ANESTHESIOLOGY

Patient Sex and Postoperative Outcomes after Inpatient Intraabdominal Surgery: A Population-based Retrospective Cohort Study

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ABSTRACT

Background: Intraabdominal surgeries are frequently performed procedures that lead to a high volume of unplanned readmissions and postoperative complications. Patient sex may be a determinant of adverse outcomes in this population, possibly due to differences in biology or care delivery, but it is understudied. The authors hypothesized that there would be no association between patient sex and the risk of postoperative adverse outcomes in intraabdominal surgery.

Methods: This retrospective, population-based cohort study involved adult inpatients aged 18 yr or older who underwent intraabdominal surgeries in Ontario, Canada, between April 2009 and March 2016. The authors studied the association of patient sex on the primary composite outcome of all-cause death, hospital readmission, or major postoperative complications, all within 30 postoperative days. Inverse probability of exposure weighting based on propensity scores (computed using demographic characteristics such as rural residence status and median neighborhood income quintile, common comorbidities, and surgery- and hospital-specific characteristics) was used to estimate the adjusted association of sex on outcomes.

Results: The cohort included 215,846 patients (52.3% female). The primary outcome was observed in 24,712 (21.9%) females and 25,486 (24.7%) males (unadjusted risk difference, 2.8% [95% CI, 2.5 to 3.2%]; $P < 0.001$). After adjustment, the association between the male sex and the primary outcome was not statistically significant (adjusted risk difference, –0.2% [95% CI, –0.5 to 0.2%]; $P = 0.378$).

Conclusions: In a large population of intraabdominal surgical patients, there was no differential risk between sexes in the composite outcome of all-cause death, hospital readmission, or major postoperative complications, all within 30 postoperative days.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Sex-based disparities exist for outcomes after cardiac surgery, trauma care, and postoperative sepsis
- Previous analyses of general surgery patients using U.S. administrative data have demonstrated that female sex may be associated with lower rates of complications, but the reproducibility of this observation is unclear

What This Article Tells Us That Is New

- Among 215,846 patients undergoing major inpatient abdominal surgery in Ontario, Canada, from 2009 to 2016, 24,712 females (21.9%) and 25,486 males (24.7%) experienced death, readmission, or major complications, all within 30 days
- After adjusting for comorbidities, surgical details, and sociodemographic factors, patient sex was not associated with a statistically significant difference in the composite outcome of death, readmission, or major complications

Research has shown that sex-based differences in the incidence of diseases as well as the efficacy and safety of therapeutic interventions may be attributed to differential exposures, susceptibilities, metabolism, physiology, immune response, and behavioral attitudes of medical personnel toward male compared with female patients.[1,2] Widely recognized sex-based differences now exist for outcomes in cardiac surgery,[3] trauma,[4] and sepsis.[5,6] In spite of this evidence, significant sex bias, as a result of inadequate sex-based reporting or the unequal inclusion of males and females, persists in surgical clinical research published in the top surgical journals.[7]

Intraabdominal surgeries such as intestinal surgery, cholecystectomy, and appendectomy are among the most common surgical procedures performed in Ontario, Canada.[8] Moreover, in the United States, cholecystectomy and

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gastrectomy are among the most frequently performed and fastest-growing procedures in females, respectively.[9] Thus, any sex-based differences in outcomes in this population should be measured and understood in order to establish that there is equitable health care being delivered to males and females.

Previous studies that have assessed whether sex may differentially affect postoperative outcomes in intraabdominal surgery have excluded many relevant procedures[10–13] (including elective procedures[10,11,13]) and have had methodologic limitations such as residual confounding and the use of stepwise regression.[11–14] As such, the objectives of this population-based study were to ascertain the association of patient sex with postoperative adverse outcomes after inpatient intraabdominal surgeries using appropriate observational study methodology and to determine whether surgical subtype, surgical priority status (*i.e.*, elective *vs.* urgent/emergency), and/or age acted as effect modifiers in this association. We hypothesized that the incidence of the composite primary outcome of all-cause death, hospital readmission, or major postoperative complications, all within 30 postoperative days, would not be different for males compared with females.

Materials and Methods

Study Design and Data Sources

This retrospective, population-based cohort study used administrative healthcare data from Ontario, Canada. All residents of Ontario (population, approximately 14 million) obtain healthcare services from a government-administered single-payer system. A unique, encoded identifier permitted linkage across several administrative databases, which were then analyzed at ICES (formerly known as the Institute for Clinical Evaluative Sciences, Canada). The analysis was conducted on an existing ICES dataset created for a previous project.[15] Databases used to construct this dataset included the Canadian Institute for Health Information's (Ottawa, Ontario, Canada) Discharge Abstract Database (in-hospital outcomes) and National Ambulatory Care Reporting System (emergency department visits), and the Ontario Ministry of Health and Long-term Care's (Toronto, Ontario, Canada) Ontario Health Insurance Plan (physician billings), Corporate Provider Database (physician demographic data), and Registered Persons Database (patient demographics and vital status). A data analysis and statistical plan was written after the data were accessed. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology[16] and Reporting of Studies Conducted Using Observational Routinely-collected Data[17] guidelines. Ethics approval for this secondary analysis was not required under Section 45 of Ontario's *Personal Health Information Protection Act*. This act defines prescribed entities, including ICES, that do not need consent from patients for the collection or analysis of routinely collected data.

