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Ultrasound-Guided Vacuum-Assisted Breast Complete Duct Excision: A Novel Minimally Invasive Surgical Technique for Pathological Nipple Discharge

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Abstract

Objective: Pathological nipple discharge (PND) is a common challenge in breast surgery, requiring surgical management. However, the noticeable scars after traditional surgical approaches become a nightmare for patients. Ultrasound-guided vacuum-assisted breast minimally invasive complete duct excision is a novel exploration attempt.

Methods: From May 2019 to May 2020, we conducted a study involving women diagnosed with PND who underwent ultrasound-guided vacuum-assisted complete breast duct excision with a minimally invasive surgical incision. To enhance preoperative localization accuracy, this study utilized the benefits of ultrasound technology to investigate the utility of breast duct contrast-enhanced ultrasound (CEUS) employing microbubble-based contrast agents for PND. Our novel operative procedure, ultrasound-guided vacuum-assisted breast duct excision, offers the advantage of a minimally invasive surgical incision, resulting in inconspicuous scarring.

Results: A total of 20 participants were enrolled in the novel minimally invasive complete duct excision procedure, which involved preoperative breast duct CEUS and vacuum-assisted minimally invasive resection. In all cases, patients underwent minimally invasive surgery with the use of small incisions.

Conclusions: The utilization of CEUS demonstrates a clear advantage in the preoperative localization and surgical management of patients with PND. We observed successful complete duct removal through minimally invasive surgery in all patients, and the initial results are encouraging.

Keywords: Pathological nipple discharge; Minimally invasive; Duct excision; Contrast-enhanced ultrasound.

Abbreviations: ND: Nipple discharge; PND: Pathological nipple discharge; IDP: Intraductal papilloma; CEUS: Contrast-enhanced ultrasound; VABB: Vacuum-assisted breast excision.

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Introduction

Nipple discharge (ND) is the third most common complaint in patients with breast diseases after breast pain and breast mass and is mainly seen in women aged 30-50 [1,3]. Physiologic nipple discharge is usually milky or water-like, spontaneous, and multiductal. In contrast, pathological nipple discharge (PND) is bloody or serous-like, spontaneous, unilateral, and single-holed [3,4]. Intraductal papilloma (IDP) is the most common cause of PND, with an occurrence of 63-77% [5,6]. However, 5-15% of patients with PND are diagnosed with malignant ductal carcinoma in situ and breast cancer [7,10]. According to the guideline of UpToDate, most PND needs surgical management. Currently, conventional examinations for diagnosing and locating the cause of PND mainly include mammary fiberoptic ductoscopy, galactography, ND cytology, and ultrasonography. However, each of these modalities has certain limitations [11,12]. Limited by the outer optical fiber diameter and different mammary duct branching modes, the observation range of ductoscopy is mainly confined to the central mammary duct [13]. Galactography is not recommended because of its high technical failure rate, invasive nature, and false-negative rate [14]. Recently, microbubble-based contrast agents have been manufactured for contrast-enhanced ultrasound (CEUS) to diagnose breast diseases [15,16]. These enhanced agents reflect more echogenic signals after intravenous injection to determine the position and features of the blood vessels. However, the application of this kind of research involving injecting microbubble-based contrast agents into the mammary duct for clear visualization has not yet been reported in PND patients. The Vacuum-assisted breast biopsy (VABB), also known as mammotome® biopsy, is a novel device used extensively in Japan, Europe, and America [17,19]. It is a minimally invasive approach to breast puncture for the qualitative diagnosis before breast cancer surgery and evaluation of breast microcalcifications and papillary lesions. For the accuracy of preoperative localization and minimally invasive results, this study combined the advantages of ultrasound to investigate the value of breast duct CEUS and minimally invasive duct excision using microbubble-based contrast agents combined with the Mammotome system in PND patients.

