Original Investigation

Association Between Cholecystectomy With vs Without Intraoperative Cholangiography and Risk of Common Duct Injury

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Editorial page 801

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IMPORTANCE Significant controversy exists regarding routine intraoperative cholangiography in preventing common duct injury during cholecystectomy.

OBJECTIVE To investigate the association between intraoperative cholangiography use during cholecystectomy and common duct injury.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study of all Texas Medicare claims data from 2000 through 2009. We identified Medicare beneficiaries 66 years or older who underwent inpatient or outpatient cholecystectomy for biliary colic or biliary dyskinesia, acute cholecystitis, or chronic cholecystitis. We compared results from multilevel logistic regression models to the instrumental variable analyses.

INTERVENTIONS Intraoperative cholangiography use during cholecystectomy was determined at the level of the patients (yes/no), hospitals (percentage intraoperative cholangiography use for all cholecystectomies at the hospital), and surgeons (percentage use for all cholecystectomies performed by the surgeon). Percentage of use at the hospital and percentage of use by surgeon were the instrumental variables.

MAIN OUTCOMES AND MEASURES Patients with claims for common duct repair operations within 1 year of cholecystectomy were considered as having major common duct injury.

RESULTS Of 92 932 patients undergoing cholecystectomy, 37 533 (40.4%) underwent concurrent intraoperative cholangiography and 280 (0.30%) had a common duct injury. The common duct injury rate was 0.21% among patients with intraoperative cholangiography and 0.36% among patients without it. In a logistic regression model controlling for patient, surgeon, and hospital characteristics, the odds of common duct injury for cholecystectomies performed without intraoperative cholangiography were increased compared with those performed with it (OR, 1.79 [95% CI, 1.35-2.36]; $P < .001$). When confounding was controlled with instrumental variable analysis, the association between cholecystectomy performed without intraoperative cholangiography and duct injury was no longer significant (OR, 1.26 [95% CI, 0.81-1.96]; $P = .31$).

CONCLUSIONS AND RELEVANCE When confounders were controlled with instrumental variable analysis, there was no statistically significant association between intraoperative cholangiography and common duct injury. Intraoperative cholangiography is not effective as a preventive strategy against common duct injury during cholecystectomy.

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Biliary anatomy misidentification during cholecystectomy can result in injury to the common hepatic duct or common bile duct. Common duct injuries cause significant short- and long-term morbidity including major operations, multiple hospitalizations, and biliary strictures.[1-5] Elimination of common duct injury is desirable, but it has remained stubbornly present with rates ranging from 0.3% to 0.5%.[1,6-10]

Intraoperative cholangiography was described by Mirrizi[11] in 1937 and is a radiologic examination of the ducts performed during cholecystectomy. When routinely used, intraoperative cholangiography is thought to prevent common duct injury.[6] However, controversy exists regarding the effectiveness of routine use in the prevention of common duct injury.[12-16]

Observational, population-based data, such as Medicare billing claims, provide study populations with sufficient statistical power to study rare events like common duct injury. However, administrative data lack information regarding the indication for intraoperative cholangiography and are subject to unmeasured confounding (ie, factors influencing outcomes not found in the database). The preferred means for overcoming unmeasured confounding is instrumental variable analysis.[17] Using instrumental variable analysis, we investigated the association between intraoperative cholangiography use and common duct injury.

Methods

Overview

This study was approved by the institutional review board at The University of Texas Medical Branch. We evaluated multivariable regression and instrumental variable methods for addressing measured and unmeasured confounding of the association between intraoperative cholangiography use and common duct injury in older patients who underwent cholecystectomy. We hypothesized that unadjusted and multivariable-adjusted regression analyses would show a strong benefit of intraoperative cholangiography as previously reported,[6-8] but that instrumental variable analyses would attenuate the association.

Data Source

Data were deidentified and informed consent was waived. The 100% complete Texas Medicare files used for this study included the Denominator File (demographics, eligibility), the Medicare Provider Analysis and Review File (inpatient claims), the Carrier Claims File (claims from physicians), and the Outpatient Standard Analytical File (claims from institutional outpatient providers).

