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Psychological Sequelae of Surgery in a Prospective Cohort of Patients from Three Intraoperative Awareness Prevention Trials

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Abstract

Background—Elective surgery can have long-term psychological sequelae, especially for patients who experience intraoperative awareness. However, risk factors other than awareness for symptoms of posttraumatic stress disorder (PTSD) after surgery are poorly defined, and practical screening methods have not been applied to a broad population of surgical patients.

Methods—The Psychological Sequelae of Surgery (Psych SOS) study was a prospective cohort study of patients previously enrolled in the United States and Canada in 3 trials for the prevention of intraoperative awareness. The 68 patients who experienced definite or possible awareness were matched, based on age, sex, surgery type, and awareness risk, with 418 patients who denied awareness. Participants completed the PTSD Checklist–Specific (PCL-S) and/or a modified Mini International Neuropsychiatric Interview telephone assessment to identify symptoms of PTSD and symptom complexes consistent with a PTSD diagnosis. We then used structural equation modeling to produce a composite PTSD score and examined potential risk factors.

Results—One hundred forty patients were unreachable; of those contacted, 303 (88%) participated a median of 2 years postoperatively. Forty-four of the 219 patients (20.1%) who completed the PCL-S exceeded the civilian screening cutoff score for PTSD symptoms resulting from their surgery (15 of 35 [43%] with awareness and 29 of 184 [16%] without). Nineteen

patients (8.7%; 5 of 35 [14%] with awareness and 14 of 184 [7.6%] without) both exceeded the cutoff and endorsed a breadth of symptoms consistent with the DSM-IV diagnosis of PTSD attributable to their surgery. Factors independently associated with PTSD symptoms were poor social support, prior PTSD symptoms, prior mental health treatment, dissociation related to surgery, perceiving that one's life was threatened during surgery, and intraoperative awareness (all $p < 0.017$). Perioperative dissociation was identified as a potential mediator for perioperative PTSD symptoms.

Conclusions—Events in the perioperative period can precipitate psychological symptoms consistent with subsyndromal and syndromal PTSD. We confirmed the high rate of postoperative PTSD in awareness patients, but also identified a significant rate in matched nonawareness controls. Screening surgical patients, especially those with potentially mediating risk factors such as intraoperative awareness or perioperative dissociation, for postoperative PTSD symptoms with the PCL-S is practical and could promote early referral, evaluation and treatment.

Introduction

More than 200 million major surgical procedures are performed each year worldwide, the majority with general anesthesia.¹ Prospective studies using structured interviews have found that between 0.1 and 0.4% of all general anesthetics are complicated by unintended intraoperative awareness with explicit recall, hereafter referred to as awareness.² Patients reporting awareness may experience ongoing psychological sequelae on a spectrum from subsyndromal to syndromal posttraumatic stress disorder (PTSD); small studies have suggested that between 0% and 71% develop PTSD.³⁻¹⁰ However, intraoperative awareness is likely to be only 1 of many perioperative experiences associated with posttraumatic stress spectrum disorder.¹¹ Certain patient factors such as depressive symptoms and pain,¹² as well as perioperative factors including intensive care unit (ICU) admission,¹³ mechanical ventilation,¹⁴ and in-hospital cardiac arrest,¹⁵ have been described as risk factors for healthcare-associated PTSD.

Many studies of healthcare-associated PTSD symptoms have used face-to-face interview techniques that, while valid, cannot feasibly be implemented for routine screening.^{4-7, 9, 10} Well-validated PTSD screening instruments have not been broadly applied to an elective surgical population. We previously conducted 3 large prospective trials of interventions to prevent awareness, enrolling more than 29,000 patients at 4 institutions.¹⁶⁻¹⁸ The assessment of psychological sequelae and/or PTSD was a prespecified secondary aim in all 3 trials and is the focus of the present Psychological Sequelae of Surgery (Psych SOS) study. The objectives of the Psych SOS study were 1) to apply practical screening instruments to detect symptoms of PTSD (e.g., subsyndromal PTSD) and symptom complexes consistent with a diagnosis of postoperative PTSD, and 2) to identify factors, such as intraoperative awareness, that are associated with increased risk of postoperative PTSD symptoms.

