Association between multidisciplinary team care approach and survival rates in patients with oral cavity squamous cell carcinoma

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ABSTRACT: *Background.* The purpose of this study was to investigate whether multidisciplinary team care (MDTC) is associated with outcomes in oral cavity squamous cell carcinoma (SCC).

Methods. We retrospectively examined 1616 patients with oral cavity SCC who underwent radical surgery between 1996 and 2011. The study participants were classified into 2 subgroups according to the use of MDTC.

Results. Five-year outcomes were significantly better in the MDTC group than in the no-MDTC group (neck control, 88% vs 84%, $p = .0397$; disease-specific survival [DSS], 83% vs 78%, $p = .0114$; and overall survival [OS], 70% vs 64%, $p = .0002$, respectively). Among patients who were scheduled to undergo adjuvant therapy, the number who completed their adjuvant treatment was significantly higher in the MDTC group than in the no-MDTC group (90% vs 60% to 70%, $p < .001$).

Conclusion. The association of MDTC with improved outcomes may be potentially explained by a better therapeutic alliance between the patient and the tumor board, and/or a greater thoroughness in clinical management. © 2016 Wiley Periodicals, Inc. *Head Neck* **38**: E1544–E1553, 2016

KEY WORDS: oral cavity cancer, squamous cell carcinoma, multidisciplinary team care, adjuvant therapy, outcomes

INTRODUCTION

Growing evidence indicates that the multidisciplinary team care (MDTC) approach may improve the quality of life of patients with malignancies, drive the cost of health care lower, and improve clinical outcomes.[1–10] As part of its continued effort to improve care for patients with cancer, the Taiwan Health Promotion Administration has taken initiative to promote MDTC and multidisciplinary case management as of April 2003. The Administration emphasizes that MDTC can span the cancer care continuum and would enhance the quality of clinical practice.

Oral cavity squamous cell carcinoma (SCC) is a major cause of cancer-related morbidity and mortality in areas where the habit of chewing betel quid is widespread. In Taiwan, oral cavity cancer ranks sixth in cancer incidence, and it is the most common malignancy diagnosed in Taiwanese men aged between 30 and 50 years.[11] We have previously shown that betel quid chewing is associated with field cancerization in patients with oral cavity SCC, which, in turn, confers a higher risk of second primary tumors and local recurrences.[12] Because outcomes in patients with oral cavity SCC largely depend on the type of surgical approach and the use of adjuvant therapy, a comprehensive strategy for decision-making, therapy, clinical management, and follow-up is mandatory in betel quid chewing endemic areas. Starting from these premises, we began implementing an MDTC approach as of January 2004.

In this study, we hypothesized that MDTC may be associated with patient compliance to treatment and consequently ameliorate clinical outcomes at 5 years. To this aim, we analyzed our cohort data of patients with oral cavity SCC who underwent surgical resection as of 1996. The study patients were classified into 2 subgroups according to the use of an MDTC approach.

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Additional Supporting Information may be found in the online version of this article.

MATERIALS AND METHODS

Study subjects

Between January 1996 and December 2011, we identified a total of 1616 consecutive previously untreated patients with first primary oral cavity SCC who were scheduled for radical surgery, either with or without neck dissection. Patients presenting with locoregional recurrences were excluded. All of the participants underwent an extensive presurgical evaluation and stage workup.[12] Patients were staged according to the 1997 (5th) and 2010 (7th) staging criteria of the American Joint Committee on Cancer. The 1997 criteria were used for patients enrolled before 2002, whereas the 2010 criteria were utilized for patients recruited after 2002. The major difference between the 2 staging systems is that some tumors with invasion of masticator space/pterygoid plate would be classified as pT4b using the American Joint Committee on Cancer 2010 criteria, but only as pT2 to T3 tumors according to the 1997 criteria. Because MDTC was formally introduced in our hospital as of January 2004, the study patients were classified into 2 subgroups accordingly (no-MDTC, patients enrolled between January 1996 and December 2003 vs MDTC, patients enrolled between January 2004 and December 2011). Intergroup analyses were performed according to different clinicopathological parameters and treatment modalities. The study protocol was approved by the Institutional Review Board of the Chang Gung Memorial Hospital (CGMH 101-4457B). Patient consent was waived because of the retrospective nature of the study.

