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Does high surgical risk affect the management and outcomes of percutaneous cholecystostomy in acute cholecystitis? A single-center retrospective analysis

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Abstract

We compared the management and results of percutaneous cholecystostomy (PC) in high surgical risk (HSR) and normal surgical risk (NSR) acute cholecystitis (AC) patients. The patients were divided into two groups: 60 patients with NSR and 30 patients with HSR. Pre-PC laboratory values, PC efficiency in terms of AC complications, catheter withdrawal method and duration, catheter-related complications, AC recurrence rate, mortality rate, presence of dyspeptic complaints in definitive PC, and cholecystectomy rate were compared. Technical and clinical success were achieved in 90 (100%) patients and, 85 (94.4%) patients with PC, respectively. The mortality developed in the HSR group; however, it was not seen in the NSR group (p=0.003). Five (83.3%) out of 6 (6.7%) patients with the American Society of Anesthesiology classification system (ASA) IV score developed mortality. With PC, clinical success was achieved in all 8 (100%) patients with suspected perforated cholecystitis and 6 (75%) of 8 patients with suspected emphysematous cholecystitis on abdominal CT in the non-acute abdomen. PC complications were seen in 8 (8.8%) and recurrent cholecystitis in 8 (12.5%) patients. The hospital stay was longer, and the rate of definitive treatment with PC was higher in the HSR group (p=0.019, p=0.008). C-reactive protein and procalcitonin levels were higher in the NSR group (p<0.001, p=0.001). Dyspeptic complaints did not observe in 28 (73.7%) of the 38 patients without operation during the 33.3-month follow-up. The rate was not different between the groups (p=0.713). PC provides high clinical success in AC-related major complications, severe infection, and the presence of serious comorbid diseases. Mortality was observed only in ASA IV patients. The definitive cure rate of PC was higher in patients with HSR.

Keywords: Percutaneous cholecystostomy, acute cholecystitis, high surgical risk, cholelithiasis, perforated cholecystitis, emphysematous cholecystitis

Introduction

Acute cholecystitis (AC) is the most common complication in patients with gallbladder stones and it is seen at a rate of 1-3% [1]. In the early stages of mild-to-moderate AC, the recommended treatment is laparoscopic cholecystectomy [2]. In severe AC, conservative treatment or percutaneous cholecystostomy (PC) is recommended as a primary option in case of the hospital is not equipped or there is a lack of experienced surgeons [3]. In AC cases with severe inflammation or severe comorbid disease, an early operation increases the morbidity and mortality rates [4].

According to the 2018 Tokyo guideline, medical treatment is recommended primarily in elderly patients and patients with high surgical risk (HSR) [5,6]. In recent studies, the American Society of Anesthesiology (ASA) classification system grade ≥3 and age ≥80 have been accepted as independent risk factors for early operation in AC [3,7].

Perforation and multiple organ failure may develop when treatment is delayed in ACs that do not respond to medical treatment and have severe inflammation. PC reduces the distension of the gallbladder by providing bile drainage, which causes rapid regression of inflammation [8,9].

In the literature, while the perioperative mortality rate in elderly and severely comorbid AC patients is 18%, the morbidity and mortality rate in early operation is 40%. The perioperative mortality rate was 1% in patients with low risk [10].

According to the World Society of Emergency surgery 2020 guidelines, sepsis and septic shock are considered contraindications for laparoscopic cholecystectomy [11]. In studies, PC is

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recommended as a bridge therapy in patients who do not respond to medical treatment and have HSR. In this group of patients, 82-93% of clinical improvement was observed within 72 hours with PC [10,12].

Recently, PC has become a definitive treatment alternative to surgery for patients with HSR. Since the treatment is achieved with PC, both the mortality risk and health expenses are reduced [5]. However, there is no consensus on the indications and contraindications of PC [13]. Uncertainty remains about the efficacy of PC in terms of AC complications, complications related to the PC procedure, the rate of AC recurrence when to remove the catheter (residence), method of catheter removal, frequency of dyspeptic complaints in non-operated patients after PC catheter removal, and patient's preference for operation after catheters' removal [8,14]. We compared the results of PC in AC patients with HSR and normal surgical risk (NSR) and investigate how HSR affects the choice of elective operation.

