Predicting Acute Pain after Cesarean Delivery Using Three Simple Questions

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ABSTRACT

Background: Interindividual variability in postoperative pain presents a clinical challenge. Preoperative quantitative sensory testing is useful but time consuming in predicting postoperative pain intensity. The current study was conducted to develop and validate a predictive model of acute postcesarean pain using a simple three-item preoperative questionnaire.

Methods: A total of 200 women scheduled for elective cesarean delivery under subarachnoid anesthesia were enrolled (192 subjects analyzed). Patients were asked to rate the intensity of loudness of audio tones, their level of anxiety and anticipated pain, and analgesic need from surgery. Postoperatively, patients reported the intensity of evoked pain. Regression analysis was performed to generate a predictive model for pain from these measures. A validation cohort of 151 women was enrolled to test the reliability of the model (131 subjects analyzed).

Results: Responses from each of the three preoperative questions correlated moderately with 24-h evoked pain intensity (r = 0.24–0.33, P < 0.001). Audio tone rating added uniquely, but minimally, to the model and was not included in the predictive model. The multiple regression analysis yielded a statistically significant model (R^2 = 0.20, P < 0.001), whereas the validation cohort showed reliably a very similar regression line (R^2 = 0.18). In predicting the upper 20th percentile of evoked pain scores, the optimal cut point was 46.9 (z =0.24) such that sensitivity of 0.68 and specificity of 0.67 were as balanced as possible.

Conclusions: This simple three-item questionnaire is useful to help predict postcesarean evoked pain intensity, and could be applied to further research and clinical application to tailor analgesic therapy to those who need it most.

What We Already Know about This Topic

- Pain intensity after surgery is highly variable
- Developing a simple test to predict pain intensity after surgery could facilitate tailored treatment of pain

What This Article Tells Us That Is New

- Responses to three simple questions moderately predicted the severity of acute postoperative pain after cesarean section
- Further refinements in such modeling may allow the development of simple tools to predict patients who may develop severe postoperative pain

INTERINDIVIDUAL variability in degree of pain and response to analgesic treatment creates a considerable clinical challenge in acute postoperative care after cesarean delivery. In addition, women with severe pain on the day after cesarean delivery have a 2.5- to 3-fold increased risk of postpartum depression and persistent pain 8 weeks later compared with those with mild pain,[1] and this persistent pain and depression may affect cognitive development of infants and induce negative behavior effects.[2–4] Given the increasing frequency of cesarean delivery, currently impacting over 1.4 million individuals in the United States annually, persistent pain represents a significant public health problem.[5]

Accurate prediction and targeted treatment of women who will experience severe postcesarean delivery pain might reduce the persistent effects associated with severe pain. The widespread use of multimodal pain control regimens, such as neuraxial opioids in combination with oral nonsteroidal antiinflammatory drugs, has improved the quality of postoperative analgesia.[6] However, most women after cesarean delivery receive a one-size-fits-all approach, with a fixed dose of intrathecal morphine and nonsteroidal antiinflammatory drug, relying on nurse-administered analgesics to treat breakthrough pain. This approach works well for many women, but not all, and preoperative identification of high-risk women for severe pain could lead to better analgesia.

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Previous work has identified some predictors of severe pain after cesarean delivery. These include reduced pain threshold or response threshold to quantitative sensory testing (QST)[7–9] and psychologic constructs, such as catastrophizing.[10] Using a combination of preoperative patient responses from physical to psychological tests,[11] we were able to predict 20–28% of the variance in acute postcesarean pain and analgesic consumption, but this preoperative testing required approximately 120 min and additional personnel, equipment, and training, making it impractical for routine clinical use or for screening for research purposes.

In this study, we examined the utility of a simplified and practical approach to predict acute pain after cesarean delivery. Our previous study using extensive preoperative testing identified four factors that contributed strongly to our predictive model of severe postcesarean pain[11]: anxiety, expected postoperative pain, expected analgesic requirement, and response to an experimental thermal painful stimulus. These factors appear in other large studies of predictors of postoperative pain in nonobstetric patients.[7,12] We also observed that intensity ratings of the volume of an audio tone correlated with pain ratings to an experimental stimulus, suggesting that audio tone ratings may be a simple and acceptable alternative to thermal QST.[11] In addition, Hollins *et al.* and others,[13,14] in an evaluation of the generalized hypervigilance hypothesis, suggested that perceived auditory intensity may correlate with other types of pain intensity reporting. Based on these observations, we developed in a large cohort a predictive model for acute postcesarean delivery pain from three single-item questions to assess preoperative anxiety, anticipated pain, and anticipated analgesic drug need and then validated this model in a second large cohort. In addition, the effect of incorporating the intensity rating of audio tones to the three single-item question model was explored.

