

ORIGINAL PAPERS

## Is cholecystectomy the treatment of choice for acute acalculous cholecystitis? A systematic review of the literature

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### ABSTRACT

**Background and objectives:** There is currently no consensus with regard to the use of cholecystectomy or percutaneous cholecystostomy as the therapy of choice for acute acalculous cholecystitis. The goal of this study was to review the scientific evidence on the management of these patients according to clinical and radiographic findings.

**Methods:** A systematic review of the literature from 2000 to 2016 was performed. The databases of PubMed, Índice Médico Español, Cochrane Library and Embase were searched according to the following inclusion criteria: publication language (English or Spanish), adult patients, acalculous etiology and appropriate study design.

**Results:** A total of 1,013 articles were identified and ten articles were selected for review. These included five observational controlled studies and five case series which described the outcome of patients treated with percutaneous cholecystostomy and emergency cholecystectomy. No prospective or randomized studies were identified using the search criteria. The data from the literature and analysis of results suggested that percutaneous cholecystostomy may be a definitive therapy for acute acalculous cholecystitis with no need for subsequent elective cholecystectomy.

**Conclusions:** Percutaneous cholecystostomy may be the first treatment option for patients with acute acalculous cholecystitis except in cases with a perforation or gallbladder gangrene. Patients at low surgical risk may benefit from cholecystectomy but both treatment options may be effective. Percutaneous cholecystostomy in patients with acute acalculous cholecystitis may be a definitive therapy with no need for a subsequent elective cholecystectomy. However, the overall quality of studies is low and the final recommendations should be considered with caution.

**Key words:** Acute acalculous cholecystitis. Percutaneous cholecystostomy. Cholecystectomy. Systematic review.

### INTRODUCTION

Acute acalculous cholecystitis (AAC) is an acute necroinflammatory condition of the gallbladder with a multifactorial pathogenesis. This condition accounts for approximately 10% of all acute cholecystitis cases and

is associated with high morbidity and mortality rates. An increasing number of cases are identified due to greater numbers of severe forms, enhanced awareness and improved imaging techniques (1). AAC is now recognized as a condition within the differential diagnosis of complications in patients with major comorbidities (2-4). Mortality rate among patients with AAC remains high at 30%, and is related to the initial clinical severity and a high prevalence of gangrene (around 50%) and perforation (approximately 10%) (5).

In contrast to calculous cholecystitis, over 80% of patients that develop AAC postoperatively are males (5). An increased incidence of AAC has been noted in individuals with severe burns and polytrauma patients, and frequencies range between 0.7% and 0.9% (6) in aortic surgery over ten years (7). AAC is also associated with conditions such as diabetes mellitus, vasculitis (8), congestive heart failure and chronic kidney disease (9). Conditions that may result in AAC include bile stasis, total parenteral nutrition, gallbladder ischemia, inflammation mediators and sepsis (10,11). Gallbladder ischemia is a key factor in the pathogenesis of AAC and there appears to be an association with stasis related to hypoperfusion. Decreased blood supply is associated with events such as hypotension, dehydration and vasoactive drug administration.

The diagnosis of acute acalculous cholecystitis is challenging due to the low prevalence and the difficulties to differentiate this condition from acute calculous cholecystitis (ACC). Most patients are in a critical condition and oral communication is impaired. Thus, taking an adequate history from these patients is challenging. However, it is important that this condition is considered for the differential diagnosis of the systemic inflammatory response syndrome. An early diagnosis is key to improve prognosis as a result of the fast progression of AAC due to gangrene and perforation.

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Ultrasonography is usually performed initially in patients with a suspected acute abdomen (12). This is a non-invasive procedure that can be performed in the hospital ward and has a good sensitivity and specificity for diagnosing AAC. Vascular wall thickening is the most reliable symptom. Early treatment is essential for patients with AAC due to the risk of developing gallbladder gangrene and a subsequent perforation (1,13). Antibiotic therapy must be initiated as soon as possible regardless of the definitive treatment of choice. An empiric antimicrobial therapy should be effective against the most commonly found pathogens in the enterobacteriaceae family, including Gram-negative bacteria and anaerobes; activity against enterococci is not required (14). The bacteria most commonly isolated from the bile in the gallbladder or the bile duct include *Escherichia coli* (41%), *Enterococcus spp* (12%), *Klebsiella spp* (11%) and *Enterobacter spp* (9%). Antibiotic choice should consider both the most common bacteria and the sensitivity studies in each institution (15).

