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Cholecystostomy: Are we using it correctly?

Alexander L. Colonna [a, *], Travis M. Griffiths [a], Douglas C. Robison [a], Toby M. Enniss [a], Jason B. Young [a], Marta L. McCrum [a], Jade M. Nunez [a], Raminder Nirula [a], Rulon L. Hardman [b]

[a] University of Utah, Department of Surgery, 30 N 1900 East, Salt Lake City, UT, 84132, USA
[b] University of Utah, Department of Radiology & Imaging Sciences, 30 North 1900 East, Salt Lake City, UT, 84132, USA

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ABSTRACT

Background: Percutaneous Cholecystostomy Tubes (PCT) have become an accepted and common modality of treating acute cholecystitis in patients that are not appropriate surgical candidates. As percutaneous gallbladder drainage has rapidly increased newer research suggests that the technique may be overused, and patients may be burdened with them for extended periods. We examined our experience with PCT placement to identify independent predictors of interval cholecystectomy versus destination PCT.

Methods: All patients with cholecystitis initially treated with PCT from 2014 to 2017 were stratified by whether they underwent subsequent interval cholecystectomy. Demographic data, initial laboratory values, Tokyo Grade, Charlson Comorbidity Index, ASA Class, complications related to PCT, complications related to cholecystectomy, and mortality data were retrospectively collected. Descriptive statistics, univariable, and multivariable Poisson regression were performed.

Results: 165 patients received an initial cholecystostomy tube to treat cholecystitis. 61 (37%) patients went on to have an interval cholecystectomy. There were 4 complications reported after cholecystectomy. A total of 46 (27.9%) deaths were reported, only one of which was in the cholecystectomy group. Age, Tokyo Grade, liver function tests, ASA Class, and Charlson Comorbidity Index were significantly different between the interval cholecystectomy and no-cholecystectomy groups. Univariable regression was performed and variables with $p < 0.2$ were included in the multivariable model. Multivariable Poisson regression showed that increasing Tokyo Grade (IRR 0.454, $p = 0.042$, 95% CI 0.194–0.969); and increasing Charlson Comorbidity Score (IRR 0.890, $p = 0.026$, 95% CI 0.803–0.986) were associated with no-cholecystectomy. Higher Albumin (IRR 1.580, $p = 0.011$, 95% CI 1.111–2.244) was associated with having an interval cholecystectomy.

Conclusion: Patients in the no-cholecystectomy group were older, had more comorbidities, higher Tokyo Grade, ASA Class, and initial liver function test values than those that had interval cholecystectomy. Since interval cholecystectomy was performed with a low rate of complications, we may be too conservative in performing cholecystectomy after drainage and condemning many patients to destination tubes.

Background

Across the American population of approximately 330 million, 10–15% of adults have gallstones. Of these, 1–4% have symptomatic cholelithiasis, and of these 20% - an estimated 400,000 patients - develop acute complications.[1–3] Cholecystectomy remains the standard of care for symptomatic or complicated cholelithiasis, with approximately 600,000 to 1.5 million cholecystectomies performed per year in the United States. While this procedure is common, it carries an overall reported complication rate of 1–12%, which includes a 0.04–0.25% chance of common bile duct injury, the most serious procedure-specific complication.

Since it was first described in the late 19th century, and with the

* Corresponding author.
E-mail addresses: Alexander.Colonna@hsc.utah.edu (A.L. Colonna), travis.griffiths@hsc.utah.edu (T.M. Griffiths), u0736886@utah.edu (D.C. Robison), toby.enniss@hsc.utah.edu (T.M. Enniss), jason.b.young@hsc.utah.edu (J.B. Young), marta.mccrum@hsc.utah.edu (M.L. McCrum), Jade.nunez@hsc.utah.edu (J.M. Nunez), r.nirula@hsc.utah.edu (R. Nirula), rulon.hardman@hsc.utah.edu (R.L. Hardman).

