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Sex Differences in the Incidence of Severe Pain Events Following Surgery: A Review of 333,000 Pain Scores

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Abstract

Objective/Background—Prior work has not addressed sex differences in the incidence of severe postoperative pain episodes. The goal of this study was to examine sex differences in clinical postoperative pain scores across an array of surgical procedures using direct comparisons of numeric rating scale pain scores as well as using the incidence of severe pain events (SPEs).

Design/Setting—Retrospective cohort study of over 300,000 clinical pain score observations recorded from adult patients undergoing nonambulatory surgery at a tertiary care academic medical center over a 1-year period.

Methods/Patients—To test the hypothesis that the number of SPE on postoperative day (POD) 1 differed by sex after controlling for procedure, we calculated Cochran–Mantel–Haenszel statistics of sex by count of SPE, controlling for type of surgery.

Assessment Tools/Outcomes—Pain scores were collected from clinical nursing records where they were documented using the numeric rating scale.

Results—In female patients, 10,989 (25.09%) of 43,806 POD 1 pain scores were considered SPE compared with 10,786 (22.45%) of 48,055 POD 1 pain scores in male patients. This produced an overall odds ratio of 1.16 (99% confidence interval 1.11–1.20) for females vs males to report an SPE for a pain score on POD 1. Estimates of the odds that a given pain observation represents an SPE for female vs male patients after controlling for type of surgery yielded an odds ratio of 1.14 (99% confidence interval, 1.10–1.19).

Conclusion—Female patients experience greater mean pain scores, as well as a higher incidence of SPE, on POD 1 for a variety of surgical procedures.

Keywords

Sex; Gender; Pain; Surgery; Severe Pain Event; Numeric Rating Scale

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Introduction

Each year, over 70 million patients undergo surgery in the United States alone. Surveys suggest that over 80% of these patients will experience postoperative pain and that for over 85% of these patients, the pain will be rated as moderate to severe [1]. Prior work in laboratory models of pain testing consistently demonstrate significant sex differences in response to a variety of nociceptive stimuli [2,3]. These findings have been replicated across numerous types of clinical chronic pain conditions, where data overwhelmingly point toward an excess prevalence of pain in females compared with males [4–7]. However, studies in the postoperative pain setting have yielded mixed results regarding sex differences in analgesic consumption and reported pain scores [8–15].

Examinations of averaged measures of pain scores, evaluated through standard regression techniques, may fail to fully evaluate a patient's pain experience during recovery from surgery. For instance, mean pain scores may not reflect repeated patterns of severe episodic pain followed by temporary pain control via bolus doses of opioids. Prior work has not addressed potential sex differences in the incidence of severe postoperative pain episodes. However, the incidence of severe pain events (SPEs) after surgery is an important feature of postoperative pain characterization given new data associating severe postoperative pain scores with the development of chronic postsurgical pain [16–21]. Analysis of the incidence of SPE, as well as changes in pain during the early recovery period, may offer further insights into the patient postoperative pain experience.

If sex differences exist for severe pain episodes after surgery, acute pain services could use this information to create tailored approaches toward optimal postoperative pain management. The goal of this retrospective cohort study was to examine sex differences in postoperative pain control across an array of surgical procedures using direct comparisons of pain scores and the incidence of SPE. We hypothesized that the incidence of SPE, defined as pain scores greater than or equal to 7 of 10, on postoperative day (POD) 1 would be greater in female compared with male surgical patients.

Methods

The Institutional Review Board at the University of Florida approved this study, and study registration was not required given the retrospective nature of this project.

All data were obtained from the University of Florida's Integrated Data Repository. Subjects were those adult patients aged 21 and over undergoing nonambulatory surgery at Shands at the University of Florida over a 1-year period beginning in May 2011. Exclusion criteria included obstetric surgery and those patients who received multiple separate surgeries within the study period to avoid contamination of pain scores from time domain interference with preceding or proceeding surgeries.

All pain scores were recorded using the numeric rating scale (NRS) on an 11-point system, ranging from 0 to 10. Pain scores were entered using the EPIC electronic medical record system; this particular implementation provides education on the administration of the NRS query at the point of data entry in order to improve the veracity of collected data. The NRS represents one of the most widely employed pain intensity measurement tools in hospitals in the United States for collection of pain scores in communicative adult patients [22]. To this end, the NRS has been widely used for clinical research involving acute pain outcomes, although there is data to suggest that the NRS may systematically underestimate patient pain states in some health care systems [23–25]. Furthermore, the NRS is a well-validated method for collecting pain intensity measurements within clinical and experimental settings, thus allowing for a common metric across experimental and clinical pain research. Therefore, we elected to employ the NRS so that our results can be clinically translated to other U.S. civilian hospital populations.

Pain scores generally were recorded every 4 hours, per nursing protocol, with a repeat query within 1 hour after administration of analgesic medications for breakthrough pain, and increased numbers of observations for patients in higher acuity patient care settings. When the patient was listed as "asleep" during the charting of pain scores, the pain score was converted to a missing value rather than zero to account for the fact that some patients had received additional sedatives that may have facilitated sleep despite a strong nociceptive load. Missing values were considered as missing at random. All pain scores were recorded with a corresponding data/time stamp, which was converted to a "time in minutes following surgery." Pain scores were filtered to include only those obtained after the listed end-surgery time through the end of POD 5. General descriptions of postoperative pain here focused on POD 1 because this was the time period with the most frequent pain observations and minimal censuring of data due to hospital discharge. Severe postoperative pain was defined as a numeric rating score between 7 and 10 on a scale ranging from 0 to 10.

Types of surgery were identified using current procedural terminology (CPT) codes. Given the large number of CPT codes, surgeries were grouped into 244 different categories using the Clinical Categorization Software (CCS) for Services and Procedures provided by the Agency for Healthcare Research and Quality (http://www.hcup-us.ahrq.gov/toolssoftware/ccs_svcsproc/ccssvcproc.jsp). Only those CCS groups with at least 41 subjects per group were included due to prior evidence suggesting that this minimum group size was necessary to detect differences in pain score by sex [3].

Statistical Analyses

To evaluate the general influence of sex on postoperative pain and to place our results within the context of prior work, female vs male pain scores were compared using *t* tests on a per-procedural basis using the Satterthwaite approximation for degrees of freedom to account for unequal variance between groups. Prior work suggests that parametric methods may be used for analyzing numeric pain scores, given that parametric methods reflect similar power and false positive rates when compared with nonparametric methods for large samples [26,27]. Mean differences between groups were also reported using Satterthwaite confidence intervals (CIs). Data are presented as the mean with 99% CI.

