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Postoperative outcomes after delayed cholecystectomy for high risk patients with percutaneous drainage for acute cholecystitis

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Abstract

Background: Laparoscopic cholecystectomy (LC) is the gold standard treatment for acute cholecystitis (AC). In high-risk patients, percutaneous drainage (PD) with delayed cholecystectomy (DC) is an alternative. However, the data on outcomes of patients who underwent DC after PD is scarce. The aim of this study was to compare the outcomes after DC in patients primarily treated either with antibiotics (ATB) or with PD.

Methods: Retrospective analysis of all consecutive patients treated primarily either with ATB or PD followed by DC at our institution between January 2006 and December 2015. Patients' co-morbidities, Charlson index at the time of acute cholecystitis, and DC outcomes (including complication comprehensive index (CCI) after surgery) were analysed.

Results: Twenty-eight patients were treated with PD [median age = 77 years (range = 73-87)] and 77 with antibiotics [median age = 78 years (range = 73-83)] at the time of AC. Both groups had a similar Charlson's comorbidity index at admission. Eighteen patients (64%) initially treated with PD underwent DC, while 10 (36%) required an emergency cholecystectomy (EC) for recurrence (n=1) or treatment failure (n=9). In the ATB group, 53 (69%) patients underwent DC, while 24 (31%) had an EC for recurrence (n=13) or treatment failure (n=11). The length of stay after DC was longer for patients initially treated with PD [26 days (range = 15-48) vs 7 days (range = 4-13) in ATB group, p<0.001]. After DC, PD group had more major complications, and higher CCI compared to the ATB group [3 vs 1 (p = 0,048) and mean 16,4 ± 32.0 vs mean 1,8 ± 5,6 (p = 0,006), respectively].

Conclusion: Percutaneous drainage is an effective initial treatment for acute cholecystitis in patients at high risk for surgery, however delayed cholecystectomy in this group is associated with a higher complications and longer hospital stay compared to patients treated primarily with antibiotics.

Key Words: acute cholecystitis, high risk patient, percutaneous drainage, delayed cholecystectomy, surgical outcomes

Table of content

Tables and Figures

Introduction

The management of acute cholecystitis (AC) is still debated in the high-risk population with the potential increased risk of morbidity after emergency cholecystectomy (1, 2). There is no generally accepted definition of high-risk patients. Often, age or the American Society of Anesthesiology (ASA) score is used as a surrogate parameter instead of a precise assessment of organ failure to define critical illness (3). The Charlson co-morbidity index (CI) was developed to predict 1-year mortality for surgically treated patients and is frequently used to estimate the patients' general condition (4). Laparoscopic cholecystectomy (LC) is the the gold standard treatment to treat acute cholecystitis (5), with a proven lower morbidity and mortality rate than with open approach (6, 7). Some recent studies even concluded that LC should be offered, regardless of age, unless the surgical risk is deemed too high (2, 8). However, the mortality and morbidity rate in the high-risk patients may be increased, with an overall morbidity rate as high as 65% and a mortality rate up to 30% (3, 9).

Percutaneous drainage (PD) is a good alternative in this population, because it allows for source control of the infection without the elevated risk of a major invasive procedure (10-14). The PD is a minimally invasive procedure performed under local anaesthesia with real-time imaging guidance while placing a drainage tube into the gallblader. The high success rate of this intervention ranges from 90 to 100% with a low complication rate, generally less than 9% (3, 4, 14, 15). Definitive treatment with cholecystectomy still necessary weeks after the acute episode to avoid a reccurence, especially in case of an acute calculous cholecystitis (3, 4, 16-18). Many publications compared the outcomes of cholecystectomy compared with PD (2, 3, 19-21). However, there is few publications comparing the outcomes after delayed cholecystectomy (DC) in patients who underwent either PD or antibiotics only to treat the acute episode of cholecystitis (22-24).

The aim of this study was to compare the postoperative outcomes of delayed cholecystectomy after resolution of the acute cholecystis with antibiotherapy (ATB) versus percutaneous drainage in the high-risk patients presenting a calculous or acalculous acute cholecystitis.