Cohort Identification

The cohort selection is summarized in the **Figure**. After identifying *Current Procedural Terminology* (*CPT*) codes for cholecystectomy with or without intraoperative cholangiography in the Carrier Claims File, we used the following inclusion criteria: (1) enrollment in Medicare Part A and Part B 12 months before and 12 months after cholecystectomy or until death, if a patient died before 12 months, (2) Texas residents, (3) aged 66 years or older, and (4) *International Classification of Diseases, Ninth Revision* (*ICD-9*) diagnosis codes for biliary colic, biliary dyskinesia, acute cholecystitis, and chronic cholecystitis. Patients with hepatobiliary, pancreatic, or duodenal cancers, gallstone pancreatitis, and common duct stones were excluded. All *CPT* and *ICD-9* codes are shown in eTable 1 in the Supplement.

Identification of Hospitals and Hospital Outpatient Facilities

Carrier claims were merged to inpatient and outpatient claims by beneficiary identification and surgery date to obtain the facility identification. Facility identification was linked to the Provider of Services File to obtain hospital type, bed size, and medical school affiliation. Medicare cholecystectomy volume was calculated for each hospital during the study period. Medicare volume and total volume have been shown to be highly correlated ($r = 0.97$) at the hospital level for other surgical procedures.[18]

Identification of Surgeons

The operating physician was identified by the Unique Physician Identification Number (UPIN, 2001-2007) or National Provider Identifier (NPI, 2008-2009) in the carrier claim. If 2 or more surgeons billed the same procedure on the same day, we selected the surgeon who billed the most inpatient services, outpatient services, and consultations within 7 days before the claim date to 30 days after the claim date.

Surgeon UPINs and NPIs were linked to the American Medical Association's Physician Masterfile to obtain surgeon age, sex, year of medical school graduation, graduation from US or foreign medical school, and specialty. The volume of cholecystectomies performed in Medicare patients was calculated for each surgeon (2001-2009) and presented as a yearly average.

Definition of Intraoperative Cholangiography and Covariates

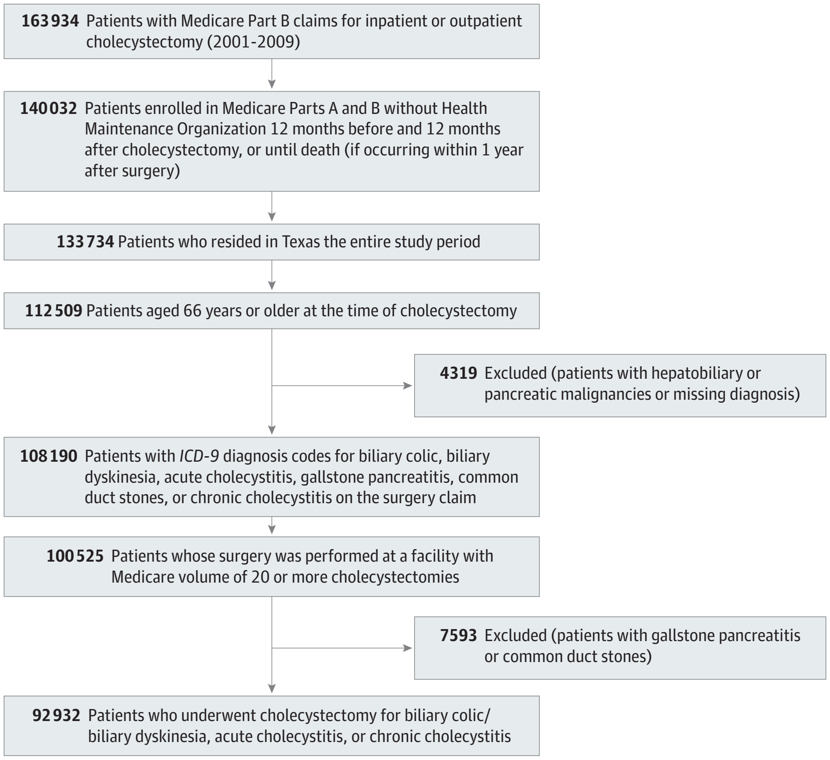
Intraoperative Cholangiography

Patients with *CPT* codes for cholecystectomy with intraoperative cholangiography or for intraoperative cholangiography and any *CPT* code for cholecystectomy were classified as having a cholecystectomy with intraoperative cholangiography (eTable 1 in the Supplement).[6] Intraoperative cholangiography use was determined at the level of the patient (yes/no), the hospital (percentage of use for all cholecystectomies at the hospital, 2001-2009), and the surgeon (percentage of use for all cholecystectomies performed by the surgeon, 2001-2009).

