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David K. Warren

Katelin B. Nickel

Anna E. Wallace

Daniel Mines

Fang Tian

See next page for additional authors

Authors
David K. Warren, Katelin B. Nickel, Anna E. Wallace, Daniel Mines, Fang Tian, William J. Symons, Victoria J. Fraser, and Margaret A. Olsen

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Risk Factors for Surgical Site Infection After Cholecystectomy

David K. Warren,[1] Katelin B. Nickel,[1] Anna E. Wallace,[4] Daniel Mines,[4] Fang Tian,[4] William J. Symons,[2] Victoria J. Fraser,[1] and Margaret A. Olsen[1,3]

[1]Division of Infectious Diseases, Department of Medicine, [2]Department of Surgery, and [3]Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri; and [4]HealthCore, Inc., Wilmington, Delaware

Background. There are limited data on risk factors for surgical site infection (SSI) after open or laparoscopic cholecystectomy.

Methods. A retrospective cohort of commercially insured persons aged 18–64 years was assembled using *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) procedure or Current Procedural Terminology, 4th edition codes for cholecystectomy from December 31, 2004 to December 31, 2010. Complex procedures and patients (eg, cancer, end-stage renal disease) and procedures with pre-existing infection were excluded. Surgical site infections within 90 days after cholecystectomy were identified by ICD-9-CM diagnosis codes. A Cox proportional hazards model was used to identify independent risk factors for SSI.

Results. Surgical site infections were identified after 472 of 66 566 (0.71%) cholecystectomies; incidence was higher after open (n = 51, 4.93%) versus laparoscopic procedures (n = 421, 0.64%; $P < .001$). Independent risk factors for SSI included male gender, preoperative chronic anemia, diabetes, drug abuse, malnutrition/weight loss, obesity, smoking-related diseases, previous *Staphylococcus aureus* infection, laparoscopic approach with acute cholecystitis/obstruction (hazards ratio [HR], 1.58; 95% confidence interval [CI], 1.27–1.96), open approach with (HR, 4.29; 95% CI, 2.45–7.52) or without acute cholecystitis/obstruction (HR, 4.04; 95% CI, 1.96–8.34), conversion to open approach with (HR, 4.71; 95% CI, 2.74–8.10) or without acute cholecystitis/obstruction (HR, 7.11; 95% CI, 3.87–13.08), bile duct exploration, postoperative chronic anemia, and postoperative pneumonia or urinary tract infection.

Conclusions. Acute cholecystitis or obstruction was associated with significantly increased risk of SSI with laparoscopic but not open cholecystectomy. The risk of SSI was similar for planned open and converted procedures. These findings suggest that stratification by operative factors is important when comparing SSI rates between facilities.

Keywords. administrative health claims data; cholecystectomy; risk factors; surgical site infection.

Surgical site infection (SSI) is the most common healthcare-associated infection [1, 2] and contributes to increased length of hospitalization and healthcare costs [1, 3]. Cholecystectomy is the most commonly performed abdominal surgery and one of the most common ambulatory procedures performed in the United States [4, 5]. The incidence of SSI is higher after open versus laparoscopic cholecystectomy, with reported SSI rates after open cholecystectomy ranging from 1.1% to 8.4% [6–16] versus 0.3% to 3.4% after laparoscopic cholecystectomy [6–16].

Although open cholecystectomy has been consistently associated with higher risk of SSI [6, 7, 10, 13, 17–19], other risk factors for SSI have not been as well established. Older age [6, 7, 18, 20, 21], male gender [6, 7, 13], longer duration of surgery [6, 13, 17, 18, 20], multiple surgical procedures [6, 20], higher severity of illness [6, 8, 10, 17, 18], and contaminated/infected wound class [6, 8, 17, 18] have been reported as independent risk factors for SSI after cholecystectomy. The impact of other patient-, operative-, and postoperative-level factors on SSI risk after cholecystectomy has not been well studied, and it may be important for risk stratification in facilities with different patient case mix. Because the majority of cholecystectomy operations are performed in ambulatory surgery, we sought to investigate risk factors for SSI in patients without serious underlying medical conditions after cholecystectomy in a large, geographically diverse cohort of privately insured persons.

