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Online Exclusive

# Neuropathic Aspects of Persistent Postsurgical Pain: A French Multicenter Survey With a 6-Month Prospective Follow-Up

Christian Dualé,[*,†,‡] Lemlih Ouchchane,[§,||,¶] Pierre Schoeffler,[‡,§,**] the EDONIS Investigating Group[1], and Claude Dubray[*,†,‡,§]

**CHU Clermont-Ferrand, Centre de Pharmacologie Clinique, Clermont-Ferrand, France.*
*†Inserm, CIC 501, Clermont-Ferrand, France.*
*‡Inserm, U1107 "Neuro-Dol," Clermont-Ferrand, France.*
*§Univ Clermont1, Clermont-Ferrand, France.*
*||CHU Clermont-Ferrand, Pôle Santé Publique, Clermont-Ferrand, France.*
*¶CNRS, ISIT, UMR6284, Clermont-Ferrand, France.*
***CHU Clermont-Ferrand, Pôle Anesthésie-Réanimation, Hôpital Gabriel-Montpied, Clermont-Ferrand, France.*

**Abstract:** **To investigate the role of peripheral neuropathy in the development of neuropathic postsurgical persistent pain (N-PSPP) after surgery, this French multicentric prospective cohort study recruited 3,112 patients prior to elective cesarean, inguinal herniorrhaphy (open mesh/laparoscopic), breast cancer surgery, cholecystectomy, saphenectomy, sternotomy, thoracotomy, or knee arthroscopy. Besides perioperative data collection, postoperative postal questionnaires built to assess the existence, intensity, and neuropathic features (with the Douleur Neuropathique 4 Questions [DN4]) of pain at the site of surgery were sent at the third and sixth months after surgery. In the 2,397 patients who completed follow-up, the cumulative risk of N-PSPP within the 6 months ranged from 3.2% (laparoscopic herniorrhaphy) to 37.1% (breast cancer surgery). Pain intensity was greater if DN4 was positive and decreased with time since surgery; it depended on the type of surgery. In pain-reporting patients, the response to the DN4 changed from time to time in about 1:4 of the cases. Older age and a low anxiety score were independent protective factors of N-PSPP, whereas a recent**

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CHU Clermont-Ferrand, Centre de Pharmacologie Clinique (Inserm CIC 501), F-63003 Clermont-Ferrand, France.

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Address reprint requests to Christian Dualé, MD, PhD, Centre de Pharmacologie Clinique – CIC, Hôpital Gabriel Montpied, CHU de Clermont-Ferrand, Rue Montalembert, BP69, 63003, Clermont-Ferrand Cedex 1, France. E-mail: cduale@chu-clermontferrand.fr

[1] The following are members of the EDONIS Investigating group: Coordinating clinical research assistant: Sylvie Soule-Sonneville, CHU Clermont-Ferrand. In-hospital investigation and coordination: Christophe Decoene, CHU Lille (StT); Denis Baylot, Clinique Mutualiste Chirurgicale Saint-Etienne (KnA); Danièle Lefebvre-Kuntz, Centre Oscar-Lambret, Lille (BKS); Patrick Reynier, CHU Bordeaux (ThT); Brigitte Sokolo, CHG Le Puy en Velay (Saph); Patrick Niccolaï, CH Princesse Grâce de Monaco, Principauté de Monaco (IHR-OM); Aline Albi-Feldzer, Centre René-Huguenin, Saint-Cloud (BKS); Monique Belon, CHG Aurillac (IHR-OM, Saph); Hammou Taheri, CHU Clermont-Ferrand (ThT); Michel Delecroix, CHU Lille (KnA); Ourdia Hadjali, Hôpital Européen Georges Pompidou, Paris (CcE, StT, ThT); Céline Biermann, CHU Strasbourg (CcE, IHR-OM); Bertrand Nougarède, Centre Jean-Perrin, Clermont-Ferrand (BKS); Brice Richez, CHU Bordeaux (Ces); Fayçale Beouche, CHU Nice (IHR-OM); Bilal El Drayi, CHG Thiers (CcE, IHR-OM, Saph); Christiane Hercule, HC Lyon (StT, ThT); Maurice Libier, Clinique de La Louvière, Lille (IHR-L); Pascal Duchêne, Clinique de la Pergola, Vichy (IHR-OM, KnA); Jean-Marc Vedrinne, Clinique du Tonkin, Villeurbanne (IHR-L); Martine Bonnin, CHU Clermont-Ferrand (Ces); Jacques Desbordes, CHU Lille (ThT); Marc Raucoules-Aimé, CHU Nice (CcE); Vedat Eljezi, CHU Clermont-Ferrand (StT); Bertrand Guillot, CHU Saint-Etienne (ThT); Yves Noudem, CHU Strasbourg (Ces); Albane Legrand, CHU Lille (Saph); Fabienne Monier, HC Lyon (CcE); Thierry Therre, Clinique de la Chataigneraie, Beaumont (Saph); Emmanuelle Schaack, Hôpital Ambroise-Paré, Boulogne-Billancourt (Saph); Laurent Vallet, CHG Riom (IHR-L); Franck Ruiz, CHG Vichy (IHR-OM); Virginie Cognet, HC Lyon (Ces); Marie-Christine Crosmary, CHG Vichy (CcE); Anne-Frédérique Dalmas, CHU Lille (Ces); Nathalie Chalons, CHU Lille (CcE); Marie-Noëlle Falewee, Centre Antoine-Lacassagne, Nice (BKS); Lise Brisebrat, CHG Roanne (Ces); Claudine Chirat, CHG Montluçon (IHR-L); Nicolas Jérémie, CHG Vichy (KnA); François Mirault, Clinique de la Chataigneraie, Beaumont (Ces). Abbreviations for each subcohort; BKS: breast cancer surgery; CcE: cholecystectomy; Ces: cesarean section; IHR-L: inguinal herniorrhaphy (laparoscopic); IHR-OM: inguinal herniorrhaphy (open mesh); KnA: knee arthroscopy; Saph: saphenectomy StT: sternotomy; ThT: thoracotomy.