Materials and Methods

Study Population—Derivation Cohort

With approval from institutional review boards at Wake Forest University and Forsyth Medical Center in Winston-Salem, North Carolina, written informed consent was obtained from 200 parturients who were scheduled for elective cesarean delivery under subarachnoid anesthesia with the addition of preservative-free morphine for postoperative analgesia. These 200 parturients were used as the derivation cohort in order to derive the predictive model for intensity of postcesarean delivery pain. The parturients were American Society of Anesthesiology physical status 1 or 2 patients, English-speaking, aged 18 years or above, and with pregnancies of at least 36 weeks gestational age. Patients with a history of documented psychiatric disease, hearing deficits, alcohol or drug abuse, chronic opioid use, unable to understand English, unable to receive subarachnoid anesthesia or intrathecal morphine, and those requiring prolonged surgery such as cesarean hysterectomy or extended vertical uterine incision were excluded. Patients scheduled for surgery were seen during their preoperative visit (1–3 days before surgical date) by research personnel, evaluated for study inclusion, and approached for informed consent.

Preoperative Assessment

Vital signs and patient demographics were obtained and recorded as part of the usual preoperative assessment. Patients were asked to rate, using a 0–100 mm visual analog scale (VAS), their surgical anxiety level ("On a scale of 0–100, with 0 being not anxious at all through 100 being extremely anxious, how anxious are you about your upcoming surgery?"), their anticipated pain ("On a scale of 0–100, with 0 being no pain at all and 100 being pain as bad as you can imagine, how much pain do you anticipate experiencing after your upcoming surgery?"), and using a categorical scale, their anticipated pain medication need ("On a scale of 0–5, with 0 being none at all, 1 being much less than average, 2 being less than average, 3 being average, 4 being more than average, and 5 being much more than average, how much pain medication do you anticipate needing after your upcoming surgery?"). Patients were also asked to use a 100-mm VAS to rate the intensity of the loudness of three series of audio tones administered through headphones in a quiet room as previously described.[12] Briefly, each series consisted of six tones of the same frequency (900 Hz) but each of different amplitude (loudness). The first series was administered in an ascending order of loudness, whereas the second and third series were administered in randomized order of loudness.[12]

Intraoperative Care

Parturients received routine anesthetic care and surgery common in our facility. All patients received subarachnoid anesthesia with intrathecal hyperbaric bupivacaine 10.5–12 mg, fentanyl 15–20 μg, and preservative-free morphine 150–200 μg. Intravenous morphine or fentanyl was administered as needed at the discretion of the attending anesthesiologist only in the case of intraoperative discomfort or pain, but no anxiolytics were administered during surgery.

Postoperative Analgesia and Outcomes Assessment

Postoperative analgesia was provided using our routine protocol for patients receiving intrathecal morphine. This included ibuprofen 800 mg orally every 6 h, as well as intravenous morphine and/or fentanyl in the postanesthesia care unit if needed and stepwise administration of oxycodone/acetaminophen and/or morphine for breakthrough pain in the postpartum ward only as needed. Systemic opioid analgesics were converted to morphine equivalents for the purpose of comparison of analgesic consumption. Nalbuphine, diphenhydramine, ondansetron, metoclopramide, and promethazine were used as needed according to the standardized orders for treatment of side effects from spinal morphine.

At 18–24 h postoperatively, research personnel blinded to results of preoperative and intraoperative assessments

evaluated the severity of pain at rest while the patient was resting in bed and pain evoked by movement from lying in the supine position in bed to a sitting upright position with legs hanging off the bed, and patient satisfaction of the postoperative analgesic treatment. Each of these was measured using a 100-mm VAS ruler, with the left side (0 mm) of the scale being no pain or not satisfied at all and the right side (100 mm) being the worst pain imaginable or most satisfied, respectively. In addition, we recorded all drugs administered in the preoperative, intraoperative, and postoperative study periods. The primary outcome measure, as in our previous study,[12] was evoked pain.

Study Population—Validation Cohort

After conclusion of the derivation cohort, the three preoperative questions assessed in the validation cohort were incorporated in our routine clinical preoperative assessment for all elective cesarean and gynecological surgery patients. For the validation cohort, the scores of the three routine preoperative questions and assessment of postoperative pain scores at rest and with movement were prospectively obtained from postcesarean patients as part of the outcome measures in that study. Given the minimal or no additional risk added to routine care of patients, institutional review board approval of exemption of consent was obtained for the study of the validation cohort. Data were obtained from 151 subjects. Preoperative management, intraoperative anesthesia, and postoperative analgesia and management in the validation cohort followed the same protocol as in the derivation cohort and as in our usual clinical practice, with the exception that no audio tone assessment was performed in the validation cohort. Postoperative pain assessment in the validation cohort also followed the same protocol as in the derivation cohort using a 100-mm VAS to obtain the intensity of resting pain and evoked pain at 18–24 h postoperatively.

Statistical Analyses

As this was a practice improvement effort, no *a priori* sample size calculation was conducted. The derivation sample was based on logistical limitations and included all patients enrolled between 10/1/2007 and 9/2/2009. The size of the validation cohort was based on a common rule of thumb of 15 measurements per predictor, whereas the number of predictors was initially estimated to be not more than seven.