Surgery and adjuvant therapy

The primary tumors were excised with safety margins of 1 cm or greater (both peripheral and deep margins). Levels I to V neck dissections were performed in patients with cN+ disease, whereas cN- patients received levels I to III neck dissections.[12] Before 2004, we performed traditional levels I to III neck dissection (ie, dissections that reached the cricoid cartilage level). As of 2004, the majority of patients received extended levels I to III neck dissection (ie, dissections that reached the transverse cervical vessel located between the cricoid cartilage and the clavicle). The modality for selecting patients for postoperative adjuvant therapy was not standardized until the implementation of MDTC. In general, postoperative radiotherapy (RT; 60 Gy) was performed for patients bearing pathological risk factors. The risk factors were classified according to the National Comprehensive Cancer Network guidelines before 2008; thereafter, the classification of risk factors was performed based on the Chang Gung guidelines outlined in our publications. The main risk factors for RT included: pT4, pT3N1, or pT1 to 2N1 (N1 at level IV/V), or close margins $\leq$2 mm, or poor differentiation with tumor depth $\geq$4 mm, or 2 minor risk factors (pN1, tumor depth $\geq$10 mm, close margins $\leq$4 mm, poor differentiation, perineural invasion, lymphatic invasion, or vascular invasion). The radiation field included the entire tumor bed area (with 1- to 2-cm margins) as well as the regional lymphatics. Concomitant chemoradiotherapy (CRT; 66 Gy) with cisplatin-based regimens was administered to patients with extracapsular spread (ECS), multiple lymph node metastases, positive margins, or $\geq$3 minor risk factors (ie, the above-mentioned minor risk factors plus pT4).[13–15] The chemotherapy regimen consisted of intravenous cisplatin 50 mg/m^2 biweekly plus daily oral tegafur 800 mg and leucovorin 60 mg, cisplatin 40 mg/m^2 weekly, or cisplatin 100 mg/m^2 every 3 weeks.[15]

Salvage therapy for locoregional recurrence

Patients with local tumor recurrence underwent radical surgical excision with safety margins of 1.5 cm or greater (both peripheral and deep margins). Patients with cervical lymph node recurrences underwent complete neck dissection (levels I–V). As of January 2004, postoperative adjuvant RT or concurrent CRT were administered when deemed necessary by the consensus reached by our tumor board conference. In presence of unresectable local tumors or nodes, the decision to use definitive RT/concurrent CRT versus the best supportive care was taken based on the disease status and the patient's general conditions. Patients with initial failure at distant sites received palliative treatment, the only exception being the presence of a single resectable lesion located in the lung.

Statistical analysis

The study endpoints included the 5-year rates of local control, neck control, distant metastases, disease-free survival (DFS), disease-specific survival (DSS), overall survival (OS), and second primary tumors. Cumulative survival plots for the study outcomes were univariately evaluated using the Kaplan–Meier method (log-rank test). All calculations were performed using the SPSS 17.0 statistical package (SPSS, Chicago, IL). Two-tailed p values $< .05$ were considered statistically significant.

RESULTS

Patients

A total of 1616 patients with oral cavity SCC (1506 men and 110 women) were included in the study. The age at onset ranged from 25 to 89 years, with a mean of 51 years and a median of 50 years. The tumor subsites were as follows: tongue (n = 594; 37%), buccal mucosa (n = 560; 35%), alveolar ridge (n = 218; 14%), retromolar trigone (n = 94; 6%), mouth floor (n = 59; 4%), lip (n = 54; 3%) and hard palate (n = 37; 2%).