Patient Covariates

Sociodemographic characteristics of the patients included age, sex, and race/ethnicity. Indication for cholecystectomy was classified as biliary colic or biliary dyskinesia, acute cholecystitis, or chronic cholecystitis. Type of procedure was classified as open vs laparoscopic. Charlson comorbidity index[19] based on inpatient and outpatient claims in the year prior to surgery was used for comorbidity.

Figure. Study Selection Summary



ICD-9 indicates *International Classification of Diseases, Ninth Revision*.

Outcome Measure

Patients with *CPT* or *ICD-9* procedure codes for choledochojejunostomy or hepaticojejunostomy (eTable 1 in the Supplement) within 1 year of surgery were considered to have had a major common duct injury during cholecystectomy. These procedures also may be performed for reasons other than repair of common duct injuries; therefore, we applied the following exclusion criteria: patients with (1) a diagnosis for pancreatic, duodenal, or biliary tract cancer or (2) a diagnosis for fistula of the duct (eTable 1 in the Supplement) and a repair operation the same day as cholecystectomy were not considered to have had an injury.

Statistical Methods

Descriptive Analysis

Descriptive statistics on patient-, surgeon-, and hospital-level characteristics were compared for patients with and without intraoperative cholangiography using χ^2 tests for categorical variables and *t* tests for continuous variables.

To explore potential bias in the association between intraoperative cholangiography and common duct injury, we evaluated injury rates in cholecystectomies performed with and without intraoperative cholangiography based on hospital frequency of use. Hospitals were stratified into quartiles of use and the unadjusted percentage of common duct injuries was estimated within each quartile for operations performed with and without intraoperative cholangiography. Chi-squared tests were used to evaluate the statistical significance of differences in injury rates between intraoperative cholangiography groups within each stratum. Bonferroni corrections were used for multiple comparisons.

Multivariable Analyses

Multivariable logistic regression was used to evaluate the association between intraoperative cholangiography use and common duct injury after adjusting for patient, surgeon, and hospital characteristics. Surgeon and hospital characteristics were limited to those that were statistically significant ($P < .05$) in bivariate analyses with common duct injury. The association between intraoperative cholangiography and common duct injury also was evaluated using a 2-level hierarchical generalized linear model with patients clustered within hospitals.

Instrumental Variable Analysis

The instrumental variable was a continuous measure of the percentage of hospital intraoperative cholangiography use. To confirm that the percentage of hospital use was not a weak instrument, we used a partial *F* test. The null hypothesis was that there was no association between hospital use and patient's receiving intraoperative cholangiography. An *F* statistic greater than 10 suggests that the instrument is not weak.[20] The null hypothesis was rejected at $P < .001$, with an *F* statistic of 22 801. We also evaluated the balance of measured covariates across levels of the instrumental variable (≤ median vs > median) to provide additional information to assess its validity. Standardized difference scores, which are independent of sample size, were calculated from the Mahalanobis distance method and compared between groups.[21] The standardized difference for categorical variables shows the overall differences across all levels of the categorical variable between 2 groups. A difference of 0.2 (or 20%) indicates a small effect size. A standardized difference of 20% indicates that a non-overlap region between the 2 populations is only 14.8%.

The percentage of hospital intraoperative cholangiography use was used as a continuous measure in the instrumental variable analyses. We estimated the parameters using 2-stage residual inclusion models because the outcome was dichotomous. The standard error of the instrumental variable parameter was estimated robustly to account for correlation among patients within hospitals.

Additional Analyses

We conducted additional analyses using a second instrumental variable and a second outcome. The second instrumental variable was percentage of intraoperative cholangiography use by surgeon. A partial *F* test confirmed that the percentage of surgeon use was not a weak instrument (*F* statistic = 29 584, *P* < .001). These models included only hospitals performing 20 or more cholecystectomies and surgeons performing 5 or more cholecystectomies during the study period.

As a control, we examined an alternative outcome that we did not expect to be subject to unmeasured confounding: the use of procedures to remove common duct stones. Previous studies have shown that patients undergoing routine intraoperative cholangiography were more likely to require postoperative endoscopic retrograde cholangiopancreatography (ERCP) or common duct exploration (eTable 1 in the Supplement) due to identification of common duct stones that might otherwise have been asymptomatic.[22,23] Our hypothesis was that the use of postoperative ERCP or common duct exploration would be significantly lower in cholecystectomies performed without intraoperative cholangiography and that instrumental variable analysis would not attenuate this association.

All analyses were performed using SAS, version 9.2 (SAS Institute Inc) and STATA, version 12 (StataCorp). All statistical tests were 2-sided with *P* < .05 considered to be statistically significant.