METHODS

Primary Data Source

We conducted a retrospective cohort study using the HealthCore Integrated Research Database, which includes all fully adjudicated claims submitted for reimbursement from providers, facilities, and outpatient pharmacies linked to private health plan enrollment information, as described previously [22].

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Correspondence: D. K. Warren, Washington University School of Medicine, Division of Infectious Diseases, Campus Box 8051, 660 S. Euclid Ave., St. Louis, MO 63110 (dwarren@wustl.edu).

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Cholecystectomy Patient Population

We identified cholecystectomy procedures performed at a hospital on an inpatient or outpatient basis or at a freestanding ambulatory surgery center (ASC) using *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) and Current Procedural Terminology, 4th edition (CPT-4) procedure codes from facility and provider claims between December 31, 2004 and December 31, 2010 among members aged 18–64 years (Supplementary Appendix 1). To capture comorbidities, we excluded members lacking prescription drug coverage and/or 365 days of prior insurance enrollment before cholecystectomy.

Exclusion of Erroneous Claims for Cholecystectomy

We excluded erroneous claims (ie, facility claims with apparent CPT-4, Healthcare Common Procedure Coding System, or UB-04 revenue codes truncated to 4 digits and populated in the fields reserved for ICD-9-CM procedure codes) as described previously [22]. We also excluded claims in which a cholecystectomy procedure code was present only on 1 line on a single claim, with no other claims on the same date.

Exclusion of Complicated Patients and Procedures

Because our focus was on SSI risk in patients who would be eligible to have their procedure performed in ambulatory surgery, we excluded cholecystectomy procedures performed in medically complicated patients (ie, coded for cancer, chemotherapy, end-stage renal disease, or prior organ transplant) from 30 days (365 for organ transplant) before to 7 days after cholecystectomy (Supplementary Appendix 1). We also excluded complex operations, defined as those in which motor vehicle accident, fracture involving the skull or trunk, abdominal compartment syndrome, or gunshot wound were coded on the same claim as the cholecystectomy or on a contemporaneous ambulance or emergency department claim, and other complicated procedures, as defined in Supplementary Appendix 1. We also excluded cholecystectomy procedures performed on the day of or after another surgical procedure during the same hospitalization; additional surgical procedures were identified using the procedure codes used for SSI surveillance by the National Healthcare Safety Network (NHSN) [23] and additional CPT-4 codes for abdominal surgeries (Supplementary Appendix 1). We did not exclude a cholecystectomy if another procedure occurred after the cholecystectomy, because these might have been performed as a result of a complication of the cholecystectomy. Finally, we excluded cholecystectomies performed on or after day 3 of an inpatient hospital stay because these patients would not have had the opportunity for surgery in an ambulatory facility.

Surgery Date and Classification of Cholecystectomy

All provider and facility claims for cholecystectomy within 7 days were collapsed into a single surgery due to the potential for inaccuracy in dates [24]. When there was more than one date within 7 days coded for cholecystectomy, we compared facility and provider surgery dates and incorporated supplemental evidence from other unique providers to determine the most likely surgery date (Supplementary Appendix 1). After consolidating service dates, if there was still more than 1 claim date for cholecystectomy within an individual person, we used the first claim date as the study procedure date.

We classified the cholecystectomy as laparoscopic or open based on ICD-9-CM procedure and CPT-4 codes from the provider and facility (Supplementary Appendix 1). As described previously [22], to obtain more accurate SSI rates by surgical approach, we excluded cholecystectomy procedures that were coded by a provider- or facility-only, or when the provider and facility coded discordant surgical approaches.

Identification of Surgical Site Infection

Surgical site infections recorded 2–90 days after cholecystectomy were identified using ICD-9-CM diagnosis codes from inpatient and outpatient facilities and provider claims. We did not include claims with SSI diagnosis codes from service locations inconsistent with a provider diagnosis of SSI (eg, home, ambulance) and claims with CPT-4 codes for laboratory services (88104-88399) to avoid "rule-out" diagnoses. Persons with claims for SSI, peritonitis, retroperitoneal infection, or septicemia (ICD-9-CM diagnosis 038.0–0.38.9, 790.7) between 30 days before to 1 day after the cholecystectomy date were excluded due to pre-existing infection.

