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Analysis of Intraoral Squamous Cell Carcinoma Reconstructed with Radial Forearm Flap

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전완부 유리 피판으로 재건한 구강내 편평상피암환자의 예후분석

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= 국문초록 =

미세외과 수술에 의한 유리 피판술의 도입은 두경부 종양제거후 재건에 괄목할 만한 진보를 가져왔다. 특히 광범위한 종양의 제거가 필요하며 인근의 조직으로 수복이 어렵고 기능 및 외모상의 재건이 문제가 되는 경우 유리 피판은 절대적인 적응이 된다.

구강은 언어구사 와 연하(deglutition)기능을 담당하므로 재건을 위해서는 얇고 부드러운 조직으로 수복하여 주어야 한다. 전완부 유리피판은 혈관경의 위치가 대부분 일정하고 종양제거후 결손의 모양에 따라 피판을 계획할 수 있기 때문에 구강암 제거후 가장 많이 이용되는 유리피판이다. 저자는 1982년 부터 1988년까지 영국 글라스고우 소재 서부 스코틀랜드 성형 및 구강외과 병원에서 구강의 편평상피암환자로 암종제거 후, 전완부 피판에 의한 재건 및 방사선 치료를 받은 151명의 치료결과(재발율 및 생존율)를 분석하였다.

절제연의 종양조직의 양성($P<0.05$), 경부 임파절의 extracapsular node spread여부($P<0.001$), 경부 임파절 곽청술의 종류($P<0.05$) 등은 재발율과 관련하여 통계적으로 유의하였다. 반면에 종양의 구강내 위치, 하악골의 침범여부등은 통계적의의가 없었다.

생존율에 관하여는 종양의 구강내 위치 ($P<0.05$), 종양절제연 종양여부($P<0.005$), 하악골의 침범여부($P<0.05$), 경부 임파절의 extracapsular node spread여부($P<0.001$) 등이 통계적으로 유의할 만한 요소로 밝혀졌다. 젊은 나이의 환자들에서(50세이하) 특징적으로 높은 사망율을 보였다.

하악골절제방법의 차이는 환자의 생존예후에 통계적으로 유의할 만한 영향을 주지 못했다.

Introduction

The introduction of free flap transfer by means of microvascular technique has brought remarkable progress in reconstruction following resection of cancer in the head and neck region[1-3].

Without the use of free flap the ability to close wounds is limited and radical excision sometimes must be compromised because of the lack of epithelial lining and unacceptable function, or disfigurement.

Because the oral cavity has function in speech and deglutition, thin and pliable skin is mandatory for its reconstruction.

Myocutaneous flaps such as pectoralis major flap has frequently been used[4)5)], but the major drawbacks of this flap are its bulk and contraction due to gravity which make it less suitable for intraoral defects.

The radial forearm flap has become one of the most reliable methods for head and neck cancer reconstruction because of its predictable and constant vascular anatomy and versatile design[3)6)7)].

Postoperative irradiation is a major component in the management of locally advanced head and neck cancer but no detrimental effects on transferred free flap have been reported[8)].

This report presents our experience in intraoral squamous cell carcinoma managed with surgery, with radial forearm flap transfer for reconstruction and adjuvant radiotherapy.

Materials and Methods

The survival of any patient with cancer is determined by three types of factor : those determined by the host, those by the tumor and those by the treatment. The study was designed to determine the influence of certain types of factors regarding tumor recurrence and survival in patients with squamous cell carcinoma in oral cavity. A series of 152 patients of squamous cell cancer of oral cavity who underwent tumor extirpation and immediate reconstruction with radial forearm flap in Canniesburn Hospital, Bearsden, Glasgow, from 1982 to 1988 were included in this study. Each patient's chart was reviewed and information was obtained regarding the patient's age, primary tumor site, tumor stage, pathologic findings, treatment, and outcome results. Information from a retrospective analysis of the patient's age, primary site, neck dissection, and from surgical pathology reports regarding extracapsular node spread, resection margins, bony invasion of mandible, were correlated with treatment outcome. All tumors were restaged after the pathologic report to conform to the TNM classification as adopted by teh UICC[10)]. The patient's ages ranged from 31 to 85 years with a mean age of 62 years. Sixty eight percent(103/152) of the patients were male and thirty two percent(49/152) were female(Table 1). The stage and sites of the disease are described in Table 2.

