

Surgical treatment of cutaneous squamous cell carcinoma in Japanese patients aged 85 years and older compared with those below 85 years

Natsuko Kounoike, Minekatsu Akimoto, Mitsuru Nemoto,
Shinsuke Ishikawa, Takayuki Sugimoto, Akira Takeda

Department of Plastic and Aesthetic Surgery, Kitasato University School of Medicine

Objective: Case of cutaneous squamous cell carcinoma (cSCC) in elderly patients are increasing. We analyzed the characteristics of patients aged 85 years and older who underwent surgery for cSCC.

Methods: The clinical records of 178 patients with cSCC who were treated surgically were reviewed. Twenty-six patients aged 85 years or older were treated. We evaluated the following tumor characteristics: sex, tumor size, symptom duration, and lymph node metastasis. We also examined surgical margins, lymph dissection, and the postresection reconstruction procedure.

Results: The symptom duration was significantly shorter, and the surgical margin range was smaller in the elderly patients compared with the younger patients. However, no difference was observed in the frequency of lymph node metastasis or dissection. Half of the cases were operated on under a local anesthesia or an axillary block, and primary suture was the most common reconstruction method in the elderly.

Conclusions: cSCC surgery for elderly patients who have loose skin, should not be identical to that for younger patients because it is easier to close. Rather, for elderly patients with cSCC, it is advisable to select a surgical procedure taking into account the importance of performance status and outcome.

Key words: cutaneous squamous cell carcinoma, surgery, elderly patients

Introduction

In 2014, in Japan, the life expectancy at birth was 81.13 years for men and 87.99 years for women, which ranks third worldwide. With regard to the Japanese aged 65 years and older, males comprise 20.6% of the population and females comprise 26.0%.¹ Malignant tumors are one of the primary causes of death in Japan, and cutaneous squamous cell carcinoma (cSCC) is the second most common malignant skin tumor after basal cell carcinoma (BCC).² In contrast to BCC, lymph node metastasis is observed in cSCC; and, because this influences prognosis, in Japan, cSCC management is based on surgical excision more than it is on Mohs' microscopic surgery³ — a method by which cutaneous cancers can be excised under complete microscopic control by systematic use of frozen sections. Surgical excisions of sSCC in elderly patients have been increasing in recent years.

Although there are various definitions of "elderly,"

however, studies regarding treatment outcomes for elderly patients have been conducted over a wide age range, from 70 to 90 years.⁴⁻⁷ According to the WHO (World Health Organization) classification of the very old, we defined "elderly patients" as those aged 85 years or older. The purpose of the present study was to identify the effects of age on tumors and their management, treatment, and outcome.

Patients and Methods

This study targeted 198 sites in 178 patients who underwent surgical treatment for cSCC at the Department of Plastic and Aesthetic Surgery, Kitasato University Hospital. Patients whose age at the time of surgery was 85 years or older were categorized in the elderly patients group (n = 26), and they were compared with a non-elderly group (n = 152) comprised of patients aged less than 85 years. In addition to comparing all the sites, we also evaluated the differences regarding facial cSCC,

Received 26 January 2015, accepted 29 January 2015

Correspondence to: Natsuko Kounoike, Department of Plastic and Aesthetic Surgery, Kitasato University School of Medicine

1-15-1 Kitasato, Minami-ku, Sagami-hara, Kanagawa 252-0374, Japan

E-mail: natsull@hotmail.com

which involve anatomical structures that affect surgical margins as well as reconstructive surgery. The following parameters were evaluated: sex, maximum tumor diameter, symptom duration, lymph node metastasis, tumor surgical margin, and whether or not lymph node dissection was performed. The follow-up periods ranged from 6 months to 24 years. The results are presented as mean \pm SD.

Tumor size (maximum diameter), symptom duration, and surgical margin for both groups were compared using the paired *t*-test; moreover, lymph node metastasis and dissection and disease recurrence were compared using Fisher's exact test.

