The Effect of Ductoscopy in the Surgical Selection of Patients with Pathological Nipple Discharge

Kenan Çetin

Objective: Surgical excision of the ductus is the current conventional means of treatment and diagnosis of pathological nipple discharge (PND). However, a review of the histopathology results of cases of routine duct excision reveals that a large number of unnecessary surgical interventions are performed. The aim of this study was to determine the rate of lesion detection after a ductoscopic evaluation in patients who underwent surgery.

Methods: Between November 2005 and December 2010, a microductectomy was performed following a ductoscopic evaluation for 129 patients who were admitted to our clinic with PND. The characteristics of the discharge, and the ductoscopic and pathological findings were assessed.

Results: The final pathology results confirmed lesions in 76% of the patients (85/112) who underwent surgery based on only ductoscopic findings. Seventeen patients with ductoscopic findings who were operated on based on the findings of a physical examination and classical imaging methods could be followed up. Lesions were detected in 11 (6 potential neoplastic and malignant lesions, 5 papillomatous lesions).

Conclusion: The results of this study indicate that ductoscopy appears to predict the patients who will require surgical treatment and so can decrease the number of operations. However, conventional imaging and physical examination findings of patients should also be considered in the follow-up after ductoscopy in PND patients.

ABSTRACT

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INTRODUCTION

Intermittent or continuous nipple discharge is the third most frequent (up to 10%) reason for women to present at medical facilities with complaints of the breast after breast pain and mass. The reason for most nipple discharge is physiological.[1,2] Pathological nipple discharge (PND) is described as spontaneous, unilateral, hemorrhagic, serohemorrhagic, and serous exudate from a single duct apart from pregnancy and lactation.[3–5] The most common cause of nipple discharge is a benign breast lesion, such as a solitary intraductal papilloma or papillomatosis.[6] However, an important cause of PND is breast cancer, which constitutes between 5% and 21% of cases.[6,7]

Imaging methods play an essential role in the diagnostic approach to PND, following complete anamnesis and physical examination. The classical modalities preferred are mammography, ultrasonography (USG), magnetic resonance imaging (MRI), cytology of discharge smear, fine-needle aspiration biopsy, and core biopsy. Mammography and USG have a low sensitivity for detecting small intraductal lesions.[6] MRI may not always be successful in determining all intraductal neoplasms.[6,10]

Galactography offers an indirect view of the milk ducts, while ductoscopy can provide direct visualization. The combined use of these imaging modalities may increase the reliability of the diagnosis, but may nonetheless be inadequate. Therefore, the general approach used to create a definitive diagnosis for women with PND is ductal excision.[11,12] Although it has not yet been accepted all over the world, the recognition of the value of breast ductoscopy is increasing worldwide as a new method that can help to investigate nipple discharge.[13,14]

Ductoscopy is the use of an endoscope to image breast milk ducts in patients with nipple discharge. It provides a direct view of the inside of the ducts and it is possible to evaluate and locate epithelial abnormalities and lesions. In addition, intraductal polypoid lesions can be excised endoscopically through the working channel of the endoscope.[13] Although ductoscopy is currently performed in a limited number of centers, a consensus has not yet been reached concerning interpretation of the findings.[14,17]
Studies are underway to evaluate its place in the diagnosis and treatment nipple discharge.

The aim of this study was to retrospectively compare the results of ductectomy and postoperative surgical pathology results in patients whose indication for surgical treatment was based on preoperative examination, conventional imaging, and ductoscopy findings.

MATERIAL AND METHODS

Between November 2005 and December 2010, 129 patients with nipple discharge who underwent a ductectomy and an isolated duct excision performed by the general surgery department of the Okmeydani Training and Research Hospital were included in the study. The nipple discharge characteristics of the patients, the ductoscopic findings and demographic details were retrospectively obtained and analyzed. The study protocol was approved by the Okmeydani Training and Research Hospital’s ethics committee, and all patients provided written informed consent before ductoscopy and surgery.