The majority of patients(132/152) underwent planned dual-modality treatment, comprising surgery followed by early postoperative radiotherapy beginning 3 to 6 weeks after operation.

Nine percent(13/152) of the patients required adjuvant chemotherapy.

All patients were followed for a minimum of 5 years or until death. Any data which was ambiguous or insufficient for complete analysis was excluded from presentation.

Chi-square was employed to determine the significance of difference between variables[9)]. Significa-

Table 1. Distribution of patients

Age	Male	Female
<40	3	2
41−50	10	8
51−60	30	7
61−70	39	18
71−80	20	12
81<	1	2
Total	103	49

Table 2. Stages and primary sites(N=152)

Site Stage	I	II	III	IV	Total(%)
Tongue	2	11	9	13	35(23.0)
F.O.M.*	5	14	9	23	51(33.6)
Alveolus	0	3	2	7	12(7.9)
Buccal	1	0	1	3	5(3.3)
R.M.T.**	1	6	10	13	30(19.7)
Tonsillar F.	0	4	4	4	12(7.9)
Others	1	1	3	2	7(46.1)
Total	10(6.6)	39(25.7)	38(25.0)	65(42.8)	152(100.0)

* Floor of mouth
* Retromolar trigone

nce level is set at $P<0.05$.

Results

In this series of 152 cases, 23(15%) patients required revision of their anastomosis, of which, 13 cases were successfully salvaged. The overall flap success rates was 93.4%(142/152). The noteworthy feature was that all anastomotic falilures(10 patients) occurred early in the series. Even though there was not a strong significant sex bias in the 10 patients whose anastomoiss failed, the percentage of flap failure was higher among female patients than among male patients(Table 3).

The gross survival rate was 42.6%(60/141) and the death rate from cancer was 43.9%(62/141)(Table 4). Twenty percent(30/152) of the patients had composite tissue transfer (with radius) for mandibular reconstruction.

Table 5 shows the relationship between primary tumor site and recurrence. There was no significant correlation between primary site and recurrence. Floor of mouth lesions had a better survival rate 52.3%(23/44), than that of tongue 37.1%(13/35). Patients with tongue lesions had a cancer death rate of 51.4(18/35). Floor of mouth lesion had a cancer death rate of 36.4(16/44). Correlation of survival by primary sites was significant($P<0.05$)(Ta-

Table 3. Flap success rates

	Female	Male	Total(%)
Success	44(89.9%)	98(95.1%)	142(93.4%)
Failure	5(10.2%)	5(4.9%)	10(6.6%)
Total	49(100.0%)	103(100.0%)	152(100.0%)

Non-significant

Table 4. Survival data(n=141)

Alive free from tumor	52(36.9%)
Alive with tumor	8(5.7%)
Dead of tumor	62(43.9%)
Dead of other causes	19(13.5%)
Total	141(100%)

Table 5. Recurrence related to primary sites(n=132) (%)

	Tongue	F.O.M.*	Alveolus	Buccal	R.M.T.	Tonsillar**	Others
Free	12(38.7)	23(35.9)	7(70.0)	2(3.1)	10(35.7)	6(9.4)	4(6.3)
Local recurrence	7(22.6)	6(14.0)	1(10.0)	2(50.0)	8(28.6)	1(10.0)	—
Regional recurrence	7(22.6)	9(20.9)	2(7.4)	—	6(21.4)	2(20.0)	1(16.7)
Distant metastasis	5(16.1)	5(31.3)	—	—	4(14.3)	1(10.0)	1(16.7)
Total	31(100.0)	43(100.0)	10(8.3)	4(100.0)	28(100.0)	10(100.0)	6(100.0)

Non-significant

ble 6).

