Micrometastasis and Recurrent Neck Node in Supraomohyoid Neck Dissection field

Somjin Chindavijak, MD*

** Otolaryngology Division, National Cancer Institute Thailand*

Objectives: *Supraomohyoid neck dissection (SOHND) is one of the treatment for clinically negative neck disease in carcinoma of the oral cavity when primary is treated with surgery. Neck tumor recurrence in these patients who were treated by SOHND with and without post-operative radiotherapy was evaluated.*
Material and Method: *Forty-four patients with squamous cell carcinoma of the oral cavity aged between 33-78 years was studied. Every case had clinically negative neck and was treated with SOHND.*
Results: *There were 53 supraomohyoid neck dissections. The overall recurrence rate was 11.3% (6/53). The duration of recurrence ranged from six to nine months and was seen in five of pathologically negative neck and one in pathologically positive neck. Five of six of the recurrence cases were in the field of SOHND without post-operative radiotherapy. Histopathological review with immunohistochemistry study of all recurrent cases that was previously reported as negative by H&E stain showed no micrometastasis. The 5-yr survival of neck node metastasis was 64% versus 82% of these with no lymph node metastasis which showed no statistically significant difference.*
Conclusion: *The SOHND was useful for treating clinical negative neck of oral cancer with high percentage of occult lymph node. The pathological report influenced the adjuvant treatment. Micrometastasis and other indicators for this pathologically negative neck is still await further study to improve survival of this particular group of patients.*

Keywords: *Micrometastasis, Recurrent, Supraomohyoid neck dissection*

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Neck lymph node metastasis of oral cancer increases the risk of loco-regional recurrence as well as distant metastatic spread and correlate with 50 % decrease in survival. Supraomohyoid neck dissection plays an important role in treating clinical non-palpable neck lymphadenopathy because of the high incidence of occult nodal disease when surgery is the treatment of choice for primary. Pathological data gained from the surgical specimen can be used for post-operative treatment. Medina and Byers[1] recommended post-operative radiotherapy if there are multiple lymph nodes or there is evidence of extracapsular spread based on the reduction of regional recurrence from 24% to 15% in their series of 389 patients. Much of the literature supports the usefulness of this selective neck dissection.

Correspondence to : Chindavijak S, Otolaryngology Division, National Cancer Institute Thailand, Bangkok 10400, Thailand.

However, the failure rate in the neck after treatment by this protocol is still challenging. Shah et al reported the incidence of neck failure in pathological negative to be 5%.There were both in the field and outside the field of supraomohyoid neck dissection, more than half of those with neck recurrence did not receive post-operative radiotherapy. Analysis of micrometastasis (tumor size less than 3 mm) by immunohistochemical studies found 5-50 % of the patients who had no evidence of metastases at the time of routine pathological examinations[2]. This method may increase the sensitivity of detection of metastasis.

The present report studied the efficacy of supraomohyoid neck dissection in control of regional metastasis and to look for the characteristics of recurrent neck lymph node metastasis in patients whose pathological results were no neck nodes metastasis. The result will guide the way for treatment and improve survival for these patients.

Material and Method

The retrospective review of supraomohyoid neck dissection operations that were performed between 1997-2001 in the National Cancer Institute Bangkok. In our instiure alll cases of high occult node which are tongue and floor of mouth of all stage, buccal from stage II, the surgery at primary that performed through the neck such as mandibulectomy of gum and lip cancer were included. Cases that were treated by chemotherapy, radiation or recurrent cases before the operation were excluded. There were 63 cases of oral cancer with non-palpable neck node with only 44 records available for review. These cases were studied in age, sex, clinical staging (AJCC 1997), operation, pathological report, follow up, recurrent.