The diagnosis codes used to identify SSIs included postoperative wound infection (998.5, 998.51, 998.59), peritonitis (567.2–567.29, 567.9), and retroperitoneal infection (567.3–567.39). We also considered a diagnosis code of cellulitis of the trunk (682.2) on the same claim as a CPT-4 code for incision and drainage (10060, 10061, 10180, 11005, 49020, 49021, 49040, 49041, 49060, 49061) as evidence of SSI, consistent with the NHSN definition of SSI [23]. The ICD-9-CM diagnosis code for unspecified cellulitis (682.9) was also used to identify SSIs, but only if it was on the same claim as an abdomen-specific CPT-4 code for incision and drainage (11005, 49020, 49021, 49040, 49041, 49060, 49061), or if it was coded on the same claim as an incision and drainage procedure by the operating surgeon. We defined the SSI onset date as described previously [25]. We categorized SSIs as serious if they were coded during an inpatient admission or within 14 days of a laparotomy (ICD-9-CM procedure 54.11, 54.12, 54.19; CPT-4 49000, 49002) or incision and drainage procedure (as per codes defined above).

We identified SSIs up to 90 days after surgery, with earlier censoring for the end of insurance enrollment or the day after subsequent abdominal surgery. We excluded nonabdomen-specific ICD-9-CM diagnosis codes for SSI (eg, 998.59) if the code was first recorded after a nonabdominal NHSN surgery. We extended surveillance beyond the standard NHSN definition of symptom onset within 30 days because an SSI is not detectable in claims data until the patient presents for care, which could be delayed from symptom onset. In addition, previous work has shown that limiting identification of SSI to 30 days can miss

a large proportion of infections, depending on the procedure [26].

Identification of Risk Factors for Surgical Site Infection

We obtained patient age and sex from enrollment files. Patient home zip code was matched to year 2000 census median household income [27] to determine income quartile and linked to the 2006 National Center for Health Statistics (NCHS) urban-rural classification scheme [28] through a 5-digit Federal Information Processing Standard code to determine patient urban-rural status.

Patient comorbidities and postoperative risk factors were identified using ICD-9-CM diagnosis codes [29], ICD-9-CM/CPT-4 procedure codes, and outpatient prescription drug claims. All inpatient facility claims were included; we excluded provider and outpatient facility claims containing only CPT-4 or UB-04 revenue codes for pharmacy, diagnostic radiology/cardiology/pulmonology, clinical laboratory, physical/occupational therapy, speech pathology, or ambulance services, to increase the likelihood that the diagnosis was assigned by a clinician. One or more inpatient claim(s) or ≥2 provider or outpatient facility claims from −365 to + 7 days after cholecystectomy were required to establish the diagnosis of most comorbidities (Supplementary Appendix 2) [30]. Postoperative risk factors were restricted to those factors coded before SSI.

We included cholecystectomy-related diagnoses on the same claim as the cholecystectomy procedure and concurrent procedures as potential operative risk factors (Supplementary Appendix 2). Conversion to an open procedure was defined based on the ICD-9-CM diagnosis code for laparoscopic to open conversion in patients coded for open cholecystectomy; if the provider and facility coded a laparoscopic cholecystectomy, we assumed the conversion code referred to another procedure on the same claim because the conversion diagnosis code is not specific to cholecystectomy.

We used the American Hospital Association (AHA) Annual Survey of Hospitals (Health Forum, LLC, Chicago, IL) and the Outpatient Surgery Center Profiling Solution data (IMS Health, Plymouth Meeting, PA) to determine whether the cholecystectomy was performed at a hospital or freestanding ASC. These sources were matched to the facility where the cholecystectomy was performed using National Provider Identifier codes (when available) or facility name and address fields. Among facilities matching to a hospital in the AHA survey, determination of inpatient or outpatient procedure was based on an inpatient designation by the facility for admissions with length of stay of 1 day or inpatient designation by the facility or provider for admissions with length of stay greater than 1 day. Number of beds, medical school affiliation, residency program, and ownership were captured from the AHA data for hospitals, whereas number of surgical procedures, urban location of facility, and region in the United States were available for hospitals and ASCs. Urban-rural location of the facility was available in the AHA data directly; we used the NCHS urban-rural classification scheme linked to ASC zip code for the IMS Health data.

