Predictive Factors of Recurrence Following Surgical Treatment of Phyllodes Tumors in Ramathibodi Hospital

Suragit Pornchai MD*, Prakasit Chirappapha MD*, Panuwat Lertsithichai MD*,
Youwanush Kongdan MD*, Thongchai Sukarayothin MD*, Monchai Leesombatpaiboon MD*

** Department of Surgery, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Background: *Phyllodes tumor is rare fibroepithelial lesion of breast tumor. The main stay treatment is surgery. Although surgery has an adequate surgical margin, the tumor has a tendency to recur locally and occasionally to metastasis.*
Objective: *To determine parameters that influence recurrence in this uncommon neoplasm.*
Material and Method: *Data from Ramathibodi Hospital since 1 January 2000 to 31 December 2016 were reviewed retrospectively. 168 patients were newly diagnosed with phyllodes tumors at the Ramathibodi Hospital. We reviewed and analyzed factorsfor recurrence of phyllode tumors after surgery.*
Results: *The median age of the patients was 43.65 years, ranging from 16 to 66 years. The mean of the tumor size was 4.92 cm, ranging from 0.5 to 32 cm. Based on the criteria proposed by WHO, 107 cases were benign tumors (63.69%), 39 borderline tumors (23.21%), and 21 malignant tumors (12.5%). The median duration of follow-up was 11.92 months that ranged from 3.07 to 62.30 months. Of the 168 cases, 8 (4.76%) patients had recurrence. The mean age of these patients was 46.37 years, and the mean follow-up was 40.02 months. The mean time to recurrence was 17.47 months, with a median of 11.92 months, and ranged of 0.3.07 to 62.30 months. Incidence rate of recurrence tumors was 2.43% and the median follow-up time to recurrence was 34.07 months (95% CI = 21.83 to 30.10). The event free probability of all patient was 5.72% and 50% median time to recurrence was 10.77 month (95% CI = 18.5 to 28.73). Factors of recurrence in the present study were histology ($p<0.001$) and tumor size ($p<0.001$).*
Conclusion: *The tumor size and histology of phyllodes were the principal determinants of the recurrence. Complete surgical excision by either wide local excision or mastectomy if necessary is important in the primary surgical treatment of phyllodes tumors.*

Keywords: *Phyllodes tumor*

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Phyllodes tumor is rare fibroepithelial lesion of breast tumor found in approximately 1% of the primary breast tumor.[1, 2] Phyllodes tumors were initially describedas "cystosarcomaphyllodes" by Johannes M□ller in 1838[3], and these tumors have as many as 62 different synonyms[3]. Phyllodes tumor's structural pathology is similar to fibroadenoma; however, the Phyllodes tumor have a leaflike projection of stroma and increased stromal cellularity from histopatholgy[1]. For those patients most likely to have breast mass, the size of the mass have been reported since 1 to 40 cm[4]. Approximately 20% of patients had a mass larger than 10 cm[5] (Fig. 1). The evaluation of phyllodes tumor was carried out by triple assessment i.e clinical, radiological and histological examination forms the fundamentalbasis. The diagnosis of phyllodes tumor was based on the criteria defined by the World Health Organization in 2003, including the degree of stromal hypercellularity, mitoses and cytologic atypia, stromal overgrowth, and the nature of tumor borders. The WHO classification distinguished 3 histological subtypes of phyllodes tumors: benign, borderline, and malignant[1], which account for 58.4% to 74.6%, 15.0% to 16.1%, and 9.3% to 31% of all phyllodes tumors, respectively[6-8]. The behavior is unpredictable and the distinction between benign, borderline, and malignant tumors is often difficult and does not always reflect the clinical behavior[9]. The main stay treatment of phyllodes tumor is surgery, which should have an adequate margin of at least 1 cm[10]. In some cases, the mass was large and may require immediate reconstruction for improved cosmetic outcome[10,11] (Fig. 2).

Prognosis of Phyllodes tumor was quite good. In a retrospective study of 101 patients treated between

Correspondence to:
Chirappapha P, Breast & Endocrine Surgery Unit, Department of Surgery, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.
Phone: +66-2-2011315, Mobile: +66-84-4574059
E-mail: onco.prakasit@gmail.com

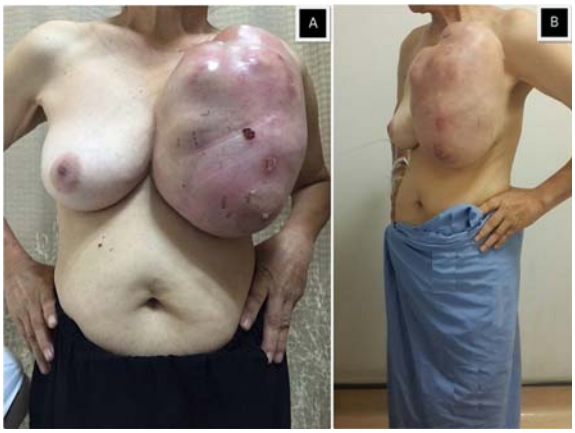

Fig. 1 Presentation of a malignant phyllodes tumor. A 56-year-old woman presented with a large mass in the left breast, the tumor size was 32 cm. CNB was reported as "malignant phyllodes tumor". A) Preoperative presentation with a bulging mass apparent on Straight inspection view, B) Preoperative presentation with a bulging mass apparent on Semi-lateral inspection view.

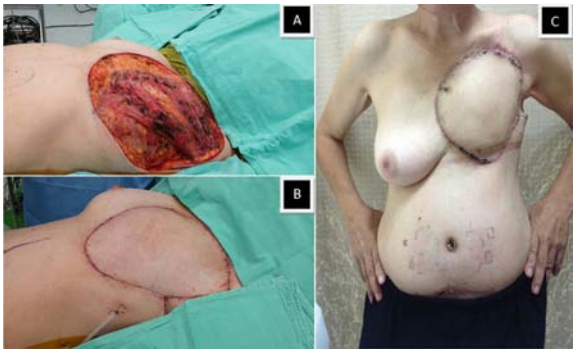

Fig. 2 Intraoperative and Post operative views of patient with large phyllodes tumor of left breast. A) Intra operative after remove breast and tumor with large defect, B) The TRAM flap reconstruction for coverage large defect, C) Post operative 1 week without complication.

1944 and 1998, the overall survival for patients combined with benign and borderline tumors was 91 percent at 5 years. The five year survival rate for malignant phyllodes tumors was 82 percent[12].