Operative technic: Supraomohyoid neck dissection was performed in the cases that had no palpable neck nodes in oral cancer. The primary site in all the cases was treated by surgery and there was no radiation and chemotherapy before the operation. Bilateral SOHND was performed for midline primary site. This operation was performed to achieve a compartment excision of levels I, II, III neck lymph nodes. The unilateral dissection was performed through an apron-like incision from the mastoid to the mandibular symphysis. The flap was elevated to the mandible superiorly and to the level of the omohyoid muscle inferiorly. The fascia was incised along the anterior border of the sternomastoid muscle. The muscle was retracted and the dissection continued toward the level of its posterior border with preservation of cutaneous branches of the cervical plexus. The accessory nerve was carefully dissected and preserved. The first part of the dissection began at the level of the omohyoid muscle intersection with the internal jugular vein. The dissection was then carried along the jugular vein, carotid arteries, and vagus nerve from the inferior limit of operation to the subdigastric level. All fibroadipose tissue and lymphatics sited over the accessory nerve were included in the specimen. The dissection continued through the submandibular triangle and ended at the submental area.

Histopathological report: Pathological reports in all cases were reviewed for size, type, grade, margin of the primary and number of lymph nodes remove and number of lymph nodes containing metastasis. All paraffin blocks of the recurrent cases at the neck which were previously reported H&E negative were reviewed. These lymph nodes were proceeded in order to identify micrometastasis in tumor free nodes. Each lymph node was serially cut 24 levels of each node with 3 microns thickness. The slide levels 1-5, 7-11, 13-17 and 19-23 were stained with H&E. The slide levels 6,12,18 and 24 were stained with keratin immunostaining (AE_1/AE_3)

Radiation:Adjuvant post-operative radiotherapy was indicated when the pathological report revealed either involved/close resection margin and/or tumor metastasis in lymph nodes specimen. The treatment was started within 6-8 weeks after the operation. The field of radiation included primary and neck below the surgical scar. The patient received a conventional dose of radiation (200 cGy/day) for 5-6 weeks. Shrinking field technic was used to boost the dose at the primary site and lymph nodes at 5,000 to 6,000 cGy. Spinal cord was always protected at doses greater than 4,500 cGy.

Statistical Analysis:The overall survival probability was calculated using the method of Kaplan and Meier and the log-rank test was used to test for differences between groups.

Results

Among 44 cases there were 22 males and 22 females. Aged between 33-78 years (mean 60.7 yrs). Stage I = 25 cases (56.8%), stage II = 13 cases (29.5%), stage III = 1 cases (2.3%) and stage IV = 5 cases (11.4%). The site of the tumor were: Tongue = 30 cases (68.2%), gum = 7 cases (15.9%), floor of the mouth = 3 cases (6.8%), buccal = 2 cases (4.5%) and lip = 2 cases (4.5%). There were 53 neck lymph node specimens (9 cases did bilateral SOHND).

Lymph nodes metastasis

All cases in the present study, did not have lymph nodes palpable at the neck.The routine pathological report revealed 17%(9/53) of occult metastatic rate. There were no cases of recurrent neck lymph nodes found micrometastasis from cytokeratin immunohistochemistry stain.

The overall rate of neck recurrence was 11.3% (6/53). For the SOHND-treated group without radiotherapy (26 cases) this rate was 9.4%(5/53), and for the combined treatment group (18 cases) it was 1.9% (1/53) ($p = 0.3$). Details of these cases are shown in Table 1.

There were 6 cases that had neck recurrence. Only one case was recurrent outside the field of dissection and others recurred in the field that supraomohyoid neck dissection was performed. Almost all of the recurrent cases were pathological negative node and therefore were only treated with surgical modality only (Diagram).

Eight cases were pathological positive and received post-operative radiation. The course of disease is shown in Table 2.

Two patients failed to receive planned post-operative radiation, one alive without disease after19 months and one recurred at the neck after 8 months.

Twelve cases with no neck nodes metastasis but received post-operative radiation due to close or involves margin at primary. Among these there was only 1 case recurred at neck and outside the field of SOHND and 3 cases recurred at primary.

5-year survival for cases with neck node metastasis was 64% and 82% for cases of without lymph node metastasis. But this is not statistically significant.

Discussion

The presence of nodal metastasis is an important prognostic factor in head and neck cancer and is used to direct further treatment plan. Pathological upstaging of the clinically N0 neck was 17% in the present study. These patients had undergone adjuvant radiation therapy which was influenced by the pathological report and the result of regional control was demonstrated in table 2 which showed no neck recurrence in these cases.