Statistical Analysis

We used univariate and multivariable Cox proportional hazards models to examine risk factors for SSI, and we accounted for censoring before the 90-day follow-up period. For multivariable models, backward selection was used with $P < .05$ as the cutoff for inclusion among variables with $P < .2$ in univariate models. We assessed multicollinearity by examining the tolerance values in each model to ensure independence of explanatory variables. In the event of multicollinearity, we considered model performance (C-statistic) to determine which variable to use in the final model. Post hoc testing was performed to determine whether related risk factors had significantly different hazard ratios (HRs) in the multivariable model. As sensitivity analyses to determine the robustness of our model, we developed models for early SSI (within 30 days of surgery) and serious SSI. All data management and analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC). This study was approved by the Washington University Human Research Protection Office with a waiver of informed consent.

RESULTS

A total of 160 817 cholecystectomy patients met initial eligibility criteria during the 7-year study period. The number of patients was reduced to 66 566 after removing procedures coded by either provider or facility alone (n = 10 738), procedures performed at the time of another abdominal operation (n = 15 698), procedures performed after the second day of hospitalization or at the same time or after another NHSN surgery (n = 14 232), procedures in medically complicated patients (n = 5622), procedures with discordant coding for open versus laparoscopic approach (n = 727), procedures performed at the time of pre-existing infection (n = 753), and patients without prescription drug coverage (n = 5204) or without 1 year of prior insurance coverage (n = 41 277).

Over 98% of the cholecystectomy procedures were performed laparoscopically (65 532 of 66 566). Of the 1034 open procedures, 499 were planned open procedures and 535 were laparoscopic converted to open procedures. Seventy-five percent of operations were performed in females, and the median age at time of surgery was 45 years (range 18–64). Persons who had a laparoscopic procedure were more likely to be female and younger than those with open cholecystectomy ($P < .001$). Most operations were performed as same day surgery in a hospital (58%) or during an inpatient hospital admission (16%). Planned open or converted procedures were more likely than laparoscopic procedures to be performed during an inpatient hospitalization (861 [83.3%] vs 15 586 [23.8%]; $P < .001$).

Four hundred seventy-two surgical site infections were identified after the 66 566 procedures (0.71%) (Table 1). Eighty-one

Table 1. Univariate Cox Proportional Hazards Model of Risk Factors for SSI After Cholecystectomy[a]