Statistical analyses were conducted using SPSS software version 19.0 for Windows (SPSS Inc., Chicago, IL). Descriptive statistics were calculated for all variables such that mean (SD) were used for normally distributed variables; median (range) for data that were not normally distributed or for data with outliers or ordinal data; and number (percentage) for categorical data. For all analyses, P was set at 0.05 for statistical significance. The primary outcome variable was 24-h postcesarean evoked pain VAS. Predictor variables were the three questions and audio tone responses described in the preoperative assessment. In order to guide calculations, an interim analysis was performed, but no attempts were made to adjust the P value from the interim analysis.

Before conducting analyses, histograms of the distributions and normal probability plots of predictor and pain outcome variables were studied to assess normality. The residual series were examined to determine model fit and evidence of misestimating among predictor variables. Multicollinearity was examined among predictors through examination of bivariate correlations. To analyze the demographic difference of the two subgroups of the derivation cohort, two-tailed independent samples t tests and chi-square tests of independence were utilized. As the distributions of the predictor and pain outcome variables were skewed, a Spearman correlation was chosen to examine their relationship.

To investigate whether the predictors could be used to improve the prediction of the pain outcome variable, a multiple regression analysis was performed with two blocks (with and without audio tone assessment) using a generalized linear model with normal distribution and identity function. The contributory effect from audio tone assessment was assessed using chi-square likelihood ratio test and Bayesian information criterion.

The regression and residual plots of predicted pain outcome *versus* actual pain outcome for both the derivation and validation cohorts were examined to assess the replication and precision of the regression model. Finally, in order to index the predictive ability of the model and for clinical replication applicability, a receiver operating characteristic curve of the two cohorts was used to estimate the sensitivity and specificity of the model's ability to predict the above 80th percentile of individuals' evoked pain intensity. The optimal standardized cut-point value of the prediction equation was chosen using the Youden index in Z-metric such that sensitivity and specificity were as high as possible in derivation cohort,[15] while still remaining balanced. The above 80th percentile was chosen based on our previous studies suggesting that about one-fifth of the postcesarean delivery parturients had evoked pain intensity in the severe range (defined as ≥70/100).

Results

In the derivation cohort, 200 subjects were enrolled and 8 were excluded (three due to surgical reasons: one cesarean hysterectomy, two extended vertical uterine incision, and five due to anesthetic reasons: not receiving intrathecal morphine or not receiving subarachnoid anesthesia; fig. 1). The remaining 192 parturients had a mean body weight of 92 ± 21 kg, height of 163 ± 7.1 cm, a mean estimated gestational age of 38.5 ± 0.8 weeks, and a median parity of 1 (0–4). All subjects had low uterine transverse incision and the duration of surgery was 77 ± 21 min. Complete descriptive statistics for demographics are provided in table 1. Women who experienced evoked pain on the day after cesarean delivery above the 80th percentile were younger, were less highly educated, and more likely to be single than those reporting pain below the 80th percentile (table 1).

