Radical Surgery for T1 and T2 Squamous Cell Carcinoma of the Vulva Through Separate Incisions

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Objectives: *The aim of the study was to retrospectively evaluate treatment results in patients with T1 and T2 vulvar carcinoma.*
Material and Method: *The medical records of 46 patients with T1 and T2 SCC of the vulva undergoing radical excision of the tumor and groin node dissection at Chiang Mai University Hospital between January 1998 and December 2004 were reviewed. The tumor size, histologic grade, nodal status, lymph-vascular space invasion, lesion location, surgical marginal status, complications, recurrence and survival were analyzed.*
Results: *Mean age of the 46 patients (T1 = 15, T2 = 31) was 59 years with a range of 34–84 years. The incidence of lymph node metastases for T1 lesions was 13% compared to 35% for T2 lesions. Twenty nine patients (63%) experienced surgical complications, the most common one was lymphedema (16) while wound breakdown was noted in only 1 patient. With a median follow–up of 15 months, 14 patients (30%) developed recurrence, 3 (20%) and 11 (35%) in patients with T1 and T2 lesions respectively. The overall 5–year disease-free survival and 5-year survival were 37% and 40%, respectively. The 5–year survival of patients with T1 lesion was significantly higher than that of patients with T2 lesion (64% vs 31%, P = 0.04). Patients with negative nodes had significantly better survival than those with positive nodes (56% vs 18%, P = 0.02). In multivariable analysis, only the status of groin node remained as independent prognostic factors for survival.*
Conclusion: *Radical excision and groin node dissection through separate incision for T1 and T2 squamous cell carcinoma of the vulva in this study has a less favorable survival outcome compared with the literature.*

Keywords: *Vulvar carcinoma, Radical surgery, Separate incision*

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Squamous cell carcinoma of the vulva is the most common malignancy of the female external genitalia. Surgery has been the mainstay of management of this tumor since the earliest reports of Taussig and Way[1,2]. Radical vulvectomy and bilateral groin node dissection remains the standard surgical approach for all patients with operable vulvar cancer. Over the past 20 years, significant advances of surgical treatment have occurred in the management of squamous cell vulvar cancer from a resection of the vulva en bloc with the groin lymph nodes to a more individualized approach. The trend has been toward more conservative resection of the primary tumor sparing as much of the vulva as possible[3]. For localized lesions, the less radical surgery called "radical local excision" or "separate incision technique" is as effective as an en bloc radical vulvectomy in preventing local recurrence[4-8]. Morbidity has been shown to reduce considerably when separate groin incisions are used in stead of the en bloc procedure. Most notably, the frequency of major wound breakdown is decreased by almost a half in the various series reported[9,10]. Skin bridge recurrences are reported in 1–2% of patients treated by this method. These bridge recurrences are found more

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frequently in patients with positive nodes and, less frequently, in those with negative nodes[9–13].

This study was performed to evaluate treatment results in patients with T1 and T2 squamous cell carcinoma of the vulva undergoing radical excision and groin node dissection through separate incision, based on the experience of the Gynecologic Oncology Service, Department of Obstetrics and Gynecology, Chiang Mai University Hospital, Thailand.

Material and Method

The medical records of women with T1 and T2 squamous cell carcinoma of the vulva (FIGO staging 1994, T1 = tumor size £ 2 cm and T2 = tumor size > 2 cm in greatest diameter) treated at the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Chiang Mai University Hospital between January 1998 and December 2004 were reviewed. The clinical and pathological features were analyzed including age, surgical procedure, tumor size and site, histologic grade, depth of invasion, lymph–vascular space invasion (LVSI), surgical margin status, number of groin nodes removed, lymph node status, interval to and site of recurrence, and survival.

The type of surgical treatment included radical vulvectomy, radical hemivulvectomy and radical local excision with ipsilateral or bilateral groin node dissection depending on the size and site primary tumor and the clinical assessment of groin nodes. Radical excision of the primary tumor was performed deep to the inferior fascia of the urogenital diaphragm with at least 1-cm of tumor–free margins regardless of the tumor size. Groin node dissection was defined as inguino–femoral lymphadenectomy that completely removed the superficial inguinal nodes and deep femoral nodes located around the femoral vessels. Unilateral groin node dissection was carried out for lateral vulvar lesion while bilateral dissection was done for midline tumors of the clitoris and perineum.