Resection margins related with recurrence were available for study in 129 of 152 patients. Of the patients with tumor negative resection margin, 63.6 %(56/88) were free of recurrence and 13.6%(12/88) had local recurrence. Of the patients with tumor postive resection margin, 17.1%(7/41) were free of recurrence and 31.7%(13/41) had regional and neck recurrence. There was a strong correlation between resection margins and recurrence($p<0.001$)(Table 7).

Resection margin related with survival data was available for the study in 136 of 152 patients. Of the patients with tumor negative resection margin, 51.6%(47/91) survived. Of the patients with tumor positive resection margin, the survival rate declined, to 26.7%(12/45). Patients with complete resection margin had a far better cure rate than incomplete resection margin. Tumor positive resection margins resulted in a highly significant decrease in survival ($p<0.001$)(Table 8).

Bone involvement related with recurrence and survival data is shown in Table 9 and Table 10. Patients with bone involvment had a lower survival rate(23.7%, 9/38) and a higher death rate from tumor(57.9%, 22/38) than non-involved patients. The survival rates were statistically significant when compared to bone involvement($p<0.05$).

There was no statistically significant difference in the correlation between recurrence and bone involvement.

Table 11 and Table 12 show the effects of mandi-

Table 6. Survival related to primary sites(n=137) (%)

	Tongue	F.O.M*	Alveolus	Buccal	R.M.T.**	Tonsillar	Others
Alive without tumor	10(28.5)	22(50.0)	4(33.3)	3(75.0)	8(28.6)	1(14.3)	
Alvie with tumor	3(8.3)	1(2.2)	–	1(25.0)	2(7.1)	–	1(14.3)
Dead of tumor	18(51.4)	16(36.4)	3(25.0)	–	17(60.7)	5(61.4)	3(42.9)
Dead of other causes	4(11.4)	5(11.4)	5(41.7)	–	1(3.6)	2(28.6)	2(28.6)
Total	35(100.0)	44(100.0)	12(100.0)	4(100.0)	28(100.0)	7(100.0)	7(100.0)

$x^2=33.22$ df=18 $P<0.05$

* Floor of mouth

** Retromolar trigone

Table 7. Recurrence related to resection margin(N=129) (%)

	T.N.R.M.*	T.P.R.M.**	Total
Free of recurrence	56(63.6%)	7(17.1%)	63(48.8%)
Locar recurrence	12(13.6%)	13(31.7%)	25(19.4%)
Combined recurrence	12(13.6%)	13(31.7%)	25(19.4%)
Distant metastasis	8(9.1%)	8(19.5%)	16(12.4%)
Total	88(100.0%)	41(100.0%)	129(100.0%)

$x^2=20.92$ df=3 $P<0.001$

* Tumor negative resection margin

** Tumor positive resection margin

Table 8. Survival related resection margin(N=136) (%)

	T.N.R.M.*	T.P.R.M.**	Total
Alive free from tumor	44(48.4)	7(15.6)	51(37.5)
Alive with tumor	3(3.3)	5(11.1)	8(13.2)
Dead of tumor	29(31.9)	30(66.7)	59(43.4)
Dead of other causes	15(16.5)	3(6.7)	18(13.2)
Total	91(100.0)	45(100.0)	136(100.0)

$x^2=22.51$ df=3 $P<0.001$

* Tumor negative resection margin

** Tumor positive resection margin

Table 9. Recurrence related to bone Invasion(N=125) (%)

	Yes	No	Total
Free of recurrence	11(32.4)	51(56.0)	62(49.6)
Local recurrence	7(20.6)	16(17.6)	23(18.4)
Combined recurrence	11(32.4)	15(16.5)	26(20.8)
Distant metastasis	5(14.7)	9(9.9)	14(11.2)
Total	34(100.0)	91(100.0)	125(100.0)

Non significant

Table 10. Survival related to bone invasion(N=131) (%)