Methods

Patients

This study was approved by The Medical Ethics Committee of Beijing Friendship Hospital, Capital Medical University, and it is registered at ClinicalTrials.gov.cn (ID: ChiCTR1900022776). All participants were provided with written informed consent before enrollment in this study between May 2019 and May 2020. In addition, all PND patients registered in the Department of General Surgery were subjected to qualification screening. The inclusion criteria of this study were as follows: (1) underwent ultrasound-guided breast-focused minimally invasive resection using the Mammotome system; (2) subjected to preoperative breast duct CEUS; (3) age>18 years; and (4) voluntarily enrolled in this study and provided written informed consent. The exclusion criteria were as follows: (1) definitive diagnosis of breast cancer with puncture pathology or ND cytology; (2) history of malignant tumors of the breast or other organs; and (3) poor general physical condition, incapable of undergoing an operation.

I**nstruments and materials:** The instruments used in our study included the iU22 color Doppler ultrasound system with a superficial L9-3 linear transducer for contrast-enhanced sonography (Philips Healthcare, USA), 8-gauge Mammotome breast biopsy system (Devicor Medical Products, USA), and PD-VC-0210 endoscope camera system of the mammary duct (Ethicon Endo-surgery, USA). In addition, SonoVue (Bracco Suisse SA, Switzerland) sulfur hexafluoride microbubbles were used for injection.

Surgical procedures: Routine ultrasound examination. The patient was placed in the supine position. Ultrasonography examination of the PND patients included a review of breast tissue, dilated mammary ducts, hypoechoic nodules, and bilateral axillary lymph nodes. In addition, clear and comprehensive ultrasound images were selected and stored for comparison with the CEUS breast duct images.

Ductoscopy: The nipple-areola complex was cleaned with a povidone-iodine solution, and ductoscopy was performed under local anesthesia using diluted lidocaine (0.5%). First, a rude pinhead was placed in the dilated ductal orifice. The expander system was then introduced into the ductal orifice to expand the duct gently to submit the fiberoptic scope. A ductoscopy examination is done in a regular way and is well documented [20-22]. Finally, a soft syringe needle was inserted into the dilated ductal orifice for further injection.

Breast duct CEUS: Breast duct CEUS was conducted to monitor the branching and pathway of the mammary duct. First, physiological saline (5 ml) was mixed with SonoVue lyophilization and vigorously shaken for 20 seconds to obtain the SonoVue suspension. Next, 1-4 ml of the configured SonoVue suspension was injected into the mammary duct through the soft syringe needle into the dilated ductal orifice. The pathway of the mammary duct was visualized immediately on the contrast pulse sequence after injection. The contrast ultrasound can help surgeons identify the scope of the mammary duct lesions to achieve complete duct resection.

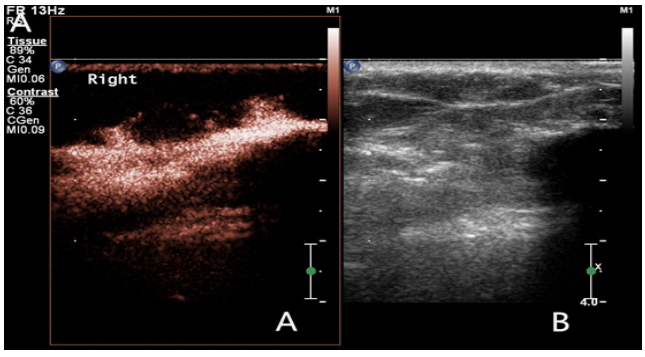

Figure 1: Mammotome-assisted minimally invasive duct resection.

Statistical analysis: All statistical analyses were two-tailed. The confidence interval was 5-95%; p-values<0.05 were considered statistically significant. Categorical variables were analyzed using the chi-square test with Fisher's exact test, and continuous variables using an unpaired t-test with Welch's correction. Categorical variables and continuous variables are presented as frequencies (percentages) and means ± standard deviations, respectively. All the analyses were performed using Statistical Product and Service Solutions (version 26.0; IBM Inc., Chicago, IL, USA). We have de-identified all the patient's details. The reporting of this study conforms to STROBE guidelines.