Overall survival was defined as the time from surgery until death. Univariable analysis of survival was used to evaluate the potential prognostic significance of clinical and pathologic variables, i.e. lesion location, tumor size, grade, presence of LVSI, surgical margin status and groin node status. Survival analysis was carried out using the method of Kaplan and Meier with the log–rank test used for statistical evaluation of these data. Statistical significance was judged at the level of £ 0.05. This study was approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University.

Results

Of the total 46 patients, 15 (33%) and 31 (67%) had T1 and T2 lesions, respectively. The mean and median ages of the patients were 62 and 59 years, respectively with a range of 34–84 years. Seventeen patients (36%) presented with vulvar mass followed by pruritus (34%), vulvar ulcer (18%) and pain (12%). The clinical and pathological features of the patients are shown in Table 1.

The mean length of hospital stay was 18.5 days (range 7–37 days). Associated vulvar carcinoma in situ was identified in 11 (24%) patients. Thirty–one (67%) patients had lateral lesions, 19 were left– sided, 10 were right–sided, and 2 were both–sided. Fifteen (33%) patients had midline lesions in the clitoral area. Although grossly normal surgical margins could be achieved in all cases, histologic evaluation documented invasive lesion at surgical margins in 4 (9%) patients, and near margin (< 1 cm) in 18 (39%) patients. Tumor

Table 1. Clinicopathological features of 46 patients with vulvar carcinoma

Age (years)	
Mean (range)	59 (34 – 84)
Tumor size	
T1	15 (33%)
T2	31 (67%)
Type of surgery*	
RV	17 (37%)
RHV	12 (26%)
RLE	17 (37%)
Groin node dissection	
Unilateral	3 (7%)
Bilateral	43 (93%)
Mean node number	16 (4–32)
Tumor size (mm)	
Mean (range)	30 (3–80)
Depth of invasion (mm)	
Mean (range)	4.8 (1–12)
Tumor grade	
Grade I	36 (78%)
Grade II	7 (15%)
Grade III	3 (7%)
Positive LVSI*	3 (7%)
Surgical margin status	
Free	24 (52%)
Close	18 (39%)
Positive	4 (9%)

*RV = radical vulvectomy,
RHV = radical hemivulvectomy,
RLE = radical local excision,
LVSI = lymph – vascular space invasion.

size, histologic grade , surgical margin, LVSI and location of the tumor had no impact on the incidence of lymph node metastases as shown in Table 2.

Lymphedema was the most common complication occurring in 16 (35%) patients. Groin wound infection, groin lymphocyst and cellulitis occurred in 10 (22%), 3 (7%) and 2 (4%) patients, respectively. Wound breakdown occurred in only 1 (2%) patient undergoing radical vulvectomy and groin node dissection. One patient developed deep vein thrombosis at 2 months after the operation. There was no perioperative death. There was no significant difference in complications among the 3 surgical techniques of radical surgery for vulvar lesions.

Thirteen (28%) of 46 patients had positive groin nodes. All of these 13 patients had unilateral groin node metastases. None of 7 patients with lateral lesions and ipsilateral positive groin nodes had contralateral groin node metastases. Eleven patients received adjuvant groin and pelvic radiation therapy. The remaining 2 patients with one unilateral positive groin node refused adjuvant radiation and were alive without relapse at 8 months and 50 months postoperatively. With a median follow-up of 15 months (range 6-81 months), 14 (30%) patients developed recurrence with a median time to recurrence of 21 months (range 4-52 months). Eight (57%) of these recurrences occurred within 2 years after initial operation. Of the 14 patients with recurrence, 10 had vulvar recurrence (4 alive and 6 died within 12 months), 2 had groin recurrence (1 alive and 1 died at 17 months), and 2 had simultaneous vulvar and groin recurrences (all died within 6 months). All patients with groin recurrence had previously negative groin nodes. There was no recurrence at the skin bridges. Among 10 patients with vulvar recurrence, 5 were treated with radiation, 2 were treated with surgery, 1 was treated with surgery followed by radiation, and 2 refused treatment. Four patients who had groin recurrence with or without vulvar recurrence were treated with radiation [3] and chemoradiation [1]. There was no significant difference in recurrence among the 3 surgical techniques of radical excision. The incidence of recurrence for T1 lesions was 20% (3 in 15) compared with 35% (11 in 31) for T2 lesions (P = 0.25). The overall 5–year disease-free survival was 37%, there was a difference in disease-free survival based on only surgical margin status. The 5-year disease-free survival of patients with the healthy lateral margin was < 1 cm was 22% compared with 64% of those with more than a 1 cm lateral margin (P = 0.02).