	Yes	No	Total
Alive free from tumor	9(23.7)	42(45.2)	51(39.8)
Alive with tumor	–	7(7.7)	7(5.5)
Dead of tumor	22(57.9)	33(35.5)	55(43.0)
Dead of other causes	7(18.4)	11(11.8)	18(14.1)
Total	38(100.0)	93(100.0)	131(100.0)

$x^2=8.04$ df=3 $P<0.05$

Table 11. Recurrence after mandibular resection(N=34)
(Histologic bone invasion positive only) (%)

	Marginal gorup	Segmental group	Total
Free of recurrence	5(35.7%)	7(35.0%)	12(35.3%)
Local recurrence	3(21.4%)	4(20.0%)	7(20.6%)
Combined recurrence	3(21.4%)	8(40.0%)	11(32.4%)
Distant metastasis	3(21.4%)	1(5.0%)	4(11.8%)
Total	14(100.0%)	20(100.0%)	34(100.0%)

bular resection on survival data. Menthods of mandibular resection did not significantly affect the survival rate and recurrence as well.

Patients without extracapsular node spread had a higher rate of free of recurrence(65.8%) than those with extracapsular node spread(26.7%). The correlation of extracapsular node spread and recurrence was highly significant($p<0.001$) (Table 13).

Extracapsular node spread related with survival data were available for the study in 125 of 152 patients. Of patients without extracapsular node spread, 29.2%(26/89) died from tumor. Of the extracapsular node spread patients, the death rates from tumor increased, to 71.7%(33/46). The correlation of extracapsular node spread patients, the death rates from tumor increased, to 71.1%(33/46). The corre-

lation of extracapsualr node spread and survival was highly significant($p<0.001$)(Table 14).

The age related with survival data showed peculiar findings. From the younger group(<50 years of age), 63.6%(14/22) died from tumor. This was higher than older group (43.7%, 31.2% respectively) (Table 15). The oldest group(>71 years of age) showed a high mortality rate from other causes(28.1 %). The correlation of age group to survival was statistically significant($p<0.05$).

Patients treated with functional neck dissection had a higher tumor free rate(58.5%) than those with radical neck dissection or bilateral neck dissection(36.9%, 42.9% respectively). Patients treated with radical neck dissection had a higher combined recurrence rate(30.4%) than those with functional neck dissection(13.2%)(Table 16) Patients treated with radical neck dissection or bilateral neck dissec-

Table 12. Survival after mandibular resection(N=38)
(Histologic bone invasion positive only) (%)

	Marginal group	Segmental group	Total
Alive	2(13.3%)	7(30.4%)	9(23.7%)
Dead of tumor	11(73.3%)	11(47.8%)	22(57.9%)
Dead of other causes	2(13.3%)	5(21.7%)	7(18.4%)
Total	15(100.0%)	23(100.0%)	38(100.0%)

Non-significant

Table 13. Recurrence related to extracapsular node spread(N=127)

	Yes	No	Total
Free of recurrence	12(26.7)	54(65.8)	66(51.9)
Local recurrence	10(22.2)	12(14.6)	22(17.3)
Combined recurrence	15(33.3)	8(9.8)	23(18.1)
Distant metastasis	8(17.8)	8(9.8)	16(12.6)
Total	45(100.0)	82(100.0)	127(100.0)

$x^2=20.08$ df=3 $P<0.001$

Table 14-1. Survival related to extracapsular node spread(N=135) (%)

	Yes	No	Total
Alive free from tumor	10(21.7)	42(47.2)	52(38.5)
Alive with tumor	3(6.5)	4(4.5)	7(5.2)
Dead of tumor	33(71.7)	26(29.2)	59(43.7)
Dead from other caues	-	17(19.1)	17(12.6)
Total	46(100.0)	89(100.0)	135(100.0)

$x^2=26.66$ df=3 $P<0.001$

Table 14-2. Survival related to extracapsular node spread(N=90)
(Tumor negative Resection margin only) (%)

