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Operative vs Nonoperative Treatment of Acute Cholecystitis in Older Adults With Multimorbidity

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Supplemental content

IMPORTANCE Acute cholecystitis in older patients with multimorbidity is associated with a high risk of morbidity and mortality. Debate exists as to whether operative or nonoperative treatment is the most appropriate approach.

OBJECTIVES To compare the effectiveness of operative and nonoperative treatment in older adults with multimorbidity who are hospitalized emergently with acute cholecystitis.

DESIGN, SETTING, AND PARTICIPANTS This was a nationwide retrospective comparative effectiveness research study conducted in the US from 2016 to 2018 that used both an inverse propensity weight analysis and an instrumental variable analysis. The study participants were Medicare beneficiaries with multimorbidity hospitalized emergently with acute cholecystitis. Previously validated qualifying comorbidity sets were used to identify multimorbidity. Data were analyzed from April 1, 2016, to December 31, 2018.

EXPOSURES Treatment assignment of operative or nonoperative treatment for acute cholecystitis.

MAIN OUTCOMES AND MEASURES The primary outcome was 30- and 90-day mortality. Secondary outcomes included readmission rates, emergency department (ED) revisit rates, and cost. A preference-based instrumental variable approach was used to isolate circumstances for which the decision to operate is in clinical equipoise. Our hypothesis was that operative treatment would be associated with decreased mortality compared with nonoperative management.

RESULTS Among the 32 527 included patients, the median age was 78.8 years (IQR, 72.4-85.2 years), and 21 728 patients (66.8%) underwent cholecystectomy. Of the 10 799 patients (33.2%) who received nonoperative treatment, 3462 (32.1%) received a percutaneous cholecystostomy tube. Among all patients, operative treatment was associated with a lower risk of 30-day mortality (risk difference [RD], −0.03; $P < .001$) and 90-day mortality (RD, −0.04; $P < .001$) compared with nonoperative treatment. Among patients for whom the treatment decision was in clinical equipoise, mortality was similar for the operative and nonoperative treatment groups; operative treatment was associated with a lower risk of 30-day readmissions (RD, −0.15; $P < .001$) and 90-day readmissions (RD, −0.23; $P < .001$) as well as a lower risk of 30-day ED revisits (RD, −0.09; $P < .001$) and 90-day ED revisits (RD, −0.12; $P < .001$). The risk-adjusted cost of operative treatment was higher at the index hospitalization (+$2870.84; $P < .001$) and lower at 90 days (−$5495.38; $P < .001$) and 180 days (−$9134.66; $P < .001$) compared with nonoperative treatment.

CONCLUSIONS AND RELEVANCE The findings of this comparative effectiveness research study suggest that risk-adjusted operative treatment of acute cholecystitis in older patients with multimorbidity was associated with lower rates of 30- and 90-day readmissions and ED revisits compared with nonoperative treatment and a lower cost by 90 days. These findings further suggest that when uncertainty exists regarding the most appropriate treatment approach for this challenging population, strong consideration should be given to operative treatment.

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Key Points

Question Is operative or nonoperative treatment better for treating acute cholecystitis in older adults with multimorbidity?

Findings In this comparative effectiveness research study including 32 527 older adults with multimorbidity and acute cholecystitis, operative treatment was associated with similar mortality rates, lower readmission rates, lower emergency department revisit rates, and lower cost by 180 days after hospitalization when compared with nonoperative treatment.

Meaning These findings suggest that in older patients with multimorbidity for whom the management decision is in clinical equipoise, operative treatment should be considered.

The prevalence of gallstone disease has doubled over the last 3 decades in the US,[1] resulting in the use of significant health care resources and an average cost of $48 000 per admission.[2] Treatment with antibiotics alone fails in an estimated 23% of patients, and approximately 27% of patients who do not receive up-front surgery ultimately require unplanned, emergent surgery in the future.[3] Many older patients receive percutaneous cholecystostomy tubes as the initial treatment.[4] Previous published data show that up-front surgery for acute cholecystitis is associated with decreased rates of biliary complications, morbidity, and readmission, as well as decreased length of stay and overall cost.[5-12] However, despite these data, there continues to be wide variation in the initial treatment of acute cholecystitis.[3,9,11,13-17] Furthermore, these studies focused on all adult patients, without a clear focus on the patients for whom the decision to operate is often the most challenging: older patients with multiple medical conditions.

