Original Study

Annals of Surgery Open

OPEN

Preoperative Depression and Anxiety Impact on Inpatient Surgery Outcomes

A Prospective Cohort Study

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Objectives: To determine the association of preoperative mood symptoms and postoperative adverse outcomes; to explore sex-specific differences.

Background: Depression and anxiety can increase postoperative mortality. Psychological stress is associated with a chronic inflammatory response unfavorable to postsurgical healing.

Methods: Prospective cohort study. Patients were recruited from surgical preadmission clinics at a university hospital. Preoperative depression and anxiety were measured via the Beck Depression and Beck Anxiety Inventories (BDI-II and BAI). Our primary outcome was a composite of postoperative complications, extended length of stay (ELOS) and early readmission. Associated variables included demographics, preoperative pain, pain tolerance/catastrophizing, coping mechanisms, postoperative pain, and opioid use. We adjusted for age, comorbidities, and surgical specialty.

Results: Of 1061 recruited patients (ten surgical specialties, 2015–2020), 455 males and 486 females had preoperative and postoperative data available. Mean age was 62.9 (range 20.2–96.2). At baseline, 9.3% of patients had moderate or severe depression; 7.4% had moderate or severe anxiety. Females were more likely to be moderately or severely depressed (11% vs 7%, $P = 0.036$) and moderately or severely anxious (9% vs 6%, $P = 0.034$). Females had significantly fewer reported comorbidities and lower American Society of Anesthesiologists category ($P < 0.001$). Increasing BDI-II and BAI scores significantly increased likelihood of postoperative complications, ELOS, and/or hospital readmission in females (adjusted odds ratio [aOR] = 2.57 for BDI-II 1-19 vs 0, $P = 0.041$; aOR = 4.48 for BDI-II > 19 vs 0, $P = 0.008$; aOR = 1.54 for BAI ≤ 6 vs >6, $P = 0.038$) but not in males. Mood symptoms did not influence postoperative pain or opioid use.

Conclusion: Preoperative depression and anxiety negatively impact surgical outcomes in female patients undergoing major surgery.

INTRODUCTION

Depressive disorders have persistently ranged in the top 3 global causes of nonfatal disease burden (measured in years lived with disability)[1] and have been named a World Health Organization priority.[2] Disability is defined as health loss associated with a single given health state.[1] Psychiatric disorders cause higher disability, yet are undertreated compared with physical disorders in high-, middle-, and low-income countries.[3] Among mental and substance use disorders, depression and anxiety account for 40.5% and 14.6% of disability-adjusted life years, respectively.[4] Psychological stress in patients is associated with a chronic inflammatory response that can impair or delay normal postsurgical healing.[5] In addition, depression and immune inflammatory activation may share common genetic predispositions.[6] Certain genetic characteristics regulating immune function may also be associated with reduced responsiveness to antidepressants.[6] After surgery, normal immune function is required for tissue repair and prevention of infections. Despite available treatment strategies for mood disorders, mental health optimization is infrequently addressed before major surgery. Some surgeons do not consider their patients' depressive symptoms in operative planning,[7] and yet psychological distress is a significant predictor for postoperative pain in many surgical specialties.[8] Moreover, depression has been associated with increased analgesic use,[9] length of stay,[10] early readmission,[11] and higher complication rates[12] in various surgical disciplines. Depression and anxiety have been well studied in cardiac surgery, where they significantly increase postoperative mortality.[13] Adult women have a greater burden from psychiatric disorders than men,[4] yet the impact of sex on postsurgical outcomes is unclear and conflicting in various studies.[8]

We hypothesized that depression and anxiety increase adverse surgical outcomes and postoperative pain. We aimed to quantify the association of preoperative depression and anxiety symptoms on postoperative complications, length of stay, readmission, and pain, and to explore sex differences and sex-specific coping mechanisms in patients undergoing major surgery.

METHODS

We conducted a prospective cohort study of depression and anxiety symptoms in patients undergoing major surgery at a university hospital. Major surgery was defined as a need for postoperative

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Disclosure: The authors declare that they have nothing to disclose.

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Annals of Surgery Open (2021) 1:e049

Received: 17 November 2020; Accepted 31 January 2021

Published online 16 March 2021

DOI: 10.1097/AS9.0000000000000049

inpatient admission. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for this study.[14] Institutional review board approval was obtained. We included all adult patients who presented to preoperative assessment clinics one day before or same day as their surgery (February 2015 to January 2020). We excluded patients who were unable to complete English language questionnaires. Patients were recruited at baseline before surgery, written informed consent was obtained and demographic data collected including age, sex, body mass index, ethnicity, level of education, smoking, alcohol use, recreational drug use, exercise and activity levels, changes in sleep patterns, and a coping mechanism questionnaire consisting of questions about support at home after surgery, trust in the surgical team, expectations of surgical results, satisfaction with preoperative educational materials received, additional sources of information sought, anticipation of surgical pain, and self-reported pain tolerance. Patients also completed validated questionnaires including the Beck Depression Inventory (BDI-II),[15,16] the Beck Anxiety Inventory (BAI),[17] the Pain Catastrophizing Scale,[18] and the Brief Pain Inventory Short Form (BPI).[19] Depression and anxiety questionnaires asked about symptoms in the weeks before questionnaire administration, with the anxiety questionnaire asking participants to exclude feelings the day of questionnaire completion to mitigate stress of upcoming surgery. Following the planned surgery, we collected demographic, intraoperative, and postoperative data from hospital charts up to 30 days postoperatively. Intraoperative data included American Society of Anesthesiologists (ASA) physical status classification[20] and type of surgery (specialty). Postoperative data included Visual Analog Scale (VAS)[21] for pain, narcotic use up to 72 hours, postoperative complications, length of hospital stay, and readmissions. Narcotic use was quantified using morphine milligram equivalents (MME).[22] Adverse events for each patient were categorized using the modified Clavien-Dindo surgical complication grading scale.[23,24]

Our primary analysis was to determine the association of preoperative depression and anxiety with postoperative complications, length of stay, and readmission in males versus females. Our primary outcome measure was a composite of Clavien-Dindo score >0, extended length of stay (ELOS, >90th percentile of specialty-specific LOS) and early readmission (up to 30 days postoperatively). Secondary analyses explored the association between primary outcome and patient demographics/coping mechanisms, impact of depression and anxiety on early postoperative pain, sex differences, and correlations between depression/anxiety and patient demographics, coping mechanisms and pain catastrophizing. Participants were analyzed by sex; if they indicated "other" under the sex category, they were excluded from comparative analyses of males versus females. Although there are notable gender effects on mood, we specifically asked participants to report their identified sex, as male, female, or other. As such, we refer to sex differences and use these terms throughout this article.