The site of neck recurrence after SOHND has been shown by Byers et al who found that the recurrence occurred more frequently inside the limits of SOHND. In contrast with Spiro et al., the neck recurrence preferentially occurred beyond the limit of SOHND. In the present study, most of the neck recurrences occurred in the field and in patients without post-operative radiation. Although in this study statistical significance between the two group (with and without post-operative radiation) cannot be demonstrated due to limit number of cases but relevant information can be gathered due to the fact that only one patient had neck recurrence after post-operative radiation compared to five patients in the only surgery group.

Spiro et al. reported neck recurrence in 5 % of patients with pathological N0 neck. Other studies revealed neck recurrence after SOHND varied from 4.8% to 16%. In this study we found 9.4% (5/53). There were no indications for adjuvant therapy in these patients. The micrometastasis for detection tumor size

Table 1. The duration after surgery to recurrence at neck ranged from 6-9 months

Diagnosis	Stage	No. of lymph nodes metastasis from SOHND	Follow up (months)	primary	Duration of recurrence at neck (months)	Status
Gum	T1N0M0	0/12	43	normal	9	Alive without disease after RND and post-operative radiation
Gum	T1N0M0	3/17	6	normal	8	Death , pt. failed to receive post operative radiation
Tongue	T1N0M0	0/20	19	normal	7	Death of disease
Tongue	T2N0M0	0/15	10	normal	8	Death of disease in 10 months after treatment primary : Margin not free
Tongue	T2N0M0	0/9	10	normal	6	Alive with lung metastasis
Tongue	T1N0M0	0/12	36	normal	7	Death unknown cause

Table 2. The course of disease in pathological positive neck

Primary	Stage	No. of lymph nodes metastasis	Last follow up (months)	Status
Tongue	T1N0M0	1/6	39	Alive without disease
Tongue	T2N0M0	1/9	13	Death from disease at primary
Tongue	T1N0M0	2/9	60	Alive without disease
Tongue	T2N0M0	3/9	10	Death , no neck recurrence
Tongue	T1N0M0	3/31	57	Alive without disease
Gum	T4N0M0	4/13	24	Death from liver metastasis

