

Effect of Axillary Lymph Node Dissection on Prevalence and Intensity of Chronic and Phantom Pain After Breast Cancer Surgery

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Abstract: Chronic pain after breast cancer surgery is a major problem and is expected to increase in the coming years because of an increased prevalence of breast cancer coupled with better survival. Axillary lymph node dissection (ALND) in patients with breast cancer is associated with nerve damage. The present study investigated the effect of ALND on the prevalence and intensity of chronic pain after breast cancer surgery. Furthermore, we studied the effect of chemotherapy and radiotherapy on chronic pain and the quality of life after breast cancer surgery. We analyzed 317 questionnaires of patients who underwent surgery for breast cancer between 2002 and 2004. In the first part, questions were asked concerning the prevalence of chronic pain, its intensity (visual analog scale), and phantom breast pain. The second part covered quality of life and included the EORTC QLQ-C30/BR-23. The prevalence of chronic pain after breast cancer surgery with ALND is double that without ALND (51% vs 23%). Chronic pain intensity and prevalence of phantom breast pain were not influenced by ALND. Chemotherapy and radiotherapy in interaction with ALND were associated with increased prevalence of chronic pain. The quality of life in patients was mainly affected by chronic pain and to a lesser extent by type of surgery.

Perspective: Nerve injury is particularly efficient at producing central sensitization. ALND in conjunction with breast cancer surgery is associated with a doubled prevalence of chronic pain, which has not been described to date. ALND and nerve injury may play a major role in pain chronification after breast cancer surgery.

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Key words: Chronic pain, neuropathic pain, postoperative pain, visceral pain, screening questionnaires, thoracotomy, video-assisted thoracotomy (VATS).

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Chronic pain after breast cancer surgery is increasingly recognized and reported. The population at risk will increase in the coming years because of increased breast cancer prevalence and survival rates.^{20,40} Numerous investigators have reported chronic pain prevalences after breast cancer surgery, with results between 20% and 56% according to study design and quality.^{2,11,12,18,28,32,41,43,45,46,49}

Nerve injury is particularly efficient at producing the central sensitization and hyperalgesia associated with chronic neuropathic pain^{6,16,24} and chronic pain in general^{6,47,51} and is at present considered the most important single factor for chronic pain after surgery.^{24,50} The presence of neuropathic components in chronic pain syn-

dromes is associated with poor prognosis; thus its presence in low back pain correlates with more intense pain, more severe comorbidity, and poorer quality of life.¹⁵ Nerve damage plays an important role in pain after breast cancer operations, with neuropathic pain being the most prevalent type of chronic pain thereafter.²² This is because major nerves trespass the surgical field in axillary lymph node dissection (ALND), making it a surgical procedure in which nerve damage is easily caused as a precondition for subsequent development of chronic pain. However, to date the effect of ALND on chronic pain after breast cancer surgery has not been formally studied, because most prevalence studies of chronic pain included only patients with ALND.

The quantified degree of nerve damage after thoracotomy correlates with pain intensity 1 month after surgery, suggesting a causal role for nerve damage in chronic postoperative pain.⁸ In patients with chronic pain after breast cancer surgery with ALND, psychophysical testing near the scar shows increased evoked pain intensity after repetitive pinprick stimulation, suggesting central sensitization.¹⁶ Pain-free patients do not show this phenomenon. The decreased risk of developing chronic pain after breast cancer surgery in a high-volume surgical unit supports this idea: More experienced surgeons can be expected to cause less nerve damage.⁴⁵ Further support accrues from studies showing less morbidity in general and better quality of life in breast surgery patients without ALND (eg, only sentinel lymph node biopsy) compared with ALND.^{28,29,31,35,36,38,39,44} Phantom breast pain is well described after mastectomy, with a broad range (1%–53%) of reported prevalences.^{13,26,34,37} Central sensitization and cortical reorganization, considered to have an important role in pain chronification, also play an important part in the genesis of phantom pain, again associated with nerve damage.¹⁴ The influence of ALND on phantom breast pain has not been described.

The primary aim of the present study was to investigate the effect of ALND, as a surrogate for nerve damage, on the prevalence and intensity of chronic postsurgical pain, the prevalence of phantom breast pain, and its impact on the quality of life. A secondary aim was to explore effects of radiotherapy and chemotherapy, both associated with further nerve damage, on chronic pain development after breast cancer surgery with and without ALND.

Materials and Methods

Patient Selection

We investigated women undergoing surgical treatment for breast cancer in the Canisius Wilhelmina Hospital (CWZ), Nijmegen, The Netherlands. The study was conducted in March 2005 and included all 495 patients undergoing breast cancer surgery in the period January 2002 to July 2004. We chose this time interval to ensure that patients could remember their pain and to cover a minimum postoperative period of 6 months. The surgical

procedures included (1) lumpectomy without ALND (including sentinel node dissection), (2) mastectomy without ALND, (3) lumpectomy with ALND, and (4) mastectomy with ALND.

Definition

Chronic pain was defined as “pain persisting continuously or intermittently for more than 3 months after surgery” as per the International Association of Study of Pain.¹⁹ Phantom breast pain was defined as painful sensations experienced in the (partially) amputated breast.

Study Procedures

The ethical committee CMO (commissie voor mensgebonden onderzoek [human research commission]) region Arnhem-Nijmegen approved the study. Patients were sent a questionnaire with a cover letter and a stamped, addressed reply envelope, followed by a telephone reminder if there was no response within 4 weeks. Informed consent was also requested for viewing the patients’ medical records.

Study Questionnaire

The study questionnaire used consisted of 2 parts. The first part included 19 questions concerning pain due to the breast cancer surgery present at the time of answering the questionnaire. Questions were asked concerning the intensity visual analog scale (VAS), character (stinging, burning, nagging, and phantom) and the location of pain. We also asked about other pain disorders and the use of medication for pain. The second part covered quality of life and included the Dutch version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 and the module BREast-23 (EORTC QLQ C30 and BR-23)⁴² and the Dutch version of Concerns About Recurrence Scale (CARS).⁴⁸ The first 2 self-report questionnaires are for measuring health-related quality of life. The EORTC QLQ-C30 and BR-23 questionnaires are internationally validated with an integrated modular approach for evaluating quality of life in several areas of daily living¹ and symptoms and side effects related to different treatment modalities, body image, sexuality, and future perspective.⁴² The internationally validated CARS systematically assesses the extent and nature of women’s fears about the possibility of breast cancer recurrence,⁴⁸ which can negatively influence quality of life.³⁰

Patient’s Medical Record Study

Patients’ medical records were studied after obtaining written informed consent and sought to identify factors contributing to chronic pain development. The following data were obtained: (1) Date of surgery, (2) date of birth, (3) postoperative complications, for example, wound infections, secondary hemorrhage, and hematomas, (4) supplementary therapy, for example, radiotherapy and chemotherapy, (5) reoperation due to tumor in resection border, (6) type of surgery, (7) presence or ab-

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