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addition of ultrasonography and fluoroscopy guidance in the late 1970s and early 1980s, rates of percutaneous cholecystostomy tube (PCT) placement have been rising. It is regarded as an increasingly safe destination treatment or as a bridge to cholecystectomy for both acute calculous and acalculous cholecystitis in those considered high-risk candidates for surgery.[3–6] Cholecystostomy can be a lifesaving maneuver, but it is accompanied by relatively high morbidity and high utilization of interventional radiology with tube checks and repositioning, leading to increased costs. Per Medicare data, approximately 6.5% of patients older than 65 admitted with cholecystitis will be managed with a cholecystostomy tube.[7] Since cholecystectomy remains the definitive treatment for gallstone related disease, interval cholecystectomy with PCT removal is often subsequently performed.

Despite increasing usage of PCT, the literature regarding indications for this procedure is highly variable.[7–10] Current data regarding outcomes for PCT and its impact on mortality are limited by study design and variability of outcomes, with some investigators calling for a robust review of outcomes from tertiary centers with a history of performing PCT.[11] This variability of data, much of it conflicting, leaves treating physicians to rely on surgical gestalt to decide which patients would best be served by PCT versus cholecystectomy.

Given this uncertainty regarding indications for PCT, the acute care surgery and interventional radiology groups at our University-based, tertiary referral center performed a retrospective review of our experience to identify independent predictors of eventual interval cholecystectomy versus destination cholecystostomy and evaluate the appropriateness of our use of PCT for the treatment of cholecystitis.

Methods

Database and study population

All patients with cholecystitis initially treated with PCT at the University of Utah Hospital from January 2014 to March 2017 were stratified by whether they underwent non-operative management with either destination PCT or PCT with subsequent tube removal (no-cholecystectomy group) or underwent interval cholecystectomy and entered into a database (n = 165). Follow up was obtained from chart review up to November 2018. In most cases, the decision to pursue PCT over cholecystectomy was based on our institutional protocol for the management of acute cholecystitis and attending surgeon judgement (Fig. 1). This protocol was derived from the Tokyo 2013 guidelines, a thorough literature review, and the consensus of the acute care surgery service at the University of Utah. For Tokyo Grade II cholecystitis every effort is made to perform an early (within 48 h) laparoscopic cholecystectomy if the patient is an appropriate surgical candidate. If the patient is a poor candidate for general anesthesia, has had symptoms for more than 72 h, or has advanced metastatic disease, PCT is considered. For Grade III cholecystitis PCT is more strongly considered, unless the patient is an otherwise acceptable surgical candidate that resuscitates appropriately and can then have a laparoscopic cholecystectomy. The ultimate decision to proceed with PCT or not for acute cholecystitis was made by the attending acute care surgeon and interventional radiologist in all cases.

Percutaneous cholecystostomy tubes are placed under imaging guidance by the interventional radiology service. Ultrasound is performed of the right upper quadrant. Typically, a trans-hepatic approach is chosen to enter the gallbladder, with moderate sedation used for nearly all cases. An 18G Chiba needle (Cook Medical, Bloomington, IN) is inserted into the gallbladder, and using Seldinger technique, a 10 Fr multipurpose drain is then placed. The gallbladder is decompressed by aspirating all bile from the gallbladder, and a sample is sent for gram stain and culture. A small amount of contrast is injected to confirm location of the cholecystostomy tube.

The decision to leave the drain in as destination therapy, remove the drain, or proceed to interval cholecystectomy was based on clinical status and surgeon judgement. Patients with destination therapy are discharged from surgery service follow up once the episode of acute cholecystitis has resolved and are subsequently followed by interventional radiology clinic for tube checks and exchanges. Most patients are seen every 12 weeks for cholecystostomy exchange. The existing cholecystostomy is removed over a wire and a new drain of the same size is placed. The exchange is a quick procedure (usually less than 30 min) performed as an outpatient.