Patients

The study included adults (aged 18 yr or older) undergoing one of eight broad categories of intraabdominal surgery (esophageal, gastric, intestinal, appendiceal, rectal, biliary, pancreatic, hepatic), according to Canadian Classification of Health Intervention codes, from April 1, 2009, to March 31, 2016. A list of the surgical procedures included in this study and corresponding Canadian Classification of Health Intervention codes are provided in Supplemental Digital Content 1 (http://links.lww.com/ALN/C789). We included inpatients (*i.e.*, patients admitted to hospital for at least 1 night after surgery), both laparoscopic and open surgeries, as well as elective and urgent/emergency surgeries. Elective surgeries comprised patients who were admitted for scheduled treatment. Urgent/emergency surgeries comprised patients who were admitted for a serious or life-threatening condition, patients who required immediate assessment and treatment, patients who had a scheduled admission but had to be admitted earlier than the scheduled admission because they required immediate assessment/treatment, and patients admitted from another facility who required an unscheduled immediate assessment/treatment. We excluded outpatients because, by definition, they did not have a measurable hospital length of stay, and they were unlikely to have major complications, intensive care unit (ICU) admission, or death.[18] For patients who had multiple surgeries within the accrual period, only the first eligible surgery was included.

Exposure and Outcomes

Patient sex was recorded in the Registered Persons Database. This database contains a person's sex as coded on their Ontario Health Insurance Plan card (biologic sex at birth determined by caregivers that can be changed to self-identified gender upon demand). The primary and all secondary outcomes were specified *a priori*. The primary outcome was a composite of all-cause death, hospital readmission, or major postoperative complications, all within 30 days of the index surgery. Secondary outcomes included the three separate components of the primary outcome, ICU admission during the hospitalization, hospital length of stay, number of emergency department visits in Ontario within 90 days and any emergency department visit within 90 days. Major postoperative complications such as respiratory and cardiac complications, bleeding and blood clots, severe life-threatening or major vital organ–threatening adverse outcome, hospital- and surgery-related complications, acute kidney injury, new-onset hemodialysis, and stroke were defined by Canadian Classification of Health Intervention codes, International Statistical Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes, and/or Ontario Health Insurance Plan physician billings.[19,20] See Supplemental Digital Content 2 (http://links.lww.com/ALN/C790) for a list of the major complications and corresponding Canadian Classification of Health Intervention codes, ICD-10 diagnostic codes, and/or Ontario Health Insurance Plan physician billing codes.

Statistical Analysis

Our study sample consisted of all cases in the existing fixed dataset that met our eligibility criteria, and thus, an *a priori* power analysis was not performed. Using the inverse probability of exposure weighting based on propensity scores, we controlled for measured confounding, accounting for systematic differences in baseline characteristics between male and female surgical patients.[21]

The propensity score was estimated using a multivariable logistic regression model,[22] specified *a priori,* where the dependent variable was sex, and the covariates included age, comorbidities ascertained using a 5-yr look-back window (hypertension, coronary artery disease, heart failure, peripheral arterial disease, diabetes, previous stroke or transient ischemic attack, chronic liver disease, cancer, chronic kidney disease, and chronic obstructive pulmonary disease), duration of the surgery (categorized into deciles), fiscal year of hospital admission, region of the province, hospital teaching status (academic or not), institutional surgical case volume (in quintiles), patient's rural residence status, patient's median neighborhood income quintile, surgical priority status (elective or urgent/emergency), and surgical subtype. Absence or presence of individual comorbidities was determined using validated inpatient and outpatient records *via* ICES data holdings.[23] Comparable to the use of hierarchical modeling to analyze the association of patient characteristics with adverse outcomes, covariate adjustment for hospital-specific characteristics was used to account for clustering within institutions.[24] Observations were then weighted to give those who were likely to be in the particular exposure group to which they belonged a lower weight than those who were unlikely to be in the exposure group to which they belonged. This approach created a pseudosample in which the distribution of covariates would be, on average, the same between exposed (*i.e.*, male) and unexposed (*i.e.*, female) patients. A limitation of covariate balancing using inverse probability of exposure weighting based on propensity scores is that very large weights can arise if exposed subjects have low propensity scores or if unexposed subjects have propensity scores close to 1. These large weights may unduly influence results and increase the variance of estimates. To mitigate this problem, we used weight truncation, wherein a threshold is prespecified, and weights exceeding this threshold are set to the threshold.[25,26] In our primary analysis, we truncated at the 98th percentile (*i.e.*, weights greater than the weight value at the 98th percentile were set to that weight value). This threshold was found to improve CI coverage without increasing bias for linear and additive propensity score–estimating logistic regression models.[25] Results were expressed as potential outcome means, adjusted risk differences, and adjusted relative risks. The balance of covariates pre- and postweighting were assessed using standardized differences.[21]

In sensitivity analyses that were specified *a priori*, the primary outcome was re-analyzed with (1) inverse probability of exposure weighting without truncation using the *teffects ipw* package in Stata (StataCorp LLC, USA), (2) 1:1 propensity score matching using a caliper width of 0.2 of the SD of the logit of the propensity score, (3) covariate adjustment using the propensity score as a continuous covariate in a logistic regression model, and (4) doubly robust regression adjustment with inverse probability of exposure weighting using the *teffects ipwra* package, in which the propensity score–weighted exposure as well as covariates used in propensity score estimation were included in the outcome regression model.

Homogeneity of subgroup effects were tested *via* a joint test of interaction between the exposure and the subgroup levels in a logistic regression model that was weighted by inverse probability of exposure weighting. For each of the three analyses, the subgroup variable of interest (surgical subtype, surgical priority status, or age group) was removed from the propensity score estimation model to ensure that this variable was not balanced between sexes before subgroup analysis.