Methods

This multicenter study was approved by the Human Studies Committees at Washington University in St. Louis (USA), the University of Manitoba in Winnipeg (Canada), and the University of Michigan in Ann Arbor (USA). Verbal informed consent was obtained for

each telephone interview; return of a completed study form implied consent for the written portion of the study.

The requirement for written informed consent was waived by the IRB. The study was not registered before patient enrollment. The parent studies (B-Unaware, BAG-RECALL, and MACS) were registered at clinicaltrials.gov as NCT00281489, NCT00682825, and NCT00689091, respectively. Evaluation of psychological sequelae was a secondary outcome of interest of these studies.

Study design

Psych SOS was designed as a matched double-cohort study. Patients who experienced definite or possible awareness were matched 1:4 with control patients who denied awareness from the same institution and trial. Other matching factors were sex, age (in study population quartiles: 18-50, 51-60, 61-70, and 71 years and older), ICU care after surgery, and surgical procedure (if possible) or service. Screening tools were used to identify patients with postoperative PTSD-complex symptoms (Supplemental Figure 1) and are described in detail below.

Patient population

Patients were drawn from participants in the B-Unaware trial (September 2005 to October 2006), BIS or Anesthetic Gas to Reduce Explicit Recall trial (BAG-RECALL) (May 2008 to May 2010), and the Michigan Awareness Control Study (MACS) (May 2008 to May 2010). Thus, inclusion criteria were based on those trials.¹⁶⁻¹⁸ In brief, the B-Unaware and BAG-RECALL trials recruited only patients who were considered to be at high risk of experiencing awareness and who were receiving potent volatile anesthetics. High-risk patients were defined in BAG-RECALL as those who had at least 1 of the following: preoperative long-term use of anticonvulsants, opiates, benzodiazepines, cocaine, or daily alcohol consumption; history of cardiac ejection fraction <40%, aortic stenosis, end-stage lung disease, marginal exercise tolerance, pulmonary hypertension, intraoperative awareness, difficult intubation, or anticipated difficult intubation; ASA physical status 4 or 5; or planned open-heart surgery. B-Unaware used fundamentally similar criteria. By contrast, MACS recruited patients at all risk levels receiving both inhaled and IV anesthetics. All 3 studies excluded non-English speakers and patients younger than 18 years. Postoperatively, all participants underwent structured modified Brice interviews to detect awareness.¹⁹ Patients from Washington University (BAG-RECALL, B-Unaware), the University of Manitoba (BAG-RECALL), and the University of Michigan (MACS) who experienced definite or possible awareness were matched with patients who denied awareness, as above. The decision to include patients with adjudicated definite or possible awareness was made *a priori*, as reflected in the study protocol submitted to the study site ethics committees. This decision was based on the possibility that any credible awareness experience could potentially cause psychological distress in a patient.

Assessment for psychological sequelae

Participants were contacted between August 2010 and December 2011. Two types of assessment were used: the PTSD Checklist – Specific (PCL-S),²⁰ which was mailed to

participants, and a modified version of the Mini International Neuropsychiatric Interview (MINI),²¹ which was administered by telephone. The modified version of the MINI is referred to herein as “mMINI.”

PCL-S

The PCL-S is a validated measure of PTSD symptoms after a defined incident (e.g., surgery).²⁰ A copy of the PCL-S and an explanatory letter were mailed to study participants (Supplemental Document 1). Based on recommendations from the Department of Veterans' Affairs PCL-S scoring guide, the civilian cut-off score of 30 was selected to discriminate between patients with potentially clinically meaningful levels of PTSD symptoms and those without.²² We selected the cutoff score based on our goal to screen for, rather than diagnose, PTSD. We also evaluated the PCL-S responses of those with severity scores above the civilian cutoff to determine whether the participant endorsed a breadth of symptoms consistent with the Diagnostic and Statistical Manual Fourth Edition (DSM-IV) symptom criteria for diagnosis of PTSD (Supplemental Figure 1).