To test the hypothesis that the number of SPE on POD 1 differed by sex after controlling for procedure, we calculated Cochran–Mantel–Haenszel statistics of sex by a count of SPE, controlling for CCS groups. Overall sex differences in the frequency of SPE reported between the end of surgery and the conclusion of POD 5 were calculated for comparison.

Additionally, the difference in proportions of POD 1 pain scores considered SPE between females and males was calculated globally and on a per-procedural level via chi-squared testing.

Given the large number of observations, an overall significance level of 0.01 was chosen. To correct for the many procedure-wise comparisons, corrections for multiple comparisons was performed using the method of Holm [28]. The Holm method is similar to that of Bonferroni but uses a step-down process that is less conservative while still maintaining the family-wise error rates of the Bonferroni method [29]. Given the retrospective nature of this study and the prespecified number of included observations, no power analysis was conducted. All analyses were conducted using sas version 9.3 (SAS Institute, Cary, NC, USA).

Results

A total of 349,797 pain observations from 8,332 subjects undergoing 147 different CCS categories of surgery were reviewed. The median number of observations was 38 (interquartile range of 20–60, total range of 1–181). A total of 69 CCS categories, representing 601 patients, and 16,351 pain observations were removed because female and/or male sex groups had less than 41 subjects for a given CCS category. The analyzed dataset included 333,446 pain observations from 7,731 subjects undergoing 78 different CCS categories of surgery.

Patient Demographics

An overview of patient demographics is given in Table 1. The mean age for females was 56.4 years (99% CI 55.7–57.1), and for males, 56.6 years (99% CI 55.9–57.3), a difference that was not statistically significant ($P = 0.7$). The mean body mass index for females was 29.5 kg (99% CI 29.2–29.9), and for males, 28.5 kg (99% CI 28.2–28.9), with a statistically significant mean difference of 0.99 kg (99% CI 0.5–1.5, $P < 0.0001$). The mean number of separate CPT codes per surgery was 1.74 (99% CI, 1.69–1.78) for females vs 1.65 (99% CI 1.61–1.70) for males, with a mean difference of 0.08 (99% CI 0.02–0.15, $P = 0.0001$). The mean Charlson Comorbidity Index for females was 1.04 (99% CI, 0.99–1.09) and for males, 1.18 (99% CI, 1.12–1.23), with a mean difference of 0.14 (99% CI, 0.07–0.21, $P < 0.0001$), indicating that males had more comorbid conditions than females.

Pain Scores

Pain scores recorded between the end of surgery and the end of POD 5 were statistically different between female and male patients (mean difference 0.36, 99% CI 0.33–0.40, $P < 0.0001$), with a mean score of 4.11 (99% CI 4.08–4.13) for females and 3.74 (99% CI, 3.72–3.76) for males (Figure 1). Given the change in pain scores over time for many patients, this comparison was repeated for pain scores obtained on POD 1. For POD 1 pain scores, there was a small but statistically significant difference according to sex (mean difference 0.22, 99% CI 0.16–0.28, $P < 0.0001$), with female mean pain scores of 4.20 (99% CI, 4.15–4.24) and male pain scores of 3.98 (99% CI, 3.94–4.02).

Table 2 compares the mean pain scores for female and male patients on POD 1 for the CCS categories of surgery. The mean difference between female and male patients, in addition to the 99% CI, are included to demonstrate the small magnitude of difference between female and male patients for a given surgery. These values range in absolute value from 0 to 2.03. There were 15 CCS categories for which the Holm's correction changed the significance from <0.01 to greater than the cutoff.

SPE by Sex from End of Surgery to End of POD 5

Of the 7,731 subjects, 6,797 (87.92%) reported at least one SPE between the end of surgery and the conclusion of POD 5. Of 3,739 female subjects, 3,166 (84.68%) reported at least one SPE between the end of surgery and POD 5 compared with 3,058 of 3,992 (76.60%) male subjects (chi-squared 80.92, $P < 0.0001$), giving an odds ratio of 1.69 (99% CI 1–1.96), which indicates female patients are at greater risk than male patients for experiencing at least one SPE.

Between the end of surgery and the conclusion of POD 5, 77,419 of 256,027 (23.22%) pain scores were considered SPE. Of the 160,709 pain scores recorded in female patients, 40,470 (25.18%) were considered SPE compared with 36,949 (21.39%) SPE of 172,737 pain scores for male patients. This suggested an overall odds ratio of 1.24 (99% CI 1.21–1.26) for female vs male patients for any given pain score to be an SPE from the end of surgery through the conclusion of POD 5, indicating that females are 24% more likely than males to have a SPE when they have pain.

SPE by Sex on POD 1

On POD 1, 7,485 subjects had recorded pain scores; this difference from the 7,731 subjects with scores documented between the end of surgery and POD 5 reflects those subjects who were intubated and/or had undocumented pain scores on POD 1 but subsequent recordings on POD 2 through POD 5. Of the 7,485 patients with pain scores recorded on POD 1, 4,559 (60.91%) reported at least one SPE. For females, 1,292 (64.44%) of 3,633 patients reported at least one SPE on POD 1 compared with 1,634 (57.58%) of 3,852 male patients (chi-squared 36.98, $P < 0.0001$). This suggested an overall odds ratio of 1.34 (99% CI 1.18–1.51) for the risk of female vs male patients experiencing at least one SPE on POD 1.

On POD 1, 21,775 (23.7%) of 91,861 pain observations were rated as an SPE. In female patients, 10,989 (25.09%) of 43,806 POD 1 pain scores were considered an SPE compared with 10,786 (22.45%) of 48,055 POD 1 pain scores as an SPE for male patients. This suggested an overall odds ratio of 1.16 (99% CI 1.11–1.20) for female vs male patients, indicating that female patients were 16% more likely than male patients to report an SPE for a pain score on POD 1.

SPE on POD 1 by Sex and Type of Surgery

To further characterize differences in postoperative pain experience while accounting for differing lengths of stay and for different types of surgical procedures, we examined the overall frequencies of POD 1 SPE in female and male patients for each CCS category of surgical procedures (Table 3). Cochran–Mantel–Haenszel statistics of sex by overall number of SPE on POD 1, controlling for CCS categories, supported the hypotheses for nonzero correlation, difference in mean scores, and general association of SPE frequency with sex, all at the $P < 0.0001$ level of significance. Estimates of the odds that a given pain observation represents an SPE for female vs male patients after controlling for CCS group yielded an odds ratio of 1.14 (99% CI 1.10–1.19).