Demographic data, initial laboratory values, Tokyo Grade (2013), Charlson Comorbidity Index, American Society of Anesthesiologists Physical Status Classification (ASA Class), complications related to cholecystostomy, complications related to cholecystectomy, and mortality data were retrospectively collected. Race was self-reported and divided into White, Hispanic, and other. Comorbidities were obtained from each patient's medical record and used to calculate the Charslon Comorbidity Index.[12] Comorbid conditions were defined as follows using previously published guidelines: cardiovascular disease: coronary artery disease, New York Heart Association functional classification system III or IV, moderate to severe valve disease, peripheral vascular disease, cerebral vascular disease; pulmonary disease: chronic obstructive pulmonary disease, pulmonary fibrosis, chronic bronchitis; malignancy: not including nonmelanoma skin cancer, with or without metastases; chronic renal insufficiency: glomerular filtration rate less than 60 mL/min/1.73m2, baseline creatinine more than 1.5 mg/dL; liver disease: moderate to severe liver disease; organ failure: as defined by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference.[13] ASA Class was recorded in most cases in the procedure note for the cholecystostomy tube. In instances where it was not recorded, a single author (A.C.) reviewed the chart and assigned an ASA Class based on published guidelines.[14]

Statistical analysis

Student's t-test, chi-squared test, and Fisher's exact test were used as appropriate. Univariable Poisson regression was performed to identify variables associated with having an interval cholecystectomy. Variables with a p-value <0.2 were considered clinically relevant and included in the multivariable model to reduce residual confounding. Multivariable Poisson regression was then performed to identify independent predictors of proceeding to interval cholecystectomy or not. The Poisson regression approach directly estimates the risk ratio in cohort study designs, or prevalence ratio in cross-sectional designs, which is more intuitive to interpret than an odds ratio from a logistic regression approach.[15] The regression analysis was performed twice, once using the presence of gallstones as a variable, and subsequently, a sensitivity analysis performed which only analyzed patients with calculous cholecysitis. This was done as it was presumed that having acalculous cholecystitis is a relative contraindication for cholecystectomy. A p-value of < 0.05 was considered statistically significant. All analyses were performed using STATA15 (StataCorp, 2018, Stata Statistical Software, Release 15, College Station, TX).

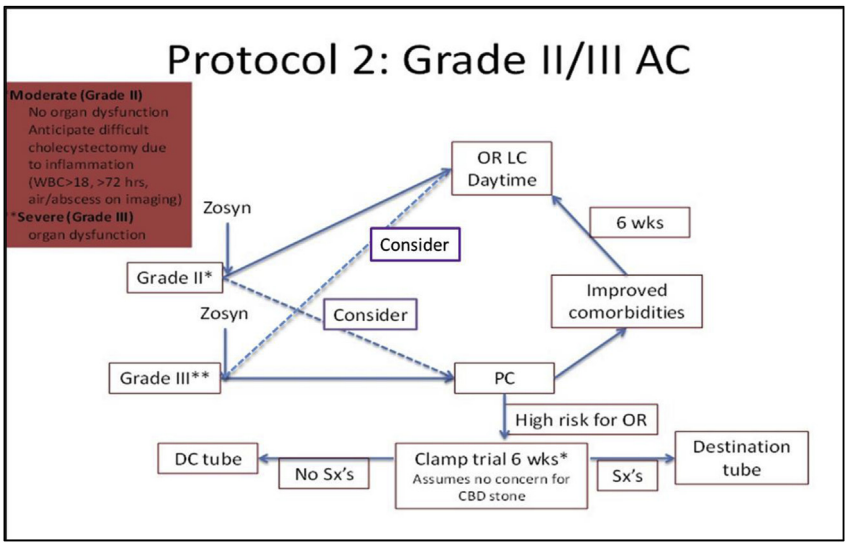

Fig. 1. Grade II and III Acute Cholecysitis Protocol.
DC, discontinue; LC, laparoscopic cholecystectomy; PC, percutaneous cholecystostomy tube; OR, operating room; Sx's, symptoms.
For Grade II cholecystitis the patient should have early cholecystectomy if possible, unless poor surgical candidate or prolonged duration of symptoms precludes safe operation. For Grade III cholecysitis consideration should be for cholecystostomy tube unless patient is otherwise an appropriate surgical candidate and responds to resuscitation.