Results

Patient, Surgeon, and Hospital Characteristics

A total of 92 932 Medicare beneficiaries 66 years or older underwent cholecystectomy at 307 hospitals in Texas from 2001 through 2009 (**Table 1**). There were 37 533 cholecystectomies with intraoperative cholangiography (40.4% [95% CI, 40.1%-40.7%]) and 55 399 without (59.6% [95% CI, 59.3%-59.9%]). Patients undergoing intraoperative cholangiography were more likely to have acute cholecystitis, jaundice, laparoscopic procedures, and a high-volume surgeon and hospital. They were less likely to have had surgery at a nonprofit or teaching hospital than patients not undergoing intraoperative cholangiography (selected surgeon- and hospital-level variables in Table 1, see eTable 2 in the Supplement for all variables). Table 1 shows the variable match for hospitals above and below the median percent of hospital intraoperative cholangiography use. Standardized differences between groups are shown. When patient characteristics were compared using instrumental variable status, the imbalance between intraoperative cholangiography groups was reduced for diagnosis, type of procedure, length of stay in the hospital, jaundice, and Charlson comorbidity index. Race/ethnicity, surgeon volume, medical training in the United States, hospital bed size, and medical school affiliation had standardized differences exceeding 10%, but less than 25%.

Evidence of Selection Bias

Common duct injury occurred in 280 patients (0.30% [95% CI, 0.27%-0.34%]). There were 201 common duct injuries (0.36% [95% CI, 0.31%-0.41%]) in patients undergoing cholecystectomy without intraoperative cholangiography and 79 injuries (0.21% [95% CI, 0.17%-0.26%]) for those having an intraoperative cholangiography (**Table 2**). Table 2 shows the rates of common duct injury for cholecystectomies performed with and without intraoperative cholangiography based on the hospital's frequency of use. In hospitals that routinely performed intraoperative cholangiography, common duct injury occurred in 26 cholecystectomies with intraoperative cholangiography (0.12% [95% CI, 0.07- 0.17]) and 43 cholecystectomies without intraoperative cholangiography (0.76% [95% CI, 0.54-0.99]; *P*<.001). Conversely, in hospitals that performed intraoperative cholangiography infrequently, common duct injury occurred in 11 cholecystectomies with intraoperative cholangiography (0.96% [95% CI, 0.39-1.52]) and 42 cholecystectomies without intraoperative cholangiography (0.25% [95% CI, 0.18-0.33]; *P*<.001).

Multivariable and Multilevel Analyses

Table 3 shows the results for the unadjusted and multivariable logistic regression models and instrumental variable analyses. Cholecystectomy performed without intraoperative cholangiography was associated with common duct injury when compared with those performed with intraoperative cholangiography (OR, 1.76 [95% CI, 1.34-2.32]) after controlling for patient, surgeon, and hospital characteristics (Table 3, model 2). A multilevel logistic regression model adjusting for clustering of patients within hospitals produced similar estimates of association (Table 3, model 3; full model shown in eTable 3 in the Supplement).

Instrumental Variable Analyses

Table 1 demonstrates a good balance of covariates across levels (above and below the median) with the instrumental variable. The standardized differences are expressed as percentages, where a difference of 20% corresponds to a nonoverlap region of only 14.8% between the 2 populations. Only hospital bed size and medical school affiliation had standardized differences of more than 20%.

Instrumental variable analysis (Table 3, model 4) was performed to control for suspected unmeasured confounding. The percentage of hospital intraoperative cholangiography use ranged from 0% to 97.0% across hospitals. Using

Table 1. Balance of Covariates Across Treatment Groups and Levels of the Instrumental Variable (Percentage of Hospital Intraoperative Cholangiography Use)