Gallbladder drainage is indicated for patients with a high surgical risk in order to remove purulent material from the gallbladder. Drainage may be carried out percutaneously or endoscopically; the former is the most commonly used method. Percutaneous cholecystostomy (PCo) (16) may manage AAC in 85% to 90% of patients. However, success rates range from 56% to 100% (17). In a series of 57 patients with AAC, PCo was successful in all cases and symptom remission occurred within four days in 93% of patients (18), with a morbidity rate of 21%. PCo is a minimally invasive technique that may be carried out under local anesthesia via a percutaneous puncture and has been used for patients with a contraindication for general anesthesia (19). Endoscopic drainage of the gallbladder may be performed in patients where PCo is contraindicated or anatomically unfeasible (20). The most common approach is transpapillary. Endoscopic retrograde cholangiography is used to insert a drainage tube inside the gallbladder via the cystic duct, passing the opposite catheter end to the duodenum or through the nose, as with a nasobiliary tube (21,22). When technically feasible, transpapillary drainage resolves the acute condition in 80-90% of patients (23).

Traditionally, the definitive treatment of AAC is open or laparoscopic cholecystectomy (Ct) (1,3,24), which allows a review of the gallbladder. The presence of a perforation, empyema or gangrene can be confirmed and a resection can be performed (25). Collections and diffuse peritonitis may be adequately managed and other overlooked disorders may be identified. The laparoscopic approach may be chosen due to its lower surgically invasive nature. However, the gallbladder is usually affected by an inflammatory process in these patients that complicates the laparoscopic approach with a concomitant increased risk for vascular or biliary damage. Antibiotic therapy cannot replace cholecystectomy or PCo for the treatment of AAC, although concomitant administration is important. The treatment regimen should focus on the organisms most commonly

isolated in the bile collected from these individuals, including *E. coli*, *Klebsiella spp*, and *Enterococcus faecalis*.

The traditional treatment for AAC is cholecystectomy, both open and laparoscopic. PCo has been used as a rescue option for patients with a poor baseline status who cannot undergo emergency surgery with general anesthesia. Patients successfully treated with PCo do not require a subsequent cholecystectomy. Therefore, some professionals suggest that PCo should be the treatment of choice in the absence of gallbladder gangrene or perforation (18,26). Currently, no clinical trials or literature reviews demonstrate the superiority of either therapeutic technique. A systematic review by Treinen et al. (27) of 20 studies including patients with AAC attempted to identify the best treatment option. However, significant patient inclusion bias and difficulties with regard to appropriate data collection were identified and, therefore, their conclusions should be taken with caution.

AAC is an uncommon condition, and selecting a percutaneous or surgical therapy will depend on the patients' health status, disease stage and the availability of technical equipment. The goal of this study was to systematically review scientific evidence regarding the management of patients with AAC according to clinical characteristics and imaging findings. PCo and Ct were compared as treatment options and complications and mortality were primary outcome measures.

## METHODS

### Study design

The PRISMA method (28) was used for article identification, selection and data collection. A systematic review was performed to compare Ct and PCo as a definitive management for patients with AAC regardless of the use of antibiotics or support therapy.

### Study inclusion criteria

The review process included articles in English or Spanish and the search was restricted to articles published from the 1<sup>st</sup> of January 2000 to the 28<sup>th</sup> of February 2016. The search included the Cochrane Library, Medline, Embase, Índice Médico Español and Scopus databases using the following keywords: (acute acalculous cholecystitis OR acute cholecystitis OR severe cholecystitis OR cholecystitis) AND (cholecystectomy OR laparoscopic cholecystectomy OR open cholecystectomy) AND (cholecystostomy OR percutaneous cholecystostomy OR gallbladder drain OR gallbladder tube OR transhepatic gallbladder drain OR transhepatic gallbladder tube OR cholecystostomy tube).

The list of eligible articles was manually reviewed by two researchers. Studies were selected based on their title and abstract and two independent researchers checked the inclusion criteria. The article selection strategy included the reading of abstracts for non-excluded articles. The full paper was read when the acalculous nature of the condition was specified in the abstract. Each investigator pro-

vided a reason to rule out any given article and a third investigator was consulted when there was a disagreement.

### Data collection

A worksheet was designed to collect the data obtained from the systematic review. Researchers extracted data independently for all studies included. Disagreements were settled by discussion. A third investigator was consulted when there was a persistent disagreement in order to resolve the controversy.