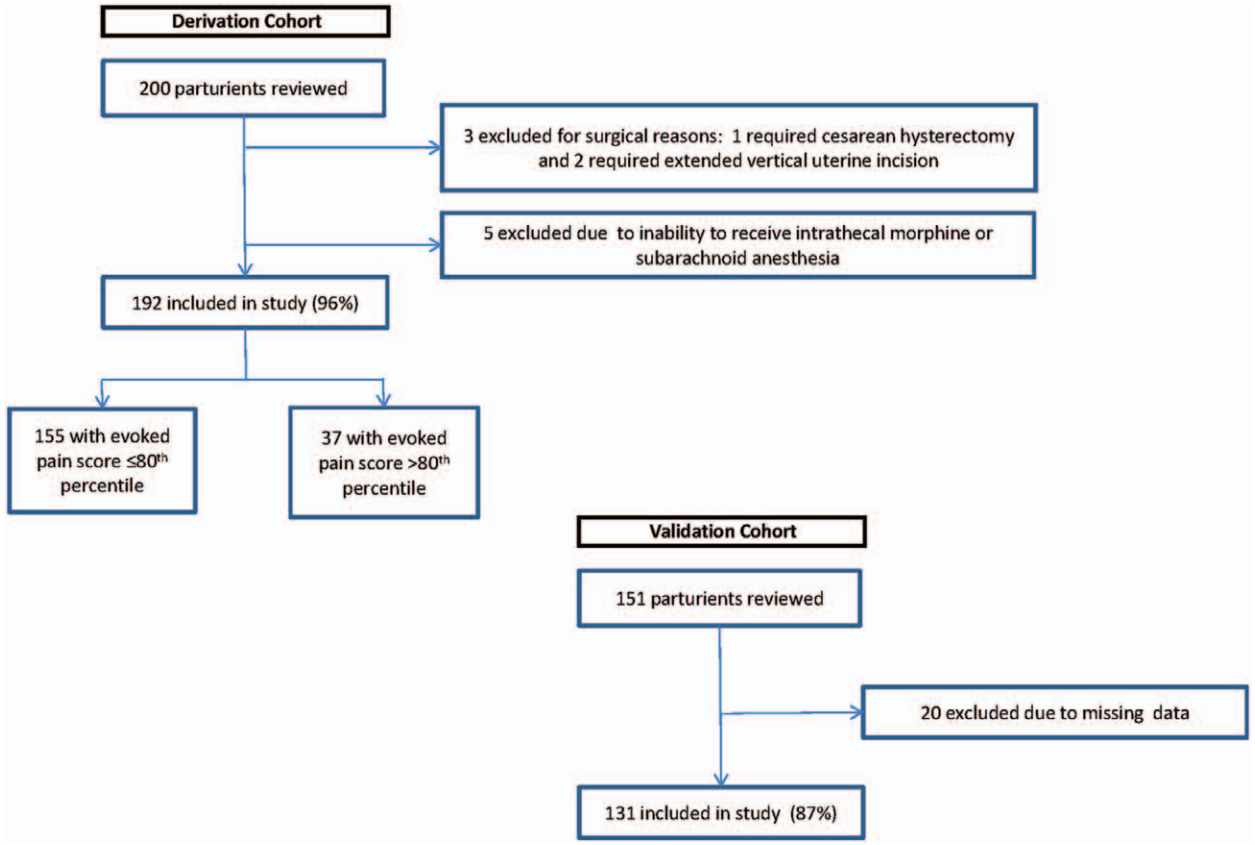

Fig. 1. Flow chart for subject inclusions and exclusions for derivation and validation cohorts.

Preoperative Assessment and Postoperative Outcomes in Derivation Cohort

There was a large interindividual variability in the results of all three preoperative predictive question scores, as well as the ranges of postoperative pain scores and analgesic requirements. Women with evoked pain on the day after cesarean delivery above the 80th percentile scored higher on all three preoperative questions and received more opioids in the postanesthesia care unit and in the first 24 h after surgery, and had higher resting pain scores and lower patient satisfaction scores. The actual and predicted 24-h evoked pain VAS for all subjects in the derivation cohort were 44 ± 26 and 44 ± 12, respectively, whereas the scores for the three preoperative questions were 52 ± 32 for anxiety, 57 ± 26 for anticipated postoperative pain, and 3 (0–5) for anticipated pain medication need. The actual 24-h evoked pain VAS was 83 (71–100) for parturients above the 80th percentile of observed pain intensity, and 35 (0–68) for those equal to or below the upper 80th percentile.

Spearman Correlations and Multiple Regression Analyses for Pain Outcomes in Derivation Cohort

Scores from three preoperative screening questions on anxiety, anticipated pain, and anticipated pain medication showed minimal to moderate correlation with each other but were only moderately correlated with the 24-h evoked pain VAS (primary outcome) ($P < 0.001$), 24-h resting pain VAS, and 24-h systemic opioid requirement (table 2).

Audio tone ratings showed minimal correlation to the standardized scores of the three preoperative questions, minimal to moderate correlation to evoked pain intensity, and minimal correlation to the other secondary pain outcomes on univariate analyses (table 2). The primary outcome multiple regression analysis is shown in table 3. Average audio tone intensity scores added uniquely but only minimally (2% of the variance) to the predictive power of the model (table 3). The regression model was not statistically significant for the secondary outcomes of resting pain and analgesic consumption, with minimal additional utility by addition of audio tone ratings (data not shown).

The final multiple regression model included the three predictive variables (answers to the three questions) and all the second- and third-order interaction terms. The multiple regression analysis yielded a statistically significant model using the three preoperative questions to the primary outcome ($R^2 = 0.20$, $P < 0.001$). Using the regression coefficients of the three predictors and their combinations in the multiple regression analysis, the formula used to calculate the predicted 24-h evoked pain VAS was as follows:

Predicted pain = 49.12 + (PM × (−4.27)) + (PA × (−1.37)) + (AS × (−0.74)) + (PM × PA × 0.46) + (PM × AS ×0.24) + (PA × AS × 0.03) + (PM × PA × AS × (−0.008)), where AS