Variable	Category	SSI n (%)	No SSI n (%)	*P*	Hazards Ratio (95% CI)
Total		472	66 094		
Patient factors					
Demographics					
Age	18–25 years	19 (4.0)	4675 (7.1)	.008	1.00
	26–30 years	40 (8.5)	5742 (8.7)		1.71 (0.99–2.95)
	31–35 years	53 (11.2)	6962 (10.5)		1.86 (1.10–3.14)
	36–40 years	48 (10.2)	8160 (12.3)		1.44 (0.84–2.44)
	41–45 years	49 (10.4)	9157 (13.9)		1.31 (0.77–2.22)
	46–50 years	72 (15.3)	9604 (14.5)		1.83 (1.10–3.03)
	51–55 years	73 (15.5)	9054 (13.7)		1.97 (1.19–3.26)
	56–60 years	74 (15.7)	7800 (11.8)		2.31 (1.39–3.82)
	61–64 years	44 (9.3)	4940 (7.5)		2.18 (1.27–3.73)
Male		167 (35.4)	16 609 (25.1)	<.001	1.63 (1.35–1.97)
Comorbidities/Medications					
Anticoagulopathy drugs		n < 10	437 (0.7)	.107	1.94 (0.87–4.34)
Blood loss anemia		13 (2.8)	660 (1.0)	<.001	2.80 (1.61–4.86)
Chronic anemia		36 (7.6)	1417 (2.1)	<.001	3.75 (2.67–5.27)
Congestive heart failure		22 (4.7)	1314 (2.0)	<.001	2.41 (1.57–3.70)
Depression		30 (6.4)	2953 (4.5)	.048	1.45 (1.00–2.10)
Diabetes mellitus		79 (16.7)	5835 (8.8)	<.001	2.07 (1.63–2.64)
Drug abuse		n < 10	318 (0.5)	<.001	3.98 (2.06–7.70)
Hypertension		191 (40.5)	21 795 (33.0)	.001	1.38 (1.15–1.66)
Liver disease		11 (2.3)	617 (0.9)	.002	2.52 (1.39–4.59)
Malnutrition/weight loss		21 (4.4)	1234 (1.9)	<.001	2.44 (1.57–3.77)
Obesity		82 (17.4)	7511 (11.4)	<.001	1.64 (1.29–2.08)
Peripheral vascular disease		n < 10	414 (0.6)	.005	2.72 (1.35–5.47)
Pneumonia or urinary tract infection		26 (5.5)	2208 (3.3)	.010	1.69 (1.14–2.51)
Psychoses		23 (4.9)	2139 (3.2)	.047	1.53 (1.01–2.33)
Renal failure		n < 10	219 (0.3)	<.001	5.18 (2.58–10.43)
Smoking		74 (15.7)	8538 (12.9)	.073	1.26 (0.98–1.61)
Smoking-related diseases		39 (8.3)	2371 (3.6)	<.001	2.42 (1.74–3.36)
Staphylococcus aureus infection		n < 10	85 (0.1)	<.001	6.56 (2.45–17.55)
Operative Factors					
Facility					
Type of facility	Inpatient hospital	166 (35.2)	10 798 (16.3)	<.001	1.00
	Outpatient hospital	188 (39.8)	38 711 (58.6)		0.32 (0.26–0.39)
	ASC	20 (4.2)	4038 (6.1)		0.32 (0.20–0.51)
	Missing facility[b] or uncertain inpatient designation[c]	98 (20.8)	12 547 (19.0)		0.51 (0.40–0.65)
Number of beds	1–299	253 (53.6)	32 714 (49.5)	.121	1.00
	300–499	81 (17.2)	13 508 (20.4)		0.78 (0.60–1.00)
	500+	62 (13.1)	8728 (13.2)		0.92 (0.70–1.21)
	ASC	20 (4.2)	4038 (6.1)		0.64 (0.41–1.01)
	Missing facility[b]	56 (11.9)	7106 (10.8)		1.02 (0.77–1.37)
Medical school affiliation	Yes	175 (37.1)	22 267 (33.7)	.140	1.16 (0.95–1.42)
	No	221 (46.8)	32 683 (49.4)		1.00
	ASC	20 (4.2)	4038 (6.1)		0.73 (0.46–1.16)
	Missing facility[b]	56 (11.9)	7106 (10.8)		1.17 (0.87–1.57)
Residency program	Yes	142 (30.1)	17 126 (25.9)	.063	1.23 (1.00–1.52)
	No	254 (53.8)	37 824 (57.2)		1.00
	ASC	20 (4.2)	4038 (6.1)		0.74 (0.47–1.17)
	Missing facility[b]	56 (11.9)	7106 (10.8)		1.18 (0.88–1.57)
Ownership	Government	49 (10.4)	5594 (8.5)	.178	1.00
	Nongovernment, not for profit	303 (64.2)	42 194 (63.8)		0.82 (0.61–1.11)
	Investor owned, for profit	44 (9.3)	7162 (10.8)		0.70 (0.47–1.05)
	ASC	20 (4.2)	4038 (6.1)		0.57 (0.34–0.95)
	Missing facility[b]	56 (11.9)	7106 (10.8)		0.90 (0.62–1.33)