Results

The age distribution, in decades, of all the cSCC patients is shown in Figure 1. The mean age was 68.7 ± 13.3 years (range, 29–95 years), which peaked for patients in their 60s (53 sites) and for those in their 70s (52 sites). There were 106 males (53.5%) and 92 females (46.5%). Tumor characteristics and the TNM classification (UICC [Union for International Cancer Control] 2009)⁸ of the elderly patients are summarized in Table 1. A female patient, No. 11, underwent surgery three times for temporal, forearm, and cheek region cSCC. Moreover, a male patient, No. 23, who had undergone radiotherapy for tinea manuum, underwent surgery of the hand three times for cSCC in his 60s and 70s; but then, at the age of 89 years, he had to undergo amputation of his right middle finger.

A comparison was made between all the patients in the elderly and non-elderly groups (Table 2). The non-elderly group accounted for 170 sites. Facial cSCC was

the most common, accounting for 109 non-elderly patient sites (64.1%) and 20 elderly patient sites (71.4%); however, cSCC did not occur in any hairy sites of the head. Furthermore, no cases of cSCC of the trunk were reported in the elderly group.

Tumor size (maximum diameter) was 38.8 ± 40.5 mm in the non-elderly group and 29.4 ± 23.1 mm in the elderly group. Moreover, in the non-elderly group, a number of patients with tumors exceeding 100 mm in the limbs were also observed. Based on the responses given by the patients, and their families, the symptomatic period leading up to surgery was significantly shorter in the elderly group (17.1 ± 24.4 months) than in the non-elderly group (31.7 ± 49.7 months; $P < 0.05$). In addition, tumor margins tended to be smaller in the elderly patients (11.1 ± 7.2 mm) than those in the non-elderly patients (13.6 ± 9.6 mm). Furthermore, lymph node metastasis was observed in 4 elderly patients, and lymph node dissection was performed in 2 patients. Nevertheless, no significant differences were observed in the frequencies of lymph node metastasis or dissection between the elderly and non-elderly patients. We did not perform Mohs' microscopic surgery.

Table 3 summarizes the clinical data on cSCC of the face that was operated on at 20 and 109 sites in the elderly at non-elderly groups, respectively. Moreover, the ratio of males to females was smaller in the elderly group (56 : 53) than that in the non-elderly group (8 : 14). Furthermore, in the elderly group, cheek region cSCC was most prevalent (30%), whereas in the non-elderly group, lower lip cSCC was most prevalent (21%).

Facial tumor size was 31.8 ± 26.5 mm in the elderly patients and 30.9 ± 29.6 mm in the non-elderly patients. In the patients with facial cSCC, tumor size did not

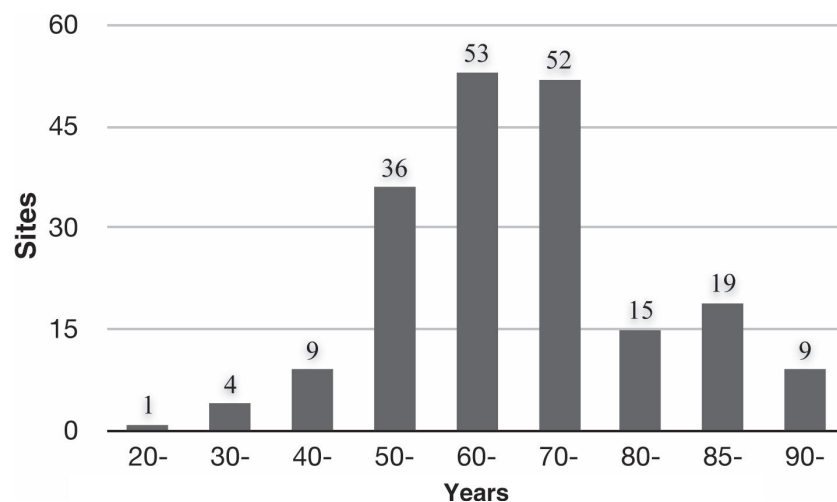


Figure 1. The age distribution of the patients sites with cSCC in decades (N = 198)

Table 1. Characteristics of patients 85 years old or older with cutaneous squamous cell carcinoma (cSCC)