For those procedures where the mean differences in pain score and the proportions of pain scores that were SPE were statistically different for females vs males, there was general agreement in the direction of difference (e.g., female greater than male incidence for SPE comparison along with female greater than male pain score for mean difference comparison) for those 11 procedures where the mean difference in pain scores and the incidence of SPE were statistically different according to sex (Figure 2).

Discussion

Our results support earlier clinical findings that suggest an overall sex difference in pain after surgery when pain scores are measured using the NRS in a clinical setting. Furthermore, these results demonstrate that for a wide variety of surgical procedures, there are differences in the incidence of SPE between female and male patients. These results were not limited to a single type of surgery but instead encompassed cardiothoracic, orthopedic, visceral, vascular, and soft tissue surgeries. In addition, these differences were observed despite a very conservative approach to avoiding type I errors. Despite the relatively small magnitude of the differences, the scale of our data allowed us to demonstrate the observed differences with a very high degree of certainty. Our aggregate results suggest that female patients may be at slightly higher risk for the severe pain scores that have been associated with the development of chronic postsurgical pain, although the nature of our retrospective study design obviously cannot identify the mechanisms driving these effects.

When evaluating differences in pain intensity within the postoperative setting, it is important to consider the multiple variables that influence the pain experience, including preoperative pain, psychological status, pain modulatory function, the degree of tissue injury posed by the surgery, and the patient's response to analgesic interventions [7,30–34]. All of these factors (and more) interact within an individual patient to generate a rating of pain intensity, which can generate skepticism regarding the value of simple self-report measures of pain, such as the NRS. However, it is important to note that the NRS has been well validated in clinical and experimental settings [35–37].

Moreover, single-item ratings of experimental pain intensity correspond to activation in pain-related brain regions in response to the same pain stimulus [38]. More recently, grey matter density in pain-related brain regions was found to predict intensity ratings of experimental heat pain [39]. Thus, single-item pain ratings remain a highly efficient and valid window into an individual's pain experience.

Our data build upon prior work suggesting higher pain scores for female patients after surgery, all of which also used the NRS within clinical settings [4]. The results shown in Table 2, where the differences in pain scores between females and males are compared using mean differences in pain scores on POD 1, concur with these prior findings. By grouping types of surgeries into broader categories of associated procedures, we were able to identify small differences in pain scores between sexes in a manner similar to that of Ruau et al. [13]. These findings are highly consistent with abundant data demonstrating greater experimental pain sensitivity and higher risk for clinical pain among women compared with men [4]. Although our findings reflect small mean differences between sexes on a per-procedural basis, even for procedures with high statistical significance (see Table 2), the results still have important implications. Specifically, the observed sex differences were highly reliable and suggest the need for additional research to identify the contributing factors. Moreover, at a public health level, interventions designed to improve postoperative pain management at either the hospital or systems level should take into account the higher risk for severe postoperative pain among women.

Eleven of the procedures with sex differences in mean pain scores also had statistically significant differences between the sexes in the incidence of SPE. Unlike the direct global comparison of pain scores in Table 2, the comparison of SPE in Table 3 demonstrates a number of procedures for which the per-procedure difference in percentages of SPE between the sexes was quite large. The concordance between SPE and mean differences in pain scores for lobectomy or pneumonectomy is especially notable, given that the requisite thoracotomy used for such procedures often leads to the development of chronic post-thoracotomy pain and that poorly controlled acute postoperative pain is associated with the development of chronic postsurgical pain as well [20,21,40]. Our results suggest that despite the widespread use of thoracic epidural analgesia at our institution for female and male patients undergoing thoracotomies, females are at greater risk for SPE compared with male patients.

Our findings should be interpreted in light of the study’s limitations, one of which is the lack of data regarding analgesic administration because sex differences in the effectiveness or administration of analgesics could influence the results. Previous evidence regarding sex differences in opioid analgesia are mixed, but on balance, the data suggest that females experience greater analgesia in response to mu-opioid and mixed-action opioids when administered for postoperative pain [41]. Any sex differences in reported pain scores should ideally also account for the possibility of differences in analgesic responsiveness related to sex; clinically, partitioning the effects of nociceptive loading and analgesic efficacy on reported pain intensity scores remains challenging. This informed our decision to focus on POD 1 for the testing of SPE using the logic that the patient’s care team likely optimized a pain management regimen throughout the hours after surgery on POD 0 (zero). Thus, continued SPE suggested effects from atypical analgesic requirements not addressed by the customary processes and the effects attributable to underlying surgical nociception along with the biopsychosocial characteristics of patients.

Our study shared additional limitations inherent to large-outcomes studies. First, the documentation of pain scores certainly deviated from the ascribed clinical protocol of a recording at least every 4 hours, with more frequent assessments conducted after analgesic interventions or in patient care settings with more intensive monitoring. Patients suffering from pain may have had their pain scores documented more frequently, whereas those comfortably sleeping may have been undersampled. Furthermore, the process used for collecting NRS pain scores used no standardization or specific training on pain assessment beyond that of the routine clinical education of nurses; this was an unavoidable salutary effect of such a large-scale collection of NRS data and mimics the limitation inherent to pain score assessments employed throughout the United States. Importantly, such limitations may be minimized through the use of multi-item pain assessment scales such as the Defense and Veterans Pain Rating Scale (DVPRS) [42]. Although the assignment of surgical procedures to CCS groups degrades the granularity of modeling particular procedures, CCS group assignment has been well validated in prior studies [43–45]. Interpretation of CCS group differences was most complicated for catch-all "other" categories of procedures, which is an inescapable effect of examining outcomes from a variety of types of surgery in a quaternary care facility. The inclusion of these "other" categories also minimized the attribution of component procedures to less appropriate categories, thus preserving low-variance categories and allowing for improved interpretation. Further work is necessary using multidimensional pain assessment tools (e.g., DVPRS), as well as with even larger data platforms and methods that enable testing of interactions and conditioning of factors upon pain outcomes.

In conclusion, our results suggest that females, on average, report higher numeric ratings of pain intensity in a clinical environment, and they experience a higher incidence of SPE on POD 1 for a variety of surgical procedures. Furthermore, the difference in clinically reported NRS pain scores between female and male patients increases through POD 5, reflecting a more rapid decrease in male compared with female patients. These results may inform future work in delineating which patient characteristics and treatment regimens are likely to influence the risk of severe acute postoperative pain. Further work is necessary to better characterize the use of SPE incidence in selecting patient cohorts to help health care providers better anticipate not just average pain needs but also comprehensive pain experience over the duration of the early postoperative recovery period.