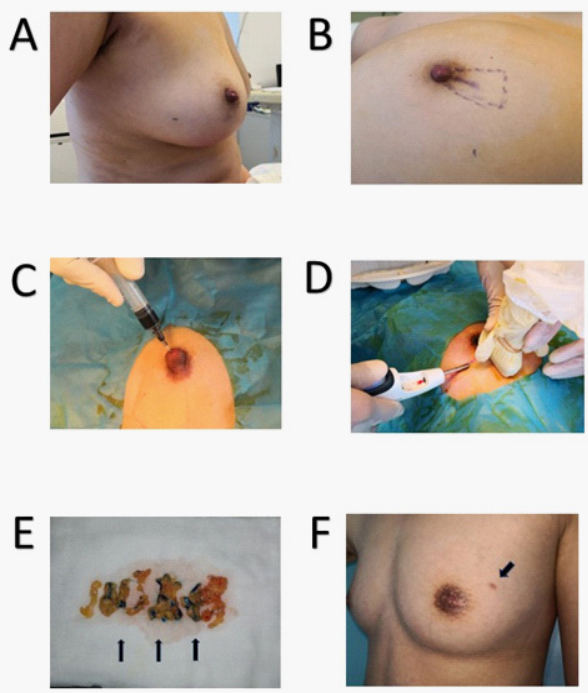

Figure 2: The patients were placed in the supine position **(Figure 2A)**. As shown in **Figure 2B**, the surgical margin was determined according to the position localized by the breast duct CEUS and the thickness of the gland and fat. Methylene blue was first injected into the mammary duct using a soft syringe needle through the dilated ductal orifice **(Figure 2C)**. This helped stain the resected ductal lesions. The operation was performed under local anesthesia with 1% lidocaine. The cutting head of the Mammotome was used to puncture the skin at the appropriate exterior margin of the breast and to penetrate the selected region. Guided by ultrasound, resection of the mammary duct lesions was started from the surrounding area of the glands **(Figure 2D)**. The mammary duct, stained Oxford blue color by the methylene blue dye, could be resected thoroughly in the delineated area. Excessive resection should be avoided when removing the mammary duct below the nipple and areola to prevent ischemic necrosis because of insufficient blood supply. As shown in **Figure 2E**, blue-stained mammary duct tissues were observed in the excised tissue, and a pathological examination was performed to identify the histological type. After the complete removal of the lesion, the affected area was pressed to confirm no further bleeding. The incision was closed using histoacryl **(Figure 2F)** and covered with a sterile dressing and compression bandage. Drainage tubes were not inserted because the bleeding was minimal. After observing for 30 minutes, the patients were discharged.

Results

Clinical and demographic characteristics: This study enrolled 20 patients with PND who underwent preoperative breast duct CEUS and Mammotome-assisted minimally invasive resection between May 2019 and May 2020. Table 1 shows the clinical and demographic characteristics of the patients. All patients were women, and the average age was 47.5 years. Notably, the occurance of the right- and left-sided lesions was the same. Regarding the pathological classification, 14 patients were diagnosed with IDP, 5 with duct ectasia, and 1 with intraductal papillary carcinoma. Of the 20 patients, 7 did not show positive findings for lesions on ductoscopy, and only 1 did not show positive results on duct CEUS.

Postoperative effect and patient satisfaction: The follow-up period ranged from 12 to 24 months (average, 18±6 months). Postoperative evaluation was performed by the patients and the surgeon at each follow-up visit. Patient satisfaction, recurrence, symmetry, infection, and scarring were evaluated. There was no recurrence reported in any patient. The bilateral breast tissue was assessed during follow-up using ultrasound. None of the patients experienced severe postoperative complications, and all were very satisfied with the results. Incision scars were nearly invisible [6-8] months after the procedure. All patients recovered well without infection and were very satisfied with the results.