In compliance with the regulatory requirements of ICES, cells with counts of five or fewer were reported as less than six. All continuous variables were expressed as the mean ± SD, and differences between groups were assessed using a Student's *t* test. Categorical variables were reported as the total number of cases and prevalence, and differences between groups were compared by Pearson chi-square test. Absolute standardized differences were calculated and expressed as percentages, with a standardized difference of less than 10% typically denoting unimportant differences between groups.[21]

A *P* value less than 0.05 was considered statistically significant (two-sided). A complete case analysis was used to analyze data. No corrections were made for multiple comparisons, so comparisons of secondary outcomes (including all-cause death, hospital readmission, individual organ system complications within 30 days of the index surgery, ICU admission during the hospitalization, hospital length of stay, number of emergency department visits in Ontario within 90 days, and any emergency department visit within 90 days) and subgroups (including surgical subtype, surgical priority status, and age group) between males and females were deemed exploratory. Analyses were conducted with Stata version 15.1.

Results

Of the 215,846 patients included in this study, 112,802 (52.3%) were female (fig. 1). Missing data occurred in three variables: 2,705 (1.3%) patients were missing data on duration of surgery; 885 (0.4%) patients were missing data on neighborhood income quintile; and fewer

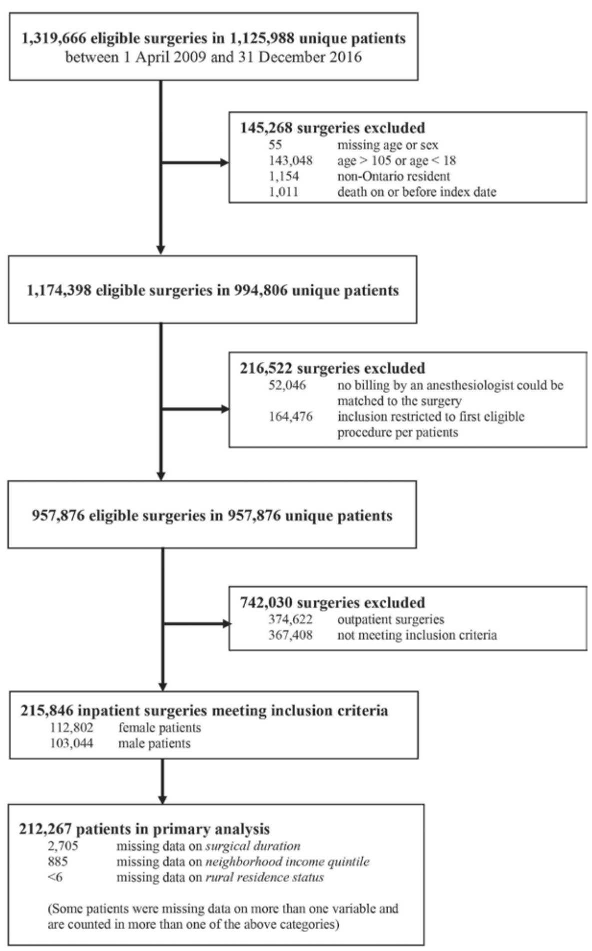

Fig. 1. Flow diagram of cohort build and missing data.

than 6 patients were missing data on rural residence status. From April 2009 to March 2016, the total number of patients receiving the surgeries that met our study's inclusion criteria declined slightly for both females and males. Important baseline differences between females and males were noted on several characteristics; notably, the prevalence of all individual comorbidities was higher in males (table 1).

The composite primary outcome of all-cause death, hospital readmission, or major complication within 30 days of the index surgery was observed in 24,712 (21.9%) females and 25,486 (24.7%) males (risk difference, 2.8% [95% CI, 2.5 to 3.2%]; $P < 0.001$). Before adjustment, males had a higher rate of the primary composite outcome and each component of the main outcome (table 2). The incidence of ICU admission was also higher and the hospital length of stay was longer for males. Male sex was associated with a statistically significant higher proportion of all postoperative complications, with the exception of stroke and venous thromboembolic events (table 3).

After adjustment, the absolute event rate was 23.0% in males and 23.2% in females, and males did not have a statistically significant increased risk of the primary composite outcome (adjusted risk difference, −0.2% [95% CI, −0.5 to 0.2%]; $P = 0.378$). Conversely, male sex was found to be associated with a statistically significant lower risk than female sex in exploratory secondary outcomes such as all-cause death within 30 days (adjusted risk difference, −0.2% [95% CI, −0.3 to −0.06%]; $P = 0.004$) and major complications within 30 days (adjusted risk difference, −0.4% [95% CI, −0.7 to −0.08%]; $P = 0.012$). Male sex was also associated with shorter hospital length of stay (adjusted risk difference, −0.3 days [95% CI, −0.4 to −0.1 days]; $P < 0.001$), a decreased number of emergency department visits within 90 days (adjusted risk difference, −0.03 visits [95% CI, −0.04 to −0.02 visits]; $P < 0.001$), and a lower proportion of any emergency department visits within 90 days (adjusted risk difference, −2.0% [95% CI, −2.4 to −1.6%]; $P < 0.001$). After adjustment in the analyses of the individual organ system complications, the risk of some complications was statistically significantly higher for males (table 3).

Across multiple sensitivity analyses, point estimates and 95% CIs were similar and consistent with the primary analysis. In Supplemental Digital Content 3 (http://links.lww.com/ALN/C791), the results of sensitivity analyses carried out for the primary outcome are displayed.

In our subgroup analyses, heterogeneity was observed among the two surgical subtype groups (*i.e.*, esophageal, gastric, intestinal, appendiceal, rectal *vs.* biliary, pancreatic, hepatic) and among surgical priority groups (*i.e.,* elective *vs.* urgent/emergency), but the differences were larger for the latter. No statistically significant heterogeneity was observed among age groups (fig. 2).

Discussion

This large, population-based retrospective study investigated the association between sex and postoperative outcomes in Ontario's inpatient intraabdominal surgery population. Before adjustment, males fared worse than females in the primary outcome. After adjusting for prognostically important covariates, we did not find a statistically or clinically significant association of sex with the primary composite outcome.

