diagnosing and management of GBD^[13].

Previous research articles have shown that GBEF can be accessed via HIDA scan after a high-fat meal and helps identify patients with impaired GB emptying below 35%, implicating dyskinesia^[14].

Cholescintigraphy also known as HIDA scan, is a nuclear medicine imaging procedure used to evaluate the function of the GB and bile ducts. The procedure involves intravenous administration of a radioactive tracer agent known as technetium-99m (99mTc) IDA, which is taken up by the liver and secreted into the bile. Scintigraphic images are then obtained at regular intervals using a specialized gamma camera to visualize the movement of radioactive tracers through the hepatobiliary system^[15].

This study aims to determine if low GBEF predicts GBD and guides decisions about cholecystectomy for patients with normal anatomy but persistent colicky pain.

A total of 29 patients were enrolled, with an average age of 18–54 years, and 24 of them were females, resembling the demographics of the study. These patients have undergone fasting and postprandial (after a fatty meal) US to measure GB change of diameter and all of them have shown incomplete bile evacuation. After that, all patients had a HIDA scan to determine GBEF. Eight patients were excluded from the study due to normal GBEF and were investigated for alternative causes of abdominal pain.

A total of 21 patients with biliary colic but a normal GB on US and GBEF less than 35% underwent laparoscopic cholecystectomy. Symptom duration averaged 8.2 months within the 6–24 month spectrum.

Female preponderance 18 (86%) patients of patients with BD. This data is aligned with prior studies in the Cochrane review done by Gudsoorkar *et al.*^[12].

Mean operative duration of 66±4 min represents rapid attainment of the critical view of safety, a key determinant of reduced complications. The absence of conversions to open underscores the advantage of laparoscopy for this indication. This is near the average duration of laparoscopic cholecystectomy^[16].

Complete pain resolution by 3 months postcholecystectomy achieved in all 21 patients reproduces prior reports of symptomatic resolution rates exceeding 85%. It implicates GB as likely etiology responsive to definitive extirpation. No early adverse events occurred in any case. This result is consistent with previous research done by Jagannath *et al.*, Yap *et al.*^[17,18].

Significant improvements in daily functioning, quality of life, and medication cessation substantiated true clinical benefit rather than transient placebo effects as seen in rigorous long-term follow-up investigations. Early recovery timelines align with existing literature. A study done by Richmond *et al.*^[19] showed similar results.

Histopathology: Mild inflammation in 1 case does not negate primary neuromuscular pathophysiology since normal mucosa occurs in up to 95.2% of resected specimens in comparable series. The absence of an obvious abnormality reinforces the limitations of histology alone in diagnosing dyskinesia.

Low GBEF independently predicted the need for surgery, and the postoperative course is consistent with its role as a diagnostic parameter. Cholecystectomy has played a significant role in pain relief and quality of life improvement. These results were consistent with previous research done by Jagannath *et al.*, Yap *et al.*, and Richmond *et al.*^[17–19].

