The Breast 49 (2020) 242–245

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Ultrasound-guided vacuum-assisted excisional biopsy to treat benign phyllodes tumors

Qiu Jing Shang [a, 1], Nan Li [a, 1], Meng Ke Zhang [a], Yan He [a], Gang Liu [b, **], Zhi Li Wang [a, *]

[a] Department of Ultrasound, Chinese People's Liberation Army General Hospital, 28 Fuxing Road, Beijing, 100853, China
[b] Department of Radiology, Chinese People's Liberation Army General Hospital, 28 Fuxing Road, Beijing, 100853, China

ARTICLE INFO

Article history:
Received 17 April 2019
Received in revised form
6 December 2019
Accepted 12 December 2019
Available online 18 December 2019

Keywords:
Ultrasound-guided vacuum-assisted breast biopsy
Excisional biopsy
Phyllodes tumor
Recurrence

ABSTRACT

Purpose: To evaluate the value of ultrasound (US)-guided vacuum-assisted excisional biopsy (VAB) in treating benign phyllodes tumors (PTs) of the breasts and to investigate the lesion characteristics that could affect the local recurrence rate.
Patient and methods: From December 2008 to February 2018, 93 patients with PTs diagnosed on histology underwent US-guided, 7-gauge VAB. The recurrence rate of benign PT and complications of VAB were evaluated on follow-up US every three to six months. The lesion characteristics were analyzed to identify the factors affecting the recurrence rate.
Results: Of the 87 patients, local recurrence was found in 15 patients (17%) in a mean follow-up period of 35.8 months, and the rate of complete excision was 82.8% (72/87). PTs with a largest diameter less than 3.3 cm had a significantly lower recurrence rate than PTs with a largest diameter larger than 3.3 cm ($P < 0.05$).
Conclusions: In conclusion, US-guided VAB is an effective method to treat benign PT, especially in lesions with a diameter less than 3.3 cm.

1. Introduction

Phyllodes tumors (PTs) are rare fibro-epithelial lesions with an incidence rate of approximately 1% of all primary breast lesions [1] and occur in women aged 35–55 years [[2]]. Fibro-epithelial lesions also include fibroadenomas (FAs), which are composed of balanced proliferation of glands and stroma [3]. However, PTs disturb the balance, with overgrowth of stroma, resulting in a leaf-shaped appearance. According to the World Health Organization, PTs are classified as benign, borderline, and malignant based on five factors: the cellular pleomorphism, degree of mitosis, overgrowth of the stroma, appearance of the margin, and distribution of stoma [4]. Local recurrence can occur in all subtypes of PTs. The recurrence rates of benign, borderline, and malignant PTs are 10%–17%, 14%–25%, and 23%–30%, respectively [5].

Ultrasonography (US) is an important diagnostic modality for PTs. On US, PTs often present as a heterogeneous hypoechoic mass with internal cystic space, distended veins, and thickening of surrounding skin. On color Doppler US, PTs may appear hypervascular.

Usually, surgical excision is necessary for PTs of all subtypes: benign, borderline, or malignant. With the rapid development of vacuum-assisted biopsy (VAB), benign breast tumors, such as FAs and intraductal papillomas, can be excised in a minimally invasive manner [6–10]. To date, there have been no systematic reports on the treatment of benign PTs using US-guided VAB or the factors affecting the local recurrence.

The aim of this study was to evaluate the value of ultrasound-guided vacuum-assisted excisional biopsy in the treatment of benign PTs of the breast and to investigate the lesion characteristics that could affect the local recurrence rate.