The following information was obtained for each article: publication language, year, country of origin, basic patient associated data (including age, sex, ASA and body mass index [BMI]), sample size, study design, inclusion criteria, intervention type (cholecystectomy or cholecystostomy) and the criteria for either technique, length of stay (days) in the Intensive Care Unit (ICU), hospital stay (days), length of follow-up, mortality and morbidity rates, re-intervention due to therapy failure, the elective cholecystectomy rate, readmission due to biliary complications and treatment cost. The quality of selected papers was assessed using the STROBE template for observational studies (29).

### Procedures

The Ct and PCo procedures were compared. Cholecystectomy was defined as the removal of the gallbladder, whether laparoscopic

or via an open approach. Percutaneous cholecystostomy refers to the placement of a drain or tube to clear the gallbladder contents. This procedure is usually performed under local anesthesia and is aided by ultrasound or CT imaging. The primary outcome data included intra-hospital mortality, the overall complication rate (any complications during admission) and the procedure-related complication rate. Secondary outcome measures reviewed in the selected articles included re-intervention (any form of surgery or radiographic/endoscopic procedure after cholecystectomy or cholecystostomy), length of stay in the ICU, length of hospital stay, biliary-related readmission and treatment cost. A meta-analysis of the results was not possible due to the heterogeneity of the selected studies.

## RESULTS

A total of 1,013 articles were identified in the various databases according to the search terms used in the review (Fig. 1).

### PubMed

Three-hundred and ninety articles were identified using the search terms previously described. Twenty-four articles were excluded based on the title as a calculous origin was specified, and thirteen were then excluded due to the lack of an abstract. Thus, 353 articles were retained. The abstracts were reviewed