Patients and methods

Patients

This is a single-center retrospective study of patients treated for AC with delayed cholecystectomy between January 2006 and December 2015. The study was approved by the internal Institutional Review Board (ID number 437/15). Medical charts, radiological, surgical and pathological reports were reviewed to extract data and outcome parameters. Demographics data and major comorbidities such as diabetes, obesity, chronic obstructive pulmonary disease (COPD), hypertension were analysed. The Charlson comorbidity index adjusted to the age is a weighted score of 17 comorbid conditions developed as a 1-year mortality predictor after hospital discharge. Charlson's index variables were defined as previously described (25, 26).

All consecutive patients treated with percutaneous drainage for acute calculous or acalculous cholecystitis were reviewed. Patients who had a delayed cholecystectomy after PD constituted the study group (Figure 1) and patients treated primarily with antibiotics followed by DC constituted the control group (Figure 2). The indication for PD was failure to control cholecystitis sepsis despite the use of antibiotherapy and/or high-risk patients for general anesthesia. Figure 3 shows the flowchart of the study.
Patients who underwent LC for other indications such as symptomatic choledocholithiasis, biliary pancreatitis without acute cholecystitis, or those who underwent LC during the acute event were excluded (348 patients). Patients with additional pancreatitis or cholangitis were also included.

Diagnosis of acute cholecystitis

The diagnosis of AC was based on the patient's history, clinical signs (i.e., positive Murphy's sign, fever, pain in the right upper quadrant), laboratory finding (CRP > 10mg/l, WBC > 10 g/l), and positive computed tomography (CT) and/or ultrasound (US) imaging. Acute cholecystitis was considered on imaging if there was greater than 10-cm enlargement of the antero-posterior gallbladder axis and a gallbladder wall thickening greater than 3 mm.

Antibiotherapy

All patients were initially treated with intravenous antibiotherapy according to the institutional guidelines. Penicillin was mostly administered with possible modification according to the severity of the infection or the risk of resistant pathogen. The therapy was administered for at least 5 days.

Percutaneous drainage of the gallbladder

All procedures were performed under local anesthesia by an experimented radiologist. After percutaneous transhepatic puncture of the gallbladder under US or CT guidance, an 8-Fr Autolock catheter (Boston Scientific, Natick, MA, USA) was inserted using the standard Seldinger technique. PD was associated with an antibiotherapy (27). The catheter was removed after resolution of the cholecystitis sepsis and after cholecystography to exclude cystic duct obstruction that prevents catheter removal (i.e. high risk of recurrent cholecystitis).

Success of initial treatment (ATB or PD) was defined as improvement in clinical signs (reduction of abdominal tenderness, pain, fever) and in biological signs (reduction of leucocytosis, CRP of at least 25%) 24 hours after the initial treatment. Failure of initial treatment was defined as no improvement in clinical signs and in biological signs 24 hours after treatment provided that no other cause of sepsis was found. Recurrence of symptoms was defined as any acute cholecystitis initially improved with recurrence of symptoms during the first admission or at readmission. For failure or recurrence, emergency cholecystectomy was performed.

Cholecystectomy

Delayed cholecystectomy was generally performed at least 6 weeks after the acute event to allow resolution of the inflammation, if no emergency cholecystectomy was needed. Laparoscopic cholecystectomy was always attempted if there were no contraindication for a minimally invasive approach. While open cholecystectomy was performed by using a subcostal incision, a 3-trocars technique was the standard approach for a laparoscopic cholecystectomy. In all cases, the gallbladder was removed in toto, i.e., no subtotal cholecystectomy was performed. Intraoperative cholangiography was only selectively performed. Specimens were sent for routine pathological examination. Postoperative complications were classified according to Dindo-Clavien classification (28). Major complications were classified as grade III-IV and referred to any life-threatening morbidity requiring either surgical or radiological intervention, while minor complications where classified as grade I-II. Mortality (grade V) was defined as any death occurring during the surgical procedure up to 90 days after the operative day. We also used the Comprehensive Complication index (CCI) to assess the overall surgical complications of a single patient as previously described (29).

