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The Role of Psychological Factors in Persistent Pain After Cesarean Delivery

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Abstract: **This French multicenter prospective cohort study recruited 391 patients to investigate the risk factors for persistent pain after elective cesarean delivery, focusing on psychosocial aspects adjusted for other known medical factors. Perioperative data were collected and specialized questionnaires were completed to assess reports of pain at the site of surgery. Three dependent outcomes were considered: pain at the third month after surgery (M3, n = 268; risk = 28%), pain at the sixth month after surgery (M6, n = 239; risk = 19%), and the cumulative incidence (up to M6) of neuropathic pain, as assessed using the Douleur Neuropathique 4 questionnaire (n = 218; risk = 24.5%). The neuropathic aspect of reported pain changed over time in more than 60% of cases, pain being more intense if associated with neuropathic features. Whatever the dependent outcome, a high mental component of quality of life (SF-36) was protective. Pain at M3 was also predicted by pain reported during current pregnancy and a history of miscarriage. Pain at M6 was also predicted by report of a postoperative complication. Incident neuropathic pain was predicted by pain reported during current pregnancy, a previous history of a peripheral neuropathic event, and preoperative anxiety.**

Trial Registration: **ClinicalTrials.gov, NCT00812734.**

Perspective: ***Persistent pain after cesarean delivery has a relatively frequent neuropathic aspect but this is less stable than that after other surgeries. When comparing the risk factor analyses with published data for hysterectomy, the influence of preoperative psychological factors seems less important, possibly because of the different context and environment.***

Key words: *Neuropathic pain, chronic pain, cesarean delivery, postsurgical pain, Douleur Neuropathique 4.*

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Postsurgical persistent pain (PSPP) is a recognized issue that deserves attention.[17,21] Cesarean delivery is one of the various surgeries that may be responsible for PSPP,[23,32] and the frequency of this technique is increasing worldwide.[11,43] In addition, the role of preoperative psychological factors in the development of PSPP, such as depression, psychological vulnerability, stress,[19] anxiety, and pain catastrophizing,[45] has been highlighted. Anxiety and catastrophizing have recently been shown to favor PSPP regardless of the surgical model.[28] Other more specific predictors of the preoperative context, such as emotional illness, representation of the condition leading to surgery,[39] fear of surgery,[36] physical condition,[37] or recent capacity overload,[1] have also been reported. As the effects of psychological factors on PSPP are likely to be influenced by the surgical context, it seemed interesting to compare the effects of psychological risk factors on hysterectomy and on cesarean delivery, two surgical models that share some technical aspects (transverse low abdominal and uterine incision) but differ in many other aspects. Cesarean delivery, although a stressful event, is performed on younger women anticipating a happy event and involves a specific hormonal status with high levels of circulating gonadic steroids. On the other hand, hysterectomy is often performed on patients reporting preoperative pain,[6,18,46] generally due to a tumor that is to be removed, whereas a cesarean procedure targets the safety of the child or the mother. Psychological risk factors of PSPP have been studied previously in hysterectomy for benign disorders,[39] but only acute pain after cesarean delivery has been investigated with reported evidence of a role of preoperative anxiety and anticipated pain.[35] Data were available for analysis from a wide prospective cohort that estimated the risk of occurrence of neuropathic PSPP (nPSPP) within 6 months after surgery.[10] In this study, which pooled nine different surgeries, the occurrence of nPSPP was favored by anxiety, low preoperative quality of life, and catastrophizing, but additional information was available about the cesarean subcohort. In particular, the psychosocial aspects of pregnancy were addressed using a preoperative questionnaire. Therefore, our aim was to assess the respective roles of various psychosocial factors in the development of PSPP after cesarean delivery, adjusted for other known medical risk factors, with a methodology as close as possible to that conducted by Pinto et al[39] on hysterectomy. The analyses also focused on the risk of occurrence of nPSPP, given that reporting of a neuropathic mechanism for PSPP is a risk factor for pain chronicization.[2]

Methods

The methods are described in detail in the report of the main multicenter French study,[10] which was undertaken after approval by the appropriate research ethics committee (CCPPRB d'Auvergne and CPP Sud-Est VI for amendments). The cesarean study was coordinated by a referent anesthetist at each center and was conducted by the anesthesiology team. The study population consisted of all patients over 18 years of age scheduled for cesarean delivery in a recruitment center, following written informed consent. The exclusion criteria were expected difficulties with comprehension or completion of the questionnaires; patients who would be unreachable in 6 months' time; cesarean delivery in an emergency or during labor. Parturients with previous experience of cesarean delivery could be included. Consecutive recruitment of patients was required. The inclusion visit was undertaken by the anesthetist the day before scheduled surgery. The patient was first asked to complete a questionnaire about her history of previous painful events (before and during this pregnancy), pregnancies (miscarriages and childbirths), and cesarean deliveries, as well as if the current pregnancy was desired, and if pain was expected during the postcesarean period. This questionnaire, which was specific to the cesarean subcohort, is presented in Appendix 1. In addition, the patient had to complete standard questionnaires: (i) the Medical Outcomes Study (MOS) 36-item Short Form (SF-36) to assess health-related quality of life,[24,33] (ii) the Pain Catastrophizing Scale,[44] and (iii) the Hospital Anxiety and Depression Scale (HADS).[51]