The standard approach in patients with at least 2 criteria of PND was a complete mammography (though not preferred in patients under 40 years of age) followed by a physical examination, breast ultrasonography, ductoscopy, and ductal lavage cytology. Patients with only a single criterion of PND were evaluated with a physical examination and conventional imaging.

Patients with no significant findings from the ductoscopy and normal physical examination, conventional imaging and lavage cytology results in terms of intraductal lesion are routinely followed up in our clinic. Surgical intervention is recommended for all other patients (i.e., for those with positive ductoscopic findings and/or suspect physical examination, conventional imaging or cytology findings with persistent nipple discharge).

The ductoscopic images were evaluated according to findings of a normal appearance, changes in ductal calibration (ductal stenosis or ectasia), intraluminal secretion or debris, lesion, ductal epithelial color changes, irregular intraluminal mass, ductal wall irregularities, solitary papilloma (SP), or multiple papillomas (MP). Based on the pathology results, lesions were classified as papillomatous lesions, atypical ductal hyperplasia (ADH), ductal carcinoma in situ (DCIS), invasive carcinoma potential neoplastic and malignant lesions (PNML), SP, or MP.

Ductoscopy procedure

Prior to ductoscopy, the areola was cleansed with a disinfectant (10% polyvinylpyrrolidone iodine solution) and 1 cc local anesthetic (2% prilocaine) was applied around the nipple to ensure minimal discomfort. A 55-mm diameter, single-channel (irrigation channel) 3000 pixel LaDuScope-S and a 1.1-mm diameter, dual channel (working and irrigation channels), 6000 pixel LaDuScope-T flex (Polydiagnost GmbH, Pfaffenhofen, Germany) optical system were used to perform the ductectomy (Fig. 1). The sphincter of the duct with discharge was dilated with the aid of the dilator bougies and the shaft of the ductoscope was positioned.

The ductoscope was passed through the prepared shaft. The single-channel scope was used initially to provide the intraductal image. When a papillomatous structure (Fig. 2), intraluminal irregular mass, ductal wall irregularity, or epithelial discoloration was observed and surgical intervention was required, the ductoscope with a working channel was used. A 2-0 Prolene suture (Ethicon, Inc., Somerville, NJ, USA) was advanced to the lesion through the working channel of the ductoscope, and the duct to be excised was marked. After removing the ductoscope from the channel, the areola was closed with a square sponge to ensure that the suture remained in the duct, and the four sides of the sponge were taped. This procedure was performed within 2 days. Dilatation of the working channel and insertion of the ductoscope into the working channel were the most difficult stages of the ductoscopy.

Microductectomy procedure

The operations were performed under general anesthesia in operating room conditions. A blue-tipped angiocath was advanced over Prolene suture material into the duct, the labeled suture was removed from the lesioned area, and approximately 1–2 cc of methylene blue was delivered to the lesioned area using an angiocath. Afterward, the main duct, stained blue through a periareolar incision, was iso-
lated with its branches as distally as possible and excised (Fig. 3).

**Statistical analysis**

In this study, the pathology results were accepted as optimal method of determining the etiology of the nipple discharge. SPSS for Windows, Version 15.0 (SPSS Inc., Chicago, IL, USA) was used to perform statistical calculations. Chi-square tests and Pearson correlation coefficient techniques were used in the statistical analysis. P≤0.05 was considered statistically significant.

**RESULTS**

The age range of the patients was 17 to 76 years (mean: 41.3±11.8 years). Among the operated patients, 77 (59.7%) women were of reproductive age and 52 (40.3%) were menopausal. In 74.4% (96/129) of the patients, lesions (papillary lesions+PNML) were detected. PNML was seen in 21% (27/129) of the patients without color separation and in 21.2% (25/118), hemorrhagic or serohemorrhagic discharge was observed. Lesions were confirmed in 8 of 11 patients who did not comply with the colors described in the PND criteria (hemorrhagic, serohemorrhagic, and serous) (Table 1). Lesions were determined in 80% (75/106) of PND3+, and in 91.3% (21/23) of PND2+ patients. PNML was detected in 20.7% (22/106) of PND3+ and 21.7% (5/23) of PND2+ patients (p>0.05) (Table 2).

