Psychological Predictors of Acute Postoperative Pain After Hysterectomy for Benign Causes

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Objectives: Psychological parameters have been shown to contribute significantly to the development of acute postoperative pain (APOP). For the prediction of APOP in chest malformation patients and cancer patients, we found pain-specific psychological predictors to be of higher relevance than general psychological predictors. The current study aims to further substantiate these findings.

Materials and Methods: In a sample of 73 middle-aged hysterectomy patients, 3 predictor sets were assessed 1 day before surgery: attitudinal biases (toward pain-related, social threat, and positive words in a dot-probe task), pain-related emotions and cognitions (pain anxiety, pain catastrophizing, and pain hypervigilance), and affective state variables (depression and somatization). APOP intensity rated 2 to 3 days after surgery and analgesic consumption during the first 48 postoperative hours were used as outcome measures.

Results: APOP intensity ratings were significantly explained by their best single predictors in a multiple regression analysis: social threat words of the dot-probe task, pain anxiety, and somatization (14.7% of explained variance). When comparing standardized β coefficients, pain-specific psychological predictors appeared to be of higher explanatory relevance than general psychological predictors. In contrast, analgesic consumption could not be significantly predicted by the psychological variables.

Discussion: Hysterectomy patients at risk for high APOP intensity could be characterized by the psychological variables used, whereas their predictive value for analgesic consumption was limited. The high predictive potency of pain-specific psychological variables should be considered for further improvement of pain management and prevention, because pain-specific variables such as pain anxiety can be the target of focal psychological interventions when preparing for surgery.

Key Words: acute postoperative pain, analgesic consumption, psychological predictor, pain anxiety, hysterectomy (Clin J Pain 2017;33:595–603)

Postoperative pain in its acute form is a fundamental aspect of surgery. In patients undergoing various types of surgeries, 10% to 57% reported moderate or even severe acute postoperative pain (APOP) on postoperative day 2.1 In the case of hysterectomy patients, up to about two thirds of the patients have reported moderate or even severe APOP 48 hours after surgery.2

APOP is a crucial issue because it is not only an unpleasant experience, but also a significant stressor for patients, which can have many adverse effects. For example, it has been found to have an influence on immune function, wound healing, physical ability, recovery time, time until discharge, and quality of life.3,4 Furthermore, it is a strong predictor of chronic postoperative pain,5—7 which can seriously impair a patient’s long-term quality of life. Better prediction of APOP would therefore not only allow for more efficient postoperative acute pain management, but also increase fundamental knowledge about the complex processes of the genesis of APOP.

General psychological factors (eg, depression, anxiety, distress, neuroticism) have been found to contribute significantly to APOP and analgesic consumption after various kinds of surgeries, including gynecological surgery.3—9 The investigation of pain-specific emotions and cognitions that are more directly related to APOP (eg, pain catastrophizing, pain anxiety, pain hypervigilance) has gained importance because current research points toward pain-specific predictors being of higher predictive relevance than general psychological predictors.2,4,10—15

Pain-specific variables such as pain anxiety, pain catastrophizing, and pain hypervigilance are usually measured by self-report questionnaires. Consequently, patients are aware that they are supposed to monitor pain-related emotions and cognitions, and responses can differ depending on their introspective abilities and self-representations. It is also of considerable interest to investigate other levels of processing; therefore, variables that assess automatic and implicit attentional processing of pain-related stimuli (eg, in a dot-probe task) should also be included. By adding this additional processing level, the amount of explained variance of APOP might be further increased.

Parameters of the dot-probe task, as well as pain-related emotions and cognitions, have been shown to be
predictors of APOP in patients undergoing surgical correc-
tion of a chest malformation\textsuperscript{12} and cancer patients.\textsuperscript{14} Whereas in one study by Lautenbacher et al.,\textsuperscript{12} pain ca-
tastrophizing and avoidance of pain-related dot-probe words were significant predictors of APOP intensity, in another study by Lautenbacher et al.,\textsuperscript{14} avoidance of social threatening dot-probe words was a significant predictor of acute postoperative analgesic consumption. In both studies, pain-specific predictors were of higher explanatory rele-
vance than general psychological predictors such as depression. Yet, it has to be noted that different pain-
specific psychological predictors were found to be relevant in the 2 samples. The differences concerning the best single predictors might be due to varying psychological pop-
ulation profiles (differences in sex, gender, age, pain-
nativity, extent and type of surgery, threat of disease) and might indicate that different maladaptive coping styles are associated with a poor postoperative outcome.

In this study, we included hysterectomy patients to further assess the variations among surgical models. We selected hysterectomy not only because it is a common surgical procedure with high frequencies of APOP but also because it is possible to select patients who do not report presurgical acute and/or chronic pain. Thus, the likelihood of postoperative pain being due to causes other than the surgery is strongly decreased, keeping pathophysiology overseen.