Based on the BDI percentiles reported in Roelofs,[25] we hypothesized that the distribution of BDI in preoperative patients can be approximated by a Gamma distribution with shape and scale parameters being 2 and 3, respectively. Assuming the primary outcome rate is 40% for patients with BDI score of 6 (ie, mean score of the assumed Gamma distribution), the sample size required to detect an odds ratio of 2 (per 10 unit of BDI increase) with 80% power at the 5% significance level would be 398 for each sex group. To account for a potential loss to follow up of 10%, a sample size of 442 was planned for each sex group (male and female participants, respectively).

Comparisons of preoperative and postoperative variables between sexes and groups defined by selected patient variables were made by Chi-square test, Fisher exact test, ANOVA, or Kruskal-Wallis test as appropriate. Comparison of MME between sexes was based on quantile regression adjusted for patient's weight. The relationship between preoperative BDI-II/BAI scores and the primary outcome within each sex group was assessed univariately using the Cochran-Armitage trend test. Logistic regression analysis adjusted for clinically relevant confounders including age, ASA, and surgical specialty (type of surgery) was also performed for each sex group separately. Upon examination of the data, the association between BDI-II/BAI scores and the primary outcome was nonlinear, and thus, BDI-II/BAI was considered as categorical variables in the regression analysis and adjacent categories were combined if their observed primary outcome rates were similar. Comparisons of primary outcome rate across levels of ordinal or categorical patient variables were based on the Cochran-Armitage trend test or Chi-square test as appropriate. Logistic regression analysis adjusted for the same confounders as in the primary analysis was also performed. Spearman correlation (rho) was used to assess the association between pairs of variables. No adjustment was made to the P value to account for comparisons of multiple secondary outcomes. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Demographics

Preoperative

In total, 1061 preoperative patients were recruited and 942 (455 males, 486 females, and 1 other) had preoperative BDI-II/BAI scores and surgical and postoperative data available. The baseline median BDI-II score was 6.3 (interquartile range [IQR] 3–11) and 9.3% of patients had moderate or severe depression; median BAI score was 6 (IQR 2–11) and 7.4% of patients had moderate or severe anxiety. Females were more likely than males to be moderately or severely depressed (11% vs 7%, $P = 0.036$) and moderately or severely anxious (9% vs 6%, $P = 0.034$).

Patients' mean age was 62.9 years (range 20.2–96.2) and most described their ethnicity as Canadian (69.6%). Some demographic characteristics were significantly different between men and women (Table 1). Most did not require any assistance with basic daily activities preoperatively (91.5%). Over half of patients reported exercising lightly >4× per week (57.2%), but less than half for moderately strenuously >1× per week (37.7%). Recent moderate-severe changes in their sleeping patterns were noted by 16.6% of patients. Similar proportions in both males and females reported no recent change in sleeping pattern (38% vs 39%), but more males reported getting more sleep than usual when compared to females (27% vs 18%, $P = 0.003$). Most (79.8%) described having quite a bit or a lot of support at home for recovering after surgery, with no difference between males and females. Male patients placed significantly more trust in their surgical team compared with females (complete trust: 71% vs 58%, $P < 0.001$). Both sexes thought surgeries for their condition would most likely be successful (89%) and were quite satisfied or very satisfied with the amount of medical information received (95%). Females were more likely than males to consult the Internet for additional surgical information (57% vs 50%, respectively, $P = 0.036$). Significantly more females anticipated early postoperative pain to be moderate or severe (75% vs 66%, $P < 0.001$). The sexes had similar reported pain tolerance, but females had higher pain catastrophizing total scores and in each subscale of rumination, magnification, and helplessness ($P < 0.001$). Females also had higher baseline pain score on the BPI (median 1.3 vs 0.5, IQR 0–3.3 and 0–2.3, respectively, $P = 0.001$).

Intraoperative

Ten different surgical specialties were represented (Table 2). Females had significantly fewer reported comorbidities and lower ASA category ($P < 0.001$).

TABLE 1.

Patient Characteristics

Variable	ALL (N = 942)	MALE (N = 455)	FEMALE (N = 486)	*P*
Body mass index, mean (SD), kg/m^2	27.2 (5.8)	27.4 (5.0)	27.0 (6.4)	0.003
Missing, n	49	22	27	
Age, mean (SD), y	62.9 (15.0)	65.9 (13.4)	60.0 (16.0)	<0.001
Missing, n	34	15	19	
Ethnicity, n (%)*				
Canadian	654 (69.6)	324 (71.7)	329 (67.7)	0.185
European origins	243 (25.9)	130 (28.8)	113 (23.3)	0.054
Asian	101 (10.8)	34 (7.5)	67 (13.8)	0.002
Aboriginal/North American Indian	21 (2.2)	11 (2.4)	10 (2.1)	0.697
Other	54 (5.8)	23 (5.1)	31 (6.4)	0.397
Cancer as indication for surgery, n (%)	161 (17.1)	88 (19.3)	73 (15.0)	0.079
Highest level of education, n (%)				0.017
Unknown	1	1	0	
8th grade or less	52 (5.5)	32 (7.0)	20 (4.1)	
High School	275 (29.2)	135 (29.7)	139 (28.6)	
College/University	480 (51.0)	212 (46.7)	268 (55.1)	
Postgraduate	134 (14.2)	75 (16.5)	59 (12.1)	
Exercise lightly, n (%)				0.484
Unknown	17	11	6	
Once a month or less	54 (5.8)	30 (6.8)	24 (5.0)	
Few times each month	111 (12.0)	55 (12.4)	55 (11.5)	
2–3 times each week	231 (25.0)	115 (25.9)	116 (24.2)	
4 times or more each week	529 (57.2)	244 (55.0)	285 (59.4)	
Exercise moderately to strenuously, n (%)				0.833
Unknown	61	29	32	
Once a month or less	375 (42.6)	177 (41.5)	198 (43.6)	
Few times each month	174 (19.8)	84 (19.7)	89 (19.6)	
2–3 times each week	209 (23.7)	101 (23.7)	108 (23.8)	
4 times or more each week	123 (14.0)	64 (15.0)	59 (13.0)	
Smoked cigarettes in the last year, n (%)	86/930 (9.2)	44/447 (9.8)	42/482 (8.7)	0.553
Any use of alcohol, n (%)	475/929 (51.1)	264/447 (59.1)	211/481 (43.9)	<0.001
Any use of recreational drugs, n (%)	100/927 (10.8)	69/443 (15.6)	31/483 (6.4)	<0.001

*Multiple categories can be selected for each patient. Data were missing for 3 patients.

TABLE 2.

