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Predictors of early readmission in patients awaiting interval cholecystectomy after conservative treatment of acute cholecystitis: A retrospective cohort study

Akut kolesistitte konservatif tedavi sonrası interval kolesistektomi bekleyen hastalarda erken yeniden yatışın prediktörleri: Retrospektif kohort çalışması

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ABSTRACT

Aim: Although interval cholecystectomy is a common strategy in the treatment of acute cholecystitis, a significant proportion of patients are readmitted due to complications during the waiting period. This study aims to identify factors affecting early readmission in patients scheduled for interval cholecystectomy after conservative treatment.

Material and Methods: In this retrospective cohort study, patients hospitalized with acute cholecystitis between January 2023 and December 2024 who received conservative treatment and were scheduled for interval cholecystectomy were evaluated. Patients were classified as Early Presentation Group (EPG) and Normal Presentation Group (NPG) based on whether they were readmitted within six weeks after discharge. Demographic, clinical, and laboratory data were compared; risk factors were evaluated by logistic regression analysis.

Results: A total of 110 patients were included in the study (NPG: 78, EPG: 32). In multivariate analysis, male gender (OR: 5.108; 95% CI: 1.758-14.852; p=0.003) and diabetes mellitus (OR: 8.521; 95% CI: 2.933-24.756; p<0.001) were identified as independent predictors of early readmission. Age, inflammatory markers, and gallbladder stone size showed no significant association.

Conclusion: Male gender and diabetes mellitus are independent risk factors for early readmission in patients awaiting interval cholecystectomy. Early surgical intervention should be considered instead of prolonged conservative treatment in patients with these risk factors.

Keywords: Acute cholecystitis, cholecystectomy, patient readmission, diabetes mellitus, risk factors

ÖZ

Amaç: Akut kolesistit tedavisinde interval kolesistektomi yaygın bir strateji olmasına rağmen, bekleme döneminde hastaların önemli bir kısmı komplikasyonlar nedeniyle yeniden hastaneye yatmaktadır. Bu çalışma, konservatif tedavi sonrası interval kolesistektomi planlanan hastalarda erken yeniden yatışı etkileyen faktörleri belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmasında, Ocak 2023-Aralık 2024 tarihleri arasında akut kolesistit tanısıyla yatırılarak konservatif tedavi uygulanan ve interval kolesistektomi planlanan hastalar değerlendirildi. Hastalar, taburculuk sonrası altı hafta içinde yeniden başvurup başvurmamalarına göre Erken Başvuru Grubu (EBG) ve Normal Başvuru Grubu (NBG) olarak sınıflandırıldı. Demografik, klinik ve laboratuvar verileri karşılaştırıldı; risk faktörleri lojistik regresyon analizi ile değerlendirildi.

Bulgular: Çalışmaya 110 hasta dahil edildi (NBG= 78, EBG= 32). Çok değişkenli analizde erkek cinsiyet (OR: 5,108; %95 GA: 1,758-14,852; p=0,003) ve diyabetes mellitus (OR: 8,521; %95 GA: 2,933-24,756; p<0,001) erken yeniden yatış için bağımsız prediktörler olarak saptandı. Yaş, inflamatuar belirteçler ve safra kesesi taşı boyutu anlamlı ilişki göstermedi (p>0.05).

Sonuç: Erkek cinsiyet ve diyabetes mellitus, interval kolesistektomi bekleyen hastalarda erken yeniden yatış için bağımsız risk faktörleridir. Bu risk faktörlerine sahip hastalarda uzun süreli konservatif tedavi yerine erken cerrahi müdahale düşünülmelidir.

Anahtar Kelimeler: Akut kolesistit, kolesistektomi, hasta yeniden yatışı, diyabetes mellitus, risk faktörleri

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Highlights

- Male gender and diabetes mellitus are independent predictors of early readmission in patients awaiting interval cholecystectomy.
- Diabetic patients have an 8.5-fold increased risk of readmission compared to non-diabetic patients.
- Male patients show a 5-fold higher risk of readmission compared to female patients.
- Age, C-reactive protein, white blood cell count, and gallbladder stone size measured at initial admission did not show a significant association with readmission.
- Early cholecystectomy should be considered instead of delayed surgery in high-risk patients.