Patient Characteristics	Patient Treatment Status: IOC Use, No. (%) Yes	Patient Treatment Status: IOC Use, No. (%) No	Patient Treatment Status: Standardized Differences,[21] %	Instrumental Variable Status: Hospital IOC Use Rate, No. (%) ≤Median (28.7%)	Instrumental Variable Status: Hospital IOC Use Rate, No. (%) >Median (28.7%)	Instrumental Variable Status: Standardized Differences,[21] %[a]
No. of patients	37 533	55 399		41 019	51 913	
Common duct injury	79 (0.21)	201 (0.36)	−2.85	119 (0.29)	161 (0.31)	−0.36
IOC				4952 (12.07)	32 581 (62.76)	
Age, mean (SD), y	75.13 (6.61)	75.17 (6.64)	−0.64	75.15 (6.61)	75.16 (6.64)	−0.20
Sex						
Men	14 311 (38.13)	21 269 (38.39)	−0.54	15 643 (38.14)	19 937 (38.40)	−0.55
Women	23 222 (61.87)	34 130 (61.61)		25 376 (61.86)	31 976 (61.60)	
Race/ethnicity						
White	31 984 (85.22)	47 904 (86.47)	9.87	35 912 (87.55)	43 976 (84.71)	18.39
Black	1769 (4.71)	3121 (5.63)		2452 (5.98)	2438 (4.70)	
Hispanic	3224 (8.59)	3442 (6.21)		1920 (4.68)	4746 (9.14)	
Other	556 (1.48)	932 (1.68)		735 (1.79)	753 (1.45)	
Diagnosis						
Acute cholecystitis	27 251 (72.61)	37 880 (68.38)	9.63	28 180 (68.70)	36 951 (71.18)	5.41
Biliary colic/biliary dyskinesia	6664 (17.76)	11 749 (21.21)		8502 (20.73)	9911 (19.09)	
Chronic cholecystitis	3618 (9.64)	5770 (10.42)		4337 (10.57)	5051 (9.73)	
Type of surgical procedure						
Open	3203 (8.53)	10 149 (18.32)	29.00	6164 (15.03)	7188 (13.85)	−3.36
Laparoscopy	34 330 (91.47)	45 250 (81.68)		34 855 (84.97)	44 725 (86.15)	
Hospital stay, mean (SD), d	4.20 (5.67)	4.89 (6.61)	−11.18	4.67 (6.24)	4.57 (6.26)	1.60
Jaundice	1329 (3.54)	1416 (2.56)	5.73	1162 (2.83)	1583 (3.05)	−1.28
Charlson comorbidity index						
0	16 766 (44.67)	23 699 (42.78)	6.57	17 837 (43.48)	22 628 (43.59)	0.83
1	8703 (23.19)	12 413 (22.41)		9383 (22.87)	11 733 (22.60)	
2	4218 (11.24)	6222 (11.23)		4564 (11.13)	5876 (11.32)	
≥3	7846 (20.90)	13 065 (23.58)		9235 (22.51)	11 676 (22.49)	
Year of surgery						
2001	3773 (10.05)	6001 (10.83)	4.72	4213 (10.27)	5561 (10.71)	3.33
2002	4284 (11.41)	6549 (11.82)		4830 (11.78)	6003 (11.56)	
2003	4353 (11.60)	6655 (12.01)		5031 (12.27)	5977 (11.51)	
2004	4641 (12.37)	6802 (12.28)		5105 (12.45)	6338 (12.21)	
2005	4410 (11.72)	6479 (11.70)		4821 (11.75)	6068 (11.69)	
2006	4218 (11.24)	6314 (11.40)		4659 (11.36)	5873 (11.36)	
2007	3982 (10.61)	5778 (10.43)		4301 (10.49)	5459 (10.52)	
2008	3841 (10.23)	5479 (9.89)		4033 (9.83)	5287 (10.18)	
2009	4031 (10.74)	5342 (9.64)		4026 (9.81)	5347 (10.30)	
Surgeon annual volume quartile						
<0.9	667 (1.78)	1587 (2.86)	18.94	1012 (2.47)	1242 (2.39)	11.46
0.9 to <4.1	1859 (4.95)	4280 (7.73)		3064 (7.47)	3075 (5.92)	
4.1 to <11.2	7832 (20.87)	13 994 (25.26)		10 457 (25.49)	11 369 (21.90)	
≥11.2	27 175 (72.40)	35 538 (64.15)		26 486 (64.57)	36 227 (69.78)	
US medical school training	29 362 (79.76)	44 432 (82.20)	−6.22	33 875 (84.50)	39 919 (78.61)	15.23
Hospital bed size						
<200	11 729 (31.28)	20 744 (37.45)	16.96	16 765 (40.87)	15 708 (30.29)	24.50
200 to 324	7629 (20.35)	10 322 (18.63)		8053 (19.63)	9898 (19.08)	
325 to 500	9922 (26.46)	11 368 (20.53)		8128 (19.82)	13 162 (25.38)	
>500	8212 (21.90)	12 957 (23.39)		8073 (19.68)	13 096 (25.25)	
Medical school affiliation						
Major	3072 (8.19)	6638 (11.98)	26.82	5506 (13.42)	4204 (8.11)	24.30
Limited	4041 (10.78)	8930 (16.12)		6463 (15.76)	6508 (12.55)	
Graduate	1415 (3.77)	3645 (6.58)		2726 (6.65)	2334 (4.50)	
No affiliation	28 964 (77.25)	36 178 (65.31)		26 324 (64.16)	38 818 (74.85)	

Abbreviation: IOC, intraoperative cholangiography.

