Early Cholecystectomy for Acute Cholecystitis: A Population-based Analysis of Variability in Practice

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Funding: The project was funded by operating grants from the Canadian Surgical Research Fund and Physician Services Inc. Foundation. In addition, this study was supported by the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

ABSTRACT

BACKGROUND: Randomized controlled trials and expert opinion support early cholecystectomy performed on first admission for most patients with acute cholecystitis. We sought to characterize the extent and potential sources of variability in the performance of early cholecystectomy for acute cholecystitis within a large regional healthcare system.

METHODS: We used a population-based retrospective cohort design. The cohort was limited to adults with a first episode of AC, admitted through the Emergency Department (ED). Subjects were identified using administrative databases comprising all ED visits and hospital admissions in Ontario, Canada, from 2004 to 2010. Patient and hospital-level characteristics associated with early cholecystectomy (within 7 days of ED presentation) were identified using multilevel logistic regression.

RESULTS: We identified 24,347 patients admitted to 106 hospitals with a first episode of AC. A majority (58%, N=14,286) underwent early cholecystectomy. Rates of early cholecystectomy varied widely across hospitals (median 51%, IQR 25%-72%), even among 18-49 year old healthy patients with uncomplicated cholecystitis (median 74%, IQR 41%-88%). On multivariable multilevel analysis, hospitals in the top quartile for acute cholecystitis admission volume had the highest adjusted odds of early cholecystectomy and hospital effects accounted for half of the explained variability in early cholecystectomy.

INTERPRETATION: Across a large regional healthcare system's hospitals, similar patients with acute cholecystitis did not receive comparable care consistent with best available evidence and expert consensus. Hospital-level factors, independent of patient characteristics, appear strongly related to practice variability. This finding suggests that hospital-specific initiatives should be considered to facilitate early cholecystectomy for acute cholecystitis.

INTRODUCTION

Acute cholecystitis (AC) is a ubiquitous cause of hospitalization for gastrointestinal disease and is definitively managed with cholecystectomy.(1,2) Randomized controlled trials, meta-analyses and expert consensus support a practice of early laparoscopic cholecystectomy on first hospital admission for most patients with AC, without severe sepsis.(3–11) In fact, when compared to delaying cholecystectomy until after discharge, early laparoscopic cholecystectomy within up to 7 days of symptom onset is associated with a shorter total hospital length of stay and a similar risk of conversion to open cholecystectomy.(3,7–11) Further support for early intervention can be drawn from reports showing an approximately 20% risk of recurrent gallstone-related symptoms, if delaying cholecystectomy.(9-12)

In spite of this evidence favouring early intervention, inconsistency in delivering what many consider best practice has been reported worldwide. In fact, reports out of the United Kingdom, Japan and the United States show rates of early cholecystectomy ranging from 36% to 88%.(13–17) However, because of differences in the setting and cohort characteristics across published studies, our understanding of the extent and underlying etiology of the inconsistent application of early cholecystectomy remains circumstantial. We postulated that a better understanding of the factors associated with the performance of early cholecystectomy would provide opportunities to address the gap between evidence and practice. Our objective was therefore to evaluate the extent of variation across hospitals in a large regional healthcare system and, to identify the patient and hospital characteristics associated with performing early cholecystectomy.

METHODS

Study design

This is a population-based retrospective cohort study of all adults with a first episode of acute cholecystitis emergently admitted to an acute care hospital between April 1, 2004 and March 31, 2010, in the province of Ontario, Canada. We compared rates of early cholecystectomy across hospitals and used multivariable multilevel logistic regression to identify patient and hospital characteristics associated with performing early cholecystectomy. This study was approved by the Research Ethics Board of Sunnybrook Health Sciences Center.

Setting

This study used data from Ontario, Canada's most populous province with over 13 million persons. All medically necessary hospital and physician services for Ontario residents are paid by the provincial Ministry of Health. There are no private general hospitals in Ontario.