INTRODUCTION

Acute cholecystitis is a major cause of emergency department visits and the third leading cause of abdominal complications requiring hospitalization. The incidence of the disease increases with age, and approximately 10-15% of the adult population in Western societies has gallstones. The optimal timing of surgery for acute cholecystitis remains a controversial issue. Although the Tokyo Guidelines 2018 (TG18) criteria define treatment strategies based on disease severity, the applicability and outcomes of these recommendations in clinical practice vary (1,2).

There are two basic approaches to the treatment of acute cholecystitis: early cholecystectomy, performed within 72 hours of symptom onset, and interval (delayed) cholecystectomy, performed after 6-12 weeks of conservative treatment. Although randomized controlled trials have shown that early cholecystectomy shortens hospital stays and is cost-effective, many centers prefer interval cholecystectomy, particularly in high-risk patients, due to technical difficulties and concerns about complications (2-4).

Patients who are successfully discharged with conservative treatment and scheduled for interval cholecystectomy may develop significant complications during the waiting period. The literature reports that rehospitalization rates during this period range from 15% to 40% due to complications such as recurrent cholecystitis, acute cholangitis, biliary pancreatitis, and gallbladder perforation. These readmissions not only increase patient morbidity, but also place additional burden on the healthcare system and increase the risk of complications by requiring planned surgery to be performed in emergency settings (5).

Identifying patients at high risk for complications and early readmission during the interval period is critical for individualizing treatment strategies. Current literature suggests that factors such as advanced age, male gender, the presence of diabetes mellitus, elevated CRP and white blood cell counts, gallbladder wall thickness, and the presence of pericholecystic effusion may be associated with the risk of readmission. However, there is no consensus on the predictive value of these factors and in which patient groups early cholecystectomy is absolutely indicated (5,6).

Recent systematic reviews and meta-analyses highlight the lack of reliable predictive models for risk stratification in patients awaiting interval cholecystectomy (2,5,7). This retrospective study aims to identify factors affecting early readmission in patients undergoing conservative treatment for acute cholecystitis and scheduled for interval cholecystectomy.

MATERIAL and METHODS

Study Design

The study was approved by the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Research Ethics Committee (Decision No: 2025/436). The study then began by reviewing the data of patients with a history of a single hospitalization for acute cholecystitis at the same institution. Due to the retrospective nature of the study, patient consent was not obtained. Patients hospitalized with a preliminary diagnosis of acute cholecystitis between January 2023 and December 2024 were screened for the study.

Inclusion Criteria

To ensure a homogeneous patient cohort, specific criteria were established for inclusion in the study. These criteria included emergency hospital admission with only a preliminary diagnosis of acute cholecystitis, diagnosis supported by abdominal ultrasonography, age 18 years or older and younger than 80 years, initial follow-up with standard daily treatment of 2 g ceftriaxone and 3 x 0.5 g metronidazole for at least 3 days, and discharge after planned cholecystectomy following medical follow-up.

Exclusion Criteria

To reduce the variability of the study, specific exclusion criteria were established. These included the presence of acute biliary pancreatitis or cholangitis at presentation, the

presence of an additional inflammatory or neoplastic disease of hepatobiliary origin, being younger than 18 or older than 70 years, a history of prior hospitalization for acute cholecystitis, having undergone non-invasive procedures or direct cholecystectomy at initial hospitalization, receiving treatment other than standard antibiotics at admission, or being allergic to metronidazole or penicillin.

Patient Follow-up Protocols

The study began by scanning hospital records for patients admitted to the hospital with a diagnosis of acute cholecystitis. Patients who were admitted to hospital with a preliminary diagnosis of acute cholecystitis were excluded. Their hemogram and biochemistry parameters were evaluated during admission and at discharge. Ultrasound findings from the initial admission were also included. The ultrasound findings assessed increased gallbladder wall thickness and stone size. Stone sizes were recorded separately as millimeters and as large as 1 cm. Comorbidities were also assessed based on patient demographics.