No.	Age Sex	Site	TNM	Anesthesia	L/N dissection
1	85 M	Lower lip	T2N0M0	G	
2	88 M	Lower leg	T1N0M0	L	
3	87 M	Hand	T3N0M0	G	
4	87 M	Lower leg	T3N0M0	G	
5	88 M	Cheek	T2N1M0	G	Radical neck
6	88 M	Lower lip	T2N1M0	G	Upper neck
7	87 M	Ear	T2N0M0	G	
8	89 M	Cheek	T3N1M0	G	
9	89 F	Cheek	T2N0M0	G	
10	90 M	Cheek	T1N0M0	L	
11	86 F	Temple	T2N0M0	G	
	91 F	Forearm	T2N0M0	L	
	91 F	Cheek	T1N0M0	L	
12	95 F	Middle finger	T2N0M0	Ax	
13	86 F	Upper eyelid	T3N0M0	G	
14	93 F	Little finger	T1N0M0	L	
15	89 F	Lower leg	T2N0M0	G	
16	90 F	Upper eyelid	T3N0M0	G	
17	93 M	Ear	T2N0M0	L	
18	85 M	Temple	T2N0M0	L	
19	86 M	Cheek	TisN0M0	G	
20	95 F	Lower eyelid	T2N0M0	L	
21	88 F	Lower lip	T2N1M0	G	
22	85 F	Nose	TisN0M0	L	
23	89 M	Middle finger	T2N0M0	L	
24	94 F	Cheek	T2N0M0	L	
25	86 M	Index finger	T4N0M0	L	
26	89 F	Upper lip	T1N0M0	L	

TNM, tumor, node, metastasis; L/N, lymph node; G, general anesthesia; L, local anesthesia; Ax, axillary block

Table 2. Patients' sites and tumor characteristics

Variables	Number of patients' sites (%)		
	<85 yo 170 (85.9)	≥85 yo 28 (14.1)	
Male	106 (62.4)	13 (46.5)	
Site			
Head and/ or face	109 (64.1)	20 (71.4)	
Upper limb	21 (12.6)	6 (21.4)	
Lower limb	28 (16.5)	2 (7.1)	
Torso	12 (7.0)	0 (0)	
Size (mm)	38.8 ± 40.5	29.4 ± 23.1	ns
Symptom duration (months)	31.7 ± 49.7	17.1 ± 24.4	P < 0.05
Recurrence			ns
L/N metastasis	16	4	ns
L/N dissection	23	2	ns
Surgical margin (mm)	13.6 ± 9.6	11.1 ± 7.2	ns

yo, years old; L/N, lymph node; ns, not significant

significantly differ according to age. Moreover, no statistically significant difference was observed regarding recurrence, with only one (52.6%) recurrence case in the elderly group and 11 (13.8%) recurrence cases in the non-elderly group. Although no statistically significant differences were observed regarding the symptom durations, which were 13.5 ± 16.3 months in the elderly group and 23.9 ± 35.2 months in the non-elderly group, these results showed that symptom durations were shorter in the elderly group. Lymph node metastasis was observed in 4 patients with cervical lymph node metastasis. Lymph dissection was performed in 2 of these patients. The results indicated smaller facial surgical margins in the elderly group than those in the non-elderly group without a statically significant difference.

The surgical procedures for reconstruction after resection of head and facial cSCC are presented in Table 4. Eight patients in the elderly group (40%) were sutured. Skin grafts were performed in 6 patients: 4 received full-thickness skin grafts, 1 patient received a split thickness skin graft, and 1 patient received an artificial skin graft. The donor site for the full-thickness skin grafts was the neighboring area in 3 patients and the lower abdomen in 1 patient. In the non-elderly patients, reconstruction with skin flaps was the most common. The free-flap reconstruction performed in 3 non-elderly cases was not performed in any of the elderly patients. Of the 28 surgical procedures performed in the elderly patients, 14 received general anesthesia and the others local anesthesia and/or nerve blocks.