2. Materials and methods

2.1. Patient

Informed consent was not required because of the retrospective nature of the study. From March 2008 to May 2016, 6788 lesions of 5112 patients underwent percutaneous vacuum-assisted excisional biopsy under ultrasound guidance. There were 93 cases of benign

* Corresponding author.
** Corresponding author.
E-mail address: wzllg@sina.com (Z.L. Wang).
[1] The co-first author.

https://doi.org/10.1016/j.breast.2019.12.008

PT. The age of the patients was 11–55 years (mean age ± standard deviation, 38.8 ± 10.7 years). Among the 93 cases of benign PT, six were excluded because the patients had been lost to follow-up, and the remaining 87 cases were enrolled. Nine patients had a history of benign breast lesions treated with local surgical excision in the breast. Six of the nine patients were confirmed to have FA while the others had benign PT. However, they presented with recurrent local lesions and chose US-guided VAB for the retreatment. The flow chart of the patients' follow-up is showed in Fig. 3.

US-guided VAB was indicated for patients with Breast Imaging Reporting and Data System (BI-RADS) category 3 or 4 lesions who refused to follow-up, those who felt extremely uneasy because of their lesions or complained of pain or other symptoms, those whose lesions were increasing in size, and those who suffered from severe anxiety.

US-guided VAB was contraindicated for patients with BI-RADS category 5 lesions or lesions confirmed to be malignant previously and for patients allergic to local anesthetics or suspected with bleeding tendencies because of the use of anticoagulants within seven days before the US-guided VAB.

2.2. US-guided VAB procedure

First, US examinations were performed by a well-organized team headed by Zhi Li Wang, and two other doctors, Nan Li and Yan He, using the iU22 ultrasound system (Philips Medical Systems, Andover, Massachusetts), with a L12-5 linear array probe, to determine the direction and largest diameter of the lesions and to ensure the insertion site for the probe. Second, local anesthesia was induced with the injection of 10 mL of 1% lidocaine around the mass, including the space along the estimated course of the probe and the cutaneous layer. Subsequently, the probe of the 7-gauge EnCor® system (EnCor® MR, SenoRx, Allso Viejo, CA) was inserted into the mass or close to the mass via a 3-mm incision, and multiple core samples were transported automatically into a collection basket until the lesion was seen as completely excised on US. The operation lasted from 3 to 30 min (10.6 ± 7.3 min), depending on the size of the lesion. Finally, after 10–15 min of direct pressure for bleeding control, US examination was performed to ensure that there were no residual lesions or hematomas. An adhesive elastic band was used for 24–48 h. The overall duration for the procedure was 15–40 min (25.6 ± 9.4 min). The vacuum-assisted rotation procedures were mainly performed by two experienced radiologists, Zhi Li Wang and Nan Li.

2.3. Follow-up

The follow-up US examinations were performed one, three, and six months later, and subsequently, at one-year intervals to check for new nodules at or near the VAB sites. New nodules in the region of the previous excision were classified as recurrent lesions.

2.4. Data and statistical analysis

For each PT, data included the age of the patient at presentation, lesion dimensions, original lesion edge, blood flow, BI-RADS category, follow-up period, interval to recurrence, and history of surgical excision. All statistical analyses were performed using SPSS 23.0, standard version (SPSS Inc, Chicago, IL). Statistical comparisons were performed using the χ^2 test or Fisher's exact test for categorical variables and Mann–Whitney *U* test for continuous variables. Differences were considered to be statistically significant at p-values < 0.05.

3. Result

3.1. Recurrence rate

The follow-up duration was 12–86 months (35.8 ± 24.3 months). Table 1 summarizes the clinical and US features of the 87 cases of PT. Of all the 87 lesions diagnosed as benign PT, 15 showed recurrences in the follow-up period. The recurrence rate after VAB was 17.2% (15/87). Ultrasound imaging of the recurrence PT is showed in Fig. 1 (1a, 1b, 1c, 1d), and the no recurrence PT is showed in Fig. 2 (2a, 2b, 2c).

All the recurrences occurred 1–12 months after VAB (mean interval ± standard deviation, 7.8 ± 4.6 months). Fifteen patients with recurrence underwent further surgery, three of whom chose to follow-up. Among the remaining 12 patients, the pathology demonstrated that three, six, and three had benign PT, FA, and borderline PT, respectively. The largest diameter of the lesions was 2.0–3.8 cm (mean size ± standard deviation, 3.1 ± 0.8 cm) in the recurrence group and 1.3–3.5 cm (mean size ± standard deviation, 2.2 ± 0.5 cm) in the non-recurrence group. There was no significant difference in the lesion size between the recurrence and non-recurrence groups ($P > 0.05$).