	Yes	No	Total
Alive free from tumor	9(39.1)	35(52.2)	44(48.9)
Alive with tumor	-	3(4.5)	4(3.3)
Dead of tumor	14(60.9)	15(22.4)	29(32.2)
Dead from other caues	-	14(20.9)	14(15.6)
Total	23(100)	67(100.0)	90(100.0)

$x^2=14.44$ df=3 $P<0.01$

Table 15. Survival related to age groups(N=109) (%)

	Group I (<50 years)	Group II (51-70 years)	Group III (>71 years)
Alive free from tumor	8(34.4%)	31(35.6%)	12(37.5%)
Alive with tumor	-	7(8.1%)	1(3.1%)
Dead of tumor	14(63.6%)	38(43.7%)	10(31.2%)
Dead of other causes	-	11(12.6%)	9(28.1%)
Total	22(100.0%)	87(100.0%)	109(100.0%)

$x^2=13.39$ df=6 $P<0.05$

Table 16. Recurrence related to neck dissection(N=127) (%)

	F.N.D.*	R.N.D.**	Bilateral N.D.	Selective N.D.	Total
Free of recurrence	31(58.5)	17(36.9)	9(42.9)	5(55.6)	62(48.1)
Local recurrence	11(20.7)	9(19.6)	2(9.5)	2(22.2)	24(28.6)
Combinel recurrence	7(13.2)	14(30.4)	6(28.6)	-	27(20.9)
Distant metastasis	2(7.5)	6(13.1)	4(19.0)	2(22.2)	14(12.4)
Total	51(100.0)	46(100.0)	21(100.0)	9(100.0)	127(100.0)

$x^2=18.09$ df=9 $P<0.05$

* functional neck dissection

** radical neck dissection

Table 17. Survival related to neck dissection(N=103) (%)

	Functional N.D.	Radical N.D.	Total
Alive free from tumor	25(36.5)	14(28.0)	39(37.9)
Alive with tumor	2(3.8)	3(6.0)	5(4.9)
Dead from tumor	16(30.2)	28(56.0)	44(42.7)
Dead from tumor	10(18.9)	5(10.0)	15(14.6)
Dead from other causes	10(18.9)	5(10.0)	15(14.6)
Total	53(100.0)	50(100.0)	103(100.0)

$x^2=8.19$ df=3 $P<0.05$

tion had higher death rates from cancer(56.0%, 60.9 % respectively) than those with functional neck dissection (30.2%), however, the correlation of neck dissection and survival was not statistically significant(Table 17).

Discussion

There has been increasing clinical use of free tissue transfer for reconstruction of functional and cosmetic defects after surgical treatment of head and neck tumors. The surgeon is able to make custom-designed flaps tailored for major defects in the head and neck region and thus provide better cosmesis and function for the patient.

The radial froearm flap has proved to be a reliable free flap in many areas of reconstructive surgery and has made free flap reconstruction of the oral cavity a real possibility[3)6)7)] Much of this reliability results from the constant vascular pattern of the forearm and the large size of the vessels, which greatly simplify the technical aspects of microvascular surgery. It has been shown that the flap can tolerate radical radiotherapy early in the postoperative period without significant detrimental effects and in particular with no evidence of wound breakdown or subsequent fistula.

The thin, pliable nature of the forearm skin is well suited to replace oral mucosa, particularly in small defects in which the import of tissue is requi-

Table 18. Comparasion of recurrence after neck dissection(N=97) (%)

	Functional N.D.	Radical N.D.	Total
Free of recurrence	31(58.5)	17(36.9)	48(48.5)
Local recurrence	11(20.7)	9(19.6)	20(20.2)
Combined recurrence	7(13.2)	14(30.4)	21(21.2)
Distant metastasis	2(7.5)	6(13.1)	10(11.1)
Total	51(100.0)	46(100.0)	97(100.0)

$x^2=8.33$ df=3 $P<0.05$

red to maintain tongue mobility and oral function but where bulk may be a positive disadvantage. A segment of vascularized bone can be included as an osteofasciocutaneous flap for composite tissue reconstruction, enabling immediate reconstruction of the mandible. The bone appears to be well vascularized and can tolerate early postoperative radiotherapy.