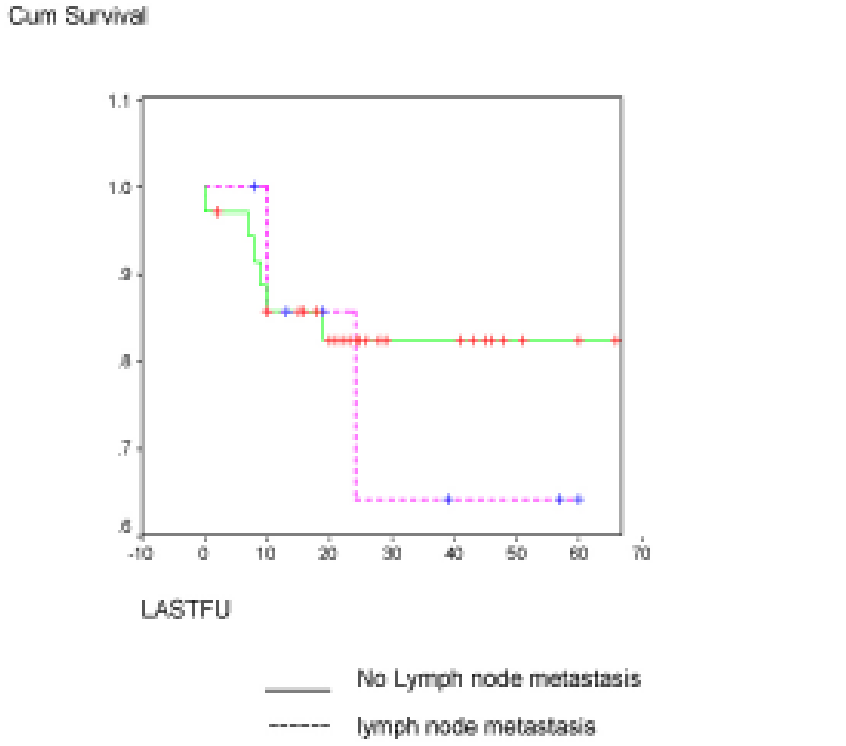
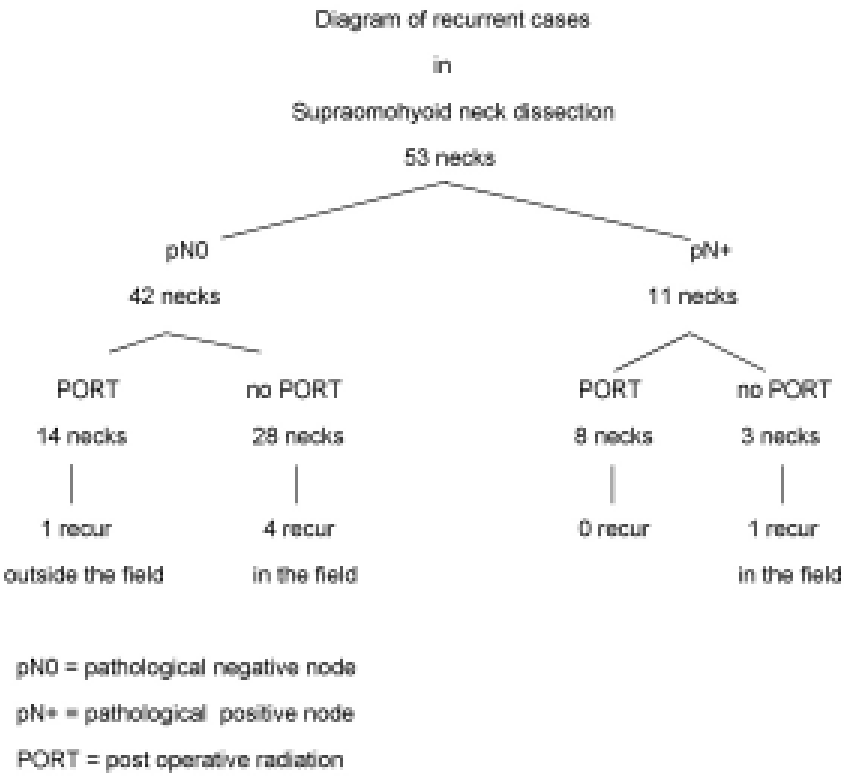


Fig. 1 5-yr survival between lymph node metastasis & no lymph node metastasis



pN0 = pathological negative node

pN+ = pathological positive node

PORT = post operative radiation

less than 3 mm. were reported by immunohistochemical studies with a mean incidence rate of 15.2% [2] of the patients who had no evidence of metastases from routine pathological examination that resulted in recurrence at later date. Pathologist in this study cannot find any micrometastasis in 168 slides in these 5 cases with neck node recurrence and were re-evaluated. The primary site of these cases were controlled and no evidence of carcinoma at the time of neck recurrence. So the rationale that can explain maybe that occult nodes were left at the time of neck dissection or the method for study of micrometastasis is not sensitive enough to identify the spot of metastasis in lymph nodes. Becker et al[21] reported in 2004 that quantitative reverse transcriptase polymerase chain reaction (RT-PCR) detection of cytokeratin 5 or 14 is a promising new molecular technique that may be used for detection of cervical micrometastases in head and neck cancer. Considering the method of the micrometastasis study, this process depends very much on the effort put into the histological examination, the number of lymph nodes examined and the number of sections that were examined. AT present the treatment for non-palpable neck lymphadenopathy in oral cancer is supraomohyoid neck dissection when the primary was treated with surgery. Sentinel nodes study may assist in identifying lymph node that contain micrometastasis. Further studies in this direction are needed to find the best method to treat oral cancer patients with pathological negative neck.