Discussion

In Japan, the most common non-melanoma skin cancers are BCC and SCC as in Canada, South Wales, Finland, Singapore, and Australia.^{2,9-13} Research conducted in Canada suggested that, compared with BCC, the male-to-female ratio is predominantly male in all age ranges; moreover, although the ratio decreases in patients 80 years or older, there is still a higher proportion of males.⁹ The results of the present study, which indicated that the male-to-female ratio was equal in the patients aged 85 years or older, may have been due to the influence of the female patients who underwent surgery three times. Moreover, the difference between the mean life expectancy in Japan for males (81.13 years) and females (87.99 years) could have influenced the results as well.¹

Sites of occurrence of cSCC in the patients aged 85 years or older were limited to the face or limbs and were all sun-exposed sites. Sun-exposed skin areas are considered a risk factor for local recurrence and metastasis in the literature review by Rowe et al.¹⁴ and increase metastatic potential of cSCC in the UK.^{15,16} The fact that a majority of the 28 sites of patients aged 85 years or older were on the face (20 sites) compared with those on the limbs (8 sites) could evidently be related to the sun-exposed skin.

Regarding facial SCC, there was no statically significant difference in tumor size between the elderly and non-elderly patients. The tendency for shorter symptom duration and relatively rapid growth seen in many cases

Table 3. Patients with head or facial cSCC and their characteristics

Variables	Number of patients (%)		
	<85 yo 109	≥85 yo 20	
Male	56 (53%)	8 (47%)	
Site			
Cheek	16 (15%)	6 (30%)	
Lower lip	22 (21%)	3 (15%)	
Upper eyelid	8 (8%)	2 (11%)	
Ear	8 (8%)	2 (11%)	
Temple	9 (9%)	2 (11%)	
Nose	17 (16%)	2 (11%)	
Size (mm)	30.9 ± 29.6	31.8 ± 26.5	ns
Symptom duration (months)	23.9 ± 35.2	13.5 ± 16.3	ns
Recurrence	11	1	ns
L/N metastasis	9	3	ns
L/N dissection	12	2	ns
Surgical margin (mm)	10.93 ± 8.8	8.13 ± 5.7	ns

L/N, lymph node; ns, not significant

Table 4. Surgical procedures for head and neck cSCC

Surgical procedure	Number of patients (%)	
	<85 yo n = 109	≥85yo n = 20
Open/cryosurgery	1 (0.9%)	1 (5%)
Primary closure	18 (16.5%)	8 (40%)
Skin graft	29 (26.6%)	6 (30%)
Flap	58 (53.3%)	5 (25%)
Free flap	3 (2.7%)	0 (0%)

could also have been a contributing factor. The reason for shorter symptom duration in facial cases for both elderly and non-elderly patients compared with all the cases could be that those patients sought earlier treatment for the sites on their faces. The concerns of elderly patients' families regarding the sudden growth of facial tumors and their encouragement for patients to seek treatment could be an exclusive feature of elderly facial skin tumors that warrants further investigation.

Lymph node metastasis has been reported in 10% of all cSCC patients at our hospital,¹⁷ which is consistent with the results of previous reports.^{18,19} In elderly patients, the lymph nodes have been reported to undergo structural changes with age.²⁰ The decision to perform lymph dissection is one that should be made with extreme care. Elective lymph node dissection has been shown to have no effects on the prognosis of malignant melanomas.²¹ A comparison of upper aerodigestive tract SCC in patients aged 80 years or older with that in patients aged less than 65 years revealed that neck lymph node dissection was performed at the same frequency, but the prognosis for the patients aged 80 years or older was poor. We believe that the decision to perform lymph dissection in elderly patients should be made extremely carefully, while taking performance status into account. Selection of lymph dissection in the elderly group was also influenced by the patients' general conditions. We select this surgical procedure with caution because it can lead to longer hospital stays.

The results indicating smaller surgical margins in the elderly group than in the non-elderly group may have been influenced by many factors, including alteration of the reconstruction procedure according to the margin in order to avoid increased invasiveness. In Japan, Mohs' micrographic surgery is not yet standard treatment for skin cancer. Similar to lymph dissection, in such cases, a good understanding of the patient's state and the performance of surgical procedures to avoid prolonged hospitalization periods and associated long-term bed rest are factors that can help prevent lowering the performance status of patients.