We investigated 3 sets of psychological predictors: pain-specific psychological variables ("pain-related emo-
tions and cognitions"): pain anxiety, pain catastrophizing, pain hypervigilance), general psychological variables ("affective state": depression, somatization), and implicit attentional processing variables as assessed by a dot-probe task ("attentional biases": pain-related, social threat, and positive words). The main objectives were to first investi-
gate as to which variables from the 3 predictor sets would be the best single predictors for APOP and analgesic con-
sumption in the first few days after surgery. Second, we wanted to compare pain-specific and general psychological variables concerning their predictive value (using standardized beta coefficients in linear regression analyses). We hypothesized that pain-specific psychological vari-
ables would be of higher predictive influence than general psychological predictors, and that APOP after hystere-
tomy would be predicted by variables similar to those that were predictive after chest malformation surgery and cancer surgery (pain catastrophizing, attentional avoidance of pain-related, and social threatening stimuli). On the basis of our current knowledge, we expected attentional avoidance of negative dot-probe stimuli and pain catastrophizing, or the related concept “pain anxiety,” to be of predictive value for APOP in hysterectomy patients.

MATERIALS AND METHODS

Participants, Surgery, and Medication

Participants

There were 73 female patients included in the study, who were undergoing laparoscopic hysterectomy (LH) for benign causes at the Gynecological Department of the University Hospital Erlangen. Only patients aged from 30 to 65 years were included (mean age: 45.2 $\pm$ 4.5 y). Exclu-
sion criteria encompassed acute or chronic pain conditions, previous extensive surgeries, severe somatic diseases (eg, diabetes, multiple sclerosis, epilepsy), malignant illnesses (patients with cervical intraepithelial neoplasia class-
fications were included, if histologic results postoperatively showed nonmalignancy), additional larger surgical pro-
dure in the course of the hysterectomy (eg, due to prolapse or incontinence), current or previous psychological disorders (except depression and specific phobia; cf. Lautenbacher et al\textsuperscript{12}), and conditions requiring psycho-
pharmacological treatment.

Antibiosis and Anesthetic Procedure

All patients included in the study received standard antibiotic prophylaxis with cephalexin (2 g cefalexin) preoperatively and standard anesthesia: midazolam (3.75 to 7.5 mg) for premedication (when called to the operating room); mivacurium (0.2 mg/kg) as muscle relaxant for intubation; propofol (target controlled infusion, target value: 4 to 5 mg/mL) and fentanyl (2 to 5 lg/kg) for anes-
thetic induction; propofol (target controlled infusion, target value: 3 mg/mL) and remifentanil (permanent infusion: 0.1 to 0.5 lg/kg/min) for maintenance of anesthesia.

Postoperative Acute Pain Management

All patients were scheduled for patient-controlled IV analgesia (PCA); using a standard PCA pump; Graseby 3300 Smiths Medical Deutschland GmbH; Grashruen, Germany) immediately after surgery, for the first 48 hours postoperatively. There was no basal rate, but patients could access a bolus of 0.2 mg hydromorphone on demand (by pressing a button) with a lock-out interval of 10 minutes and with a 1-hour maximum of 1.2 mg (maximum of 6 boluses in 1 hour). Nonopioids (peralgan) were available as rescue analgesia on demand. Patients were instructed by trained nurses from the acute pain service on how to use the pump in a way that should prevent ratings higher than 3 on a numerical rating scale (NRS) ranging from 0 to 10 (verbal anchors "no pain" and "strongest pain imaginable").

Surgical Technique

The surgical technique for LH is described in detail in Müller et al.,\textsuperscript{16} therefore, only a short description is given here: The Hohi instrument is inserted into the vagina and the uterus. After separating the uterus from the parametrial tissue, the uterus is morcelled and extracted vaginally. The vaginal vault is closed by laparoscopic or vaginal suturing.

Tissue lesions are due to separating the uterus (and in some cases also the cervix) from the surrounding peritoneal and parametrical tissue. Furthermore, surrounding vessels are cut and tied. Moreover, other surrounding tissues such as the bladder, the ureter, and the bowel can be irritated due to intraoperative manipulation, mobilization, dis-
section, and electrocauterization. In addition, the laparo-
scopic ports can cause small-sized lesions in skin and muscles (one 10-mm subumbilical port for the optical tele-
scope and three 5-mm ports in the middle, left, and lower right abdomen).

APOP after LH develops due to nociceptive, inflamma-
atory, and neuropathic consequences of surgical tissue lesions. These lesions affect muscle, nerves, and visceral tissue, and comprise microlesions and irritations of sur-
rounding tissues. Additional factors contributing to the development of APOP include disturbances of wound healing, development of internal and external scar tissue.
(adhesions as normal consequence of trauma-related tissue healing), infection, and hematoma.\textsuperscript{17,18}

Two LH patients had an intraoperative injury (1 vaginal and 1 bladder injury; no treatment beyond intraoperative care in the form of additional suturing was necessary). Because they were both found to be within 2 SDs from the mean of the whole group concerning APOP ratings, they were not excluded. None of our patients had to be reoperated for any reason.