Materials and Methods

Study Design

The information on the patients who applied to the emergency department of a tertiary education and research hospital due to abdominal pain between 2014 and 2019 and were clinically (non-acute abdomen) and radiologically diagnosed with AC was obtained from the hospital's electronic database and retrospectively evaluated with the approval of the local ethics committee (Decision no: 2019/8-9, Date 08.05.2019).

Written informed consent was obtained from patients admitted to the clinics for medical treatments, invasive procedures, and operative interventions for use in scientific studies evaluating the methods and results of these practices.

Study groups

In the study, AC patients were divided into HSR and NSR groups. Risk groups were determined according to previous studies [7,13]. The HSR group included patients with ages greater than or equal to 70 and <80 years with ASA score III, patients aged ≥80 years, and patients with ASA score IV. NSR group included patients with age <70 with ASA score I, II, and III and patients with age greater than or equal to 70 and <80 years with ASA score I, and II. The workflow was planned as shown in the graph (Figure 1).

Inclusion and exclusion criteria of the study

The inclusion criteria are as follows; 1) Murphy's sign positivity in the abdominal examination, 2) distension and increased wall thickness in the gallbladder in abdominal ultrasonography (USG), 3) abdominal computerized abdominal tomography (CT) does not detect any other intra-abdominal pathology other than AC, and 4) no stone or stenosis in the biliary tract in Magnetic Resonance Cholangiopancreatography (MRCP) performed in patients with higher than normal blood bilirubin levels whose abdominal USG or CT showed dilatation of the bile ducts.

The exclusion criteria include; 1) detection of stones in the common bile duct, 2) suspicion of malignancy or benign stenosis in the bile ducts, 3) inability to reach the patients after removal of the PC catheter, and 4) acute abdomen in clinical examination.

Evaluation of patients and performed procedures

In patients with NSR first, emergency operation was planned, but before a medical treatment (including parenteral fluid, antibiotherapy, and analgesia) had to be started because of the rejection of emergency operation (when the patient is informed about interval cholecystectomy and emergency operation). In patients with HSR, medical treatment is planned first. In patients who started medical treatment, PC was performed when there was no regression in AC, and systemic inflammation markers (white blood cell (WBC), C-reactive protein (CRP), procalcitonin) were monitored within 48 hours. Additionally, antibiotherapy was started in patients with poor systemic conditions or suspected perforated cholecystitis or emphysematous cholecystitis on abdominal CT (non-acute abdomen on physical examination). In these patients, PC was performed without waiting for treatment response. PC drainage catheter [8 Fr pigtail (Flexima and Percuflex, Boston Scientific)] was inserted in the interventional radiology unit by a radiologist who is specialized in interventional radiology under local anesthesia [prilokain (Citanest; Zenica Medical)] with the Seldinger technique (either transhepatically or transperitoneal under USG guidance) [15].

Percutaneous cholecystostomy catheter removal method

Catheter removal time: a) spontaneous dislocation; spontaneous removal of the catheter against the patient's will, b) scheduled removal (by the doctor) in the outpatient clinic; 1) if the catheter has been in place for at least four weeks if there were no problems with the gallbladder during the catheter residence inserted, and laboratory values were regular, 2) if ductus cysticus (DC) is patent in the cholangiography and patient's clinical and biochemical tests were within normal range, 3) if DC cannot be visualized in the cholangiography, but the patient's clinical and laboratory values are regular.

Alternatively, the catheter was removed during operation: a) if the operation coincided with the time of catheter withdrawal, b) the development of complications related to the catheter, and the patients did not want the catheter removed until the operation.

Surgical plan

According to the Society for American Gastrointestinal and Endoscopic Surgeon's guideline, our goal in PC is to bridge from emergency operation to elective cholecystectomy in patients with AC [16]. The surgical risks were explained to the patients after the AC manifestations had passed. Moreover, the decision of interval cholecystectomy was left to patients' preference. The interval cholecystectomy was applied to patients who wanted operation at least four weeks after the AC manifestations resolved. Emergency operations were also performed in patients who developed acute abdomen after insertion or removal of a PC catheter and those with recurrent AC who did not respond to any medical treatment and did not want repeat PC.

Conducting and evaluating the study

After removing the PC catheter, patients who did not undergo operation in our clinic and did not come for follow-ups called on their phones, and information about the process was questioned. The type of operation (open, laparoscopic, or conversion) was noted. Those who did not undergo operation were asked whether

they had a recurrence of AC attacks or dyspeptic complaints after the removal of the PC catheter. The patients also questioned why they did not accept surgical treatment.