At the time of analysis, 29 (63%) were alive, 23 were alive without disease and 6 were alive with disease recurrence. Seventeen (37%) women had died (13 died of disease and 4 died of intercurrent diseases). The overall 5–year survival was 40%. In univariable analysis, tumor size and the status of groin node were

Table 2. Incidence of lymph node metastasis by tumor and operative factors

	Groin node status				
	Positive(%)	Negative(%)	Odd ratio	CI	p value
Surgical margin status					
Free	5 (21)	19 (79)	2.17	0.58-7.40	0.40
Close	7 (39)	11 (61)			
Positive	1 (25)	3 (75)			
Tumor grade					
Grade I	11 (31)	25 (69)	0.56	0.14-3.14	0.80
Grade II	2 (29)	5 (71)			
Grade III	0 (0)	3 (100)			
Tumor size					
T1	2 (13)	13 (87)	3.57	0.66-14.00	0.22
T2	11 (35)	20 (65)			
LVSI					
Negative	12 (28)	31 (72)	1.29	0.18-12.70	0.64
Positive	1 (33)	2 (67)			
Location of tumor					
Lateral	7 (23)	24 (77)	2.28	0.61-8.12	0.37
Midline	6 (40)	9 (60)			

CI = 95% confidence interval

significant prognostic indicators for survival. The 5–year survival of patients with T1 lesions was 64% compared with 31% of those with T2 lesions (P = 0.04) as shown in Fig. 1. Patients with groin node metastases had significantly lower 5–year survival than those without nodal metastases (18% vs 56%, P = 0.02) as shown in Fig. 2. The type of radical excision, location of tumor, histologic grade, LVSI and surgical margin status had no significant impact on survival. However, in multivariable analysis, only the status of groin node remained as independent prognostic factors for survival as shown in Table 3.

Discussion

Currently, radical excision and groin node dissection using the three separate incision technique has been universally accepted as a primary treatment for patients with early stage vulvar carcinoma. Equivalent survival outcome and reduced complications have been reported with this technique compared with the traditional en bloc procedure[5–10]. The overall wound dehiscence rate of 50–70% reported in the series for en bloc technique remains a significant problem, as is the long hospital stay[10,14]. With the separate incision approach, wound breakdown occurs in approximately

Table 3. Multivariable analysis of prognostic factors for survival

	HR	CI	p-value
Tumor size	3.29	0.77-14.03	0.08
Groin node status	4.26	1.10-16.53	0.03