All patients were admitted to the ward with oral feedings off. In addition to intravenous (IV) antibiotics, analgesia, antiemetics, and crystalloids and fluid replacement were administered. Oral feeding was gradually initiated in patients who responded clinically and laboratory tests and who did not undergo early surgery. Patients who received at least 3 days of treatment and were able to receive oral feedings were then discharged with elective surgery scheduled for at least 6 weeks later. Length of stay was recorded. Upon discharge, patients were prescribed two 1-gram ceftriaxone tablets with analgesia. Patients who presented earlier after discharge were grouped as the “Early Presentation Group (EPG)” and the “Normal Presentation Group (NPG).” The extracted demographic and clinicopathological data were compared between the two groups.

Statistical Analysis

SPSS 27.0 (SPSS Inc., Chicago, IL) was used for statistical analyses. The Kolmogorov–Smirnov test was used for the distribution of numerical data. The Mann–Whitney U test was used to evaluate non-parametric data. The Pearson Chi-Square test was used for the distribution of categorical data. Fisher’s exact test was applied when any expected cell count was less than 5. Parameters found to be significant as risk factors for early hospitalization were subjected to regression analysis. Non-parametric variables were processed as median (25th–75th percentile). Categorical data are presented as frequencies (%). p-value <0.05 was considered statistically significant.

RESULTS

There were total of 110 patients included in the study. NPG group consisted 78; EPG group consisted 32 patients. In the comparison of demographic, clinical, and laboratory variables; two variables demonstrated statistically significant differences between groups. Regarding gender distribution, a notably higher proportion of female patients was observed in the EPG compared to the NPG (56.3% vs 19.3%, p<0.001), suggesting that women tend to seek medical attention earlier following symptom onset. Similarly, diabetes mellitus showed a striking association with early presentation, with 62.5% of EPG patients having diabetes compared to only 17.9% in the NPG (p<0.001) (Figure 1). This finding may reflect heightened health awareness or closer