Intraoperative and Postoperative Characteristics

Variable	All (n = 942)	Male (n = 455)	Female (n = 486)	*P*
Surgical specialty, n (%)				<0.001
Cardiac	305 (32.4)	215 (47.3)	89 (18.3)	
Colorectal	117 (12.4)	67 (14.7)	50 (10.3)	
ENT	15 (1.6)	6 (1.3)	9 (1.9)	
General	134 (14.2)	67 (14.7)	67 (13.8)	
Gynecology	99 (10.5)	0 (0.0)	99 (20.4)	
Orthopedic	2 (0.2)	1 (0.2)	1 (0.2)	
Plastic	1 (0.1)	1 (0.2)	0 (0.0)	
Urogynecology	135 (14.3)	0 (0.0)	135 (27.8)	
Urology	99 (10.5)	70 (15.4)	29 (6.0)	
Vascular	35 (3.7)	28 (6.2)	7 (1.4)	
Comorbidities score, median (IQR)	1.0 (0.0, 2.0)	1.0 (0.0, 3.0)	0.0 (0.0, 2.0)	<0.001
Missing, n	31	12	19	
ASA physical status, n (%)				<0.001
1	76 (8.2)	10 (2.3)	66 (13.7)	
2	290 (31.4)	81 (18.4)	209 (43.5)	
3	237 (25.7)	128 (29.0)	109 (22.7)	
4	320 (34.7)	222 (50.3)	97 (20.2)	
Clavien-Dindo classification, n				<0.001
0	589 (64.0)	249 (56.0)	340 (71.6)	
1	160 (17.4)	82 (18.4)	78 (16.4)	
2	112 (12.2)	74 (16.6)	37 (7.8)	
3	45 (4.9)	30 (6.7)	15 (3.2)	
4	13 (1.4)	8 (1.8)	5 (1.1)	
5	2 (0.2)	2 (0.4)	0 (0.0)	
Clavien-Dindo > 0, n (%)	332/921 (36.0)	196/445 (44.0)	135/475 (28.4)	<0.001
Length of stay, median (IQR), d	2.9 (1.2, 5.1)	3.9 (1.9, 6.0)	2.0 (1.1, 4.1)	<0.001
Missing, n	23	12	11	
ELOS, n (%)	68/919 (7.4)	28/443 (6.3)	40/475 (8.4)	0.225
Early readmission to hospital, n (%)	91/918 (9.9)	48/441 (10.9)	43/476 (9.0)	0.349
Primary outcome (postoperative complication, ELOS or early readmission), n (%)	412/915 (45.0)	231/440 (52.5)	180/474 (38.0)	<0.001

ASA indicates American Society of Anesthesiologists; ENT, ear nose and throat; IQR, interquartile range.

Postoperative

Males had more postoperative complications (Clavien-Dindo score > 0, $P < 0.001$) and longer median length of stay ($P < 0.001$), but similar proportion with ELOS ($P = 0.23$) or early postoperative readmission to hospital when compared with females ($P = 0.35$) (Table 3). Postoperatively, females reported more severe pain at 48 to 72 hours (mean VAS: 2.5 vs 2.1, $P = 0.045$) but not in the first 48 hours (2.8 vs 2.6, $P = 0.46$). No difference in MME was observed by sex in any time increment after adjusting for patients' weight.

Primary Analysis

Increasing BDI-II scores was significantly associated with more postoperative complications, ELOS, and/or hospital readmission in female patients (unadjusted $P = 0.002$ [Fig. 1] and adjusted $P \le 0.041$ when compared with BDI-II = 0 [Table 3]) but not in males (unadjusted $P = 0.615$ and adjusted $P > 0.124$). Increasing BAI scores was also significantly associated with more postoperative complications, ELOS, and/or hospital readmission in females (unadjusted $P = 0.048$ and adjusted $P = 0.038$) but not in males (unadjusted $P = 0.092$ and adjusted $P = 0.12$) (Fig. 1 and Table 3).

Secondary Analyses

Infrequent light exercise (unadjusted $P = 0.007$ and adjusted $P = 0.047$) and sleep disturbance (unadjusted $P = 0.014$ and adjusted $P = 0.022$) were associated with worsening of the primary outcome in females, but not in males. Other coping mechanisms did not influence the primary outcome (Table A1).

Both BDI-II and BAI showed moderate positive correlations with preoperative pain catastrophizing (rumination, magnification, and helplessness) and with pain interference on daily activities (Spearman rho: 0.4–0.5) for both sexes, but not with postoperative pain or opioid requirements (Spearman rho ≤ 0.23). Preoperatively, for both sexes, depressive symptoms were significantly associated with levels of exercise and assistance for basic daily activities; overall sentiments about success of surgery; and anticipation of pain (Table A2). The level of exercise and anticipation/tolerance of pain were significantly associated with BAI in males, but not in females.

Anticipation of higher pain severity was associated with significantly greater VAS and MME scores in all time increments, as well as with more complications and longer length of stay for both sexes ($P < 0.05$ for all; Table A3). In both sexes, those with lower subjective pain tolerance reported significantly higher VAS in the first 24 hours postoperatively, with similar length of stay. There were no significant correlations between preoperative pain catastrophizing, or BPI scores and postoperative VAS, MME, or length of stay (Spearman rho ≤ 0.3).

There were no significant correlations between exercise or sleep and VAS or MME scores (Spearman rho < 0.3). Trust in the surgical team was not consistently associated with pain across all time intervals in both sexes (Table A4). Trust did not affect opioid consumption. Anticipated success of surgery was significantly associated with less pain yet similar MME use for both sexes. Satisfaction with the amount of surgical information was associated with less pain in males and females at 24 to 48 hours and less opioid consumption in females in the same time interval.

DISCUSSION

Our study described the association of preoperative depression and anxiety symptoms with postsurgical outcomes, and how these differed by sex of participants. We showed both depression and anxiety were associated with postoperative complications, length of stay, and readmission in female patients. Greater preoperative perceptions of pain were correlated with higher subjective pain, greater opioid use, more complications and longer length of stay postoperatively. There was also an overall difference by sex, independent of outcomes, with females reporting more surgical pain than males at 48 to 72 hours, with similar opioid consumption for pain control. Exercise and sleep were significant predictors of successful surgical outcomes in females.

A systematic review and meta-analysis including data from 236,595 patients undergoing cardiac surgery showed perioperative depression and anxiety may be associated with increased postoperative mortality.[13] Emotional distress has shown a multifactorial association with coronary artery disease, explained by factors such as tendency to sedentary behaviors and poor adherence to preventative measures such as diet and exercise. The association between depression and greater risk of postoperative complications has been demonstrated in other surgical specialties

TABLE 3.