Ethics

The study protocol was approved by the ethics committee of the medical faculty of the Friedrich-Alexander University Erlangen-Nürnberg (FAU). All participants gave written informed consent.

Materials and Procedures

There were 2 sessions: the first session took place 1 day before surgery to assess the predictor variables (attentional biases, pain-related emotions and cognitions, and affective state); the second session was scheduled for the assessment of the outcome variable APOP intensity ratings and took place \textasciitilde2 to 3 days after surgery (1 day before or on the day of discharge from hospital).

Session 1 took place between 11 AM and 7 PM and lasted for \textasciitilde2 hours 15 minutes. It included screening for psychological disorders using a standardized psychological interview (Mini-DIPS\textsuperscript{19}; \textasciitilde25 min), assessment of the 3 predictor sets “pain-related emotions and cognitions” (questionnaires; \textasciitilde30 min), “attentional biases” (dot-probe task; \textasciitilde25 min), and “affective state” (questionnaires; \textasciitilde20 min), and assessment of experimental pain sensitivity (thermal and pressure pain; \textasciitilde35 min). For ensuring the statistical strength of the regression analyses (relatively small sample size), we could not consider all predictors at once and decided to exclude the variable group “experimental pain sensitivity” for the present report.

Session 2 included assessment of the outcome variables (eg, APOP intensity ratings) and reassessment of the predictor variables. Analgesic consumption was assessed during the first 48 hours after surgery. Table 1 provides an overview of all predictor and outcome variables used, which are described in detail in the following sections.

Assessment of the Predictor Variables

Assessment of Attentional Biases

The selective attention task used in the current study was based on the dot-probe task of Keogh et al.\textsuperscript{20} The German version of this dot-probe task has already been used successfully in previous investigations by our work group (for details, see eg Lautenbacher et al\textsuperscript{21}) and contains 3 emotional word categories: pain-related (eg, schreckhaft/shameful), social threat (eg, beschämung/shameful), and positive words (eg, glücklich/lucky). During visual presentation, these words are paired with neutral words (eg, Anstrich/paintwork); neutral-neutral word pairs serve as filler items.

Following Keogh et al,\textsuperscript{20} a fixation cross was presented in the center of a computer screen for 500 ms. Then, 2 words (a neutral one paired with an emotional one) were presented for another 500 ms: 1 below and 1 above the fixation cross. After this, a dot appeared at the location of 1 of the 2 words. Participants were required to indicate where the dot had appeared (below and above) as quickly as possible by pressing 1 of 2 keys. A reaction time measurement was taken. After 20 practice trials, participants had to complete 128 test trials (32 trials per word-pair category), all of which were presented in a random order by the computer. Bias indices were calculated on the basis of reaction times to assess, separately, the attentional bias toward each emotional word category (for more details, see eg Lautenbacher et al\textsuperscript{21}). A positive score indicates an attentional preference for the location of the emotional word, whereas a negative score may suggest avoidance. In addition, patients completed a reading task to ensure the patient’s capacity to read and understand words quickly enough (analog to the dot-probe task, word pairs of real and nonsense words were presented at a computer screen for 500 ms and participants had to indicate by key press where the real word appeared). If \textasciitilde50% of the reactions were erroneous, the dot-probe data of this patient were excluded from the analysis. On this basis, the dot-probe task data of 3 patients were excluded.

Assessment of Pain-related Emotions and Cognitions

Pain-related emotions and cognitions were assessed by different questionnaires, namely the Pain Anxiety Symptoms Scale (PASS\textsuperscript{22}), the Pain Catastrophizing Scale (PCS\textsuperscript{23}), and the Pain Vigilance and Awareness Questionnaire (PVAQ\textsuperscript{24}).

The PASS\textsuperscript{25} (German version by Walter et al\textsuperscript{25}) is designed to measure pain anxiety across cognitive, behavioral, and physiological domains. It comprises 40 items (potential range of scores: 0 to 240) and is composed of 4 subscales: cognitive anxiety, escape/avoidance, fear/appraisal, and physiological anxiety.

The PCS\textsuperscript{26} was developed as a measure of catastrophizing related to pain. It contains 13 items that can be divided into 3 subscales, namely rumination, magnification, and helplessness (potential range of scores: 0 to 52).

The PVAQ\textsuperscript{27} was developed as a comprehensive measure of attention to pain and has been validated for use in chronic pain and nonclinical samples.\textsuperscript{26,27} It targets awareness, vigilance, preoccupation, and observation of pain. There are 16 items rated on a 6-point scale. The potential range of scores is from 0 to 80.