Data sources

Patients were identified from the Canadian Institute for Health Information Discharge Abstract Database (DAD), which contains demographic, diagnostic and procedural information on all hospitalizations in Ontario. Admission via the Emergency Department (ED) was confirmed through linkage to the National Ambulatory Care Reporting System database, which captures all ED visits. To derive certain covariates (patient comorbidities and hospital after-hours procedure volume), DAD was supplemented with data from the Ontario Health Insurance Plan (OHIP) billing database that contains all physician claims. These datasets were deterministically linked through a unique encrypted patient identifier and have been validated for a variety of exposures and comorbidities.(18-22) In a multicenter validation study, almost perfect agreement was found between Ontario's DAD and reabstracted data for cholecystectomy coding and coding of gallstone disease as the most responsible diagnosis.(18)

Cohort

The cohort included residents of Ontario, 18 years of age or older, who were admitted to hospital via the ED with a most responsible diagnosis of AC (ICD-10-CA codes K80.0, K80.1, K80.4, K81.0, K81.8, K81.9). We restricted our analysis to those with a first episode of AC and without other prior gallstone-related admissions or ED visits in the two years preceding their index admission. We also excluded patients directly admitted to an intensive care unit (ICU). ICU admission was considered a surrogate for cholecystitis with severe sepsis, consistent with the Tokyo consensus definition of severe cholecystitis.(23) Patients who underwent cholecystostomy tube placement were also excluded since this suggests either severe cholecystitis or significant pre-existing disease that might preclude operative intervention at any time. Less than 0.5% of patients were excluded due to missing covariate information.

We also had two exclusions at the hospital level. First, we wished to exclude hospitals where there was no general surgeon, because patients presenting to these hospitals could not have had an early cholecystectomy. Since data on the availability of physicians at specific hospitals were not directly available, we excluded hospitals where no appendectomy was recorded over the six year study period. Finally, to provide more robust estimates of rates, we also excluded hospitals with fewer than 5 patients meeting entry criteria per study year. These two criteria resulted in the exclusion of 52 of 158 hospitals.

Outcome

The primary outcome of interest was early cholecystectomy, defined as cholecystectomy within 7 days of ED presentation.

Patient and hospital-level characteristics

Several patient and hospital-level characteristics were considered as potential explanatory variables influencing the performance of early cholecystectomy. Patient-level characteristics included age, sex, income level, comorbidity level, concomitant common bile duct (CBD) obstruction and pancreatitis. Income quintile was used as crude surrogate for socioeconomic status and was derived from the median household income of the patient's postal code of residence based on 2001 and 2006 census data.(24) Comorbidity level was captured using the John Hopkins Aggregated Diagnosis Group (ADG) scoring system.(25) Using inpatient and outpatient records in the two years preceding the index admission, an ADG-based comorbidity index was calculated according to an algorithm validated for the prediction of 1 year mortality in a large cohort of adult Ontarians.(26)

The hospital-level characteristics we considered included teaching status (academic teaching / non-teaching) as recognized by the Ontario Ministry of Health(27), annual volume of AC admissions (quartiles) and, annual volume of elective cholecystectomies (quartiles). We also considered the possibility that a hospital's policy regarding the use of operating room resources after hours (evenings, nights and weekends) or operating room availability might influence the likelihood of early cholecystectomy. Therefore, as a standardized measure of operating room (OR) utilization after hours, we derived a variable corresponding to the ratio of total after-hours operative cases (for all surgical specialties) divided by the number of all-cause ED visits. Lower values are indicative of lesser after-hours OR utilization.

Statistical analysis

Exploration of variation across hospitals

We calculated the crude rate of early cholecystectomy at each hospital for all patients. To better understand the source of variability, we also explored rates across hospitals for young healthy patients (<50 years old in lowest comorbidity quartile) with uncomplicated disease (without CBD obstruction or pancreatitis). Variability across hospitals is presented using funnel plots in which each hospital's early cholecystectomy rate is plotted against their volume of AC admissions, with ninety-nine percent control limits around the overall mean cholecystectomy rate.(28) A hospital outside the control limits is interpreted as having an early cholecystectomy rate outside the range of random variability related to their volume of AC admissions.

Exploration of factors associated with early cholecystectomy

We evaluated the association of patient and hospital characteristics with early cholecystectomy using multilevel (two-level) logistic regression, which accounts for the non-independence of patients admitted to the same hospital.(29) Model calibration was examined through observed versus predicted outcome plots and discrimination was quantified with the c-statistic.