Association Between BDI-II and BAI and the Primary Outcome (Rate of Postoperative Complications, ELOS, and/or Hospital Readmission)

	BDI-II				BAI			
	Male		Female		Male		Female	
Variable	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
BDI-II								
1–19 vs 0	0.87 (0.41, 1.83)	0.707	2.57 (1.04, 6.37)	0.041	—		—	
>19 vs 0	2.29 (0.56, 9.35)	0.247	4.48 (1.48, 13.56)	0.008	—		—	
>19 vs 1–19	2.65 (0.77, 9.15)	0.124	1.74 (0.86, 3.53)	0.124				
BAI: ≤6 vs >6	—		—		1.40 (0.92, 2.14)	0.119	1.54 (1.02, 2.32)	0.038
ASA (per category increase)	1.74 (1.15, 2.63)	0.009	1.32 (0.95, 1.82)	0.095	1.79 (1.19, 2.69)	0.005	1.37 (0.99, 1.89)	0.056
Age (per 5 y decrease)	1.07 (0.98, 1.16)	0.124	1.11 (1.03, 1.19)	0.005	1.05 (0.97, 1.15)	0.216	1.10 (1.03, 1.19)	0.008
Surgical specialty								
General	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Cardiac	0.91 (0.41, 1.98)	0.807	2.38 (1.03, 5.53)	0.044	0.85 (0.39, 1.84)	0.675	2.43 (1.05, 5.65)	0.038
Colorectal	0.88 (0.42, 1.85)	0.733	1.00 (0.45, 2.22)	0.991	1.01 (0.49, 2.11)	0.974	1.15 (0.52, 2.55)	0.731
Gynecology	—		0.88 (0.42, 1.81)	0.719	—		0.93 (0.45, 1.92)	0.848
Urogynecology	—		0.98 (0.49, 1.99)	0.961	—		1.14 (0.56, 2.32)	0.708
Urology	0.56 (0.26, 1.18)	0.128	1.08 (0.40, 2.91)	0.886	0.75 (0.36, 1.57)	0.447	1.04 (0.38, 2.87)	0.943
Vascular	0.49 (0.17, 1.37)	0.173	1.43 (0.24, 8.54)	0.694	0.67 (0.24, 1.88)	0.452	1.08 (0.18, 6.28)	0.935
Other	0.37 (0.06, 2.11)	0.263	0.54 (0.11, 2.67)	0.454	0.42 (0.08, 2.37)	0.328	0.60 (0.12, 2.94)	0.528

ASA indicates American Society of Anesthesiologists.

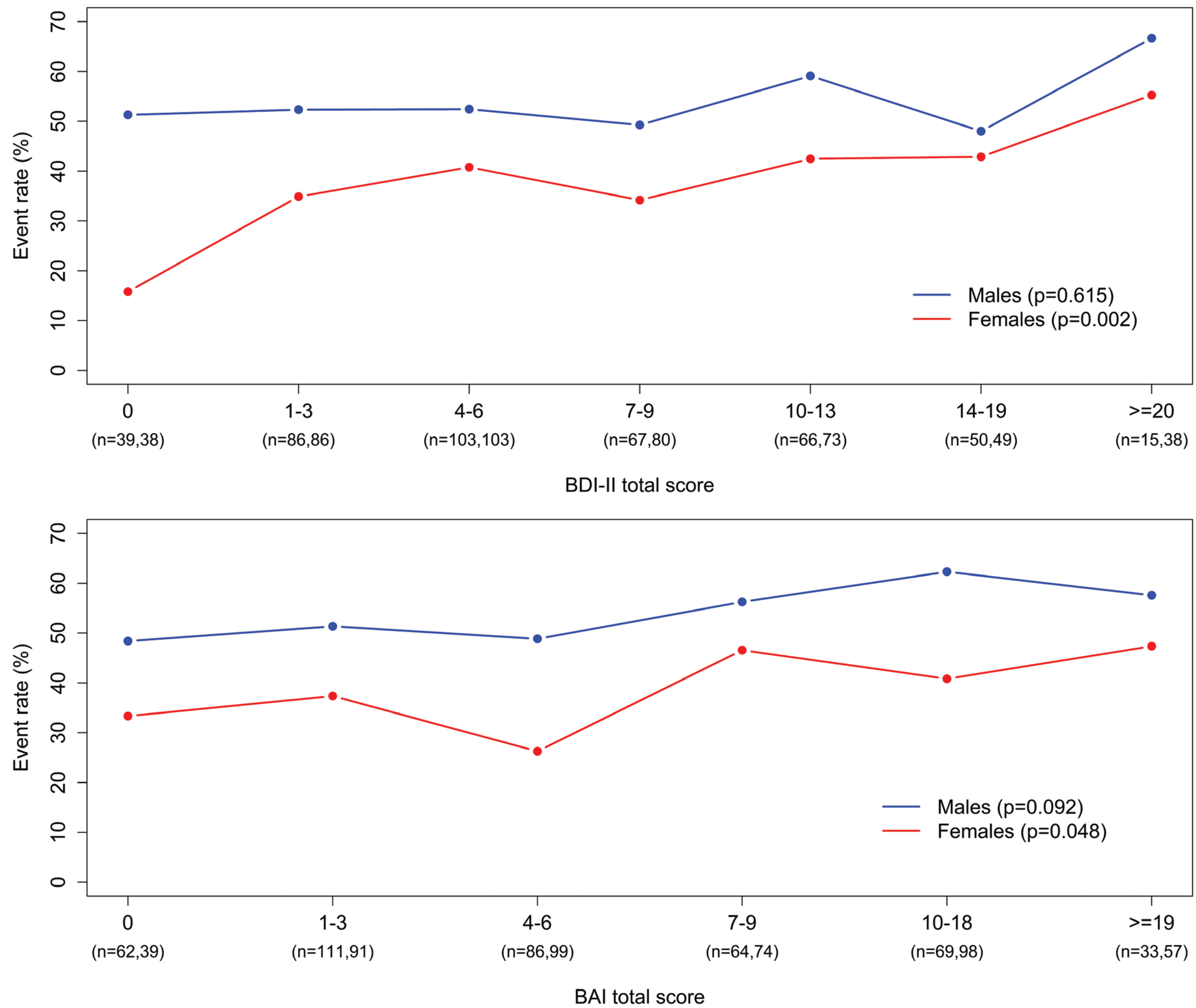

FIGURE 1. Primary outcome: rate of postoperative complications, ELOS, and/or hospital readmission by preoperative BDI-II/BAI scores for males and females.