[a] Standardized differences (expressed as percentages in Table 1) are independent of sample size. They were calculated from the Mahalanobis distance method and compared between groups. In general, a difference of 0.2 (or 20%) indicates a small effect size. A standardized difference of 20% means the non-overlap region between the 2 populations is only 14.8%. The standardized difference for categorical variables shows the overall differences across all levels of the categorical variable between the 2 groups.

Table 2. Rate of Common Duct Injury in Cholecystectomies Performed With and Without Intraoperative Cholangiography Based on the Hospital's Frequency of Intraoperative Cholangiography Use

Hospital IOC Use Quartile, %[a]	No. of Patients	Rate of Common Duct Injury, No. (%) [95% CI]			*P* Value[b]	Bonferroni Adjusted *P* Value[b]
		Overall	Without IOC	With IOC		
<11.6	17 869	53 (0.30) [0.22-0.38]	42 (0.25) [0.18-0.33]	11 (0.96) [0.39-1.52]	<.001	<.001
11.6 to <28.8	23 150	66 (0.29) [0.22-0.35]	53 (0.27) [0.20-0.35]	13 (0.34) [0.16-0.53]	.47	>.99
28.8 to <67.8	24 479	92 (0.38) [0.30-0.45]	63 (0.46) [0.35-0.57]	29 (0.27) [0.17-0.37]	.02	.06
≥67.8	27 434	69 (0.25) [0.19-0.31]	43 (0.76) [0.54-0.99]	26 (0.12) [0.07-0.17]	<.001	<.001
All	92 932	280 (0.30) [0.27-0.34]	201 (0.36) [0.31-0.41]	79 (0.21) [0.17-0.26]	<.001	

Abbreviation: IOC, intraoperative cholangiography.

[a] Statistical significance of overall rates across hospital intraoperative cholangiography quartiles: $P = .07$.

[b] Statistical significance of differences between cholecystectomies performed without and with intraoperative cholangiography for each strata of percentage of hospital intraoperative cholangiography use.

the percentage of hospital intraoperative cholangiography use as an instrumental variable eliminated the significant association between intraoperative cholangiography and common duct injury (OR, 1.26 [95% CI, 0.81-1.96]). The percentage of surgeon intraoperative cholangiography use ranged from 0% to 100% across 1234 surgeons. Using the percentage of use by surgeon as an instrumental variable yielded a similar estimate of association (n = 90 095; OR, 1.31 [95% CI, 0.91-1.89]). The full instrumental variable model with the percentage of hospital use is shown in eTable 4 in the Supplement. Model comparison and goodness-of-fit statistics for all models in Table 3 are in eTable 5 in the Supplement.

Instrumental Variable Analyses of Unrelated Outcome

Table 3 also shows the associations between intraoperative cholangiography and procedures to remove common duct stones. In the multivariable logistic regression models, cholecystectomies performed without intraoperative cholangiography were associated with lower use of ERCP or common duct exploration than those with intraoperative cholangiography (Table 3, models 2 and 3). As hypothesized, the association between intraoperative cholangiography and ERCP, common duct exploration, or both was not attenuated in the instrumental variable analyses with the percentage of either surgeon or hospital intraoperative cholangiography use as the instrument (Table 3, model 4).

Discussion

Significant controversy exists regarding the role of intraoperative cholangiography in the prevention of common duct injury during cholecystectomy.[6,12-16] Previous population-based studies using data from Medicare claims, hospital discharge records, and national inpatient registries report nearly 2-fold higher rates of injury in cholecystectomies performed without intraoperative cholangiography.[6-8,24] In the present study using Texas Medicare claims data, the association between intraoperative cholangiography and common duct injury was highly sensitive to the analytic method used. Results from standard risk-adjustment methods indicated that not using an intraoperative cholangiography during cholecystectomy was significantly associated with an increase in common duct injury, even after controlling for patient, surgeon, and hospital characteristics. When we used instrumental variable methods, the relative increase in injury was attenuated and the association was no longer statistically significant.