The general clinicopathological characteristics and the main risk factors for adverse outcomes in the 2 groups are summarized in Table 1. Patients in the MDTC group were more likely to have a history of preoperative alcohol drinking ($p < .001$), preoperative betel quid chewing ($p = .005$), and tumors located in the buccal mucosa ($p = .009$). More aggressive treatment strategies were also observed in the MDTC group in terms of neck dissections ($p = .039$), extended levels I to III neck dissection ($p < .001$), bone excision ($p = .040$), free flap reconstructions ($p = .021$), and adjuvant concurrent CRT ($p < .001$). Additionally, a higher prevalence of skin invasion ($p = .014$) and perineural invasion ($p < .001$) was observed in the MDTC group. In contrast, the no-MDTC group was characterized by a higher frequency of tongue tumors ($p = .009$), tumor depth $\geq$10 mm ($p = .002$), and lymphatic

TABLE 1. General characteristics of patients with oral cavity squamous cell carcinoma in the no-multidisciplinary team care (1996–2003; $n = 789$) and multidisciplinary team care (2004–2011; $n = 827$) groups.

Characteristics (no. of patients; %)	No-MDTC No. of patients (%)	MDTC No. of patients (%)	*p* value
Sex			1.000
Male (1506; 93.2)*	735 (93.2)	771 (93.2)	
Female (110; 6.8)	54 (6.8)	56 (6.8)	
Age at onset, y			.148
<65 (1394; 86.3)*	691 (87.6)	703 (85.0)	
≥65 (222; 13.7)†	98 (12.4)	124 (15.0)	
Preoperative alcohol drinking			<.001
No (577; 35.7)	364 (46.1)	213 (25.8)	
Yes (1039; 64.3)*	425 (53.9)	614 (74.2)	
Preoperative betel quid chewing			.005
No (335; 20.7)	187 (23.7)	148 (17.9)	
Yes (1281; 79.3)*	602 (76.3)	679 (82.1)	
Preoperative cigarette smoking			.945
No (248; 15.3)	122 (15.5)	126 (15.2)	
Yes (1368; 84.7)	667 (84.5)	701 (84.8)	
Postoperative alcohol drinking			.032
No (1387; 85.8)	662 (83.9)	725 (87.7)	
Yes (229; 14.2)	127 (16.1)	102 (12.3)	
Postoperative betel quid chewing			.799
No (1601; 99.1)	781 (99.0)	820 (99.2)	
Yes (15; 0.9)	8 (1.0)	7 (0.8)	
Postoperative cigarette smoking			.056
No (1220; 75.5)	579 (73.4)	641 (77.5)	
Yes (396; 24.5)	210 (26.6)	186 (22.5)	
Tumor subsite			.009
Tongue (594; 36.8)	314 (39.8)	280 (33.9)	
Buccal (560; 34.7)†	246 (31.2)	314 (38.0)	
Others (462; 28.6)†	229 (29.0)	233 (28.2)	
Pathological T classification*,†			.068
pT1–2 (967; 59.8)	454 (57.5)	513 (62.0)	
pT3–4 (649; 40.2)	335 (42.5)	314 (38.0)	
Pathological N classification*,†			.874
pN0 (899; 60.3)	434 (60.5)	465 (60.0)	
pN1–2 (593; 39.7)	283 (39.5)	310 (40.0)	
Pathological stage*,†			.422
I–II (697; 43.1)	332 (42.1)	365 (44.1)	
III–IV (919; 56.9)	457 (57.9)	462 (55.9)	
Extended levels I−III neck dissection			<.001
No (1063; 65.8)	788 (99.9)	275 (33.3)	
Yes (553; 34.2)	1 (0.1)	552 (66.7)	
Skin excision			.316
No (1066; 66.3)	527 (67.6)	539 (65.2)	
Yes (541; 33.7)	253 (32.4)	288 (34.8)	
Bone excision			.040
No (726; 44.9)	375 (47.5)	351 (42.4)	
Yes (890; 55.1)	414 (52.5)	476 (57.6)	
Free flap reconstruction			.021
No (257; 15.9)	143 (18.1)	115 (13.9)	
Yes (1359; 84.1)	646 (81.9)	712 (86.1)	
Neck dissection			.039
No (124; 7.7)	72 (9.1)	52 (6.3)	
Yes (1492; 92.3)	717 (90.9)	775 (93.7)	
ECS			1.000
No (1262; 78.2)	615 (78.2)	647 (78.2)	
Yes (351; 21.8)*,†	171 (21.8)	180 (21.8)	
Tumor differentiation			.360
Well/moderate (1486; 92.0)	731 (92.6)	755 (91.3)	
Poor (130; 8.0)*,†	58 (7.4)	72 (8.7)	
Tumor depth, mm			.002
<10 (834; 51.7)	375 (47.8)	459 (55.5)	
≥10 (778; 48.3)*,†	410 (52.2)	368 (44.5)	