Demographic data and data about potential symptoms of peripheral neuropathy and possible risk factors for peripheral neuropathy were collected by the physician. All the questionnaires are presented in Appendix 1. After surgery, on discharge from the surgical ward, the physician completed data about the intraoperative anesthetic used, the postoperative analgesia given, and the occurrence of early complications. At M3 and M6, a questionnaire was mailed to the patient, in which she was asked if she experienced pain in the operated area (study definition of PSPP). If PSPP was present, additional information was asked about the intensity of this pain over the last 48 hours, with a drawn visual analog scale. Other questions related to the time course since surgery and the clinical features of the pain. Some of these questions were derived from the Douleur Neuropathique 4 (DN4) questionnaire, a screening tool validated to assess the neuropathic aspect of PSPP, and included within the study's questionnaire.[4] nPSPP was defined as PSPP with at least four positive items on the DN4. If documents were not completed and returned, the patient was contacted by telephone. Throughout the follow-up period, the patient was able to consult a referent practitioner for analgesia if required or could be referred on request to the closest specialist pain center.

Three dependent outcomes were considered separately, each in samples with a full dataset. The first outcome was the presence of reported PSPP at M3, whatever the mechanism (neuropathic or not). The initial aim was to study the intensity of PSPP at this time point, but the distribution of the data (too many null values and highly skewed positive values) did not allow for relevant analysis. This analysis was similar to that conducted by Pinto et al[39] and provided information about the role of non-neuropathic cases. The second outcome was the presence of reported PSPP at the sixth month after surgery, considering that the features of PSPP could have changed with time. The third outcome was the risk of

nPSPP, either at M3 or M6 (i.e., cumulative incidence within 6 months after surgery); these two measurement points were considered to avoid missing information due to a possible fluctuation of the symptoms.[9] This outcome was considered to be a good predictor of the likelihood of subsequently experiencing chronic pain.[2]

The end point was to investigate the risk factors for PSPP/nPSPP with a multistep approach similar to that used by Pinto et al[39] in their hysterectomy model. The first step consisted of a basic model in which only sociodemographic and clinical factors were considered, according to current knowledge and the results of the main study.[10] These factors were (i) morphometric and demographic factors such as the patient's age and body mass index, and the center in which the surgery was performed; (ii) factors likely to favor PSPP (neuropathic or not), such as the report and location of any pain before pregnancy and of any pain directly linked to pregnancy, a previous history of cesarean delivery, a previous history of a peripheral neuropathic event, and the report of any putative neurotoxic condition (see Dualé et al[10] for a description of the construction of the two last outcomes); (iii) other obstetric outcomes such as the history of childbirths and miscarriages, and whether the current pregnancy was desired; and (iv) other outcomes such as the use, and time of use, of locoregional anesthesia and the report of any early postoperative maternal complication. To conduct the analyses free from any constraint or assumption of a linear relationship with the dependent outcome, continuous variables were transformed into ordinal variables according to their terciles taken as cut-off values. Following Hosmer and Lemeshow,[20] certain variables were selected (those for which the *P* value of the univariate Wald test did not exceed .25) using an automated backward elimination procedure with a .05 significance level to stay in the model. This was taken into account for all variables except age and body mass index, which were forced into the model whatever the *P* value in order to systematically control for these possible confounding factors.

The final models tested the predictive power of different psychological presurgical factors, with an adjustment for relevant sociodemographic and clinical factors. Due to the effect of multicollinearity, a phenomenon likely to appear in psychometry, the psychological factors were separated into different sets, as reported by Pinto et al,[39] who treated emotional distress, illness perceptions, and coping strategies separately. This study was the first in which the patients' perception of illness was tested as a determinant of PSPP. This concept derives from the Common-Sense Self-Regulation Model, and assumes that, "in the context of an illness, people tend to develop individual cognitive and emotional illness representations of their illness" (see Pinto et al[39] for review). A fourth set, quality of life, was also tested as this information was also available to us. For each of these four final models, the selected covariates were (i) those identified as predictive following the initial basic model, plus (ii) the age and body mass index, which were forced into the model whatever the results of the analysis. The model testing emotional distress studied the adjusted effect of the anxiety and the depression subscores from the HADS and the report of a negative event within the past 6 months. In the model testing illness perception, the added factor was the expectation of pain during the postcesarean period. In the model testing coping strategies, the global score of catastrophizing was added. In the model testing quality of life, the physical component and the mental component summaries, calculated from the MOS SF-36,[24] were added.

The quantitative data were expressed as the mean ± SD for normally distributed data and as median and interquartile range otherwise. The categorical data were expressed as frequencies and percentages. When a pain score of PSPP was available, the difference between the two observation points (M3 and M6) was calculated, and the factors influencing this difference were analyzed with a generalized linear model. To avoid data skewness, the analysis was conducted on ranks. Analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC) with a double-sided type I error set at .05. The sample size calculation was performed to reach 5% precision for the width of the 95% confidence interval (95% CI), i.e., the type I error was set at 5%. Each 95% CI was built around the point estimate of the risk of PSPP being reported in the available literature at the time of conception of the project, i.e., 5.9%.[32] The sample size was systematically inflated expecting 20% of patients lost to follow-up during the study. The targeted size of the recruited sample (N = 103) had to be adjusted up to 352 during the study, according to the results of an intermediate analysis, which showed that the cumulative risk of nPSPP was closer to .5 than expected.