To evaluate the relative importance of hospital characteristics and patient case-mix, we compared the proportion of explained outcome variation in the multilevel logistic model with patient and hospital-level characteristics to a standard logistic model containing only the patient-level covariates. Each model's respective proportion of explained outcome variation was calculated as the squared Pearson correlation coefficient between the probabilities of early cholecystectomy predicted by the model and the observed outcomes.(30)

In addition, the multilevel model was used to quantify the extent of variability between hospitals, adjusted for differences in patient case-mix, by calculating the median odds ratio (MOR).(31) The MOR is the median value of all possible ratios of the odds of cholecystectomy in two patients with the same covariates admitted to two randomly selected, distinct hospitals. By convention, the odds of the patient at the hospital with the highest propensity for cholecystectomy is used as the numerator of the ratio, such that the MOR is always greater or equal to 1. As an example, a MOR of 3.0 suggests a threefold median difference in the odds of early cholecystectomy for two similar patients admitted to distinct randomly selected hospitals.

All analyses were performed using SAS 9.2. Given the large sample size, a two-tailed $\alpha < 0.01$ was considered statistically significant.

RESULTS

Study cohort

We identified 24,437 patients, admitted to 106 hospitals, with a first episode of acute cholecystitis who met inclusion criteria (figure 1). The median number of patients per hospital was 196 (IQR 71–357). Teaching hospitals comprised 13% of hospitals and cared for 21% of patients. The cohort was evenly distributed across study years. Over half of patients were female (59%) and the mean age was 56±18 years. Concurrent common bile duct obstruction and pancreatitis were present in 11% and 5% of patients, respectively. Overall, 14,286 (58%) patients underwent early cholecystectomy.

Variability in rate of early cholecystectomy across hospitals

There was marked variability in the rate of early cholecystectomy across hospitals: median 51%, IQR 25%–72%. This variability remained evident even when limited to young (<50 years) healthy (lowest comorbidity quartile) patients with uncomplicated disease (without CBD obstruction or pancreatitis): median early cholecystectomy rate 74%, IQR 41%–88%. In both the full cohort and in the younger healthy subgroup, the variation in early cholecystectomy was in excess of that expected by chance alone as evidenced by the large number of hospitals lying outside the ninety-nine percent control limits shown in the funnel plots (figures 2A and 2B).

Association of patient and hospital-level characteristics with early cholecystectomy

On multivariable multilevel analysis, patients who were younger, female, with a lower comorbidity burden and without common bile duct obstruction were more likely to undergo early operative intervention (Table 1). At the hospital level, a high volume of AC admissions was associated with increased odds of early cholecystectomy (Table 1). Albeit significant, the level of OR utilization after hours showed an inconsistent association with performance of early cholecystectomy. The model showed good discrimination (c-statistic=0.80) and calibration. Univariable analysis results are available in the supplemental appendix

We then used the multilevel model to quantify the extent of variability between hospitals, adjusted for differences in patient case-mix. The MOR was 3.7, which can be interpreted as a nearly 4-fold median difference in the odds of early cholecystectomy for two similar patients admitted to randomly selected hospitals.

Finally, we examined the explained outcome variation attributable to patient and hospital level effects. Our multilevel model explained 53% of the variation in the frequency of early cholecystectomy. Of this explained variation, about half (27%) could be attributed to hospital-level effects, and half (26%) to patient-level effects.

DISCUSSION

In this population-based study evaluating the practice of early cholecystectomy for AC, we demonstrated significant variability across hospitals, even when considering only young, healthy patients with uncomplicated disease. Our analysis suggests that two similar patients presenting to randomly selected hospitals have an almost 4-fold median difference in their respective odds of early cholecystectomy. Furthermore, hospital effects, as opposed to patient effects, accounted for half of the explained variability in early cholecystectomy. Admission to a hospital with a high AC admission volume was associated with the highest rate of early intervention.