The recurrence rate was 8% for lesions with a largest diameter of less than 3.3 cm and 75% for lesions with a largest diameter of more than 3.3 cm, showing a significant difference ($P = 0.01$). The recurrence and non-recurrence groups showed no significant differences in terms of age, original lesion edge, blood flow, BI-RADS category, or history of local surgical excision.

3.2. Complications

The complications of US-guided VAB included hematoma, pain, and ecchymosis. Of the 87 patients, three experienced pain and six had hematoma after the procedure. Two months later, both the complications had disappeared. Two of the 87 patients had skin scratches during VAB, so the patients' postoperative appearance satisfaction was 97.7%.

4. Discussion

PTs and FAs account for most cases of fibroepithelial lesions. Differentiating between benign PT and FA is still a challenge

Table 1
Characteristics of patients undergoing Excision for Benign Phyllodes tumors on Ultrasound-guided vacuum-assisted.

	No recurrence	recurrence	p value
Age			0.339
< 40.5	48	6	
≥40.5	24	9	
History of local surgical excision			0.68
Yes	3	6	
No	69	9	
Lesion dimensions (cm)			0.01
< 3.3	69	6	
≥3.3	3	9	
Original lesion edge			1.0
clear	66	15	
unclear	3	0	
blood flow			0.597
Yes	54	9	
No	18	6	
BI-RADS category			0.172
3	72	12	
4	0	3	

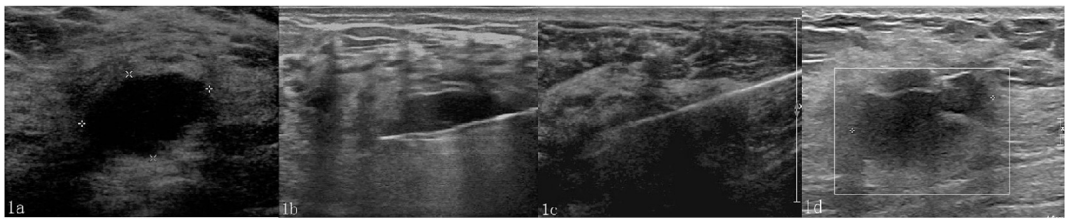

Fig. 1. A lesion in a 52 years old woman, which was demonstrated to be Phyllodes tumors by pathology. 1a Ultrasound imaging showed a hypoechoic mass; 1b The probe in the mass; 1c Complete resection of the mass; 1d Ultrasound showed a recurrence mass in the same place (which was demonstrated to be Phyllodes tumors by pathology).

clinically and histologically [11]. When the tumor is fast-growing, histological examination is necessary to exclude benign PT. The common treatment of PT is surgical resection, which includes local excision and wide local excision. Local excision is defined as excision with a 5-mm safe surgical margin, and wide local excision is defined as excision with at least 1-cm surgical margin [12]. A previous study showed no significant difference between the two types of excisions in the recurrence of benign PT [13].

In this study, the local recurrence rate of the lesion was 17.2%. It was slightly higher than previous VAB studies [6,14,15]. The study by Quyang et al. showed that the local recurrence rate of 108 cases of benign PT after VAB was 11.1% [16]. The study by Park et al. showed that the recurrence rate of 67 cases of benign PT was 7.5% [17]. The higher recurrence rate in this study can be clarified with two explanations. First, the standard for recurrence in our study was strict. Any new nodule in the region of the previous excision