Both patient groups were compared in terms of AC grade, AC complications (those with suspected emphysematous cholecystitis and perforation cholecystitis on CT), the time interval from hospitalization to PC, the duration of PC catheter residence, ERCP history, PC complications, mortality rates, laboratory values before PC (WBC, neutrophil, lymphocyte, CRP, procalcitonin, urea, creatinine, aspartate aminotransaminase (AST), alanine aminotransferase (ALT), total bilirubin), PC catheter removal method, recurrence rates after PC removal, interval cholecystectomy rates, type of operation (laparoscopic, open, conversion), and dyspeptic complaint rates in patients that did not undergo the operation.

Statistical analyses

The SPSS 25.0 (IBM Corporation, Armonk, New York, USA) program was used in the analysis of variables. The conformity of univariate data to a normal distribution was evaluated with the Shapiro-Wilk test, while the homogeneity of variance was evaluated with the Levene test. Mann-Whitney U test was used together with the Monte Carlo test to compare the two independent groups' quantitative data. Categorical variables were compared with the Pearson Chi-Square, Fisher Exact, and Fisher-Freeman-Halton tests used with the Monte Carlo Simulation technique, and column ratios were compared with each other and expressed according to Benjamini-Hochberg corrected p-value results. Quantitative variables were expressed as mean (standard deviation), median (minimum/maximum), and median (percentile 25/percentile 75) in the tables, while categorical variables were shown as n (%). Variables analyzed at a 95% confidence level with a p-value less than 0.05 were considered statistically significant.

Results

In the study, 32 (35.6%) of 90 patients were male, and 58 (64.4%) were female. The mean age was 69 (31/94) years (Table 1). There were 38 (63.3%) women and 22 (36.6%) men in the NSR group and 20 (66.6%) women and 10 (33.3%) men in the HSR group. There was no significant difference between the groups in terms of gender distribution (p=0.999) (Table 2).

The results of abdominal USG, CT, and MRCP used during diagnosis when patients applied to the emergency department are summarized in Table 1. The patient distribution was similar in both groups in terms of AC grade (p=0.246) (Table 2). In terms of major AC complications, 5 (8.3%) perforated cholecystitis and 4 (6.6%) emphysematous cholecystitis cases were suspected in the NSR group, whereas 3 (10%) perforated cholecystitis and 4 (13.3%) emphysematous cholecystitis cases were suspected in the HSR group. There was no difference between the two groups in terms of AC complications (p=0.688). Acute pancreatitis accompanying AC attack was present in 5 (8.3%) patients in the NSR group and 3 (10%) patients in the HSR group and the difference between the groups was not significant (p=0.999) (Table 2).

Gallbladder fluid culture results were obtained from 47 (52.2%) patients. Growth was detected in 22 (46.8%) of these cultures: 14 (43.8%) in the NSR group and 8 (53.3%) in the HSR group. There was no significant difference between the groups (p=0.755) (Tables 1 and 2).

The PC catheter was removed spontaneously in 5 (8.3%) patients in the NSR group. In 26 (68.5%) of 38 (63.4%) patients in the NSR group, PC catheters were removed without cholangiography. DC was patent in 11 (91.7%) of 12 (31.5%) patients who underwent cholangiography, and DC could not be visualized in the remaining 1 (8.3%) patient. In 17 (28.3%) patients in the NSR group, the catheter was removed during the operation.

In 2 (8%) patients in the HSR group, the PC catheter was removed spontaneously. The catheters of 13 (68.5%) out of 19 in the HSR group were removed without cholangiography, while in 6 (31.5%) patients it was removed after cholangiography. DC could not be visualized in 1 (16.6) patient who underwent cholangiography. In this group, the catheter was removed during operation in 4 (19%) patients. There was no significant difference between the NSR and HSR groups in terms of catheter withdrawal method (p=0.769) (Table 2).

The median residence time of the PC catheter was 42 (30/60) days in the NSR group and 45 (30/45) days in the HSR group. There was no significant difference between the groups (p=0.829). The median hospital stay in the NSR group was 6 (5/10) days, while in the HSR group it was longer than 9 (6/14) days (p=0.019) (Table 3).