Table 1. Demographic Characteristics for Derivation Cohort

	Entire Population (n = 192)	Evoked Pain Score ≤ 80th Percentile (n = 155)	Evoked Pain Score > 80th Percentile (n = 37)	*P* Value
Age, yr	30 (4.8)	30.4 (4.8)	28.2 (4.5)	0.01
Height, cm	163.2 (7.0)	163.0 (7.2)	161.5 (6.2)	0.42
Weight, kg	91.5 (21.2)	91.6 (22.2)	91.0 (16.6)	0.89
BMI, kg/m^2	34.3 (7.4)	34.4 (7.7)	33.9 (6.1)	0.69
Parity	1 (0, 4)	1 (0, 4)	1 (0, 3)	0.55
Previous cesarean delivery	169 (88.0)	135 (87.1)	34 (91.9)	0.68
Race				0.25
African American	44 (22.9)	39 (25.2)	5 (13.5)	
Hispanic	8 (4.2)	7 (4.5)	1 (2.7)	
White	140 (72.9)	109 (70.3)	31 (83.8)	
Current health				0.51
Excellent	70 (36.5)	58 (37.4)	12 (32.4)	
Good	102 (53.1)	83 (53.6)	19 (51.4)	
Fair	19 (9.9)	13 (8.4)	6 (16.2)	
Poor	1 (.5)	1 (.6)	0 (0)	
Education				0.01
Some high school	12 (6.3)	7 (4.5)	5 (13.5)	
High school graduate	34 (17.6)	23 (14.8)	11 (29.7)	
Some college	47 (24.5)	38 (24.5)	9 (24.3)	
College graduate	99 (51.6)	87 (56.2)	12 (32.5)	
Employment status				0.06
Employed	105 (54.7)	90 (58.1)	15 (40.5)	
Unemployed	87 (45.3)	65 (41.9)	22 (59.5)	
Marital status				<0.01
Married	140 (72.9)	121 (78.1)	19 (51.4)	
Divorced	7 (3.6)	4 (2.6)	3 (8.1)	
Single	42 (21.9)	29 (18.7)	13 (35.1)	
Separated	3 (1.6)	1 (.6)	2 (5.4)	
Cumulative morphine equivalents, mg				
24 h postsurgery	12 (0–98)	9 (0–67)	30 (1–98)	<0.01
48 h postsurgery	26 (0–148)	20 (0–142)	65 (12–148)	<0.01

All values are n (%) except age, height, weight, BMI are mean (SD); and parity and morphine equivalents are median (range).
BMI = body mass index.

Table 2. Spearman Correlations between Primary Outcome and Individual Predictor Factors (n = 192)

Predictor Factor Variables*	Anxiety	Anticipated Pain	Average Audio Score‡	24-h Evoked Pain (Primary Outcome)§
Anticipated pain medication usage	0.20†	0.47†	0.17	0.33†
Anxiety		0.36†	0.17	0.24†
Anticipated pain			0.16	0.33†
Average audio score				0.24†

These audio tones were administered in three series. Each series consisted of six tones of same frequency (900 Hz) but each of different amplitude (loudness). The first series was administered in ascending order of loudness, whereas the second and third series were administered in randomized order of loudness. The patient's intensity rating on the loudest tone in each series was obtained and averaged to obtain an average audio score.

* Predictor factor variables are as defined previously in text. † $P \leq 0.001$. ‡ Visual analog scale (VAS) was used to rate the intensity of three series of audio tones administered through headphones in a quiet room. § Twenty-four hour evoked pain is the visual analog score (0–100) for the intensity of pain when changing position from supine to sitting up at 24 h after surgery.

Table 3. Multiple Regression Analyses for Primary Pain Outcome in Derivation Cohort (n = 192)

Predictor Factor Variables	β	95% CI Lower	95% CI Upper	*P* Value
Block 1				
1. Anxiety	−0.74	−1.68	0.21	0.13
2. Anticipated pain medication usage	−4.30	−24.26	15.72	0.68
3. Anticipated pain	−1.40	−2.50	−0.21	0.02*
4. Anxiety × anticipated pain medication usage	0.24	−0.12	0.59	0.19
5. Anxiety × anticipated pain	0.03	0.01	0.04	0.01†
6. Anticipated pain medication usage × anticipated pain	0.46	0.07	0.86	0.02*
7. Anxiety × anticipated pain medication usage × anticipated pain	−0.01	−0.01	0.00	0.01†
Block 2				
1. Anxiety	−0.78	−1.71	0.15	0.10
2. Anticipated pain medication usage	−5.55	−25.20	14.10	0.58
3. Anticipated pain	−1.44	−2.58	−0.31	0.01†
4. Anxiety × anticipated pain medication usage	0.25	−0.10	0.59	0.16
5. Anxiety × anticipated pain	0.03	0.01	0.04	0.01†
6. Anticipated pain medication usage × anticipated pain	0.49	0.10	0.88	0.01†
7. Anxiety × anticipated pain medication usage × anticipated pain	−0.01	−0.01	0.00	0.01†
8. Average audio score‡	0.18	0.05	0.31	0.01†

* $P < 0.05$. † $P \leq 0.01$. ‡ Visual analog scale (VAS) was used to rate the intensity of three series of audio tones administered through headphones in a quiet room.These audio tones were administered in three series. Each series consisted of six tones of same frequency (900 Hz) but each of different amplitude (loudness). The first series was administered in ascending order of loudness, whereas the second and third series were administered in randomized order of loudness. The patient's intensity rating on the loudest tone in each series was obtained and averaged to obtain an average audio score.

β = regression coefficient.

= anxiety score (0–100), PA = pain anticipated (0–100), and PM = pain medicine anticipated (0–5).

The relation between the predicted 24-h evoked pain intensity outcome and evoked pain was examined using the regression plot and the residual plot as shown in figure 2, A and B. In a final step, the sensitivity and specificity of the model for predicting the top 20th percentile were evaluated using receiver operating characteristic curves. The optimal cut point was found to be 46.9 (z = 0.24) such that the sensitivity of 0.68 and the specificity of 0.67 were as balanced as possible. This cut point is provided in both real and standard units as it is sample and institution dependent.