Results

Baseline characteristics

A total of 165 patients underwent PCT to treat cholecystitis. Subsequently 61 (37%) patients went on to have an interval cholecystectomy, 104 (63%) did not and comprise the no-cholecystectomy group. Demographics are summarized in Table 1. Patients were evenly balanced by gender, with 53.3% male. Mean age was 60.9 (±18.8). The no-cholecystectomy group was significantly older (65.2 (±17.2) vs. 52.5 (±19.4), $p < 0.001$) than the interval cholecystectomy group. Patient race followed expected patterns in Utah; 123 (74.6%) identified as White, 23 (13.9%) as Hispanic, and 15 (9.1%) were grouped as other, which included Black, Asian, Pacific Islander, and Native American. Four patients did not have a listed race. There was no difference between the

Table 1
Demographics.

Variable	Total (165)	No Cholecystectomy (104)	Interval Cholecystectomy (61)	p-value
Age	60.87 (±18.84)	65.19 (±17.18)	53.0 (±19.38)	<0.001
Gender				
Male	88 (53.6%)	58	31	
Female	77 (46.7%)	46	30	0.413
Race				
White	123 (74.6%)	78	45	
Hispanic	23 (13.9%)	15	8	
Other	15 (9.1%)	9	6	
Missing	4 (2.4%)	2	2	0.933
Tokyo Grade				
I	21 (12.7%)	10	11	
II	112 (67.9%)	67	45	
III	32 (19.4%)	27	5	0.008
Body Mass Index, kg/m^2	29.5 (±9.94)	28.6 (±10.19)	31.62 (±9.96)	0.127
White Blood Cell Count, $10^3/dL$	14.5 (±7.78)	14.25 (±7.63)	15.16 (±8.14)	0.812
Bilirubin, *mg/dL*	2.98 (±3.68)	3.67 (±4 .30)	1.80 (±1.75)	0.002
Aspartate Aminotransferase, *IU/L*	95.44 (±133.18)	116.96 (±156.63)	50.62 (±59.55)	0.002
Alanine Aminotransferase, *IU/L*	85.91 (±117.04)	105.25 (±135.54)	52.93 (±64.45)	0.005
Alkaline Phosphatase, *IU/L*	207.87 (±213.79)	252.57 (±247.66)	131.62 (±100.45)	<0.001
Albumin, *g/dL*	3.27 (±0.69)	3.05 (±0.63)	3.64 (±0.63)	<0.001
ASA[a] Class				
I	2 (1.2%)	0	2	
II	81 (49.1%)	43	38	
III	67 (40.6%)	49	18	
IV	15 (9.1%)	12	3	0.007
Charlson Comorbidity Index	4.6 (±3.02)	5.6 (±2.68)	2.9 (±2.82)	<0.001
Cholecystitis				
Acalculous	25 (15.1%)	24	1	
Calculous	140 (84.9%)	80	60	<0.001
Mortality	46 (27.9%)	45	1	<0.001

Values reported as n(%) or mean(±SD).
[a] ASA, American Society of Anesthesiologists.

interval cholecystectomy and the no-cholecystectomy group with regards to race.