Results

The whole sample for cesarean delivery has been described in Dualé et al[10] Fig 1 shows the flowchart of the cohort, as well as the main results describing the PSPP and nPSPP outcomes. At M3 and M6, 28% and 19% of patients reported PSPP, respectively; the odds of a neuropathic case (on the basis of the DN4) for one non-neuropathic case were 3.3 (62:19) and 1.6 (30:19), respectively. The samples considered for each analysis are described in Table 1; they differ because a full dataset was required for the studied outcomes, which depended on the analyses. Two centers with less than 10 inclusions were pooled in one modality.

At M3 and M6, for the 75 cases of PSPP with information about pain intensity (visual analog scale ranging from 0 to 10), the median pain scores were 1.1 (.4–2.6) and .2 (.0–1.5), respectively. A pain score >3 was reported by 16 and 6 women, respectively; this represented 21.3 and 8.0% of the painful cases and 5.5 and 2.4% of the whole. Three patients were taking medication for pain at the sixth month after surgery (all DN4 (+)); two were treated by dextropropoxyphen and acetaminophen, and one by acetaminophen alone. The Neuropathic Pain Symptom Inventory score, which was collected only at the first report of nPSPP, was available for 46 patients (37 and 9 patients, respectively at M3 and M6 after surgery). Its median value was 11 (range = 5–21;

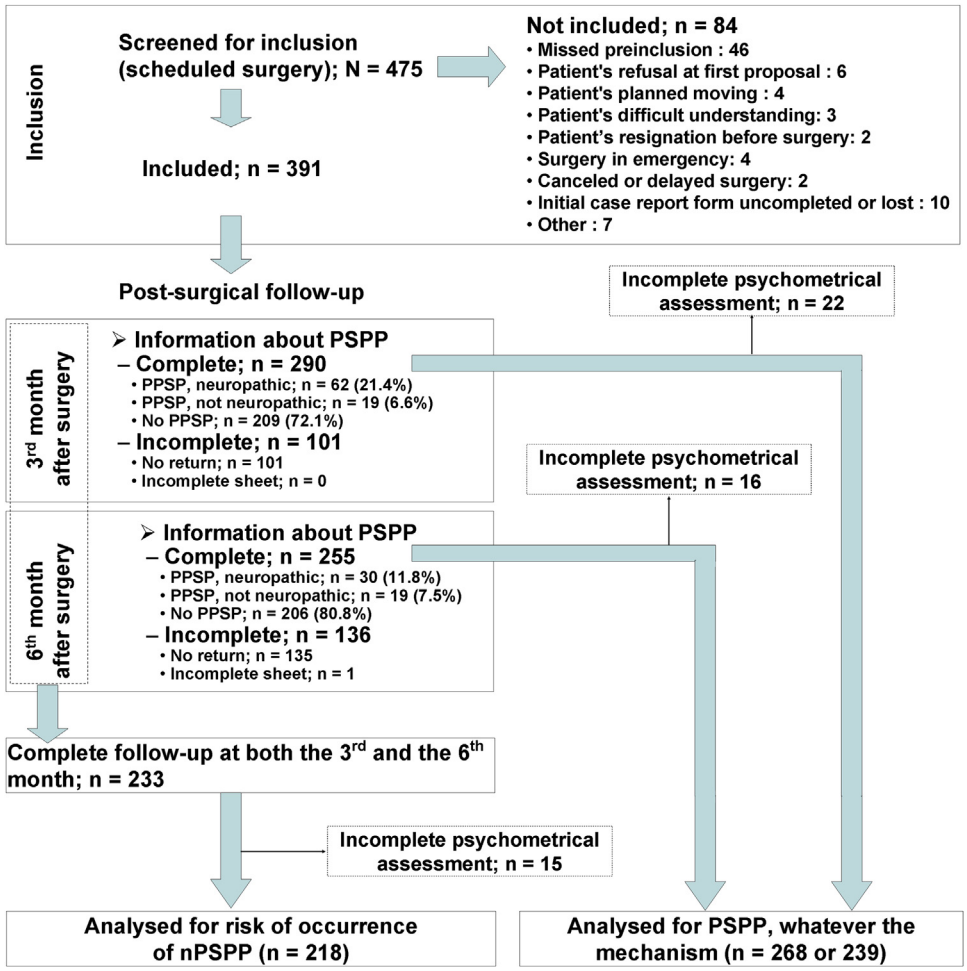

Figure 1. Flowchart of the patients from the time of screening to the end of follow-up, i.e., at the sixth month after surgery. The cumulative incidence of neuropathic pain is defined on the basis of self-report of persistent pain at the operated site with four or more positive items on the DN4 questionnaire.

max = 61). As observed in Dualé et al[10] in pooled surgeries, four different profiles of painful cases could be identified, depending on the response to the DN4 (Fig 2). The change in pain intensity with time was influenced by the profile ($P < .0001$, analysis of variance on ranks, post hoc analysis with the Tukey test).

Table 2 shows the results of the risk factor multivariable analyses for each dependent outcome. For the risk of PSPP at M3, the basic model found report of pain during current pregnancy and history of miscarriage as independent predictors, so these two factors were retained in the final models. None of the psychological factors were found to be predictive after adjustment, except the mental component of quality of life; the upper tercile (corresponding to subjects with the best mental-based quality of life) was protective compared with the lower tercile taken as the reference class. The factors found to be predictive by the basic model were generally still predictive in these models, except history of miscarriage in the emotional distress model.