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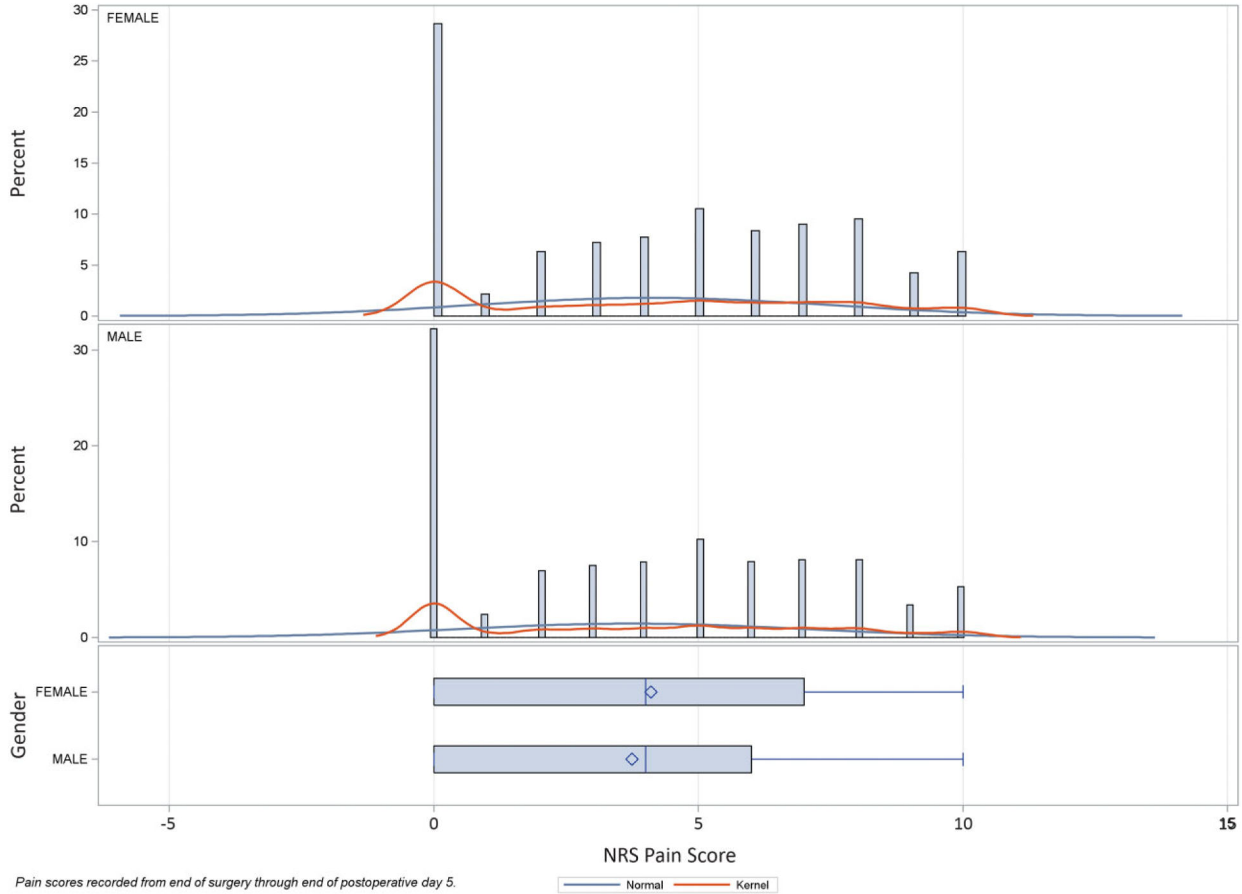

Figure 1.

Distribution of pain scores by sex. Pain scores for female and male patients recorded between the end of surgery and the end of postoperative day (POD) 5 are shown. The sample comprised 333,446 pain scores, documented using the numeric rating scale (NRS), from 7,731 subjects undergoing 78 separate Clinical Categorization Software (CCS) categories of surgery. There was a statistically significant difference between female and male patients (mean difference 0.36, 99% confidence interval [CI] 0.33–0.4, $P < 0.0001$), with a mean score of 4.1 (99% CI 4.1–4.1) for females and 3.74 (99% CI 3.7–3.8) for males.