Todate, the local recurrence rate in PT is approximately 15%[13-15]. Local recurrence usually occurs within the first few years following surgery, especially if it was with incomplete excision[7]. Some authors argue that histologicalcriteria can be used to predict the likelihood of local recurrence[16]. Local recurrence can usually be controlledby another surgery including wider excision or even mastectomy[9]. It was unclear whether malignant phyllodes tumor were associated with high recurrence rate[17,18] or whether the positive margins are responsible for this recurrence[9,19]. Approximately 20% of patients with malignant phyllodes tumor developed distant metastasis[5,13,19]. Most distant metastasis develops without evidence of local recurrence, while several studies have shown that local recurrenceis a strong predictor of metastatic spread[20-22]. The most common sites for distant metastasis are the lung, bone, limbs but rarely to the abdominal viscera[23]. When tumors recur, they typically recur locally within two years of initial excision[24]. Approximately 15% have a propensity to recur locally and about 10% chance of distant recurrence[24].

The objective of this study was to determine factors that influenced the outcome of local recurrence and distant metastasis in PT patients managed at Ramathibodi Hospital.

Material and Method

After permission was obtained from our institutional review board, we reviewed the pathology and cancer registry records at Ramathibodi Hospital. Between January 2002 and December 2016, 168 cases of Phyllodes tumor were identified. All of patients had their definitive surgery and follow-up at Ramathibodi Hospital. Clinical data retrieved from the charts included age, duration of symptoms, signs, tumor size, location, type of surgery, and time to recurrence. Follow-up information was obtained from the charts review. Surgical therapy was categorized as follows:

1) Local excision: Removal of tumors with a subjectively healthy tissue margin, including excision, enucleation, lumpectomy, or simple excision of the breast mass.

2) Wide excision: Removal of tumors with a margin of healthy tissue more than 1.0 cm, including wide excision, partial mastectomy, quadrantectomy, or reoperation after enucleation to achieve a clear margin.

3) Mastectomy: Complete removal of breast tissue, including simple mastectomy, total mastectomy, radical mastectomy, or modified radical mastectomy, regardless of whether axillary dissection was done or not.

The reconstruction type was categorized as LD flap, TRAM flap, Implant, and combines. The classification of the Phyllodes tumor as benign, borderline, and malignant histotype was recorded from the original pathology report issued at the time of

diagnosis and treatment. All of the original haematoxylin and eosin slides were prepared using formalin fixedparaffin embedded. Routine haematoxylin and eosin staining procedure were done. Our pathologist retrieved all available pathology slides (166 of 168 cases, 98.8%)and recorded the following histologic characteristics: size, margins, tumor borders, stromal pattern, stromal cellularity, cellular pleomorphism, number of mitoses, and presence of necrosis. Histologically, the diagnosis of PT was based on established morphologic criteria defined by the World Health Organization in 2003[1] as a "group of circumscribed biphasic tumours, basically analogous to fibroadenomas, characterized by a double layer edepithelial component arranged in clefts surrounded by an overgrowing hypercellular mesenchymal component typically organized in leaf-like structures".

Clinical size measurements were only used when pathology determinations were not available. This occurred in 10 patients (4%) whose mean tumor size was 5.3 cm (range, 0.6 to 13.4 cm). The margin of a phyllodes tumor was defined as positive if the tumor was present atthe inked tissue edge on histopathologic evaluation. If a subsequent surgery was performed (reexcision, mastectomy), margin status will be determined by the last surgical procedure. The border between the tumor and the surrounding breast parenchyma was characterized as either well circum scribed/pushing or invasive/infiltrative. The stromal pattern of each PT was categorized asuniform, stromal expansion, or marked stromal overgrowth. Uniform stromal distribution showed little to no increase in the stroma. Stromal expansion was defined as a proliferation of the stroma, displacing the epithelium. Marked stromal overgrowth was characterized by stromal proliferation such that breast epithelial elements were not seen in at least onelow-power field (x4 objective; x40 total power)[25]. Stromal cellularity was classified as either minimal/modest (resembling that of a fibroadenoma) or marked (with dense cellularity such that many intracellular nuclei appear to make contact). Cellular pleomorphism was categorized as minimal/modest or marked, depending on the varying sizeand shape of nuclei in tumor cells. Mitotic count is expressed as the enumerating number of mitotic figures per 10 high-power fields (HPF). Low and high mitotic activity were defined by established criteria of the Armed Forces Institute of Pathology[26]. Low mitotic activity had <5 mitoses per 10 HPF, and high mitotic counts were defined as having at least 5 mitoses per 10 HPF. Ghosts of tumor cells, without viable nuclei, retaining phyllodes architecture in proximity to a phyllodes tumor were recognized as tumor necrosis.

Statistical analysis

Statistical analysis was performed using STATA V.14 (StataCorp LP 4905 Lakeway Drive College Station, Texas 77845 USA). Descriptive statistics including frequency, percent, mean, standard deviation, median, inter-quartile range / range were used to present the data; Analytic statistics included t-test, Wilcoxon Mann-Whitney test, Chi-square test, Fisher's test exact, Kruska wallis, Event-free probability of recurrence.

Results

Table 1 to 6 shows the demographic and clinical characteristics of 168 patients with phyllode tumor treated at Ramathibodi Hospital with follow-up. Of the 168 patients in the study, 8 (4.76%) had a recurrence and 5 (2.97%) had distant metastases. Table 7 shows the demographic and clinical characteristics of 8 patients with recurrent phyllodes tumors.

Clinical features

All patients were female. The mean duration of symptom was 0.4 months, ranging from 0 to 121.67 months. The mean follow-up was 11.92 months, ranging from 3.07 to 62.30 months. The greatest dimension of the tumors ranged from 0.5 to 32 cm and had a mean of 4.92 cm. The greatest dimension of the tumors were approximately 73.21% less than or equal to 5 cm in dimension and 26.75% more than 5 cm.

Patients' age ranged from 16 to 66 years, with a mean of 43.65 years. 66 patients (39.29%) were 40 or younger, and 18 (35.29%) of them had a tumor size of more than 5 cm. 102 patients (60.71%) were older than 40, of whom 33 (64.71%) had a tumor size of more than 5 cm, but there was no significant difference between the two age groups ($p = 0.484$). Patients' age were not associated with recurrence ($p = 0.483$). 68 (40.48%) had right-sided lesions; 92 (54.76%) had left-sided lesions, and eight (4.76%) had bilateral phyllodes tumor.