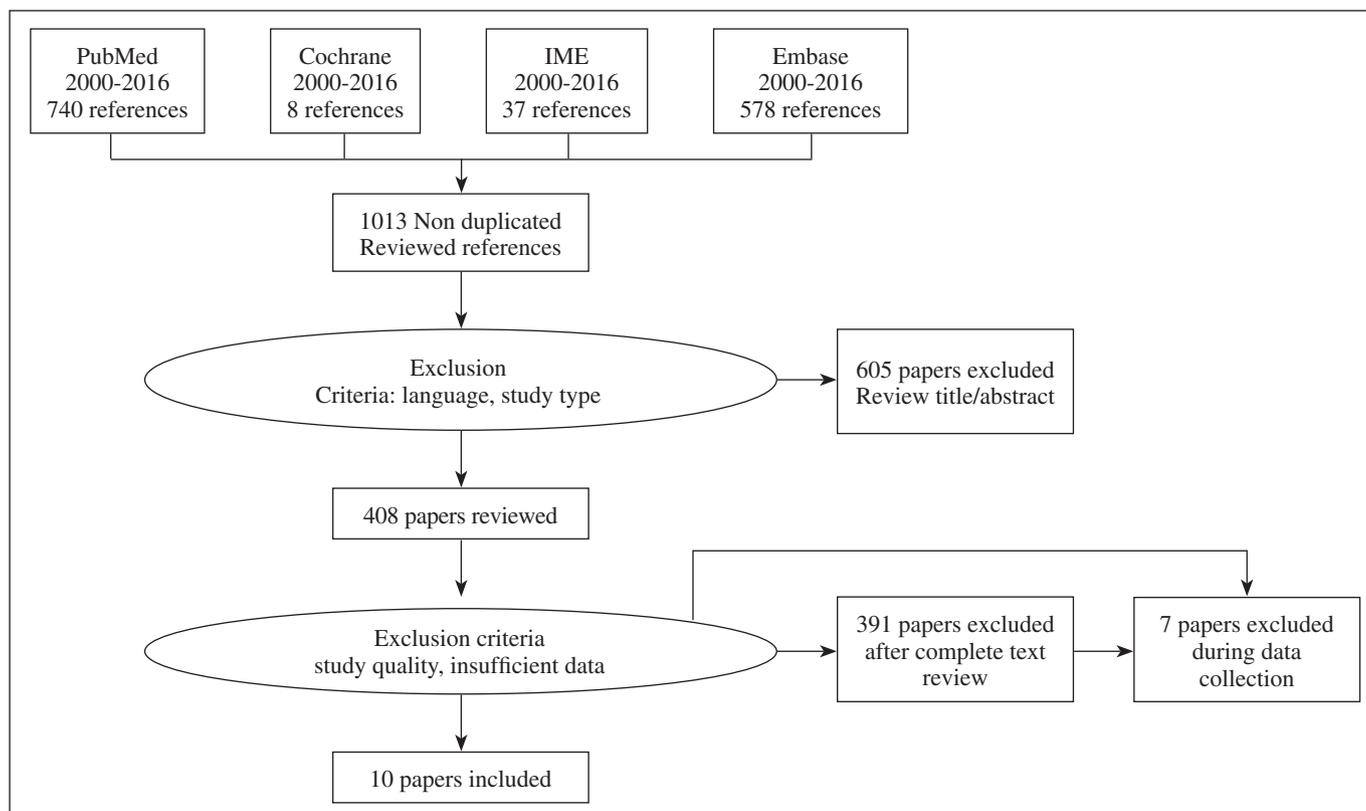


Fig. 1. Process of identification and selection of references included in the review according to search sources.

using language and study design related exclusion criteria. Articles with non-qualifying designs (e.g., case reports) which focused on specific patient populations (immunosuppressed children, patients with specific conditions) or had an inadequate data collection were excluded; ten articles were finally selected. Following review, four articles were excluded due to insufficient data required for analysis and the remaining six studies were included in the study.

### Cochrane Library

Eight articles were identified using the search terms previously described. Three articles were excluded based on their publication date, i.e., prior to the 1<sup>st</sup> of January 2000. One article was selected based on the abstract and the four remaining articles were discarded as they were not related with the objective of this review. The final article was excluded after reviewing the full text due to insufficient data required for analysis.

### Índice Médico Español

A total of 378 articles were identified. Thirty-three articles were excluded based on their publication date (i.e., prior to the 1<sup>st</sup> of January 2000). Two of the remaining four papers were excluded since they were not related with the objective of this review. The final two articles were excluded as they did not meet the criteria required for the methodology of this study, being based on reports of only one and two cases, respectively.

### Embase

Using the aforementioned keywords, 578 articles were identified. Duplicate articles in other databases were excluded and, after application of the publication filters, 293 articles were selected. Two-hundred and forty-one articles were excluded based on the title and study design as they failed to meet the review criteria, and 52 were selected. After reviewing the abstracts, seven articles were selected and 45 documents were excluded as they were not related to the objective of this review, they did not specify an acalculous etiology or were published in languages other than English or Spanish. Three articles were excluded after review of the full text as the data required in this study could not be retrieved. The remaining four articles were included in the qualitative analysis (30-32).

### Articles selected

Ten articles were selected; all were written in English and published between 2001 and 2015 from different coun-

tries and continents. These included retrospective, observational, comparative studies (detailing the results of PCo and Ct) and retrospective case series (detailing the results of only one treatment option). Sample size was strikingly variable among the studies included, with study populations ranging from 23 to 58,518 patients according to the various databases and related institutions (Table 1). The three retrospective, observational studies with over 100 cases were from clerical databases at several institutions: A Simorov et al., 1,725(30); JE Anderson et al. (2012), 58,518 (32); and JE Anderson (2014), 43,341 (31). All three were published in English in the United States.

With regard to the criteria for therapy choice, most case series used one treatment modality and no significant differences were found in the results or patient characteristics. In the study of PCo-treated patients by Chung (18) and Peters (26), this modality was excluded for patients with gallbladder gangrene or evidence of biliary peritonitis. With regard to cases treated with both modalities, Ct was chosen for patients with a lower anesthetic risk and PCo was selected for patients with an impaired status or at increased anesthetic risk (26,30) (Table 1).

Follow-up differed according to the study. The median follow-up for patients treated with PCo was 32, 35 and 55 months, respectively, in the three studies by Yung Hee Chung et al. (18), A Granlund et al. (19) and R Peters et al. (26). Anderson et al. (31) reported a shorter median follow-up of patients who underwent PCo (10.5 months) as compared to those treated with Ct (38 months) (Table 2).

### Mortality

All papers that provided comparative mortality rates between both therapies reported higher rates for patients that underwent PCo. Mortality among patients treated with PCo oscillated between 10.6% (33) and 26% (18) and from 0% to 12% among those who underwent Ct in series from a single institution (12). The series by Anderson based on clerical databases from the State of California (31) recorded mortality rates of 23% for Ct and 61.7% for PCo, which have not been replicated in the other series derived from clerical databases (Table 3).