PASS and PVAQ were translated using a standard “forward-backward” procedure. Translation accuracy was considered to be sufficient if the resulting backward English version was very similar to the original version according to the evaluation of a native English speaker. These translated versions have been used successfully in several investigations by our work group.\textsuperscript{12,14,21} The intercorrelations of the German versions of PASS, PCS, and PVAQ ranged between \(r = 0.458\) and \(r = 0.741\). This is in accordance with findings for the English and Dutch versions.\textsuperscript{27-30}

Assessment of Affective State

The affective state was assessed with 2 different questionnaires, namely the German versions of the Screening of Somatoform Symptoms (SOMS\textsuperscript{31}) and the German version of the Center for Epidemiological Studies Depression scale (CES-D; German version: ADS\textsuperscript{32}).

The SOMS\textsuperscript{31} is a self-rating scale, which assesses 5 medically unexplained symptoms. The state version of the SOMS was applied, wherein participants are asked to rate the intensity of each symptom during the last 7 days. For further analyses, we used the sum of all items (potential range of scores: 0 to 208).

The CES-D\textsuperscript{32} is a self-rating scale (20 items) that was designed to assess emotional, somatic, and cognitive
TABLE 1. Descriptive Statistics and Correlation Coefficients for All Predictor and Outcome Variables

<table>
<thead>
<tr>
<th>Predictor Variables</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Correlation Coefficient ((r)) With Outcome Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>APOP Intensity (NRS)</td>
</tr>
<tr>
<td>Pain-related words (ms)</td>
<td>70</td>
<td>5.29</td>
<td>37.43</td>
<td>-100.00</td>
<td>87.25</td>
<td>0.259 +</td>
</tr>
<tr>
<td>Social threat words (ms)</td>
<td>70</td>
<td>12.24</td>
<td>42.37</td>
<td>-92.65</td>
<td>106.30</td>
<td>0.258 +</td>
</tr>
<tr>
<td>Positive words (ms)</td>
<td>70</td>
<td>-2.40</td>
<td>40.54</td>
<td>-92.05</td>
<td>112.55</td>
<td>0.198</td>
</tr>
<tr>
<td>Pain-related emotions and cognitions (questionnaires)</td>
<td>75</td>
<td>11.76</td>
<td>8.19</td>
<td>0.00</td>
<td>32.00</td>
<td>0.225</td>
</tr>
<tr>
<td>PCS</td>
<td>73</td>
<td>62.85</td>
<td>31.06</td>
<td>14.74</td>
<td>135.00</td>
<td>0.281 +</td>
</tr>
<tr>
<td>PASS</td>
<td>73</td>
<td>34.68</td>
<td>11.80</td>
<td>1.07</td>
<td>56.00</td>
<td>-0.036</td>
</tr>
<tr>
<td>Affective state (questionnaires)</td>
<td>73</td>
<td>11.22</td>
<td>8.16</td>
<td>0.00</td>
<td>33.00</td>
<td>0.124</td>
</tr>
<tr>
<td>CES-D</td>
<td>73</td>
<td>11.91</td>
<td>11.60</td>
<td>0.00</td>
<td>48.00</td>
<td>0.136</td>
</tr>
<tr>
<td>SOMS</td>
<td>73</td>
<td>3.68</td>
<td>2.10</td>
<td>0.00</td>
<td>9.00</td>
<td>0.369*</td>
</tr>
<tr>
<td>Outcome variables</td>
<td>67</td>
<td>3.37</td>
<td>2.48</td>
<td>0.20</td>
<td>12.40</td>
<td></td>
</tr>
</tbody>
</table>

APOP indicates acute postoperative pain; CES-D, Center for Epidemiological Studies Depression scale; NRS, Numerical Rating Scale; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; PVAQ, Pain Vigilance and Awareness Questionnaire; SOMS, Screening for Somatoform Disorders.

Symptoms of depressive mood during the last week (potential range of scores: 0 to 60).

Assessment of the Outcome Variables

APOP Intensity Ratings

Two to 3 days after surgery, patients were asked to rate the average intensity of their pain since surgery on an 11-point NRS from 0 to 10. The NRS is labeled with the verbal anchors “no pain” and “strongest pain imaginable.”

Analogic Consumption

The amount of requested hydromorphone (mg) through a PCA system in the first 48 hours after surgery was used as a measure of the subjective need for analoges. Six patients did not receive PCA (eg, due to patients’ refusal of opioid medication) and were therefore excluded from PCA analyses.

Statistical Analyses

In case of missing single values (eg, 1 item of a questionnaire), mean imputation was conducted. In case of missing variables (eg, a complete questionnaire), no imputation was conducted, but the paitent was excluded from the analyses containing missing variables (pairwise deletion). For the statistical description, means, SDs, minima and maxima of all variables are given; for the description of simple relationships, Pearson correlation coefficients were computed. To check for potentially relevant covariates, Pearson, Spearman, and point-biserial correlation coefficients were computed between the 2 outcome variables and physical (body mass index, number of childbirths, and smoking behavior), psycho-physical (experimental pain sensitivity), and demographic (age, education level, professional activity, and marital status) variables. The variables that were not significantly correlated to both outcome variables were not included in the following analyses.