Table 1: Clinical and demographic characteristics of patients.

Characteristics	Total
Sex	
Female, n(%)	20(100 %)
Age (mean ± standard deviation)	47.50±12.95 years
Lesion location	
Left, n(%)	10(50%)
Right, n(%)	10(50%)
Pathological classification	
Intraductal papilloma, n(%)	14(70%)
Duct ectasia, n(%)	5(25%)
Intraductal papillary carcinoma, n(%)	1(5%)
Ductoscopy	
Positive, n(%)	13(65%)
Duct contrast-enhanced ultrasound	
Positive, n(%)	19(95%)

Discussion

ND is classified as pathologic if it is spontaneous, unilateral, or bloody. Alternatively, serous, and clear discharge is usually associated with a tumor [12]. IDP, duct ectasia, carcinoma, and infection are common causes of PND. Benign papilloma is the most common cause of these diseases, identified in up to 57% of cases presenting PND [23]. Currently, conventional examinations for diagnosing the cause of PND include mammary fiberoptic ductoscopy, galactography, ND cytology, and ultrasonography. However, each of these has certain limitations. Limited by the outer optical fiber diameter and different mammary duct branching modes, the observation range of ductoscopy is mainly confined to the central mammary duct [23]. Although mammography is recommended for all women with PND over 30 years, the sensitivity (7-68%) for detecting malignancy associated with PND is not sufficient and satisfactory [24]. Mammary ductoscopy has been used for over 40 years since its introduction in 1988 to evaluate spontaneous and bloody ND patients. Ductoscopy is a minimally invasive procedure that helps in the visualization of the ductal epithelium of the breast via the nipple. Although some studies [25,26] have shown a strong correlation between intraductal morphological images and histopathologic diagnosis, others have shown that this relationship is only valid for papillomas [22,27,28]. Ductoscopy provides good visualization of approximately 94% of lesions, the specificity for malignancy it's much higher than benign lesions [20]. These results indicate that histological diagnosis or surgery

is necessary to exclude malignancy in patients with PND [20]. The primary indications for mammary ductoscopy are to evaluate PND and assess the risk of developing breast cancer and other diseases [29]. Using an endoscope with a 1.0 mm outer diameter may not allow the detection of lesions in the margin of the breast. In other words, we concluded that false-negative results might mainly be due to the possibility of lesion development from the distal ductal units. Peripheral distribution of lesions results in a false-negative rate of 18% with ductoscopy. Additionally, galactography is contraindicated in pregnant women because of the radiation-induced damage. As for ND cytology, its low sensitivity makes it difficult to improve the detection rate; therefore, only positive results in ND cytology are considered clinically significant [30]. Ultrasonography provides good resolution for hypoechoic nodules in the breast. However, PND patients often have multiple small hypoechoic nodules, making it challenging to identify the nature of the hypoechoic areas with ultrasound [31]. Therefore, a more precise preoperative examination to determine the scope of the mammary duct is highly desirable.

To overcome the limitations of ductoscopy, we suggest that all PND cases be subjected to breast duct CEUS, a noninvasive technique that can solve the above problem [32]. The new generation of ultrasound contrast agents, in combination with low acoustic power contrast-specific ultrasound imaging, has enabled a major clinical breakthrough in some organs' diagnostic and interventional procedures [33,34]. In China, the only licensed contrast agent is SonoVue, a sulfur hexafluoride-filled microbubble contrast agent stabilized by phospholipids. CEUS plays a crucial role in evaluating breast lesions by the intravenous injection of contrast agents. However, there are few reports of the use of CEUS in diagnosing intraductal lesions and localizing them after SonoVue injection in the mammary duct in clinical settings.