The rate of operation after the removal of the PC catheter was 26 (51.6%) in the NCR group, and 5 (20%) in the HSR group (p=0.008). These groups did not differ significantly in terms of the type of operation (elective or emergency cholecystectomy) (p=0.999) (Table 2). Additionally, there were no significant differences between the groups in terms of surgical method: laparoscopic, open, or conversion rates (p=0.440) (Table 2).

Mortality developed in 5 (9.25%) out of 54 (60%) patients who did not undergo operation and the rest of those patients 49 (90.75%), 11 (22.4%) (4 patients in the HSR group, 7 patients from the NSR group) found to have died of other causes during follow-up after discharge. The remaining 38 patients were questioned in terms of dyspeptic complaints during a median follow-up of 33.3 (7.96/76.37) months (Table 1). Dyspeptic complaints did not observe in 17 (77.3%) of 22 patients in the NSR group and were observed in 5 (22.7%) patients. In the HSR group, dyspeptic complaints were not observed in 11 (68.8%) of 16 patients and were detected in 5 (31.3%) patients. There was no significant difference between the two groups (p=0.713) (Table 2).

The two groups were not significantly different in terms of laboratory values (WBC, neutrophil, lymphocyte, urea, creatinine, AST, ALT, total bilirubin) (p>0.05). However, infection markers (CRP, procalcitonin) were found to be higher in the NSR group than in the HSR group (p <0.001, p=0.001 respectively) (Table 3).

PC complications developed in 8 (8.8%) of 90 patients in our study. Complications were observed in 7 (11.6%) of 60 patients in the NSR group. In the HSR group, complications developed in 1 (3.3%) of 30 patients. There was no significant difference between the two groups (p=0.261) (Table 2). Complications observed in the two groups are summarized in figure 1. Of the complications, hemobilia and subcapsular fluid accumulation

were treated conservatively. Bile leakage from the catheter hole into the abdomen was prevented by catheter repositioning. An emergency operation was performed for biliary peritonitis in one patient after the catheter was inserted and in another patient after the catheter was removed. Among the other complications, pericholecystic abscess, closed gallbladder perforation, and an abscess in the fistula tract were detected intraoperatively during interval cholecystectomy. Since these complications were not seen in preoperative radiological examinations, they were attributed to the process after the PC procedure. A biliocutaneous fistula was detected on physical examination because it developed from the catheter site. This patient was treated with cholecystectomy under elective conditions.

Table 1. Demographic, radiological, and clinical characteristics, duration of cholecystostomy catheter residence, follow-up periods of patients who could not undergo operation, and length of hospital stay of patients who underwent percutaneous cholecystostomy

	n, n/n(present/absent)		%
Gender			
Female	58		6404
Male	32		35.6
Acute cholecystitis grade			
II	74		82.2
III	16		17.8
ASA			
I	22		24.4
II	28		31.1
III	34		37.8
IV	6		6.7
Cholecystitis type			
Acute cholecystitis	74		82.2
Emphysematous Cholecystitis	8		8.9
Perforated cholecystitis	8		8.9
Biliary tract			
Normal	81		90.0
Minimal dilate	9		10.0
Radiological examination			
US + CT	73		81.1
US + MRCP	3		3.3
US + CT + MRCP	14		15.6
Acute Pancreatitis (present/absent)	8/82		9.0/81
Growth in gallbladder fluid culture (present/absent)	22/25		46.8/53.2
PC Complication (present/absent)	8/92		8.8/91.2
Cholangiography (present/absent)	18/46		28.1/71.2
Recurrent AC (present/absent)	8/56		12.5/87.5
PC removal method			
Spontaneous	7		8.2
Radiologist + clinician	57		67.1
During operation	21		24.7
Operation type			
Laparoscopic	21		58.3
Open	8		22.2
Conversion	7		19.4
Dyspeptic complaints (present/absent)	10/28		26.3/73.7
Timing of operation			
Interval cholecystectomy	30		83.3
Emergency	6		16.7
Mortality	5		5.6
	n	**Mean (SD.)**	**Median (min/max)**
Age	90	69.13(13.41)	69(31/94)
PC residence time	90	46.04(27.94)	43(1/180)
Time between hospitalization and PC	90	3.92(3.25)	3(1/22)
Time to operation with PC	36	77.25(58.68)	60(1/210)
Length of hospital stay	90	9.63(7.80)	6.50 (3/43)
Follow-up time in non-surgical patients	38	33.78(15.6)	33.3(7.96/76.37)