Table 1. Continued

Variable	Category	SSI n (%)	No SSI n (%)	*P*	Hazards Ratio (95% CI)
Cholecystectomy					
Acute cholecystitis/obstruction		205 (43.4)	17 481 (26.4)	<.001	2.13 (1.78–2.56)
Other/chronic cholecystitis		386 (81.8)	56 202 (85.0)	.047	0.79 (0.62–1.00)
Choledocholithiasis		37 (7.8)	2652 (4.0)	<.001	2.03 (1.45–2.84)
Surgical approach	Laparoscopic approach	421 (89.2)	65 111 (98.5)	<.001	1.00
	Laparoscopic converted to open approach	28 (5.9)	507 (0.8)		8.48 (5.79–12.44)
	Planned open approach	23 (4.9)	476 (0.7)		7.40 (4.87–11.26)
Endoscopic retrograde cholangiopancreatography		n < 10	302 (0.5)	<.001	3.74 (1.86–7.52)
Bile duct exploration		12 (2.5)	426 (0.6)	<.001	3.97 (2.24–7.04)
Postoperative Factors					
Chronic anemia		33 (7.0)	1289 (2.0)	<.001	3.76 (2.64–5.35)
Pneumonia or urinary tract infection		28 (5.9)	1386 (2.1)	<.001	2.91 (1.99–4.27)

Abbreviations: ASC, ambulatory surgery center; CI, confidence interval; SSI, surgical site infection.

[a]The following factors had $P \geq 0.2$ and were excluded from the table: patient home urban/rural location, patient income quartile, alcohol abuse, cancer, coagulopathy, disease-modifying antirheumatic drugs or biologic drugs, oral corticosteroids, skin disease, total annual surgical procedures quartile for performing facility, facility urban/rural location, facility region of the United States, cholelithiasis, cholangiography, and other bile duct procedures.

[b]Missing facility type due to no match to a facility in the American Hospital Association Annual Survey of Hospitals or the IMS Health Outpatient Surgery Center Profiling Solution data or a match to multiple facilities.

[c]Uncertain inpatient hospital admission due to inpatient designation based on a same-day nonfacility claim.

percent of SSIs were first identified 2–30 days postsurgery, 12.9% between 31–60 days, and 5.7% between 61–90 days after the procedure. The incidence of SSI was significantly higher after an open (4.93% [51 of 1034]) versus laparoscopic cholecystectomy (0.64% [421 of 65 532]; $P < .001$). Overall, 63.1% of SSIs were serious. There was no significant difference between

Table 2. Multivariable Cox Proportional Hazards Model of Significant Risk Factors for SSI After Cholecystectomy

Variable	Category	Adjusted Hazards Ratio (95% CI)
Patient Risk Factors		
Male		1.42 (1.17–1.72)
Chronic anemia		2.46 (1.67–3.63)
Diabetes mellitus		1.53 (1.19–1.98)
Drug abuse		2.85 (1.46–5.54)
Malnutrition/weight loss		2.09 (1.34–3.25)
Obesity		1.39 (1.09–1.77)
Smoking-related diseases		1.63 (1.16–2.28)
Staphylococcus aureus infection		3.43 (1.26–9.31)
Operative Risk Factors		
Type of facility	Inpatient hospital	1.00
	Outpatient hospital	0.57 (0.45–0.74)
	ASC	0.65 (0.40–1.05)
	Missing facility or uncertain inpatient hospital designation[a]	0.81 (0.62–1.06)
Surgical approach and acute cholecystitis/obstruction	Laparoscopic approach without acute cholecystitis/obstruction	1.00
	Laparoscopic approach with acute cholecystitis/obstruction	1.58 (1.27–1.96)
	Laparoscopic converted to open approach without acute cholecystitis/obstruction	7.11 (3.87–13.08)
	Laparoscopic converted to open approach with acute cholecystitis/obstruction	4.71 (2.74–8.10)
	Planned open approach without acute cholecystitis/obstruction	4.04 (1.96–8.34)
	Planned open approach with acute cholecystitis/obstruction	4.29 (2.45–7.52)
ERCP/bile duct exploration[b]		2.08 (1.31–3.30)
Postoperative Risk Factors (Before SSI)		
Chronic anemia		1.68 (1.12–2.53)
Pneumonia or urinary tract infection		2.15 (1.45–3.17)

Abbreviations: ASC, ambulatory surgery center; CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; SSI, surgical site infection.

[a]Missing facility type due to no match to a facility in the American Hospital Association Annual Survey of Hospitals or the IMS Health Outpatient Surgery Center Profiling Solution data or a match to multiple facilities. Uncertain inpatient admission due to inpatient designation based on a same-day nonfacility claim.