CONCLUSION

Patients with biliary colic and normal anatomy by the US must undergo fasting and postprandial (after fatty meal) US to measure GB change of diameter. Patients with incomplete evacuation of bile must undergo a HIDA scan to determine GBEF. If GBEF is less than 35%, the patient should have a cholecystectomy. The patient will require medical attention, and further reasons for abdominal pain will be investigated if the GBEF is greater than 35%.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Aziz I, Palsson OS, Törnblom H, Sperber AD, Whitehead WE, Simren MJOjotACoG, *et al.* The prevalence and impact of overlapping Rome IV-diagnosed functional gastrointestinal disorders on somatization, quality of life, and healthcare utilization: a cross-sectional general population study in three countries. *Am J Gastroenterol* 2018; 113:86–96.
2. Cotton PB, Elta GH, Carter CR, Pasricha PJ, Corazziari ESJG. Gallbladder and sphincter of Oddi disorders. ■ 2016; 150:1420–1429. e2
3. Nasri B, Glass T, Singh K, Saxe JJSE. Biliary hyperkinesia: an indication for cholecystectomy? *Surg Endosc* 2021; 35:3244–3248.
4. Clark CJJSC. An update on biliary dyskinesia. *Surg Clin North AM* 2019; 99:203–214.
5. Szepes A, Bertalan V, Várkonyi T, Pávics L, Lonovics J, Madácsy LJCnm. Diagnosis of gallbladder dyskinesia by quantitative hepatobiliary scintigraphy. *Clin Nucl Med* 2005; 30:302–307.
6. Paaianen H, Miilunpohja S, Joukainen S, Heikkinen JJSLE, Techniques P. Role of quantitative cholescintigraphy for planning laparoscopic cholecystectomy in patients with gallbladder dyskinesia and chronic abdominal pain. *Surg Laparosc Endosc Percutan Tech* 2009; 19:16–19.
7. Geiger TM, Awad ZT, Burgard M, Singh A, Davis W, Thaler K, *et al.* Prognostic indicators of quality of life after cholecystectomy for biliary dyskinesia. *Am Surg* 2008; 74:400–404.
8. Behar J, Corazziari E, Guelrud M, Hogan W, Sherman S, Toouli JGG. Functional gallbladder and sphincter of oddi disorders. *Gastroenterology* 2006; 130:1498–1509.
9. O'Connor OJ, O'Neill S, Maher MMJAJoR. Imaging of biliary tract disease. ■ 2011; 197:W551–W558.
10. Wehrman A, Waisbourd-Zinman O, Wells RG. Recent advances in understanding biliary atresia. *F1000Res.* 2019 Feb 25;8:F1000 Faculty Rev-218.
11. Vyas PK, Vesly TL, Konez O, Ciavellara DP, Hua K, Gaisie GJJoMRIAOJotISfMRiM. Estimation of gallbladder ejection fraction utilizing cholecystokinin-stimulated magnetic resonance cholangiography and comparison with hepatobiliary scintigraphy. *J Magn Reson Imaging* 2002; 15:75–81.
12. Gudsoorkar VS, Oglat A, Jain A, Raza A, Quigley EMJAP, Therapeutics. Systematic review with meta-analysis: cholecystectomy for biliary dyskinesia-what can the gallbladder ejection fraction tell us? *Aliment Pharmacol Ther* 2019; 49:654–663.
13. Treinen C, Lomelin D, Krause C, Goede M, Oleynikov DJLsAoS. Acute acalculous cholecystitis in the critically ill: risk factors and surgical strategies. *Langenbecks Arch Surg* 2015; 400:421–427.
14. Prince J, Hancu DJJotNDoSS. Acute Cholecystitis and the Controversies of Treatment: Case Study. ■ 2020; 1:1.
15. Turner MA, Fulcher AS. 73 - Gallbladder and Biliary Tract: Normal Anatomy and Examination Techniques. In: Gore RM, Levine MS, editors. *Textbook of Gastrointestinal Radiology, 2-Volume Set (Fourth Edition)*. Philadelphia: W.B. Saunders; 2015. 1281–1302.
16. Haji A, Khan A, Haq A, Ribeiro BJTS. Elective laparoscopic cholecystectomy for surgical trainees: predictive factors of operative time. *Surgeon* 2009; 7:207–210.
17. Yap L, Wycherley AG, Morphett AD, Toouli JGG. Acalculous biliary pain: cholecystectomy alleviates symptoms in patients with abnormal cholescintigraphy. *Gastroenterology* 1991; 101:786–793.
18. Jagannath SB, Singh VK, Cruz-Correa M, Canto MIF, Kalloo ANJTAjos. A long-term cohort study of outcome after cholecystectomy for chronic acalculous cholecystitis. ■ *Am J Surg* 2003; 185:91–95.
19. Richmond BK, Grodman C, Walker J, Dean S, Tiley EH, Hamrick RE, *et al.* Pilot randomized controlled trial of laparoscopic cholecystectomy vs active nonoperative therapy for the treatment of biliary dyskinesia. *J Am Coll Surg* 2016; 222:1156–1163.