Reviewer's report

Title: The Role of Major Duct Excision in the Detection of Breast Carcinoma.

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Reviewer: Neslihan Cabioglu

Reviewer's report:

General
The manuscript submitted by Dillon et al. reports a cohort of 211 patients who were operated with a diagnosis of nipple discharge using the major duct excision procedure or lacrimal probe guided surgery. They investigated the risk factors including patient and discharge characteristics associated with cancer. However, there are several important points to be reconsidered in the study design and in the manuscript to be clarified.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1) They presented the histopathologic diagnosis of lesions of the surgical excisions in Table 3. Of note, there are so many patients diagnosed with benign lesions and duct ectasia who could be followed without any surgical excision in this large series. Therefore, two important comparisons could be made from this cohort to answer the questions who could be identified with the diagnosis of cancer or other specific lesions for nipple discharge (papilloma, ADH, LCIS) to justify the surgical approach and who could be followed without any surgery. First, they could compare the patients with cancer (n=9) with other patients (n=202) as they did in Table 1. Second, they could compare the patients with benign lesions (benign/nonspecific lesions, n=60; duct ectasia, n=51; total, n= 111) with other patients with specific lesions as a cause for nipple discharge (papilloma, n=86; cancer, n=9; ADH/LCIS, n=5; total, n=100) in terms of patient and nipple discharge characteristics. Furthermore, according to the AJCC TNM classification of breast cancer, LCIS has been considered as T in situ carcinoma because of the difficulty to distinguish the pleomorphic LCIS from the classic type of LCIS. Therefore, either the authors should state that the LCIS lesions are all classic type LCIS or they should consider LCIS as malignancy by stating that they used the AJCC 2003 criteria seperating the LCIS from ADH lesions and including those lesions into the malignancies. It might be easier to make these comparisons in 2 separate tables and all the p values should be exactly given even though they are not significant. Nipple discharge characteristics such as spontaneous vs evoked, unilateral vs bilateral, single duct vs multiduct, bloody vs non-bloody, Clear/serous vs other, brown/black vs other, green/milky vs other, cytology findings (abnormal vs normal), mammographic findings (abnormal vs normal), and ultrasonographic findings (abnormal vs normal) should be also investigated in these tables. As a result of these analyses, more interesting findings could be obtained from this study.
2) In the results section, they should give the period when the patients returned to the clinic with recurrent discharge. They should also clarify whether those 3 patients diagnosed later with cancer had also recurrent nipple discharge.

Furthermore, the recurrence rate of nipple discharge by using the major duct excision and microdochectomy procedures, is very high in this series along with the high rate of benign/nonspecific lesions in the histopathologic diagnosis. It is known that a histopathologic etiology is not always found on major duct or lacrimal-probe guided excision, which raises the possibility that the causative lesion might have been left in situ as found by several studies. Therefore, diagnostic ductography allows preoperative determination of location, and extent of any underlying lesions for nipple discharge. It is also known that preoperative use of ductography with methylene blue injection to localize lesions has been shown to increase the likelihood that a specific
pathologic lesion will be found at surgery. The authors should discuss these issues in the discussion by giving more references in this subject in the discussion section even though ductography is not their practice (their references 3 and 7, and Van Zee KJ, Perez GO, Minnard E, Cohen MA. Preoperative galactography increases the diagnostic yield of major duct excision for nipple discharge. Cancer 1998; 82: 1874-1880).

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1) In comparison analyses (Table 1), the ranges (the min and max values) should be given for ages along with the median values in parentheses. All abbreviations should be defined clearly in the tables such as NS (not significant).
2) Major duct excision and lacrimal probe guided surgery are 2 different surgical procedures that were performed in these study. In the lacrimal probe guided surgery (microdochectomy), only the affected duct was excised whereas all the ducts were excised in the major duct excision technique. Therefore, the title and the abstract should be corrected as using a more general terminology such as “The role of surgical approach in the detection of breast carcinoma in patients with nipple discharge”. The major duct excision in the abstract should be replaced by “surgical procedures including microdochectomy or major duct excision”.
3) In the results section and 1st paragraph, they stated that 9 patients were incompletely categorised. They should clarify the discharge characteristics of these patients and why they defined them as incompletely categorised.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
I declare no competing interests.