SD. Standard deviation; **AC;** Acute cholecystitis; **PC:** Percutaneous cholecystostomy; **ASA:** American Society of Anesthesiology classification system; **US:** Ultrasonography; **CT:** Computed tomography; **MRCP:** Magnetic Resonance Cholangiopancreatography

Table2. Comparison of demographic, radiological, and clinical results of patients in high and normal surgical risk groups who underwent percutaneous cholecystostomy

	NSR	HSR	
	n(%), n/n (present/absent) (%)	n(%), n/n (present/absent) (%)	
Gender			0.999[c]
Female	38(63.3)	20(66.6)	
Male	22(36.6)	10(33.3)	
AC Grade			0.246[c]
II	50(83.3)	21(70)	
III	10(16.6)	9(30)	
Cholecystitis type			0.688[ff]
Acute cholecystitis	51(82.3)	23(76.7)	
Emphysematous cholecystitis	4(6.6)	4(13.3)	
Perforated cholecystitis	5(8.3)	3(10)	
Pancreatitis (present/absent)	5/(8.3/91.7)	3/27(10/90)	0.999[f]
Growth in gallbladder fluidculture (present/absent)	14/18(43.8/56.3)	8/7(53.3/46.7)	0.755[c]
ERCP history (present/absent)	10/50(16.6/83.4)	3/27(10/90)	0.532[f]
PC complications (present/absent)	7/53(11.6/88.4)	1/29(3.3/96.7)	0.261[f]
Cholangiography (present/absent)	12/31(27.9/(72.1)	6/15(28.5/71.5)	0.999[c]
PC catheterremoval method			0.769[f]
Spontaneous	5(8.3)	2(8)	
Radiologist+clinician	38(63.4)	19(76)	
During operation	17(28.3)	4(16)	
Operation type			0.440[ff]
Laparoscopic	18(58.0)	3(60.0)	
Open	6(19.3)	2(40.0)	
Conversion	7(22.5)	0(0.0)	
Operation (present/absent)	31/29(51.6/48.4)[B]	5/20(20/80)[A]	0.008[c]
Operation type			0.999[f]
Interval cholecystectomy	26(83.8)	4(80)	
Emergency	5(16.1)	1(20)	
Mortality	0	5(16.6)	0.003[f]
Recurrent cholecystitis (present/absent)	6/37(13.9/86.1)	2/19(9.6/90.4)	0.999[f]
Dyspeptic complaints (present/absent)	5/17(22.7/77.3)	5/11(31.3/68.7)	0.713[f]
PC residence time (days),median(q1/q3)	42(30/60)	45(30/45)	0.829[u]
Time between hospitalization and PC (days)	3(2/4)	4(2/5)	0.568[u]
Time to operation with PC	67(41/132.5)	51.(43.5/59)	0.446[u]
Length of hospital stay(day)	6(5/10)	9(6/14)	0.019[u]

[f] Fisher Exact Test (Monte Carlo); [ff] Fisher Freeman Halton Test (Monte Carlo); c Pearson Chi-Square Test (Monte Carlo; A Significant compared to the group with normal surgical risk; B Significant compared to the group with high surgical risk; **NSR:** Normal surgical risk; **HSR:** High surgical Risk; **ERCP:** Endoscopic Retrograde Cholangiopancreatography; **PC:** Percutaneous cholecystostomy

Table 3. Comparison of laboratory values in high and normal surgical risk groups

	NSR	HSR	P
AST (U/L)	21(15/33)	23(14/36.5)	0.634[u]
ALT (U/L)	20(13/31)	20(12/39)	0.799[u]
WBC (x103/µl)	14(9.7/19)	11.3(9.1/14.4)	0.161[u]
Neutrophil (x103/µl)	10.8(7.7/15.8)	9.25(7.05/11.25)	0.187[u]
Lymphocytes (x103/µl)	1.2(0.9/1.7)	1.1(0.75/1.5)	0.442[u]
Creatinine (mg/dl)	0.95(0.8/1.2)	1.2(0.9/1.35)	0.183[u]
Urea (mg/dl)	33.5(23/50)	42.5(26/55)	0.251[u]
T.bil (mg/dl)	0.665(0.365/1.49)	0.54(0.355/0.865)	0.265[u]
CRP (mg/l)	227(174.5/313)	96(44.5/221)	<0.001[u]
Procalcitonin (ng/ml)	1.365(0.48/4.92)	0.21(0.02/1.22)	0.001[u]