The data obtained from the comparison of the ductoscopic findings with the pathology results (n=129) were as follows:

Of the 17 patients whose ductoscopy was evaluated as normal, duct ectasia, or intraluminal secretion, 12 underwent surgery due to the presence of an intraductal lesion, 4 for persistent discharge after ductoscopy, and 1 for a palpable mass. Postoperative histopathology reports confirmed the presence of PNML in 6 (35.3%) of the 11 (64.7%) patients in this group that could be followed-up (Table 3).

A ductal excision was performed for 112 patients whose ductoscopy was evaluated as positive for intraductal lesions (intraluminal irregular mass: n=7; SP: n=41; MP: n=28), suspect (ductal epithelial discoloration: n=10; duct-

<p>| Table 1. Histopathology results based on the color of the discharge (n=129) |
|-----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|</p>
<table>
<thead>
<tr>
<th>Color of the discharge</th>
<th>SP</th>
<th>MP</th>
<th>Debris</th>
<th>Mastitis</th>
<th>DCIS</th>
<th>Invasive carcinoma</th>
<th>ADH</th>
<th>Ductal hyperplasia</th>
<th>Ductal ectasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhagic (72)</td>
<td>20</td>
<td>18</td>
<td>8</td>
<td>5</td>
<td>7</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Serohemorrhagic (46)</td>
<td>13</td>
<td>12</td>
<td>1</td>
<td>6</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td></td>
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<tr>
<td>Milky (3)</td>
<td>1</td>
<td>2</td>
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<td></td>
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<tr>
<td>Other (8)</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
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</tbody>
</table>

ADH: Atypical ductal hyperplasia; DCIS: Ductal carcinoma in situ; MP: Multiple papillomas; SP: Solitary papilloma.

<p>| Table 2. Histopathology results based on PND criteria (n=129) |
|-----------------|-------|-------|-------|-------|-------|-------|-------|-------|---------------|-------|</p>
<table>
<thead>
<tr>
<th>Number of PND criteria</th>
<th>SP</th>
<th>MP</th>
<th>Debris</th>
<th>Mastitis</th>
<th>DCIS</th>
<th>Invasive carcinoma</th>
<th>ADH</th>
<th>Ductal hyperplasia</th>
<th>Ductal ectasia</th>
<th>Cases with lesions n (%)</th>
<th>PNML n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PND 2+ (n=23)</td>
<td>11</td>
<td>5</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>21 (91.3%)</td>
<td>5 (21.7%)</td>
</tr>
<tr>
<td>PND 3+ (n=106)</td>
<td>25</td>
<td>28</td>
<td>0</td>
<td>11</td>
<td>8</td>
<td>10</td>
<td>4</td>
<td>9</td>
<td>6</td>
<td>75 (70.8%)</td>
<td>22 (20.7%)</td>
</tr>
</tbody>
</table>

ADH: Atypical ductal hyperplasia; DCIS: Ductal carcinoma in situ; MP: Multiple papillomas; PND: Pathological nipple discharge; PNML: Potential neoplastic and malignant lesions; SP: Solitary papilloma.
tal wall irregularities: n=26), and lesions were confirmed with histopathology results in 85 (76%). PNML was detected in 3 of 10 patients with epithelial discoloration, 2 of 7 cases with irregular intraluminal mass lesions, and in 10 of 26 cases with ductal wall irregularities. In other words, 35% (15/43) of cases with PNML were confirmed pathologically. The PNML rate was lower in the other lesion groups (14%, 12/86; p=0.006) (Table 3).

One patient developed mastitis requiring oral antibiotic treatment for one week after the ductoscopy. No complication was observed in any patient after the microductectomy.