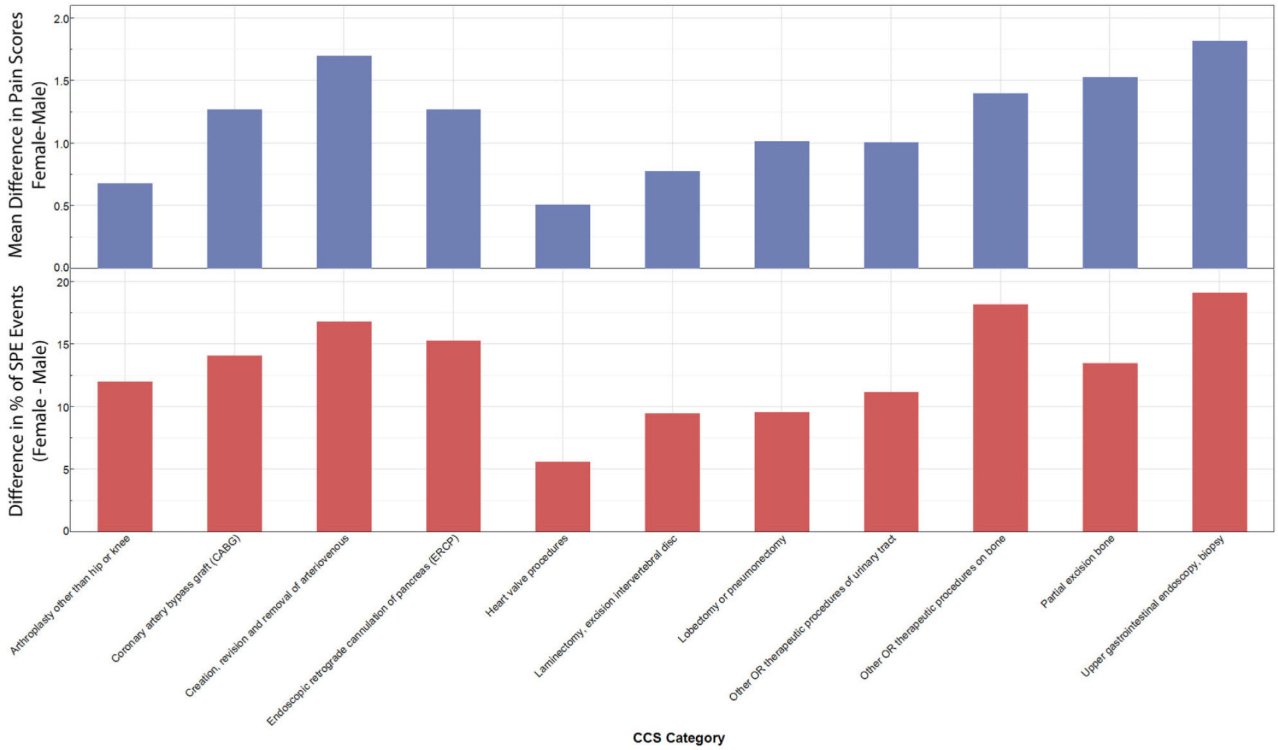

Figure 2.

Comparison of mean difference in pain scores with the difference in percentage of severe pain episode events between female and male patients. There were 11 procedures with statistically significant sex differences in mean difference in pain scores and incidence of severe pain event (SPE) for pain scores recorded on postoperative day (POD) 1.

Table 1

Characteristics of male and female patients

Characteristic	Female (Number)	Male (Number)	*P* value
Total patient count	3,739	3,992	0.4947
Age group			0.0829
21–39	639	677	
40–64	1,794	1,891	
65–84	1,197	1,340	
85 or greater	109	84	
BMI category			<0.0001
Morbidly obese (BMI ≥ 40)	366	184	
Normal (BMI 19–24)	820	769	
Obese (BMI 30–40)	937	946	
Overweight (BMI 25–29)	686	1,080	
Underweight (BMI < 19)	532	526	
Unknown BMI status	398	487	
Number of CPT codes per surgery			0.0015
3–5	650	591	
Greater than 5	61	47	
Less than 3	3,028	3,354	
Charlson comorbidity index			0.0127
<3	3,305	3,430	
3–6	418	541	
7–10	6	6	
Unknown	10	15	

BMI = body mass index; CPT = current procedural terminology.

Table 2

Comparison of pain scores by sex on POD 1

CCS Group	Female		Male		Mean Difference (99% CI) Female–Male	*t* Test *P* Value	Holm's Corrected *P* Value
	Number of Observations	Mean Pain Score ± SD	Number of Observations	Mean Pain Score ± SD			
Amputation of lower extremity	1,683	5.5 ± 3.6	1,561	5.5 ± 3.2	0.03 (−0.64, 0.71)	0.8954	1
Aortic resection, replacement, or anastomosis	538	3.0 ± 3.1	378	2.6 ± 3.0	0.35 (0.01, 0.70)	0.0085	0.3650569
Appendectomy	125	4.8 ± 2.8	251	5.6 ± 2.8	−0.82 (−1.52, −0.11)	0.0028	0.1433189
Arthroplasty knee	286	4.1 ± 3.2	578	4.2 ± 3.0	−0.09 (−0.34, 0.15)	0.3303	1
Arthroplasty other than hip or knee	490	4.2 ± 3.3	1,274	3.5 ± 3.1	0.68 (0.23, 1.13)	0.0001	0.0057522
Cholecystectomy and common duct exploration	392	4.9 ± 3.4	307	4.9 ± 3.0	0.00 (−0.56, 0.55)	0.9871	1
Colonoscopy and biopsy	165	2.1 ± 3.0	233	2.1 ± 3.5	−0.07 (−1.30, 1.15)	0.8797	1
Colorectal resection	326	4.0 ± 3.3	339	4.2 ± 3.4	−0.17 (−0.67, 0.34)	0.4017	1
Colostomy, temporary and permanent	1,334	4.4 ± 3.5	1,006	4.4 ± 3.5	0.08 (−1.67, 1.83)	0.9016	1
CABG	310	4.2 ± 3.6	387	2.9 ± 2.7	1.27 (0.74, 1.81)	0	1.04E-07
Creation, revision, and removal of arteriovenous fistula or vessel-to-vessel cannula for dialysis	282	4.8 ± 3.6	262	3.1 ± 3.4	1.70 (0.95, 2.46)	0	7.67E-07
Debridement of wound, infection, or burn	1,712	5.6 ± 3.2	2,214	5.2 ± 2.9	0.43 (0.05, 0.82)	0.0033	0.1599523
Embolectomy and endarterectomy of lower limbs	569	3.6 ± 3.2	672	4.7 ± 3.4	−1.09 (−2.14, −0.03)	0.0079	0.3480715
Endarterectomy, vessel of head and neck	453	1.6 ± 2.5	421	2.1 ± 2.7	−0.47 (−1.10, 0.16)	0.0559	1
ERCP	790	4.5 ± 3.3	852	3.1 ± 3.2	1.35 (0.67, 2.04)	0	3.14E-05
Endoscopy and endoscopic biopsy of the urinary tract	367	4.3 ± 3.7	565	3.4 ± 2.9	0.88 (−0.52, 2.28)	0.104	1
Excision of skin lesion	823	3.8 ± 2.7	606	4.4 ± 3.4	−0.58 (−1.78, 0.62)	0.2082	1
Exploratory laparotomy	396	4.2 ± 3.3	611	5.1 ± 3.4	−0.84 (−1.26, −0.43)	0	1.40E-05
Extracorporeal lithotripsy, urinary	1,246	4.8 ± 3.8	1,805	3.1 ± 3.4	1.68 (0.34, 3.02)	0.0013	0.0703855
Gastric bypass and volume reduction	752	3.8 ± 3.0	727	4.6 ± 3.0	−0.71 (−1.56, 0.14)	0.0308	1
Gastrostomy, temporary and permanent	147	4.6 ± 3.5	78	2.6 ± 3.2	2.03 (0.16, 3.90)	0.0054	0.2421155
Heart valve procedures	954	3.2 ± 3.0	1,078	2.7 ± 2.8	0.51 (0.24, 0.79)	0	7.06E-05
Hip replacement, total and partial	301	3.9 ± 3.3	435	4.1 ± 3.0	−0.24 (−0.49, 0.01)	0.0142	0.5684356
Ileostomy and other enterostomy	155	3.9 ± 3.1	95	3.7 ± 3.1	0.19 (−0.39, 0.78)	0.3957	1
Incision and drainage, skin and subcutaneous tissue	489	5.2 ± 3.3	894	4.9 ± 3.2	0.26 (−0.23, 0.75)	0.1761	1