HR = hazard ratio, CI = 95% confidence interval

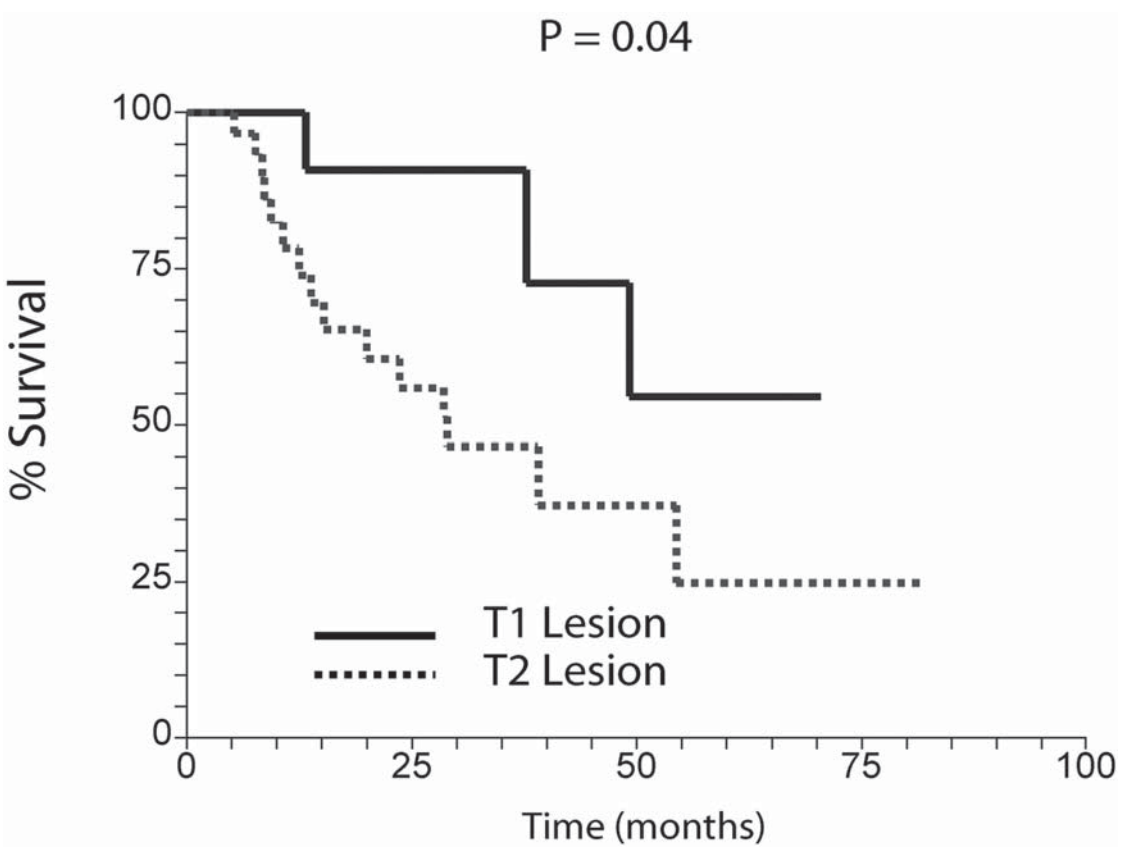

Fig. 1 Survival curve comparing between T1 and T2 lesion

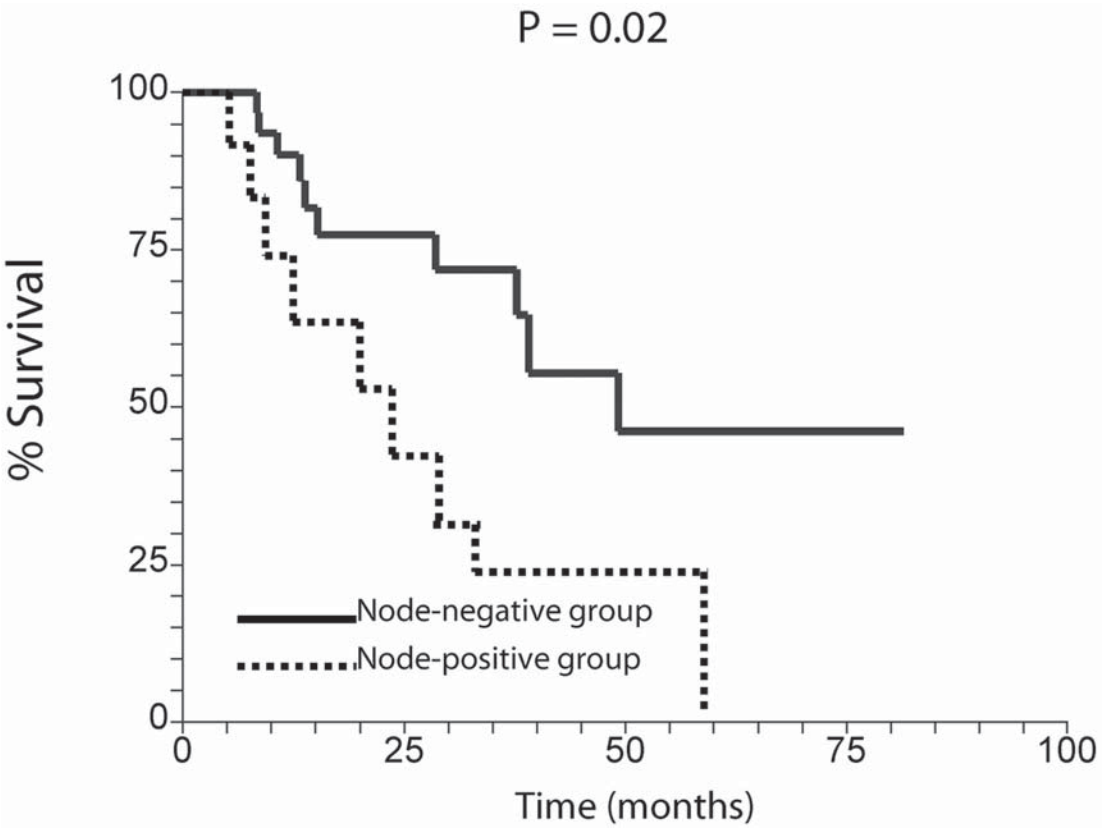

Fig. 2 Survival curve comparing between node negative and node positive group

8–14% of cases[15,16]. Wound breakdown was found in only 2% of patients in our study using the separate incision technique. Chronic leg edema or lymphedema, the major late complication of groin node dissection was noted in 35% of patients in this study which was slightly lower than those reported of 40–70% in other series[16,17].

The incidence of groin node metastases (28%) in our study was comparable to that of 30% in the collective series of Hacker's[3]. In the present study, the incidence of groin node metastases in T2 tumor (35%) was higher than that in T1 tumor (13%), but was not significantly different (P = 0.22). Such incidences were slightly higher than those reported of 26% and 11% respectively in the literature[3]. Groin node metastases was a significant prognostic factor in our study. Patients with negative nodes had a 5–year survival rate of 56% compared to 18% for patients with positive nodes. We did not perform bilateral groin node dissection if the primary tumor was unilateral. However, if the ipsilateral groin nodes were found to be positive, contralateral groin node dissection was performed. None of 7 patients with lateral tumors and ipsilateral positive groin nodes had contralateral groin node metastases in this study. The incidence of positive contralateral groin nodes in patients with lateral T1 squamous cell vulvar carcinomas and negative ipsilateral groin nodes is considerably low at 0.4%[3]. For midline lesions, i.e. clitoris, perineum, and anterior labia minora; bilateral groin node dissection is recommended and should be a thorough inguinofemoral lymphadenectomy which includes dissection of both superficial inguinal and deep femoral lymph nodes.