Previous research has been discordant. In contrast to our findings, a large multicenter study[12] concluded that males fared worse in postoperative mortality and hospital length of stay. Consistent with our results, a small study focused on gastrointestinal surgeries[14] did not find a statistically significant association between sex and 30-day readmission. However, in both of these studies, the construction of the multivariable model was either unclear or had excluded prognostically important covariates such as socioeconomic status,[27] comorbidities,[28] and duration of surgery,[29] which may have confounded the association between sex and the outcomes of interest.

Table 1. Baseline Characteristics of the Patients: Before and After Inverse Probability of Exposure Weighting

	Observed Data (n = 215,846)			Inverse Probability of Exposure-weighted Data (Pseudosample) (n = 212,267)		
Characteristic	Females (n = 112,802)	Males (n = 103,044)	Absolute Standardized Difference (%)	Females (n = 106,154.6)	Males (n = 106,112.4)	Absolute Standardized Difference (%)
Age, yr						
Mean ± SD	55.0 ± 19.8	55.5 ± 19.1	2.3	55.3 ± 19.9	55.3 ± 19.0	0.5
Median [interquartile range]	56 [39–71]	58 [41–71]	—	—	—	—
Comorbidities						
Charlson comorbidity index						
Mean ± SD	0.89 ± 1.5	1.35 ± 1.7	28.4	—	—	—
Median [interquartile range]	0 [0–2]	1 [0–2]	—	—	—	—
Charlson comorbidity index, number of conditions						
0	49,781 (44.1%)	31,766 (30.8%)	27.7	—	—	—
1	7,943 (7.0%)	6,710 (6.5%)	2.2	—	—	—
2+	21,543 (19.1%)	27,723 (26.9%)	18.3	—	—	—
No hospitalizations in previous 5 yr (*i.e.*, no data available)	33,535 (29.7%)	36,845 (35.8%)	13	—	—	—
Hypertension	46,459 (41.2%)	43,855 (42.6%)	2.7	44,364.9 (41.8%)	44,467.9 (41.9%)	0.2
Coronary artery disease	16,281 (14.4%)	20,768 (20.2%)	15.1	18,081.6 (17.0%)	18,358.6 (17.3%)	0.03
Congestive heart failure	5,523 (4.9%)	5,858 (5.7%)	3.4	5,608.9 (5.3%)	5,639.4 (5.3%)	0.03
Peripheral vascular disease	785 (0.7%)	1,214 (1.2%)	5	946.1 (0.9%)	986.3 (0.9%)	0.09
Diabetes	18,846 (16.7%)	21,501 (20.9%)	10.7	19,724.5 (18.6%)	19,949.2 (18.8%)	0.04
Previous stroke or transient ischemic attack	1,945 (1.7%)	2,152 (2.1%)	2.5	2,014.2 (1.9%)	2,030.2 (1.9%)	0.004
Chronic liver disease	6,441 (5.7%)	7,388 (7.2%)	5.8	6,756.2 (6.4%)	6,819.5 (6.4%)	0.1
Chronic kidney disease	4,926 (4.4%)	5,794 (5.6%)	5.7	5,229.6 (4.9%)	5,291.8 (5.0%)	0.05
Chronic obstructive pulmonary disease	15,920 (14.1%)	15,863 (15.4%)	3.6	15,641.6 (14.7%)	15,721.9 (14.8%)	0.1
Cancer	15,748 (14.0%)	21,452 (20.8%)	18.1	18,059.0 (17.0%)	18,364.3 (17.3%)	0.1
Duration of surgery (min)						
Mean ± SD	136.4 ± 113.3	154.3 ± 122.1	15.2	144.4 ± 125.4	145.4 ± 112.8	0.2
Median [interquartile range]	110 [74–172]	123 [78–199]	—	—	—	—
Fiscal year of hospital admission						
2010	17,647 (15.6%)	16,053 (15.6%)	0.3	16,125.4 (15.2%)	16,118.5 (15.2%)	0.005
2011	16,297 (14.5%)	14,742 (14.3%)	0.06	14,828.0 (14.0%)	14,817.2 (14.0%)	0.01
2012	16,429 (14.6%)	15,055 (14.6%)	0.1	15,665.8 (14.8%)	15,648.9 (14.8%)	0.009
2013	15,757 (14.0%)	14,150 (13.7%)	0.9	14,905.9 (14.0%)	14,881.4 (14.0%)	0.003
2014	15,582 (13.8%)	14,381 (14.0%)	0.3	14,891.5 (14.0%)	14,899.1 (14.0%)	0.02
2015	15,581 (13.8%)	14,207 (13.8%)	0.2	14,836.7 (14.0%)	14,839.3 (14.0%)	0.006
2016	15,509 (13.8%)	14,456 (14.0%)	0.6	14,901.4 (14.0%)	14,908.0 (14.1%)	0.01
Region						
Metropolitan Toronto	38,544 (34.2%)	36,696 (35.6%)	3.0	36,972.9 (34.8%)	37,016.4 (34.9%)	0.06
Southwestern Ontario	33,969 (30.1%)	30,818 (29.9%)	0.3	31,799.6 (30.0%)	31,786.7 (30.0%)	0.06
Eastern Ontario	27,892 (24.7%)	24,578 (23.9%)	2.1	25,932.5 (24.4%)	25,883.4 (24.4%)	0.005
Northern Ontario	12,397 (11.0%)	10,952 (10.6%)	1.3	11,449.6 (10.8%)	11,425.9 (10.8%)	0.005
Hospital teaching status			1.0			0.06
Academic	36,475 (32.3%)	33,777 (32.8%)		34,344.7 (32.4%)	34,380.5 (32.4%)	
Non-academic	76,327 (67.7%)	69,267 (67.2%)		71,809.9 (67.7%)	71,731.9 (67.6%)	
Patient's rural residence status			1.5			0.03
Rural area	14,430 (12.8%)	13,688 (13.3%)		13,634.6 (12.8%)	13,652.0 (12.9%)	
Urban area	98,372 (87.2%)	89,355 (86.7%)		92,519.9 (87.2%)	92,460.5 (87.1%)	
Surgical priority status			7.4			0.2
Elective	38,501 (34.1%)	38,602 (37.5%)		37,462.4 (35.3%)	37,617.2 (35.5%)	
Urgent/emergency	74,301 (65.9%)	64,442 (62.5%)		68,692.2 (64.7%)	68,495.2 (64.6%)	
Institutional surgical case volume (quintiles: 1 = low; 5 = high)						
1	266 (0.2%)	217 (0.2%)	0.4	210.6 (0.2%)	207.2 (0.2%)	0.04
2	3,709 (3.3%)	3,387 (3.3%)	0.09	3,485.9 (3.3%)	3,477.5 (3.3%)	0.02
3	15,318 (13.6%)	13,427 (13.0%)	1.6	14,209.9 (13.4%)	14,174.6 (13.4%)	0.01
4	30,253 (26.8%)	27,014 (26.2%)	1.3	28,219.9 (26.6%)	28,168.4 (26.6%)	0.008
5	63,256 (56.1%)	58,999 (57.3%)	2.3	60,028.4 (56.6%)	60,084.7 (56.6%)	0.03