Aging is often accompanied by an accrual of comorbidities, and specific combinations of these conditions confer increased risk of death and serious morbidity in a surgical setting. This phenomenon is known as multimorbidity, and it contributes to particularly challenging decision-making in emergency general surgery.[18,19] The World Society of Emergency Surgery Consensus guidelines advocate for up-front, early laparoscopic cholecystectomy even in patients who are pregnant, are older, and have cirrhosis,[3] but these data are not based on large comparative studies. Other studies demonstrate increased rates of major complications and postoperative morbidity and mortality for older patients undergoing surgery compared with younger patients (up to 7-fold in patients aged >80 years).[9,14] However, to date there are no large national studies comparing operative and nonoperative management of acute cholecystitis in a population of older adults with multimorbidity, leaving the optimal treatment course unknown.

We therefore performed a comparative effectiveness study of operative vs nonoperative treatment for acute cholecystitis in older patients with multimorbidity who presented to the emergency department (ED). We hypothesized that operative intervention would be associated with lower mortality and readmission rates.

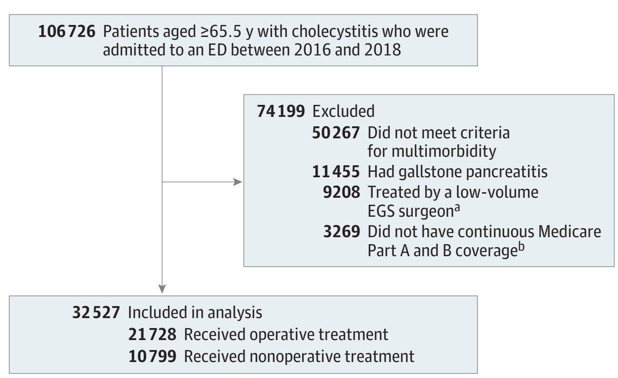
Methods

This comparative effectiveness research study was approved by the University of Pennsylvania Institutional Review Board. The requirement of informed consent was waived owing to the use of deidentified data. The study was performed in compliance with the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) reporting guideline.

Data Sources and Patient Population

This was a national retrospective comparative effectiveness research study of multimorbid Medicare beneficiaries aged 65.5 years and older who were admitted through the ED with a principal diagnosis of cholecystitis over a 3-year period (from 2016 to 2018). The cohort was defined using Medicare inpatient, master beneficiary, and Part B carrier claims files in accordance with previously described methods.[20] To define multimorbidity, we used qualifying comorbidity sets defined by Silber et al[19] and others[18,21] to identify patients for study inclusion. Comorbidity sets include specific combinations of comorbidities that have been shown to be associated with higher rates of death and serious morbidity in surgical patients, rather than providing a sum of the total number of medical problems per patient. We used *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) codes to identify patients with cholecystitis. Patients with choledocholithiasis were only included if they also had cholecystitis (eTables 1 and 2 in the Supplement). Patients with gallstone pancreatitis were excluded (**Figure 1**). We allowed for a 6-month look-back period to confirm the diagnoses and comorbidities. Patients were excluded if they were not enrolled in continuous Medicare Part A and B coverage or if they were enrolled in a health maintenance organization plan in the 6 months before or after their index admission.

Figure 1. Study Flow Diagram



ED indicates emergency department, EGS, emergency general surgery.

[a]Surgeons who performed 5 or fewer emergency general surgery operations per year on Medicare patients (ie, we were unable to calculate surgeon tendency to operate).

[b]Patients who were not enrolled in health maintenance organization coverage 6 months before and 6 months after their index emergency general surgery admission.

Exposure

Operative management was the exposure of interest, which was defined using *International Statistical Classification of Diseases, Tenth Revision* procedure and *Current Procedural Terminology* codes (eTable 3 in the Supplement). Patients were considered to have operative management if they underwent an operation during their index hospitalization. Patients who underwent both a procedure and an operation within this time frame (ie, endoscopic retrograde cholangiopancreatography followed by laparoscopic cholecystectomy) were considered operative patients. Patients who underwent only procedures such as percutaneous cholecystectomy were considered nonoperative.

Outcomes

Our primary outcome was mortality measured at 30 and 90 days after hospitalization. Secondary outcomes included 30- and 90-day readmission rates (excluding patients that died during these periods) and 30- and 90-day ED revisit rates. Reasons for readmission and ED revisit were also collected by examining the principal diagnoses for these visits. Cost was also examined for index admission and at 30, 90, and 180 days after hospitalization. Patients who died during or after the index hospitalization were excluded from the cost analyses for each respective time interval.