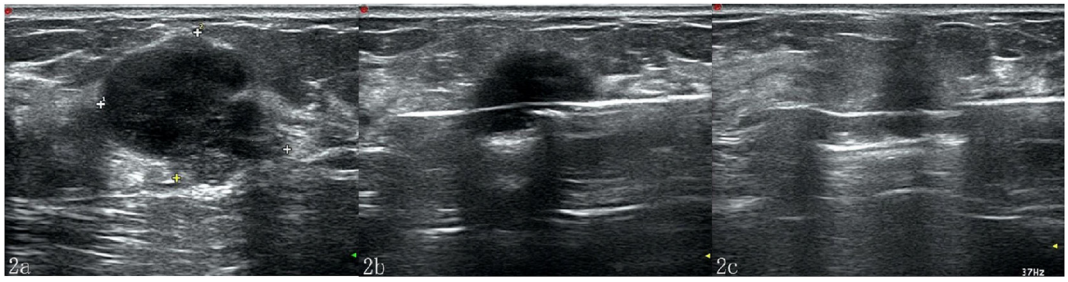

Fig. 2. A lesion in a 25 years old woman, which was demonstrated to be Phyllodes tumors by pathology. 2a Ultrasound imaging showed a hypoechoic mass; 2b The probe in the mass; 2c Complete resection of the mass.

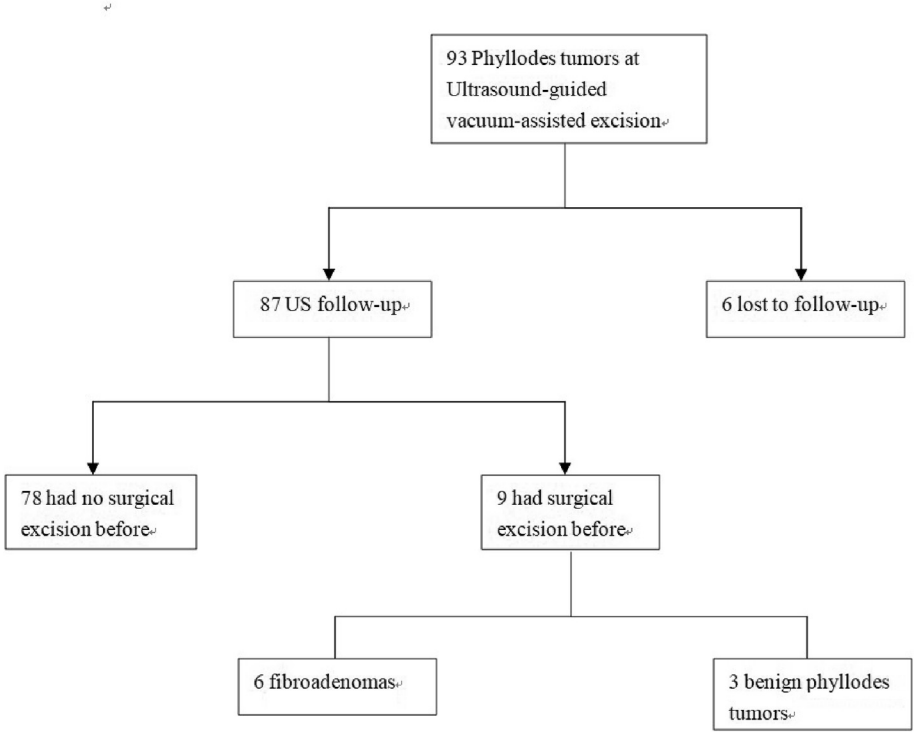

Fig. 3. The flow chart of the patients' follow-up.

was classified as a recurrent lesion, without histological examination. Second, the largest diameter of the lesions was larger in our study than in the previous studies, which might have affected the complete excision rate. In the study by Park, the mean tumor size at the time of diagnosis was 1.97 ± 0.84. In our study, the mean tumor size at the time of diagnosis was 2.36 ± 0.65.

In this study, the mean time to recurrence after VAB was 7.8 months (1–12 months). Previous studies showed the average interval to recurrence of benign PT was two years after the treatment with surgical resection [18–21]. The recurrence time after VAB was shorter in this study than in previous studies, which might be explained by the fact that a small amount of residual cells after VAB could not be detected on US, resulting in early recurrence.