CCS Group	Female: Number of Observations	Female: Mean Pain Score ± SD	Male: Number of Observations	Male: Mean Pain Score ± SD	Mean Difference (99% CI) Female–Male	*t* Test *P* Value	Holm's Corrected *P* Value
Incision and excision of CNS	1,635	3.3 ± 3.2	1,384	3.4 ± 3.2	−0.11 (−0.37, 0.16)	0.2953	1
Insertion, replacement, or removal of extracranial ventricular shunt	698	4.0 ± 3.4	1,481	3.2 ± 3.2	0.75 (0.27, 1.23)	0.0001	0.0041286
Insertion, revision, replacement, removal of cardiac pacemaker or cardioverter/defibrillator	192	3.6 ± 3.0	325	1.6 ± 2.8	2.00 (1.11, 2.90)	0	1.20E-06
Kidney transplant	41	3.9 ± 3.1	50	3.9 ± 3.3	−0.03 (−0.68, 0.62)	0.9023	1
Laminectomy, excision intervertebral disc	846	5.6 ± 3.1	1,196	4.8 ± 3.2	0.78 (0.48, 1.07)	0	2.21E-09
Laparoscopy	1,105	3.5 ± 3.4	1,345	3.7 ± 2.5	−0.13 (−0.91, 0.65)	0.663	1
Lobectomy or pneumonectomy	528	3.8 ± 3.2	1,040	2.8 ± 2.9	1.02 (0.39, 1.65)	0	0.0020145
Nephrectomy, partial or complete	462	4.3 ± 3.2	686	3.5 ± 3.1	0.76 (0.32, 1.20)	0	0.0005741
Nephrotomy and nephrostomy	61	4.4 ± 3.3	53	4.9 ± 2.9	−0.53 (−1.20, 0.15)	0.0433	1
No procedure	147	3.9 ± 3.1	180	3.5 ± 3.0	0.39 (0.05, 0.73)	0.0034	0.1642764
Other diagnostic nervous system procedures	1,019	2.8 ± 3.1	2,461	1.6 ± 2.7	1.21 (0.30, 2.11)	0.0006	0.0357079
Other diagnostic procedures on lung and bronchus	174	2.9 ± 2.8	300	3.4 ± 3.1	−0.50 (−0.95, −0.05)	0.0042	0.193488
Other diagnostic procedures on musculoskeletal system	345	4.2 ± 3.0	449	3.8 ± 3.0	0.38 (−0.32, 1.08)	0.1568	1
Other diagnostic radiology and related technique	2,353	3.0 ± 3.6	2,116	4.1 ± 3.5	−1.14 (−3.10, 0.83)	0.1302	1
Other fracture and dislocation procedure	320	4.6 ± 3.2	542	5.2 ± 3.1	−0.61 (−1.10, −0.12)	0.0014	0.0752244
Other hernia repair	2,908	5.4 ± 3.0	1,686	5.2 ± 3.1	0.20 (−0.33, 0.73)	0.3254	1
Other non-OR therapeutic cardiovascular procedures	592	2.8 ± 3.3	444	4.3 ± 3.3	−1.42 (−2.68, −0.16)	0.0039	0.1812885
Other OR gastrointestinal therapeutic procedures	108	3.9 ± 3.4	106	3.1 ± 3.3	0.80 (0.34, 1.25)	0	0.0004353
Other OR heart procedures	743	2.9 ± 3.1	646	3.4 ± 2.9	−0.52 (−1.07, 0.02)	0.0136	0.5588774
Other OR lower GI therapeutic procedures	80	4.1 ± 3.1	55	4.2 ± 3.1	−0.03 (−0.69, 0.62)	0.8926	1
Other OR procedures on vessels of head and neck	239	3.6 ± 3.1	343	3.7 ± 3.2	−0.18 (−0.69, 0.33)	0.3635	1
Other OR procedures on vessels other than head and neck	86	4.1 ± 3.5	77	3.4 ± 3.3	0.74 (0.18, 1.31)	0.0007	0.037895
Other OR therapeutic nervous system procedures	82	4.5 ± 3.1	130	4.5 ± 3.1	−0.02 (−0.35, 0.32)	0.8978	1
Other OR therapeutic procedures of urinary tract	712	4.5 ± 3.4	109	3.5 ± 3.1	1.01 (0.51, 1.51)	0	1.38E-05
Other OR therapeutic procedures on bone	492	5.9 ± 2.9	500	4.5 ± 3.1	1.4	0	2.61E-08
Other OR therapeutic procedures on joints	613	4.8 ± 3.2	740	4.3 ± 2.8	0.45 (−0.14, 1.05)	0.0478	1

