Clinico-Pathological Profile of Vulva Cancer in Southern Thailand: Analysis of 66 Cases

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Objective: *To evaluate the clinico-pathologic findings and treatment outcome of women with vulva cancer in Southern Thailand.*
Material and Method: *The authors retrospectively reviewed the medical records of 66 women who had been treated with surgery from June 1984 to October 2003 at the Department of Obstetrics and Gynecology, Prince of Songkla University.*
Results: *The patients' age ranged from 30 to 87 years, mean 58.2 years. Two most common presentations were vulva mass (89.4%) and pruritus (57.6%). Duration of symptoms at presentation ranged form 1 month to 5 years. Most cases were squamous cell carcinoma (82.0%). The distribution by FIGO surgical stage I, II, III and IV was 9.1%, 47.0%, 34.8% and 9.1%, respectively. The most common complication was wound infection (45.5%), followed by wound dehiscence, lymphosis and leg edema (each 15.2%). The 5-year survival (and 95% CI) for stages I, II, III and IV was 100%, 96% (76-99%), 94% (63-99%) and 60 (13-88%), respectively. The 5-year survival for node-positive cases was 82% (54-94%) versus 100% for node-negative cases (p = 0.0003). Stage was a significant predictor of survival (p = 0.0142) and disease-free survival (p = 0.0112).*
Conclusion: *Stage and nodal involvement are predictors of survival, and stage is a predictor of disease-free survival.*

Keywords: *Vulva cancer, Survival, Prognostic factors*

J Med Assoc Thai 2005; 88(5): 575-81
Full text. e-Journal: *http://www.medassocthai.org/journal*

Vulva cancer is an uncommon disease and accounts for 3% to 5% of all female gynecologic malignancies[1-4]. In Thailand, vulva cancer is the fourth most common gynecologic malignancy after cervical, ovarian, endometrial cancer. Pengsaa et al reported that vulva cancer accounted for 0.4% of all gynecologic malignancies[5].

The disease typically develops in elderly women. Commonly, vulva cancer occurs in 60 and 70 year old women[2,4,6-9]. On the other hand, vulva cancer can also occur in young patients; Al-Ghamdi et al noted that 5% of all vulva squamous cell carcinoma occurs in women younger than 40 years[10]. More than 85% of vulva cancer are squamous cell carcinoma followed by adenocarcinoma, malignant melanoma, basal cell carcinoma, and Paget's disease of the vulva[2,5,11,12].

The main treatment of vulva cancer remains surgery. The original surgical procedure was introduced by Bassett, Taussing, and Way[1,3,4,13-15]. Surgical treatment in the past required a radical triangular incision (Butterfly-type) that excises the entire vulva en bloc down to the urogenital diaphragm and extends laterally to include the groin lymph nodes as a common procedure. Recently, surgical modification has been described to decrease associated morbidities and improve patient quality of life[1,3,4,15,16].

Department of Obstetrics and Gynecology, Songklanakarind Hospital, Faculty of Medicine, Prince of Songkla University is the only tertiary referral

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center for surgical cases of vulva cancer in Southern Thailand, so most case of vulva cancer in this region are treated at this hospital. There have been very few studies concerning the correlation of clinical profile and histopathology of vulva cancer, especially from Thailand[5].

The objective of the present study is to evaluate the clinico-pathologic findings and treatment outcome of women with vulva cancer in Southern Thailand.

Material and Method

A total of 81 consecutive patients underwent surgery for vulva cancer during the period June 1984 to October 2003 at the Department of Obstetrics and Gynecology, Prince of Songkla University. Among these complete clinical records were available in 66 patients. The authors reviewed the clinical records (age, parity, chief complaints, duration of symptoms, site of lesions, diameter of lesions, type of surgery, surgical stage, adjuvant treatment, and complication), pathology reports (histological type, grade, margin, and nodal status), and outcome of treatments for all 66 patients.

Type of surgery included the following: radical vulvectomy and bilateral groin node dissection (en bloc butterfly incision technique or three separate incision technique) plus or minus pelvic node dissection; modified radical vulvectomy (radical local excision) plus or minus groin node dissection (ipsilateral or bilateral); local excision. The groin lymph node dissection consisted of removal of all superficial and deep lymphatic tissue around the femoral vessels, and great saphenous vein in the femoral triangle.

Further treatment depended on the malignant involvement of the inguinofemoral lymph nodes or the surgical margin not being free after attempted surgical removal. If they were involved then radiotherapy was given to the groin and pelvis varying from 4,500 to 5,000 cGy. No chemotherapy was provided to any patient included in this series.