Statistics

For continuous variables, a Mann-Whitney U test or Student's t-test was used depending on the normality of the distribution and homogeneity of the variances. For discrete variables, a Fisher's exact test was performed. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using GraphPad Prism© 5.0 for Mac OS X.

Results

One hundred and five patients were included in the study. Twenty-eight patients had a PD and 77 had an ATB to treat the acute cholecystitis (Figure 3). The indication for the drainage was failure of the ATB in 43% (12/28) or high-risk patients in 57% (16/28). Success of the primary treatment of AC was observed in 19/28 (68%) and 66/77 (86%) patients after PD and ATB, respectively (p=0,039) (Table 1). Delayed cholecystectomy could not be performed in 10/28 (36%) patients after PD and in 24/77 patients (31%) after ATB (p=0,664) due to either early recurrence of symptoms [1/28 (3.5%) after PD; 13/77 (17%) after ATB, p=0,073] or failure of the initial treatment [9/28 (32%) after PD; 11/77 (14%) after ATB, p=0,039].

Successful initial treatment with antibiotherapy or percutaneous drainage without recurrence

Patient's characteristics at the time of acute cholecystitis (Table 2)
There were 10 men and 8 women [median age = 74 years (range = 73 - 84)] included in the successful PD who underwent delayed cholecystectomy compared with 32 men and 21 women [median age = 79 years (range = 73-81)] in the ATB group. The two groups had similar characteristics except for the renal failure and the COPD that were more frequent in the percutaneous drainage [9/18 vs 11/53 in the ATB group (p=0,033) and 5/18 vs 1/53 (p=0,003), respectively]. The Charlson Comorbidity Index was similar between the two groups [median = 4 in both groups (range = 3-6 in PD group, range = 3-5 in ATB group)]. The PD group had more acalculous cholecystitis (7/18 vs 1/53, p<0.001) and more admission in ICU and a longer hospital stay for the initial treatment [5/18 vs 0/53 admission, p<0.001 and 27 days (range = 16-44) vs 6 days (range = 3-10), p<0.001, respectively].

Postoperative outcomes after delayed cholecystectomy (Table 3)
Patients successfully treated with PD had a longer hospital stay after DC [10 days (range = 3-29) vs 3 days (range = 2-4), p=0,001]. Open surgery were more frequent in the PD group with 4 OC and 14 LC vs 0 OC and 53 LC in the ATB group (p=0,003). Decisions for laparotomy as initial approach were all based on the history of previous abdominal surgery. Conversion from LC to OC was also higher in the PD group (2/18 vs 0/53, p=0,041). The cause of conversion was enterotomy (small bowel, n=1; colon, n=1) consecutive to severe intra-abdominal adhesions. DC in patients successfully treated with PD showed a higher rate of major complications (3/18 vs 1/53, p=0,048) with an associated higher CCI (mean 14 ± 26,7 vs 1,8 ± 5,6, p=0,006). Major complications after DC included one pulmonary failure treated with non-invasive ventilation (NIV), one bilioma requiring percutaneous drainage and one

multiorgan dysfunction (respiratory failure after postoperative extubation from excessive opioide administration, chronic kidney disease with fluid overload treated with combination of Naloxone, diuretic and NIV; and neurological failure with decreased glasgow coma scale after excessive opioide administration) requiring ICU in the study group, and one pleural effusion requiring percutaneous drainage in the control group. Other outcomes, such as operative time, minor complications and mortality showed no statistically significant difference between the two groups. Two deaths occurred in patients initially treated with PD. One patient died after a respiratory failure (pulmonary embolism) 44 days after the DC (patient denied further therapeutic intervention). Another patient died 24 days after the DC from a septic shock after a persistent Enterococcus faecalis bacteriema originating from a mesenteric abcess despite two drainages and antibiotherapy.