CCS Group	Female Number of Observations	Female Mean Pain Score ± SD	Male Number of Observations	Male Mean Pain Score ± SD	Mean Difference (99% CI) Female–Male	*t* Test *P* Value	Holm's Corrected *P* Value
Other OR therapeutic procedures on musculoskeletal system	2,299	4.6 ± 2.5	2,042	4.8 ± 3.4	−0.14 (−1.41, 1.13)	0.7684	1
Other OR therapeutic procedures on nose, mouth, and pharynx	335	3.3 ± 3.2	378	3.7 ± 3.4	−0.35 (−0.99, 0.29)	0.16	1
Other OR therapeutic procedures on respiratory system	329	2.1 ± 2.8	192	3.4 ± 3.4	−1.29 (−1.97, −0.61)	0	7.83E-05
Other OR therapeutic procedures on skin and breast	386	4.5 ± 2.7	272	5.1 ± 2.7	−0.65 (−1.50, 0.19)	0.0463	1
Other OR upper GI therapeutic procedures	351	3.8 ± 3.0	365	2.8 ± 3.0	0.99 (0.33, 1.66)	0.0001	0.0078213
Other organ transplantation	1,050	3.3 ± 2.7	423	3.3 ± 3.1	−0.03 (−0.67, 0.62)	0.915	1
Other therapeutic ear procedures	1,359	3.9 ± 2.7	1,248	2.1 ± 2.2	1.82 (0.25, 3.39)	0.0031	0.1545763
Other therapeutic endocrine procedures	41	2.4 ± 3.0	190	2.2 ± 2.9	0.24 (−0.30, 0.78)	0.2567	1
Other therapeutic procedures on muscles and tendons	286	4.0 ± 3.0	669	4.9 ± 3.2	−0.83 (−1.37, −0.30)	0.0001	0.0041286
Other therapeutic procedures, hemic and lymphatic system	286	4.0 ± 3.6	121	4.4 ± 3.5	−0.47 (−1.71, 0.77)	0.325	1
Other vascular bypass and shunt, not heart	694	4.7 ± 2.7	818	4.3 ± 3.2	0.38 (−0.47, 1.22)	0.2465	1
Other vascular catheterization, not heart	442	4.3 ± 3.3	200	2.8 ± 3.2	1.52 (0.74, 2.31)	0	5.20E-05
Partial excision bone	41	4.7 ± 3.4	67	3.2 ± 3.3	1.53 (0.91, 2.15)	0	2.31E-08
Peripheral vascular bypass	457	4.1 ± 3.3	529	4.4 ± 3.6	−0.36 (−1.08, 0.36)	0.1973	1
Skin graft	242	5.7 ± 3.1	487	5.3 ± 3.1	0.46 (0.07, 0.86)	0.0027	0.1394749
Small bowel resection	540	4.0 ± 3.1	376	4.7 ± 3.0	−0.76 (−1.95, 0.42)	0.0955	1
Spinal fusion	77	5.3 ± 3.1	299	4.9 ± 3.2	0.39 (0.07, 0.70)	0.0017	0.0875771
Thyroidectomy, partial or complete	148	4.3 ± 2.9	300	3.9 ± 3.1	0.40 (−0.37, 1.18)	0.1756	1
Tracheoscopy and laryngoscopy with biopsy	308	2.7 ± 3.2	589	3.8 ± 3.2	−1.12 (−2.74, 0.50)	0.072	1
Tracheostomy, temporary and permanent	108	1.2 ± 2.3	120	1.3 ± 2.3	−0.03 (−0.74, 0.68)	0.9097	1
Transurethral excision, drainage, or removal urinary obstruction	323	4.0 ± 3.6	195	4.5 ± 3.2	−0.52 (−1.86, 0.83)	0.3157	1
Treatment, facial fracture or dislocation	75	4.9 ± 3.4	79	4.7 ± 3.2	0.25 (−1.09, 1.59)	0.6275	1
Treatment, fracture or dislocation of hip and femur	137	4.7 ± 3.3	205	4.9 ± 3.1	−0.21 (−0.55, 0.13)	0.1142	1
Treatment, fracture or dislocation of lower extremity (other than hip or femur)	72	5.2 ± 3.2	205	5.7 ± 3.0	−0.47 (−0.78, −0.16)	0.0001	0.0047918

CCS Group	Female: Number of Observations	Female: Mean Pain Score ± SD	Male: Number of Observations	Male: Mean Pain Score ± SD	Mean Difference (99% CI) Female–Male	*t* Test *P* Value	Holm's Corrected *P* Value
Treatment, fracture or dislocation of radius and ulna	70	6.0 ± 3.3	168	5.2 ± 3.1	0.83 (−0.03, 1.69)	0.0124	0.5220135
Upper gastrointestinal endoscopy, biopsy	1,426	4.1 ± 4.0	1,254	2.3 ± 3.2	1.82 (1.08, 2.57)	0	5.34E-08
Ureteral catheterization	258	4.5 ± 3.2	191	4.7 ± 3.5	−0.23 (−1.15, 0.69)	0.522	1

CABG = coronary artery bypass graft; CI = confidence interval; CCS = Clinical Categorization Software; ERCP = endoscopic retrograde cannulation of pancreas; GI = gastrointestinal tract; OR = operating room; POD = postoperative day; SD = standard deviation.

Table 3

Severe pain episodes on postoperative day 1 by procedure and sex

	Female			Male			Chi-Squared	
	Severe Pain Episode?			Severe Pain Episode?				
CCS Group	No	Yes	Percent of Pain Scores as SPE	No	Yes	Percent of Pain Scores as SPE	*P* Value	Adjusted *P* Value (Holm)
CABG	379	111	22.7	1,165	109	8.6	1.00E-15	7.81E-14
Upper gastrointestinal endoscopy, biopsy	192	94	32.9	498	80	13.8	5.30E-11	4.08E-09
Other OR therapeutic procedures on bone	254	199	43.9	313	108	25.7	1.55E-08	1.18E-06
Laminectomy, excision intervertebral disc	998	685	40.7	1,074	487	31.2	1.80E-08	1.35E-06
Heart valve procedures	1,474	238	13.9	2,030	184	8.3	2.04E-08	1.51E-06
Arthroplasty other than hip or knee	519	233	31.0	589	138	19.0	1.02E-07	7.45E-06
Other OR therapeutic procedures of urinary tract	383	145	27.5	870	170	16.3	2.08E-07	1.50E-05
Creation, revision, and removal of arteriovenous fistula or vessel-to-vessel cannula for dialysis	261	131	33.4	256	51	16.6	5.03E-07	3.57E-05
ERCP	213	97	31.3	325	62	16.0	1.81E-06	0.000126355
Partial excision bone	373	165	30.7	313	65	17.2	3.67E-06	0.000252904
Lobectomy or pneumonectomy	296	71	19.3	510	55	9.7	2.76E-05	0.001873536
Debridement of wound, infection or burn	490	356	42.1	800	396	33.1	3.48E-05	0.002330097
Nephrectomy, partial or complete	612	178	22.5	721	131	15.4	0.000209892	0.01385288
Other OR therapeutic procedures on respiratory system	275	26	8.6	356	79	18.2	0.000281347	0.018287569
Exploratory laparotomy	1,023	311	23.3	705	301	29.9	0.000317732	0.02033485
Other therapeutic procedures on muscles and tendons	309	87	22.0	417	194	31.8	0.0007238	0.045599419
Treatment, fracture or dislocation of lower extremity (other than hip or femur)	804	442	35.5	1,056	749	41.5	0.000803041	0.049788549
Other OR therapeutic procedures on joints	226	119	34.5	342	107	23.8	0.0009658	0.058913772
Treatment, fracture or dislocation of radius and ulna	91	83	47.7	202	98	32.7	0.001164523	0.069871351
Other vascular catheterization, not heart	205	77	27.3	220	42	16.0	0.001481174	0.087389257
Endoscopy and endoscopic biopsy of the urinary tract	57	29	33.7	67	10	13.0	0.001950886	0.111807554
Insertion, replacement, or removal of extracranial ventricular shunt	623	200	24.3	500	106	17.5	0.001927716	0.111807554
Other OR gastrointestinal therapeutic procedures	783	171	17.9	934	144	13.4	0.004533025	0.253849427
Gastrostomy, temporary and permanent	40	21	34.4	46	7	13.2	0.008662414	0.476432791
Spinal fusion	1,055	580	35.5	955	429	31.0	0.009368234	0.505884662