The no-cholecystectomy group had a larger proportion of higher Tokyo Grade acute cholecystitis, with 10 grade I (9.6%), 67 grade II (64.4%), and 28 grade III (26.0%) versus 11 (18.0%), 45 (73.8%), and 5 (8.2%) respectively in the interval cholecystectomy group, $p = 0.008$. Body mass index and white blood cell count were not significantly different. Patients in the no-cholecystectomy group had higher overall liver function tests and lower albumin. The proportion of patients with a higher ASA Class was significantly higher in the no-cholecystectomy group; class I: 0 vs 2; class II: 43 vs 38, class III: 49 vs 18, class IV: 12 vs 3, $p = 0.007$. The no-cholecystectomy group also had significantly higher Charlson Comorbidity Index scores 5.60 (±2.68) vs 2.90 (±2.82), $p < 0.001$. Patients with acalculous cholecystitis were more likely to not have an interval cholecystectomy, 24 vs 1, $p < 0.001$. Data for days of symptoms at presentation was available for 124 patients precluding statistical analysis. Mean days of symptoms was 6.48 (±8.68) for the entire cohort and 7.1 (±10.6) for the interval cholecystectomy group.

Outcomes

There were 46 deaths in the full cohort, corresponding to a 27.9% mortality. The no-cholecystectomy group accounted for the vast majority of mortalities, with 45 deaths. The one death in the interval cholecystectomy group was not related to surgery. Complications from PCT and interval cholecystectomy are summarized in Table 2. There were 54 complications from PCT itself for an overall complication rate of 32.7%. The first 27 (50%) were displaced tubes treated with tube replacement. The next 26 (48.1%) were various minor complications including displaced tubes that were not replaced. The final complication was one pulmonary embolus treated with anticoagulation. Four patients were lost to follow up. After interval cholecystectomy, there were three minor complications and one bile leak treated with ERCP and common bile duct stent for a complication rate of 6.5%. In this group, eight patients were lost to follow up.

The 104 patients in the no-cholecystectomy group had a mortality rate of 43.3% during the study period. Twenty-nine (27.9%) patients had advanced metastatic cancer, and 23 (22.1%) patients died of their cancer during the study period. Fifty-four (57.9%) patients were considered poor surgical candidates due to due medical comorbidities, and 18 (17.3%) patients died of their medical comorbidities. In the follow up period, 47 patients had their destination PCT removed in clinic. Of these, five (10.6%) had recurrent cholecysitis. One patient recurred two years after tube removal and had a destination PCT placed due to his medical comorbidities precluding surgery. One patient initially refused cholecystectomy but had an interval cholecystectomy after recurring. Two patients were treated with antibiotics only after their recurrences. The final patient had acalculous cholecystitis during treatment for chronic myelogenous leukemia (CML), recovered and had the PCT removed. During subsequent bone marrow transplant this individual developed colon ischemia which involved the gallbladder and had an emergency colectomy and cholecystectomy.

Table 2
Complications.

Complications from interval cholecystectomy	4 (6.5%)
bleeding from trochar site	1
intraabdominal bleed	1
e.coli sepsis	1
bile leak	1
Complications from cholecystostomy tube	54 (32.7%)
Tube displacement/replacement	27
Other (site infection, tube accidentally pulled, leaking)	26
Pulmonary Embolism	1

There were 25 patients with acalculous cholecystitis, 24 were treated with PCT only, except for the aforementioned patient with CML. Sixteen (64%) of these patients died within the study period. The majority of these patients had advanced cancer, two were polytrauma patients that developed acalculous cholecysitis while in the Surgical Intensive Care Unit, two patients developed acalculous cholecystitis while critically ill in the Medical Intensive Care Unit. Only 6 (24%) patients ultimately had their PCT removed. The remaining patients with destination PCT were deemed to have too many comorbidities for surgery and not able to be medically optimized.