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References

1. Medina JE, Byers RM. Supraomohyoid neck dissection: rationale, indications and surgical technique. Head Neck 1989; 11: 111-22.
2. Kim I, Jung KY, Woo JS, Kim HJ, Kwon SY. The usefulness of cytokeratin immunohistochemistry in detection of lymph node micrometastasis in neck dissection specimens. Otolaryngol Head Neck Surg 2004; 131: 300-6
3. Spiro RH, Morgan GJ, Strong EW, Shah JP. Supraomohyoid Neck Dissection. Am J Surg 1996; 172: 650-7.
4. Brazillian Head and Neck Cancer Study Group. Results of a prospective trial on elective modified radical classical versus supraomohyoid neck dissection in the management of oral squamous carcinoma. Am J Surg 1998; 176, 422-7.
5. Hao SP,Tsang NM. The role of supraomohyoid neck dissection in patients of oral cavity carcinoma. Oral Oncology 2002; 38: 309-12.
6. Chone CT, Crespo AN,Silva AR, Schlupp WR, Regional Tumor Recurrence After Supraomohyoid Neck Dissection. Arch Otolaryngol Head Neck Surg 2003; 129: 54-8.
7. Magrin J. Ipsilateral Neck Cancer Recurrences After Elective Supraomohyoid Neck Dissection. Arch Otolaryngol Head Neck Surg 2000; 126: 410-6.
8. Pitman KT,Johnson JT, Myers EN. Effectiveness of Selective Neck Dissection for Management of the Clinically Negative Neck. Arch Otolaryngol Head Neck Surg 1997; 123: 917-22.
9. Committee for Head and Neck Surgery and Oncology American Academy of Otolaryngology-Head and Neck Surgery, Neck Dissection Classification Update. Arch Otolaryngol Head Neck Surg 2002; 128: 751-8.
10. Detsky A, Biem J, Davidson J. The Clinically Negative Neck in Patients with Early Oral Cavity Carcinoma: A Decision-Analysis Approach to Management. J Otolaryngol 1995; 24: 323-9.
11. Ferlito A, Shaha AR, Rinaldo A. The Incidence of Lymph Node Micrometastasis in Patients Pathologically Staged N0 in Cancer of Oral Cavity and Oropharynx. Oral Oncology 2002; 38: 3-5.
12. van den Brekel MWM,van der Waal I,Meijer CJLM,Freeman JL, Castelijns JA,Snow GB. The incidence of Micrometastases in Neck Dissection Specimens obtained from Elective Neck Dissections.Laryngoscope 1996; 106: 987-91.
13. Woolgar JA. Micrometastasis in Oral/Oropharyngeal squamous cell carcinoma: Incidence, histopathological features and clinical implication. Br Oral Maxillofacial Surg 1999; 37: 181-6.
14. Karalak A. Occult Axillary Lymph Node Metastases Discovered by Serial Section in Node negative Breast Cancer. J Med Assoc Thai. 1999; 82: 1017-9.
15. Yarbrough W, Funkhouser W, Yin X, Shores CG. Clinical Evaluation of a New Molecular Method for Detection of Micrometastases in Head and Neck Squamous Cell Carcinoma. Arch Otolaryngol Head Neck Surg 2004; 130: 937-42.
16. Siberchicot F, Demeaux H, Duroux S, Majoufre C,Pinsolle V, Pinsolle J. Prognostic Value of Histologic Findings in Neck Dissections for Squamous cell carcinoma. Arch Otolaryngol Head Neck Surg

1997;123:145-8.
17. Rinaldo A, Shaha A, Devaney KO, Ferlito A, Pitman KT. Sentinel lymph node biopsy in head and neck cancer. Oral Oncology 2003; 39: 343-9.
18. Alex JC. The Application of Sentinel Node Radiolocalization to Solid Tumors of the Head and Neck: A 10-year Experience. Laryngoscope 2004;114: 2-19.
19. Kim I, Jung KY, Woo JS, Kim HJ, Kwon SY. The usefulness of cytokeratin immunohistochemistry in detection of lymph node micrometastasis in neck dissection specimens. Otolaryngol Head Neck Surg 2004; 131: 300-6.
20. Piombino P. Surgical management of the neck in squamous cell carcinoma of the tongue. B J Oral Maxillofacial Surg 1999; 37: 320-3.
21. Becker MT, Shores CH, Yu KK, Yarbrough WG. Molecular assay to detect metastatic head and neck squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 2004; 130: 21-7.