### Complications

The overall complication rate was not deemed reliable as most studies did not separate comorbidity from overall complications. Thus, in the articles comparing both therapies (30-32), morbidity after treatment is slightly higher for patients undergoing Ct *versus* PCo (Table 3). When series from clerical databases were excluded, the morbidity for patients that underwent PCo ranged from 6.9% (32) to 39% (18). Morbidity rates oscillated between 22% (31) and 52% (32) for patients treated with Ct.

**Table 1. Articles selected for data collection including study design information and patient inclusion criteria**

Articles included	Language, year of publication, country of origin	Basic patient associated data	n (sample size)	Study design	Inclusion criteria
Anton Simorov et al. (24)	English, 2013, United States	Adult patients categorized by age, gender and race	1,725	Retrospective comparative observational study	Patients older than 18 years of age included in the UHC (University HealthSystem Consortium) database
Yung Hee Chung et al. (18)	English, 2012, South Korea	Patients with a median age of 71 years and underlying chronic disease in 89% of cases	57	Retrospective case series	Patients with AAC treated with PCo between 1995 and 2010 at the Samsung Medical Center
Merhdad Nikfarjam et al. (28)	English, 2012, Australia	Adult patients categorized by age, sex, anesthetic risk, clinical, laboratory and radiographic parameters	35	Retrospective comparative observational study*	Patients with histologically confirmed AAC between 2005 and 2011 at the Austin tertiary hospital, Melbourne
A Granlund et al. (15)	English, 2001, Sweden	High surgical risk (ASA IV) adult patients (ASA IV), categorized according to clinical and laboratory parameters	23	Retrospective case series	Adult patients treated with PCo between 1987 and 1999 at Uppsala University Hospital
Jamie E Anderson et al. (26)	English, 2013, United States	Adult patients categorized by age, sex, race and the Charlson's comorbidity index	58,518	Retrospective comparative observational study	Adult patients undergoing PCo or Ct between 1998 and 2010 included in the US Nationwide Inpatient Sample (NIS) database
Jamie E Anderson et al. (25)	English, 2014, United States	Adult patients classified according to clinical parameters, age, sex, race, and the Charlson's comorbidity index	43,341	Retrospective comparative observational study	Adult patients treated with PCo or Ct between 1995 and 2009 included in the OSHPD (Office of Statewide Health Planning and Development, California) database
Daisuke Ueno et al. (35)	English, 2015, Japan	Patients categorized by age, sex, comorbidities and both clinical and laboratory parameters and indices	27	Retrospective case series	Patients who underwent Ct between 2010 and 2014 at the digestive surgery unit, Kawasaki Medical School
Ay-Jiun Wang et al. (31)	English, 2003, China	Adult patients classified by age, sex, clinical parameters and ultrasonographic findings	52	Retrospective case series	Adult patients undergoing Ct between 1997 and 2002 at the Mackay Memorial Hospital
R Peters et al. (19)	English, 2014, Netherlands	Adult patients classified by demographic data, clinical manifestations, ultrasonographic findings, complications and expected outcome	24	Retrospective comparative observational study*	Adult patients treated with PCo between 2004 and 2012 at the radiology unit, ZGT Almelo/Hengelo hospital
J Kirkegård et al. (27)	English, 2015, Denmark	Adult patients categorized according to age, sex, clinical data and PCo approach	56	Retrospective case series	Adult patients undergoing PCo between 2002 and 2012 at the Aarhus University Hospital

PCo: Percutaneous cholecystostomy; Ct: Cholecystectomy (either open or laparoscopic). \*Comparative observational study of patients with acute cholecystitis treated with Ct (M. Nikfarjam et al.) or PCo (R Peters et al.); patients were stratified according to calculus/acalculous status etiology. Only the group of patients with acute acalculous cholecystitis (AAC) were considered in this study, which was a retrospective case series.