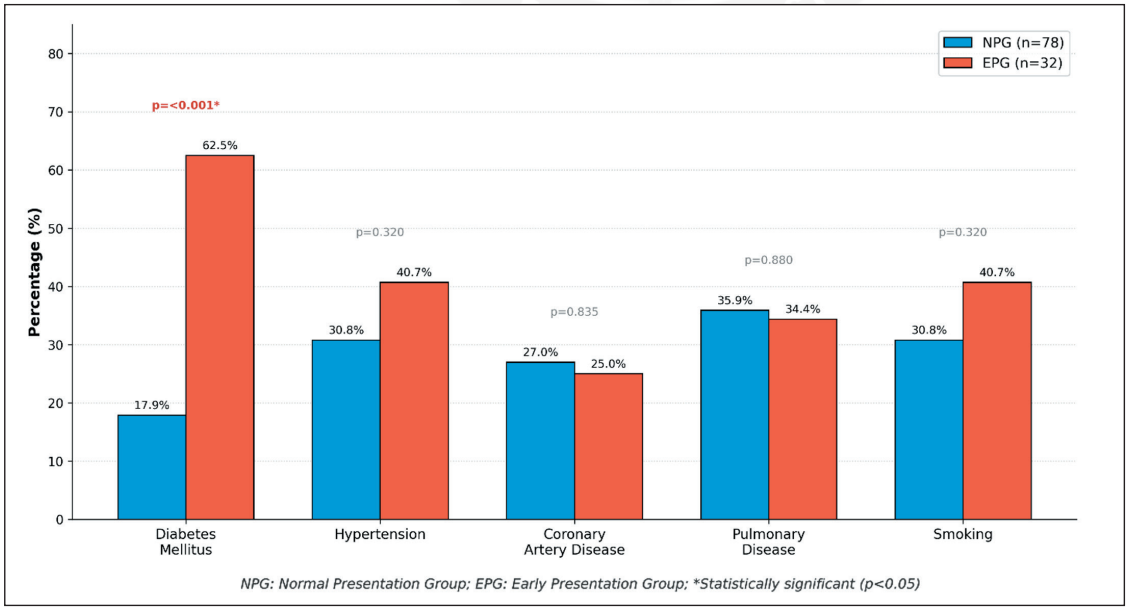

Figure 1: Distribution of Comorbidities Between Study Groups

Table 1: Variable comparison based on early admission

		NPG (n = 78)	EPG (n = 32)	p value •
		n (%)	n (%)	
Gender	Male	63 (80.7)	14 (43.7)	<0.001
	Female	15 (19.3)	18 (56.3)	
DM	No	64 (82.1)	12 (37.5)	<0.001
	Yes	14 (17.9)	20 (62.5)	
HT	No	54 (69.2)	19 (59.3)	0.320
	Yes	24 (30.8)	13 (40.7)	
CAD	No	57 (73.0)	24 (75.0)	0.835
	Yes	21 (27.0)	8 (25.0)	
Pulmonary Disease	No	50 (64.1)	21 (65.6)	0.880
	Yes	28 (35.9)	11 (34.4)	
Smoking	No	54 (69.2)	19 (59.3)	0.320
	Yes	24 (30.8)	13 (40.7)	
USG	Mm GB Stones	68 (87.1)	27 (84.3)	0.762
	>1 cm GB Stones	10 (12.9)	5 (15.7)	
		Median (IQR)		p value ••
Age	Years	43.00 (42.00-46.00)	45.00 (40.00-56.00)	0.600
Lymphocyte Count	µl	13.50 (10.90-16.10)	12.45 (10.40-15.80)	0.838
Crp	mg/dL	9.70 (7.90-11.00)	7.80 (6.50-10.70)	0.730
Alt	(U/L)	20.80 (17.90-23.70)	21,65 (18.20-26.90)	0.359
Ast	(U/L)	35.70 (32.30-38.70)	36.65 (33.20-41.90)	0.342
Ggt	U/L	51.65 (45.20-57.70)	51.05 (43.80-60.90)	0.703
Alp	U/L	97.95 (82.90-112.10)	105.10 (93.80-113.00)	0.435
PA Complaint Period	Days	6.00 (6.00-7.00)	6.50 (5.00-7.00)	0.021
Admission Period	Days	2.00 (2.00-3.00)	2.00 (2.00-3.00)	0.474

NPG: Normal Presentation Group, **EPG:** Early Presentation Group, **DM:** Diabetes, **HT:** Hypertension, **CAD:** Coronary Artery Disease, **USG:** Ultrasonography, **CRP:** C Reactive Protein, **Ast:** Aspartate Aminotransferase, **Alt:** Alanine Aminotransferase, **GGT:** Gamma-Glutamyltransferase, **Alp:** Alkaline Phosphatase, **PA:** Pre-application, **GB:** Gallbladder, **IQR:** Interquartile Range.
•: Pearson Chi-square test, **••:** Mann-Whitney U test.

medical follow-up among diabetic patients due to their existing chronic condition. The pre-application complaint period also differed significantly between groups (median 6.5 vs 6.0 days, p=0.021), though the clinical relevance of this difference appears limited given the overlapping interquartile ranges.

Conversely, no statistically significant differences were identified for hypertension (p=0.320), coronary artery disease (p=0.835), pulmonary disease (p=0.880), smoking status (p=0.320), gallbladder stone size on ultrasonography (p=0.697), age (p=0.600), or any of the laboratory parameters including white blood cell count, C-reactive protein, and liver enzymes (all p>0.05). The admission period was also comparable between groups (median 2 days for both, p=0.474) (Table 1).

In univariate logistic regression analysis, three variables demonstrated statistically significant associations with early readmission following discharge. Male gender was associated with a 5.4-fold increased odds of early readmission compared to females (OR 5.400, 95% CI 2.202-13.244, p<0.001), while the presence of diabetes mellitus conferred the highest risk with approximately 7.6 times greater odds (OR 7.619, 95% CI 3.036-19.121, p<0.001). Additionally, admission period showed a modest but significant association, with each additional day of hospitalization increasing the odds of early readmission by approximately 46% (OR 1.458, 95% CI 1.054-2.018, p=0.023).