DISCUSSION

Spontaneous, unilateral, hemorrhagic, or serous discharge from a single duct, excluding conditions of pregnancy and lactation defines PND.[3] The most common causes of PND are benign breast lesions, such as solitary intraductal papilloma and papillomatosis (35–48%), but it can be a sign of malignancy in rare cases.[4] For this reason, surgeons should evaluate the complaints and symptoms of these patients very carefully.

The literature provides a description to be used to distinguish PND from physiological discharge, but there is no consensus about for whom ductoscopy should be performed. In our clinic, we perform ductoscopy in patients who have at least 2 of these criteria (spontaneous, single duct, hemorrhagic/serous discharge). Ductoscopy resulted in the determination of a lesion in 74.4% (96/129) of the patients. The literature offers a comparable detection rate of between 36% and 81%.[18] When we classified PND cases based on predefined criteria, our lesion detection rate was 91.3% in PND2+ and 70.8% in patients with PND3+. Our higher rate of lesion detection rate in PND2+ cases may have been due to the fact that ductal excision for PND2+ patients is viewed as more difficult, while PND3+ cases are considered more straightforward. We elect to perform surgery if the findings of a physical examination and conventional imaging methods support the presence of a lesion.

The rate of PNML has been reported as 7% in the literature, if the color of the discharge is not taken into consideration. If there is bloody discharge, the rate increases to 31%.[19] In our study, we found PNML in 21% (27/129) of the total patient group in this study. Among the PND3+ patients the rate observed was 20.7%, and it was 21.7% in the PND2+ group (p>0.05).

In the literature, the sensitivity of smear cytology made from nipple discharge has been reported as 16% to 40%.[19,20] This may be helpful in diagnosis, but cannot distinguish between ADH, intraductal papilloma, and DCIS.[21] In the last 20 years, ductoscopy has begun to be used to help make this distinction. The rigid ductoscopies that were initially used have been replaced with semi-flexible endoscopes with a working channel and the capability to yield high-resolution images and taking a biopsy from the lesion.[22,23] These developments have reduced the technical difficulties of ductoscopy and provided an easily applicable procedure. Now, it is possible to perform a ductoscopy with minimal risk and complications in the course of outpatient diagnosis and treatment.[24]

Of the patients in this study with suspicious findings (color changes in wall epithelium, irregular intraluminal mass, wall irregularities, or intraductal lesion), we found a false positivity rate of 24.1% (27/112). Assessment of the subgroup of patients with discoloration of the wall epithelium revealed a rate of false positivity of 70% (7/10), while it was 42.3% (11/26) among those with wall irregularities. This is likely due to the presence of mastitis (n=8) and ductal hyperplasia (n=7). Both pathologies can cause structural changes and discoloration of the duct wall. We believe that this confusion can be overcome using higher resolu-