The relationship between operative procedures, tumor size, and recurrence are shown in Table 1 and 4. Of 66 (39.29%) patients undergoing local excision, 3 (4.54%) had a recurrence; 69 (41.07%) patients were managed with wide excision, and 1 (1.45%) patient had a recurrence. 33 (19.64%) patients had a mastectomy, and 4 (12.12%) had a recurrence, but there was no significant difference between the other two procedures ($p = 0.054$). 6 (11.77%) patients who underwent excisionhad a tumor size of more than 5 cm

Table 1. Clinical demographic data (by tumor)

Characteristics	Total n = 168 (%)	Tumor ≤5 n = 123 (%)	Tumor >5 n = 45 (%)	*p*-value
Age (year)				
<40	66 (39.29)	48 (41.03)	18 (35.29)	0.484
≥40	102 (60.71)	69 (58.97)	33 (64.71)	
Side				
Right	68 (40.48)	46 (39.32)	22 (43.14)	0.159
Left	92 (54.76)	63 (53.84)	29 (56.86)	
Both	8 (4.76)	8 (6.84)	0	
Clinical				
Palpable mass	155 (92.26)	105 (89.74)	50 (98.04)	0.112
Screening	13 (7.74)	12 (10.26)	1 (1.96)	
Operation				
Excision	66 (39.29)	60 (51.29)	6 (11.77)	<0.001
Wide excision	69 (41.07)	56 (47.86)	13 (25.49)	
Mastectomy	33 (19.64)	1 (0.85)	32 (62.74)	
Reconstruction				
Yes				<0.001
LD	2 (1.19)	0	2 (3.92)	
TRAM	8 (4.76)	0	8 (15.69)	
Prosthesis	9 (5.36)	0	9 (17.65)	
LD with prosthesis	1 (0.60)	0	1 (1.96)	
Reduction mammoplasty	1 (0.60)	1 (0.85)	0	
No	147 (87.49)	116 (99.15)	31 (60.78)	
Reoperation				
No	153 (91.07)	105 (89.74)	48 (94.12)	0.557
Yes	15 (8.93)	12 (10.26)	3 (5.88)	
Reoperation type				
Re-excision	12 (80.00)	9 (75.00)	3 (100)	0.999
Mastectomy	3 (20.00)	3 (25.00)	0	
Recurrent				
No	160 (95.24)	115 (98.29)	45 (88.24)	0.010
Yes	8 (4.76)	2 (1.71)	6 (11.76)	

13 (25.49%) patients who underwent wide excision had a tumor size of more than 5 cm 32 (62.74%) treated with mastectomy had a tumor size of more than 5 cm, which is a significant difference compared to the other two procedures (p<0.001). Of 21 patients undergoing reconstruction operation, 2 (1.19%) had a LD flap; 8 (4.76%) had a TRAM flap; 9 (5.36%) had prosthesis; 1 (0.6%) had LD flap with prosthesis; 1 (0.66%) had mammoreduction.

Pathologic features

Table 2 shows the pathologic features of all PT categorized by tumor size. Tumor size in these patients ranged from 0.5 to 32 cm, with a mean of 4.92 cm and a median of 4.20 cm. Tumor size also significantly correlated with recurrence (p = 0.010). Recurrent tumor size of more than 5 cm was significant recurrence compared to tumors less than or equal to 5 cm. The association between tumor size and histology was observed: 6 (5.17%) were labeled as malignant having a tumor of more than 5 cm, and 18 (35.29%) were labeled as borderline with a tumor of more than 5 cm, and 18 (35.29%) had benign phyllodes (p<0.001). Histology type was also significantly correlated with recurrence (p<0.001). Of the 168 cases, 100 (59.52%) had pathologically negative margins after surgery; 33 (19.64%) had pathological closed margin, and 15 (8.94%) had positive margin. Margins in 20 (11.90%) cases could not be evaluated. An association between tumor size and margin was observed: 2 (4.26%) labeled as positive with a tumor of more than 5 cm; 12 (25.53%) labeled as closed to having a tumor of more than 5 cm,

Table 2. Pathological demographic data (by tumor)

Characteristics	Total n = 168 (%)	Tumor ≤5 n = 123 (%)	Tumor >5 n = 45 (%)	*p*-value
Histology				
Benign	107 (63.69)	89 (76.73)	18 (35.29)	<0.001
Borderline	39 (23.21)	21 (18.10)	18 (35.29)	
Malignant	21 (12.50)	6 (5.17)	15 (29.42)	
Unknown	1 (0.60)			
Mitotic count				
<5 per 10 HPF	49 (29.17)	29 (74.36)	20 (57.14)	0.118
≥5 per 10 HPF	25 (14.88)	10 (25.64)	15 (42.86)	
Unknown	94 (55.95)			
Margin status				
Not free	15 (8.94)	13 (12.87)	2 (4.26)	0.254
Closed or < 0.1 cm	33 (19.64)	21 (20.79)	12 (25.53)	
≥0.1 cm (free)	100 (59.52)	67 (66.34)	33 (70.21)	
Unknown	20 (11.90)			
Borders				
Well define	86 (51.19)	63 (87.50)	23 (71.87)	0.052
Infiltrative/invasive	18 (10.71)	9 (12.50)	9 (28.13)	
Unknown	64 (38.10)			
Stromal status				
No overgrowth	19 (11.31)	16 (80.00)	3 (21.43)	0.001
Present overgrowth	15 (8.93)	4 (20.00)	11 (78.57)	
Unknown	134 (79.76)			
Stromal cellularity				
Minimal/modest	41 (24.41)	29 (90.63)	12 (92.31)	0.999
Marked	4 (2.38)	3 (9.37)	1 (7.69)	
Unknown	123 (73.21)			
Cellular pleomorphism				
No atypia	3 (1.79)	2 (8.70)	1 (5.88)	0.999
Present atypia	37 (22.02)	21 (91.30)	16 (94.12)	
Unknown	128 (76.19)			
necrosis				
No	1 (0.60)	1 (33.33)	0	0.231
Present	12 (7.14)	2 (66.67)	10 (100)	
Unknown	155 (92.26)			

Chi-square test, Fisher's exact test

and 33 (70.21%) had a negative margin (p = 0.254). Margin was not significantly correlated with recurrence (p = 0.740). Of the 168 cases, 49 (29.17%) had mitotic activity greater than 5 per 10 HPF; and 25 (14.88%) had mitotic activity less than or equal 5 per 10 HPF. Mitotic activity in 94 (55.95%) could not be evaluated. The association between tumor size and mitotic activity was observed: 20 (57.14%) had mitotic activity greater than 5 per 10 HPF and a tumor of more than 5 cm, and 15 (42.86%) with mitotic activity less than or equal 5 per 10 HPF (p = 0.118). Mitotic activity was not significantly correlated with recurrence (p = 0.328). Although borders, stromal cellularity, tumor necrosis, stromal status, and cellular pleomorphism appeared to be associated with tumor size and recurrence, the association was not statistically significant (Table 2 and 4).