The predictive power of the 3 predictor sets (attentional biases towards emotionally loaded words in a dot-probe task, self-report of pain-related emotions and cognitions, and affective state) was tested in 2 consecutive regression protocols. In the first regression protocol, 6 multiple regression analyses were conducted (separately for each predictor set and separately for the 2 outcome measures). The aim was to select the best single predictor from each predictor set (highest value of the standardized \(\beta\) coefficients) for each outcome. Given our small sample size, this was necessary to reduce the number of variables, which should serve as predictors in the second protocol. Thus, in the second regression protocol, we entered only the best single predictors of each predictor set in 2 regression analyses (separately for the 2 outcome measures). To investigate possible differences between pain-specific and general psychological predictors of APOP intensity ratings and analogic consumption, we descriptively compared their standardized \(\beta\) coefficients in these 2 regression models (given that the whole model reached significance). In all analyses, testing was 2-sided and findings were considered to be statistically significant at \(\alpha < 0.05\). Both Bonferroni-adjusted significant results (marked with *) and non-Bonferroni-adjusted significant results (marked with +) are reported.

RESULTS

Descriptives

Detailed information about descriptive statistics for all predictor and outcome variables are shown in Table 1. The varying numbers of patients are due to the exclusion of 3 patients’ dot-probe task data (several errors in the reading task) and 6 patients who could not receive PCA.
TABLE 2. Descriptive Statistics and Correlation Coefficients for Potential Covariates

<table>
<thead>
<tr>
<th>Physical variables</th>
<th>n</th>
<th>Mean ± SD (Range)/n (Valid %)</th>
<th>Correlation Coefficients With Outcome Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>73</td>
<td>24.7 ± 2.4 (17.4-39.1)</td>
<td>APOP Intensity (NRS) Analgesic Consumption</td>
</tr>
<tr>
<td>No. childbirths</td>
<td>65</td>
<td>1.8 ± 1.1 (0-6)</td>
<td></td>
</tr>
<tr>
<td>Smoking behavior</td>
<td>70</td>
<td>Nonsmoker: 62 (88.6%)</td>
<td>0.028 (NS) -0.123 (NS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Occasional smoking: 1 (1.4%)</td>
<td>-0.209 (NS) 0.165 (NS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-4 cigarettes per day: 0 (0%)</td>
<td>0.186 (NS) 0.035 (NS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-8 cigarettes per day: 0 (0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 8 cigarettes per day: 7 (10%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psycho-physical variables: experimental pain sensitivity</th>
<th>n</th>
<th>Mean ± SD (Range)/n (Valid %)</th>
<th>Correlation Coefficients With Outcome Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure pain threshold</td>
<td>71</td>
<td>432.5 ± 131.5 (171.5-770.5)</td>
<td>-0.110 (NS) -0.157 (NS)</td>
</tr>
<tr>
<td>Cold pain threshold</td>
<td>72</td>
<td>10.5 ± 7.7 (0.0-29.0)</td>
<td>0.093 (NS) 0.085 (NS)</td>
</tr>
<tr>
<td>Heat pain threshold</td>
<td>72</td>
<td>45.3 ± 2.1 (39.8-49.3)</td>
<td>0.057 (NS) -0.164 (NS)</td>
</tr>
<tr>
<td>Temporal heat pain summation</td>
<td>71</td>
<td>1.2 ± 1.5 (2.3-4.7)</td>
<td>0.218 (NS) 0.119 (NS)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>n</th>
<th>Mean ± SD (Range)/n (Valid %)</th>
<th>Correlation Coefficients With Outcome Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>73</td>
<td>45.2 ± 4.5 (33-57)</td>
<td>-0.149 (NS) -0.016 (NS)</td>
</tr>
<tr>
<td>Education level</td>
<td>73</td>
<td>8-9 school years: 13 (17.8%)</td>
<td>0.053 (NS) -0.072 (NS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 school years: 32 (43.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-13 school years: 28 (38.4%)</td>
<td></td>
</tr>
<tr>
<td>Professional activity</td>
<td>70</td>
<td>Yes: 65 (92.9%)</td>
<td>-0.113 (NS) -0.037 (NS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No: 5 (7.1%)</td>
<td></td>
</tr>
<tr>
<td>Married/in permanent relationship</td>
<td>72</td>
<td>Yes: 63 (87.5%)</td>
<td>-0.115 (NS) -0.068 (NS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No: 9 (12.5%)</td>
<td></td>
</tr>
</tbody>
</table>

BMI indicates Body Mass Index; NS, not significant; NRS, Numerical Rating Scale.

Screening for Potentially Relevant Covariates

Physical, psycho-physical, and demographic variables were significantly correlated neither to pain intensity ratings nor to analgesic consumption. Detailed information for all potential covariates is presented in Table 2.