**Table 2. Treatment decision criteria and duration of follow-up**

Articles included	n (sample size)	Type of procedure	Decision criteria for either technique	Duration of follow-up	
				PCo	Ct
Anton Simorov et al. (24)	1,725	PCo and Ct (comparative study)	No unified criteria available due to the variety of centers involved in the database	Not specified	Not specified
Yung Hee Chung et al. (18)	57	PCo	PCo approach and the need for a subsequent elective Ct were established according to the judgment of the attending physician	Median follow-up of 32 months	
Merhdad Nikfarjam et al. (28)	35	Ct	Only patients undergoing Ct with histological confirmation or those undergoing elective Ct after PCo were included	Not specified	
A Granlund et al. (15)	23	PCo	Patients with a high surgical risk (ASA IV) for whom PCo was chosen for therapy	Median follow-up of 35 months	
Jamie E Anderson et al. (26)	58,518	PCo and Ct (comparative study)	Unified criteria cannot be extrapolated due to the wide variety of sites involved in the NIS database	Not specified*	
Jamie E Anderson et al. (25)	43,341	PCo and Ct (comparative study)	Criteria cannot be established due to the wide variety of centers involved in the OSHPD database	10.5 months	38 months
Daisuke Ueno et al. (35)	27	Ct	No data collected for patients with AAC and Ct contraindicated based on surgical risk. Results support a surgical technique as a valid option for the management of carefully selected patients	Not specified	
Ay-Jiun Wang et al. (31)	52	Ct	Only patients undergoing Ct with histological or intraoperative confirmation were included	Not specified	
R Peters et al. (19)	24	PCo	A primary approach with PCo was warranted for all patients in this study due to the potential morbidity and mortality risks associated with Ct	55 months	
J Kirkegård et al. (27)	56	PCo	To determine the effectiveness of PCo as a single therapy, patients with AAC were included when surgery was precluded	Not specified	

PCo: Percutaneous cholecystostomy; Ct: Cholecystectomy (either open or laparoscopic). \*Follow-up data could not be collected for these patients as the NIS database only included data for one admission.

**Table 3. Morbidity and mortality rates according to therapeutic option**

Articles included	n (sample size)	Morbidity rate		Mortality rate	
		PCo	Ct	PCo	Ct
Anton Simorov et al. (24)	1,725	5%	8%	2.6%	2.1%
Yung Hee Chung et al. (18)	57	39% PCo		26% PCo	
Merhdad Nikfarjam et al. (34)	35	17% Ct			0% Ct
A Granlund et al. (15)	23	Not specified		17% PCo	
Jamie E Anderson et al. (26)	58,518	6.9%	10%	14%	2.6%
Jamie E Anderson et al. (25)	43,341	Not specified		61.7%	23%
Daisuke Ueno et al. (35)	27		22% Ct		0% Ct
Ay-Jiun Wang et al. (31)	52		52% Ct		12% Ct
R Peters et al. (19)	24	29% PCo		17% PCo	
J Kirkegård et al. (27)	56	16% PCo		10.6% PCo	

PCo: Percutaneous cholecystostomy; Ct: Cholecystectomy (either open or laparoscopic). Mortality and morbidity rates during 30 days.

### Re-intervention for therapeutic failure

After a failed PCo, 1.8% of patients needed a repeat Ct procedure according to the studies by Yung Hee Chung et al. (18) and J Kirkegård et al. (33). In the study by R Peters et al. (26), none of the 17 patients treated with PCo required surgery during follow-up. The remaining authors provide no data on repeat procedures for patients undergoing PCo or Ct (Table 4).

### Readmission due to biliary complication

In the series of PCo cases from a single site, readmission for biliary complications occurred in 7% of subjects in the series by Yung Hee Chung et al. (18) and in 4.3% of subjects in the study by A Granlund et al. (19). With regard to series from diverse institutions, readmission was only reported by A Simorov et al. (30), with rates of 16.1% for patients treated with Ct and 29% for those treated with PCo (Table 4).

**Table 4. Repeat PCo due to elective procedure or therapy failure, conversion of Ct and readmission for a biliary complication**

Articles included	n (sample size)	Repeat PCo		Conversion of Ct	Readmission for biliary complication	
		Therapy failure	Elective Ct	To open surgery	PCo	Ct
Anton Simorov et al. (24)	1,725	Not specified*		26.5%	29%	16.1%
Yung Hee Chung et al. (18)	57	1.8%	32%		7% PCo	
Merhdad Nikfarjam et al. (28)	35	0%**		6%	0%	
A Granlund et al. (15)	23	Not specified	4.3%		4.3% PCo	
Jamie E Anderson et al. (26)	58,518	Not specified			Not specified***	
Jamie E Anderson et al. (25)	43,341	Not specified	1.2%		Not specified	
Daisuke Ueno et al. (35)	27	Not specified		18.5%	Not specified	
Ay-Jiun Wang et al. (31)	52	Not specified			Not specified	
R Peters et al. (19)	24	0%	4.2%		8.3% PCo	
J Kirkegård et al. (27)	56	1.8%****	7.1%		14.3% PCo	