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**negative event, a low preoperative quality of life, and previous history of peripheral neuropathy were risk factors. The type of anesthesia had no influence on the occurrence of N-PSPP. Trial registration: ClinicalTrials.gov, NCT00812734.**

***Perspective:** This prospective observational study provides the incidence rate of N-PSPP occurring within the 6 months after 9 types of elective surgical procedures. It highlights the possible consequences of nerve aggression during some common surgeries. Finally, some preoperative predispositions to the development of N-PSPP have been identified.*



***Key words:** Chronic pain, postoperative, DN4, complications, nerve lesion.*

Postsurgical persistent pain (PSPP) has frequently been reported in the literature.[16,38,43] Although this fact is now well identified for some types of surgery, there is a need for more precise information such as level of risk (especially for frequently performed procedures), intensity, and time course. The role of neuropathy needs also to be better identified, as there is growing evidence that it is one of the main mechanisms in the development of PSPP. Such a role is supported by 1) anatomic (ie, some surgeries are likely to harm nerves),[8,61] 2) semiological (ie, neuropathic aspects have been reported in patients suffering from PSPP),[13,26,46] and 3) exploratory arguments (ie, peripheral nerve dysfunction has been noted after certain surgeries).[3,20,29]

The present study ("EDONIS") is a prospective epidemiologic multicentric study of PSPP. Only certain surgical procedures were included in the project, and each procedure represented a subcohort of the whole cohort. The types of procedures were chosen to achieve 2 goals in parallel: 1) to give a precise estimate of the risk of PSPP and its neuropathic components following frequent procedures, where this the information was incomplete, and 2) to be able to conduct an analysis in which predictive factors of the occurrence of neuropathic PSPP (N-PSPP)—whatever the type of surgery—could be identified. Then, some other surgical procedures (such as thoracotomy, breast cancer surgery, and inguinal herniorrhaphy) were considered because they were already identified as inducing frequent, and often neuropathic-like, PSPP.[1,13,46,57,64] The other procedures were chosen on the basis of case series of PSPP, or anatomic arguments for a nerve lesion during a procedure. These were sternotomy,[13,34,45] cesarean section,[50] cholecystectomy,[9] saphenectomy,[13] and knee arthroscopy.[47,73] For inguinal herniorrhaphy, it was estimated at the conception of the study that 3 types of procedures (ie, open meshless, open mesh, and laparoscopic) were equally represented in the French practice, and each represented a different cohort instead of pooling the 3 procedures. For cholecystectomy, only the laparoscopic procedure was considered, as this technique was by far the most practiced in France. The primary endpoint was to estimate the risk of N-PSPP within the 6 months following surgery. Another important endpoint was to identify risk factors of N-PSPP. To improve power and therefore predictability, the risk factor analysis was performed by pooling the different surgeries, a method used previously in risk factor analysis of PSPP.[6,30]

# Methods

## Organization

This prospective observational study was approved by the appropriate institutional review boards (CCPPRB d'Auvergne and CPP Sud-Est VI for amendments) and declared on ClinicalTrials.gov (ref. NCT00812734). The steering committee made up of the authors and a coordinating clinical research assistant (CRA) designed the study with the help of scientific collaborators, regularly followed the pattern of inclusions, and could decide to recruit new centers if necessary. It was helped by a French network of regional coordinators, each head of a Department of Anesthesia at a regional University Hospital, who contacted other sites. A regional CRA was appointed to monitor the quality of the research at each site, to mail the questionnaires, and to keep contact with the coordinating CRA. One coordinating investigator was appointed at each site.

## Study Sample

The study sample consisted of all patients over 18 years of age scheduled in a recruitment center for one of the selected procedures (Table 1). To avoid inclusion bias, consecutive recruitment was required, and off-inclusion periods were defined by the coordinating CRA when centers were unable to include patients because of local constraints.

## Data Collection

All the questionnaires are detailed in the Appendix. The inclusion visit was undertaken by the anesthetist at the preanesthetic visit (1–2 weeks before surgery). After providing information and obtaining verbal consent, the patient was given a preoperative questionnaire about his or her working activities and history of previous pain. The anesthetist completed the preoperative part of the medical data sheet, including the patient's demographic data, potential symptoms of peripheral neuropathy, and possible risk factors for peripheral neuropathy. On discharge from the surgical ward, he or she completed the peri- and postoperative parts of the medical data sheet concerning general and/or locoregional anesthesia, per- and postoperative analgesia, and possible early complications.

If surgery had been completed as planned, the inclusion was confirmed to the regional CRA, who posted a questionnaire to the patient at the third and the sixth months after surgery, to be returned to the