Validation Cohort

Of the 151 parturients included in the validation cohort, 20 were excluded due to missing or incomplete data. Demographic characteristics of the remaining 131 subjects were similar to those in the derivation cohort (data not shown). The actual and predicted 24-h evoked pain VAS for all subjects in the validation cohort were 42 ± 24 and 50 ± 17, respectively, whereas the scores for the three preoperative questions were 44 ± 30 for anxiety, 48 ± 26 for anticipated postoperative pain, and 3 (1–5) for anticipated pain medication need. The 24-h evoked pain VAS were 77 (69–100) for parturients above the 80th percentile of observed pain intensity, and 34 (0–68) for those below the upper 80th percentile.

The utility and reliability of the predictive model obtained from the derivation cohort for predicting 24-h evoked pain VAS were examined by comparing the regression line plots and residual plots of the evoked pain VAS outcome, as well as the receiver operator characteristic curves between derivation and validation cohort (figs. 2, A, B, and 3). The slopes and intercepts of the regression lines (fig. 2A) from the two cohorts were similar with $R^2 = 0.20$ for the derivation cohort and $R^2 = 0.18$ for the validation cohort. The utility of the model for predicting the top 20th percentile was similar and modest in both the derivation and validation cohorts.

Discussion

These results suggest that using the responses to a three-item preoperative screening questionnaire in assessing anxiety, anticipated postcesarean pain, and anticipated analgesic need in a homogenous population provides a meaningful parsimonious combination of predictors that reliably yields a validated model with significant improvement over single variable and comparable with the more time-consuming QSTs for predicting severe evoked pain after cesarean delivery. This simple model accounts for 20% of the variance in postcesarean evoked pain and replicates closely in the validation cohort.

Despite uniform multimodal and preemptive analgesic treatment, we confirmed a large variability in pain with