Recurrence of vulvar carcinoma is related to the stage of disease, the status of groin nodes and surgical margins[3,6,10,13]. In this study, the recurrence was slightly higher in patients with T2 (35%) compared with that of 20% in T1 tumors, but was not significantly different. Such recurrences were comparable to 18% and 35% of patients with T1 and T2 tumors in the report of Rodolakis et al.[16] Local vulvar recurrence are commonly noted in patients with primary tumor larger than 4 cm[18] and is usually curable by further radical excision or radiation. In our study, recurrences were

more frequently localized to the vulva irrespective of the type of radical excision. Furthermore, no recurrence was found in the skin bridge between the vulva and the site of groin node dissection.

Survival of the patients with vulvar cancer not only depends on the lymph node status but also depends on the clinical stage of disease[3]. Patients with T1 tumors in our study had significantly higher 5–year survival than those with T2 tumors (64% and 31%, respectively). Tumor size, in general influences patient survival through the status of groin nodes.

In our study had a 5-year survival of 40% compared with 70% in the collective series of Hacker's[3]. We cannot clarify the definite reasons for these discrepancies of unfavorable outcomes in survival. The potential explanations could be a large number of loss to follow-up and incomplete information about exact causes of death in this study. In addition, recall bias especially on the definite types and techniques of surgery as well as detailed postoperative adjuvant therapy could have a significant impact on the study result.

Although we could demonstrate that only inguinal lymph node status was an independent prognostic factor for survival on this study. There exists a trend toward tumor stage as another prognostic factor (P = 0.08). Larger study with complete follow up information might exhibit clearer association.