Because this series of intraoral cancer patients were reconstructed with vascularized free radial forearm flap, there has been virtually no limitation on radical excision of tumor and objective analysis for determining the influence of clinical and histopathological findings regarding recurrence and survival thus became possible.

The overall flap survival rate were 934% and anastomotic failures occurred mostly early in the series. This shows the excellent reliability of free radial forearm flap for reconstruction in oral cavity.

Though we failed to reveal a statistically significant sexual bias regarding anastomotic failure, we are still under impression that forearm dissection from women patients needs great care because they have more subcutaneous fat and finer blood vessles.

As was expected, anatomic subsites had a significant correlation with results of tratment. In our series, survival rates were significantly higher for patients with floor of mouth as compared with tongus tumors(68.6% vs 31.3% respectively). These findings showed the importance of reporting the intraoral cancer by specific subsites different treatment options according to primary site as well[11)12)]. As Zelefsky et al. recommended, tongue tumors should be treated to doses greater than what are conventionally used for postoperative radiotherapy in an effort to enhance local control[11)]. The combination of external radiotherapy with interstitial brachytherapy to boost the primary site is worthy of investigation.

Among the factors affecting treatment failure in carcinoma of the oral cavity, positive excision margins are known to contribute both to local recurrence and to eventual treatment failure[13)]. Our data show that tumor negative resection margin patients had better survival rates(47%) than the tumor positvie resection margin patients(14.7%).

Even though there is no data available on the significance of the number of positive resection margin or the location of the positive margin, resection margin is one of the most important prognostic factors in the treatment of intraoral cancer.

Since Willis had described the tendency for metastatic squamous cell carcinoma of the head and neck to breach the capsules of cervical lymph nodes and infiltrate surrounding tissue[14)], extracapsular node spread has been regarded as an important prognostic factor of local recurrence of tumor in the neck.

There is evidence that risk of local recurrence in patients with extracapsular spread is reduced by postoperative radiotherapy[15)16)], but the effects of postoperative radiotherapy need to be evaluated because radiation therapy has not been found to effectively prevent the development of local recurrence in patients with positive margins[17)].

For surgical treatment of oral carcinomas suspected to involve the mandible, marginal mandibulr resection has the advantage of maintaining the con-

tinuity of the mandible, although it undoubtedly involves a compromise between eradication of the tumor and conservation of the form and function of the mandible. In this study, from the histologically bony invaded patients, recurrence and survival rates between two groups did not show any significant difference. Based on these observations, we agree with the suggestion that marginal mandibular resection combined with radiotherapy is comparable to that following segmental mandibulectomy[18)19)].

Segmental mandibulectomy should be reserved for those tumors invading deeply into the mandible or wrapping around it.

Age has been one of the most controversial host factors in relation to survival. Some authors state that the prognosis is better in younger patients, some that it is better in older patients, some that age has no effect whatsoever. Most of these authors give no data to support their views[20)]. We are under the impression that intraoral carcinoma is more often anaplastic in younger patients[21)], while other reported that carcinoma is more often anaplastic in older patients[22)].

The result that patient treated with functional neck dissection had lower recurrence than those with radical neck dissection gave us some suggestions. Patients treated with radical neck dissection might have more serious neck node involvement before treatment. But it also implies that functional neck dissectin was more or just as effective as radical neck dissection with less morbodity. At a point in time in the treatment of cancer when concern about the cosmetic and functional results of treatment is mounting, attempts at modifying our therapeutic approach in order to achieve a better quality of life and lesser morbidity have taken great importance.

Therefore, functional neck dissection can be a acceptable alternative to radical neck dissection without compromising cancer control[23)24)].

Radical neck dissection should be performed in cases of advanced neck node involvement, however, attempts to be more selective in the choice of patients for radical neck dissection.

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