Failure of initial treatment with antibiotherapy or percutaneous drainage

Patient's characteristics at the time of acute cholecystitis (Table 4)

There were 4 men and 5 women [median age = 87 years (range = 72 - 91)] with failure of PD who underwent emergency cholecystectomy compared with 5 men and 6 women [median age = 78 years (range = 72-91)] in the ATB group. The two groups had similar characteristics except for the renal failure that was more frequent in the percutaneous drainage (5/9 vs 0/11 in the ATB group, $p < 0.008$). The Charlson Comorbidity Index was similar between the two groups [median = 4 (range = 3-4)]. The PD group had a longer hospital stay [24 days (range = 16-58) vs 14 days (range = 7-16), $p<0.04$]. There was no statistically significant difference for the admission in ICU (1 in the PD group vs 0 in the ATB group, p=0,450).

Postoperative outcomes after emergency cholecystectomy (Table 5)

The operative time was longer in the ATB group [123 min (range = 81-196) vs 87 min (range = 76-109), p=0,111]. In the PD group 4 OC and 5 LC was performed with 1 conversion to laparotomy, compared with 1 OC and 10 LC (p=0,127) with 3 conversions in the ATB group (p=1). Decisions for laparotomy as initial approach were all based on the history of previous abdominal surgery. Three conversions (PD group n=1, ATB group n=2) occurred because of dense adhesions with inability to identify the anatomy of the cystic pedicle structures correctly. In the ATB group, one patient had peroperative complication with a common bile duct section that needed conversion and an hepaticojejunostomy, another had an haematoma that needed transfusion without conversion. The overall morbidity rate was 6/9 (67%) and 6/11 (55%) in PD and ATB groups respectively (p=0,642) with 4 major complications in the PD group vs 2 in the ATB group (p=0,336). In the PD group, one patient died of sepsis from a subhepatic abcess with multiorgan failure and another died from an advanced pancreatic adenocarcinoma with peritoneal carcinomatosis and pulmonary failure. Although not significant, the mortality and the CCI tended to be higher in the PD group [2 vs 0 (p=0,189) and mean 34 ± 35.0 vs mean 14,6 ± 18,6 (p=0,254), respectively].

Discussion

This study shows that PD is a good alternative to surgery to treat the acute episode of cholecystitis when needed. However, hospital stays are longer and complications after delayed cholecystectomy are higher compared to patients initially treated with antibiotics alone. In addition, in patients with failure of PD, emergency cholecystectomy is not associated with higher complications than in patients with failure of antibiotics treatment.

One third of patients primarily treated with PD or antibiotics required an emergency cholecystectomy. In this group of patients, emergency cholecystectomy was associated with similar outcomes whether treated primarily with PD or ATB. This should advocate a more aggressive approach with emergency cholecystectomy as the primary treatment even in the high risk population. However, more data are needed to confirm our results. In addition, major complications after DC were as high as 16% after successful PD with higher morbidity and CCI than after successful antibiotics. Other studies showed overall complications after DC from 0 to 18% (4, 15, 17, 30-33), however the classification of complications was not standardized. Chikamora and al. (23) reported a rate of complication of DC after ATB of 25%. In a recent randomized control trial, overall morbidity was significantly lower in patients with early LC compared to patients treated primarily with ATB and DC (34). In addition, median total length of stay and duration of antibiotic therapy were shorter in the early LC group. Total hospital costs were also lower after early LC. Despite similar Charlson index at admission, the 90 days mortality after delayed cholecystectomy was 11% in the PD group, while no death occurred in the ATB group after DC. Those results support previous reports (8, 14-17, 22, 23, 30-32, 35, 36). Of note, mortality after DC in the PD group was related to patients' comorbidities rather than the surgery. Conversion rates after DC or EC were similar. The literature shows a high variability for the rate of conversion from laparoscopy to open surgery ranging from 3% to 86% after PD (4, 14-18, 30-33, 35-40) and from 13% to 33% after ATB (22, 23, 35). However, the risk of bile duct lesion during DC or emergency cholecystectomy after PD seems not to be increased.

This study has several limitations. First, it is a single centre retrospective study, which entails inherent limitations. Some patients underwent PD after failure of antibiotics treatment, however those patients did not have a higher Charlson comorbidity score. No comparison was made between the complication rates of the initial therapy but the PD has already been reported to be safe with a low complication rate from many studies (3, 4, 14, 15).