Correlations Between Predictor and Outcome Variables

Correlation coefficients for the relationships between predictor and outcome variables are listed in Table 1: significant (+) positive correlations with APOP intensity ratings were found for PASS, pain-related and social threat words of the dot-probe task. Significant (+) positive correlations with analgesic consumption were found for PASS, PCS, CES-D, and SOMS. The 2 outcome variables were significantly (*) and positively correlated.

First Regression Protocol: Selection of the Best Single Predictors

The results of the multiple regression analyses are presented in Table 3. The predictor sets “attentional biases” and “pain-related emotions and cognitions” were significantly (+) associated with the outcome variable APOP intensity ratings. The predictor set “affective state” was significantly (+) associated with the outcome variable analgesic consumption.

On the basis of the relative size of the standardized β coefficients in the respective multiple regression equations, we selected the best single predictor from each predictor set for each outcome (see Table 3, right side, best single predictors are marked in bold). For both outcomes, namely APOP intensity and analgesic consumption, the best single predictors were attentional preference for social threat words (dot-probe task), PASS, and SOMS; only the first 2 reached significance levels (+) when considering their relationship to the APOP intensity ratings. Significant correlations between best single predictor variables were found only for the relationship between PASS and SOMS (r = 0.465, P < 0.001).

Second Regression Protocol: Predictive Value of the Best Single Predictor Combinations

The combination of the 3 best single predictors was significantly (+) predictive of APOP intensity ratings (14.7% explained variance), but not of analgesic consumption (Table 4). Therefore, we excluded analgesic consumption from further analyses.

In the regression model for APOP intensity ratings, single standardized β coefficients for the social threat words of the dot-probe task and PASS reached significance (+) (Table 4). Furthermore, these 2 variables were sufficient for significant (+) prediction alone, because removing somatization from the regression equation resulted in a reduction of the explained variance by only 0.1%. Hence, the pain-specific questionnaire PASS seems to be of much stronger weight in the regression equation compared with the general psychological variable somatization (SOMS). In contrast to our expectations, the attentional preference of negative stimuli (i.e., social threat words) was predictive of APOP intensity ratings (not attentional avoidance as in our earlier studies12,14).

DISCUSSION

The first main objective of the present study was to investigate as to which variables from the 3 predictor sets “pain-related emotions and cognitions,” “attentional biases,” and “affective state” would be the best single predictors of APOP intensity and analgesic consumption, in a
sample of hysterectomy patients. The second was to compare pain-specific and general psychological variables concerning their predictive value (standardized β coefficients in linear regression analyses).

Our main findings were as follows: (1) APOP intensity was significantly explained by a combination of the best single predictors from the 3 predictor sets, namely the attentional bias towards social threat words of the dot-probe task, pain anxiety, and somatization (14.7% of the explained variance). In contrast, analgesic consumption was not significantly predicted by a combination of the best single predictors, but there were significant single correlations with pain anxiety, pain catastrophizing, somatization, and depression. (2) Regarding standardized β coefficients in the linear regression models, pain-specific psychological predictors seemed to be of higher relevance in predicting APOP intensity ratings than general psychological predictors. Consequently, omitting the best general psychological predictor “somatization” only reduced the explained variance from 14.7% to 14.6%.

### TABLE 3. Multiple Regression Analyses for Each Predictor Group and the 2 Outcome Variables

<table>
<thead>
<tr>
<th>Predictor Group</th>
<th>R²</th>
<th>Analgesic Consumption</th>
<th>Single Predictors</th>
<th>APOP Intensity (NRS)</th>
<th>Analgesic Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attentional biases (dot-probe)</td>
<td>0.155 +</td>
<td>0.004</td>
<td>Pain-related words, Social threat words, Positive words</td>
<td>0.232 +</td>
<td>0.015</td>
</tr>
<tr>
<td>Pain-related emotions and cognitions</td>
<td>0.130 +</td>
<td>0.115</td>
<td>PCS</td>
<td>0.236 +, P = 0.041</td>
<td>0.061, P = 0.637</td>
</tr>
<tr>
<td>Affective state</td>
<td>0.021</td>
<td>0.128 +</td>
<td>PASS, PVAQ, CES-D, SOMS</td>
<td>0.371 +, P = 0.040</td>
<td>0.271, P = 0.153</td>
</tr>
</tbody>
</table>

* + P ≤ 0.05 (non-Bonferroni adjusted).

APOP indicates acute postoperative pain; CES-D, Center for Epidemiological Studies Depression Scale; NRS, Numerical Rating Scale; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; PVAQ, Pain Vigilance and Awareness Questionnaire; SOMS, Screening for Somatoform Disorders.