Recurrence

Of the 168 cases, 8(4.76%) patients had recurrence. 3 patients had local recurrence, 2 patients had second recurrence, and 5 patients had distant recurrence; to the lung in all. The mean age of these patients was 46.37 years, and the mean follow-up was 40.02 months. The mean time to recurrence was 17.47

Table 3. Clinical characteristics (continuous data by tumor)

Characteristics	Total n = 168 (%)	Tumor ≤5 n = 117 (%)	Tumor >5 n = 51 (%)	*p*-value
Age				
Mean	43.66	42.75	45.75	0.086
SD	10.39	10.16	10.71	
Median	42.50	42	46	
Range	16 to 66	16 to 66	16 to 64	
Inter-quartile range	38 to 51	37 to 48	39 to 55	
Time detect (month)				
Mean	4.25	3.15	6.64	<0.001
SD	12.11	12.84	12.11	
Median	0.40	0.27	1.73	
Range	0 to 121.67	0 to 121.67	0.03 to 60.83	
Inter-quartile range	0.13 to 2	0.13 to 1.73	0.47 to 12.13	
Time to recurrent (month)				
Mean	17.47	15.98	17.97	0.505
SD	18.88	7.37	22.06	
Median	11.92	15.98	27.37	
Range	3.07 to 62.30	10.77 to 21.20	0.27 to 114.57	
Inter-quartile range	7.98 to 17.31	10.77 to 21.20	13.30 to 42.73	
Time follow-up (month)				
Mean	32.34	32.10	32.85	0.966
SD	24.76	24.16	26.27	
Nedian	27.07	11.10	26.82	
Range	0.27 to 114.57	3.07 to 62.30	0.40 to 113.47	
Inter-quartile range	13.43 to 41.80	6.83 to 13.43	13.43 to 38.50	

Age >normal distribution >t-test; Time detect, Time to recurrent, Time follow-up >non-normal distribution >wilcox on mann-whitney test

months with a median of 11.92 months, and ranged from 0.3.07 to 62.30 months. Two patient's tumors were less than or equal to 5 cm, but the other six tumors were more than 5 cm (mean 7.43 cm). 6 patients underwent mastectomy while others underwent breast conserve surgery. The pathologic diagnosis in six patients was malignant tumor, and the other a borderline tumor. 6 patients had pathologically negative margins after surgery and 1 patient had pathological closed margin. All local recurrence patients can be managed with wide local excision.

Fig. 3 show event free probability of all patient was 5.72% and 50% median time to recurrence was 10.77 month (95% CI = 18.5 to 28.73).

Discussion

Phyllode tumor constitute less than 1% of all breast tumors and only 2.3% of all mammary fibroepithelial neoplasms[27]. These tumors occur over a wide age range among women, with a median age of 45 years, and 15 to 20 years later than that for fibroadenomas[13,28]. Few cases have been reported in men and these have invariably been associated with gynecomastia[29,30]. In our series, all patients were women, with an age of range of 16 to 66 years (mean 43.66 years).

Phyllode tumors usually present as rapidly growing but clinically benign breast lumps. In some patients, a lesion may have been apparent for several years, but they only come for evaluation when the mass increases suddenly in size. Other symptoms and signs are non-specific, including dilated skin veins, blue discoloration of the skin, nipple retraction, fixation to the skin or the pectoralis muscle, a skin ulcer, pressure necrosis of the skin, or palpable axillary lymphadenopathy[13]. In the current study, 155 of 168 patients presented with a palpable breast mass, with a time to detect tumor of ranging from 0.33 to 121.67 months (mean 4.25 months); another presented with breast mass on screening. No patient had skin ulcer,

Table 4. Clinical demographic data (by recurrence)

Characteristics	Total n = 168 (%)	Non-recurrence n = 160 (%)	Recurrence n = 8 (%)	*p*-value
Age				
<40	66 (39.29)	64 (40.00)	2 (25.00)	0.483
≥40	102 (60.71)	96 (60.00)	6 (75.00)	
Side				
Right	68 (40.48)	63 (39.38)	5 (62.50)	0.521
Left	92 (54.76)	89 (55.63)	3 (37.50)	
Both	8 (4.76)	8 (5.00)	0	
Clinical				
Papillary mass	155 (92.26)	147 (91.88)	8 (100)	0.999
Screening	13 (7.74)	13 (8.13)	0	
Operation				
Excision	66 (39.29)	63 (39.38)	3 (37.50)	0.054
Wide excision	69 (41.07)	68 (42.50)	1 (12.50)	
Mastectomy	33 (19.64)	29 (18.13)	4 (50.00)	
Reconstruction				
Yes	21 (12.50)	19 (11.88)	2 (25.00)	0.262
LD	2 (9.52)	2 (10.53)	0	
TRAM	8 (38.10)	8 (42.11)	0	
prosthesis	9 (42.86)	7 (36.84)	2 (100)	
LD with prosthesis	1 (4.76)	1 (5.26)	0	
Reduction mammoplasty	1 (4.76)	1 (5.26)	0	
No	147 (87.50)	141 (88.13)	6 (75.00)	
Re op				
No	153 (91.07)	147 (91.88)	6 (75.00)	0.152
Yes	15 (8.93)	13 (8.13)	2 (25.00)	
Reoperation type				
Excision	12 (80.00)	11 (84.62)	1 (50.00)	0.371
Mastectomy	3 (20.00)	2 (15.38)	1 (50.00)	
Pathologic reoperation				
Non-residual	14 (93.33)	12 (92.31)	2 (100)	0.999
Residual	1 (6.67)	1 (7.69)	0	

nipple discharge, or axillary lymphadenopathy.

In the literature review, Phyllodes tumors reported a recurrence rate of approximately 20%, regardless of its classification as benign or malignant[16,25,31-36]. In the current study, 8 of 168 (4.76%) had treatment failures, with an incidence rate of recurrence tumors of 2.43%, and a median follow-up time to recurrence of 34.07 months (95% CI = 21.83 to 30.10). Incidence rate cumulative hazard of recurrence patients was4.96%, and the median time to recurrence was 11.92 months (95% CI 3.07 to 21.20).