Stages were defined according to the revised International Federation of Gynecology and Obstetrics (FIGO) staging system[17]. Most of the patients were scheduled for post-treatment follow up every 1-3 months for 2 years and every 6 months afterward. All living patients who did not show up at the scheduled check up or loss to follow up were reminded by phone or mail. All deaths are registered by the Medical Statistical Unit and Cancer Registry Unit of Songklanagarind Hospital and the Department of Provincial Administration, Ministry of Interior, according to death certificates issued by a physician stating the cause of death.

Survival time was calculated from the date of beginning of treatment until the date of death or last follow up. Recurrence-free survival was calculated from the date of original treatment to the date of appearance the new lesion. Survival profiles of the entire group and subgroups were examining using Kaplan-Meier method. The significance of differences in survival was evaluated using the log-rank test. P-value of less than 0.05 was considered to be significant. The Stata 7 statistical software was used to perform the analysis.

Results

The characteristics of the 66 patients are summarized in Table 1. The mean age at diagnosis was 58.2 years (range 30-87 years). Nine patients (13.6%) were nulliparous and fifty seven patients (86.4%) had at least one child at the time of diagnosis. The mean parity of the parous patients was 4.3 (range 1-12). The most prominent presenting symptoms were vulva mass (89.4%) and pruritus (57.6%). The duration of vulva symptoms varied, ranging from 1 month to 5 years (mean 11.5 months). In most of the patients the primary site of vulva cancer was labia majora (56.1%)

Table 1. Characteristics of 66 patients with vulva cancer

	No. (%) of patients
Age (yrs)	
< 35	3 (4.6)
35-50	17 (25.8)
50-65	24 (36.4)
> 65	22 (33.3)
Chief complaints	
Vulva mass	59 (89.4)
Pruritus	38 (57.6)
Bleeding	11 (16.7)
Vulva pain	9 (13.6)
Abnormal discharge	8 (12.1)
Abnormal pigmentation	2 (3.0)
Site of first detection	
Labia majora	37 (56.1)
Labia minora	27 (41.0)
Clitoris	23 (34.9)
Other (vagina, fourchette, urethra)	11 (16.7)
Size of lesions (cm)	
<1	2 (3.0)
1-2	16 (24.2)
2-3	18 (27.3)
>3	30 (45.5)

and labia minora (41.0%). Tumor diameter at the time of diagnosis ranged between 1-10 cm.

Histopathology results of the 66 patients are shown in Table 2. Squamous cell carcinoma was the most common histological form of vulva cancer. Lymph node metastasis was found in 21 patients (31.8%). The distribution by FIGO surgical stage I, II, III and IV was 9.1%, 47.0%, 34.8% and 9.1%, respectively. The surgical procedure varied from radical vulvectomy and bilateral groin node dissection by the en bloc butterfly incision technique to local excision (Table 3). Forty four patients (66.7%) were treated by surgery alone, 22 patients (33.3%) by surgery followed by radiation.

The complications related to surgery were evaluated for all patients (Table 4). The most common complication was wound infection (45.5%), followed by wound dehiscence, lymphosis and leg edema (each 15.2%). Ten patients had no follow up data and therefore were omitted from the survival calculations. The median follow up time for the remaining 56 patients was 4.2 years (range 0.15-15.74 years). At the time of analysis, 44 patients (78.6%) were alive without disease, 4 patients (7.1%) were alive with disease, 7 patients (12.5%) had died of vulva cancer and 1 patient (1.8%) had died without vulva cancer. Of 66 patients, 10 (15.2%) developed recurrence. Distribution of recurrence by site was as follows: perineal 8 patients (80%), liver 1 patient (10%) and spine 1 patient (10%).The 5-year survival (and 95% CI) of 56 patients with stage I was 100%, falling to 96% (76-99%) in stage II, 94% (63-99%) in stage III and 60% (13-88%) in stage IV (p = 0.0142) (Fig. 1). The 5-year survival for node-positive patients was 82% (54-94%) versus 100% for node-negative patients (p = 0.0003) (Fig. 2). The effect of size of lesion on survival reached borderline significance (p = 0.0563) (Table 5).