Best available evidence supports early over delayed laparoscopic cholecystectomy for most patients with AC, based on findings of a shortened total hospital stay, a similar conversion rate and the elimination of the risk of recurrent gallstone symptoms associated with delayed elective cholecystectomy.(3,7–12) While the trials were published between 1998 and 2005, inconsistency in the practice of early cholecystectomy remains evident across different practice environments internationally, with reported early cholecystectomy rates ranging from 36% to 88%.(13–17) Previous studies have also shown that, in those 66 years of age or older, early cholecystectomy is less likely in patients of greater age and comorbidity level and that early cholecystectomy is less likely with limited insurance status in the United States.(16,17) Other determinants of management identified in surveys of physicians include the surgeon's competing elective clinical obligations, the surgeon's comfort with laparoscopy, as well as the availability of hospital resources for emergency surgery.(32-34) While we found patient characteristics associated with management that are consistent with the prior literature, our study is the first to describe the extent of variability across hospitals within a large regional healthcare system and quantify the importance of hospital-level effects as a source of variability in practice.

While many hospitals are providing early cholecystectomy for most patients in Ontario, we have shown that similar patients managed at different hospitals did not receive comparable care. We postulate that these results may in part be related to logistic barriers to early cholecystectomy at certain institutions. Variability across hospitals in the management of AC may be reduced in the future because of a recent focus on the efficient delivery of emergency surgical care. This focus includes the American College of Surgeons' support for the emerging field of acute care surgery as well as the Royal College of Surgeons of England's promotion of the separation of emergency and elective surgery practice.(35,36) Initiatives targeting better delivery of emergency surgical care, including a dedicated service for emergency surgery referrals, a surgeon-of-the-week practice model, and operating room time during the day dedicated to emergency cases, are likely to facilitate early cholecystectomy. In fact, recent evidence supports a dedicated emergency surgery team as the catalyst for more efficient management of gallstone disease.(37-41)

The main strengths of this study include its population-based scope, the quality of the data sources, as well as the study setting - a health care system where emergency surgical care is only accessed through single-payer funded public hospitals. However, the study also has limitations. The first is potential residual confounding related to the severity of cholecystitis. We attempted to reduce this potential bias by excluding patients with severe cholecystitis and prior gallstone disease. While a gradient of severity (captured by duration of symptoms, white blood cell count, gallbladder wall thickness on ultrasound) is likely present in our study cohort, it is reasonable to expect that this gradient be similarly distributed across hospitals, particularly after adjusting for age, sex, socioeconomic status and comorbidity level. Furthermore, we believe the extent of variability across hospital is too large to be fully explained by unmeasured differences in cholecystitis severity. The second limitation is that we are unable to identify the decision-making surgeon in our data sources. Nevertheless, many surgeon characteristics such as physician practice type and cholecystectomy volumes would be expected to overlap with the hospital characteristics we included. As such, the measured hospital effects are likely partly attributable to the characteristics of a hospital's surgeons. Finally, definitions of the timeframe for early cholecystectomy range in the literature between 24 hours and 7 days from symptom onset or diagnosis.(5) While we chose a broad timeframe definition (within 7 days from ED presentation), when we defined early cholecystectomy as occurring within 3 days of ED presentation, we found the same extent of variability and similar associations on multivariable analysis (data available on request).

In conclusion, hospital-level factors, independent of patient characteristics, appear strongly related to practice. This finding suggests that hospital-specific initiatives should be considered to facilitate early cholecystectomy for acute cholecystitis.

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FIGURES

Figure 1 - Exclusion flowchart

Figure 2A - Variability in the rate of early cholecystectomy across hospitals (N=24,437 patients, 106 hospitals)

Figure 2B - Variability in the rate of early cholecystectomy rate across hospitals among young (<50 years) healthy patients without concurrent biliary tract obstruction or pancreatitis (N=2,894 patients, 102 hospitals)

TABLES

Table 1 - Multilevel multivariable logistic regression results showing association of patient and hospital characteristics with early cholecystectomy