In this study, the recurrence and non-recurrence groups showed no differences in terms of age, original lesion edge, blood flow, or BI-RADS category. Further, the recurrence rate of the lesions with a largest diameter ≤3.3 cm was significantly lower than that of lesions with a largest diameter >3.3 cm. This result was similar with the result reported by Park et al., who demonstrated that benign PTs with tumor size <3 cm and low recurrence could be safely monitored on US after being excised and diagnosed using VAB [17]. Many reports indicated that the local recurrence rate was low in tumors smaller than 2 cm in size [5]. All these studies suggested that benign PTs of small size could be more sufficiently excised using VAB.

In this study, three recurrent lesions after VAB had worse histologic grade than the primary tumor, upgrading from benign to borderline PT. This phenomenon was also seen in other studies [20]. Reinfuss et al. explained that this upgrade might be caused by the missing malignant foci on histological examination and that the recurrence of benign PTs had the potential to progress to borderline PTs [22]. It has been reported that the therapeutic effect of borderline PTs was closely associated with the surgical method, and wide local excisions led to a lower recurrence rate than local excisions [20,23]. Therefore, the recurrence of benign PT should be treated with wide local excision instead of VAB or local excision.

The analysis of our data showed that there were no significant differences between the recurrence and non-recurrence groups in terms of history of local surgical excision before VAB. This suggested that the therapeutic effect of benign PTs was independent of prior surgery. Furthermore, in our study, two recurrences of FAs after prior surgery were found to be benign PTs. This was the same as previous studies, which showed the possibility of progression from FAs to PTs [24,25].

The current study had some limitations. First, we could not differentiate between recurrent and residual PTs. Further studies with histological characteristics are necessary to obtain a more robust conclusion on the recurrence of PTs.

In conclusion, US-guided VAB is an effective method for the treatment of benign PTs, especially in lesions with a largest diameter less than 3.3 cm.

Acknowledgements

FundingThis work was supported by the National Natural Science Foundation [grant number: 81771832], Military Top project of Youth Training for Medical Science and Technology [grant number: 19QNP071], and Military Health-care Topic [grant number: 17BJZ34].