Telephone interview

The MINI was developed as a broad screening tool for many psychiatric diagnoses, according to the criteria described in the DSM-IV²¹ (Supplemental Figure 1). A psychologist with expertise in anxiety disorders expanded the questions in the PTSD section of the MINI by (a) including assessments for each symptom and (b) including severity scales for those symptoms for which it was possible to assess symptom severity. This brought a degree of dimensionality to the mMINI similar to that found in the PCL-S, which is appropriate when considering PTSD symptoms along a spectrum from mild to severe. We supplemented the MINI with an assessment of social support based upon the Multidimensional Perceived Social Support Scale,²³ questions about mental health history, and the depression items from the 21-item version of the Depression Anxiety and Stress Scales.²⁴ We also inquired about past PTSD symptoms attributed to the index surgery that had resolved before the interview, and past experiences with PTSD symptoms due to other events. Finally, 2 items to evaluate perioperative experiences of dissociation, i.e., a feeling that one is numbed, dazed, or dreaming during real events, were inserted. The telephone interview script is reproduced in Supplemental Document 2.

Interviewers from all 3 institutions received a standardized training regimen and were blinded to awareness status.

Statistical analysis

Descriptive and univariate statistics were performed using SPSS Statistics versions 19 and 20 (IBM Corporation, Somers, NY). Modeling of risk factors for the PTSD symptom complex using mMINI and PCL-S data was conducted using structural equation modeling with the software package Mplus (Version 7, Muthén&Muthén, Los Angeles, CA). For each participant, we estimated a composite PTSD factor corresponding to PTSD symptom severity using available information from the mMINI, PCL-S, or both. Self-report and interview responses to PTSD symptoms in the B, C, and D clusters (Supplemental Figure 1) were treated as ordered categorical variables and used to estimate the composite PTSD

factor; missing data were estimated using available information.²⁵ We then regressed the PTSD factor on predictors to determine what variables predicted PTSD symptom severity. This approach avoids the statistical and scientific problems associated with the use of a single measure of a construct, falsely dichotomizing dimensional scores,²⁶ and inappropriately discarding cases with partially missing data. Indirect effects were assessed using bias-corrected bootstrapping with 5000 draws.²⁷ A *p* value less than 0.05 was considered to indicate statistical significance.

Results

Patients

We attempted to recruit all 68 patients from the 3 institutions with definite or possible intraoperative awareness and an additional 418 who denied awareness. After exclusions for those who were deceased or unreachable, and those who refused participation, 49 patients with awareness and 254 without participated and contributed to the study (Figure 1) by completing the mMINI (*n* = 84), the PCL-S (*n* = 23), or both (*n* = 196). Because of the iterative process of matching within then on awareness cohort, more nonawareness patients were recruited than the planned 1:4 match. Nonawareness patients who completed 1 or both surveys were not excluded from analysis if it became apparent later that the awareness patient with whom they had been matched would not be participating in Psych SOS.

Those who participated were not significantly different from those who did not, in terms of sex, whether or not they reported awareness, their study intervention, age at surgery, and the type of surgery they received. However, patients who participated were significantly more likely to have reported distress during their initial awareness experience (Table 1).²⁸ Those who participated also had a significantly shorter time between their surgery and entry into the Psych SOS study, were more likely to have had an ICU stay, and were less likely to have been judged at high risk for awareness (Table 1).

Assessment for psychological sequelae and the PTSD symptom complex using the PCL-S

Of all patients who completed the PCL-S, 20.1% exceeded the civilian PCL-S cutoff score for the presence of significant PTSD symptoms attributed to their surgery and hospitalization. Twenty-nine of 184 patients (15.8%) who did not experience awareness and 15 of 35 (42.9%) who experienced definite or possible awareness screened positive (unadjusted absolute risk increase = 27.1%; 95% CI, 11.1% to 44.0%). Patients with a PCL-S total severity score higher than 30 were more likely to have reported definite or possible awareness (Table 2). Nineteen patients (8.7%; 14/184 who denied awareness and 5/35 with definite or possible awareness) had both a total severity score higher than 30 and reported symptoms on the PCL-S or during the mMINI interview from the B, C and D clusters consistent with presumptive DSM-IV criterion-based diagnosis of PTSD related to their surgery.