Covariates

Covariates included age, sex, race and ethnicity, dual eligibility for Medicare and Medicaid, transfer status (ie, from one hospital to another), year of admission, individual comorbid conditions,[22] and principal diagnosis category. Race and ethnicity data were collected to control for potential confounding owing to the known differences in surgical consultation receipt based on patient race and ethnicity in an emergency general surgery setting.[23] Frailty was calculated using the Claims-Based Frailty Index.[24] The presence of septic shock on admission was defined using the previously validated Angus criteria, which requires both a code for a qualifying infection and a code indicating the presence of end-organ dysfunction.[20,25] This was included because the degree of critical illness is important in operative decision-making and risk of mortality.

Statistical Analysis

Descriptive statistical analyses were performed, including imaging modality used for diagnosis, the type of operation, and additional procedures (such as endoscopic retrograde cholangiopancreatography) performed during the index hospitalization. Univariate analyses were performed using generalized Wilcoxon and χ^2 tests to compare unadjusted outcomes.

We used balancing weights, an alternative form of estimation for inverse propensity score weights (IPWs), to control for measurable confounders.[26] The balancing weights minimize differences in the distribution of 65 different covariates between operative and nonoperative patients. To evaluate balance across the groups, the absolute standardized mean differences between groups were calculated, and covariates with differences of less than 0.10 were considered well balanced.

To evaluate the effectiveness of operative treatment across the entire population of older, multimorbid patients with acute cholecystitis, we estimated the average treatment effect of the treated (ATT). The ATT reflects the difference in mean outcomes of all patients in our cohort who received operative treatment compared with those who received nonoperative treatment. This was done using a linear regression model after application of balancing weights across the treatment groups (IPW analysis). This approach allowed us to assess all included patients.

Not all patients are offered both treatments, as treating physicians may consider that certain patients clearly require surgery and that certain other patients could not sustain surgery. To address the role of this selection bias in treatment assignment, an instrumental variable analysis was performed to control for selection bias due to unobservable factors such as patient physiology. In prior work, a preference-based instrumental variable (PBIV) was validated for use in emergency general surgery,[20,27] and we used this PBIV to control for selection bias. The PBIV represents an individual surgeon's preference for operative treatment and is calculated as the number of operations performed divided by the number of total hospitalizations for the same condition. To ensure the strength of the instrumental variable, patients who were treated by surgeons with 5 or fewer emergency general surgery operations per year were excluded. The PBIV analysis quantifies the local average treatment effect (LATE), or the treatment effect among patients for whom the decision to operate is in clinical equipoise. Unlike the ATT, the LATE measures the treatment effect of only patients who receive operative treatment based on the PBIV assignment. In this way, the PBIV acts as a pseudorandomizer as patients do not select their surgeon when they present to the ED. The PBIV was combined with balancing weights to perform an instrumental variable analysis.

The primary analysis was performed comparing the operative and nonoperative treatment groups. Two subsequent analyses (using both an IPW and a PBIV analysis) were performed comparing operative patients to nonoperative patients who underwent percutaneous cholecystostomy tube placement and operative patients to nonoperative patients who did not undergo percutaneous cholecystostomy tube placement.

Data were analyzed from April 1, 2016, to December 31, 2018. All analyses were performed in R, version 4.4.1 (R Project for Statistical Computing) and SAS, version 9.4 (SAS Institute Inc), and a 2-sided $\alpha \le 0.05$ was considered statistically significant. There were no missing data in our cohort. A Bonferroni correction was used on the adjusted outcomes to control for multiple tests.

Results

We identified 32 527 older adults with multimorbidity who were hospitalized emergently for cholecystitis and met inclusion criteria (Figure 1). Their median age was 78.8 years (IQR, 72.4-85.2 years); 17 640 (54.2%) were male, 14 887 (45.8%) were female, and 6388 (19.6%) were eligible for both Medicare and

Table 1. Selected Patient Characteristics Stratified by Treatment Before and After Application of Balancing Weights[a]