TABLE 1. *Continued*

Characteristics (no. of patients; %)	No-MDTC No. of patients (%)	MDTC No. of patients (%)	*p* value
Margin status, mm			.800
≤4 (154; 9.6)*,†	76 (9.8)	78 (9.4)	
>4 (1446; 90.4)	697 (90.2)	749 (90.6)	
Skin invasion			.014
No (1495; 92.5)	743 (94.2)	752 (90.9)	
Yes (121; 7.5)*,†	46 (5.8)	75 (9.1)	
Bone marrow invasion			.437
No (1382; 85.5)	669 (84.8)	713 (86.2)	
Yes (234; 14.5)*,†	120 (15.2)	114 (13.8)	
Perineural invasion			<.001
No (1137; 70.4)	602 (76.4)	535 (64.7)	
Yes (478; 29.6)*,†	186 (23.6)	292 (35.3)	
Lymphatic invasion			.002
No (1531; 94.9)	733 (93.1)	798 (96.5)	
Yes (83; 5.1)*,†	54 (6.9)	29 (3.5)	
Vascular invasion			.310
No (1579; 97.8)	773 (98.2)	806 (97.5)	
Yes (35; 2.2)	14 (1.8)	21 (2.5)	
Perioperative mortality (≤30 d)			.720
No (1609; 99.6)	785 (99.5)	824 (99.6)	
Yes (7; 0.4)	4 (0.5)	3 (0.4)	
Treatment modality			<.001
Surgery alone (790; 48.9)	387 (49.0)	403 (48.7)	
Surgery plus RT (463; 28.7)	296 (37.5)	167 (20.2)	
Surgery plus concurrent CRT (263; 22.5)	106 (13.4)	257 (31.1)	

Abbreviations: MDTC, multidisciplinary team care; ECS, extracapsular extension; RT, radiotherapy; CRT, chemoradiotherapy.
* The following variables were identified as significant adverse prognostic factors ($p < .05$) for relapse (local, neck, or distant) in this study: male sex, age <65 y, history of alcohol drinking, history of betel quid chewing, pT classification, pN classification, p-stage, ECS(+), poor differentiation, tumor depth ≥10 mm, margin ≤4 mm, skin invasion, bone marrow invasion, perineural invasion, and lymphatic invasion.
† The following variables were identified as significant adverse prognostic factors ($p < .05$) for death in this study: age ≥65 y, subsites other than tongue, pT classification, pN classification, p-stage, ECS(+), poor differentiation, tumor depth ≥10 mm, margin ≤4 mm, skin invasion, bone marrow invasion, perineural invasion, and lymphatic invasion.

invasion ($p = .002$). There were no intergroup differences in terms of pathological tumor classification ($p = .068$), nodal classification ($p = .874$), and pathological stage ($p = .422$), although the presence of the above-mentioned risk factors had a more adverse impact on relapse and death in the MDTC group (namely, preoperative alcohol drinking, preoperative betel quid chewing, buccal subsite, skin invasion, and perineural invasion) than in the no-MDTC group (namely, tumor depth and lymphatic invasion; Table 1, footnote). To provide a more comprehensive description of the changes observed in the entire cohort study over time, the general characteristics of the study participants were analyzed at 4-year intervals (Supplementary Table S1, online only). Most of the investigated features were in line with those originally depicted in the no-MDTC and MDTC subgroups.