Regression analysis

Univariate Poisson regression with cholecystitis type as a variable identified the following covariates as associated with a lower likelihood of interval cholecystectomy: Tokyo Grade III cholecystitis; increasing age; increasing bilirubin; increasing alkaline phosphatase; increasing aspartate aminotransferase; increasing alanine aminotransferase; ASA Class II, III, and IV; and higher Charlson Comorbidity Index. Increasing albumin level and the presence of calculous cholecystitis were associated with a higher chance of progressing to interval cholecystectomy. Body Mass Index was included in the multivariable regression as it had a $p < 0.2$ (Table 3).

Multivariable Poisson regression with cholecystitis type as a variable showed that increasing Tokyo Grade II (IRR 0.662, $p = 0.044$, 95% CI 0.443–0.990); III (IRR 0.434, $p = 0.042$, 95% CI 0.194–0.969); and Charlson Comorbidity Score (IRR 0.890, $p = 0.026$, 95% CI 0.803–0.986) were independently associated with a lower likelihood of interval cholecystectomy. Increasing albumin (IRR 1.580, $p = 0.011$, 95% CI 1.111–2.244) was independently associated with having an interval cholecystectomy (Table 4).

Regression analysis for the calculous cholecystitis subgroup produced similar results. Higher Tokyo Grade, increasing age, increasing liver function test, higher Charlson Comorbidity Index, and higher ASA Class were associated with a lower chance of having an interval cholecystectomy in univariate analysis. Higher albumin was associated with having an interval cholecystectomy. White blood cell count was included in the multivariable model as it had a $p < 0.2$. The multivariable regression also did not significant differ from that of the complete population. Tokyo Grade II (IRR 0.589, $p = 0.016$, 95% CI 0.383–0.906); III (IRR 0.407, $p = 0.015$, 95% CI 0.197–0.841); and Charlson Comorbidity Index (IRR 0.895, $p = 0.27$, 95% CI 0.812–0.988) were independently associated with no-cholecystectomy. Higher albumin (IRR 1.706, $p = 0.001$, 95% CI 1.229–2.368) and white blood cell count (IRR 1.039, $p = 0.001$, 95% CI 1.016–1.063) were independently associated with interval cholecystectomy. These data are summarized in Appendix 1 (Tables 5 and 6).

Discussion

As surgical technology has improved, we have seen a shift in the treatment of gallbladder disease from open cholecystectomy for acute cholecystitis only, to laparoscopic cholecystectomy for acute cholecystitis, symptomatic cholelithiasis, and biliary dyskinesia. In effect, as the surgery becomes easier and more tolerable for patients, many more gallbladders are removed. In a retrospective review of cases at our academic tertiary referral center, we found

Table 3
Univariable Poisson Regression of factors associated with interval cholecystectomy.

Variable	IRR (95% CI)	p-value
Male Gender	0.847 (0.568–1.262)	0.414
Tokyo Grade		
I	reference	
II	0.767 (0.481–1.224)	0.266
III	0.298 (0.121–0.738)	0.009
Race		
White	reference	
Latino	0.951 (0.518–1.746)	0.871
Other	1.093 (0.562–2.124)	0.792
Unknown	1.366 (0.498–3.753)	0.545
Body Mass Index	1.013 (0.995–1.031)	0.150
Age	0.980 (0.971–0.990)	<0.001
White Blood Cell Count	1.00 (0.978–1.028)	0.808
Bilirubin	0.842 (0.751–0.943)	0.003
Alkaline Phosphatase	0.996 (0.992–0.998)	0.003
Aspartate Aminotransferase	0.994 (0.990–0.998)	0.006
Alanine Aminotransferase	0.995 (0.992–0.999)	0.014
Albumin	2.266 (1.685–3.048)	<0.001
ASA Classification		
I	reference	
II	0.469 (0.372–0.592)	<0.001
III	0.269 (0.181–0.399)	<0.001
IV	0.200 (0.072–0.552)	0.002
Charlson Comorbidity Index	0.817 (0.780–0.879)	<0.001
Calculous Cholecystitis	10.714 (1.546–74.241)	0.016

that our experience is in line with currently published data and that we were able to treat complicated acute cholecystitis safely.