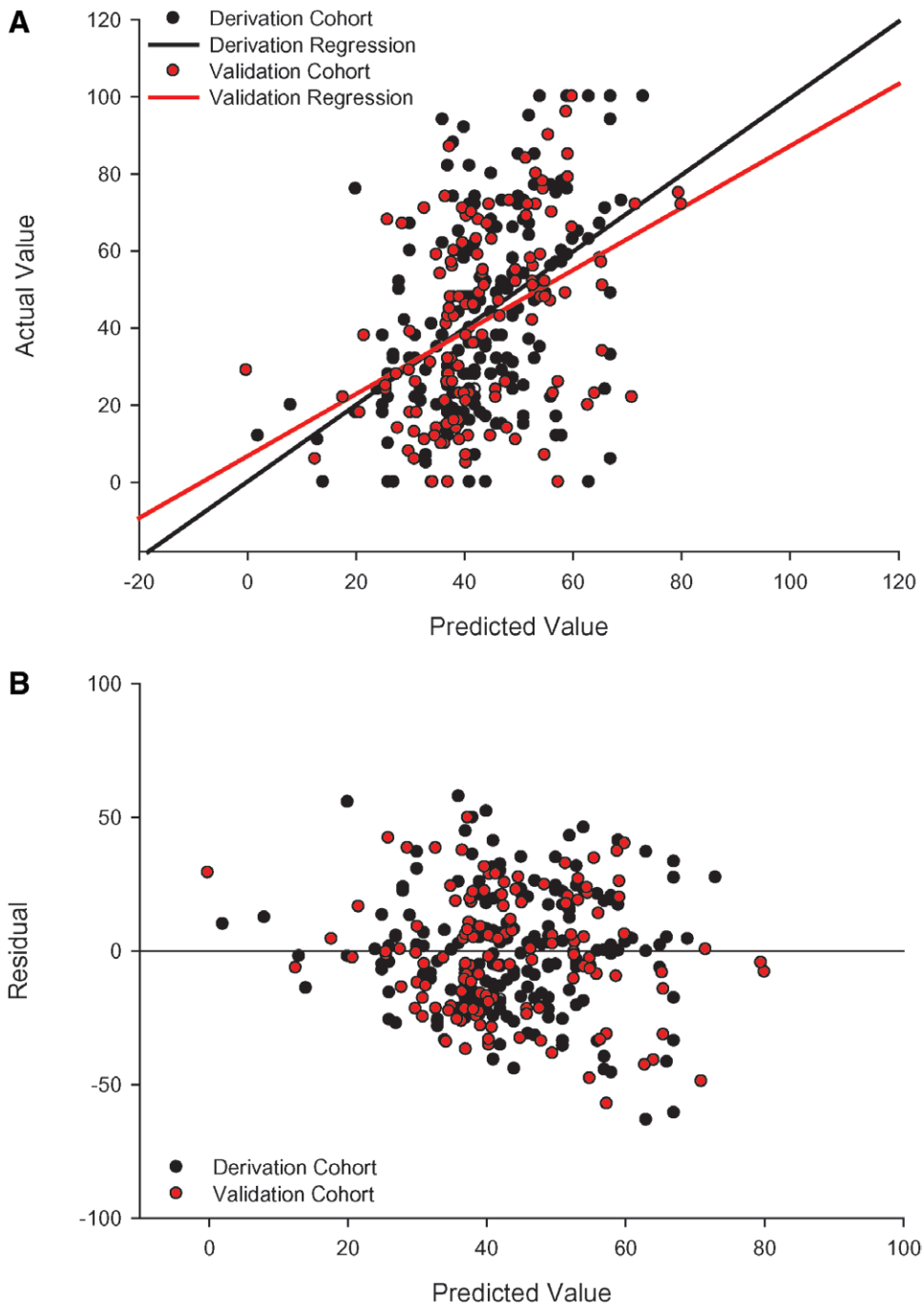

Fig. 2. (*A*) Linear regression line plot between predicted and actual 24-h evoked pain intensity (visual analog scale) in the derivation cohort (n = 192, R^2 = 0.20, $P < 0.001$) and the validation cohort (n = 131, R^2 = 0.18, $P < 0.001$). R^2 = the variance in pain outcome accounted for by the predictors. (*B*) 24-h evoked pain outcome predicted value residual plots of both derivation and validation cohorts.

activity in women after elective cesarean section. Of the 323 women included in this study, 49, 33, and 18% experienced mild, moderate, and severe pain with activity on the first postoperative day (defined as VAS 0–39, 40–69, and 70–100, respectively). Some women clearly have inadequate analgesia, whereas some have likely received more analgesics than required, which is not surprising given when applying a one-dose-fits-all approach with intrathecal morphine and oral ibuprofen in this patient population. That breakthrough pain treatment is available on an as-needed basis does not meaningfully change this conclusion, and severe pain despite availability of such add-on treatment is associated with a 2.5- to 3-fold increased risk of persistent pain and postpartum depression in this patient population.[11] If we want to be able

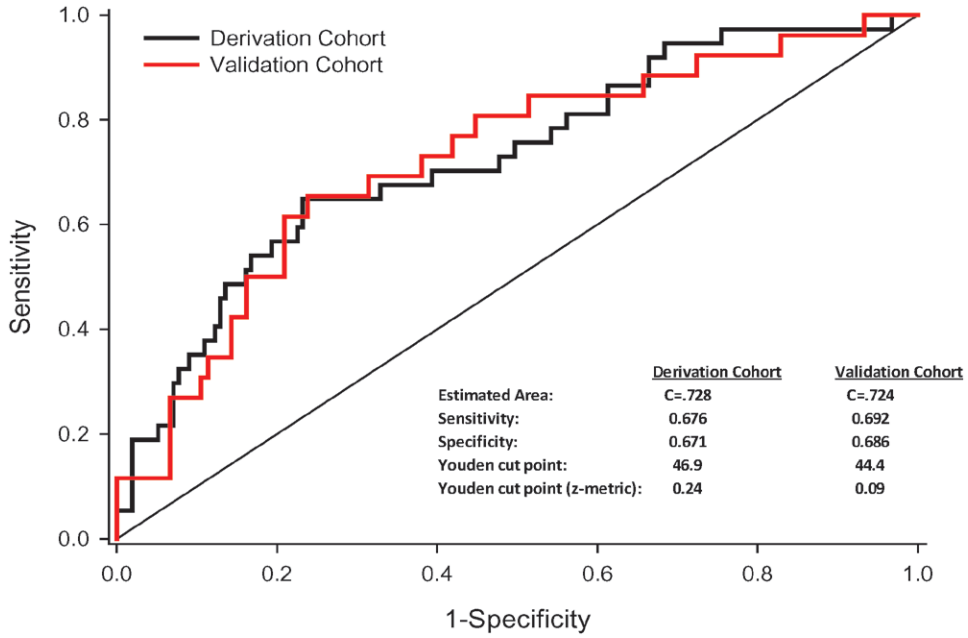

Fig. 3. Receiver operator characteristic curves of both derivation (n = 192) and validation (n = 131) cohorts.

to administer appropriate fixed doses of analgesics preemptively, or to examine the causality between acute and persistent pain and depression in high-risk groups, we would need tools to predict preoperatively the severity of postoperative acute pain. This study, building upon previous observations of key predictive factors, provides a practical approach to address this need in this population.

The predictive power of our simple approach is comparable with more complex and time-consuming approaches reported previously.[7,8] Although preoperative QST results predict postoperative pain, this method is time-consuming, requires special equipment and trained personnel, and is comparable or only marginally better than the simple approach in the current study.[8] For example, VAS pain response to a 48°C stimulus accounted for 28% of the variance in postcesarean delivery pain intensity with activity in one study,[9] whereas another study showed pain response to tonic heat stimuli accounted for only 14% of the variance in postcesarean pain intensity.[10] Similarly, pain threshold to electrocutaneous stimuli accounted for 27% of the variance in postcesarean delivery pain in one study,[16] but only 6 and 4.8% of the variance in others.[17,18] We do not argue with the value of QST studies to examine mechanisms of response to postoperative pain, but this approach does not appear to provide better predictive power than the three questions examined in the current study. Although we were hopeful that using the simpler approach to rate the loudness of audio tones would act as a surrogate for QST and further enhance the predictive utility of the three questions, their addition added less than we feel is worth the additional time and effort.