The basic model found report of a postoperative complication to be an independent predictor for the risk of PSPP at M6, so this factor was kept in the final models. None of the psychological factors were found to be predictive after adjustment, except the mental component of quality of life, as in the analyses of the risk of PSPP at M3. Similarly, postoperative complication was still predictive in all these final models.

For the risk of nPSPP within the 6 months after surgery, the basic model found a previous history of a peripheral neuropathic event and report of pain during the current pregnancy as independent predictors, so these two factors were kept in the final adjusted models. Psychological factors were found to be predictive in only two of these models. In the model testing emotional distress, anxiety was a risk factor of nPSPP, as both the upper and median terciles differed from the lower tercile, taken as the reference class. Similar to the previous analyses of the risk of PSPP at M3 and M6, the mental component of quality of life was protective. The two factors that had been found to be predictive by the basic model were generally still predictive in these models, except pain during pregnancy in the emotional distress model.

Discussion

As in other traumatic events, PSPP may be a complex phenomenon involving various peripheral and central

Table 1. Description of the Population

Sample For Analysis	*PPSP At M3*	*PPSP At M6*	*Cumulative Risk Of nPPSP*
Sample size	268	239	218
Demographic/morphometric data			
Age, y	31.9 ± 5.0	32.2 ± 5.3	32.1 ± 5.0
Body mass index (kg/m^2)	28.4 ± 5.1	28.1 ± 5.1	28.2 ± 5.2
Center			
CES-1	63 (23.5)	50 (20.9)	46 (21.1)
CES-2	147 (54.9)	133 (55.7)	117 (53.7)
CES-3	15 (5.6)	13 (5.4)	13 (6.0)
CES-4	21 (7.8)	21 (8.8)	21 (9.6)
CES-5	22 (8.2)	22 (9.2)	21 (9.6)
Putative predisposition to pain (preoperative)			
Preoperative pain			
None	131 (48.9)	118 (49.4)	109 (50.0)
Elsewhere	78 (29.1)	76 (31.8)	72 (33.0)
Unknown location	51 (19.0)	37 (15.5)	29 (13.3)
At the site of surgery or close	8 (3.0)	8 (3.4)	8 (3.7)
Pain during current pregnancy	135 (50.4)	114 (47.7)	104 (47.7)
Other obstetric outcomes			
Previous cesarean delivery	149 (55.6)	131 (54.8)	116 (53.2)
History of miscarriage	67 (25.0)	58 (24.3)	55 (25.2)
Desired current pregnancy	248 (92.5)	219 (91.6)	200 (91.7)
Previous births			
None	86 (32.1)	80 (33.5)	75 (34.4)
One	128 (47.8)	110 (46.0)	99 (45.4)
Two or more	54 (20.2)	49 (20.5)	44 (20.2)
Putative predisposition to neuropathy (preoperative)			
History of neuropathic events	80 (29.9)	73 (30.5)	65 (29.8)
Neuropathy-facilitating condition	22 (8.2)	18 (7.5)	16 (7.3)
Anesthetic data			
Locoregional anesthesia			
None (general only)	5 (1.9)	7 (2.9)	4 (1.8)
Intraoperative only	236 (88.1)	203 (84.9)	190 (87.2)
Intra- and postoperative	27 (10.1)	29 (12.1)	24 (11.0)
Indicators of emotional distress			
Anxiety (HADS)	8 [6–10] (1–18)	7 [5–10] (1–17)	7 [5–10] (1–17)
Depression (HADS)	3 [1–6] (0–23)	3 [2–6] (0–23)	3 [2–6] (0–23)
Negative event in the past 6 months	54 (20.2)	46 (19.3)	41 (18.8)
Indicators of illness perception			
Expected postoperative pain (before surgery)			
None	63 (23.5)	58 (24.3)	55 (25.2)
Mild pain	97 (36.2)	89 (37.2)	79 (36.2)
Important pain	108 (40.3)	92 (38.5)	84 (38.5)
Indicators of coping strategies			
Catastrophizing global score (preoperative)	12 [6–22] (0–45)	12 [6–22] (0–45)	12 [6–22] (0–45)
Indicators of quality of life (SF-36)			
Physical component summary	39.3 ± 8.8	39.3 ± 8.9	39.3 ± 8.8
Mental component summary	47.6 ± 9.9	47.8 ± 9.9	47.6 ± 9.8
Postoperative complication	14 (5.2)	13 (5.4)	12 (5.5)

NOTE. Description of the samples considered for the risk factor analyses of PSPP at M3 and M6 and incident nPSPP within the 6 months after surgery. Numerical data are expressed as the mean ± SD or median [interquartile range] (range). Categorical data are expressed as frequencies and (%).