[u] Mann Whitney U test (Monte Carlo); **q1**:percentile 25; **q3**:percentile 75; **PC**: Percutaneous cholecystostomy; **AST:** Aspartate Transaminase; **ALT:** Aspartate Aminotransferase; **WBC:** White Blood Cell; **CRP;** C-reactive protein; **NSR**: Normal surgical risk; **HSR**:High surgical risk

After the catheter was removed, recurrent AC was observed in 8 (12.5%) of 64 patients: 6 (13.9%) of 43 patients in the NSR group and 2 (9.6%) of 21 patients in the HSR group. There was no significant difference between the two groups (p=0.117) (Table 2). Recurrence of AC was observed 1 month after the removal of the PC catheter, in 2 patients 3 months after the procedure, and in 4 patients 6 months after the procedure. Emergency surgery was performed in 3 (50%) of 6 (13.9%) patients who developed recurrence in the NCR group, as no response to medical treatment could be obtained. Three (50%) patients responded to medical treatment and underwent interval cholecystectomy. When 2 patients (10%) in the HSR group who developed, recurrences did not respond to medical treatment, emergency operation was performed in 1 (50%) patient, and PC was performed in another (50%). After the catheter was removed, no further complications developed during the follow-up.

While mortality did not develop in the NSR group, it developed in 5 (16.6%) patients in the HSR group (p=0.003). Mortality developed in 5 (83.3%) of 6 (6.7%) patients with ASA IV. Demographic, clinical characteristics, comorbid diseases, and hospitalization reasons for patients who developed mortality were summarized in Table 4.

There was no significant difference in age between those who developed mortality and those who did not (p=0.338) (Table 5). AST and ALT values of patients who developed mortality were higher than those who did not (p=0.001, p=0.043) (Table 5). Moreover, WBC, neutrophil, and urea levels were higher in patients who developed mortality (p=0.024, p=0.034, p=0.006). However, no difference was observed in procalcitonin and creatinine values (p>0.05) (Table 5).

Table 4. Demographic characteristics, ASA score, comorbid diseases, and reasons for hospitalization of patients who developed mortality after percutaneous cholecystostomy

Age/	ASA score	Comorbidities	Reason for hospitalization
Gender			
82/M	4	DM, CHF	Diabetic ketoacidosis coma and acalculous cholecystitis
69/F	4	DM, Addison, craniopharyngioma	Confusion and acalculous cholecystitis
78/F	4	AKF, DM, CAD	Diabetic ketoacidosis coma and emphysematous cholecystitis
83/M	4	CHF	Confusion, acalculous cholecystitis, sepsis
64/F	4	DM, hyperlipidemia,	Pancreatitis, acute stony cholecystitis, sepsis

ASA: American Society of Anesthesiology classification system; **AKF:** Acute Kidney Failure; **DM:** Diabetes Mellitus; M:Male; F:Female; **CAD:** Coronary artery disease; **CHF:** Congestive Heart Failure

Table 5. Demographic characteristics, ASA score, comorbid diseases, and reasons for hospitalization of patients who developed mortality after percutaneous cholecystostomy

	Mortality		p
	Absent	Present	
	median (q1/q3)	median (q1/q3)	
Age (years)	69(59/81)	78(69/82)	0.338
AST (U/L)	21(15/32)	118(37/227)	0.001
ALT (U/L)	20(13/31)	51(20/176)	0.043
WBC (x10³/µl)	12.1(9.6/15.6)	22(20/29)	0.024
Neutrophil (x10³/µl)	10.1(7.4/13.5)	21(17.6/25)	0.034
Lymphocytes (x10³/µl)	1.2(0.8/1.7)	0.8(0.6/1.1)	0.280
Creatinine (mg/dl)	1(0.8/1.2)	2(1.5/2.4)	0.091
Urea (mg/dl)	34(23/50)	55(52/151)	0.006
T.bil (mg/l)	0.57(0.36/1.21)	3.88(0.49/4.15)	0.225
Procalcitonin (ng/ml)	0.63(0.14/2.79)	28.295(1.435/58.77)	0.095