<table>
<thead>
<tr>
<th>Ductoscopy findings</th>
<th>Surgical indications</th>
<th>SP (36)</th>
<th>MP (33)</th>
<th>Debris (1)</th>
<th>Mastitis (16)</th>
<th>DCIS (11)</th>
<th>Invasive carcinoma (10)</th>
<th>ADH (6)</th>
<th>Ductal hyperplasia (10)</th>
<th>Ductal ectasia (6)</th>
<th>Total</th>
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<tr>
<td>Normal (2)</td>
<td>Radiological indication</td>
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<td></td>
<td>Persistent discharge</td>
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<tr>
<td>Changes in ductal calibration (8)</td>
<td>Radiological indication</td>
<td>3</td>
<td>I</td>
<td>I</td>
<td>2</td>
<td>7</td>
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<td></td>
<td>Palpable mass on examination</td>
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<tr>
<td>Intraluminal secretion/debris (7)</td>
<td>Radiological indication</td>
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<tr>
<td></td>
<td>Persistent discharge</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>1</td>
<td>4</td>
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<tr>
<td>Epithelial discoloration (10)</td>
<td>Discoloration of ductal wall +Suspect cytology</td>
<td>3</td>
<td>I</td>
<td>I</td>
<td>3</td>
<td>7</td>
<td></td>
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<tr>
<td>Intraluminal irregular mass (7)</td>
<td>Irregular appearance</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>7</td>
<td></td>
<td></td>
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<tr>
<td>Ductal wall irregularity (26)</td>
<td>Ductal wall irregularity +Suspect cytology</td>
<td>I</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>25</td>
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<tr>
<td>Solitary papilloma (41)</td>
<td>Solitary papilloma</td>
<td>31</td>
<td>7</td>
<td>I</td>
<td>I</td>
<td>1</td>
<td>41</td>
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<tr>
<td>Multiple papillomas (28)</td>
<td>Multiple papillomas</td>
<td>19</td>
<td>4</td>
<td>I</td>
<td>2</td>
<td>1</td>
<td>28</td>
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ADH: Atypical ductal hyperplasia; DCIS: Ductal carcinoma in situ; MP: Multiple papillomas; SP: Solitary papilloma.
tion endoscopes that will be developed in the future. We determined a false negativity rate of 64.7% (11/17) in patients whose ductoscopy was evaluated as non-suspicious (normal, ductal calibration change, intraluminal secretion/debris findings), but for whom surgery was performed as a result of the physical examination (n=1), conventional imaging findings (n=12), or persistent discharge (n=4). We attributed this high rate of false negativity to our exclusion of patients for whom we decided to follow-up without surgery based on the ductoscopy findings. Nonetheless, these data indicated that ductoscopy alone cannot exclude the possibility of lesions in patients with persistent PND or suspect findings detected using conventional imaging and physical examinations.

As with every method, there are some technical limitations to the ductoscopy. There are approximately 15 to 30 main breast ducts opening into each nipple. As it is impossible to access each ductolobular area and obtain images during ductoscopy. It is also highly dependent on the experience and ability of the ductoscopist and there is a learning curve to achieving expertise in the technique. Possible complications of the procedure include pain, inflammation, and infection; however, they are rarely seen. In our study, only 1 patient had mastitis, which was limited to the breast skin and responded to antibiotics within a short time.

CONCLUSION
The findings of this study suggest that ductoscopy is a good predictor both in determining the patients who need surgical treatment and in reducing the number of unnecessary surgical procedures. Combined use with ductal lavage and classic imaging modalities may help to detect malignant cases during an early stage of disease. Therefore, patients with at least 2 criteria of PND should be evaluated with ductoscopy. Conventional imaging and physical examination findings should be taken into consideration for post-ductoscopy follow-up plans. Ductoscopy is a candidate to be the gold standard in the diagnosis and treatment of patients with PND.

Ethics Committee Approval
Approved by the Okmeydani Training and Research Hospital’s ethics committee.

Informed Consent
All patients provided written informed consent before ductoscopy and surgery.

Peer-review
Internally peer-reviewed.

Authorship Contributions

Conflict of Interest
None declared.

REFERENCES
Amaç: Günümüzde patolojik meme başı akıntılarının (PMA) konvansiyonel tanı ve tedavisi cerrahi duktus eksizyonudur. Rutin duktus eksizyonu uygulanan olguların patoloji sonuçları incelendiğinde yüksek oranda gereksiz cerrahi girişim yapıldığı ortaya çıkmaktadır. Bu çalışmada amacımız duktoskopik değerlendirme sonrası cerrahi yapılan hastalarda lezyon saptama oranlarını belirlemektir.


Bulgular: Sadece duktoskopik bulgular ile cerrahi kararı verilen hastaların %76’sında (85/112) lezyonlar final patoloji sonuçları ile doğrularıldı. Duktoskopi bulguları ile tekik karar verilebilecek 17 hasta fizik muayene ve klasik görüntüleme yöntemlerindeki bulgular nedeniyle ameliyat edildi ve bunların 11’inde (%64.7) lezyon saptandı (6’sı PNML, 5’si papillamatöz).


Anahtar Sözcükler: Cerrahi seçim; duktoskopi; patolojik meme başı akıntısı.

Patolojik Meme Başı Akıntılı Hastaların Cerrahi Seçiminde Duktoskopinin Etkisi