Our results demonstrate that the estimated association between intraoperative cholangiography and common duct injury in previous studies is possibly attributable to unmeasured confounding. The intent of intraoperative cholangiography is impossible to determine using administrative or hospital discharge data. Intraoperative cholangiography could have been done as a matter of routine, to delineate unclear biliary anatomy, to confirm injury, or to detect common duct stones. In hospitals using intraoperative cholangiography routinely (>67.8% of cholecystectomies), the rate of injury was 6 times higher in cases when it was not performed. In these cases, routine users may have been unable to perform intraoperative cholangiography because of complicating factors (eg, unclear anatomy) also associated with increased risk of injury. Conversely, in hospitals that use intraoperative cholangiography infrequently, the rate of injury was higher in cases for which intraoperative cholangiography was performed, suggesting it may have been used to confirm suspected common duct injury.

Observational data sets commonly lack complete information on factors influencing selection of treatment. Clinical indications for intraoperative cholangiography (such as bilirubin levels and liver function tests) and factors that influence its successful completion (such as severe inflammation or aberrant anatomy) are not captured. Our analysis indicates that the estimated benefit of intraoperative cholangiography using observational data and standard risk-adjustment methods may be due to residual confounding related to the selection of higher-risk patients into the no–intraoperative cholangiography group. Previous studies using administrative and registry data have documented an approximately 2-fold benefit of intraoperative cholangiography in preventing common duct injury.[6,8,24,25] These studies only adjusted for a limited number of covariates such as age, sex, race, diagnosis, surgeon volume, hospital volume, emergency surgery, and comorbidity and were not able to control for clinical variables and indication for intraoperative cholangiography. Conversely, 3

Table 3. Associations Between Patient Intraoperative Cholangiography Use (No vs Yes) and Odds of Common Duct Injury and ERCP or Common Duct Exploration According to Method of Risk-Adjustment

	Risk-Adjustment Method							
	Model 1		Model 2		Model 3		Model 4	
	Unadjusted Logistic Regression, OR (95% CI)	*P* Value	Multivariable Logistic Regression, OR (95% CI)	*P* Value	Multilevel Logistic Regression, OR (95% CI)[a]	*P* Value	Instrumental Variable Analysis, OR (95% CI)	*P* Value
Common duct injury[b]								
Percentage of hospital IOC use[c]	1.73 (1.33-2.24)[c]	<.001	1.76 (1.34-2.32)[d]	<.001	1.79 (1.35-2.36)[d]	<.001	1.26 (0.81-1.96)[d]	.31
Percentage of surgeon IOC use[e]	1.81 (1.38-2.37)[e]	<.001	1.74 (1.32-2.29)[f]	<.001	1.77 (1.34-2.36)[f]	<.001	1.31 (0.91-1.89)[f]	.14
ERCP/common duct exploration[g]								
Percentage of hospital IOC use[c]	0.65 (0.62-0.68)[c]	<.001	0.65 (0.62-0.69)[d]	<.001	0.67 (0.64-0.72)[d]	<.001	0.61 (0.56-0.67)[d]	<.001
Percentage of surgeon IOC use[e]	0.65 (0.62-0.69)[e]	<.001	0.66 (0.62-0.69)[f]	<.001	0.69 (0.65-0.74)[f]	<.001	0.60 (0.56-0.64)[f]	<.001

Abbreviations: ERCP, endoscopic retrograde cholangiopancreatography; IOC, intraoperative cholangiography; OR, odds ratio.

[a] The multilevel model is based on patients clustered within hospitals. The model was also repeated with patients clustered within surgeons. The results were similar, so only 1 model is shown. The full multilevel models (outcome = common duct injury) for patients clustered within hospitals are shown in eTable 3 in the Supplement.

[b] Models 2 through 4 for common duct injury are adjusted for age, sex, race, diagnosis, comorbidity, year of surgery, surgeon volume, US medical school training, hospital teaching status, and hospital bed size.

[c] Model is restricted to hospitals with 20 or more cholecystectomies during the study period (n = 92 932).

[d] The adjusted analyses sample size was 90 818 patients; 2.2% of the sample (n = 2114) patients had missing surgeon-level data: 1238 did not have a surgeon identification, 827 patients had a surgeon who was missing American Medical Association data, and 49 were missing hospital-level data. Sensitivity analyses excluding the missing surgeons and hospitals from the models showed similar results with no change in conclusion.