To conclude, whenever it is possible, emergency cholecystectomy should be performed to treat acute cholecystitis sepsis even in the high risk population since delayed cholecystectomy, particularly in the PD group is associated with a high risk of postoperative complications. Further studies are needed in this particular group of patients to confirm the results of the present study.

Figures and Tables

Figure 1. Flow diagram of patients treated with PD followed by cholecystectomy

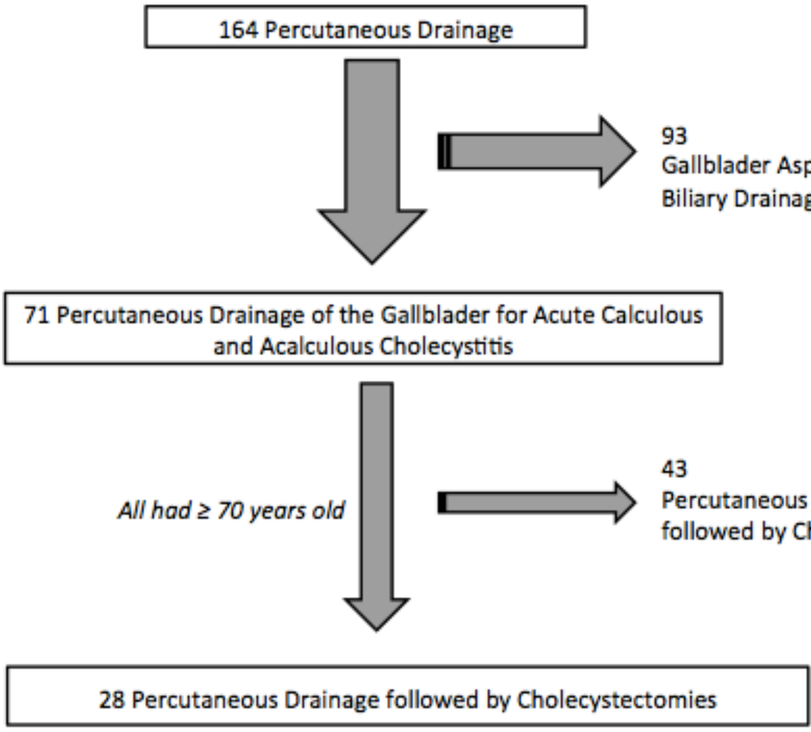

Figure 2. Flow diagram of patients treated with ATB followed by cholecystectomy

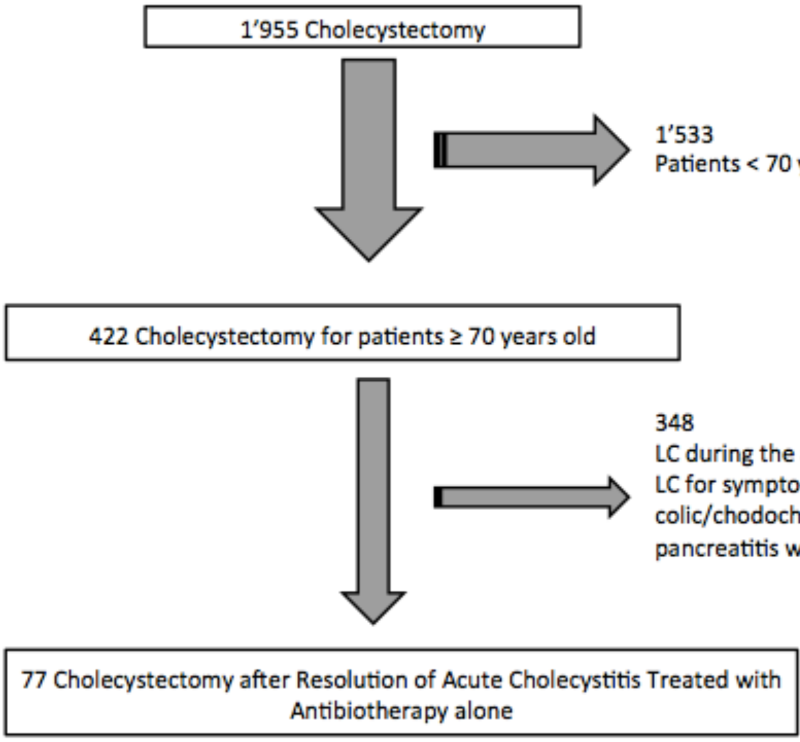

Figure 3. Flowchart of high-risk patients treated for acute cholecystitis

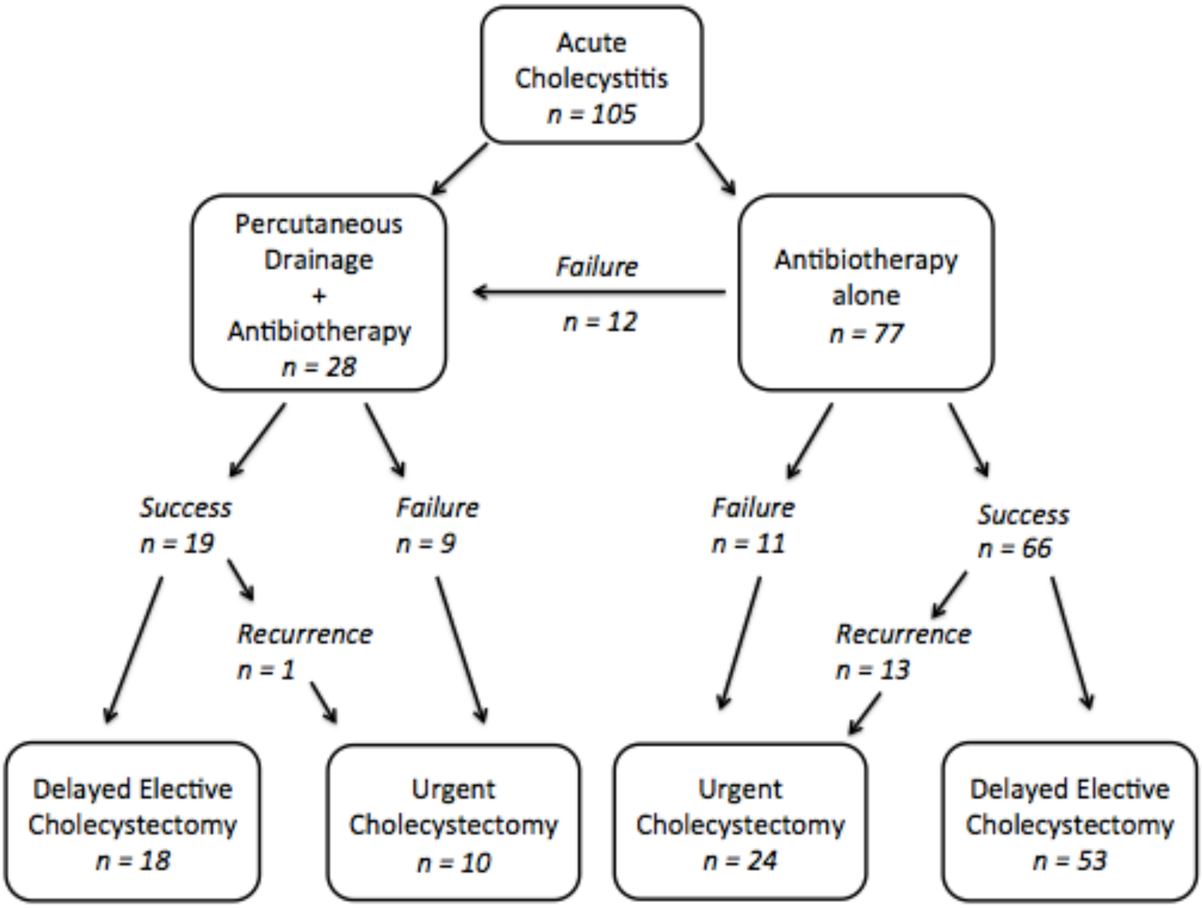

Table 1. Comparaison of the number of patients included in the different subgroups with the associated p-value