After adjusting for potential confounders in multivariate analysis, both male gender and diabetes mellitus retained their statistical significance as independent predictors of early readmission. Male patients demonstrated a five-fold

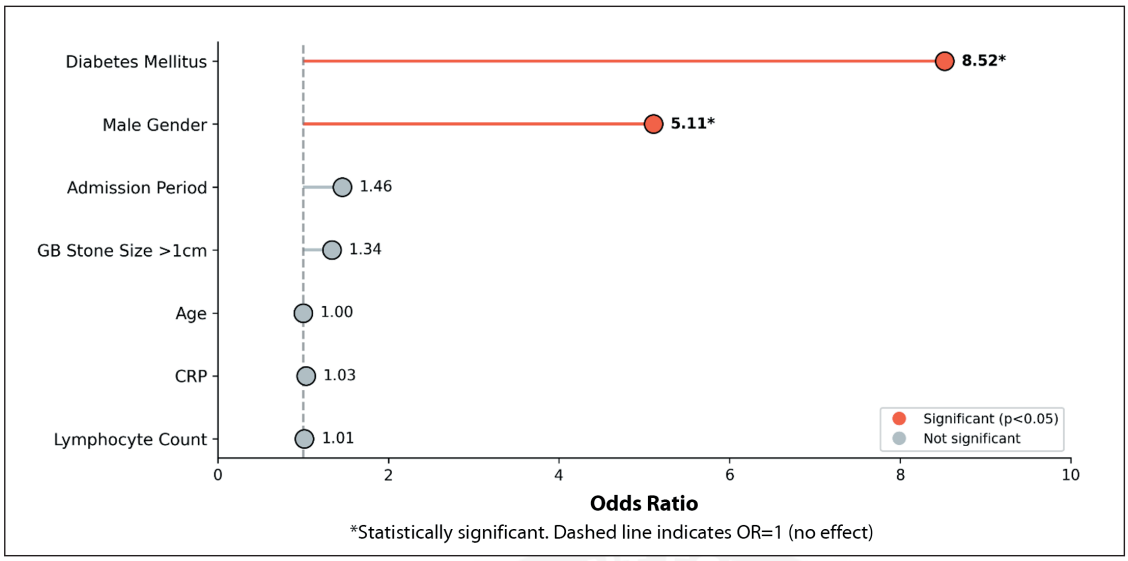

Figure 2: Multivariate Analysis: Predictors of Early Readmission

Table 2: Regression analysis on Early Admission After Discharge

		Univariate			Multivariate		
		OR	%95 CI	p	%95 CI	IQR	p
Lymphocyte count	µl	0.993	0.926-1.065	0.849	1.015	0.929-1.109	0.737
Crp	mg/dL	0.981	0.891-1.080	0.694	1.033	0.916-1.165	0.595
Gender	Male	5.400	2.202-13.244	<0.001	5.108	1.758-14.852	0.003
Age	Years	1.009	0.974-1.045	0.622	1.001	0.960-1.043	0.976
DM	Yes	7.619	3.036-19.121	<0.001	8.521	2.933-24.756	<0.001
GB stone size	>1 cm	1.259	0.394-1.027	0.698	1.338	0.310-5.770	0.696
Admission Period	Days	1.458	1.054-2.018	0.023	1.460	0.981-2.173	0.062

NPG: Normal Presentation Group, **EPG:** Early Presentation Group, **CRP:** C Reactive Protein, **DM:** Diabetes, **GB:** Gallbaldder, **OR:** Odds Ratio, **CI:** Confidence Interval

increased risk compared to females (OR 5.108, 95% CI 1.758-14.852, p=0.003), while diabetic patients showed an 8.5-fold increased odds of early readmission (OR 8.521, 95% CI 2.933-24.756, p<0.001) (Figure 2). The admission period, however, lost its statistical significance after adjustment (OR 1.460, 95% CI 0.981-2.173, p=0.062), suggesting that its univariate association may have been influenced by confounding factors, although the borderline significance indicates a potential trend warranting further investigation. Lymphocyte count, C-reactive protein, age, and gallbladder stone size demonstrated no significant associations in either univariate or multivariate analyses (Table 2).