(spinal and supraspinal) processes.[40,49] However, it is a peculiar model of chronic pain in which a trigger event is easily identified in time, and it occurs in addition to many possible predispositions.[1,19] For example, in the main study of nPSPP occurring after several pooled surgeries, the risk factors identified were either somatic (previous history of peripheral neuropathy, protection of older age) or psychological, such as a recent negative event, quality of life, or anxiety.[10] The idea that all patients are not all equally at risk of nPSPP was also supported by some discordance between nerve lesion and PSPP after thoracotomy.[9] In the current study, the adjusted effects of preoperative somatic and psychological factors of PSPP after cesarean delivery were analyzed in multivariable models by separating the latter in different dimensions. The main result was that the weight of the psychological factors was quite mild except for mental of quality of life, which appeared as a robust protective factor. There is also a strong need to identify the factors that have a stable effect on PSPP

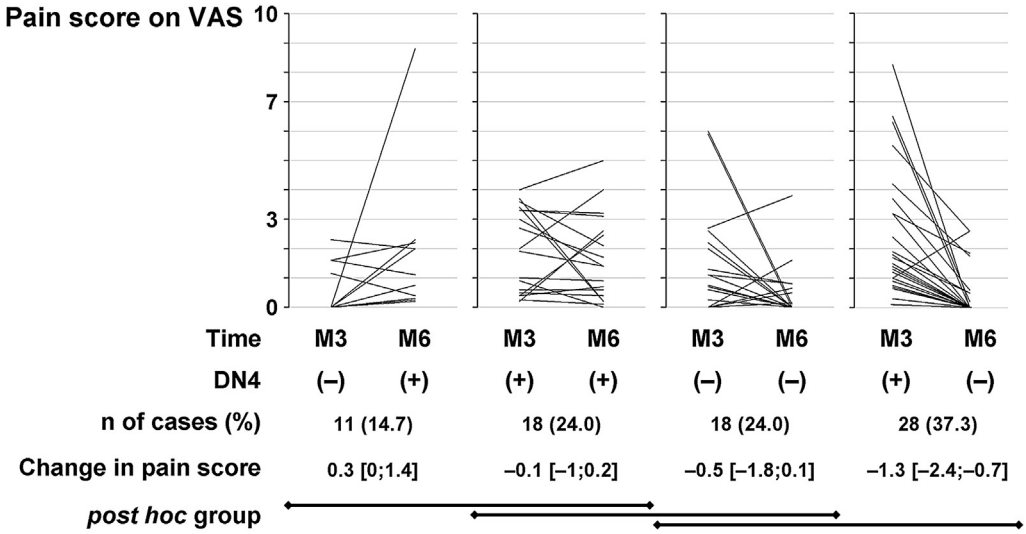

Figure 2. Raw values and evolution of pain intensity as measured on a visual analog scale (VAS) out of 10, from M3 to M6, in the 75 patients who reported persistent postsurgical pain and who rated it at both time points. Four profiles were identified depending on the response to the DN4 associated with the report of pain; this response was either positive (i.e., at least four items positive on the DN4) or negative. The change in pain score between M3 and M6 is expressed as the median [first quartile; third quartile]. After an analysis of variance on ranks showed an effect of the pain profile on the change in pain score, three groups were defined by the post hoc analysis with the Tukey test, each identified by a horizontal line.

whatever the surgical model, as this may indicate that this effect is poorly influenced by the surrounding context (age, gender, medical history, or external factors). Based on an approach developed by Masselin-Dubois et al[28] who found similar predictors in total knee arthroplasty and breast cancer surgery, the results of the current study may be compared with those of Pinto et al[39] on hysterectomy, and differences in terms of risk factors identified. This supports the hypothesis of a context effect in the development of PPSP.

Internal Validity

The rates of PSPP after cesarean delivery reported here are higher than those reported in the published prospective studies, which were 9 to 23% at M3[15,23,30,31] and 3 to 16% at M6.[23,31,34] This was probably due to different methods of measurement and to the low number of published studies. However, the highest published rates were also reported in studies conducted in Western Europe.[23,31] The risk of PSPP seems to decrease after the sixth month,[16,25,34] and few patients in our cohort (2.4%) reported relevant pain at M6, indicating that few patients will have a life-impairing disease, as noted by other authors.[23,32] The risk of PSPP estimated here can therefore be considered an imperfect surrogate of chronic pain, but may be a useful tool to build mechanistic hypotheses.

In the current report, nearly 3 of 4 cases of reported pain were associated with symptoms evocative of neuropathy. This finding is supported by a survey of 866 women who had undergone a Pfannenstiel incision 2 years previously, of which about 90% were cesarean deliveries.[26] Local numbness, a sign of nerve lesion, predicted chronic pain, and 17 of the 32 pain cases examined had signs of a trapped nerve. A recent prospective survey also reported symptoms of associated neuropathy, especially in the cases of long-term PSPP.[34] There have also been reports of pain relief by elective neurectomy in 22 patients with PSPP after a Pfannenstiel incision.[27] Neurectomy targeting the iliohypogastric or the ilioinguinal nerves was directed by preoperative screening with a search for the Carnett sign and a lidocaine nerve block test. The putative nerve lesions were cause by a direct lesion during dissection, trapping by constricting sutures, or perioperative retraction.[27] In addition, a recent trial suggested that avoiding peritoneal closure to avoid nerve entrapment might prevent persistent pain.[41]

Studying only preoperative psychological factors may also be questionable, as psychology might also be a factor at late stages when PSPP is established. In this last scenario, there may be go-and-return interactions between psychological factors and pain, which require understanding of specific models.[7,8] Nevertheless, such simple transverse preoperative psychometry might be enough to identify a relationship, and it has given reproducible results.[28,45] Furthermore, it may help to determine strategies to prevent PSPP. However, it can also be argued that such an approach misses possible fluctuations of variables over the perioperative period. Such one-shot measurements reflect a sum of the timeless and the contextual aspects of the patient's predisposition, and only a long preoperative longitudinal assessment could study both aspects separately.