Regarding surgical margins, aging skin contributes greatly to reconstruction after resection. The ratio of suturing was higher in the elderly group. Skin slackness leads to reduced tautness after a wide local resection and suturing; and, therefore, makes it easier to perform skin grafts or skin flaps created with adjacent skin. Nemoto et al.²² performed three-dimensional analysis, using histological results to demonstrate the presence of collagen in forehead wrinkles. The face is not only easily influenced by skin condition but also by subcutaneous fat and skeletal structure.^{23,24}

As in the aging face, so it is easier to collect skin in elderly patients than in non-elderly patients. In the present study, 4 of the 6 skin grafts for facial SCC surgery in patients aged 85 years or older involved full-thickness skin grafts from the neighboring areas or redundant abdominal regions. Period of epithelialization for split thickness donor sites is longer than that of full thickness wound healing. In fact, it is often possible to select a minimally invasive procedure for postresection reconstruction because elderly patients have looser skin.

The safety of reconstruction performed with microsurgery for elderly patients has been reported,²⁵⁻²⁷ however, in those reports, there are only a few patients aged 85 years or older. Considering the sacrifice made by donor sites, reconstruction performed with microsurgery is not actively selected as a treatment method; free-tissue transfer reconstruction for treatment of head and neck SCC was performed in 17% of patients aged less than 65 years but only in 4.6% of patients aged 80 years or older.⁵ Studies on cancer in elderly patients have been conducted in various fields, and radiotherapy has been shown to produce favorable treatment outcomes in the elderly. Age does not significantly influence the effects of radiotherapy in patients aged 90 years or older.²⁸ Moreover, it has also been reported that radiotherapy for patients aged 90 years or older made local control possible for 70% of the patients and nodal control possible for 87%.⁴ Although most radiotherapy outcomes for elderly patients are favorable, the same cannot be said for surgical treatment outcomes. However, there are various definitions for the age range referred to by the term, "elderly." In addition, complications and occurrence rates also increase in elderly patients aged older than the mean life expectancy, which influences treatment outcomes.

Syrigos et al.²⁹ stated that treatment for skin malignancies should be determined taking the estimation of life expectancy, functional status, comorbidity, nutrition, polypharmacy, social support, and potential existence of depression into consideration. Treatment strategies for malignant skin tumors in patients in their 80s, when individual differences in chronological age and biological age become significant, should be carefully selected. Although age cannot determine ineligibility for surgery, the same surgical procedures as those performed in younger patients will not necessarily improve prognosis in the elderly.

Conclusions

cSCC surgery for elderly patients, who have looser skin, should not be identical to that for younger patients.

Rather, it is best to select a surgical procedure that considers the importance of performance status. Skin condition should be taken into consideration when selecting surgical procedures for elderly cSCC patients. Additionally, the surgical approach for lymph node metastasis should be extremely carefully selected.