[b]ERCP and bile duct exploration combined for multivariable model due to small cell counts.

the proportion of serious SSIs that were early (within 30 days of surgery) compared with nonserious SSIs (83.9% [250 of 298] vs 77.0% [134 of 174], respectively; $P = .064$). Infection rates were similar for planned open and converted-to-open procedures (4.61% [23 of 499] and 5.23% [28 of 535], respectively; $P = .643$).

Univariate risk factors for SSI are noted in Table 1. For the multivariable analysis, an interaction term was included in the model to analyze the impact of acute cholecystitis/obstruction depending on the operative approach (Table 2). Patient-level risk factors for SSI included male gender, chronic anemia, diabetes mellitus, drug abuse, malnutrition/weight loss, obesity, smoking-related diseases (eg, lung cancer, chronic obstructive pulmonary disease), and previous *Staphylococcus aureus* infection. Patients whose cholecystectomy was performed as an outpatient procedure at a hospital (HR 0.57) were at lower risk of SSI. Laparoscopic approach with acute cholecystitis/obstruction was associated with significantly increased risk of SSI compared with laparoscopic approach without acute cholecystitis (HR 1.58). Open cholecystectomy was associated with increased risk of SSI regardless of whether acute cholecystitis/obstruction was present (HR 4.29 and 4.04, respectively; $P = .891$ for post hoc comparison of the HRs). Conversion to open cholecystectomy was also associated with similar risk of SSI, regardless of whether acute cholecystitis/obstruction was present (HR 4.71 and 7.11, respectively; post hoc $P = .283$). In addition, the HRs for SSI for planned open compared with converted procedures were similar among those with ($P = .796$) and without ($P = .217$) acute cholecystitis/obstruction. Concurrent endoscopic retrograde cholangiopancreatography (ERCP)/bile duct exploration, postoperative chronic anemia, and postoperative pneumonia/urinary tract infection were also associated with significantly higher risk of SSI post-cholecystectomy.

In a sensitivity analysis comparing early SSI only versus no SSI, risk factors were generally similar to the original model. Previous *S aureus* infection, ERCP/bile duct exploration, and postoperative chronic anemia dropped out of the model and were among the factors with the smallest number of patients with SSI. The general trends and magnitude of HRs in the early SSI model were similar to the total SSI model, and in all cases the HRs in the early SSI model were within the 95% confidence interval of the HR from the total SSI model.

In the second sensitivity analysis restricting the outcome to serious SSI versus no SSI, new risk factors included older age and choledocholithiasis. Obesity, smoking-related diseases, and ERCP/bile duct exploration were dropped from the model. The general trends and magnitude of HRs in the serious SSI model were similar to the total SSI model, and in all cases the HRs in the serious SSI model were within the 95% confidence interval of the HR from the total SSI model.

DISCUSSION

There are few published data on risk factors for SSI after cholecystectomy, particularly after ambulatory procedures. Our study identifies new patient-, operative-, and postoperative risk factors for infection after cholecystectomy to the literature and confirms some risk factors identified in previous reports.

We found a 6-fold higher risk of SSI after open versus laparoscopic cholecystectomy, consistent with previous findings [6–16]. The incidence of SSI after laparoscopic cholecystectomy converted to an open procedure was the same as the SSI incidence after planned open cholecystectomy (5.23% and 4.61%, respectively). This contrasts with the finding of Bogdanic et al [13] who reported a higher SSI rate after laparoscopic to open conversion (17.9%) compared with open (6.1%) surgery, although only 28 operations in that study involved conversion. Two groups reported significantly increased risk of SSI after conversion from laparoscopic to open procedure compared with laparoscopic cholecystectomy, but neither study included planned open procedures [20, 31]. Our results suggest that in the present era, uncomplicated patients undergoing either planned or converted open cholecystectomy are at similar risk of SSI.