Modeling risk factors for the PTSD symptom complex using composite scores

Validity testing for confirmatory factor analysis—We first tested whether all the PTSD items regarding the B, C, and D clusters could be used to estimate a single PTSD

factor by using a confirmatory factor analysis. A single factor fit the model well according to standard definitions, both locally and globally,²⁹ indicating that both the self-report and interview essentially measure a single construct. Supporting this interpretation, when scaled scores were created from the same items, the interview and self-report severity scores correlated well ($r = 0.77$, $p < 0.001$).

Impact of intraoperative awareness and other hypothesized risk factors on PTSD symptom complex severity factor—Evaluation of independent relationships among the PTSD factor, awareness, and the additional predictors described in Table 3 excluded 25 participants who did not complete the interview and thus had incomplete data for 1 or more predictor. A sensitivity analysis excluding those predictors, so all participants could be included, yielded substantively identical results.

The significant independent predictors of the PTSD factor were dissociation related to surgery, perceiving that one's life was threatened during surgery, history of PTSD before surgery, low current social support, and a history of mental health treatment (Table 3). Awareness continued to be a significant predictor of PTSD-complex symptom severity with all other variables in the model. Age, sex, ICU care, and whether the patient underwent cardiac surgery were not independent predictors of PTSD symptoms attributed to the surgery itself in this sample.

Indirect effects—Tests for indirect effects provide a surrogate for a causal chain of events. There was a significant indirect effect for awareness on PTSD through dissociation ($p < 0.01^a$). Furthermore, multiple regression demonstrated patients reporting awareness were more likely to uniquely endorse depersonalization and derealization ($p = 0.04$), as opposed to feeling numbed or dazed ($p = 0.21$), even after accounting for the overlap between the 2 dissociation items.

Discussion

Using practical screening tools, this study identified a striking percentage of postoperative patients with significant PTSD symptoms attributed to surgery and, through indirect analysis, demonstrated that the experience of dissociation in the perioperative period may be a mediating step to the development of PTSD symptoms after surgery (as has been shown for other trauma-related precipitants of PTSD).³⁰ Although the cohort studied included patients with awareness who might be expected to be at risk for psychological sequelae, a large number of matched nonawareness controls also reported psychological symptoms attributed to surgery.

The presence of PTSD is regarded as dichotomous in terms of strict diagnostic criteria, but PTSD symptoms have a spectrum of severity, with even subsyndromal PTSD having major implications for patients' functionality and quality of life.³¹⁻³⁵ The screening and analytic approaches used in Psych-SOS allowed for the fact that all participants in the study had the

^aThe MPlus bias-corrected bootstrapped point estimate with 99% two-sided confidence interval for the effect of awareness (on PTSD) via dissociation is 0.211 [0.036-0.470]. The “ $p < 0.01$ ” is reported based on the 99% confidence interval not including 0. These estimates do not have a clinical meaning (e.g., they cannot be translated into a standardized coefficient).

potential for some level of PTSD symptoms (whether very low, average or very high) attributable to their surgery that could be predicted within the model. The novel and practical approach to screening for postoperative PTSD in the current study yielded findings that are commensurate with previous studies of patients reporting intraoperative awareness (Table 4)³⁻¹⁰ and confirmed that awareness substantially increases the risk of PTSD symptoms. The findings are also consistent with a previous study identifying postoperative PTSD in 3 of 25 patients (12%) from a matched surgical cohort not experiencing awareness,⁵ and in 14 of 73 consecutive patients after elective lumbar spine arthrodesis, for whom awareness status was not assessed.³⁶

It is impractical to perform detailed psychological assessment of every patient who undergoes surgery. However, targeted screening could identify those at highest risk for subsequent referral to assessment or support services. In this study, we demonstrated 6 major risk factors for the PTSD symptom complex attributed to surgery (i.e., poor social support, history of PTSD symptoms, prior mental health treatment, dissociation related to surgery, perceiving that one's life was threatened during surgery, intraoperative awareness), that substantially overlap with known risk factors for PTSD after psychological trauma. These (and potentially other validated) risk factors could be applied to patients who have undergone surgery to identify a target population for further screening, progressing to formal assessment and intervention as needed (Figure 2). A similar step-wise care pathway has been shown to improve PTSD symptoms and remission rates in traumatic injury survivors.³⁷