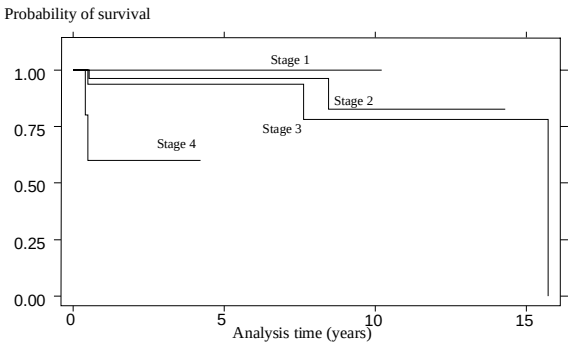

Fig. 1 Survival according to tumor stage (n = 56)

Table 2. Histopathology of 66 patients with vulva cancer

	No. (%) of patients
Histology	
Squamous cell carcinoma	54 (82.0)
Melanoma	3 (4.5)
Adrenocarcinoma	2 (3.0)
Basal cell carcinoma	2 (3.0)
Verrucous carcinoma	1 (1.5)
Basosquamous cell carcinoma	1 (1.5)
Invasive paget disease	1 (1.5)
Malignant eccrine hidradenocarcinoma	1 (1.5)
Leiomyosarcoma	1 (1.5)
Grade	
1	38 (57.6)
2	6 (9.1)
3	3 (4.5)
no data	19 (28.8)
Node	
negative	37 (56.0)
positive	21 (31.8)
not done	8 (12.2)
Margin	
free	57 (86.3)
not free	9 (13.7)

Table 3. Surgical procedures in 66 patients with vulva cancer

Surgical procedures	No. (%) of patients
Radical vulvectomy and bilateral groin node dissection - En bloc butterfly incision technique (1 patient), - Three separate incision technique (42 patients)*	43 (65.2)
Modified radical vulvectomy plus or minus groin node dissection (ipsilateral or bilateral)	18 (27.2)
Local excision - simple vulvectomy (2 patients) - wide local excision (3 patients)	5 (7.6)

* Four patients underwent pelvic node dissection

Table 4 Complications after surgery for vulva cancer

Type of complications	No. (%) of patients
Wound infection	30 (45.5)
Wound dehiscence	10 (15.2)
Lymphosis	10 (15.2)
Leg edema	10 (15.2)
Urinary tract infection	5 (7.6)
Abnormal voiding	5 (7.6)
Deep vein thrombosis	2 (3)

Table 5. Clinico-pathological prognostic factors for overall survival

	5 year survival (%)	95%CI	p value
Age			0.7205
< median	92.44	73.02-98.06	
> median	92.59	73.50-98.09	
Size of lesion			0.0563
< 2 cm	100.00		
2-3 cm	100.00		
> 3 cm	84.28	63.34-93.80	
FIGO stage			0.0142
I	100.00		
II	96.30	76.49-99.47	
III	93.75	63.23-99.10	
IV	60.00	12.57-88.18	
Lymph node status			0.0003
Negative	100.00		
Positive	81.93	53.77-93.80	
Grade			0.9182
1	93.55	76.59-98.35	
2	83.33	27.31-97.47	
3	100.00		

FIGO: International Federation of Gynecology and Obstetrics

Table 6. Clinico-pathological prognostic factors for disease-free survival

	5 year disease-free survival (%)	95%CI	p value
Age			0.5082
< median	28.57	13.54-45.61	
> median	42.86	24.57-59.96	
Size of lesion			0.7511
< 2 cm	26.67	8.26-49.63	
2-3 cm	42.86	17.73-66.04	
> 3 cm	37.04	19.60-54.59	
FIGO stage			0.0112
I	16.67	0.77-51.68	
II	46.43	27.56-63.33	
III	37.50	15.42-59.77	
IV	0.00		
Lymph node status			0.1182
Negative	46.67	28.39-63.04	
Positive	22.22	6.91-42.88	
Grade			0.2994
1	36.36	20.59-52.34	
2	16.67	0.77-51.68	
3	50.00	0.6-91.04	

FIGO: International Federation of Gynecology and Obstetrics

Table 6 shows risk of disease-free survival according to clinico-pathologic findings. Only FIGO stage was statistically significantly associated with disease-free survival (p = 0.0112) (Fig. 3).