(*Continued*)

Table 1. (Continued)

Characteristic	Observed Data (n = 215,846)			Inverse Probability of Exposure-weighted Data (Pseudosample) (n = 212,267)		
	Females (n = 112,802)	Males (n = 103,044)	Absolute Standardized Difference (%)	Females (n = 106,154.6)	Males (n = 106,112.4)	Absolute Standardized Difference (%)
Census-based neighborhood income quintile (1 = low; 5 = high)						
1	22,987 (20.5%)	19,468 (19.0%)	3.8	21,006.7 (19.8%)	20,901.6 (19.7%)	0.09
2	22,661 (20.2%)	20,425 (19.9%)	0.7	21,258.3 (20.0%)	21,224.4 (20.0%)	0.03
3	22,285 (19.8%)	20,562 (20.0%)	0.5	21,170.0 (19.9%)	21,176.7 (20.0%)	0.01
4	23,061 (20.5%)	21,544 (21.0%)	1.2	22,003.1 (20.7%)	22,026.8 (20.8%)	0.02
5	21,351 (19.0%)	20,617 (20.1%)	2.8	20,716.4 (19.5%)	20,783.0 (19.6%)	0.1
Surgical subtype			18.7			0.1
Esophageal, gastric, intestinal, appendiceal, rectal	84,116 (74.6%)	84,574 (82.1%)		82,896.6 (78.1%)	83,123.6 (78.3%)	
Biliary, pancreatic, hepatic	28,686 (25.4%)	18,470 (17.9%)		23,258.0 (21.9%)	22,988.8 (21.7%)	

All numbers are n (%) unless otherwise specified. The inverse probability of exposure-weighted data is a pseudosample that was created after weighting based on propensity scores and was not directly observed.[26] Due to this weighting, there is an apparent fraction of patients in the pseudosample. Since the Charlson comorbidity index was not included in the statistical model, the pseudosample observation numbers were not provided for this variable. Comorbidities were ascertained with a 5-yr look-back period. The Charlson comorbidity index is a list of 17 comorbidities identified by the International Classification of Diseases, Tenth Revision. Each comorbidity has an associated weight (1–6), with the sum of all weights resulting in a single score for a patient. Patients with no identified comorbidities receive a score of zero, and patients with more comorbidities have higher scores. Standardized differences compare imbalance among variables and are uninfluenced by sample size. Many authors consider a standardized difference of less than 10% as indicative of good balance between groups.[21]

Although a statistically significantly lower risk existed in males for five of seven exploratory secondary outcomes, the magnitude and clinical importance of these associations were small at the individual patient level. However, given the large number of patients in Ontario undergoing intraabdominal surgery, our findings may have importance at the level of the overall healthcare system. Our subgroup analyses demonstrated that for surgical subtype, there was a statistically significant, but clinically unimportant, difference between males and females. For surgical priority status, there was a statistically significant difference: males had an increased risk of adverse events after elective surgery as compared to females, whereas the opposite was true for urgent/emergency surgery. If this association of sex with the outcomes is real, it would be clinically important. However, we caution that since no corrections were applied to account for the multiple comparisons among secondary outcomes and subgroups, results from these analyses could have been associated with false positive discoveries. These results are also incongruent with previous studies in which male sex predicted postoperative death after emergency gastrointestinal surgery and not elective surgery,[10,13] or where no association was observed between male sex and mortality after emergency gastrointestinal surgery.[11] These contradictions may possibly be explained by the omission of prognostically important covariates, whether through the use of stepwise regression to select for variables to include in the final multivariable model[10,11] or limitations in data collection.[13]

Several contextual aspects of our Canadian study may influence generalizability to the intraabdominal surgery population in the United States and should be considered. First, Canada's universal healthcare system may confer better overall access to care and better management of chronic health conditions, particularly among those who are economically vulnerable.[30] This is unlikely to affect our propensity score–adjusted results. However, race is another determinant of quality of care and satisfaction with care, the effect of which is more pronounced within the United States.[31] If found to be a confounder in the relationship between sex and our primary outcome, the generalizability of our results may be limited as we did not account for race in our propensity score. Second, female patients in the United States may experience more sex-inequitable surgical care than female patients in Canada. A 2018 study[32] found that female patients in the United States experienced the least positive quality of care compared with 10 other high-income countries, including Canada. If found to be true within intraabdominal surgical care, there may be implications for the generalizability of our outcome event rates and size of association of sex with outcomes to the United States. Last, there is a notable difference between the two countries regarding elective surgery wait times. In Canada, wait lists are common for surgical procedures; the procedures are scheduled according to relative need and availability of service. In the United States, wait times are shorter for most medical services and are determined by availability of service and ability to pay (insurance status).[33,34] Since we were unable to account for surgical wait time, a possible confounding variable, our results may differ in the context of the United States.