DISCUSSION

The present study identified male gender and diabetes mellitus as independent predictors of early readmission in patients awaiting interval cholecystectomy following conservative management of acute cholecystitis. In multivariate analysis, male patients demonstrated a five-fold increased risk of readmission within six weeks of discharge, while diabetic patients exhibited an even more pronounced association with an 8.5-fold increased odds of early readmission. These findings carry significant clinical implications, as they suggest that a substantial proportion of patients managed conservatively may benefit from closer surveillance or earlier surgical intervention based on readily identifiable risk factors assessed at the time of initial presentation.

The management of acute cholecystitis remains a subject of ongoing debate, with interval cholecystectomy representing a widely adopted strategy particularly for patients deemed high-risk for immediate surgical intervention. This delayed approach, typically performed six to twelve weeks following the initial episode, offers several theoretical advantages including resolution of acute inflammation, optimization of comorbid conditions, and the opportunity for elective surgical planning in a controlled setting. However, the waiting period

is not without consequences, as a considerable proportion of patients experience recurrent biliary symptoms or complications necessitating unplanned hospital readmission. These early readmissions are clinically concerning not only because they increase patient morbidity and healthcare costs, but also because patients presenting with recurrent or complicated cholecystitis often require emergency surgery under less favorable conditions than originally planned. Therefore, accurate identification of patients at heightened risk for early readmission is essential to guide individualized treatment decisions and determine which patients may benefit from expedited surgical intervention rather than prolonged conservative management (8,9).

In our cohort, males demonstrated a five-fold increased risk of readmission compared to females. Köstenbauer et al. reported similar results in their population-based study of over 47,000 cholecystectomies, where male sex was significantly associated with delayed surgical intervention and poorer outcomes. The underlying mechanisms may involve later presentation with more severe disease, differences in pain perception, or higher prevalence of antiplatelet and anticoagulant use among males. However, our finding contrasts with the pediatric literature, where Pathak et al. reported that female patients had higher odds of 30-day readmission. This discrepancy likely reflects the distinct characteristics of our adult cohort, in which male patients tended to be older and had a substantially higher prevalence of diabetes mellitus, both of which may have contributed to the observed gender-related differences in readmission risk (9,10).

Diabetes mellitus emerged as the strongest independent predictor of early readmission in our study, with diabetic patients demonstrating an 8.5-fold increased risk compared to non-diabetic individuals. This finding is consistent with the established literature indicating that acute cholecystitis follows a more aggressive clinical course in diabetic patients. Several pathophysiological mechanisms may explain this association. Diabetic autonomic neuropathy has been shown to impair gallbladder motility, resulting in increased fasting gallbladder volume and reduced ejection fraction, which promotes bile stasis and facilitates stone formation and recurrent inflammation. Furthermore, hyperglycemia itself directly reduces gallbladder contractility in response to cholecystokinin stimulation, independent of neuropathy. Diabetic patients also exhibit impaired immune responses, with altered neutrophil function and compromised microvascular circulation, predisposing them to more severe infectious complications and rapid disease progression. Additionally, the metabolic derangements associated with diabetes, including hypertriglyceridemia and altered bile composition with cholesterol supersaturation, create a favorable environment for gallstone formation and recurrence. These factors collectively explain why diabetic patients managed conservatively may be at substantially higher risk of developing recurrent biliary symptoms necessitating unplanned readmission during the interval period, supporting consideration of expedited surgical intervention in this population (11-13).