as well.[26] In cancer patients in particular, depression is common and may be a consequence of their particular diagnosis. However, tumor growth and progression of disease can be affected by inadequate immune responses and treatment of depression may be of benefit. For example, in a population of women undergoing surgery for breast cancer, individual psychotherapy and pharmacologic management resulted in a significant difference in disease-free survival 1 year postoperatively when compared with a control group.[27] Prior studies from various surgical fields have shown associations of depression and anxiety with ELOS.[10,11,28,29]

It is difficult to tease out cause and effect relationships given the confounding effect of pain around the time of surgery. In accordance with the sleep and pain diathesis model, in a group of women with chronic pain from fibromyalgia, more disrupted sleep was associated with higher psychological and physical disability, and this was mediated by pain.[30] Preoperatively, females in our cohort had more pain, more mood symptoms and reported less sleep than males. However, unlike participants in the Hamilton study, our participants were not recruited from a chronic pain clinic and preoperative pain scores were low. Sex differences in pain perception may have a basis in the immune system; research shows different sex hormone-mediated immune reactivities before and following injury,[31] and surgery is a type of injury. Both infrequent exercise and poor sleep were associated with worse surgical outcomes in our patient population. There is a medium effect between sleep deprivation and pain perception, as demonstrated via meta-analysis.[32] Acute sleep deprivation lowers pain thresholds.[33] Exercise and sleep are related, with exercise showing clear benefits on sleep for patients with depressive symptoms and sleep disorders.[34] Exercise and mental health optimization are among strategies suggested as part of a larger package of preoperative conditioning to facilitate return to baseline activities of daily living.[35,36] In women, aerobic and anaerobic exercise can be an option to reduce negative mood.[37]

Mood and anxiety influence pain perceptions independent of sleep quality.[38] Although higher depression and anxiety scores were correlated with preoperative pain catastrophizing and interference from pain, we did not show an association with postoperative pain or opioid consumption. Studies from different surgical fields seem contradictory: in patients undergoing abdominal surgery, for example, moderate to intense acute postoperative pain was associated with high-trait anxiety and depressive mood,[39] whereas adult spine surgery did not show this association.[40] A systematic review of predictive factors for postoperative pain[8] showed preexisting pain, anxiety, younger age, and type of surgery to be the most significant predictors. Our baseline pain intensity score was low and our patient population was older. It is possible that depression and anxiety, in the absence of pre-existing chronic pain, contribute to pain perceptions (such as catastrophizing about pain) rather than actual pain once the surgery is completed. On the other hand, higher anticipated pain and lower subjective pain threshold did predict higher postoperative pain and higher postoperative opioid consumption for both male and female participants in our study. This is consistent with studies of objective preoperative pain threshold measurement as a predictor of postoperative pain.[41,42]

Another predictor of pain and opioid consumption in females was patients' satisfaction with the amount of information received about their surgery. An educational workshop on pelvic floor health interventions improved women's knowledge, symptoms, and quality of life scores evaluated three months later.[43] A Cochrane review of the effect of preoperative education in orthopedic hip or knee replacements concluded that it may have benefits for patients with depression or anxiety.[44] In an era of opioid misuse, tailored patient education in the context of surgical interventions may lead to less pain and safer behaviors. Interestingly, although females in our study reported more pain at 48 to 72 hours, they did not receive more opioids than males at any time point. There are significant biases reported in the literature regarding pain management in men versus women. For example, women's pain reports are taken less seriously (which may have resulted in prescribing of fewer opioids) and their medication is less effective for pain control than treatments prescribed to men (which may have resulted in female patients asking for fewer opioids or perhaps more nonprescription anti-inflammatories, for example).[45]

A strength of our study is that this represents one of the largest prospective cohort investigations of mental health in both sexes recruited from various surgical specialties. Another strength is our use of validated brief questionnaires that can be used in the clinical setting. The results from our study can be used to build individualized mental health optimization tools in vulnerable patients prior to surgery.

Limitations include patient selection bias. Depressed or anxious patients may have declined participation in our study before their upcoming surgery more often than other patients. Additionally, as we did not collect a treatment history, we may have also included patients with well controlled symptoms of depression and anxiety. This may explain the lower than expected incidence of clinical depression and anxiety in our patient population, which can limit our power to detect the relationship between depression, anxiety and patient characteristics or outcomes. On the other hand, although we tried to capture symptoms of the weeks before hospital admission, the patients who did elect to answer our questionnaires may have had heightened mood symptoms due to the imminent stress of surgery. Our study was likely underpowered to show significance in the male population. It could be that depression and anxiety are less prominent in males versus females undergoing surgery. On the other hand, our screening questionnaires may be sex-biased, thus resulting in an under-diagnosis of mood disorders in male participants. Psychological research shows that males and females experience depression differently: although men and women report similar severity of depression on the BDI, they endorse different symptoms within the questionnaire; men are also more likely to conceal symptoms.[46] Research needs to focus on male-specific symptom clusters when assessing men for depression.[46] Perhaps, our study tools were not sensitive enough to capture these subtle diagnostic nuances. Additionally, we did not examine the effect of self-identified gender, a socioculturally driven sex identification[31] in our patients and our baseline measure only asked about sex, namely male versus female. Gender does play a role in the experience of pain, for example.[31] Future research should ask participants to identify both their birth assigned sex, and their identified gender, which may include trans- and nonbinary identities, to better understand how we might optimize mental health prior to surgery in a more precise manner. Another limitation of our study is the inclusion of a great variety of patient surgeries, even within the same specialty category. This is associated with variation in length of stay and introduces variability in outcomes such as pain and pain perceptions. Surgery-specific anticipated versus actual length of stay was not available at our hospital. We hope the number of included patients ensured enough representation for many different surgical procedures within specialties. Given the limited sample size of different subgroups, we did not have sufficient statistical power to conduct subgroup analyses (such as by comorbidity, for example). Our current findings will hopefully encourage further research with mental health of particular subgroups.

In summary, our study showed preoperative depression, anxiety, and coping mechanisms were associated with adverse surgical outcomes and postoperative pain in a sex-specific way, with female patients significantly more impacted than males. It highlighted the importance of holistic preoperative medical care, patient education, and the emergence of sleep and exercise as novel therapeutic targets to potentially optimize outcomes for patients undergoing major surgery.

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APPENDIX

TABLE A1.