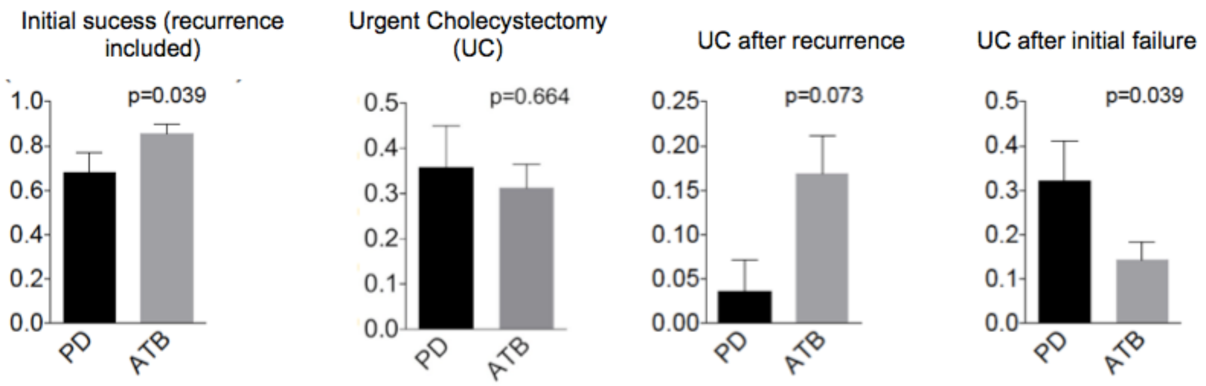

Table 2. Demographics, etiology, and length of primary stay of patients with cholecystitis who underwent successful percutaneous drainage or antibiotherapy without recurrence before elective cholecystectomy.

	Percutaneous drainage n=18	**Antibiotics n=53**	**p-value**
Gender, *men/women*	10/8	32/21	0.785
Age, *years**	74 (73-84)	79 (73-81)	0.407
Cardiomyopathy	1	0	0.254
Renal failure	9	11	**0.033**
Diabetes	6	13	0.542
Obesity	1	6	0.669
COPD	5	1	**0.003**
Hypertension	11	26	0.424
Charlson Comorbidity Index*	4 (3-6)	4 (3-5)	0.492
Acalculous cholecystitis	7	1	**<0.001**
Patients admitted in ICU	5	0	**<0.001**
Length of hospital stay, *days**	27 (16-46)	6 (3-10)	**<0.001**

* Median plus interquartile range

Table 3. Postoperative outcomes after elective cholecystectomy for patients who underwent successful primary treatment without recurrence before the operation.

	Percutaneous drainage n=18	**Antibiotics n=53**	**p-value**
Length of stay, *days**	10 (3-29)	3 (2-4)	**0.001**
Operative time, *min**	103 (77-165)	97 (72-136)	0.273
Open/laparoscopy	4/14	0/53	**0.003**
Conversion to laparotomy	2	0	**0.041**
Morbidity rate	7	6	**0.015**
Minor complications	4	5	0.218
Major complications	3	1	**0.048**
Mortality	1	0	0.254
Comprehensive Complication Index (CCI)‡	14.0 ± 26.7	1.8 ± 5.6	**0.006**

* Median plus interquartile range.
‡ Mean plus standard deviation.

Table 4. Demographics, etiology, and total length of stay of patients with cholecystitis who had failure of percutaneous drainage or antibiotherapy and necessitated an emergent cholecystectomy.

	Percutaneous drainage n=9	**Antibiotics n=11**	**p-value**
Gender, *men/women*	4/5	5/6	1
Age, *years**	87 (72-91)	78 (72-91)	0.819
Cardiomyopathy	0	0	1
Renal failure	5	0	**0.008**
Diabetes	2	2	1
Obesity	2	1	0.565
COPD	4	2	0.336
Hypertension	6	4	0.369
Charlson Comorbidity Index*	4 (3-4)	4 (3-4)	0.311
Acalculous cholecystitis	4	1	0.127
Patients admitted in ICU	1	0	0.450
Length of hospital stay, *days**	24 (16-58)	14 (7-16)	**0.040**

* Median plus interquartile range.