PCo: Percutaneous cholecystostomy; Ct: Cholecystectomy (either open or laparoscopic). Repeat PCo: re-intervention due to therapy failure and elective conversion to Ct. Conversion of Ct: conversion from laparoscopy to open surgery. \*Based on UHC characteristics, patient identification as needed to establish repeat PCo rate was not feasible. \*\*The two patients undergoing PCo who required conversion to Ct had no AAC histopathology confirmation and could not be included in the sample according to the methodological criteria of the study. \*\*\*Follow-up data cannot be collected for these patients as the NIS database only includes one admission. \*\*\*\*Of the total number of re-intervened patients, 8.9% were intervened with a second PCo and conversion to Ct was selected in 1.8%.

### Conversion of laparoscopic Ct to open surgery

The need to convert laparoscopy to laparotomy was considerably higher in the study by A Simorov et al. (30) (26.5%) than in the study of M Nikfarjam (34) (6%). However, the study by M. Nikfarjam et al. included 35 patients, whereas the one by A Simorov et al. assessed the results from 1,725 subjects. Of the latter, 822 were treated with laparoscopic Ct and 218 (26.5%) converted to open Ct due to intraoperative complications. Patients that did not require a conversion to laparotomy had a better outcome in terms of morbidity, hospital stay, readmission to ICU and the need for readmission (Table 4).

### Admission to ICU

Yung Hee Chung et al. (18) and R Peters et al. (26) reported ICU readmission rates of 24.6% and 50%, respectively, for patients managed with PCo. The retrospective series by M Nikfarjam et al. (34) and D Ueno (35) assessed ICU admission rates in patients undergoing Ct and found rates of 9% and 7.4%, respectively. These data may be due to comorbidities and the high surgical risk of the patients selected for the assessment of PCo. The study by A Simorov et al. (30) is the only one that assessed both therapy options and no significant differences were reported (28.1% for PCo and 34.6% for Ct) (Table 5).

### Elective cholecystectomy

The need for or indication of elective cholecystectomy after the resolution of the AAC event was reported at

varying rates from high to low in most studies. However, the majority of patients did not undergo an elective Ct. In the series by Yung Hee Chung et al. (18), elective Ct was performed in 18 of 57 patients, representing 32% of patients that underwent PCo. The case series by A Granlund et al. (19), R Peters et al. (26) and J Kirkegård et al. (33) reported rates of 4.3%, 4.2% and 7.1%, respectively. In the observational comparative study by JE Anderson et al. (32) of 43,341 patients, 1.2% of subjects received Ct after therapeutic drainage (Table 4). Recurrence risk was low for patients treated with PCo, 7% in the series by Chung et al. (32).

### Hospital stay and treatment costs

The studies by Simorov et al. (30) and Anderson et al. (32), based on clerical registries, assessed hospital stay for patients undergoing both techniques. In the series by Simorov et al. (30), patients treated with PCo had a mean stay of seven days as compared to eight days for those treated with Ct. Anderson et al. (32) reported a mean stay of 15 days for patients undergoing Ct and 6.7 days for those undergoing PCo (Table 5). Treatment costs were collected from the observational comparative studies by A Simorov et al. (30) and JE Anderson et al. (32), and these were \$40,516 for PCo and \$53,011 for Ct, and \$106,846 for PCo and \$49,787 for Ct, respectively (Table 5).

### DISCUSSION

AAC is an uncommon condition and the choice between percutaneous or surgical treatment will depend on patient

**Table 5. Hospitalization days, ICU stay and treatment cost by therapeutic option**

Articles included	n (sample size)	Hospitalization days		ICU stay		Treatment cost	
		PCo	Ct	PCo	Ct	PCo	Ct
Anton Simorov et al. (24)	1,725	7 (5-10)	8 (5-12)	28.1%	34.6%	\$40,516	\$53,011
Yung Hee Chung et al. (18)	57	Not specified		24.6% PCo		Not specified	
Merhdad Nikfarjam et al. (28)	35	5 (0-20) Ct		9% Ct		Not specified	
A Granlund et al. (15)	23	7 (0-30) PCo		Not specified		Not specified	
Jamie E Anderson et al. (26)	58,518	15 (14-15)	6.7 (6.6-6.8)	Not specified		\$106,846	\$49,787
Jamie E Anderson et al. (25)	43,341	Not specified		Not specified		Only funding type is described with no data on total cost	
Daisuke Ueno et al. (35)	27	14.5 (2.6-26.4) Ct		7.4% Ct		Not specified	
Ay-Jiun Wang et al. (31)	52	Not specified		Not specified		Not specified	
R Peters et al. (19)	24	Not specified		50% PCo		Not specified	
J Kirkegård et al. (27)	56	Not specified		Not specified		Not specified	

PCo: Percutaneous cholecystostomy; Ct: Cholecystectomy (either open or laparoscopic). PCo or Ct specified in case series.

status, disease stage and technical equipment availability. Thus, patients that present with gallbladder gangrene or perforation at the time of diagnosis can only be treated with Ct (18,26) and patients in poor health or unfit for general anesthesia can only be treated with PCo.