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การผ่าตัดเนื้องอกออกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองบริเวณขาหนีบ โดยผ่านแผลผ่าตัดแบบแยกต่างหากในผู้ป่วยมะเร็งปากช่องคลอดชนิดเซลล์สเควมัส T1 และ T2

อภิชาติ ขอบใจ, จตุพล ศรีสมบูรณ์, กิตติภัต เจริญขวัญ, ชัยเลิศ พงษ์นริศร, ประภาพร สู่ประเสริฐ, สิทธิชา สิริอารีย์, ฉลอง ชีวเกรียงไกร, จารุวรรณ ตันติพลากร, ชำนาญ เกียรติพีรกุล

วัตถุประสงค์ : *เพื่อศึกษาถึงผลของการรักษาในผู้ป่วยมะเร็งปากช่องคลอดชนิดเซลล์สเควมัส T1 และ T2 ที่ได้รับการรักษาด้วยการผ่าตัดเนื้องอกออกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองบริเวณขาหนีบ โดยผ่านแผลผ่าตัดแบบแยกต่างหาก*

วัสดุและวิธีการ : *ได้ทบทวนเวชระเบียนผู้ป่วยมะเร็งปากช่องคลอดชนิดเซลล์สเควมัส T1 และ T2 จำนวน 46 ราย ที่ได้รับการผ่าตัดเนื้องอกออกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองบริเวณขาหนีบ ที่โรงพยาบาลมหาราชนครเชียงใหม่ ในช่วงเดือนมกราคม พ.ศ. 2543 ถึงเดือนธันวาคม พ.ศ. 2547 ได้วิเคราะห์ขนาดของก้อนมะเร็ง ระดับของเซลล์มะเร็ง สถานะของต่อมน้ำเหลือง การลุกลามเข้าไปในหลอดเลือดหรือหลอดน้ำเหลือง ตำแหน่งของรอยโรค สถานะของขอบชิ้นเนื้อ ภาวะแทรกซ้อน การกลับเป็นซ้ำ และการอยู่รอดของผู้ป่วย*

ผลการศึกษา : *ผู้ป่วย 46 ราย (ระยะ T1 = 15 ราย, ระยะ T2 = 31 ราย) มีอายุเฉลี่ย 59 ปี พิสัยอายุ 34-84 ปี ผู้ป่วยมะเร็งระยะ T1 มีมะเร็งแพร่กระจายไปที่ต่อมน้ำเหลืองขาหนีบน้อยกว่าผู้ป่วยมะเร็งระยะ T2 คือ ร้อยละ 13 และร้อยละ 35 ตามลำดับ มีภาวะแทรกซ้อนจากการผ่าตัด 29 ราย (ร้อยละ 63) ภาวะแทรกซ้อนที่พบมากที่สุดคือ ขาบวม (16 ราย) ในขณะที่แผลแยกพบเพียง 1 รายเท่านั้น จากการตรวจติดตามผู้ป่วยเป็นระยะเวลามัธยฐาน 15 เดือน มีมะเร็งกลับเป็นซ้ำ 14 ราย (ร้อยละ 30) โดยเป็นผู้ป่วยมะเร็งระยะ T1 3 ราย (ร้อยละ 20) และระยะ T2 11 ราย (ร้อยละ 35) ผู้ป่วยมีอัตราการอยู่รอดปลอดโรคโดยรวม 5 ปีและการอยู่รอดโดยรวม 5 ปี ร้อยละ 37 และ 40 ตามลำดับ การอยู่รอดโดยรวมในผู้ป่วยมะเร็งระยะ T1 สูงกว่าระยะ T2 อย่างมีนัยสำคัญคือร้อยละ 64 และร้อยละ 31 ตามลำดับ (ค่าพี = 0.04) ผู้ป่วยที่ไม่มีมะเร็งแพร่กระจายที่ต่อมน้ำเหลืองมีการอยู่รอดสูงกว่าผู้ป่วยที่มีมะเร็งแพร่กระจายที่ต่อมน้ำเหลืองอย่างมีนัยสำคัญคือ ร้อยละ 56 และร้อยละ 18 ตามลำดับ (p = 0.02) แต่เมื่อมีการวิเคราะห์ข้อมูลแบบพหุตัวแปรแล้ว พบว่ามีเพียงสถานะของต่อมน้ำเหลืองเท่านั้นที่เป็นปัจจัยพยากรณ์โรคอิสระสำหรับการอยู่รอดโดยรวม*

สรุป : *การผ่าตัดเนื้องอกออกแบบถอนรากถอนโคนและเลาะต่อมน้ำเหลืองบริเวณขาหนีบโดยผ่านแผลผ่าตัดแบบแยกต่างหากในผู้ป่วยมะเร็งปากช่องคลอดชนิดเซลล์สเควมัส T1 และ T2 ในการศึกษานี้มีผลของการรักษาที่ด้อยกว่าเมื่อเทียบกับงานวิจัยอื่น*