Covariate	Operative treatment (n = 21 728)	Unweighted, before balancing (n = 10 799)			Weighted, after balancing (n = 21 728)		
		Nonoperative treatment before balancing	Standard mean difference	P value	Nonoperative treatment after balancing	Standard mean difference	P value
Age, mean (SD), y	78.1 (7.5)	81.2 (8.6)	−3.09	<.001	78.1 (8.0)	<0.01	>.99
Female sex	0.45 (0.50)	0.47 (0.50)	−0.01	.02	0.45 (0.50)	<0.01	
Race and ethnicity							
American Indian or Alaska Native	0.01 (0.08)	0 (0.07)	<0.01	.11	0.01 (0.08)	<0.01	>.99
Asian	0.01 (0.12)	0.02 (0.12)	<0.01	.69	0.01 (0.12)	<0.01	>.99
Black	0.07 (0.25)	0.08 (0.27)	−0.02	<.001	0.07 (0.25)	<0.01	>.99
Hispanic	0.02 (0.15)	0.02 (0.15)	<0.01	.52	0.02 (0.15)	<0.01	>.99
White	0.86 (0.34)	0.86 (0.35)	<0.01	.04	0.86 (0.34)	<0.01	>.99
Other[b]	0.01 (0.12)	0.01 (0.11)	<0.01	.32	0.01 (0.12)	<0.01	>.99
Unknown	0.01 (0.10)	0.01 (0.08)	<0.01	.02	0.01 (0.10)	<0.01	>.99
Year of admission							
2016	0.27 (0.45)	0.28 (0.45)	−0.01	.26	0.27 (0.45)	<0.01	>.99
2017	0.37 (0.48)	0.36 (0.48)	0.01	.05	0.37 (0.48)	<0.01	>.99
2018	0.36 (0.48)	0.36 (0.48)	−0.01	.35	0.36 (0.48)	<0.01	>.99
Claims-Based Frailty Index	0.18 (0.06)	0.19 (0.07)	−0.02	<.001	0.18 (0.06)	<0.01	>.99
Sepsis	0.11 (0.31)	0.18 (0.38)	−0.07	<.001	0.11 (0.31)	<0.01	>.99
Transfer status[c]	0.05 (0.21)	0.08 (0.27)	−0.03	<.001	0.05 (0.21)	<0.01	>.99
Dual eligibility for Medicare and Medicaid	0.18 (0.38)	0.23 (0.42)	−0.05	<.001	0.18 (0.38)	<0.01	>.99
Comorbid condition							
Congestive heart failure	0.29 (0.45)	0.41 (0.49)	−0.12	<.001	0.29 (0.45)	<0.01	>.99
Uncontrolled diabetes	0.2 (0.40)	0.19 (0.39)	0.01	.09	0.20 (0.40)	<0.01	>.99
Controlled diabetes	0.23 (0.42)	0.24 (0.43)	−0.01	.06	0.23 (0.42)	<0.01	>.99
Severe liver disease	0.01 (0.10)	0.02 (0.14)	−0.01	<.001	0.01 (0.10)	<0.01	>.99
Pulmonary or circulatory disorder	0.07 (0.26)	0.1 (0.30)	−0.03	<.001	0.07 (0.26)	<0.01	>.99
Severe kidney failure	0.08 (0.27)	0.1 (0.31)	−0.03	<.001	0.08 (0.27)	<0.01	>.99

[a] Data are presented as the proportion (SD) unless indicated otherwise. The largest absolute standardized mean difference after balancing was 3.7×10^{-7}.

[b] A further breakdown of race and ethnicity categories is not available in the Medicare claims data.

[c] Refers to transfers between hospitals.

Medicaid. In terms of race and ethnicity, 189 patients (0.6%) were American Indian or Alaska Native, 492 (1.5%) were Asian, 2320 (7.1%) were Black, 752 (2.3%) were Hispanic, 28 035 (86.2%) were White, 444 (1.4%) were of other race or ethnicity, and 295 (0.9%) were of unknown race or ethnicity. For their diagnostic workup, 23 400 patients (71.9%) underwent abdominal ultrasonography, 21 120 (64.9%) underwent computed tomography, and 5262 (16.2%) underwent magnetic resonance imaging.

Among all patients, 21 728 (66.8%) received operative treatment and 10 799 (33.2%) received nonoperative treatment (**Table 1** shows the balancing table with a sample of the covariates; eTables 4-6 in the Supplement show full balancing tables). Of the patients in the operative group, 19 433 (89.4%) received a laparoscopic cholecystectomy, 2535 (11.7%) received an open cholecystectomy, 415 (1.9%) received a common bile duct exploration, and 5823 (26.8%) received an intraoperative cholangiogram (eTable 7 in the Supplement). Of the patients in the nonoperative group, 3462 (32.1%) underwent percutaneous cholecystostomy tube placement. eTable 7 in the Supplement shows the breakdown of diagnosis and treatment type.

Thirty days after their index admission, 11% of the patients who were initially treated nonoperatively underwent a subsequent cholecystectomy; this interval operative rate increased to 28% by 180 days. The rate of interval cholecystectomy by 30 days was significantly higher in patients who initially did not receive a percutaneous cholecystostomy tube compared with those who did (13.4% vs 6.1%; $P < .001$). However, by 90 days, rates of interval cholecystectomy were significantly lower in patients who did not receive a percutaneous cholecystostomy tube during their index hospitalization compared with those who did (22.0% vs 28.3%; $P < .001$) (eTable 8 in the Supplement).