FIGURES

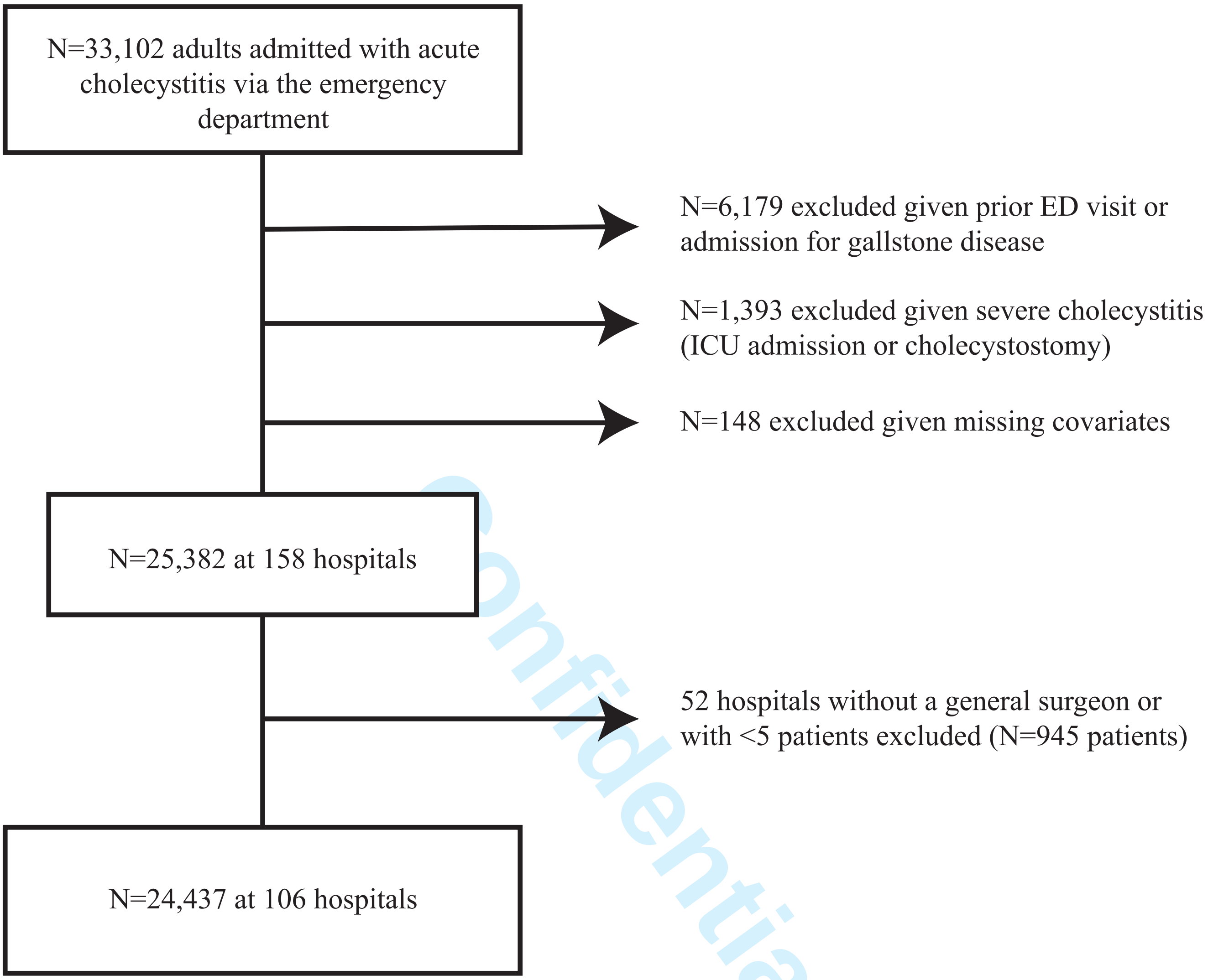

Figure 1. Exclusion flowchart

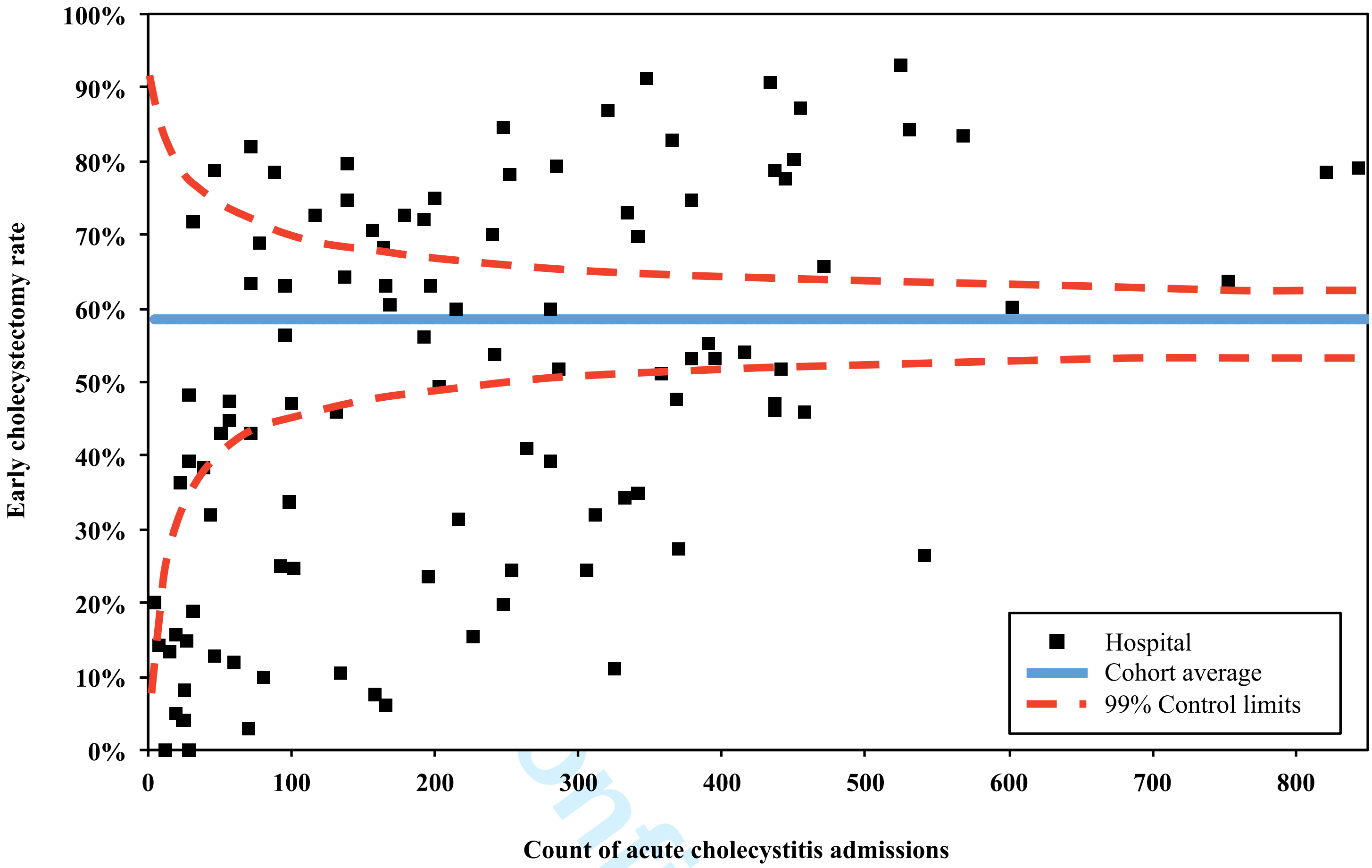

Figure 2A. Variability in the rate of early cholecystectomy across hospitals (N=24,437 patients, 106 hospitals)