References

[1] Ouyang Q, Li S, Tan C, Zeng Y, Zhu L, Song E, et al. Benign phyllodes tumor of the breast diagnosed after ultrasound-guided vacuum-assisted biopsy: surgical excision or wait-and-watch? Ann Surg Oncol 2016;23(4):1129–34.
[2] Mccarthy E, Kavanagh J, O'donoghue Y, Mccormack E, D'arcy C, O'keeffe SA. Phyllodes tumours of the breast: radiological presentation, management and follow-up. Br J Radiol 2014;87(1044):20140239.
[3] Edwards T, Jaffer S, Szabo JR, Sonnenblick EB, Margolies LR. Cellular fibroadenoma on Core needle biopsy: management recommendations for the radiologist. Clin Imaging 2016;40(4):587–90.
[4] Yii N, Read T, Tan CC, Ng SL, Bennett I. Diagnosing phyllodes tumours of the breast: how successful are our current preoperative assessment modalities? ANZ J Surg 2018;88(10):988–92.
[5] Youk JH, Kim H, Kim EK, Son EJ, Kim MJ, Kim JA. Phyllodes tumor diagnosed after ultrasound-guided vacuum-assisted excision: should it be followed by surgical excision? Ultrasound Med Biol 2015;41(3):741–7.
[6] Grady I, Gorsuch H, Wilburn-Bailey S. Long-term outcome of benign fibroadenomas treated by ultrasound-guided percutaneous excision. Breast J 2008;14(3):275–8.
[7] Kibil W, Hodorowicz-Zaniewska D, Popiela TJ, Szpor J, Kulig J. Mammotome biopsy in diagnosing and treatment of intraductal papilloma of the breast. Pol Przegl Chir 2013;85(4):210–5.
[8] Kibil W, Hodorowicz-Zaniewska D, Popiela TJ, Kulig J. Vacuum-assisted core biopsy in diagnosis and treatment of intraductal papillomas. Clin Breast Canc 2013;13(2):129–32.
[9] Wang ZL, Liu G, Li JL, Su L, Liu XJ, Wang W, et al. Breast lesions with imaging-histologic discordance during 16-gauge core needle biopsy system: would vacuum-assisted removal get significantly more definitive histologic diagnosis than vacuum-assisted biopsy? Breast J 2011;17(5):456–61.
[10] Wang ZL, Liu G, Li JL, Ding Q, Su L, Tang J, et al. Sonographically guided percutaneous excision of clinically benign breast masses. J Clin Ultrasound 2011;39(1):1–5.
[11] Marcil G, Wong S, Trabulsi N, Allard-Coutu A, Parsyan A, Omeroglu A, et al. Fibroepithelial breast lesions diagnosed by core needle biopsy demonstrate a moderate rate of upstaging to phyllodes tumors. Am J Surg 2017;214(2):318–22.
[12] Acar T, Tarcan E, Haciyanli M, Kamer E, Peskersoy M, Yigit S, et al. How to approach phyllodes tumors of the breast? Ulus Cerrahi Derg 2015;31(4):197–201.
[13] Kim S, Kim JY, Kim DH, Jung WH, Koo JS. Analysis of phyllodes tumor recurrence according to the histologic grade. Breast Canc Res Treat 2013;141(3):353–63.
[14] Yom CK, Han W, Kim SW, Park SY, Park IA, Noh DY. Reappraisal of conventional risk stratification for local recurrence based on clinical outcomes in 285 resected phyllodes tumors of the breast. Ann Surg Oncol 2015;22(9):2912–8.
[15] Organ Jr CH, Organ BC. Fibroadenoma of the female breast: a critical clinical assessment. J Natl Med Assoc 1983;75(7):701–4.
[16] Fischer KM, J S J B, Ugras SK. Invasive lobular carcinoma involving a borderline phyllodes tumor. Breast J 2018;24(6):1076–7.
[17] Park HL, Pyo YC, Kim KY, Park JS, Shin JE, Kim HR, et al. Recurrence rates and characteristics of phyllodes tumors diagnosed by ultrasound-guided vacuum-assisted breast biopsy (VABB). Anticancer Res 2018;38(9):5481–7.
[18] Carter BA, Page DL. Phyllodes tumor of the breast: local recurrence versus metastatic capacity. Hum Pathol 2004;35(9):1051–2.
[19] Zurrida S, Bartoli C, Galimberti V, Squicciarini P, Delledonne V, Veronesi P, et al. Which therapy for unexpected phyllode tumour of the breast? Eur J Cancer 1992;28(2–3):654–7.
[20] Hajdu SI, Espinosa MH, Robbins GF. Recurrent cystosarcoma phyllodes: a clinicopathologic study of 32 cases. Cancer 1976;38(3):1402–6.
[21] Wang Y, Zhang Y, Chen G, Liu F, Liu C, Xu T, et al. Huge borderline phyllodes breast tumor with repeated recurrences and progression toward more malignant phenotype: a case report and literature review. OncoTargets Ther 2018;11:7787–93.
[22] Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: an analysis of 170 cases. Cancer 1996;77(5):910–6.
[23] Ben Hassouna J, Damak T, Gamoudi A, Chargui R, Khomsi F, Mahjoub S, et al. Phyllodes tumors of the breast: a case series of 106 patients. Am J Surg 2006;192(2):141–7.
[24] Chen WH, Cheng SP, Tzen CY, Yang TL, Jeng KS, Liu CL, et al. Surgical treatment of phyllodes tumors of the breast: retrospective review of 172 cases. J Surg Oncol 2005;91(3):185–94.
[25] Noguchi S, Yokouchi H, Aihara T, Motomura K, Inaji H, Imaoka S, et al. Progression of fibroadenoma to phyllodes tumor demonstrated by clonal analysis. Cancer 1995;76(10):1779–85.