Risk Factors for PSPP: Within Study

Each of the dependent outcomes that were considered for the risk factor analysis could represent a particular aspect of PSPP. Indeed, at M3, PSPP was quite frequent (28%), with an intensity of less than 3/10 (i.e., stronger than mild) in nearly a quarter of cases, and a similar

Table 2. Sequential Logistic Regression Analysis of the Prevalence of Persistent Pain After Cesarean Delivery on Demographic, Clinical, and Psychological Measures at Baseline

Outcomes	PSPP At M3		PSPP M6		nPSPP Up To M6	
Models And Factors	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
Initial basic model: demographic and clinical predictors†						
Age: median vs lower tercile	.88 (.45–1.72)	.699	1.13 (.48–2.64)	.788	.71 (.31–1.61)	.413
Age: upper vs lower tercile	.74 (.37–1.46)	.382	1.57 (.7–3.53)	.272	1.35 (.63–2.9)	.438
BMI: median vs lower tercile	.93 (.47–1.85)	.845	.54 (.24–1.24)	.147	.86 (.4–1.87)	.710
BMI: upper vs lower tercile	.86 (.43–1.72)	.665	.78 (.36–1.68)	.519	.88 (.4–1.91)	.743
Pain during current pregnancy (yes)	2.81 (1.58–4.99)	.000*	Not passed		2.07 (1.09–3.96)	.027*
History of miscarriage (yes)	1.94 (1.04–3.61)	.036*	Not passed		Not passed	
Postoperative complication (yes)	Not passed		3.81 (1.18–12.28)	.025*	Not passed	
History of neuropathic events (yes)	Not passed		Not passed		2.46 (1.26–4.77)	.008*
Final model: emotional distress‡						
Age: median vs lower tercile	.95 (.47–1.89)	.878	1.21 (.5–2.93)	.677	.78 (.33–1.85)	.578
Age: upper vs lower tercile	.77 (.38–1.56)	.472	1.72 (.74–4.01)	.206	1.52 (.68–3.4)	.303
BMI: median vs lower tercile	.84 (.42–1.69)	.628	.44 (.19–1.04)	.061	.72 (.32–1.62)	.426
BMI: upper vs lower tercile	.8 (.39–1.62)	.527	.67 (.3–1.48)	.318	.75 (.34–1.67)	.479
Pain during current pregnancy (yes)	2.6 (1.45–4.66)	.001*	Not entered		1.73 (.88–3.4)	.111
History of miscarriage (yes)	1.86 (.98–3.51)	.058*	Not entered		Not entered	
Postoperative complication (yes)	Not entered		3.98 (1.15–13.79)	.030	Not entered	
History of neuropathic events (yes)	Not entered		Not entered		2.81 (1.4–5.64)	.004*
Anxiety: median vs lower tercile	1.85 (.91–3.77)	.089	1.6 (.69–3.69)	.272	2.48 (1.08–5.74)	.033*
Anxiety: upper vs lower tercile	1.72 (.8–3.7)	.164	1.77 (.71–4.4)	.221	2.7 (1.06–6.87)	.038*
Depression: median vs lower tercile	.96 (.46–1.98)	.907	.9 (.35–2.32)	.828	1.15 (.48–2.74)	.759
Depression: upper vs lower tercile	1.41 (.7–2.83)	.338	1.98 (.87–4.51)	.103	1.78 (.78–4.08)	.171
Negative event in the past 6 months (yes)	.8 (.39–1.66)	.553	.75 (.31–1.81)	.520	.96 (.42–2.21)	.921
Final model: illness perception‡						
Age: median vs lower tercile	.88 (.44–1.73)	.705	1.11 (.46–2.65)	.820	.68 (.3–1.57)	.367
Age: upper vs lower tercile	.75 (.37–1.49)	.404	1.6 (.71–3.62)	.261	1.33 (.62–2.85)	.471
BMI: median vs lower tercile	.94 (.47–1.86)	.849	.53 (.23–1.2)	.128	.86 (.4–1.85)	.691
BMI: upper vs lower tercile	.87 (.43–1.74)	.684	.75 (.35–1.63)	.472	.88 (.41–1.91)	.748
Pain during current pregnancy (yes)	2.75 (1.54–4.93)	.001*	Not entered		2.12 (1.1–4.06)	.024
History of miscarriage (yes)	1.91 (1.02–3.55)	.042*	Not entered		Not entered	
Postoperative complication (yes)	Not entered		3.93 (1.21–12.71)	.023*	Not entered	
History of neuropathic events (yes)	Not entered		Not entered		2.45 (1.26–4.77)	.008*
Expected pain after cesarean: mild vs none	.92 (.43–2)	.837	.78 (.34–1.82)	.571	.78 (.33–1.81)	.556
Expected pain after cesarean: important vs none	1.32 (.63–2.77)	.455	.6 (.26–1.4)	.237	.87 (.38–1.96)	.733
Final model: coping strategies‡						
Age: median vs lower tercile	.9 (.46–1.77)	.758	1.14 (.48–2.71)	.761	.72 (.32–1.63)	.428
Age: upper vs lower tercile	.75 (.38–1.5)	.418	1.66 (.73–3.76)	.225	1.4 (.65–3)	.395
BMI: median vs lower tercile	.95 (.48–1.9)	.890	.6 (.26–1.39)	.233	.9 (.41–1.97)	.797
BMI: upper vs lower tercile	.87 (.43–1.75)	.690	.82 (.37–1.78)	.612	.9 (.41–1.95)	.784
Pain during current pregnancy (yes)	2.72 (1.53–4.85)	.001*	Not entered		2.05 (1.07–3.92)	.030*
History of miscarriage (yes)	1.95 (1.05–3.64)	.036*	Not entered		Not entered	
Postoperative complication (yes)	Not entered		3.72 (1.14–12.2)	.030*	Not entered	
History of neuropathic events (yes)	Not entered		Not entered		2.49 (1.28–4.86)	.007*
Catastrophizing: median vs lower tercile	.97 (.48–1.94)	.921	.67 (.27–1.66)	.390	.82 (.36–1.85)	.625
Catastrophizing: upper vs lower tercile	1.42 (.73–2.76)	.299	1.61 (.76–3.41)	.219	1.14 (.54–2.42)	.730
Final model: quality of life‡						
Age: median vs lower tercile	.9 (.45–1.8)	.770	1.19 (.49–2.86)	.705	.79 (.34–1.83)	.580
Age: upper vs lower tercile	.78 (.39–1.58)	.491	2.14 (.91–5.06)	.083	1.58 (.71–3.53)	.263
BMI: median vs lower tercile	.95 (.47–1.92)	.890	.58 (.25–1.35)	.203	.91 (.41–2.02)	.816
BMI: upper vs lower tercile	.86 (.42–1.73)	.664	.81 (.37–1.78)	.592	.9 (.41–1.98)	.789
Pain during current pregnancy (yes)	2.61 (1.43–4.78)	.002*	Not entered		2.08 (1.04–4.15)	.038*
History of miscarriage (yes)	1.98 (1.04–3.77)	.037*	Not entered		Not entered	
Postoperative complication (yes)	Not entered		4.83 (1.43–16.34)	.011*	Not entered	
History of neuropathic events (yes)	Not entered		Not entered		2.63 (1.32–5.25)	.006*
PCs: median vs lower tercile	.67 (.34–1.35)	.262	.51 (.2–1.28)	.149	1.17 (.51–2.69)	.719
PCs: upper vs lower tercile	.79 (.39–1.61)	.523	1.31 (.6–2.89)	.498	1.36 (.6–3.08)	.462