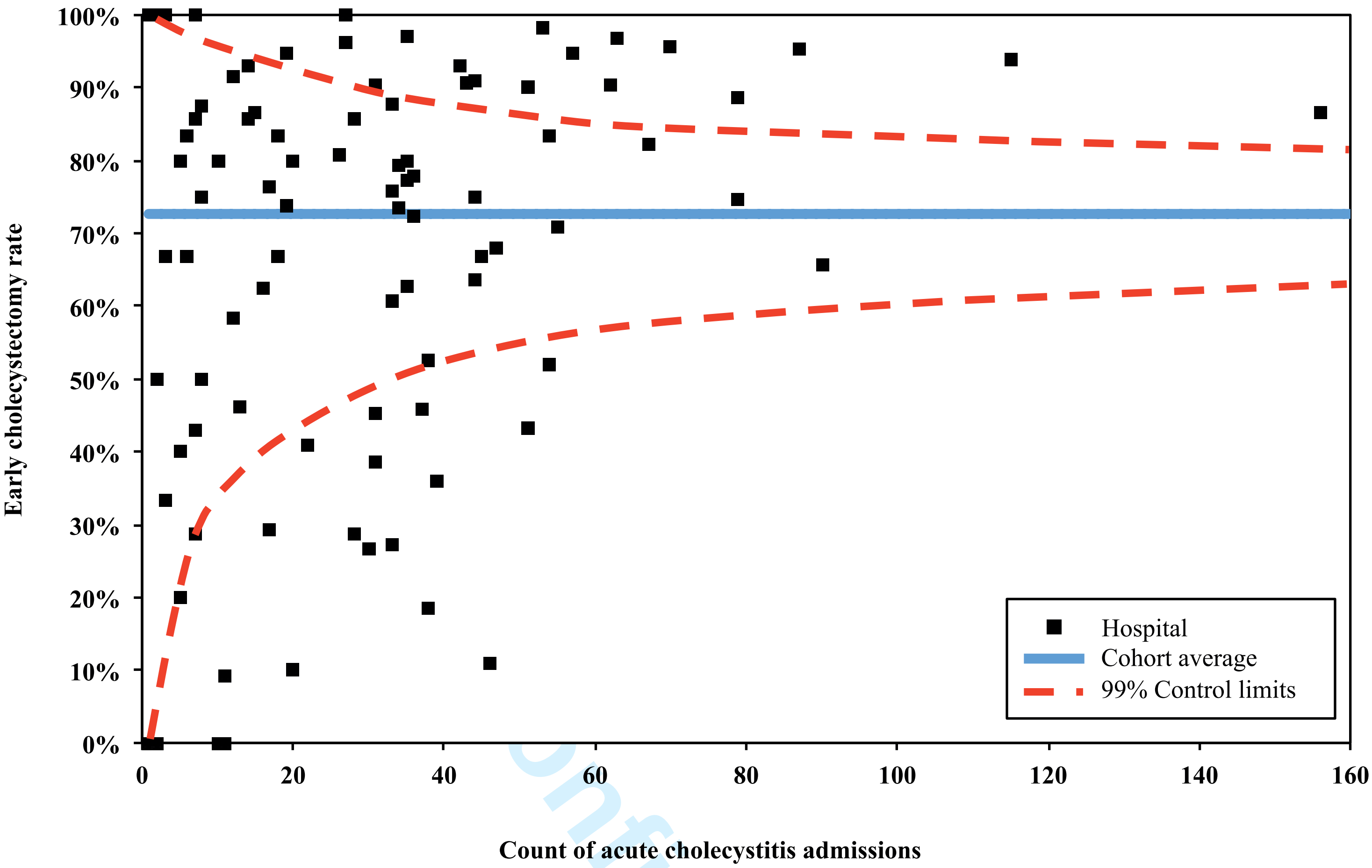

Figure 2B. Variability in the rate of early cholecystectomy rate across hospitals among young (<50 years) healthy patients without concurrent biliary tract obstruction or pancreatitis (N=2,894 patients, 102 hospitals)

Table 1. Multilevel multivariable logistic regression results showing association of patient and hospital characteristics with early cholecystectomy

Characteristic	Odds Ratio (99% CI)
Patient	
Age (years)	
18 – 35	Reference
36 – 50	0.92 (0.81 – 1.05)
51 – 65	0.69 (0.61 – 0.79)
66 – 80	0.46 (0.40 – 0.53)
>80	0.21 (0.18 – 0.25)
Female sex	0.87 (0.80 – 0.95)
Income quintile	
1	Reference
2	0.98 (0.87 – 1.10)
3	0.93 (0.82 – 1.05)
4	1.06 (0.94 – 1.21)
5 †	1.12 (0.98 – 1.27)
Comorbidity index quartile	
1	Reference
2	0.90 (0.80 – 1.01)
3	0.89 (0.79 – 1.00)
4 ‡	0.67 (0.60 – 0.75)
Common bile duct obstruction	0.41 (0.36 – 0.47)
Pancreatitis	1.14 (0.94 – 1.37)
Hospital	
Annual volume of acute cholecystitis admissions	
5-17	0.53 (0.35 – 0.78)
18-39	0.67 (0.52 – 0.87)
40-65	0.84 (0.72 – 0.97)
66-164	Reference
After-hours operating room utilization	
1	0.97 (0.72 – 1.30)
2	0.84 (0.66 – 1.07)
3	0.79 (0.64 – 0.97)
4 *	Reference
Annual volume of elective cholecystectomies	
0-74	1.02 (0.63 – 1.63)
75-159	1.15 (0.82 – 1.60)
160-279	1.11 (0.91 – 1.35)
280-905	Reference
Academic teaching hospital	0.71 (0.27 – 1.85)