Our review shows that patients requiring PCT had a markedly high mortality rate of 30% and that 98% of these deaths occurred in the group who were not operative candidates. Destination PCT is reserved for the sickest patients and that selection for interval cholecystectomy is made appropriately. These patients had a prohibitive surgical risk at presentation, either due to comorbidities or due to duration of symptoms and are treated in accordance with current evidence.[3,13,16]

PCT is a well-established therapy for the treatment of ill patients and/or patients with high Tokyo Grade.[17,18] Using the Tokyo Guidelines for the management of cholecystitis and cholangitis as a decision-making tool is helpful, but has been found by some to be too restrictive.[18,19] Reports of interval cholecystectomy being performed laparoscopically with rates of 78–90% suggest that PCT may be overused in the setting of acute cholecystitis.[20] As percutaneous gallbladder drainage has rapidly increased this newer research suggests that PCT is performed too often, and patients may be burdened with drainage tubes for extended periods of time.[21] Boules et al. at the Cleveland Clinic published in 2016 the fate of PCT tube after placement and found that of their patients with similar age and comorbidity profile to our study, only 32.9% of their patients went on to interval cholecystectomy for similar reasons.[22] Our results also reflect previous work that shows that PCT increases odds of discharge from the hospital but that less than half of patients proceed to interval cholecystectomy.[16] Our PCT experience had a relatively high re-intervention rate, most of which were related to tube dislodgment and the need for repeated interventional radiology procedures.

Table 4
Multivariable Poisson Regression of factors associated with cholecystectomy.

Variable	IRR (95% CI)	p-value
Tokyo Grade		
I	reference	
II	0.662 (0.443–0.990)	0.044
III	0.434 (0.194–0.969)	0.042
Body Mass Index	1.008 (0.993–1.023)	0.288
Age	0.995 (0.982–1.008)	0.452
Bilirubin	0.971 (0.904–1.043)	0.426
Alkaline Phosphatase	0.999 (0.996–1.001)	0.272
Aspartate Aminotransferase	0.998 (0.996–1.001)	0.270
Alanine Aminotransferase	1.000 (0.996–1.005)	0.760
Albumin	1.580 (1.111–2.244)	0.011
ASA Class		
I	reference	
II	0.785 (0.513–1.200)	0.264
III	0.919 (0.537–1.575)	0.759
IV	0.886 (0.288–2.274)	0.832
Charlson Comorbidity Index	0.890 (0.803–0.986)	0.026
Calculous Cholecystitis	5.624 (0.891–35.494)	0.066

A major concern is that we are still overusing PCT as we had a low proportion of patients progressing to cholecystectomy (37%). For the 61 interval cholecystectomy patients the most common reason for placement of PCT was duration of symptoms at presentation. We suspect this may be due to our institution's position as a major referral center, serving five largely rural states where patients may have difficulty accessing surgical care in a timely manner. Over half of the patients in the no-cholecystectomy group had advanced cancer or severe comorbidities at presentation. That we were able to remove almost half of the PCTs with a relatively low recurrence rate indicates that PCT should be strongly considered as an appropriate treatment for this group.

We further demonstrated that interval cholecystectomy can be completed on properly selected patients without a high rate of complications, consistent with Khasawneh's and colleagues' findings in their 2015 study.[20] This underlines the importance of medically optimizing post-PCT patients who are appropriate to undergo interval cholecystectomies. Larger, multi-center studies are necessary to better define this cohort of patients. Newer interventions, including endoscopic gallbladder drainage, also hold promise for patients who are not fit to undergo surgical intervention.[23] After this review, our group has moved toward more aggressive attempts at laparoscopic cholecystectomy at presentation in otherwise healthy patients whose only risk factor for complicated cholecystectomy is duration of symptoms. This has been shown to be safe even if symptoms have been present longer than 72 h.[24]