The incidence of PTSD-related symptom complexes in Psych SOS was substantially higher than would be expected from a random sample of adults in the community. Using DSM-IV criteria, the National Comorbidity Survey Replication suggested that the lifetime prevalence of PTSD in United States adults is about 6.8%.³⁸ The 12-month PTSD prevalence for adults was estimated at 3.5%.³⁹ In contrast, 8.7% of the surgical patients in the cohort studied in Psych SOS (or 7.6% of those who did not report intraoperative awareness) had symptoms consistent with PTSD in response to a single event, surgery. PTSD symptoms and diagnoses, unlike other psychiatric diagnoses, are established in reference to a specific (traumatic) event, which in the case of Psych SOS was the index surgery. Indeed, a number of surgery-specific factors were independent predictors of PTSD symptomatology in the Psych SOS study. These data suggest that a surgery confers approximately the same risk of persistent PTSD symptoms as being mugged or witnessing a killing or serious injury.⁴⁰ Although this risk appears surprisingly high, a recent study screened more than 500 stroke or transient ischemic attack survivors with the PCL-S and demonstrated that 18% of these patients had probable syndromal PTSD attributed to the event a mean of 2 years later.⁴¹

There are important limitations to consider when interpreting these results. First, we did not compare our screening methods against a "gold standard," typically a face-to-face interview with a clinician experienced in the diagnosis of PTSD using DSM-IV criteria. Second, because no outcome data were assessed, we cannot be certain about inferences regarding the clinical importance of the PTSD symptoms we identified. However, even subsyndromal levels of PTSD symptoms significantly impair function, as discussed. Future work is needed to define the quality-of-life implications for persistent psychological distress many years after surgery. Third, the prevalence of PTSD symptoms in this study may not be

generalizable to all surgical patients as this was a sample of surgical patients enriched for patients reporting intraoperative awareness and that was subject to the inclusion criteria of the parent studies. Furthermore, the awareness patients who participated in this study had a higher incidence of initial emotional distress than nonparticipants and thus might be expected to have a higher incidence of psychological sequelae attributed to awareness.⁸ Additionally, we were unable to compare patient-reported perioperative distress in control participants versus nonparticipants. Differential willingness of patients to participate in this study depending on perioperative (awareness or nonawareness) distress may have been a source of bias in our findings for which we were unable to adjust; 11% of those contacted declined to participate. Finally, no PCL-S score cutoff (above which a patient is considered to have a symptom complex consistent with PTSD) has been described for this population of postoperative patients 1-6 years after their index surgery. Therefore, further work to refine cutoff scores, taking into consideration the time elapsed since surgery, will be needed to optimize the screening. PTSD symptoms tend to wane with time, with median duration of about 60 months (although long-term longitudinal follow-up demonstrates symptoms fail to remit in approximately one-third of patients)⁴² and the distribution of PCL-S total severity scores if performed shortly after surgery may be different than the distribution we describe here. Variability in time-to-assessment may also underlie some of the differences in incidence rates reported in other peer-reviewed studies of PTSD after awareness (Table 3). Interestingly, 2 small studies of similar design to the present work found markedly different PTSD rates depending on time since the awareness event: a median of 5.3 years after surgery, 71% of the awareness patients studied had PTSD,⁵ compared with no patients a median of 17.2 years after surgery.¹⁰

One in 5 of our study population screened positive for PTSD-complex symptoms; 8.7% of the study population, including 7.6% of patients who did not experience awareness, reported lasting psychological symptoms attributed to surgery of the breadth and severity consistent with DSM-IV criteria for PTSD. This study provides evidence that there is a large population of surgical patients potentially at risk for postoperative PTSD. Our findings suggest that both perioperative physicians and general practitioners should be aware that persistent PTSD symptoms occur fairly frequently as a complication of surgery. However, this must be confirmed by further studies assessing reliability of the PCL-S screening tool and comparison with gold standard diagnostic techniques in the surgical population. Furthermore, surgical patients judged to be at risk for PTSD based on perioperative screening may benefit from a broad, multidisciplinary approach toward preoperative prevention and/or postoperative screening and treatment, as at-risk patients have in other settings.^{36,43} The data presented here provide a framework for risk identification and practical screening that could be broadly implemented in an effort to identify and appropriately refer these patients for formal psychiatric assessment and early intervention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Participant flow diagram. 1, the single patient reporting awareness from the University of Chicago in the BAG-RECALL trial was not included in Psych SOS. 2, “other” includes patients who were unable to complete their initial screening tool because of hearing, speech, or reading difficulty or other neurologic disease.