† 1 is the lowest income level, ‡ 1 is the lowest level of comorbidity, * 4 is the highest level of after-hours operating room utilization

SUPPLEMENTAL APPENDIX

Univariable analysis results showing distribution of patient and hospital characteristics between exposure groups

On univariable analysis, patients who were younger, female, with a lower comorbidity burden and without common bile duct obstruction were more likely to undergo early operative intervention (Table S1). As well, patients admitted to non-teaching hospitals, hospitals that had high OR utilization after hours and, hospitals that had a high institutional volume of acute cholecystitis admissions and elective cholecystectomies, were more likely to undergo early cholecystectomy (Table S2).

Table S1. Distribution of patient characteristics

	Early cholecystectomy N=14,286	No early cholecystectomy N=10,151	P value
Age (years)			**<0.001**
18 – 35	2791 (20)	1200 (12)	
36 – 50	3859 (27)	1863 (18)	
51 – 65	3857 (27)	2447 (24)	
66 – 80	2990 (21)	2975 (29)	
>80	809 (6)	1666 (17)	
Female sex	8,810 (62)	5,553 (55)	**<0.001**
Income quintile			**0.02**
1	3,165 (22)	2,119 (22)	
2	3,017 (21)	2,234 (22)	
3	2,754 (19)	2,086 (21)	
4	2,802 (20)	1,887 (19)	
5 †	2,548 (18)	1,745 (17)	
Comorbidity index quartile			**<0.001**
1	4,132 (29)	2,134 (21)	
2	3,799 (27)	2,370 (24)	
3	3,339 (23)	2,330 (23)	
4 ‡	3,016 (21)	3,317 (32)	
Common bile duct obstruction	1,119 (8)	1,539 (16)	**<0.001**
Pancreatitis	659 (5)	464 (5)	0.88

All values are presented as N(%), † 5 is the highest income level, ‡ 4 is the greatest level of comorbidity

Table S2. Distribution of hospital characteristics

	Early cholecystectomy N=14,286	No early cholecystectomy N=10,151	P value
Teaching status			**<0.001**
Academic teaching	2,467 (17)	2720 (27)	
Non-teaching	11,819 (83)	7,431 (73)	
After-hours operating room utilization			**<0.001**
1	1,036 (7)	1,238 (12)	
2	2,712 (18)	2,156 (21)	
3	4,505 (31)	3,154 (31)	
4 †	6,033 (44)	3,603 (36)	
Annual volume of acute cholecystitis admissions			**<0.001**
5-17	502 (3)	2,119 (9)	
18-39	1,935 (14)	2,234 (17)	
40-65	3,799 (27)	2,086 (33)	
66-164	8,050 (56)	1,887 (41)	
Annual volume of elective cholecystectomies			**<0.001**
0-74	938 (7)	1,364 (13)	
75-159	2,515 (18)	1,700 (17)	
160-279	4,481 (31)	2,712 (27)	
280-905	6,352 (44)	4,375 (43)	

All values are presented as N(%), † 4 is the highest level of after-hours operating room utilization

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
✓ **Title and abstract**	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
✓Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
✓Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
✓Study design	4	Present key elements of study design early in the paper
✓Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
✓Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
✓Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
✓Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
✓Bias	9	Describe any efforts to address potential sources of bias
✓Study size	10	Explain how the study size was arrived at
✓Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
✓Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
✓Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
✓Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
✓Outcome data	15*	Report numbers of outcome events or summary measures over time
✓Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
✓Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
✓Key results	18	Summarise key results with reference to study objectives
✓Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
✓Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
✓Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
✓Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.