Table 2. Main Outcomes in the Study Cohort

	Unadjusted Values				Adjusted Values	
Outcome	Females* (n = 112,802)	Males (n = 103,044)	Unadjusted Risk Difference† (n = 215,846)	Unadjusted Relative Risk (for Binary Outcomes)† (n = 215,846)	Adjusted Risk Difference† (n = 212,267)	Adjusted Relative Risk (for Binary Outcomes)† (n = 212,267)
Primary outcome of all-cause death, hospital readmission, or major complication within 30 days	24,712 (21.9%)	25,486 (24.7%)	2.8% (2.5–3.2)‡	1.13 (1.11–1.15)	−0.2% (−0.5 to 0.2); $P = 0.378$	0.99 (0.98–1.01)
All-cause death within 30 days	2,872 (2.5%)	2,950 (2.9%)	0.3% (0.2–0.5)‡	1.12 (1.07–1.18)	−0.2% (−0.3 to −0.06); $P = 0.004$	0.93 (0.88–0.98)
Readmission within 30 days	7,560 (6.7%)	7,550 (7.3%)	0.6% (0.4–0.8)‡	1.09 (1.06–1.13)	0.1% (−0.1 to 0.3); $P = 0.345$	1.02 (0.98–1.05)
Major complication within 30 days	18,069 (16.0%)	18,981 (18.4%)	2.4% (2.1–2.7)‡	1.15 (1.13–1.17)	−0.4% (−0.7 to −0.08); $P = 0.012$	0.98 (0.96–0.995)
Intensive care unit admission	14,403 (12.8%)	15,951 (15.5%)	2.7% (2.4–3.0)‡	1.21 (1.19–1.24)	−0.1% (−0.3 to 0.2); $P = 0.607$	0.99 (0.98–1.01)
Hospital length of stay (days)						
Mean ± SD	7.6 ± 14.7	8.4 ± 16.3	0.8 days (0.7–0.9)‡	—	−0.3 days (−0.4 to −0.1)‡	—
Median [interquartile range]	4 [2–8]	5 [2–9]	—	—	—	—
Emergency department visits in Ontario within 90 days of the index surgery						
Mean ± SD	0.5 ± 1.1	0.5 ± 1.1	0.0 visits (−0.0 to 0.0); $P = 0.610$	—	−0.0 visits (−0.0 to −0.0)‡	—
Median [interquartile range]	0 [0–1]	0 [0–1]	—	—	—	—
Any emergency department visit within 90 days of the index surgery	32,056 (28.4%)	28,928 (28.1%)	−0.3% (−0.7 to 0.0); $P = 0.076$	1.0 (1.0–1.0)	−2.0% (−2.4 to −1.6)‡	0.9 (0.9–1.0)

Data are n (%) or percent (95% CI) unless otherwise specified. Risk differences and relative risks are for the male group relative to the female group. For example, the adjusted risk difference for the primary outcome of −0.2% (95% CI, −0.5 to 0.2%) means that the male group had a non–statistically significant 0.2% absolute decrease of all-cause death, hospital readmission, or major complication within 30 days compared with the female group. Since outcomes for the three components of the composite primary outcome were not mutually exclusive, the sum of the component outcomes' events exceeds the composite event rate. Diagnostic and intervention codes used to define outcomes are specified in Supplemental Digital Content 2 (http://links.lww.com/ALN/C790). Complete case analysis resulted in some missing data (fig. 1). Adjusted values were obtained from inverse probability of exposure weighting based on propensity scores. The propensity score was estimated using multivariable logistic regression with patient sex as the dependent variable and a vector of covariates as the independent variables (age, comorbidities with a 5-yr look-back window [hypertension, coronary artery disease, heart failure, peripheral arterial disease, diabetes, previous stroke or transient ischemic attack, chronic liver disease, cancer, chronic kidney disease, and chronic obstructive pulmonary disease], duration of the surgery [categorized into deciles], fiscal year of hospital admission, region of the province, hospital teaching status [academic or not], institutional surgical case volume [in quintiles], patient's rural residence status, patient's neighborhood income quintile, surgical priority status, and the surgical subtype).

*Reference group. †95% CI. ‡$P < 0.001$.

This study represents a necessary step toward achieving sex-equitable surgical research and health care that has only recently drawn attention. Our findings serve as evidence for the relative equality of outcomes, which may suggest equitable care and proportionate distribution of resources within the intraabdominal surgery setting in Ontario. Further research could explore whether males and females have clinically meaningful differences in outcomes across specific surgeries, surgical priority groups, and surgical approach categories (*i.e.*, laparoscopic *vs.* open) in the intraabdominal surgery population.