Figure 2.
Proposed schematic for screening patients for persistent psychological sequelae following surgery.

Table 1

Comparison of baseline data between participants and nonparticipants.

Variable		Participated (% of participants)	Did not participate (% of nonparticipants)	P-value
Male sex		171 (56.4%)	112 (61.2%)	0.30 ^a
Age at surgery		54.7 ± 15.0	54.5 ±14.4	0.88 ^b
Years surgery to contact (IQR)		2 (2-3)	2 (2-5)	0.005^c
Trial source (publication year)	B-Unaware (2008)	37 (12.2%)	46 (25.1%)	<0.001^a
	BAG-RECALL (2011)	107 (35.3%)	67 (36.6%)	
	MACS (2012)	159 (52.5%)	70 (38.3%)	
Type of surgery	Cardiothoracic	103 (34.0%)	62 (33.9%)	0.12 ^a
	General	61 (20.1%)	48 (26.2%)	
	Gynecologic	39 (12.9%)	29 (15.8%)	
	Urologic	23 (7.6%)	11 (6.0%)	
	ENT or maxillofacial	19 (6.3%)	11 (6.0%)	
	Orthopedic	26 (8.6%)	6 (3.3%)	
	Other ^d	31 (10.2%)	16 (8.7%)	
Had ICU stay		115 (38.0%)	47 (25.6%)	0.005^a
Study group	End-tidal anesthetic concentration monitoring	143 (41.2%)	91 (49.7%)	0.092 ^a
	Bispectral index monitoring	117 (38.6%)	78 (42.6%)	
	No AWR monitor	43 (14.2%)	14 (7.7%)	
High risk for AWR		215 (71.0%)	146 (79.8%)	0.033^a
AWR	Definite	24 (7.9%)	7 (3.8%)	0.14 ^b
	Possible	25 (8.3%)	12 (6.6%)	
	Denied	254 (83.8%)	164 (89.6%)	
For only those patients who reported AWR:				
MACI Class	1	20 (41%)	5 (26%)	0.63 ^e
	2	15 (31%)	6 (32%)	
	3	6 (12%)	4 (21%)	
	4 or 5	8 (16%)	4 (21%)	
Distressing	No	12 (24.5%)	9 (47.4%)	0.026^a
	Yes	37 (75.5%)	10 (52.6%)	

Percentages may not sum to 100% because of rounding.

^a chi-square test.^b t-test.^c Mann-Whitney U test.^d“Other” includes surgical categories with less than 10 total patients, such as vascular surgery, neurosurgery, cardiac electrophysiology, and other miscellaneous procedure types.

^eFisher's exact test.

AWR = intraoperative awareness with explicit recall, ENT = ear, nose and throat surgery, ICU=intensive care unit, MACI = Michigan Awareness Classification Instrument

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Table 2

Univariate comparisons for patients with PCL-S scores higher than 30 versus those without.

Variable	PCL-S < 30 n (%)	PCL-S ≥ 30 n (%)	P value
Age (median [IQR])	57 [46 – 67]	53 [47 – 61]	0.11 ^a
Female gender	80 (45.7%)	19 (43.2%)	0.76 ^b
Underwent cardiac surgery	47 (26.9%)	6 (13.6%)	0.067 ^b
Stayed in ICU	63 (36.0%)	11 (25.0%)	0.17 ^b
Definite or possible AWR	20 (11.4%)	15 (34.1%)	<0.001 ^b
For patients who reported AWR:			
Nondistressing AWR experience	18 (90.0%)	12 (80.0%)	0.40 ^c

^a Mann-Whitney U test.

^b chi square.

^c Fisher's exact test.

AWR = intraoperative awareness with recall, ICU = intensive care unit, IQR = interquartile range.

Table 3

Predictors for severity of posttraumatic stress disorder (PTSD)-complex symptoms based on confirmatory factor analysis.