We found that acute cholecystitis or obstruction was associated with increased risk of surgical site infection after laparoscopic but not after open (planned or converted) cholecystectomy. This contrasts with the finding of Hussain and Khan [32] who reported no difference in the incidence of SSI in laparoscopic cholecystectomy patients in Saudi Arabia with acute versus chronic cholecystitis (1.7% and 1.3%, respectively). In other studies restricted to laparoscopic cholecystectomy, Giger et al [33] found increased risk of postoperative local and systemic complications (including SSI) with acute cholecystitis in multivariate analyses, whereas den Hoed et al [34] found an association in univariate analysis between acute cholecystitis and increased risk of SSI.

At the patient level, we found gender, chronic anemia, diabetes, drug abuse, malnutrition/weight loss, obesity, smoking-related diseases, and previous *S aureus* infection to be associated with increased risk of SSI. With the exception of diabetes [7], malnutrition [35], and male (vs female) gender [6, 7, 13], none of these conditions have been previously reported as independent risk factors for SSI after cholecystectomy. Men have also been shown to be at increased risk of conversion to open procedure [36–38] and intraoperative and postoperative local complications after cholecystectomy [33, 39]. In our study, men had more severe biliary disease compared with women, including higher proportions of men with acute cholecystitis or obstruction, choledocholithiasis, and open (planned or converted) operative approach (see Supplementary Appendix 3; data not shown). It is possible that the increased risk of SSI we found in men is due to residual confounding with increased severity of biliary tract disease that we were unable to completely capture with the claims data.

Limitations of our study include potential misclassification of diagnoses and likely undercoding of SSIs, especially minor infections diagnosed and treated only with oral antibiotics in outpatient settings during the 90-day global surgical reimbursement period [40]. Thus, our calculations for the incidence of SSI after cholecystectomy are likely underestimates of the true SSI rates. We found that slightly more than half of open cholecystectomy procedures were not planned, but due to the limitations of our data source we were unable to determine why the conversion was necessary. In addition, our findings may not be generalizable to all patients undergoing cholecystectomy, because we limited our surgical population to less complex procedures in privately insured, nonelderly adults.

A major strength of our study is the large, geographically diverse nature of the patient population. Because of this, we identified many novel risk factors, including an interesting interaction between surgical approach and the presence of acute cholecystitis/obstruction. In addition, we were able to compare the risk of SSI after open, converted to open and laparoscopic procedures, which has not been done previously. Because these data contain information from numerous urban and rural ambulatory and hospital settings, a wide variety of surgical practices are captured. In addition, we used longitudinal claims data to identify infections after discharge across the full spectrum of care. This is particularly important for procedures performed in ambulatory settings, because patients may be diagnosed and treated for SSIs at a facility other than where the surgery was performed. Another strength of our study is the robustness of our findings, because models restricted to early SSI and serious SSI yielded similar results.

CONCLUSIONS

The SSI risk factors we identified after cholecystectomy may be helpful for risk stratification to adjust for differences in patient mix between different facilities. This is important when comparing SSI rates between institutions, because facilities may have differing proportions of complex cases requiring an open approach and patients with more severe gallbladder disease. Failure to account for this complexity in case mix may result in misclassifying institutions as having a higher than expected rate of infection after cholecystectomy. In the current era of pay-for-performance and publicly reported healthcare-associated infection rates, this could have considerable negative impact for providers and facilities. Most importantly, understanding the relevant perioperative risk factors for infection will better inform patients and healthcare providers what to anticipate after this common surgical procedure and may allow targeted interventions in high-risk groups to reduce postoperative infections.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Potential conflicts of interest. D. K. W. reports consultant work with Centene Corp., Worrell Inc., Cepheid Inc., Carefusion, and Pfizer Inc. for work outside the submitted manuscript. At the time of the study, A. E. W., D. M., and F. T. were employees of HealthCore, a wholly owned subsidiary of Anthem, Inc., a health insurance company. A. E. W. has received Anthem stock options and participated in an Anthem employee stock purchase plan. D. M. is now an employee of Merck, Inc. and has received stock grants as part of his employment. V. J. F. reports her spouse is the Senior Vice President and Chief Medical Officer for Express Scripts; she has received grants from the Foundation for Barnes-Jewish Hospital. M. A. O. reports consultant work with Merck, Pfizer, and Sanofi Pasteur and grant funding through Cubist Pharmaceuticals, Pfizer, and Sanofi Pasteur for work outside the submitted manuscript. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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