Unadjusted Results

The overall 30-day mortality rate was 5.9% and the 90-day mortality rate was 9.8%. There were significantly lower unadjusted 30- and 90-day mortality rates for patients who underwent operative compared with nonoperative treat-

Table 2. Unadjusted Outcomes of Nonoperative and Operative Treatment

Variable	Patient group: Operative treatment (n = 21 728)	Nonoperative treatment (n = 10 799)	Total (N = 32 527)	*P* value[a]
Mortality, No. (%)				
30 d	811 (3.7)	1101 (10.2)	1912 (5.9)	<.001
90 d	1377 (6.3)	1819 (16.8)	3196 (9.8)	<.001
Readmissions, No. (%)				
30 d[b]	3613 (17.3)	2895 (29.9)	6508 (21.3)	<.001
90 d[c]	4949 (24.3)	3911 (43.6)	8860 (30.2)	<.001
ED revisits, No. (%)				
30 d	2673 (12.3)	2113 (19.6)	4786 (14.7)	<.001
90 d	4233 (19.5)	3379 (31.3)	7612 (23.4)	<.001
Cost, median (IQR), 2018 $				
Claim payment amount	11 055.30 (8816.15-14 452.61)	7797.94 (5683.93-10 452.61)	9966.68 (7795.34-13 571.27)	<.001
30 d[b]	14 911.55 (11 427.28-20 495.54)	12 335.58 (8544.15-20 443.19)	14 192.42 (10 668.41-20 475.79)	<.001
90 d[c]	16 461.48 (12 220.20-24381.11)	15 803.77 (9949.94-28 245.66)	16 310.90 (11 621.62-25 572.57)	<.001
180 d[d]	18 060.90 (13 089.81-28 453.92)	18 800.82 (11 253.33-34 235.56)	18 223.42 (12 618.62-30 226.62)	.007

Abbreviation: ED, emergency department.

[a] Calculated with a Wilcoxon rank sum test for cost and χ^2 test for all other variables; the values compare nonoperative vs operative treatment.

[b] Excluding 30-d mortality.

[c] Excluding 90-d mortality.

[d] Excluding 180-d mortality.

ment (3.7% vs 10.2%, respectively, at 30 days; *P* < .001 and 6.3% vs 16.8%, respectively, at 90 days; *P* < .001) (**Table 2**). Unadjusted 30- and 90-day readmissions as well as 30- and 90-day ED revisit rates were also significantly lower in the operative group compared with the nonoperative group. The median cost of operative compared with nonoperative treatment at index admission was $11 055.30 and $7797.94, respectively (*P* < .001), but by 180 days after index hospitalization, the median cost was significantly lower in the operative group compared with the nonoperative group ($18 060.90 vs $18 800.82, respectively; *P* = .007). Unadjusted comparisons between operative and nonoperative treatment both with and without percutaneous cholecystostomy tubes yielded similar results, with significantly lower rates of 30- and 90- day mortality, readmissions, and ED revisits in the operative group (eTable 9 in the Supplement). Costs were significantly higher among patients in the operative group compared with patients in the nonoperative group who underwent percutaneous cholecystostomy tube placement until 90 days, when operative treatment was associated with significantly less cost. The same relationship was observed between operative and nonoperative patients without percutaneous cholecystostomy tube placement through 180 days (eTable 9 in the Supplement). The proportion of 30- and 90-day readmissions and ED revisits related to recurrent cholecystitis and other biliary diseases such as choledocholithiasis were lower in the operative group compared with the nonoperative group (eTables 10-13 in the Supplement). For example, only 2.7% of patients in the operative group were readmitted for acute cholecystitis, whereas in the nonoperative group, 19.7% of the 30-day readmissions were due to recurrent, acute cholecystitis. Sepsis (6.4%) and postprocedural infection (4.8%) were the most frequent diagnoses associated with 30-day readmissions among patients in the operative group. Complications related to exacerbations of underlying patient comorbidities such as kidney failure, heart failure, urinary tract infection, and myocardial infarction were also common diagnoses for patients who underwent operative treatment and were readmitted within 30 days of discharge.