Factor	Estimate $\pm$ standard error of the estimate	Standardized estimate	P value
Significant:			
Past PTSD-complex symptoms	0.42 ± 0.14	0.55 if yes	0.003
Perceived social support	-0.18 ± 0.07	-0.20 per standard deviation of latent variable above zero	0.006
Prior mental health treatment	0.19 ± 0.08	0.19 if yes	0.017
Intraoperative awareness (definite or possible)	0.36 ± 0.15	0.47 if yes	0.014
Dissociation at the time of surgery	0.44 ± 0.11	0.39 per standard deviation of latent variable above zero	<0.001
Perceived degree of threat to life at the time of surgery	0.16 ± 0.05	0.21 per standard deviation of latent variable above zero	0.002
Nonsignificant:			
Age	-0.08 ± 0.07		0.21
Gender	0.09 ± 0.12		0.49
Whether the patient received care in the ICU	0.13 ± 0.18		0.40
Whether the patient underwent cardiac surgery	-0.31 ± 0.21		0.09

Standardized estimate is the amount, in standard deviations, by which the value of the predictor is expected to change the severity of PTSD-complex symptoms. Latent variables were required when the predictor was derived from more than one question on the PCL-S and/or the mMINI.

For example, if a patient reports prior PTSD-complex symptoms (+0.55), a slightly low level of social support (1 standard deviation below the mean) ($-1 * -0.20 = +0.20$), a high degree (3 standard deviations above the mean) of dissociation at the time of surgery ($3 * 0.44 = +1.31$), denies prior mental health treatment, and had average perceived degree of threat to life during surgery, their PTSD-complex symptom severity is estimated to be $0.55 + 0.20 + 1.31 = 2.06$, or 2 standard deviations above the mean severity for all people who underwent surgery.

ICU = intensive care unit

Table 4

Summary of studies evaluating psychological sequelae from intraoperative awareness.

Study	Year	Recruitment method	Mean/median time (range) since awareness event	PTSD screening test or criteria used	Data collection method	Number of awareness patients studied (number with PTSD symptoms, %)
Schwender et al ⁹	1998	Advertising and referral	9.6 (0.1-30) yr	No formal criteria used	Face-to-face	45 (3, 7%)
Ranta et al ⁷	1998	Secondary outcome of a prospective awareness study	Within 2 weeks of surgery	SCID-NP and SCID-II (DSM-III-R criteria)	Face-to-face	5 ^d (0, 0%)
Domino et al ³	1999	Closed claims	Not reported	No formal criteria used	Claim file review	61 ^b (6, 10%)
Osterman et al ⁶	2001	Advertising and referral	17.9 (0.25-38) yrs	CAPS (DSM-IV criteria)	Face-to-face	16 (9, 56%)
Lenmarken et al ⁴	2002	Secondary outcome of a prospective awareness study	27 (20-35) mos	DSM-IV (DSM-IV criteria)	Face-to-face	9 ^c (4, 44%)
Samuelsson et al ⁸	2007	Consecutive enrollment of surgical patients who reported previous awareness	21 (0-66) yrs	No formal criteria used	Telephone	46 (1, 2%) ^d
Leslie et al ⁵	2010	Secondary outcome of a prospective awareness study	5.3 (4.3-5.7) yrs	CAPS	Face-to-face	7 ^e (5, 71%)
Laukkala et al ¹⁰	2014	Secondary outcome of a prospective awareness study	17.2 (13.0-19.7) yrs	SCID-I (DSM-IV criteria)	Face-to-face	9 (0, 0%)
Whitlock et al (present study)	2014	Secondary outcome of three prospective awareness studies	2 (1-6) yrs	PCL-S	Mailed form completed at home	35 ^f (15, 43%)

^aThere were a total of 19 awareness patients, but only 5 had a completed psychiatric follow up.

^bThis does not include patients in the study who experienced awake paralysis.

^cNine other patients from the original study were lost to follow up (2), refused to participate (6), or died (1).

^dThis patient had experienced episodes of "extreme mental stress" earlier in life.

^eSix other patients from the original study died.

^fIncluded definite and possible awareness patients; only patients responding to written screening tool included.

Abbreviations: SCID, structured clinical interview for the DSM-III-R or -IV (NP, non-patient version). CAPS, clinician-administered PTSD scale.