Association Between Primary Outcome and Selected Preoperative Variables

	Male				Female			
Variable	Primary Outcome Rate	P*	aOR (95% CI)	P†	Primary Outcome Rate	P*	aOR (95% CI)	P†
Exercise lightly, n (%)		0.249				0.007		
Once a month or less	13/28 (46.4)		0.74 (0.32, 1.69)	0.470	14/23 (60.9)		2.59 (1.01, 6.61)	0.047
Few times each month	27/53 (50.9)		0.89 (0.47, 1.71)	0.734	25/53 (47.2)		1.58 (0.83, 3.03)	0.165
2–3 times each week	51/109 (46.8)		0.70 (0.43, 1.14)	0.150	42/114 (36.8)		1.14 (0.70, 1.84)	0.594
4+ times each week	132/239 (55.2)		1 (Reference)		96/278 (34.5)		1 (Reference)	
Exercise moderately to strenuously, n (%)		0.686				0.296		
Once a month or less	86/169 (50.9)		0.83 (0.44, 1.56)	0.558	79/193 (40.9)		0.93 (0.49, 1.77)	0.826
Few times each month	40/81 (49.4)		0.81 (0.40, 1.64)	0.551	35/89 (39.3)		0.92 (0.44, 1.90)	0.821
2–3 times each week	59/101 (58.4)		1.31 (0.67, 2.59)	0.432	30/106 (28.3)		0.63 (0.31, 1.30)	0.215
4+ times each week	30/61 (49.2)		1 (Reference)		23/55 (41.8)		1 (Reference)	
Change in sleeping pattern, n (%)		0.642				0.014		
No change	80/161 (49.7)		1 (Reference)		53/172 (30.8)		1 (Reference)	
More sleep than usual	58/109 (53.2)		1.04 (0.62, 1.75)	0.882	40/81 (49.4)		1.98 (1.10, 3.56)	0.022
Less sleep than usual	84/153 (54.9)		1.21 (0.75, 1.95)	0.440	79/198 (39.9)		1.25 (0.79, 1.98)	0.347
Support at home after your surgery, n (%)		0.597				0.507		
No support	15/25 (60.0)		1.30 (0.52, 3.21)	0.575	5/20 (25.0)		0.47 (0.13, 1.73)	0.257
Little support	30/61 (49.2)		0.85 (0.46, 1.57)	0.595	33/79 (41.8)		1.54 (0.87, 2.72)	0.139
Quite a bit of support	60/127 (47.2)		0.78 (0.49, 1.24)	0.295	69/164 (42.1)		1.36 (0.86, 2.15)	0.182
A lot of support	122/219 (55.7)		1 (Reference)		70/207 (33.8)		1 (Reference)	
Trust in surgical team, n (%)		0.767				0.201		
Some trust	2/7 (28.6)		0.14 (0.01, 3.73)	0.242	11/24 (45.8)		1.85 (0.73, 4.71)	0.198
A lot of trust	65/115 (56.5)		1.16 (0.73, 1.85)	0.528	71/175 (40.6)		1.32 (0.87, 2.01)	0.195
Complete trust	159/310 (51.3)		1 (Reference)		97/271 (35.8)		1 (Reference)	
Surgery for your condition, n (%)		0.668				0.603		
Perhaps be successful	25/45 (55.6)		1.11 (0.56, 2.19)	0.766	20/49 (40.8)		1.25 (0.65, 2.39)	0.509
Most likely be successful	203/389 (52.2)		1 (Reference)		154/416 (37.0)		1 (Reference)	
Amount of information received, n (%)		0.064				0.191		
Somewhat satisfied	8/20 (40.0)		0.51 (0.18, 1.45)	0.205	14/22 (63.6)		2.40 (0.90, 6.39)	0.080
Quite satisfied	57/120 (47.5)		0.69 (0.44, 1.09)	0.109	54/149 (36.2)		0.99 (0.64, 1.53)	0.951
Very satisfied	164/295 (55.6)		1 (Reference)		110/296 (37.2)		1 (Reference)	

*A *P* value was based on the Cochran-Armitage trend test or Chi-square test as appropriate.
†A *P* value was based on logistic regression adjusted for age, ASA, and surgical specialty.
ASA indicates American Society of Anesthesiologists.

Table A2.

Median BDI-II and BAI Score by Patient Demographics and Coping Mechanisms

	Male				Female			
	BDI-II		BAI		BDI-II		BAI	
Variable	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P
Exercise lightly		<0.001		<0.001		0.001		0.756
Once a month or less	9.5 (6.1, 15.0)		11.3 (4.0, 18.4)		6.7 (3.6, 11.0)		7.5 (1.5, 14.5)	
Few times each month	8.0 (4.2, 13.0)		7.0 (4.0, 12.0)		10.0 (6.0, 16.0)		7.0 (5.0, 10.0)	
2–3 times each week	5.9 (3.0, 10.0)		4.5 (1.1, 8.0)		8.0 (4.0, 14.0)		7.0 (3.0, 12.0)	
4 times or more each week	6.0 (3.0, 10.0)		4.0 (1.0, 8.4)		6.0 (3.0, 10.0)		6.0 (3.0, 12.2)	
Exercise moderately to strenuously		<0.001		<0.001		0.001		0.134
Once a month or less	8.0 (5.0, 13.0)		6.0 (3.0, 13.0)		8.0 (4.0, 13.0)		7.0 (3.2, 13.0)	
Few times each month	6.0 (3.0, 10.8)		4.0 (2.0, 7.0)		7.0 (4.0, 10.0)		7.0 (3.0, 13.0)	
2–3 times each week	4.0 (2.0, 7.4)		3.0 (1.0, 7.0)		5.0 (2.0, 9.0)		5.0 (2.0, 10.5)	
4 times or more each week	5.0 (1.5, 9.2)		4.0 (1.0, 8.6)		6.2 (2.1, 10.0)		6.2 (3.5, 10.5)	
Level of assistance required with basic daily activities		<0.001		<0.001		0.002		<0.001
None	6.0 (3.0, 10.0)		4.0 (1.0, 8.5)		6.3 (3.0, 11.0)		6.0 (3.0, 12.0)	
Some	13.8 (8.0, 18.4)		13.0 (7.0, 22.0)		11.5 (7.0, 16.6)		12.6 (8.4, 18.5)	
A lot/totally dependent on another person	8.1 (5.5, 14.5)		11.6 (6.0, 13.0)		11.6 (1.6, 14.3)		8.0 (1.0, 13.3)	
Trust in surgical team		0.055		0.092		0.308		0.223
Some trust	-		-		9.0 (5.7, 14.0)		8.7 (5.5, 13.8)	
A lot of trust	8.0 (3.0, 13.0)		5.3 (2.0, 12.0)		7.0 (4.0, 12.0)		7.0 (3.0, 13.5)	
Complete trust	6.0 (3.0, 10.0)		4.0 (1.0, 8.5)		6.3 (3.0, 11.6)		6.0 (3.0, 11.1)	
Surgery for your condition		<0.001		0.005		<0.001		0.006
Perhaps be successful	9.0 (6.0, 15.0)		8.0 (3.0, 16.0)		10.0 (7.0, 16.0)		9.2 (4.0, 17.0)	
Most likely be successful	6.0 (3.0, 10.0)		5.0 (1.0, 9.0)		6.0 (3.0, 11.0)		6.0 (3.0, 11.5)	
Pain anticipate in the first few days after surgery		<0.001		<0.001		<0.001		0.117
No pain	6.2 (3.6, 8.0)		3.5 (1.0, 8.2)		-		-	
Mild pain	5.0 (2.0, 8.0)		3.0 (0.0, 7.0)		5.3 (3.0, 9.0)		7.0 (3.0, 11.0)	
Moderate pain	6.3 (3.0, 12.0)		5.0 (2.0, 10.0)		7.0 (3.0, 12.0)		6.5 (3.0, 12.0)	
Severe pain	9.0 (5.0, 16.0)		9.0 (3.0, 19.0)		9.0 (5.0, 16.5)		7.4 (4.0, 16.0)	
Pain tolerance		0.003		0.038		0.140		0.232
Low	9.5 (5.0, 14.2)		6.0 (3.0, 13.0)		9.0 (4.9, 13.0)		7.0 (4.0, 14.0)	
Average	6.0 (3.2, 11.0)		5.0 (2.0, 10.0)		7.0 (3.0, 12.0)		7.0 (3.0, 12.0)	
High	5.0 (2.2, 9.0)		4.0 (1.0, 8.0)		6.0 (3.0, 10.8)		5.0 (3.0, 12.2)	