References

1. Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labor and Welfare: Japanese Government, 2014. Available at: http://www.indexmundi.com/japan/life_expectancy_at_birth.html. Accessed March 15, 2015.
2. Ishihara K, Saida T, Otsuka F, et al. Statistical profiles of malignant melanoma and other skin cancers in Japan: 2007 update. *Int J Clin Oncol* 2008; 13: 33-41.
3. Mohs FE. Chemosurgery for the microscopically controlled excision of skin cancer. *J Surg Oncol* 1971; 3: 257-67.
4. Schofield CP, Sykes AJ, Slevin NJ, et al. Radiotherapy for head and neck cancer in elderly patients. *Radiother Oncol* 2003; 69: 37-42.
5. Clayman GL, Eicher SA, Sicard MW, et al. Surgical outcomes in head and neck cancer patients 80 years of age and older. *Head Neck* 1998; 20: 216-23.
6. Ganly I, Gross ND, Patel SG, et al. Outcome of craniofacial resection in patients 70 years of age and older. *Head Neck* 2007; 29: 89-94.
7. Mitsuhashi N, Hayakawa K, Yamakawa M, et al. Cancer in patients aged 90 years or older: radiation therapy. *Radiology* 1999; 211: 829-33.
8. Sobin LH, Gospodarowicz MK, Wittekind C. TNM Classification of Malignant Tumors, 7th edition. *UICC International Union Against Cancer*. Chichester, West Sussex, UK; Hoboken, NJ, USA Wiley-Blackwell; 2009.
9. Demers AA, Nugent Z, Mihalciu C, et al. Trends of nonmelanoma skin cancer from 1960 through 2000 in a Canadian population. *J Am Acad Dermatol* 2005; 53: 320-8.
10. Holme SA, Malinovsky K, Roberts DL. Changing trends in non-melanoma skin cancer in South Wales, 1988-98. *Br J Dermatol* 2000; 143: 1224-9.
11. Hannuksela-Svahn A, Pukkala E, Karvonen J. Basal cell skin carcinoma and other nonmelanoma skin cancers in Finland from 1956 through 1995. *Arch Dermatol* 1999; 135: 781-6.
12. Koh D, Wang H, Lee J, et al. Basal cell carcinoma, squamous cell carcinoma and melanoma of the skin: analysis of the Singapore Cancer Registry data 1968-97. *Br J Dermatol* 2003; 148: 1161-6.
13. Staples MP, Elwood M, Burton RC, et al. Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985. *Med J Aust* 2006; 184: 6-10.
14. Rowe DE, Carroll RJ, Day CL Jr. Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. Implications for treatment modality selection. *J Am Acad Dermatol* 1992; 26: 976-90.
15. Motley R, Kersey P, Lawrence C, et al. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. *Br J Dermatol* 2002; 146: 18-25.
16. Motley R, Kersey P, Lawrence C, et al. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. *Br J Plast Surg* 2003; 56: 85-91.
17. Takeda A, Akimoto M, Nemoto M, et al. Preoperative risk factors of lymph node metastasis in cutaneous squamous cell carcinoma. *J Plast Surg Hand Surg* 2013; 47: 204-8.
18. Alam M, Ratner D. Cutaneous squamous-cell carcinoma. *N Engl J Med* 2001; 344: 975-83.
19. Dinehart SM, Pollack SV. Metastases from squamous cell carcinoma of the skin and lip. An analysis of twenty-seven cases. *J Am Acad Dermatol* 1989; 21: 241-8.
20. Pan WR, Suami H, Taylor GI. Senile changes in human lymph nodes. *Lymphat Res Biol* 2008; 6: 77-83.
21. Balch CM, Soong SJ, Bartolucci AA, et al. Efficacy of an elective regional lymph node dissection of 1 to 4 mm thick melanomas for patients 60 years of age and younger. *Ann Surg* 1996; 224: 255-63.
22. Nemoto M, Uchinuma E, Yamashina S. Three-dimensional analysis of forehead wrinkles. *Aesthetic Plast Surg* 2002; 26: 10-6.
23. Wulf HC, Sandby-Møller J, Kobayasi T, et al. Skin aging and natural photoprotection. *Micron* 2004; 35: 185-91.
24. Mendelson BC, Hartley W, Scott M, et al. Age-related changes of the orbit and midcheek and the implications for facial rejuvenation. *Aesthetic Plast Surg* 2007; 31: 419-23.
25. Chick LR, Walton RL, Reus W, et al. Free flaps in the elderly. *Plast Reconstr Surg* 1992; 90: 87-94.
26. Shestak KC, Jones NF. Microsurgical free-tissue transfer in the elderly patient. *Plast Reconstr Surg* 1991; 88: 259-63.
27. Coskunfirat OK, Chen HC, Spanio S, et al. The safety of microvascular free tissue transfer in the elderly population. *Plast Reconstr Surg* 2005; 115: 771-5.
28. Oguchi M, Ikeda H, Watanabe T, et al. Experiences of 23 patients > or = 90 years of age treated with radiation therapy. *Int J Radiat Oncol Biol Phys* 1998; 41: 407-13.
29. Syrigos KN, Tzannou I, Katirtzoglou N, et al. Skin cancer in the elderly. *In Vivo* 2005; 19: 643-52.