### TABLE 4. Multiple Regression Analyses for the Best Single Predictor Combinations and the 2 Outcome Variables

<table>
<thead>
<tr>
<th>Best Single Predictor Combination</th>
<th>Standardized β Coefficients</th>
<th>R² Whole Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>APOP intensity (NRS)</td>
<td>Social threat words (dot-probe)</td>
<td>0.238 +</td>
</tr>
<tr>
<td></td>
<td>+ PASS</td>
<td>0.299 +</td>
</tr>
<tr>
<td></td>
<td>+ SOMS</td>
<td>-0.034</td>
</tr>
<tr>
<td>Analgesic consumption</td>
<td>Social threat words (dot-probe)</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>+ PASS</td>
<td>0.095</td>
</tr>
<tr>
<td></td>
<td>+ SOMS</td>
<td>0.291 +</td>
</tr>
</tbody>
</table>

+ P ≤ 0.05 (non-Bonferroni adjusted).

APOP indicates acute postoperative pain; NRS, Numerical Rating Scale; PASS, Pain Anxiety Symptoms Scale; PVAQ, Pain Vigilance and Awareness Questionnaire; SOMS, Screening for Somatoform Disorders.

### Different Dot-Probe Parameters as Best Predictors of APOP in Earlier Surveys and the Present Study

Previous studies by our research group suggest that preoperative attentional avoidance of pain-related and social threatening stimuli is associated with higher APOP. Yet, in the present study, higher APOP intensity ratings were associated with a preoperative attentional preference for pain-related and, in particular, social threat words of the dot-probe task. Preoperative attentional biases concerning negative stimuli appear to be maladaptive and deter patients from coping with APOP successfully and could therefore be associated with higher APOP on discharge from hospital. However, interestingly, direction (attentional avoidance or preference) and word category (pain-related or social threat) appear to depend on the respective surgical patient sample studied (preoperative preference of social threatening and pain-related words in hysterectomy patients (this study); preoperative avoidance of social threatening words in cancer patients’ preoperative avoidance of pain-related words in young chest malformation patients). These conflicting findings might be due to differences concerning age and sex as well as degrees of disease severity and life threat, which could lead to different needs and fears. Whereas hysterectomy is an event that might threaten subjective womanhood (as a part of the female sex role), fears about highly needed, disease-related, social support might come to the fore in life-threatening diseases such as cancer. The preference of confrontation with social concerns might be maladaptive in hysterectomy patients, whereas the opposite applies for cancer patients. When comparing patient groups with noncancer surgical indications, pain-related fears might come to the fore, which might be associated with age; middle-aged hysterectomy patients generally might have more experience with hospitalization, pain, and pain management, whereas young patients may be worried because they could be fairly pain-naive and not have any previous experience with hospitalization and surgery. Therefore, exaggerated confrontation with pain-related stimuli might be maladaptive in the first case and avoidance in the second.
Nonetheless, the dot-probe task has performed much better as a predictor for APOP than many variables widely discussed and therefore definitely deserves further investigation. However, the cumulated findings are still very conflicting to recommend the dot-probe task already as a clinical assessment tool.

Pain-related Emotions and Cognitions as Predictors of APOP and Analgesic Consumption

Current research suggests that pain-specific emotions and cognitions (e.g., pain catastrophizing) are reliable predictors of APOP. In the present study, preoperative pain anxiety had the strongest association with high APOP intensity ratings. It has to be noted that mean scores of pain anxiety and pain catastrophizing were lower compared with that of young patients with surgical correction of chest malformations and cancer patients in our earlier studies, suggesting a smaller psychological impact of hysterectomy. Furthermore, for young chest malformation patients, the best predictor of APOP intensity ratings from the predictor set “pain-related emotions and cognitions” was pain catastrophizing and not pain anxiety. Yet given the strong theoretical and correlational overlap of these 2 measures that was found in the current study, we do not consider this to be a serious disagreement. As further evidence for its qualification as a good APOP predictor, pain anxiety was the only variable significantly correlated with both outcome variables, namely APOP intensity ratings and analgesic consumption, whereas all other predictors were related to only one or none of the outcomes (see Table 1, single correlation coefficients).

We conclude that pain-specific emotions and cognitions are important predictors of acute postoperative outcomes. In our study, the PASS (“pain anxiety,” capturing the aspects: cognitive anxiety, escape/avoidance, fearful appraisal, and physiological anxiety) and the PCS (“pain catastrophizing,” capturing the aspects: rumination, magnification, and helplessness) questionnaires were the best screening tools for this purpose.

There is no good empirical reason to assume that pain catastrophizing is preferable to pain anxiety as a pain-specific psychological predictor of APOP, although there is a strong tendency in the current research to do so. It requires further research to determine as to which variable is the superior predictor in which situation and why. Furthermore, pain anxiety and pain catastrophizing might be complementary or specific for use in certain subgroups (e.g., according to age and/or sex). Thus, both PASS and PCS questionnaires can be recommended as easily applicable screening tool(s) for patients at risk for high APOP intensity ratings and analgesic consumption.