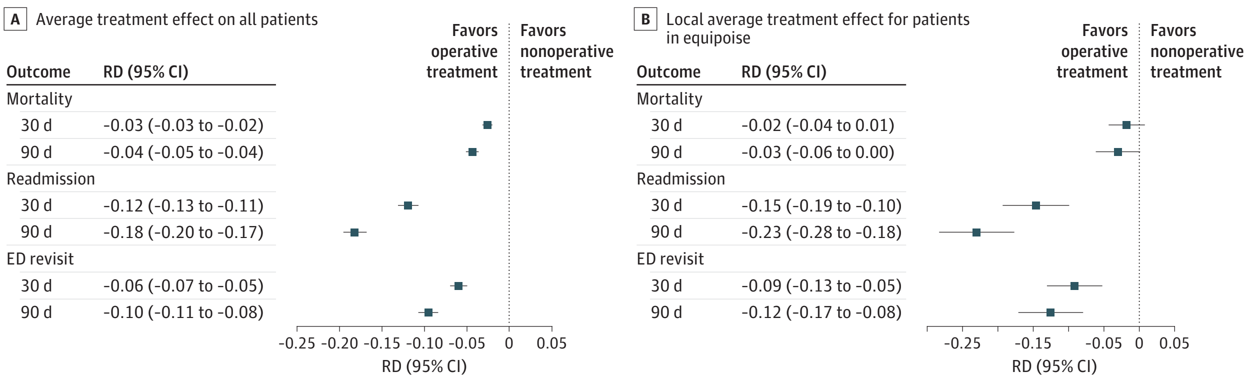
Adjusted Results: IPW Analysis (All Patients)

Operative treatment was associated with significantly lower 30-day mortality (risk difference [RD], −0.03; *P* < .001) and 90-day mortality (RD, −0.04; *P* < .001) (**Figure 2**A) compared to nonoperative treatment. Patients in the operative group had a significantly lower risk of 30- and 90-day readmissions (RD, −0.12 and −0.18, respectively; both *P* < .001), as well as 30- and 90-day ED revisit rates (RD, −0.06 and −0.10, respectively; both *P* < .001) compared with patients in the nonoperative group. Operative treatment was associated with significantly higher cost than nonoperative treatment at the index admission (cost difference compared with nonoperative treatment, +$4083.49; *P* < .001), but this pattern was reversed by 180 days with a negative cost difference favoring operative treatment (−$1459.94; *P* < .001) (**Figure 3**A).

Adjusted Results: Instrumental Variable Model (Patients in Clinical Equipoise)

The instrumental variable model down-weights patients for whom the decision to operate is not in clinical equipoise, as these patients do not have a comparator in the alternative treatment group. The instrumental variable analysis yielded 30- and 90-day mortality risk differences similar to those for the IPW analysis, but these differences did not reach statistical significance (30-day RD, −0.02; *P* = .35 and 90-day RD, −0.03;

Figure 2. Risk-Adjusted Outcome Differences by Treatment Effect



A Average treatment effect on all patients

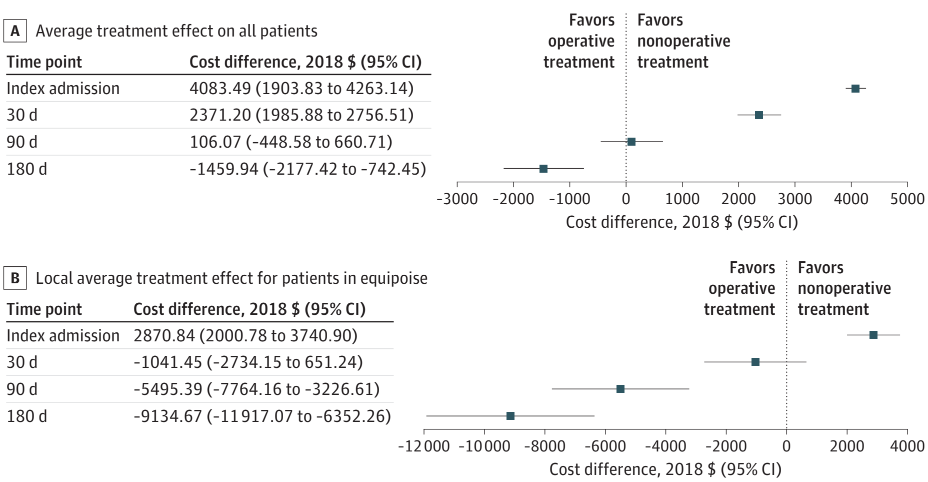
Outcome	RD (95% CI)
Mortality	
30 d	−0.03 (−0.03 to −0.02)
90 d	−0.04 (−0.05 to −0.04)
Readmission	
30 d	−0.12 (−0.13 to −0.11)
90 d	−0.18 (−0.20 to −0.17)
ED revisit	
30 d	−0.06 (−0.07 to −0.05)
90 d	−0.10 (−0.11 to −0.08)

B Local average treatment effect for patients in equipoise

Outcome	RD (95% CI)
Mortality	
30 d	−0.02 (−0.04 to 0.01)
90 d	−0.03 (−0.06 to 0.00)
Readmission	
30 d	−0.15 (−0.19 to −0.10)
90 d	−0.23 (−0.28 to −0.18)
ED revisit	
30 d	−0.09 (−0.13 to −0.05)
90 d	−0.12 (−0.17 to −0.08)

ED indicates emergency department; RD, risk difference.