Clinical course in the entire study cohort

The follow-up was continued until February 2015. All of the participants were followed for at least 36 months after primary surgery or until their death. The entire cohort was followed for a median of 71 months (mean, 79 months; range, 1–226 months). The median follow-up time of surviving patients was 108 months (mean, 108 months; range, 36–226 months). At the end of the study period, 935 patients (58%) were alive, and 681 (42%) were dead. The patterns of recurrences and second primary tumors were as follows: local, 16% ($n = 256$); neck, 14% ($n = 225$); distant metastases, 10% ($n = 161$); and second primary tumors, 25% ($n = 405$). Salvage therapy was performed in 263 of the 400 patients (66%) with local and/or neck recurrences. Among the patients who were salvaged, 122 (46%) were still alive when the data were analyzed, whereas the remaining 141 (54%) were dead.

Five-year outcomes in the multidisciplinary team care and no-multidisciplinary team care groups

In the entire study cohort, we observed the following 5-year rates: local control, 85%; neck control, 86%; distant metastases, 10%; DFS, 72%; DSS, 80%; OS, 67%; and second primary tumors, 20%. The 5-year rates observed in patients in the MDTC and no-MDTC groups were as follows: local control, 87% versus 83%, $p = .2212$; neck control, 88% versus 84%, $p = .0397$; distant metastases, 11% versus 10%, $p = .4340$; DFS, 74% vs 70%, $p = .1350$; DSS, 83% versus 78%, $p = .0114$; OS, 70% versus 64%, $p = .0002$, and second primary tumors, 22% versus 17%, $p = .2039$, respectively (Figures 1A–1G). Therefore, the largest difference in terms of tumor control was observed in the neck site. To analyze the changes in outcomes over time, we reported the main study endpoints stratified by 4-year intervals (Supplementary Table S1, lower part, online only). The comparison of OS according to the 4-year intervals is reported in Figure 1H.