Various factors were related to clinical behavior and outcome. Of these histology, stromal overgrowth, tumor necrosis, and mitotic activity were found to be most consistently associated with recurrence, metastasis, and poor survival[12,25,28,37-40]. Other factors that may correlate with the outcome were tumor size[12,28,33,39,41,42], Cellular pleomorphism[36-38,40], stromal cellularity[37,43], lymph node metastasis[41], and age[28,37,39-41,44,45]. In the present study, recurrence was not significantly correlated with age. We evaluated pathological factors including histology, tumor size, Cellular pleomorphism, stromal overgrowth, Borders, stromal atypia, mitotic activity, tumor necrosis, tumor margin, and heterologous stromal elements. Histology and tumor size were positively correlated with recurrence. Tumor size of more than 5 cm was significant for recurrence. Stromal cellularity, stromal overgrowth, Cellular pleomorphism, mitotic activity, border, and tumor margin, were not significantly correlated with recurrence; because of in the present study pathologist reported pathologic factor less of than 50%, and thus

Table 5. Pathological demographic data (by recurrence)

Characteristics	Total n = 168 (%)	Non recurrence n = 160 (%)	Recurrence n = 8 (%)	*p*-value
Tumor size (adjust)				
≤5	117 (69.64)	115 (71.88)	2 (25.00)	0.010
>5	51 (30.36)	45 (28.13)	6 (75.00)	
Pathophyllodes				
Benign	107 (63.69)	106 (66.67)	1 (12.50)	<0.001
Borderline	39 (23.21)	37 (23.27)	2 (25.00)	
Malignant	21 (12.50)	16 (10.06)	5 (62.50)	
Unknown	1 (0.60)			
Mitotic				
<5 per 10 HPF	49 (29.17)	47 (68.12)	2 (40.00)	0.328
≥5 per 10 HPF	25 (14.88)	22 (31.88)	3 (60.00)	
Unknown	94 (55.95)			
Margin status				
Not free	15 (8.93)	14 (10.00)	1 (12.50)	0.740
Closed or <0.1 cm	33 (19.64)	32 (22.86)	1 (12.50)	
≥0.1 cm (free)	100 (59.52)	94 (67.14)	6 (75.00)	
Unknown	20 (11.90)			
Borders				
Well define	86 (51.19)	83 (83.84)	3 (60.00)	0.206
Infiltrative/invasive	18 (10.71)	16 (16.16)	2 (40.00)	
Unknown	64 (38.10)			
Stromal status				
No overgrowth	19 (11.31)	18 (54.55)	1 (100)	0.999
Present overgrowth	15 (8.93)	15 (45.45)	0	
Unknown	134 (79.76)			
Stromal cellularity				
Minimal/modest	41 (24.40)	40 (90.91)	1 (100)	0.999
Marked	4 (2.38)	4 (9.09)	0	
Unknown	123 (73.21)			
Cellular pleomorphism				
No atypia	3 (1.79)	3 (7.89)	0	0.999
Present atypia	37 (22.02)	35 (92.11)	2 (100)	
Unknown	128 (76.19)			
Necrosis				
Non	1 (0.60)	1 (8.33)	0	0.999
Present	12 (7.14)	11 (91.67)	1 (100)	
Unknown	155 (92.26)			
Pathologic reoperation				
Non residual	14 (93.33)	12 (92.31)	2 (100)	0.999
Residual	1 (6.67)	1 (7.69)	0	

was not statistically significant.

Although surgery remains the mainstay of treatment, the extent of the procedure remains controversial. Margins of 1 to 2 cm have been recommended[5,12,13,35,37,39,40,46]; some authors recommended a margin of at least 1mm[47]; enucleation alone is considered insufficient[12,43]. Some authors found positive margins in all surgical specimens from patients who subsequently sustained a local recurrence after local excision[33,35,39,40,46,48]. In our study, 26 patients had positive surgical margin after the first operation. 10 of those (six underwent local excision and four had wide excision) decided to have another surgery (eight wide excision and two mastectomy, respectively) later and all margin were consequently free of tumor involvement. The ten patients' operative methods were

Table 6. Clinical characteristics (continuous data by recurrence)

Characteristics	Total n = 168	Non recurrence n = 160	Recurrence n = 8	*p*-value
Age				
Mean	43.66	43.52	46.37	0.451
SD	10.39	10.43	9.62	
Median	42.50	42.50	47.50	
Range	16 to 66	16 to 66	32 to 59	
Inter-quartile range	38 to 51	38 to 51	39 to 53.50	
Time detect (month)				
Mean	4.25	4.27	3.82	0.059
SD	12.68	12.92	4.24	
Median	0.40	0.40	2.5	
Range	0 to 121.67	0 to 121.67	0.27 to 12.17	
Inter-quartile range	0.13 to 2	0.13 to 2	2 to 3.47	
Tumor size (adjust)				
Mean	4.90	4.77	7.43	0.013
SD	4.20	4.20	3.46	
Median	3.50	3.50	6.75	
Range	0.50 to 32	0.50 to 32	3.50 to 13	
Inter-quartile range	2.05 to 6.40	2 to 5.35	5 to 9.75	
Time to recurrent (month)				
Mean	17.47	-	17.47	-
SD	18.88	-	18.88	
Median	11.92	-	11.92	
Range	3.07 to 62.30	-	3.07 to 62.30	
Inter-quartile range	7.98 to 17.31	-	7.98 to 17.31	
Time follow-up (month)				
Mean	32.34	31.87	41.15	0.278
SD	24.76	24.66	26.75	
Median	27.07	26.93	40.02	
Range	0.27 to 114.57	0.27 to 114.57	13.33 to 84.27	
Inter-quartile range	13.43 to 41.80	13.40 to 40.87	14.23 to 61.56	

initially classified as wide excision (eight patients) and mastectomy (two patients), and two of them had recurrence. Other 16 patients were observed during OPD follow-up, and one of them had recurrence.

Several authors have noted positive surgical margins to be independent predictors of recurrence[6,35,37,39,40,46,48-50]. Consistently with previous literature, our data showed positive or closed margins not associated with recurrence. The most influential factor maybe the histology factor. 16 of 26 patients who had surgical margin positive weren't reoperated, 14 patients had benign phyllode tumors, and 2 had borderline phyllode tumors. Non reoperated patients had positive margin and a favorable histology, which is probably one of the reasons that the positive margin had no influence for recurrence in the present study.

