EUROPEAN JOURNAL OF CANCER 45 (2009) 1560–1568

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

Review

Late morbidity associated with a tumour-negative sentinel lymph node biopsy in primary breast cancer patients: A systematic review

Chao-qian Liu[a], *Yan Guo*[b], *Jun-yi Shi*[a], *Yuan Sheng*[a,*]

[a]*Department of Breast Surgery, Changhai Hospital, Second Military Medical University, No. 168 Changhai Road, Shanghai 200433, China*
[b]*Department of Internal Medicine, Changhai Hospital, Second Military Medical University, Shanghai 200433, China*

ARTICLE INFO

Article history:
Received 10 October 2008
Received in revised form 23 January 2009
Accepted 11 February 2009
Available online 13 March 2009

Keywords:
Breast neoplasms
Sentinel lymph node biopsy
Axillary lymph node dissection
Morbidity
Systematic review

ABSTRACT

Aims: To evaluate the relationship between late morbidity (i.e. ≧6 months) and a tumour-negative sentinel lymph node biopsy (SLNB) in primary breast cancer patients by using a systematic review approach, and to identify the predictors of late morbidity.

Methods: We performed a systematic review of the literature for studies concerning the late morbidity of patients who had undergone SLNB alone or SLNB followed by ALND when SLN metastases were found. A literature search over the last 16 years (1993–2008) was performed in the databases MEDLINE and EMBASE. The methodological quality of the selected studies was assessed according to a list of predefined criteria. The data of assessment and predictors of late morbidity were collected.

Results: We identified a total of 32 papers reporting 27 independent cohort studies, of which 17 were high quality studies and were further analysed in this review. There was a great variation in the prevalence of pain (7.5–36%), impairment of range of motion (0.0–31.0%), oedema (0.0-14.0%), decreased strength (11.0–19.0%) and sensory disorders (1.0–66.0%). Factors such as time after surgery and young age were strong predictors of late morbidity. Breast surgery, radiation to axilla, tumour location, body mass index (BMI) and two-step procedure, especially lymph mapping techniques, could also predict the late morbidity to different extents.

Conclusions: SLNB-associated late morbidity, even with a low prevalence, remains a clinical problem which cannot be neglected in primary breast cancer patients. Time after surgery and young age are the important predictors for late morbidity in primary breast cancer patients after SLNB; breast surgery, radiation to axilla, tumour location, BMI and two-step procedure also have limited prognostic value.

1. Introduction

Sentinel lymph node biopsy (SLNB), first reported by Krag et al. using radio-guided technique,[1] is now widely used as a safe and effective procedure after routine axillary lymph node dissection (ALND) in patients with early breast cancer.[2] SLNB has been proven to be feasible and accurate to improve the staging of the axilla.[3–5] A recent meta-analysis of 69

* *Corresponding author:* Tel./fax: +86 21 25074875.
E-mail address: shengyuan.smmu@yahoo.com.cn (Y. Sheng).
0959-8049/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejca.2009.02.012

studies (comprising 8059 SLNB procedures) demonstrated the rapid and widespread acceptance of SLNB as a minimally invasive alternative to stage the axilla.[6] Furthermore, many long-term studies have proven that the prevalence of axillary recurrences after negative SLNB was much lower than expected.[7–10] Another meta-analysis reported that the axillary recurrence rate after a tumour-negative SLNB in breast cancer patients was 0.3%, and the sensitivity of SLNB was 100%.[11] Reportedly, the survival of patients following SLNB was equivalent to that of patients following ALND.[2,12]

SLNB also results in less upper limb morbidity since it can reduce unnecessary ALND that may result in considerable arm morbidity. Several papers have reported that SLNB was associated with reduced morbidity and better quality of life compared with standard ALND procedure.[13–16] However, it is not clear how strong the relationship is between late morbidity (pain, lymphoedema, range of motion, loss of strength and sensory disorders) and SLNB alone. As late morbidity may interfere with activities of daily life (ADL) and quality of life (QOL),[17–19] recently the SLNB-associated late morbidity has drawn increasing attention despite its safety and accuracy. Prevalence of late morbidities after SLNB, including pain, lymphoedema, range of motion, loss of strength, and sensory disorders, was found to be variable in different studies, probably due to differences in study population, surgical procedures and assessment methods.[20] Thus, the primary aim of this systematic review is to identify the prevalence of the late morbidity after SLNB alone by evaluating the results of relevant studies, and also to discuss the predictors of late morbidity after SLNB.

2. Methods

2.1. Search strategy

A computerised search of the literature was performed in databases MEDLINE and EMBASE from 1993 to May 2008. A search strategy that combined disease-specific search terms (e.g. 'breast neoplasms'), the axillary management-class terms (e.g. 'SLNB') and terms related to treatment outcomes (e.g. 'morbidity', 'pain', 'range of motion', 'oedema', 'lymphoedema', 'muscle strength' and 'sensory disorders') or quality of life (e.g. 'well-being', 'activities of daily living', 'QOL' and 'ADL'). The search strategy employed relevant medical subject headings (MeSH) and Excerpta Medica Tree (EMTREE) terms as well as text words. We used the search terms simultaneously by 'OR' and combined them with 'AND' in the syntax of the databases. The reference lists/bibliographies of relevant papers/books were also hand searched for additional citations.

2.2. Selection criteria

The abstracts of publications which were found were screened and selected by the first author (Liu CQ) on the basis of the following criteria:

1. The patients must have primary clinical node-negative breast cancer, must not have received neoadjuvant therapy and not be pregnant.
2. All patients in the study group must receive sentinel lymph node biopsy. The cancer treatment must either be a modified radical mastectomy or be a breast-conserving therapy (BCT) alone or in combination with radiotherapy and/or chemotherapy/endocrine therapy.
3. Late morbidity of the SLNB group must be studied with a more than six-month follow-up after the surgical treatment.
4. The author must provide the data of the late morbidity after SLNB (measurement or percentage).

All articles meeting our four criteria were included in the present analysis. The criteria were applied independently by the two reviewers (LIU CQ and GUO Y) to the full text of the articles that had passed the first eligibility screening. In case of disagreement, a consensus was reached by means of discussion. When the disagreement persisted, a third

Table 1 – Criteria list for assessing the methodological quality of studies on post-SLNB morbidity of breast cancer patients.

Criteria
A. Socio-demographic and medical data are described (e.g. age, sex, tumour stage at diagnosis and menopausal status).
B. There is a clear statement of inclusion criteria or exclusion criteria for the study population.
C. The process of data collection is described (e.g. physical examination, interview and self-report).
D. A clear description of cancer treatment strategy is described (e.g. breast surgery, chemotherapy, radiation therapy and hormone therapy).
E. The study design is randomised.
F. The study size has to be more than 100 patients.
G. The results are compared between two groups or more groups (e.g. SLNB versus ALND and SLNB versus SLNB + ALND).
H. Mean or median and range or standard deviation of time since diagnosis or treatment are given.
I. Participation and response rates for patient groups have to be described and have to be more than 75%.
J. Information on patient/disease characteristics of dropouts is presented.
K. The measurement instrument to assess morbidity or quality of life has been reported by the authors or has been established in studies cited by the authors.
L. More than one type of symptoms associated with post-SLNB morbidity is assessed in the results.
M. Besides physical morbidity, results are also described for additional assessment (e.g. quality of life, activities of daily life and the psychological or social domain).
N. Frequencies of the most important outcome measures are presented.
O. Data are presented for clinically relevant prognostic factors of late morbidity after SLNB.
P. Informed consent is obtained from all participants before study.