Our study has several important limitations that should be considered. First, ICD-10 diagnostic codes do not capture severity of outcomes and may not have captured all relevant adverse postoperative outcomes. Second, our study population was limited to adults aged 18 yr and older, and therefore our results may not necessarily apply to pediatric patients, wherein appendectomy and cholecystectomy represent two of the most common surgical procedures.[35,36] Third, certain relevant data were unavailable, preventing us from including potential confounders such as depression and race in our model. Fourth, since this was a reanalysis of an existing dataset in which surgical categories were coalesced into broader surgical subtype groups, we were unable to conduct subgroup analyses among the distinct surgical subtypes. This is problematic as different surgeries may have different associated risks. Last, despite our efforts in reducing the effects of known and measured confounders, we could not capture and account for the level of detail one encounters in daily practice. Furthermore, all observational studies will have some degree of residual confounding from unknown or unmeasured confounders. Strengths of our study were its population-based multicenter design, and its inclusion of elective surgeries and a wide variety of surgical subtypes across the intraabdominal surgery category. This generally minimizes the effects of selection bias that may be present

Table 3. Details of Major Postoperative Complications (Exploratory Analyses)

	Unadjusted Values				Adjusted Values			
Complication	Females* (n = 112,802)*	Males (n = 103,044)	Unadjusted Risk Difference† (n = 215,846)	Unadjusted Relative Risk† (n = 215,846)	Female Potential Outcome Mean† (n = 106,154.6)	Male Potential Outcome Mean† (n = 106,112.4)	Adjusted Risk Difference† (n = 212,267)	Adjusted Relative Risk† (n = 212,267)
Postoperative ventilation for ≥48 h	5,300 (4.70%)	5,747 (5.60%)	0.90% (0.7 to 1.1%)‡	1.19 (1.14–1.23)	5.20% (5.1–5.4%)	5.00% (4.9–5.1%)	−0.20% (−0.4 to −0.05%); $P = 0.013$	0.96 (0.92–0.99)
Complications directly related to surgery	6,682 (5.90%)	7,216 (7.00%)	1.10% (0.9 to 1.3%)‡	1.18 (1.14–1.22)	6.20% (6.1–6.4%)	6.40% (6.2–6.5%)	0.20% (−0.04 to 0.4%); $P = 0.114$	1.03 (0.99–1.06)
Hospital-acquired infection	8,348 (7.40%)	8,753 (8.50%)	1.10% (0.9 to 1.3%)‡	1.15 (1.12–1.18)	8.20% (8.0–8.3%)	7.70% (7.5–7.8%)	−0.50% (−0.7 to −0.3%)‡	0.94 (0.92–0.97)
Bleeding	2,628 (2.30%)	3,059 (3.00%)	0.60% (0.5 to 0.8%)‡	1.27 (1.21–1.34)	2.50% (2.4–2.6%)	2.70% (2.6–2.8%)	0.20% (0.09 to 0.4%)§	1.09 (1.03–1.15)
Respiratory complications	2,422 (2.10%)	3,092 (3.00%)	0.90% (0.7 to 1.0)‡	1.4 (1.33–1.47)	2.40% (2.3–2.5%)	2.70% (2.6–2.8%)	0.40% (0.2 to 0.5%)‡	1.15 (1.09–1.22)
Cardiac complications	2,659 (2.40%)	2,759 (2.70%)	0.30% (0.2 to 0.5%)‡	1.14 (1.08–1.20)	2.60% (2.5–2.7%)	2.50% (2.4–2.5%)	−0.10% (−0.3 to −0.003%); $P = 0.045$	0.95 (0.90–0.999)
Severe life- or major vital organ–threatening adverse outcome	2,950 (2.60%)	3,527 (3.40%)	0.80% (0.7 to 1.0%)‡	1.31 (1.25–1.37)	2.90% (2.8–3.0%)	3.10% (3.0–3.2%)	0.20% (0.05 to 0.3%); $P = 0.008$	1.07 (1.02–1.12)
Unplanned return to operating room	621 (0.60%)	891 (0.90%)	0.30% (0.2 to 0.4%)‡	1.57 (1.42–1.74)	0.60% (0.6–0.7%)	0.80% (0.7–0.8%)	0.20% (0.1 to 0.2%)‡	1.29 (1.16–1.43)
Acute kidney injury	772 (0.70%)	1,022 (1.00%)	0.30% (0.2 to 0.4%)‡	1.45 (1.32–1.59)	0.80% (0.7–0.8%)	0.90% (0.8–0.9%)	0.10% (0.06 to 0.2%)§	1.18 (1.07–1.30)
Hemodialysis (new onset)	379 (0.30%)	568 (0.60%)	0.20% (0.2 to 0.3%)‡	1.64 (1.44–1.87)	0.40% (0.3–0.4%)	0.50% (0.4–0.5%)	0.10% (0.06 to 0.2%)‡	1.3 (1.13–1.48)
Stroke	270 (0.20%)	262 (0.30%)	0.01% (−0.03 to 0.06%); $P = 0.486$	1.06 (0.90–1.26)	0.30% (0.2–0.3%)	0.20% (0.2–0.3%)	−0.03% (−0.07 to 0.02%); $P = 0.210$	0.89 (0.75–1.06)
Venous thromboembolic events	277 (0.20%)	290 (0.30%)	0.04% (−0.007 to 0.08); $P = 0.104$	1.15 (0.97–1.35)	0.30% (0.2–0.3)	0.30% (0.2–0.3)	−0.01% (−0.06 to 0.03); $P = 0.630$	0.96 (0.81–1.14)