Figure 3. Risk-Adjusted Cost Differences by Treatment Effect



A Average treatment effect on all patients

Time point	Cost difference, 2018 $ (95% CI)
Index admission	4083.49 (1903.83 to 4263.14)
30 d	2371.20 (1985.88 to 2756.51)
90 d	106.07 (−448.58 to 660.71)
180 d	−1459.94 (−2177.42 to −742.45)

B Local average treatment effect for patients in equipoise

Time point	Cost difference, 2018 $ (95% CI)
Index admission	2870.84 (2000.78 to 3740.90)
30 d	−1041.45 (−2734.15 to 651.24)
90 d	−5495.39 (−7764.16 to −3226.61)
180 d	−9134.67 (−11 917.07 to −6352.26)

P = .12). Operative treatment was associated with significantly lower risk of 30- and 90-day readmissions (30-day RD, −0.15; *P* < .001 and 90-day RD, −0.23; *P* < .001) and 30- and 90-day ED revisit (30-day RD, −0.09; *P* < .001 and 90-day RD, −0.12; *P* < .001) compared with nonoperative treatment (Figure 2B). The same pattern was observed when comparing operative patients with nonoperative patients with percutaneous cholecystostomy tubes (no significant differences in mortality, but lower risk of readmissions and ED revisits in the operative group) (eFigure 1 in the Supplement). When comparing operative patients with nonoperative patients without percutaneous cholecystostomy, risk of 90-day mortality was significantly decreased in the operative group compared with the nonoperative group (eFigure 2 in the Supplement). The adjusted cost was higher in the operative group at index hospitalization (+$2870.84; *P* < .001), favoring nonoperative treatment (Figure 3B). The adjusted cost by 90 and 180 days was significantly lower in the operative group compared with the nonoperative group (−$5495.39; *P* < .001 and −$9134.67; *P* < .001, respectively). For patients who underwent percutaneous cholecystostomy tube placement, a between-group comparison yielded no significant cost difference at index hospitalization but yielded lower cost in the operative group compared with the nonoperative group by 30 days. The same pattern was observed in the operative group compared with the nonoperative group without cholecystostomy by 90 days (eFigures 3 and 4 in the Supplement).

Discussion

This nationwide retrospective comparative effectiveness research study addressed the vexing problem of how to best treat older adults with multimorbidity who are hospitalized with acute cholecystitis. A novel instrumental variable analysis provided evidence for patients who could have reasonably undergone either operative or nonoperative treatment. Furthermore, the IPW analysis yielded data on the average treatment effect across all patients, including those for whom the decision of whether to operate was clear. Across all patients, operative treatment provided a mortality benefit. However, in patients for whom the decision to operate was in clinical equipoise, mortality rates at 30 and 90 days were similar between treatment groups. In addition, among patients who survived the index admission, operative treatment was associated with significantly lower risk of 30- and 90-day readmissions and 30- and 90-day ED revisits compared with nonoperative treatment. Patients in the nonoperative group were primarily readmitted for recurrent biliary disease as opposed to patients in the operative group, who required posthospitalization care primarily for procedural complications and exacerbation of their underlying comorbidities. Patients in the operative group also had lower risk of readmissions and ED revisits compared with patients in the nonoperative group who received a percutaneous cholecystostomy tube. Operative treatment was associated with significantly lower cost of care by 90 days after hospitalization compared with nonoperative treatment.

The overall proportion of patients who received operative treatment in our study (66.8%) is similar to the rates of operative treatment for acute cholecystitis among older patients reported in the literature.[28,29] However, to our knowledge, our study is the first to examine outcomes of operative treatment in a well-defined national cohort of older patients with multimorbidity and the first to use an instrumental variable analysis to control for selection bias.[20,27] Moreover, our cohort was selected using a validated method known to identify patients at risk for higher rates of death and serious morbidity.[18] In this way, this study analyzed the treatment outcomes of one of the most challenging and common patient populations treated in emergency surgery.