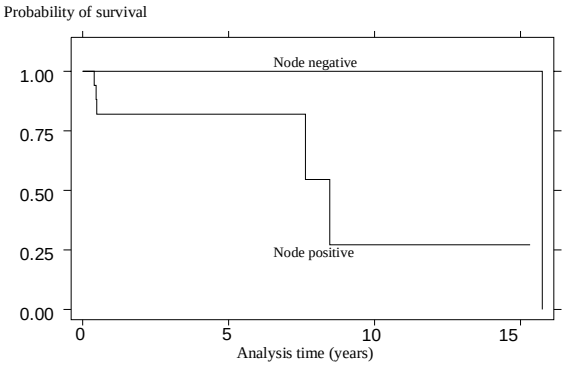

Fig. 2 Survival according to node status (n = 56)

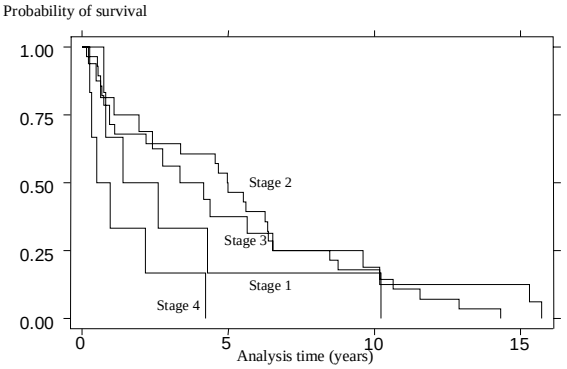

Fig. 3 Disease-free survival according to stage (n = 56)

Discussion

The present study reports on 66 surgical cases of vulva cancer. The median age of these patients was 60 years and although the age range extended from 30 to 87 years, about 30% of the patients were < 50 years. This age range is younger than what reported in most previous studies, in which the most common age group of patients with vulva cancer was 60-70 years[2,4,6-9]; however, the result was consistent with the ages reported by Pengsaa et al in northern Thailand[5]. Some studies suggest that vulva cancer among young women was associated with smoking and with human papillomavirus[6,10]. The proportion of nulliparous patients was 13.6% which is similar to previous studies[7,18] and mean parity of the parous patients was 4.3.

The most common symptoms of vulva cancer include pruritus, palpable mass, pain, bleeding, ulceration and vaginal discharge[3-7,9,12]. The present study confirmed that the most prominent presenting symptoms were vulva mass (89.4%) and pruritus (57.6%). The mean duration of patients symptom in the present study was 11.5 months which is similar to the finding of Cavanagh et al[19]. Conversely, Piura et al reported

that the mean duration of patient delay was 4 years[7]. Delay might be from two different causes. Firstly, patients delay with denial of symptoms or the growth and secondly, physician delay with treatment by creams or salves before biopsy[4,7]. The most frequent primary site of vulva cancer was the same as in other studies[3,12]: that was the labia majora followed by labia minora and clitoris. In the present study, squamous cell carcinoma (82%) was the most common malignant cell type. The result was similar to previous studies[2-6,11,12,20]. In the present study, the stages greater than stage I were more common because of the delay in diagnosis.

Since Bassett, Taussing and Way reported an improved survival rate in vulva cancer by the use of en bloc dissection of radical vulvectomy plus groin node dissection. This has become the mainstay of treatment in vulva cancer[1,3,4,13-15]. Although survival rate was excellent after introduction of this technique, the short term and long term morbidity associated with this technique is substantial. This has been replaced by radical vulvectomy and bilateral dissection using three separate incisions, modified radical or local excision of primary lesion and selective inguinal or inguinofemoral lymphadenectomy[3,4,15,16,21]. In the present study the three separate incision technique was most commonly used. Of this group, 4 patients also underwent pelvic node dissection. The selected pelvic lymphadenectomy has been routinely used in positive inguinal nodes metastasis case for over the last 20 years[4]. However, the morbidity was high. Subsequently, The Gynecology Oncology Group conducted a study randomizing patients with positive groin nodes at the time of radical vulvectomy to either pelvic lymphadenectomy or postoperative radiation therapy. The study showed a significant survival advantage for those patients receiving radiotherapy, primarily as a result of decreased groin recurrence[3,4,22]. This result had led to the use of radiotherapy when inguinal nodes are involved. In accordance with many studies[7,12,23,24], the present data confirmed that the most common complication was wound infection (45.5%), followed by wound dehiscence, lymphosis and leg edema (each 15.2%).

Wagner et al reported the 5-year survival for 80 patients with vulva cancer stage I, II, III and IV were 68.2%, 62.2%, 50.6% and 40% respectively[11]. In an earlier, large study, Podratz et al reported 5-year survival rates for 224 patients with invasive squamous cell carcinoma of vulva stage I, II, III and IV were 90%, 81%, 68% and 20% respectively[9]. The 5-year survival in the present study was higher than in the previous two studies. However, the small number of patients in the present study resulted in low precision of the survival estimates, and the lack of follow up data for 10 patients might have biased the survival estimates upwards.