Many other factors have been associated with severity of postoperative pain, including anxiety,[7,19,20] expectation,[7,20] fear, stress,[19,20] and catastrophizing behavior.[7,10,20–22] In a systematic review of 48 studies evaluating QSTs and psychosocial factors as predictors for postoperative pain outcomes among 23,036 patients, anxiety, age, surgical procedure, and preexisting pain experiences were the largest and most consistent predictive factors.[7] Of the 48 studies included in that review, only 4 were in obstetric patients, 3 of which studied primarily QSTs.[7] All four of these obstetric studies were of small sample size no larger than 65, and did not report or perform validation of their respective predictive model developed from the small derivation cohorts.[7] Building upon our previous studies[1,11] and this review,[7] we focused on the assessment of anxiety, expectation in postoperative pain, and analgesic need. Anxiety has been reported to result in lower pain threshold,[23] overestimation of pain intensity,[24] and hypersensitivity to stimuli.[12] Expectations powerfully modulate both subjective reports of acute pain and pain-induced brain activity through mechanisms likely involving the prefrontal cortex, anterior cingulated cortex, and the anterior insular cortex.[25]

Although the reliability of these three questions to predict severity of postcesarean delivery pain at other centers awaits further research, this model was remarkably reliable at our institution. The regression analysis in the validation cohort was remarkably similar to the derivation cohort, despite the application of the questions in routine clinical practice in the former and in research with informed consent in the latter. Although there are many applications of predictive models, we were initially interested in defining women at high risk for severe pain after cesarean delivery. In our validation cohort model, we consider the sensitivity and specificity of 0.69 and 0.69, respectively, with cut point of 44.4 (z = 0.09), for identifying parturients above the 80th percentile for activity-associated pain not optimal but still reasonably

acceptable, given the simplicity of the measures, and are applying these questions routinely for both clinical care and research purposes. In addition, we have performed a logistic regression analysis with evoked pain as the dependent variable and predicted pain scores from our generalized linear model as the single continuous predictor. For every five-point increase in predicted pain score, the odds of being in the upper 20% of evoked pain increases by 1.47 points.

In contrast to evoked pain, these questions were not predictive of resting pain or medication usage. This confirms previous studies and agrees with suggestions that the mechanism of resting and evoked pain may be different. Pain and analgesic consumption share a complex relationship. The relation of postoperative pain and analgesic requirement is nonlinear.[26] Therefore, predictors for postcesarean analgesic requirement may be different from those for postcesarean pain intensity.

We found similar associations in some of the secondary measures distinguishing women above the 80th percentile of acute postcesarean delivery pain from those below that level. Women with greater pain were slightly younger, less educated, and more likely to be unemployed and single than those with lesser pain. The exact contributory mechanisms of these other variables are likely complex and may reflect differences in health belief, fear, stress, and partner anxiety.[25]

In our recent multicenter, prospective, longitudinal cohort study of 1,288 hospitalized women for cesarean or vaginal delivery, it was found that the severity of acute postpartum pain, but not mode of delivery, was independently related to the risk of persistent pain and depression at 8 weeks postpartum.[1] Women with severe acute postpartum pain had a 2.5-fold increased risk of persistent pain and a 3.0-fold increased risk of postpartum depression compared with those with mild acute postpartum pain. In addition, every 1 point out of 10 points increase in acute pain scores after delivery was associated with an 8.3% increase in 8-week depressive symptoms and a 12.7% increase in the odds of experiencing persistent pain at 8 weeks.[1] Thus, it would be important to identify those patients at risk for high acute postpartum pain and to address the need for more careful pain treatment in the days after childbirth. Instead of the standard fixed dose postcesarean analgesic regimen such as fixed dose of intrathecal morphine for all patients, patients at risk for high postoperative pain could be considered for tailored therapy with more aggressive, multimodal therapy such as appropriately higher dose of intrathecal morphine plus a higher maintenance dose of nonsteroidal agents such as ibuprofen or ketorolac, and acetaminophen in combination with intravenous or epidural patient controlled analgesic under properly monitored conditions. The addition of preoperative oral gabapentin as a component of multimodal analgesic therapy for postcesarean pain is inconclusive,[27,28] whereas transversus abdominis plane block does not further improve analgesia over intrathecal morphine.[29] Continuous epidural opioid infusion for a longer postoperative period in addition to more frequent assessment and treatment is speculative but may be beneficial to further improve postoperative analgesia. However, besides the immediate benefit of reduction of acute pain, it is unclear and is currently under investigation whether reduction of acute postoperative pain score in patients at risk for high pain will reduce persistent pain or depression.

In conclusion, our results suggest that responses to three simple questions can account for a modest amount of variability in pain with activity 1 day after cesarean delivery, and that this association is reliable, at least at one institution, between research and routine practice settings. If confirmed at other institutions, this approach could further tailoring of fixed doses of analgesics commonly used in this setting and facilitate research of populations enriched in women at high or low risk for severe pain after cesarean delivery.

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