The literature review performed in this study highlights the heterogeneity within the studies of interventions for AAC. These studies discuss the benefits and disadvantages of both major treatment modalities by explicitly comparing PCo and Ct, including both open and laparoscopic cholecystectomy as subgroups. A separate analysis of open and laparoscopic Ct subgroups was not performed as comparative series provide an inadequate number of patients. There are no randomized clinical trials to date comparing both modalities, thus strong conclusions cannot be drawn in favor of one or another technique.

Caution is advised when analyzing the different mortality and morbidity rates of both techniques as they might be associated with the baseline patient status. Clinical severity and age were greater in patients treated with PCo compared to those managed with Ct, as demonstrated in the series of Anderson (31). The Charlson's index showed significant differences favoring Ct patients, and a much higher proportion of subjects with severe sepsis and shock were in the PCo group. Similarly, the mean age of patients undergoing PCo was 71 years *versus* 56.7 years for those managed with Ct.

Furthermore, three series were included from clerical databases (30-32) which provide a high number of subjects, but the results from these may be biased due to the quality of the coding systems set up in the corresponding hospitals. This is demonstrated by the reported differences in the mortality rates of patients undergoing PCo, which ranged from 2.6% (30) to 61% (31). In contrast, the primary limitation in series from a single institution (the largest study included 57 patients [18]) is the low number of cases and the fact that major outcome variables show less variability.

Elective Ct once the AAC episode has subsided is a questionable therapy due to the low possibility of recurrence. According to various studies, PCo may be a definitive therapy for AAC without the need for a subsequent Ct (36). Patients treated with PCo significantly improve with this treatment and require no further procedures following the withdrawal of the cholecystostomy tube and the resolution of their initial clinical symptoms. However, a second repeat ultrasound should be performed to assess the presence of previously overlooked stones and in the case of positive findings, the cholecystectomy should be delayed.

### Study limitations

The main limitation of this study relates to the quality of the reported articles. Most are retrospective series of patients treated with either technique according to health

status, comorbidities or radiographic findings. No randomized clinical trials or case-control studies are available that provide recommendations.

The second limitation relates to study heterogeneity. There are studies from a single institution with few cases and studies from larger institutions with high numbers of patients with AAC. The advantages and disadvantages of both data sources have been discussed in the results section and efforts were made to collect the most significant findings for each outcome variable.

The third limitation of the study derives from the challenge associated with the identification of studies. Since the incidence of AAC is much lower than that of ACC, most series include both types of cholecystitis, which made the identification of target studies for review difficult. In order to avoid this issue, all abstracts including the identified key words were reviewed, a secondary search of their associated references was performed and those that quoted AAC were finally included. Any literature references based on doctoral dissertations or conference summaries were not included.

This study discusses the benefits and drawbacks of both major treatment modalities, explicitly comparing PCo and Ct, including both open and laparoscopic cholecystectomy as subgroups. Ct subgroups (open and laparoscopic) were not separately analyzed as the comparative series reviewed provided an inadequate number of patients. There are no randomized clinical trials to date comparing both modalities that allow conclusions to be drawn in favor of one or another technique. No unified therapy choice criteria are presented in the articles included in this study, but PCo is excluded in patients with gangrenous or perforated cholecystitis.

### CONCLUSIONS

In the absence of gallbladder gangrene or perforation, PCo appears to be the first-choice therapeutic option for patients with AAC. Patients at low surgical risk may benefit from treatment with either PCo or Ct, although there is insufficient data to recommend either one of these techniques. However, PCo is associated with a lower morbidity following the procedure. PCo should be the procedure of choice instead of Ct in patients with a high surgical risk. PCo may provide a definitive treatment due to the low risk of recurrent AAC once the initial or triggering AAC episode is over. However, the quality of studies is generally low and final recommendations should be considered with caution.

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