In some series, wide local excision of the tumor with negative margins resulted in a local control rate of approximately 90%, and the authors recommended this approach whenever cosmetically feasible[12]. In the present series, 56 patients underwent wide excision had negative surgical margins, and one had recurrence. The local control rate was 98.2%, which is higher than previous reports. By comparison, 38 patients had local excision with negative margins, and one had recurrence, for a local control rate of 97.3%. 24 patients had mastectomy with negative surgical margins, and three had a recurrence with a local control rate of 87.5%. Cause mastectomy with recurrence control rate lower than local excision and wide excision in this study can be explained by patients who choose mastectomy; 22 of 24 patients had tumor size more than 5 cm. Thus, mastectomy had greater recurrence than other procedures. Most malignant PTs do not recur or

Table 7. Clinical feature of 8 patient with phyllodes tumor who had recurrence

Case	Age	Operation type	Tumor size (cm)	Histologic type	Margin status	Recurrence type	Site recurrence	Time recurrence (month)
1	41	Excision	3.7	Borderline	Free	Local	Breast	21.20
2	53	Wide excision	6.3	Malignant	Free	Distant	Lung	13.07
3	42	Mastectomy	12	Malignant	Not free	Distant	Lung	13.43
4	32	Mastectomy	7.5	Borderline	Free	Local	Chest wall	6.83
5	59	Mastectomy	6.5	Malignant	Free	Local	Chest wall	62.30
6 (1^{st})	37	Subcutaneous mastectomy	13	Benign	Free	Local	Chest wall	3.07
6 (2^{nd})	38	Mastectomy	20	Malignant	Free	Local and distant	Chest wall and Lung	67.73
7 (1^{st})	54	Wide excision	7	Malignant	Closed	Local	Breast	9.13
7 (2^{nd})	55	Mastectomy	4	Malignant	Free	Local and distant	Chest wall and Lung	3.76
8	53	Mastectomy	3.5	Malignant	Free	Local	Lung	10.77

Fig. 3 Event-free probability of recurrence tumor.

metastasize, but some histologically benign tumors have an unusually aggressive course[13,29,34,51,52]. Consequently, it has been suggested that all phyllodes tumors should be regarded as potentially malignant[13,34,44,53]. In our series, one patients with metastases initially had benign tumors.

The more common sites for distant cancers to metastasize include the lung, bones, and abdominal viscera. These often occur in the absence of lymph node metastases and only contain the stromal element histologically[13,34,39,40,54]. The lung was the site of metastases in five patients, but there was no document of bone or abdominal viscera metastasis.

The role of adjuvant radiotherapy or chemotherapy remains uncertain. Some investigators suggested that adjuvant radiotherapy improves disease-free survival[55], but not for others[47,56]. Others recommended adjuvant radiotherapy incases of incomplete resection. Chemotherapy should be examined systematically in patients with stromal overgrowth[12]. To date, neither adjuvant radiotherapy nor chemotherapy is routinely recommended. In our series, one patient received adjuvant radiotherapy because of histology was malignant tumor and surgical margin not free; this patient had local recurrence and lung metastases. One patient with a malignant lesion received adjuvant chemotherapy and subsequently remained disease-free. Due to the small numbers in our series treated with adjuvant radiotherapy or chemotherapy, statistical conclusions cannot be drawn. In our study, we does not multivariate analysis because of low incidence recurrence tumor.

In summary, we found that tumor size and histotology were associated with recurrence. The clinicopathologic factors include stromal cellularity,

stromal overgrowth, Cellular pleomorphism, mitotic activity, and margin and border, which cannot be concluded that it was associated with recurrence. The aim of this study is to determine the optimum strategy, which could form the potential basis of a prospective clinical trial.

What is already known on this topic?

Phyllodes tumor is rare fibroepithelial lesion of breast tumor. The main stay treatment is surgery. Although surgery has an adequate surgical margin, the tumor has a tendency to recur locally and occasionally to metastasis. In the literature review, various factors are related to recurrence include histology, tumor margin, stromal overgrowth, tumor necrosis, mitotic activity, tumor size, cellular pleomorphism, stromal cellularity and age. However, most of these studies are retrospective studies. Patients are not much, and no one factor causes a clear recurrence.

What this study adds?

The present study was a study of 168 patients in Ramathibodi Hospital, focusing on factors affecting the recurrence of Phyllodes tumor. These factors are the histology and size of the tumor. These maked

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Potential conflicts of interest

None.

References

1. Tavassoli FA, Devilee P. Pathology and genetics of tumors of the breast and female genital organs. WHO Classification of Tumours series-volume IV. Lyon, France: IARC Press; 2003.
2. Kraemer B, Hoffmann J, Roehm C, Gall C, Wallwiener D, Krainick-Strobel U. Cystosarcoma phyllodes of the breast: a rare diagnosis: case studies and review of literature. Arch Gynecol Obstet 2007; 276: 649-53.
3. Fiks A. Cystosarcoma phyllodes of the mammary gland—M□ller's tumor. For the 180th birthday of Johannes M□ller. Virchows Arch A Pathol Anat Histol 1981; 392: 1-6.
4. Hawkins RE, Schofield JB, Fisher C, Wiltshaw E, McKinna JA. The clinical and histologic criteria that predict metastases from cystosarcoma phyllodes. Cancer 1992; 69: 141-7.
5. 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: 910-6.
6. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M, et al. Phyllodes tumors of the breast: the role of pathologic parameters. Am J Clin Pathol 2005; 123: 529-40.
7. Karim RZ, Gerega SK, Yang YH, Spillane A, Carmalt H, Scolyer RA, et al. Phyllodes tumours of the breast: a clinicopathological analysis of 65 cases from a single institution. Breast 2009; 18: 165-70.
8. Taira N, Takabatake D, Aogi K, Ohsumi S, Takashima S, Nishimura R, et al. Phyllodes tumor of the breast: stromal overgrowth and histological classification are useful prognosis-predictive factors for local recurrence in patients with a positive surgical margin. Jpn J Clin Oncol 2007; 37: 730-6.
9. Sotheran W, Domjan J, Jeffrey M, Wise MH, Perry PM. Phyllodes tumours of the breast—a retrospective study from 1982-2000 of 50 cases in Portsmouth. Ann R Coll Surg Engl 2005; 87: 339-44.
10. Chirappapha P, Lertsithichai P, Sukarayothin T, Leesombatpaiboon M, Supsamutchai C, Kongdan Y. Oncoplastic techniques in breast surgery for special therapeutic problems. Gland Surg 2016; 5: 75-82.
11. Fang CL, Hsu CH, Tu CW. The reconstruction choice for giant phyllodes tumor of breast: Bi-pedicled deep inferior epigastric perforator flap. Aesthetic Plast Surg 2017; 41: 768-72.
12. Chaney AW, Pollack A, McNeese MD, Zagars GK, Pisters PW, Pollock RE, et al. Primary treatment of cystosarcoma phyllodes of the breast. Cancer 2000; 89: 1502-11.
13. Parker SJ, Harries SA. Phyllodes tumours. Postgrad Med J 2001; 77: 428-35.
14. Barth RJ Jr, Wells WA, Mitchell SE, Cole BF. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. Ann Surg Oncol 2009; 16: 2288-94.
15. Tan PH, Thike AA, Tan WJ, Thu MM, Busmanis I, Li H, et al. Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. J Clin Pathol 2012; 65: 69-76.
16. Kario K, Maeda S, Mizuno Y, Makino Y, Tankawa H, Kitazawa S. Phyllodes tumor of the breast: a