การศึกษาการตรวจค้นหาเซลล์มะเร็งซ่อนเร้นในต่อมน้ำเหลืองที่คอและการเกิดกลับซ้ำของต่อมน้ำเหลืองในผู้ป่วยมะเร็งช่องปากที่ได้รับการผ่าตัดเลาะต่อมน้ำเหลืองเหนือกล้ามเนื้อ omohyoid

สมจินต์ จินดาวิจักษณ์

วัตถุประสงค์*: การทำผ่าตัด Supraomohyoid neck dissection (SOHND) เป็นวิธีการรักษาผู้ป่วยมะเร็งช่องปากที่ตรวจไม่พบต่อมน้ำเหลืองเมื่อแผนการรักษามะเร็งนั้นใช้การผ่าตัด การวิจัยนี้ได้ทำการศึกษาการเกิดกลับซ้ำของต่อมน้ำเหลืองในผู้ป่วยมะเร็งช่องปากที่ได้รับการผ่าตัดและทำผ่าตัด SOHND ที่คอซึ่งได้รับและไม่ได้รับการฉายรังสีรักษาหลังผ่าตัด*

วัสดุและวิธีการ*: ผู้ป่วยมะเร็งช่องปาก 44 ราย อายุระหว่าง 33-78 ปี ซึ่งตรวจร่างกายไม่พบต่อมน้ำเหลือง และได้รับการผ่าตัด SOHND ทุกราย มีการผ่าตัดทั้งหมด 53 ครั้ง*

ผลการศึกษา*: พบว่าการเกิดกลับซ้ำทั้งหมด 11.3 % (6/53). ระยะเวลาที่เกิดกลับซ้ำอยู่ในช่วง 6-9 เดือน ผู้ป่วย 5 รายที่เกิดกลับซ้ำพบในผู้ป่วยที่ผลตรวจพยาธิ วิทยาของต่อมน้ำเหลืองหลังผ่าตัด SOHND ไม่มีการแพร่กระจายและพบผู้ป่วยเกิดกลับซ้ำ 1 รายในผู้ป่วยที่มีการ แพร่กระจายของต่อมน้ำเหลืองจากผลการตรวจทางพยาธิวิทยา การเกิดกลับซ้ำของผู้ป่วย 5 ใน 6 รายพบว่าเกิดใน บริเวณที่ได้รับการผ่าตัด SOHND และไม่ได้รับการฉายรังสีรักษาหลังผ่าตัดการตรวจค้นหา micrometastasis ในต่อมน้ำเหลืองของผู้ป่วยที่เกิดกลับซ้ำซึ่งผลการตรวจพยาธิวิทยาด้วย H&E ไม่พบการแพร่กระจาย พบว่าไม่มี micrometastasis. อัตราการรอดชีวิต 5 ปีในผู้ป่วยที่มีต่อมน้ำเหลืองแพร่กระจายคือ 64% และเป็น 82 % ในผู้ป่วยที่ไม่มีการแพร่กระจายของต่อมน้ำเหลือง ซึ่งค่าทั้งสองไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ*

สรุป*: การผ่าตัด SOHND เป็นวิธีการรักษาที่มีประโยชน์ในผู้ป่วยมะเร็งช่องปากที่ตรวจร่างกาย ไม่พบต่อมน้ำเหลืองแพร่กระจายซึ่งผู้ป่วยกลุ่มนี้มีความเสี่ยงของการแพร่กระจายต่อมน้ำเหลืองสูง ผลพยาธิวิทยาของการตรวจต่อมน้ำเหลืองมีผลต่อการวางแผนการรักษาหลังการผ่าตัด การตรวจหา micrometastasis และการตรวจหาตัวชี้วัดอื่น ๆ สำหรับผู้ป่วยที่ไม่พบการแพร่กระจายต่อมน้ำเหลืองทางพยาธิวิทยายังคงต้องศึกษา ต่อไปเพื่อให้ผลการรักษาดีขึ้น*