Table 2. Continued

Outcomes	PSPP At M3		PSPP M6		nPSPP Up To M6	
Models And Factors	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
MCs: median vs lower tercile	.67 (.34–1.32)	.245	1.04 (.48–2.28)	.920	.61 (.28–1.34)	.217
MCs: upper vs lower tercile	.37 (.18–.76)	.006*	.4 (.16–1)	.049*	.36 (.15–.82)	.016*

Abbreviation: BMI, body mass index; MCs, mental component summary (from the SF-36); PCs, physical component summary (from the SF-36).
NOTE. Three different outcomes were considered separately: PSPP at M3 and M6, and nPSPP up to M6.
*$P < .05$.
†In this model, factors had been tested previously by univariate analyses (χ^2 test) and selected under a .25 level of significance. The results shown here are those tested after a backward elimination procedure; the variable "use and time of use of locoregional anesthesia" was entered into the model but did not pass this last step.
‡In the four final models, a simple adjustment without selection has been conducted. Age, BMI (forced), and the two factors found predictive in the basic model have been added to the psychological factors to be studied.

proportion with neuropathic features. At M6, PSPP was less frequent (19%); it was mild in over 90% of cases and had neuropathic features in slightly more than half of cases. PSPP at M3 was more often related to painful neuropathy cases, most tended of which to resolve by M6 (see Fig 2). PSPP at M6 included more residual cases, with a greater propensity to develop chronic pain (especially if neuropathic).[2] The risk of nPSPP represents a propensity to develop neuropathic pain, whatever the spontaneous evolution (resolution or not, or late event occurrence). The cases of PSPP with a negative DN4 could be interpreted as related to residual inflammation, central sensitization,[22] or even neuropathy, as a result of the imperfect sensitivity of the DN4.[4] When the risk factor analyses are considered, the somatic predictors varied with the dependent outcome at M3. History of miscarriage, a somatic factor but with psychological consequences, influenced PSPP at M3 only, probably because fear of complicated childbirth or of miscarriage naturally tends to fade after the actual birth. Report of pain during the current pregnancy influenced both PSPP at M3 and nPSPP, and a relationship between preoperative pain and PSPP has been reported for various other surgeries.[1,3,5,6,12,29] At least two mechanisms may explain this: central sensitization/hyperalgesia (related or not to pregnancy) and obstetric factors that could have influenced the procedure. Unfortunately, these details were not reported in the current study so this cannot be investigated further. Postoperative complications influenced PSPP at M6, a relationship reported only once in breast cancer surgery (infectious complication).[14] This could be explained by a direct traumatic effect, but again the details are missing for a full explanation. This factor did not influence the occurrence of nPSPP, however, which argues against the role of a nerve lesion effect. The role of a psychological interaction, such as perceived injustice,[50] must also be stressed. It makes sense that a postoperative complication has more lasting effects than other factors. One of the most interesting results of the main study,[10] a previous history of a peripheral neuropathic event predicted the occurrence of nPSPP, thus argues for the role of a nerve fragility.