[e] Models are restricted to hospitals performing 20 or more cholecystectomies and surgeons performing 5 or more cholecystectomies during the study period (n = 90 932).

[f] The adjusted analyses sample size was 90 095 patients; 0.92% of the sample (n = 837) patients had missing surgeon-level or hospital-level data.

[g] Models 2 through 4 for ERCP and/or common duct exploration are adjusted for age, sex, race, diagnosis, comorbidity, year of surgery, surgeon age, years in practice, surgeon volume, type of hospital, hospital teaching status, and hospital volume.

large studies based on clinical data showed no significant difference in common duct injury rates with or without intraoperative cholangiography, supporting our hypothesis of unmeasured bias due to lack of clinical information when using administrative data.[13,26,27]

Another possibility is that surgeons who favor intraoperative cholangiography may use a generally safer surgical approach or have greater experience. Therefore, patients in the intraoperative cholangiography group would have lower injury rates as a result of their surgeon's qualities rather than because of a protective effect. However, surgeon propensity to use intraoperative cholangiography was not associated with rate of common duct injury in our study, which enabled us to use this measure as an instrumental variable.

It is important to note that instrumental variable analyses estimate the treatment effect on the marginal population—patients who would receive intraoperative cholangiography in high-use hospitals but not in low-use hospitals—rather than the average treatment effect. The association between intraoperative cholangiography and injury in our study should be interpreted as answering the policy-relevant question "What are the benefits of increasing hospital-level intraoperative cholangiography use?" rather than the question of clinical effectiveness "What is the effect of providing intraoperative cholangiography to a specific patient?"

Some surgeons advocate routine intraoperative cholangiography use as a system-level intervention to minimize common duct injuries.[6-8,22-24,28-30] Opponents document similar outcomes using operative techniques such as the critical view of safety with selective cholangiography as a complement.[9,10,13-15,26,27,31,32] Quality initiatives mandating routine intraoperative cholangiography have been implemented based on the results from previous observational studies showing a reduced risk of common duct injury. Although some report improvement in injury rates after implementation of routine intraoperative cholangiography policies,[22,23] it is not clear that improvement is attributable to the procedure itself. Implementation of a policy involves surgical training, increases awareness of the anatomy, and increases surgeon awareness of outcome measurement, all of which may improve outcomes independent of intraoperative cholangiography. The results of our instrumental variable analysis suggest that clinical protocols and quality initiatives mandating use based on expected benefits derived from standard risk-adjustment models are not supported by empirical evidence.

Our study has several limitations. The cohort included Texas Medicare fee-for-service beneficiaries 66 years or older, while the majority of patients who undergo cholecystectomy are younger than 65 years.[33-35] Our study evaluated major common duct injury, defined as having received hepaticojejunostomy or choledochojejunostomy within 1 year of the date of surgery. With advances in endoscopic and interventional radiology techniques, some major injuries may have been managed without surgery. Several previous studies also included minor injuries in their outcome variable.[13,24,26] Although the instrumental variable analysis attenuates the association between lack of intraoperative cholangiography and major common duct injury, the confidence intervals are wide. It is possible that there is an association that our study was underpowered to identify. Statistical power is often limited in instrumental variable analyses, as the precision of the estimates depends on the number of units for the instrument, rather than on the patient sample size. Whereas there were 92 932 patients in our study, there were only 307 hospitals, significantly reducing the statistical power.

In conclusion, the relationship between intraoperative cholangiography and common duct injury was sensitive to the method of statistical analysis. Failure to account for potentially confounding variables not routinely captured in administrative databases has a major effect on the interpretation of the findings. Intraoperative cholangiography was not associated with significant reduction in common duct injury using instrumental variable analysis. Instrumental variable analysis balances unmeasured confounding variables to better align risk factors in comparator groups. With better control for unmeasured confounding variables, intraoperative cholangiography was no longer associated with common duct injury. Based on these results, routine intraoperative cholangiography should not be advocated as means for preventing common duct injury.

ARTICLE INFORMATION

Author Contributions: Drs Sheffield and Riall had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Sheffield and Riall contributed equally to this study as first authors.
Study concept and design: Sheffield, Riall, Kuo, Townsend, Goodwin.
Acquisition of data: Riall, Han, Townsend.
Analysis and interpretation of data: Sheffield, Riall, Kuo, Townsend, Goodwin.
Drafting of the manuscript: Sheffield, Riall, Townsend.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Sheffield, Riall, Han, Kuo, Townsend.
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Study supervision: Riall, Townsend, Goodwin.

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