	Female			Male			Chi-Squared	
	Severe Pain Episode?			Severe Pain Episode?				
CCS Group	**No**	**Yes**	**Percent of Pain Scores as SPE**	**No**	**Yes**	**Percent of Pain Scores as SPE**	***P* Value**	**Adjusted *P* Value (Holm)**
Gastric bypass and volume reduction	566	146	20.5	75	34	31.2	0.012025097	0.637330162
Embolectomy and endarterectomy of lower limbs	117	30	20.4	122	58	32.2	0.016564906	0.861375126
Amputation of lower extremity	175	145	45.3	316	226	41.7	0.300358967	1
Aortic resection, replacement or anastomosis	887	132	13.0	2,209	252	10.2	0.020050457	1
Appendectomy	137	55	28.6	204	121	37.2	0.046546518	1
Arthroplasty knee	2,195	713	24.5	1,272	414	24.6	0.977836555	1
Cholecystectomy and common duct exploration	404	188	31.8	315	129	29.1	0.35020456	1
Colonoscopy and biopsy	94	14	13.0	87	19	17.9	0.314976975	1
Colorectal resection	579	164	22.1	492	154	23.8	0.434512083	1
Colostomy, temporary and permanent	62	18	22.5	39	16	29.1	0.386030278	1
Endarterectomy, vessel of head and neck	230	9	3.8	316	27	7.9	0.043079805	1
Excision of skin lesion	66	16	19.5	94	36	27.7	0.177604219	1
Extracorporeal lithotripsy, urinary	105	50	32.3	73	22	23.2	0.122998947	1
Hip replacement, total and partial	1,768	585	24.9	1,605	511	24.1	0.58039881	1
Ileostomy and other enterostomy	404	88	17.9	422	78	15.6	0.334809448	1
Incision and drainage, skin and subcutaneous tissue	400	213	34.7	503	237	32.0	0.290447557	1
Incision and excision of CNS	1,886	413	18.0	1,659	383	18.8	0.50102412	1
Insertion, revision, replacement, removal of cardiac pacemaker or cardioverter/defibrillator	140	25	15.2	214	19	8.2	0.02830473	1
Kidney transplant	260	75	22.4	287	91	24.1	0.594967736	1
Laparoscopy	268	61	18.5	165	27	14.1	0.188110915	1
Nephrotomy and nephrostomy	277	109	28.2	196	76	27.9	0.933456037	1
No procedure	885	220	19.9	1,109	236	17.5	0.134816463	1
Other OR heart procedures	404	58	12.6	605	81	11.8	0.703772563	1
Other OR lower GI therapeutic procedures	270	81	23.1	274	91	24.9	0.561453966	1
Other OR procedures on vessels of head and neck	864	186	17.7	340	83	19.6	0.391278803	1
Other OR procedures on vessels other than head and neck	379	110	22.5	737	157	17.6	0.026267453	1
Other OR therapeutic nervous system procedures	1,013	346	25.5	899	349	28.0	0.148491084	1
Other OR therapeutic procedures on musculoskeletal system	34	7	17.1	125	65	34.2	0.03166685	1

CCS Group	Female: Severe Pain Episode? No	Female: Severe Pain Episode? Yes	Female: Percent of Pain Scores as SPE	Male: Severe Pain Episode? No	Male: Severe Pain Episode? Yes	Male: Percent of Pain Scores as SPE	Chi-Squared: *P* Value	Chi-Squared: Adjusted *P* Value (Holm)
Other OR therapeutic procedures on nose, mouth, and pharynx	232	54	18.9	538	131	19.6	0.801945679	1
Other OR therapeutic procedures on skin and breast	216	70	24.5	90	31	25.6	0.807010758	1
Other OR upper GI therapeutic procedures	269	57	17.5	298	41	12.1	0.04995933	1
Other diagnostic nervous system procedures	107	18	14.4	227	24	9.6	0.160599232	1
Other diagnostic procedures on lung and bronchus	619	75	10.8	720	98	12.0	0.475011038	1
Other diagnostic procedures on musculoskeletal system	335	107	24.2	159	41	20.5	0.301541924	1
Other diagnostic radiology and related technique	32	9	22.0	47	20	29.9	0.368685688	1
Other fracture and dislocation procedure	413	156	27.4	449	223	33.2	0.027930624	1
Other hernia repair	288	169	37.0	332	197	37.2	0.932903016	1
Other non-OR therapeutic cardiovascular procedure	120	27	18.4	55	23	29.5	0.056213611	1
Other organ transplantation	215	27	11.2	417	70	14.4	0.228509762	1
Other therapeutic ear procedures	37	4	9.8	50	0	0.0	0.02389377	1
Other therapeutic endocrine procedures	482	58	10.7	332	44	11.7	0.649099393	1
Other therapeutic procedures, hemic and lymphatic system	55	22	28.6	216	83	27.8	0.887341347	1
Other vascular bypass and shunt, not heart	121	27	18.2	229	71	23.7	0.191538478	1
Peripheral vascular bypass	247	61	19.8	437	152	25.8	0.044894373	1
Skin graft	428	270	38.7	910	571	38.6	0.954716721	1
Small bowel resection	86	22	20.4	96	24	20.0	0.944527047	1
Thyroidectomy, partial or complete	256	67	20.7	153	42	21.5	0.829624189	1
Tracheoscopy and laryngoscopy with biopsy	68	7	9.3	67	12	15.2	0.269336331	1
Tracheostomy, temporary and permanent	132	5	3.6	196	9	4.4	0.734822204	1
Transurethral excision, drainage, or removal urinary obstruction	52	20	27.8	137	68	33.2	0.397805739	1
Treatment, facial fracture or dislocation	48	22	31.4	114	54	32.1	0.914236798	1
Treatment, fracture or dislocation of hip and femur	984	442	31.0	842	412	32.9	0.302725453	1
Ureteral catheterization	171	87	33.7	140	51	26.7	0.110986071	1

CABG = coronary artery bypass graft; CCS = Clinical Categorization Software; ERCP = endoscopic retrograde cannulation of pancreas; GI = gastrointestinal tract; OR = operating room; POD = postoperative day.