Table 5. Postoperative outcomes after emergent cholecystectomy for patients who had failure of primary treatment before the operation.

	Percutaneous drainage n=9	**Antibiotics n=11**	**p-value**
Operative time, *min**	87 (76-109)	123 (81-196)	0.111
Open/laparoscopy	4/5	1/10	0.127
Conversion to laparotomy	1	3	1
Morbidity rate	6	6	0.669
Minor complications	2	4	0.642
Major complications	4	2	0.336
Mortality	2	0	0.189
Comprehensive Complication Index (CCI)‡	37.3 ± 40.0	14.6 ± 18.6	0.254

* Median plus interquartile range.
‡ Mean plus standard deviation.

Table 6. Demographics, etiology, and length of primary stay of patients with cholecystitis who underwent successful percutaneous drainage or antibiotherapy before delayed cholecystectomy (recurrences included).

	Percutaneous drainage n=19	**Antibiotics n=66**	**p-value**
Gender, *men/women*	10/9	37/29	0.799
Age, *years**	74 (73-84)	79 (73-81)	0.688
Cardiomyopathy	1	0	0.224
Renal failure	9	14	**0.038**
Diabetes	6	13	0.349
Obesity	1	6	1
COPD	5	5	**0.040**
Hypertension	11	31	0.444
Charlson Comorbidity Index*	4 (3-6)	4 (3-5)	0.978
Acalculous cholecystitis	8	4	**<0.001**
Patients admitted in ICU	5	0	**<0.001**
Length of hospital stay, *days**	27 (15-44)	6 (3-10)	**0.001**

* Median plus interquartile range.

Table 7. Postoperative outcomes after delayed cholecystectomy for patients who underwent successful primary treatment before the operation (recurrences included).

	Percutaneous drainage n=19	**Antibiotics n=66**	**p-value**
Length of stay, *days**	15 (3-29)	3 (2-6)	**0.007**
Operative time, *min**	106 (78-162)	91 (66-122)	0.114
Open/laparoscopy	4/15	1/65	**0.008**
Conversion to laparotomy	3	1	**0.019**
Morbidity rate	7	13	0.135
Minor complications	4	8	0.453
Major complications	3	5	0.369
90-day mortality	2	1	0.124
Comprehensive Complication Index (CCI)‡	15.6 ± 31.4	5.2 ± 14.6	0.104

* Median plus interquartile range.
‡ Mean plus standard deviation.

Table 8. Demographics, etiology, and primary length of stay of patients with cholecystitis who underwent successful percutaneous drainage or antibiotherapy but presented a recurrence and necessitated an emergent cholecystectomy.

	Percutaneous drainage n=1	**Antibiotics n=13**	**p-value**
Gender, *men/women*	0/1	5/8	NA
Age, *years**	78	78 (73-86)	NA
Cardiomyopathy	0	0	NA
Renal failure	0	3	NA
Diabetes	0	0	NA
Obesity	0	0	NA
COPD	0	4	NA
Hypertension	0	5	NA
Charlson Comorbidity Index*	3	4 (3-7)	NA
Acalculous cholecystitis	1	3	NA
Patients admitted in ICU	0	0	NA
Length of hospital stay, *days**	11	6 (2-13)	NA

* Median plus interquartile range.

Table 9. Postoperative outcomes after emergent cholecystectomy for patients who underwent successful primary treatment but presented a recurrence.

	Percutaneous drainage n=1	**Antibiotics n=13**	**p-value**
Length of stay, *days**	16	9 (6-17)	NA
Operative time, *min**	142	81 (64-107)	NA
Open/laparoscopy	0/1	1/12	NA
Conversion to laparotomy	1	1	NA
Morbidity rate	0	7	NA
Minor complications	0	3	NA
Major complications	0	4	NA
Mortality	0	1	NA
Comprehensive Complication Index (CCI)‡	0	19.2 ± 27.5	NA

* Median plus interquartile range.
‡ Mean plus standard deviation.

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