A *P* value was based on the Kruskal-Wallis test.
For subgroups with less than 10 patients, they were not included in the comparison and their medians were not shown in the table.
IQR indicates interquartile range.

TABLE A3.

Association Between VAS/MME and Anticipation/Tolerance of Pain

	Male								
	Pain Anticipate in the First Few Days After Surgery					Pain Tolerance			
Variable	No Pain	Mild Pain	Moderate Pain	Severe Pain	*P*	No/Low	Average	High	*P*
VAS first 24 h, mean (SD)	1.3 (1.8)	1.8 (2.0)	2.8 (2.0)	3.6 (2.0)	<0.001	3.5 (2.2)	2.4 (2.1)	2.6 (2.0)	0.012
N	22	100	197	49		42	219	113	
VAS 24–48 h, mean (SD)	1.6 (1.7)	1.8 (1.8)	2.8 (2.0)	3.3 (1.7)	<0.001	2.9 (2.2)	2.5 (1.9)	2.6 (2.0)	0.526
N	11	62	178	43		38	167	94	
VAS 48–72 h, mean (SD)	0.6 (0.9)	1.5 (1.6)	2.2 (2.0)	2.5 (2.1)	0.021	2.1 (1.9)	1.8 (1.7)	2.5 (2.2)	0.076
N	7	42	127	35		27	122	65	
MME first 24 h, median (IQR)	0.0 (0.0, 12.5)	4.0 (0.0, 24.8)	10.0 (0.0, 34.4)	34.4 (6.5, 72.0)	<0.001	9.8 (0.0, 55.2)	8.1 (0.0, 34.4)	8.0 (0.0, 39.5)	0.661
N	29	121	239	55		51	259	141	
MME 24–48 h, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 16.0)	4.0 (0.0, 24.0)	24.0 (0.0, 48.0)	<0.001	5.3 (0.0, 33.0)	0.0 (0.0, 24.0)	6.3 (0.0, 24.0)	0.465
N	21	92	221	51		46	226	118	
MME 48–72 h, median (IQR)	0.0 (0.0, 16.0)	0.0 (0.0, 8.0)	0.0 (0.0, 16.0)	8.0 (0.0, 36.0)	0.006	8.0 (0.0, 26.0)	0.0 (0.0, 11.3)	0.0 (0.0, 24.0)	0.014
N	13	63	185	49		37	177	100	
Length of stay, median (IQR), d	1.4 (1.0, 3.9)	2.1 (1.0, 5.0)	4.1 (2.3, 6.0)	5.5 (4.0, 7.8)	<0.001	4.7 (2.2, 7.9)	3.9 (1.8, 5.8)	3.9 (1.9, 5.8)	0.127
N	28	119	234	52		48	253	138	
Clavien-Dindo > 0, n (%)	8 (28.6)	45 (37.8)	108 (46.0)	31 (58.5)	0.024	29 (59.2)	100 (39.4)	66 (47.8)	0.022

	Female								
	Pain anticipate in the First Few Days After Surgery					Pain Tolerance			
Variable	No Pain	Mild Pain	Moderate Pain	Severe Pain	*P*	No/Low	Average	High	*P*
VAS first 24 h, mean (SD)	1.4 (2.6)	1.8 (1.8)	3.1 (2.2)	3.2 (2.1)	<0.001	3.5 (2.3)	2.7 (2.1)	2.8 (2.3)	0.037
N	5	90	230	75		58	221	126	
VAS 24–48 h, mean (SD)	0.9 (1.2)	1.8 (2.1)	2.8 (2.3)	3.6 (2.5)	<0.001	3.4 (2.2)	2.7 (2.4)	2.6 (2.3)	0.216
N	2	56	168	57		41	150	94	
VAS 48–72 h, mean (SD)	0.0 (0.0)	1.5 (1.7)	2.8 (2.3)	2.9 (2.0)	0.005	2.5 (1.9)	2.6 (2.2)	2.5 (2.3)	0.985
N	2	30	93	42		25	89	54	
MME first 24 h, median (IQR)	0.0 (0.0, 0.0)	1.6 (0.0, 13.0)	12.0 (0.0, 29.4)	15.6 (0.0, 30.8)	<0.001	14.5 (4.0, 30.4)	8.0 (0.0, 27.2)	8.1 (0.0, 27.3)	0.121
N	9	109	272	86		65	264	153	
MME 24–48 h, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 16.0)	8.0 (0.0, 28.0)	<0.001	0.0 (0.0, 16.0)	0.0 (0.0, 12.0)	0.0 (0.0, 15.2)	0.516
N	5	83	225	74		53	215	122	
MME 48–72 h, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 15.0)	0.0 (0.0, 24.0)	0.022	0.0 (0.0, 20.0)	0.0 (0.0, 9.0)	0.0 (0.0, 14.4)	0.812
N	2	44	134	59		36	130	75	
Length of stay, median (IQR), d	1.0 (1.0, 1.6)	1.9 (1.0, 3.1)	2.0 (1.1, 4.0)	3.8 (1.9, 6.0)	<0.001	2.1 (1.2, 4.5)	2.0 (1.1, 4.1)	2.0 (1.1, 4.1)	0.856
N	8	105	268	85		64	256	151	
Clavien-Dindo > 0, n (%)	3 (37.5)	24 (22.9)	68 (25.3)	36 (42.9)	0.008	21 (32.8)	75 (29.4)	37 (24.3)	0.373

IQR indicates interquartile range.