The risk-adjusted mortality between our operative and nonoperative treatment groups was similar for patients in clinical equipoise. This critical finding is in contrast with a previous study by Riall et al[9] that found significantly lower mortality rates among patients undergoing operative treatment. The discordant findings most likely reflect our use of an instrumental variable analysis, which permitted the isolation of patients in clinical equipoise. In contrast, the IPW analysis examines the average treatment effect across the whole population, not just those in clinical equipoise. It therefore includes patients who do not have similar counterparts in the opposite treatment group (eg, patients who are so medically complex that no surgeon would reasonably operate on them or patients who are so healthy that most surgeons would offer them an operation). Among all of these patients, we did find a survival benefit of operative treatment, which aligns with the previously published study by Riall et al.[9] However, this finding alone does not necessarily mean that clinicians should favor operative treatment for all patients. There are likely patients in our nonoperative group who would not tolerate an operation given their functional status. The strength, therefore, of the instrumental variable analysis is that it allows us to isolate only patients who could have reasonably undergone both treatment modalities to provide information to clinicians regarding patients for whom the optimal course of treatment is unclear. This analysis, in contrast, did not show a mortality benefit. Furthermore, because previous findings have shown that patients aged 65 years and older who undergo laparoscopic cholecystectomy for acute cholecystitis have significantly increased postoperative mortality compared with younger patients undergoing surgical treatment,[14] many clinicians hesitate to offer operative treatment to older adults. These data refute conclusions that operative treatment of acute cholecystitis is less safe than nonoperative treatment when the treatment decision is in clinical equipoise.

Previously published readmission rates for recurrent cholecystitis in older adults with acute cholecystitis who were treated nonoperatively were as high as 38% by 2 years.[9] The results of this study showed a 90-day readmission rate of 24% in nonoperatively treated patients and a significantly higher risk of 30- and 90-day readmission in nonoperatively treated patients compared with operatively treated patients. At 30 days, patients in the nonoperative group who did not receive a percutaneous cholecystostomy tube had the highest rates of interval cholecystectomy. However, by 90 days, patients who received percutaneous cholecystostomy tubes during their index hospitalization had higher rates of interval cholecystectomy. This could be because patients who do not undergo any gallbladder decompression re-present early with recurrent disease, while those with cholecystostomy tubes re-present later with more elective interval operations; however, additional research into this subset of patients is warranted.

There is a dearth of data on ED revisit rates after hospitalization for acute cholecystitis. One retrospective study of patients with acute cholecystitis found 1-year ED revisit rates of 4% for patients who were initially admitted to the hospital on presentation compared with 20% for those who were discharged from the ED[30]; however, this study examined admission rather than treatment modality. Our findings in older patients with multimorbidity yielded even higher ED revisit rates of 19.6% and 31.3% at 30 and 90 days, respectively, among patients treated nonoperatively. Nonoperatively treated patients also had a significantly higher risk of ED revisits compared with operatively treated patients. These findings indicate the benefit of operative treatment on decreasing overall health care use. Finally, while operative treatment is associated with higher cost during the index admission compared with nonoperative treatment, by 90 days it becomes less expensive, further emphasizing the benefit of cholecystectomy in this patient population.

This study is the first, to our knowledge, to leverage an instrumental variable analysis to compare the effectiveness of operative treatment for acute cholecystitis with nonoperative treatment. Short of performing a large randomized clinical trial, this powerful causal inference technique controls for selection bias and provide causal evidence to support the use of operative vs nonoperative treatment of acute cholecystitis in a population of older patients with multimorbidity.

Limitations

This study has some limitations. As a retrospective cohort study using administrative claims data, any differences in patient physiology that may have influenced a surgeon's decision to operate are unknown. The instrumental variable analysis is designed to control for the impact of unmeasured confounding and helps to mitigate this shortcoming of a retrospective cohort study. We did not examine postoperative complications, which may impact how patients think about which management option to choose. However, it is well established that there is limited accuracy in documentation of surgical complications in Medicare claims data,[31] and we therefore did not include this as part of our analysis. We also did not look beyond 90-day outcomes, so it is possible that some of the differences in outcomes from each treatment modality may be more apparent with longer follow-up time. To quantify a comprehensive picture of health services use in our medically complex population, readmissions for any condition were included. This reflects hospitalization for treatment of underlying comorbidities or readmissions for elective procedures. However, as each hospitalization impacts the likelihood of a subsequent hospitalization, this holistic approach reflected relevant clinical outcomes.

Conclusions

In this comparative effectiveness research study that used a novel instrumental variable analysis in a well-defined population of older patients with multimorbidity and acute cholecystitis, we found that among patients for whom the decision to operate is in clinical equipoise, operative treatment was associated with decreased rates of 30- and 90-day hospital readmission and ED revisitation compared with nonoperative treatment without any difference in mortality among treatment groups. Cost at 90 and 180 days was also lower in the operative treatment group. This challenges the convention that this patient population is "too sick" to undergo operative management for acute cholecystitis and demonstrates the importance of considering cholecystectomy in all patients with acute cholecystitis at the index presentation.

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