Mann Whitney U test (Monte Carlo); **q1:** percentile 25; **q3:** percentile 75; **AST:** Aspartate Transaminase; **ALT:** Aspartate Aminotransferase; **WBC:** White Blood Cell; **CRP:** C-reactive protein

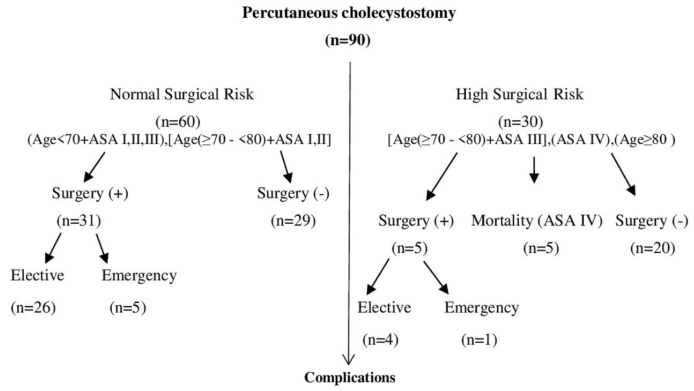

Figure 1. Flowchart of study

Discussion

Until recently, PC was used as a bridge treatment for elective operation in AC cases, but recently its use as a definitive treatment has increased [5,17]. Cholecystectomy or PC is an important step to reduce morbidity and mortality in AC cases where medical treatment is inadequate [16]. In the literature, there is not much information about the definitive treatment rate of PC and the success rate of AC-related complications in cases with high surgical risk. In our study, these rates were found to be higher.

Hsieh et al. reported that they achieved 88% clinical success with PC in cases with AC [10]. In our study, 100% technical success and 94.5% clinical success were achieved. Additionally, PC clinical success was achieved with a rate of 100% in perforated

cholecystitis and 75% in emphysematous cholecystitis (suspected perforation and emphysematous cholecystitis on abdominal CT, in the non-acute abdomen on physical examination) in our study.

Bundy et al. also reported high clinical success in perforated cholecystitis and emphysematous cholecystitis [12]. Supporting these studies, Zarour et al. reported 100% clinical success in perforated cholecystitis and pericholecystic abscess [14]. The results show that PC can be successfully applied to complications with high mortality, such as emphysematous or perforated AC.

PC-related mortality rates have been reported to be between 2-6.8% [12,18,19]. In our study, the mortality rate was found to be 5.5%, which was consistent with the literature. Studies have reported high clinical success and low complication rates with PC in patients with ASA III and IV who were unresponsive to medical therapy [10,12,20]. Hsieh et al. reported a mortality rate of 15.1% in 97% of the cases with ASA III and IV [10]. In our study, the mortality rate in the HSR group was 16.6%, which was similar to Hsieh and colleagues' report [10]. Additionally, while mortality did not observe in ASA III patients, mortality developed in 83.3% of patients with ASA IV in our study. It was monitored in AC patients whose general condition deteriorated due to comorbidities, who followed up in the intensive care unit, who had a septic state, and who were intubated, or were on respiratory support. Increased levels of inflammatory markers along with the elevated values from liver and kidney function tests in patients with mortality indicate that the existing sepsis progressed to multiple organ failure. Hence, it is stated that mortality did not develop due to PC failure or complications, but rather due to sepsis aggravated by comorbid diseases. In two studies supporting our study, a septic course in AC was found to be an independent risk factor for mortality [10,17].

In one review, the rate of complications related to PC was reported varying between 2.5-69% [8]. In two recent studies, it has been reported that major complications (biliary peritonitis, hematoma, or abscess formation) develop at a rate of 2.5-3.5% [9,17]. In our study, the complication rate was 8.8%. There was no difference between the HSR and NSR groups in terms of complications. The result shows that HSR does not increase the complication rate in PC procedures. Complication rates were lower than in recent studies compared with previous ones. This might be due to the enhanced experience in PC applications and the developments in the catheter structure.