clinicopathologic study of 34 cases. J Surg Oncol 1990; 45: 46-51.
17. Grimes MM. Cystosarcoma phyllodes of the breast: histologic features, flow cytometric analysis, and clinical correlations. Mod Pathol 1992; 5: 232-9.
18. Mokbel K, Price RK, Mostafa A, Wells CA, Carpenter R. Phyllodes tumour of the breast: a retrospective analysis of 30 cases. Breast 1999; 8: 278-81.
19. Asoglu O, Ugurlu MM, Blanchard K, Grant CS, Reynolds C, Cha SS, et al. Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. Ann Surg Oncol 2004; 11: 1011-7.
20. Kapiris I, Nasiri N, A'Hern R, Healy V, Gui GP. Outcome and predictive factors of local recurrence and distant metastases following primary surgical treatment of high-grade malignant phyllodes tumours of the breast. Eur J Surg Oncol 2001; 27: 723-30.
21. Belkac□mi Y, Bousquet G, Marsiglia H, Ray-Coquard I, Magn□ N, Malard Y, et al. Phyllodes tumor of the breast. Int J Radiat Oncol Biol Phys 2008; 70: 492-500.
22. Pezner RD, Schultheiss TE, Paz IB. Malignant phyllodes tumor of the breast: local control rates with surgery alone. Int J Radiat Oncol Biol Phys 2008; 71: 710-3.
23. Morcos BB, Baker B, Hashem SA. Ileocaecal intussusception secondary to metastatic phyllodes tumour of the breast. Ann R Coll Surg Engl 2010; 92: W29-30.
24. Telli ML, Horst KC, Guardino AE, Dirbas FM, Carlson RW. Phyllodes tumors of the breast: natural history, diagnosis, and treatment. J Natl Compr Canc Netw 2007; 5: 324-30.
25. Ward RM, Evans HL. Cystosarcoma phyllodes. A clinicopathologic study of 26 cases. Cancer 1986; 58: 2282-9.
26. Rosen PP, Oberman HA. Tumors of the mammary gland. In: Atlas of tumor pathology. Washington DC: Armed Forces Institute of Pathology; 1993: 107-13.
27. Powell CM, Rosen PP. Adipose differentiation in cystosarcoma phyllodes. A study of 14 cases. Am J Surg Pathol 1994; 18: 720-7.
28. Pandey M, Mathew A, Kattoor J, Abraham EK, Mathew BS, Rajan B, et al. Malignant phyllodes tumor. Breast J 2001; 7: 411-6.
29. West TL, Weiland LH, Clagett OT. Cystosarcoma phyllodes. Ann Surg 1971; 173: 520-8.
30. Pantoja E, Llobet RE, Lopez E. Gigantic cystosarcoma phyllodes in a man with gynecomastia. Arch Surg 1976; 111: 611.
31. Pietruszka M, Barnes L. Cystosarcoma phyllodes: a clinicopathologic analysis of 42 cases. Cancer 1978; 41: 1974-83.
32. 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: 654-7.
33. Ramakant P, Chakravarthy S, Cherian JA, Abraham DT, Paul MJ. Challenges in management of phyllodes tumors of the breast: a retrospective analysis of 150 patients. Indian J Cancer 2013; 50: 345-8.
34. Lin CC, Chang HW, Lin CY, Chiu CF, Yeh SP. The clinical features and prognosis of phyllodes tumors: a single institution experience in Taiwan. Int J Clin Oncol 2013; 18: 614-20.
35. Jang JH, Choi MY, Lee SK, Kim S, Kim J, Lee J, et al. Clinicopathologic risk factors for the local recurrence of phyllodes tumors of the breast. Ann Surg Oncol 2012; 19: 2612-7.
36. Sawalhi S, Al Shatti M. Phyllodes tumor of the breast: a retrospective study of the impact of histopathological factors in local recurrence and distant metastasis. Ann Saudi Med 2013; 33: 162-8.
37. Zhou ZR, Wang CC, Yang ZZ, Yu XL, Guo XM. Phyllodes tumors of the breast: diagnosis, treatment and prognostic factors related to recurrence. J Thorac Dis 2016; 8: 3361-8.
38. Cohn-Cedermark G, Rutqvist LE, Rosendahl I, Silfversward C. Prognostic factors in cystosarcoma phyllodes. A clinicopathologic study of 77 patients. Cancer 1991; 68: 2017-22.
39. Wei J, Tan YT, Cai YC, Yuan ZY, Yang D, Wang SS, et al. Predictive factors for the local recurrence and distant metastasis of phyllodes tumors of the breast: a retrospective analysis of 192 cases at a single center. Chin J Cancer 2014; 33: 492-500.
40. 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: 185-94.
41. Norris HJ, Taylor HB. Relationship of histologic features to behavior of cystosarcoma phyllodes. Analysis of ninety-four cases. Cancer 1967; 20: 2090-9.
42. Chen HM, Chen SC, Hsueh S, Hwang TL, Jeng LB,