Interestingly, several variables traditionally considered relevant in acute cholecystitis did not demonstrate significant associations with early readmission in our analysis. Age, white blood cell count, C-reactive protein levels, liver enzymes, and gallbladder stone size showed no predictive value for readmission within six weeks. This finding contrasts with studies examining disease severity at initial presentation, where inflammatory markers such as CRP and neutrophil-to-lymphocyte ratio have been established as reliable predictors of complicated cholecystitis and conversion to open surgery. However, these markers primarily reflect the acute inflammatory state at the time of admission rather than the likelihood of recurrent symptoms during the interval period. Similarly, while advanced age has been consistently associated with delayed surgical intervention and increased perioperative morbidity, our data suggest that age alone does not predict recurrence risk in conservatively managed patients. Regarding gallbladder stone size, although some studies have reported that larger stones may be associated with late readmissions due to mechanical obstruction, our findings align with recent evidence suggesting that stone characteristics are inconsistent predictors of gallstone disease recurrence. The RELAPSTONE multicenter study similarly found that stone-related parameters were not reliable determinants of relapse, whereas patient-specific factors such as comorbidities played a more significant role. These observations suggest that the pathophysiology driving recurrent cholecystitis during the interval period may differ from that determining initial disease severity, with metabolic and systemic factors such as diabetes exerting greater influence than acute inflammatory parameters (14-17).

This study has several limitations that should be acknowledged. First, the retrospective design inherently limits the ability to establish causal relationships and introduces potential selection bias. Also our cohort size was relatively small, which may have limited statistical power to detect associations with smaller effect sizes. Due to the retrospective nature of data collection, certain clinically relevant variables could not be consistently evaluated across all patients. Specifically, fever at presentation, gallbladder wall thickness measurements, and the presence of additional pathological findings such as pericholecystic abscess or perforation were not uniformly documented in medical records and therefore could not be included in the analysis.

Our cohort may not capture all patients who experienced recurrent symptoms during the interval period, as some patients may have sought care at different institutions or been

lost to follow-up prior to their scheduled cholecystectomy. This limitation potentially underestimates the true readmission rate and may introduce bias if patients lost to follow-up differ systematically from those retained in the study. Finally, as a single-center study, the generalizability of our findings to other healthcare settings and patient populations may be limited. Future prospective multicenter studies with standardized data collection protocols and longer follow-up periods are warranted to validate these findings and identify additional predictors of early readmission in this patient population.

Despite these limitations, our study has notable strengths. We included a homogeneous cohort of patients who received standardized conservative treatment with uniform antibiotic regimens and discharge protocols, minimizing treatment-related variability. The clearly defined endpoint of readmission within six weeks prior to scheduled cholecystectomy provides clinically relevant data for surgical planning. From a practical standpoint, the identified predictors, male gender and diabetes mellitus, are easily ascertainable at the time of initial presentation without requiring additional diagnostic workup or cost. This allows for immediate risk stratification at the bedside, enabling clinicians to identify high-risk patients who may benefit from expedited cholecystectomy during the index admission or early in the interval period rather than standard delayed surgery. Implementation of such risk-based triage could potentially reduce emergency readmissions, decrease healthcare costs, and improve patient outcomes by avoiding surgery under unfavorable emergency conditions.

Conclusion

In conclusion, this study identified male gender and diabetes mellitus as independent predictors of early readmission in patients awaiting interval cholecystectomy following conservative management of acute cholecystitis. Diabetic patients demonstrated the highest risk with an 8.5-fold increased odds of readmission, while male patients exhibited a five-fold increased risk compared to their counterparts. These findings suggest that patients with these readily identifiable risk factors may benefit from expedited surgical intervention rather than prolonged conservative management. Clinicians should consider prioritizing early cholecystectomy in diabetic and male patients to reduce the burden of recurrent biliary complications during the interval period. Further prospective studies are needed to develop and validate risk stratification tools that can guide individualized treatment decisions in this patient population.

Author Contributions

Study design and conceptualization: **Kazım Duman,** data collection: **Kazım Duman,** analysis and interpretation of results: KD; preparation of the draft article: **Kazım Duman.** The author reviewed the results and approved the final version of the article.

Conflicts of Interest

The authors have no confict of interest to declare.

Financial Support

This study received no financial support.

Ethical Approval

This study was approved by the Scientific Research Ethics Committee of Sancaktepe Martyr Prof. Dr. İlhan Varank Training and Research Hospital (Date: 26.11.2025, Decision No: 2025/436). Due to the retrospective nature of the study, patient consent was not obtained.

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