Focusing on the psychological predictors, only the mental component of quality of life was predictive of PSPP whatever the dependent outcome, with odds ratios (ORs) ranging from .36 to .4. This has been reported only once in prostatectomy,[13] but the fact of being single favored PSPP after breast cancer surgery.[14,38] In contrast, the analysis of emotional distress showed a significant effect of anxiety only on nPSPP, an effect also reported with PSPP after breast cancer surgery,[28] a highly neuropathic model.[17] However, this effect not surprisingly decreased with time, as illustrated by the ORs for PSPP at M3 and M6. The lack of statistical significance with these outcomes could be due to insufficient power, because the ORs were still greater than 1.5. In the abovementioned study, the OR for state anxiety was 1.06, and PSPP was studied only at M3.[28]

Risk Factors for PSPP: Other Studies of Cesarean Delivery

Three studies of risk factors for PSPP after cesarean delivery were identified in the literature. In a Dutch retrospective study (N = 690) of surgeries with a Pfannenstiel incision (90% of which were cesarean deliveries),[26] the factors associated with PSPP were numbness (an indicator of nerve lesion rather than a predictor), emergency cesarean delivery (excluded in the current study), and recurrent Pfannenstiel surgery (only if more than two incisions). This last covariate did not reach statistical significance in any of the basic models reported in the current study, although it was reported in more than half of patients; the difference could be due to insufficient detail of the number of previous cesarean deliveries. Another retrospective study (N = 857) undertaken in Singapore identified the following predictors: higher early postoperative pain, pain present elsewhere, and nonprivate insurance status.[42] Early postoperative pain has often been included in analyses to predict PSPP, but this was intentionally not used here, because the aim was to identify real risk factors (i.e., predisposition before the postoperative time begins), not just components of a predictive score. This may be a bias, because early postoperative pain in some cases might just be an early expression of PSPP; also, the effect of this factor is generally strong[28] and could blunt the effect of other factors. Pain present elsewhere was included in our variable preoperative pain, which did not pass in the basic models. Insurance

status is irrelevant in France where cesarean delivery is systematically funded by the social security system. In a recent Swedish study ancillary to a clinical trial (N = 260), persistent pain was significantly favored by a first cesarean delivery, a psychological indication (maternal request), and early postoperative pain[31]; however, the location of pain (at the site of surgery or elsewhere) was not considered in the analyses. The authors stressed, however, that the indications for cesarean delivery may vary with the setting, which is supported by a lower rate of psychological indications in France than in Sweden.[48] To this debate must be added one prospective study that focused on early postoperative pain after elective cesarean delivery and identified hearing sensitivity, emotional distress (anxiety), and illness perceptions (anticipated pain and pain medication usage) as risk factors.[35] Links between early and persistent postoperative pain are suggested.[1,36,37,46]

Risk Factors for PSPP: Cesarean Delivery Versus Hysterectomy

Despite differences in the tools used to explore a given domain, comparing studies of psychological preoperative risk factors is facilitated by the validity of tools that have been in use for many years.[47] To allow the current study to be compared with that of Pinto et al,[39] which analyzed 186 women undergoing hysterectomy due to benign causes and surveyed at the fourth month after surgery, similar models were produced for our analyses. On the basis of a 50% risk of reported PSPP, Pinto et al[39] first identified the type of surgery (open abdominal or Pfannenstiel) as a main risk factor, but this analysis was irrelevant in our study, as this was not a variant in cesarean delivery. They also found age to be a mild protecting factor; this was unlikely to show an effect for cesarean delivery because of the low variability in age. Contrary to our study, pain due to other causes was predictive in all the final models. This difference may be due to a lower exposure to central sensitization in the pregnant population. In the current study, very few psychological predictors, with the exception of low mental quality of life, were found to be predictive, whereas Pinto et al[39] found anxiety, emotional illness representation, and catastrophizing to be predictors, although no OR exceeded 1.8 (quality of life was not studied). The difference between the two studies may be primarily explained by the surgery and its related context. Due to different assessment tools, the baseline psychometric values between studies cannot be compared, except for anxiety on HADS, which seemed similar (for cesarean and hysterectomy: median 8 vs 7, range 1–18 vs 0–19, respectively). Although pain catastrophizing was expected from the literature to be predictive,[45] the only result of note was that the baseline values were similar in this cesarean subcohort to those in pooled surgeries (mean Pain Catastrophizing Score 14.0 vs 14.5),[10] and in which the effect was found to be significant. To summarize, a lower effect of preoperative psychological factors in cesarean delivery may not be due to a lower variability at baseline but to a lesser sensitivity to the psychological aspects of PSPP. A protective effect of the postoperative context of childbirth may have interacted.

Conclusions

The results of the current study provide information about PSPP after cesarean delivery, but larger cohorts with longer follow-up are needed, not excluding emergency procedures. More details about the surgical technique are also needed, as well as preventive trials testing nerve-protective surgical strategies or drugs. The influence of the surgical model on the risk factors of PSPP is highlighted, and such interaction should be considered if scales predicting PSPP are to be developed in the future.

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Supplementary data

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