Moreover, it has to be noted that we found no significant associations between pain-related emotions and cognitions and the attentional bias indices concerning pain-related and social threat words in the dot-probe task. This is in line with Lautenbacher et al. and Roelofs et al., who also did not find evidence for a relationship between attentional biases for pain and social threat stimuli, and pain-related emotions and cognitions. The fact that these 2 domains are largely independent of each other (very low and nonsignificant correlations), but nevertheless both predictive of APOP intensity (Table 1), is an advantage in regression analyses (Tables 3, 4) and a reason to apply both measures in future studies.

Depression as a Predictor of APOP and Analgesic Consumption

Depression scores of hysterectomy patients in the present study were comparable to those of chest malformation patients and lower than those of cancer patients. These different depression levels might be due to the differing degrees of disease severity and threat of disease. Despite this difference, all 3 studies come to the conclusion that depression does not appear to be a significant predictor of acute postoperative outcomes. Reviews have also shown heterogeneous findings regarding depression as a predictor of APOP and analgesic consumption. This might further substantiate our hypothesis that preoperative pain-specific variables (e.g., pain anxiety) are of higher relevance than more global risk factors such as preoperative depression scores for the prediction of APOP intensity. Preoperative depression (or depressive symptoms triggered by surgery and its sequels) might be of higher relevance for the development of chronic postoperative pain, because it may impair the ability to cope with pain in the long term.

Divergent Aspects of APOP Intensity Ratings and Analgesic Consumption

APOP intensity ratings and analgesic consumption were moderately correlated. This implies that they are related but not redundant, and represent different aspects of acute postoperative outcome. Furthermore, this differentiation may also be expected for theoretical reasons. Pain intensity ratings directly indicate the intensity dimension of pain experience (even though they might be affected by memory biases as they refer to the average pain up to 72 h postoperatively). Yet, analgesic consumption is not that directly and exclusively driven by the pain experience. Analgesic consumption through PCIA includes a behavioral aspect that is influenced by a variety of psychological variables beyond pain experience, which include expectations of analgesic potency, fears of using strong analgesics, and attribution of nausea to the PCIA. Thus, very frequent PCIA use could indicate high levels of pain or just high efforts to prevent any pain experience after surgery, whereas infrequent PCIA use could indicate low levels of pain or strong feelings of resentment against taking analgesic medication or its side effects. Moreover, the association between pain intensity and opioid use is moderated by interindividual variability in the pharmacodynamics of analgesics, such as sensitivity to opioids; however, controlling for this factor was beyond the scope of this study.

Limitations

The first limitation of our study is that we excluded preoperative pain conditions, although hysterectomy patients often experience preoperative pain. This exclusion may have led to an above-average pain-free and healthy sample of hysterectomy patients. Yet, this was necessary to be able to investigate pain that is only due to surgery and not due to (possibly continuing) preoperative causes. Furthermore, preoperative pain could possibly distort the relationship between psychological predictors and postoperatively developing pain.

Second, we included only LH patients and therefore generalization to other types of hysterectomy (which may differ concerning pain-related outcomes) might not be
possible. However, such limits of generalization do not apply only to hysterectomy but for every surgical model.

Third, we assessed all psychological predictor variables 1 day before surgery. The time proximity of the threatening surgical event might influence these variables and affect their relations to each other as well as to other variables. This circumstance has therefore to be kept in mind when comparing the results with studies assessing predictors several days or even weeks before surgery.

Fourth, the strong correlational overlap between the PASS, PCS, and PVAQ (0.458 ≤ r ≤ 0.741, P < 0.001 each) may have led to suppression effects concerning the regression analyses for the predictor set “pain-related emotions and cognitions.” Combined with each other, the relevance of PVAQ might be overestimated (single correlation coefficients are very small and far from significance) and the relevance of PASS and PCS underestimated. However, these suppression effects have not obscured the results, as the predictive value of PASS and PCS can also be substantiated in correlation analyses.

Finally, our sample size was relatively small (especially for PCIA). Therefore, we had to limit the number of predictors to ensure the statistical strength of the regression analyses and excluded the variable group “experimental pain sensitivity.”

CONCLUSIONS

Psychological predictors of different domains proved to be powerful predictors of APOP intensity ratings in hysterectomy patients, whereas the predictive value for analgesic consumption remains limited. Pain-specific psychological variables such as pain anxiety are important for both outcomes and appear to be of higher relevance in regression analyses than more general psychological predictors such as somatization and depression.

In consequence, patients at risk for high APOP intensity can be characterized by pain-specific psychological variables (preoperative “risk profile”). Easily applicable self-report measures such as the PASS (pain anxiety) can be recommended as a screening tool for identifying these patients. This knowledge might be beneficial for further improvement of pain management and prevention, because pain-specific psychological pain variables such as pain anxiety can be a focal target in psychological prophylaxis interventions when preparing for surgery.

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