This study has limitations associated with all retrospective reviews. We adjusted for severity of illness at presentation, Charlson Comorbidity Index, lab values, and age to attempt to capture the overall operative risk that drove the decision to place a PCT initially and then to progress to interval cholecystectomy or not. Selection bias may have occurred with surgeon discretion being the ultimate deciding factor in PCT placement. As we limited our analysis to look at initial factors at the time of PCT placement that were associated with eventual interval cholecystectomy, there may be issues with patients lost to follow-up and decisions regarding non-operative patients discharged from the surgery service that we could not account for. Finally, this is a single-center study at an institution that serves a large geographic catchment area. Remote patients may have limited access to acute care surgical services, and therefore may present later with more advanced diseases than other urban centers.

Conclusion

Percutaneous cholecystostomy tube serves an important function for patients with cholecystitis who are unable to undergo immediate cholecystectomy safely. Increasing Tokyo Grade and comorbidity status were the primary predictors of need for destination cholecystostomy tube, while good nutritional status predicted interval cholecystectomy. At our academic center, destination PCT is primarily reserved for complex patients who would be unlikely to tolerate surgical intervention, and experience

a high mortality rate even with the most conservative care. Interval cholecystectomy was performed with a very low rate of complications. Further research, such as the ongoing Dutch CHOCOLATE Trial, is needed to better delineate populations appropriate for surgical intervention versus PCT and timing of each procedure.[10]

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2019.04.002.

Appendix 1

Table 5
Univariable Poisson Regression of factors associated with interval cholecystectomy for calculous cholecystitis.

Variable	IRR (95% CI)	p-value
Male Gender	0.909 (0.619–1.385)	0.627
Tokyo Grade		
I	reference	
II	0.727 (0.469–1.127)	0.154
III	0.320 (0.133–0.767)	0.011
Race		
White	reference	
Latino	0.883 (0.489–01.59)	0.680
Other	1.070 (0.570–2.001)	0.834
Unknown	1.159 (0.423–3.178)	0.774
Body Mass Index	1.001 (0.991–1.025)	0.372
Age	0.979 (0.970–0.987)	<0.001
White Blood Cell Count	1.02 (0.995–1.040)	0.135
Bilirubin	0.876 (0.788–0.974)	0.015
Alkaline Phosphatase	0.996 (0.993–0.999)	0.011
Aspartate Aminotransferase	0.995 (0.992–0.999)	0.008
Alanine Aminotransferase	0.996 (0.993–0.999)	0.016
Albumin	2.131 (1.579–2.876)	<0.001
ASA Classification		
I	reference	
II	0.535 (0.431–0.665)	<0.001
III	0.309 (0.208–0.460)	<0.001
IV	0.250 (0.093–0.668)	0.006
Charlson Comorbidity Index	0.827 (0.771–0.887)	<0.001

Table 6
Multivariable Poisson Regression of factors associated with interval cholecystectomy for calculous cholecystitis.

Variable	IRR (95% CI)	p-value
Tokyo Grade		
I	reference	
II	0.589 (0.383–0.906)	0.016
III	0.407 (0.197–0.841)	0.015
White Blood Cell Count	1.039 (1.016–1.063)	0.001
Age	0.995 (0.982–1.008)	0.438
Bilirubin	0.988 (0.915–1.068)	0.770
Alkaline Phosphatase	0.999 (0.996–1.001)	0.316
Aspartate Aminotransferase	0.997 (0.992–1.001)	0.151
Alanine Aminotransferase	1.002 (0.997–1.007)	0.444
Albumin	1.706 (1.229–2.368)	0.001
ASA Class		
I	reference	
II	0.633 (0.406–0.988)	0.044
III	0.707 (0.425–1.176)	0.182
IV	0.625 (0.196–1.994)	0.428
Charlson Comorbidity Index	0.895 (0.812–0.988)	0.027

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