Conventionally, the standard approach in PND cases is to perform duct excision, which involves complete excision of the corresponding mammary ducts and terminal ducts. A better approach is to inject a mixture of methylene blue or an opaque dye and perform preoperative breast angiography that can show the duct progression and assist in intraoperative identification of the target ducts, which will be stained in blue dye. These surgical procedures can help detect possible premalignant lesions and carcinomas. This surgical procedure is relatively straightforward and has minimal morbidity. However, regardless of the type of traditional surgery, an incision of at least 2-3 cm is required on the breast surface, and a surgical scar is unavoidable.

Minimally invasive mastectomy, also called ultrasound-guided vacuum-assisted breast biopsy system, has been used to remove breast nodules since 1995. The Mammotome biopsy system is a complete breast disease sampling and management system. A Mammotome 8-gauge needle can yield a cylinder-shaped tissue sample measuring approximately 23 mm in length and 4.3 mm in diameter per cut, allowing for quick and precise duct and glandular tissue excision [35]. These excisions are usually limited to lesions less than 30 mm, mainly due to time, patient comfort, and tolerance. It has also been reported to be helpful in male breast development surgery [36]. However, there are only a few reports on this procedure's use in managing PND. The minimally invasive operations for ND have a shorter surgical time, but it is not significantly different from the traditional method. The complications of this technique include bleeding and hematomas that result from sharp dissection; these complications can be minimized by using the tumescent anesthesia technique and an intraoperative Doppler ultrasound to prevent cutting the large vessels. An incision only 5 mm long is considered the reason for esthetic satisfaction in all patients. After at least 1 year of follow-up, the result of this minimally invasive surgery seemed satisfactory in almost all patients.

Some risks are associated with this type of surgery, including the inability to breastfeed in younger patients, loss of nipple sensation, and possible nipple-areolar necrosis. Therefore, we believe all intraductal lesions detected on ultrasound ductoscopy, CEUS, or magnetic resonance imaging should be subjected to minimally invasive duct resection.

Limitations: This study has a few limitations. First, it was challenging to convince all the enrolled patients to undergo an ultrasound, magnetic resonance imaging, CEUS, and ductoscopy because of time constraints and high costs. Second, the number of breast PND cases was limited. Third, it is not easy to perform CEUS through the discharging duct, and a surgeon needs the full cooperation of the ultrasonography technician. Furthermore, there is a specific learning curve involved. Additionally, a larger sample size and a more extended follow-up period will be required to determine the long-term safety and efficacy of this minimally invasive surgical technique.

Conclusions

Combining conventional ultrasound, CEUS, and ductoscopy has an obvious advantage in preoperative localization and surgical treatment of patients with PND. In current clinical practice, CEUS is necessary to compensate for the limitations of ductoscopy when evaluating patients with PND. All patients who underwent vacuum-assisted breast excision reported sound therapeutic effects and cosmetic outcomes, which avoided open surgical procedures and huge scars. Minimally invasive surgery, generally well tolerated by patients, may be a safe and efficient procedure for managing breast PND with or without lesions. Moreover, the complication rate was acceptable.

Declarations

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Authors' contributions: (I) Conception and design: YG Gao; (II) Administrative support: ZC Ge; (III) Provision of study materials or patients: YG Gao, ZH Wang, HM Zhang; (IV) Collection and assembly data: ZY Yang, YG Gao; (V) Data analysis and interpretation: YG Gao, ZY Yang; (VI) Manuscript writing: YG Gao, ZY Yang; (VII) Final approval of manuscript: All authors.

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Availability of data and materials: The data will not be made available to protect the participant's identity. However, upon reasonable request, those interested parties can contact the corresponding author Dr. Yinguang Gao (gaoyinguang@gmail.com), who will provide the raw data.

Ethics approval and consent to participate: All procedures in this study involving human participants were by the Declaration of Helsinki (as revised in 2013). This study was approved and supervised by the Medical Ethics Committee of Beijing Friendship Hospital, Capital Medical University. (NO.2019-P2-062-01). All participants provided informed consent.

Consent for publication: Not applicable.

Competing interests: The authors declare that they have no competing interests.

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