TABLE A4.

Association Between VAS/MME and Coping Mechanism

Male

	Trust In Surgical Team				Surgery for Your Condition			Amount of Information Received			
Variable	**Some Trust**	**A Lot of Trust**	**Complete Trust**	***P***	**Perhaps Be Successful**	**Most Likely Be Successful**	***P***	**Somewhat Satisfied**	**Quite Satisfied**	**Very Satisfied**	***P***
VAS first 24 h, mean (SD)	2.2 (2.5)	2.9 (2.1)	2.5 (2.0)	0.301	2.9 (2.3)	2.6 (2.0)	0.284	2.9 (2.1)	2.8 (2.2)	2.5 (2.0)	0.366
N	7	95	267		40	332		16	103	254	
VAS 24–48 h, mean (SD)	3.6 (2.6)	2.9 (1.9)	2.5 (1.9)	0.112	3.7 (2.1)	2.5 (1.9)	0.002	3.7 (2.7)	2.9 (1.9)	2.4 (1.9)	0.018
N	6	75	215		30	267		14	72	212	
VAS 48–72 h, mean (SD)	3.4 (4.1)	2.6 (1.9)	1.9 (1.8)	0.041	2.9 (2.5)	2.0 (1.8)	0.014	2.8 (2.5)	2.5 (2.0)	1.9 (1.8)	0.070
N	3	59	151		26	187		12	50	152	
MME first 24 h, median (IQR)	0.0 (0.0, 34.0)	6.5 (0.0, 33.6)	8.1 (0.0, 38.4)	0.653	13.7 (0.8, 37.2)	8.1 (0.0, 37.0)	0.458	14.4 (0.0, 24.8)	6.4 (0.0, 30.5)	10.1 (0.0, 40.0)	0.315
N	7	119	321		46	403		21	123	304	
MME 24–48 h, median (IQR)	0.0 (0.0, 48.0)	0.0 (0.0, 18.4)	4.0 (0.0, 27.2)	0.305	0.0 (0.0, 39.0)	2.0 (0.0, 24.0)	0.511	0.0 (0.0, 40.0)	0.0 (0.0, 24.0)	2.0 (0.0, 24.0)	0.816
N	7	100	280		39	350		19	103	267	
MME 48–72 h, median (IQR)	20.0 (0.0, 40.0)	0.0 (0.0, 24.0)	0.0 (0.0, 14.5)	0.143	0.0 (0.0, 40.0)	0.0 (0.0, 16.0)	0.207	4.5 (0.0, 48.0)	0.0 (0.0, 32.0)	0.0 (0.0, 12.0)	0.115
N	5	80	227		33	281		15	78	221	
Length of stay, median (IQR), d	3.5 (1.9, 4.2)	3.9 (1.3, 6.2)	3.9 (1.9, 5.9)	0.966	4.2 (1.8, 7.3)	3.9 (1.9, 5.8)	0.268	3.7 (2.2, 8.0)	3.8 (1.1, 5.8)	4.0 (2.0, 6.0)	0.266
N	7	116	312		45	392		20	122	296	
Clavien-Dindo > 0, n (%)	2 (28.6)	55 (47.0)	135 (43.1)	0.546	23 (51.1)	172 (43.7)	0.340	8 (40.0)	48 (39.7)	140 (46.8)	0.375

Female

	Trust in Surgical Team				Surgery for Your Condition			Amount of Information Received			
Variable	**Some Trust**	**A Lot of Trust**	**Complete Trust**	***P***	**Perhaps Be Successful**	**Most Likely e Successful**	***P***	**Somewhat Satisfied**	**Quite Satisfied**	**Very Satisfied**	***P***
VAS first 24 h	3.7 (2.1)	3.1 (2.3)	2.6 (2.1)	0.016	3.5 (2.6)	2.7 (2.2)	0.029	4.1 (2.2)	2.8 (2.2)	2.8 (2.2)	0.118
N	18	150	236		41	363		13	131	258	
VAS 24–48 h	3.0 (2.6)	2.9 (2.5)	2.7 (2.2)	0.715	3.7 (2.7)	2.6 (2.3)	0.013	4.6 (3.0)	2.8 (2.3)	2.6 (2.2)	0.010
N	17	113	155		33	250		14	80	190	
VAS 48–72 h	1.1 (1.9)	2.7 (2.3)	2.5 (2.0)	0.168	3.5 (2.4)	2.4 (2.1)	0.048	2.4 (2.6)	2.7 (2.2)	2.5 (2.1)	0.803
N	7	75	85		18	145		13	50	104	
MME first 24 h	12.9 (6.6, 26.5)	10.1 (0.0, 29.5)	8.1 (0.0, 27.2)	0.379	9.0 (0.0, 32.0)	9.2 (0.0, 27.6)	0.463	13.4 (0.0, 48.2)	11.6 (0.0, 28.7)	8.0 (0.0, 27.0)	0.424
N	24	180	278		51	426		22	152	305	
MME 24–48 h	0.0 (0.0, 24.0)	0.0 (0.0, 8.8)	0.0 (0.0, 15.6)	0.745	0.0 (0.0, 34.4)	0.0 (0.0, 12.0)	0.158	32.5 (0.0, 50.7)	0.0 (0.0, 8.0)	0.0 (0.0, 15.2)	0.007
N	20	149	220		41	344		16	123	249	
MME 48–72 h	0.0 (0.0, 0.0)	0.0 (0.0, 10.0)	0.0 (0.0, 15.5)	0.361	0.0 (0.0, 28.0)	0.0 (0.0, 12.8)	0.975	9.5 (0.0, 52.0)	0.0 (0.0, 12.0)	0.0 (0.0, 12.8)	0.095
N	9	103	128		27	209		14	69	156	
Length of stay (d)	1.9 (1.1, 3.1)	2.3 (1.2, 4.1)	1.9 (1.1, 4.1)	0.086	2.0 (1.1, 3.1)	2.0 (1.1, 4.1)	0.737	3.2 (1.0, 6.2)	2.0 (1.1, 3.3)	2.0 (1.1, 4.1)	0.323
N	24	174	273		50	416		22	148	298	
Clavien-Dindo > 0, n (%)	8 (33.3)	53 (30.5)	73 (26.7)	0.601	13 (26.5)	117 (28.1)	0.822	12 (54.5)	41 (27.7)	81 (27.2)	0.022

IQR indicates interquartile range.