In our study, AC recurrence was observed at a rate of 12.5%. The recurrence was not different between the NSR and HSR groups, and the response to medical treatment was lower in cases with recurrence. In patients with recurrence of AC, emergency operation and medical treatment were performed in the NSR group, whereas emergency operation plus PC was performed in the HSR group. The result indicates that HSR does not affect the development of recurrence. In their study that included 144 cases, Kim et al. reported an AC recurrence rate of 6% [17]. As in our study, they performed emergency cholecystectomy, repeat PC, and interval cholecystectomy in cases with recurrence. Li et al. reported that recurrent AC, which was seen at a rate of 16.6%, responded to non-surgical methods and did not require operation [21]. In similar studies in the literature, AC recurrence rates range from 4-22% [5,22-25]. As seen in our study and similar studies, medical treatment, operation, or repeat PC can be performed in recurrent AC, depending on the patient's condition.

Our study observed that the history of acute pancreatitis, growth in bile culture, and ERCP did not change the PC success rate in AC patients. Procalcitonin and CRP values were higher in the NSR group than in the HSR group. However, clinical success was not different in both groups. These findings show that the severity of infection does not affect the success of PC.

It takes 3-6 weeks for the fistula tract to mature. Therefore, the most appropriate catheter removal time is 4-6 weeks [5,12]. Kim et al. determined that the rate of AC recurrence was higher in patients whose PC catheter was removed before 44 days [17]. In our study, the median residence time of the PC catheter in the NSR and HSR groups was 42 (30/60) days and 45 (30/45) days, respectively, and no significant difference was observed between the groups. These findings suggest that HSR does not affect catheter residence time. However, HSR did affect the length of hospital stay, as it was longer in the HSR group. Nowadays, in many centers, the PC catheter is removed during operation [8]. In our study, the PC catheter was removed during operation in 24.7% of the patients, while in 67.1% it was removed after the doctor's evaluation in the outpatient clinic. Spontaneous removal occurred in 8.2% of the patients. In our study, DC was patent in 88.8% of the patients who underwent cholangiography. None of the patients experienced any problems after catheter removal. Additionally, no difference was observed between the groups in this respect. In the literature, although cholangiography was recommended before catheter removal in every patient, it is not necessary. Additionally, it was found that there was no difference in terms of AC recurrence between those who underwent cholangiography and those who did not, and whether DC was patent or not in those who underwent cholangiography [5,10,17]. Contrary to this hypothesis, Bundy et al. suggested removing the PC catheter, either during the operation or if the cholangiogram indicates that DC is patent [12]. These findings show that there is no clear consensus on the method of withdrawal of the catheter. It is seen that the removal method may vary according to the patient's clinical course and the preference of the physician. This result suggested that HSR did not affect the PC catheter withdrawal method.

Currently, definitive cure rates for PC remain unclear. Our study determined that 80% of the patients in the HSR group did not accept the risk of interval cholecystectomy. In the NSR group, 48.4% of the patients delayed interval cholecystectomy. In Kim et al.'s study of 144 cases, PC was found to be the definitive treatment in two-thirds of patients [17]. Two different studies reported that PC was a definitive treatment in 52-54% of cases [9,14]. In our study, it was determined that 71.1% of the patients who did not undergo operation did not have dyspeptic complaints during the mean follow-up of 33.3 months. This result clarifies the fact that patients with HSR in our study accept PC as a definitive treatment.

Joseph et al. reported growth in bile fluid at a rate of 54%. Similarly, in our study, the growth in culture was found in 43.8% of the NSR group and 53.3% of the HSR group [26]. No statistical difference was observed between the two groups. This result shows that there is no relationship between HSR and growth in bile culture.

The limitations of our study were the retrospective design and small population size. Additionally, the low rate of complications of acute cholecystitis, relatively short follow-up period in non-

operational patients and dyspeptic complaints being evaluated subjectively are other limitations.

Conclusion

In conclusion, we observed a high rate of clinical success with PC in patients with major AC-related complications, and in AC cases accompanied by severe inflammation and severe comorbid diseases. Clinical success was low in AC cases with ASA IV. It has been concluded that residence time of the PC catheter, catheter withdrawal method, complications of PC, recurrence of AC, and the clinical and technical successes of PC were not affected by the surgical risk factors. It has been determined that patients with HSR have a longer hospital stay and a lower preference for interval cholecystectomy..

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical approval
This study was approved by the Izmir Tepecik SUAM non-interventional ethics committee (Decision no: 2019/8-9, Date 08.05.2019).

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