Data are expressed as n (%) or percent (95% CI) unless otherwise specified. Risk differences and relative risks are for the male group relative to the female group. For example, the adjusted risk difference for postoperative ventilation for 48 h or more of −0.2% (95% CI, −0.4 to −0.05%) means that the male group had a statistically significant 0.2% absolute decrease in this outcome compared with the female group. Diagnostic and intervention codes used to define outcomes are specified in Supplemental Digital Content 2 (http://links.lww.com/ALN/C790). Complete case analysis resulted in some missing data (fig.1). Adjusted values were obtained from inverse probability of exposure weighting based on propensity scores. The propensity score was estimated using multivariable logistic regression with sex as the dependent variable and a vector of covariates as the independent variables (age, comorbidities with a 5-yr look-back window [hypertension, coronary artery disease, heart failure, peripheral arterial disease, diabetes, previous stroke or transient ischemic attack, chronic liver disease, cancer, chronic kidney disease, and chronic obstructive pulmonary disease], duration of the surgery [categorized into deciles], fiscal year of hospital admission, region of the province, hospital teaching status [academic or not], institutional surgical case volume [in quintiles], patient's rural residence status, patient's neighborhood income quintile, surgical priority status, and the surgical subtype). Potential outcome means represent the expected average of the outcome for an individual in either the male group or the female group. They reflect the outcomes in the inverse probability of exposure-weighted pseudosample (*i.e.*, postadjustment) and therefore were not directly observed.[26]

*Reference group. †95% CI. ‡$P < 0.001$. §$P = 0.001$.

Subgroup	Primary outcome: Female potential outcome mean (95% CI) n = 106,154.6	Male potential outcome mean (95% CI) n = 106,112.4	Adjusted risk difference (95% CI) n = 212,267	P-value for interaction
Overall effect			-0.3 (-0.6, 0.05)	
Surgical subtype				P < 0.001
Esophageal, gastric, intestinal, appendiceal, rectal n = 168,690	25.30% (25.0 to 25.6%)	25.60% (25.3 to 25.9%)	0.30% (-0.09 to 0.7%)	
Biliary, pancreatic, hepatic n = 47,156	14.50% (14.0 to 14.9%)	14.50% (14.0 to 15.0%)	0.05% (-0.6 to 0.7 %)	
Surgical priority				P < 0.001
Elective n = 77,103	26.00% (25.5 to 26.4%)	27.10% (26.7 to 27.6%)	1.20% (0.6 to 1.8 %)	
Urgent or emergency n = 138,743	21.60% (21.4 to 21.9%)	20.80% (20.5 to 21.1%)	-0.90% (-1.3 to -0.5%)	
Age group				P = 0.099
18-40 n = 55,100	9.70% (9.4 to 10.1%)	9.90% (9.5 to 10.3%)	0.20% (-0.3 to 0.7%)	
41-50 n = 29,642	16.10% (15.5 to 16.6%)	15.90% (15.3 to 16.5%)	-0.20% (-1.0 to 0.6 %)	
51-60 n = 37,363	21.40% (20.8 to 21.9%)	21.40% (20.8 to 22.0%)	0.03% (-0.8 to 0.8%)	
61-70 n = 38,369	27.70% (27.1 to 28.4%)	28.30% (27.7 to 28.9%)	0.50% (-0.3 to 1.4%)	
> 70 n = 55,372	37.80% (37.2 to 38.3%)	38.40% (37.8 to 39.0%)	0.60% (-0.1 to 1.4%)	

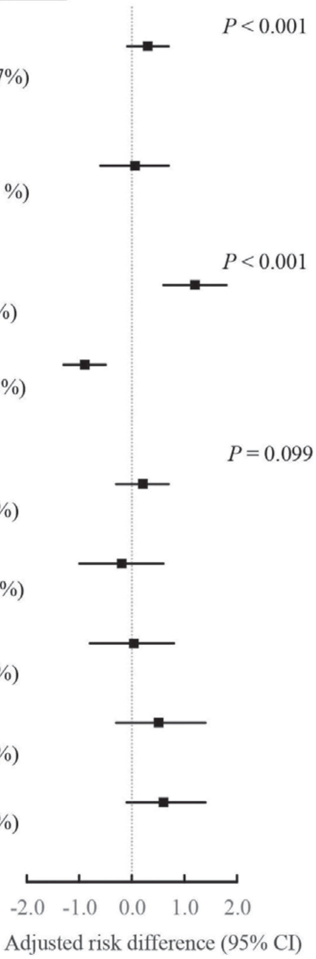

Fig. 2. Risk of adverse outcomes in the prespecified subgroups. The specified number of patients (n) in each subgroup is based on observed data. The subgroup effect was tested for homogeneity *via* a joint test of interaction between the exposure and the subgroup in a logistic regression model, which was weighted by the inverse probability of exposure, as determined by the propensity score. Risk differences are for the male group relative to the female group. Effect sizes plotted to the right of zero (line of no effect) imply superior outcomes for females, and effect sizes plotted to the left of zero imply superior outcomes for males. For example, the adjusted risk difference for the esophageal, gastric, intestinal, appendiceal, and rectal surgical subtype group of 0.3% (95% CI, –0.09 to 0.7) means that the males within this surgical subtype group had a non–statistically significant absolute increase of 0.3% in this outcome compared with the females within this surgical subtype group.

in single center studies[10,14] and may increase generalizability to other Canadian provinces. Furthermore, our study had a large sample size, with many events occurring for most outcomes in both the primary analyses and the exploratory analyses. In general, this allows for the detection of small differences in outcomes and permits more precise estimates. Finally, our principal findings were robust to analytic technique, including untruncated inverse probability of exposure weighting, propensity score matching, covariate adjustment using the propensity score, and doubly robust regression.

In a large population of adults undergoing inpatient intraabdominal surgeries from 2009 to 2016 in Ontario, Canada, we did not observe a clinically or statistically significant overall differential risk of adverse postoperative outcomes by patient sex. However, the association of sex with the primary outcome differed across surgical subtype and surgical priority groups. These findings suggest that equitable care may exist in Ontario for males and females undergoing intraabdominal surgery.

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Competing Interests

The authors declare no competing interests.

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