Jan YY, et al. Surgical treatment of phyllodes tumor of the breast - review of the clinico-pathologic features. J Surg Assoc, ROC 1993; 26: 1974-81.
43. Salvadori B, Cusumano F, Del Bo R, Delledonne V, Grassi M, Rovini D, et al. Surgical treatment of phyllodes tumors of the breast. Cancer 1989; 63: 2532-6.
44. Contarini O, Urdaneta LF, Hagan W, Stephenson SE Jr. Cystosarcoma phylloides of the breast: a new therapeutic proposal. Am Surg 1982; 48: 157-66.
45. Demian GA, Fayaz S, El Sayed EH, Nazmy N, Samir S, George T, et al. Phyllodes tumors of the breast: Analysis of 35 cases from a single institution. J Egypt Natl Canc Inst 2016; 28: 243-8.
46. Barrio AV, Clark BD, Goldberg JI, Hoque LW, Bernik SF, Flynn LW, et al. Clinicopathologic features and long-term outcomes of 293 phyllodes tumors of the breast. Ann Surg Oncol 2007; 14: 2961-70.
47. Tremblay-LeMay R, Hogue JC, Provencher L, Poirier B, Poirier □, Laberge S, et al. How wide should margins be for phyllodes tumors of the breast? Breast J 2017; 23: 315-22.
48. de Roos WK, Kaye P, Dent DM. Factors leading to local recurrence or death after surgical resection of phyllodes tumours of the breast. Br J Surg 1999; 86: 396-9.
49. Barth RJ Jr. Histologic features predict local recurrence after breast conserving therapy of phyllodes tumors. Breast Cancer Res Treat 1999; 57: 291-5.
50. Cheng SP, Chang YC, Liu TP, Lee JJ, Tzen CY, Liu CL. Phyllodes tumor of the breast: the challenge persists. World J Surg 2006; 30: 1414-21.
51. Blichert-Toft M, Hansen JP, Hansen OH, Schiodt T. Clinical course of cystosarcoma phyllodes related to histologic appearance. Surg Gynecol Obstet 1975; 140: 929-32.
52. Liu TP, JK, Yang TL. Surgical treatment of phyllodes tumors of the breast: Retrospective review of 66 cases. J Chin Oncol Soc 1995; 11: 35-42.
53. Rix DB, Tredwell SJ, Forward AD. Cystosarcoma phylloides (cellular intracanalicular fibroadenoma): clinical-pathological relationships. Can J Surg 1971; 14: 31-7.
54. Ramakant P, Selvamani, Therese MM, Paul MJ. Metastatic malignant phyllodes tumor of the breast: An aggressive disease-analysis of 7 cases. Indian J Surg Oncol 2015; 6: 363-9.
55. Stebbing JF, Nash AG. Diagnosis and management of phyllodes tumour of the breast: experience of 33 cases at a specialist centre. Ann R Coll Surg Engl 1995; 77: 181-4.
56. Kim YJ, Kim K. Radiation therapy for malignant phyllodes tumor of the breast: An analysis of SEER data. Breast 2017; 32: 26-32.

ปัจจัยที่มีผลต่อการกลับเป็นซ้ำหลังผ่าตัด Phyllodes tumor ในโรงพยาบาลรามาธิบดี

สุรกิจ พรชัย, ประกาศิต จิรัปปภา, ภาณุวัฒน์ เลิศสิทธิชัย, เยาวนุช ซงด่าน, ธงชัย ศุกรโยธิน, มนต์ชัย ลีสมบัติไพบูลย์

ภูมิหลัง: Phyllodes tumor เป็นเนื้องอกของเต้านมที่พบน้อย การรักษาหลักคือการผ่าตัด แม้ว่าจะผ่าตัดเนื้องอกชนิดนี้ได้ขอบเขตที่เพียงพอแล้วก็ตาม ก็ยังพบการกลับเป็นซ้ำทั้งเฉพาะที่และการแพร่กระจายไปยังอวัยวะต่าง ๆ จุดมุ่งหมายของการศึกษานี้ คือการศึกษาถึงปัจจัยที่มีอิทธิพลต่อการกลับเป็นซ้ำของเนื้องอกชนิดนี้

วัตถุประสงค์: เพื่อหาปัจจัยที่มีอิทธิพลต่อการเป็นซ้ำของเนื้องอก Phyllodes

วัสดุและวิธีการ: การศึกษานี้เก็บข้อมูลย้อนหลังจากเวชระเบียนในโรงพยาบาลรามาธิบดีตั้งแต่ วันที่ 1 มกราคม พ.ศ. 2543 ถึง วันที่ 31 ธันวาคม พ.ศ. 2559 ได้ผู้ป่วยเข้าร่วมการศึกษาทั้งหมด 168 คน โดยเป็นผู้ป่วยที่ได้รับการวินิจฉัยและรักษาที่โรงพยาบาลรามาธิบดีในช่วงเวลาดังกล่าว แล้วนำมาวิเคราะห์หาปัจจัยการกลับเป็นซ้ำหลังผ่าตัด

ผลการศึกษา: อายุเฉลี่ยของผู้ป่วยคือ 43.65 ปี (16 ปี ถึง 66 ปี) ขนาดเฉลี่ยของเนื้องอกคือ 4.92 เซนติเมตร (0.5 ถึง 32 เซนติเมตร) จากเกณฑ์วินิจฉัยของ WHO พบว่าเป็น benign 107 คน (63.69%), borderline 39 คน (23.21%) และ malignant 21 คน (12.5%) มัธยฐานของระยะเวลาการติดตามคือ 11.92 เดือน (3.07 ถึง 62.3 เดือน) มีการกลับเป็นซ้ำทั้งหมด 8 คน (4.76%) อายุเฉลี่ยของผู้ป่วยที่กลับเป็นซ้ำคือ 46.37 ปี มัธยฐานของระยะเวลาการติดตามผู้ป่วยที่กลับเป็นซ้ำคือ 40.02 เดือน ระยะเวลาเฉลี่ยของการกลับเป็นซ้ำคือ 17.47 เดือน อัตราการเกิดอุบัติการณ์ของการกลับเป็นซ้ำคือ 2.43% มัธยฐานของระยะเวลาการกลับเป็นซ้ำคือ 34.07 เดือน (95% CI = 21.83 ถึง 30.10 เดือน) The event free probability คือ 5.72% และ 50% ของมัธยฐานการกลับเป็นซ้ำคือ 10.77 เดือน (95% CI = 18.5 ถึง 28.73 เดือน) ปัจจัยที่มีผลต่อการกลับเป็นซ้ำคือ ขนาดและผลทางจุลพยาธิวิทยา

สรุป: ขนาดและผลทางจุลพยาธิวิทยาของเนื้องอกเป็นปัจจัยที่มีผลต่อการกลับเป็นซ้ำหลังผ่าตัดการศึกษานี้ โดยการผ่าตัดเพื่อเอาเนื้องอกออกทั้งหมดเป็นสิ่งที่สำคัญในการรักษา