In several previous studies, the prognostic value of other clinico-pathologic variables (i.e., patient age, lesion size, histologic grade, margin status, surgical status of the inguinal nodes, FIGO stage) has been demonstrated[6,7,9,23]. The present study was able to show FIGO stage ($p = 0.0142$) and nodal status ($p = 0.0003$) were significantly associated with overall survival. Only FIGO stage ($p = 0.0112$) was significantly associated with disease-free survival. This difference may probably be explained by the fact that the authors enrolled a small number of patients, with many histological cell types and a wide range of follow up time. Despite the inclusion of patients over a 19-year period, half could be followed up for less than 4.2 years. This limited the power of the study to detect prognostic factors.

In conclusion, vulva cancer is an uncommon malignancy in the southern part of Thailand. It is still a disease of the elderly. Surgery has been the mainstay of management of the disease. In the present study, stage and nodal involvement are predictors of survival, and stage is a predictor of disease-free survival.

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ลักษณะทางพยาธิวิทยาคลินิกของผู้ป่วยมะเร็งปากช่องคลอดในภาคใต้ของประเทศไทย: วิเคราะห์ในผู้ป่วย 66 ราย

จิตติ หาญประเสริฐพงษ์, สายบัว ชี้เจริญ, วิรัช วุฒิภูมิ, รักชาย บุหงาชาติ, สาธนา โตเจริญวาณิช, อลัน กีเตอร์

วัตถุประสงค์: *เพื่อศึกษาลักษณะทางพยาธิวิทยาคลินิกและผลการรักษาของผู้ป่วยมะเร็งปากช่องคลอดในภาคใต้ของประเทศไทย*

วัสดุและวิธีการ: *ศึกษาย้อนหลังจากเวชระเบียนของผู้ป่วยทั้งหมด 66 รายที่รับการรักษาโดยการผ่าตัดที่ภาควิชาสูติศาสตร์และนรีเวชวิทยา มหาวิทยาลัยสงขลานครินทร์ ระหว่างปี พ.ศ. 2527-2546*

ผลการศึกษา: *ผู้ป่วยมีอายุระหว่าง 30 ถึง 87 ปี โดยมีอายุเฉลี่ยเท่ากับ 58.2 ปี อาการนำที่มาโรงพยาบาลได้แก่ ก้อนที่ปากช่องคลอด (89%) และคันบริเวณปากช่องคลอด (57.6%) ส่วนระยะเวลาของการมีอาการมีตั้งแต่ 1 เดือนถึง 5 ปี ผู้ป่วยส่วนใหญ่ (82%) เป็นมะเร็งชนิด squamous cell carcinoma การศึกษานี้พบระยะของโรคระยะที่ 1, 2, 3 และ 4 เท่ากับ 9.1%, 47%, 34.8% และ 9.1% ตามลำดับ ผลแทรกซ้อนจากการรักษาได้แก่ แผลติดเชื้อ (45.5%), แผลแยก (15.2%), lymphosis (15.2%) และขาบวม (15.2%) อัตราการอยู่รอด 5 ปี สำหรับผู้ป่วยมะเร็งระยะที่ 1, 2, 3 และ 4 เท่ากับ 100%, 96% (95%CI 76-99%), 94% (95%CI 63-99%) และ 60% (95%CI 13-88%) ตามลำดับ พบความแตกต่างอย่างมีนัยสำคัญของอัตราการอยู่รอด 5 ปี สำหรับผู้ป่วยที่มีการกระจายของมะเร็งที่ต่อมน้ำเหลือง (82% (95%CI 54-94%)) กับผู้ป่วยที่ไม่มีการกระจายของมะเร็งที่ต่อมน้ำเหลือง (100%) ($p = 0.0003$) และพบอีกว่าระยะของโรคเป็นปัจจัยทำนายอัตราการอยู่รอด ($p = 0.0142$) และอัตราการปราศจากโรคของผู้ป่วย ($p = 0.0112$)*

สรุป: *ปัจจัยทำนายอัตราการอยู่รอดของผู้ป่วยได้แก่ ระยะของโรคและการกระจายของมะเร็งที่ต่อมน้ำเหลือง ส่วนปัจจัยทำนายอัตราการปราศจากโรคของผู้ป่วยมีเพียงระยะของโรคเท่านั้น*