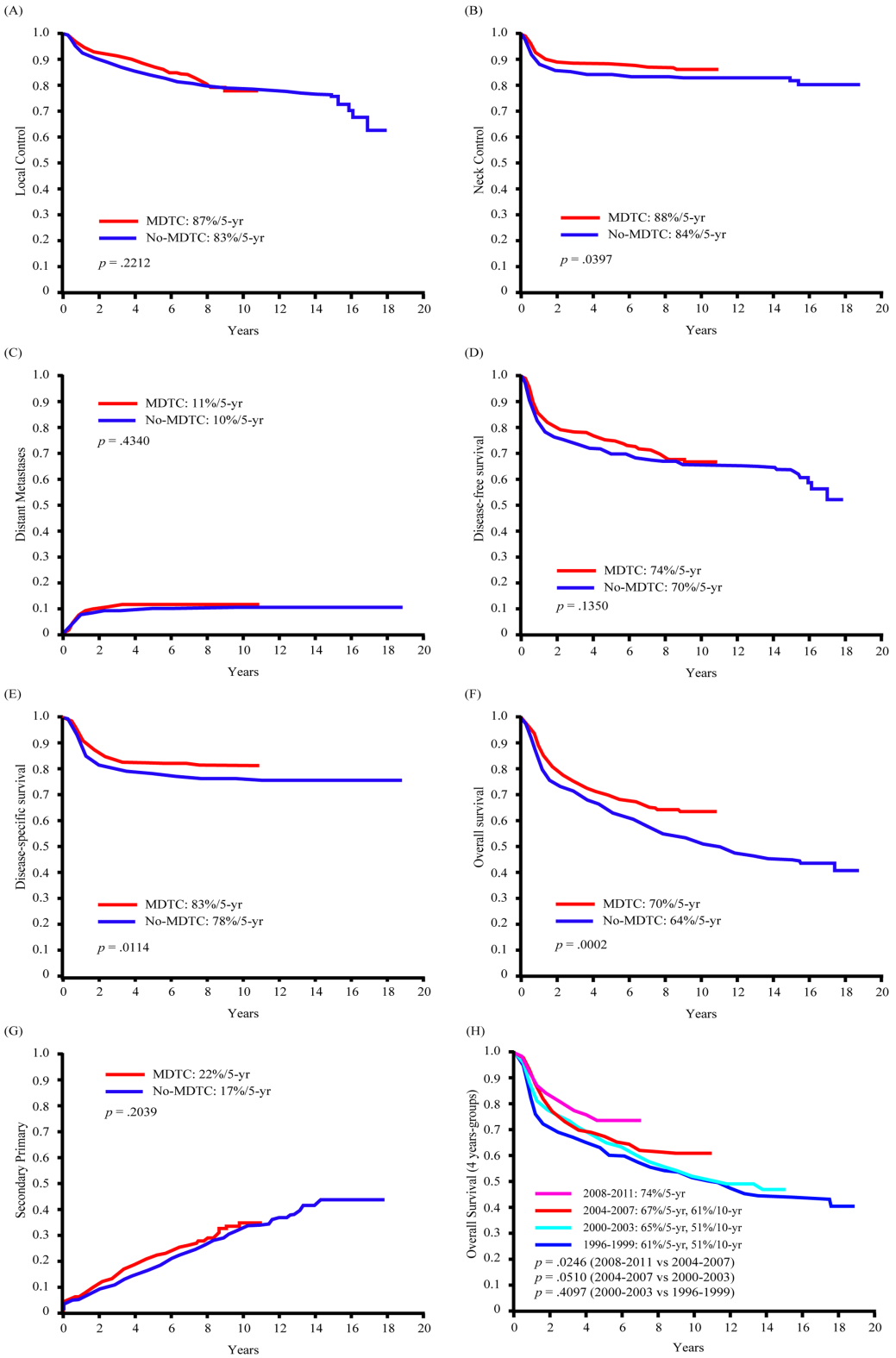

FIGURE 1. Kaplan–Meier plots of 5-year outcomes in the multidisciplinary team care (MDTC) (red line) and no-MDTC (blue line) subgroups. (A) local control, (B) neck control, (C) distant metastases, (D) disease-free survival, (E) disease-specific survival, (F) overall survival, (G) secondary primary tumors, and (H) overall survival in the early no-MDTC (blue line), late no-MDTC (light blue line), early MDTC (red line), and late MDTC (pitch red line) subgroups.

TABLE 2. Multivariate analyses of 5-year survival rates in the entire cohort of patients with oral cavity squamous cell carcinoma.

Risk factor/(no. of patients)	DFS *p* value HR (95% CI)	DSS *p* value HR (95% CI)	OS *p* value HR (95% CI)
No-MDTC (789)	NS	NS	.001 1.335 (1.122–1.587)
Preoperative betel quid chewing (1281)	.002 1.518 (1.164–1.978)	NS	NS
pT3–4 classification (649)	.034 1.263 (1.018–1.566)	.026 1.363 (1.039–1.789)	NS
pN1–2 classification (593)	<.001 1.626 (1.237–2.138)	<.001 2.375 (1.680–3.355)	NS
ECS (351)	<.001 1.788 (1.354–2.362)	<.001 2.131 (1.551–2.926)	.001 2.007 (1.656–2.433)
Poor differentiation (130)	<.001 1.671 (1.262–2.212)	<.001 2.020 (1.483–2.752)	.001 1.542 (1.200–1.981)
Tumor depth ≥10 mm (778)	.010 1.342 (1.074–1.677)	.001 1.595 (1.200–2.120)	.007 1.290 (1.073–1.550)
Margin status ≤4 mm (154)	<.001 1.691 (1.283–2.228)	.003 1.625 (1.175–2.247)	.006 1.411 (1.105–1.803)
Bone excision (890)	NS	.020 1.347 (1.048–1.732)	.003 1.305 (1.095–1.555)
Age ≥65 y (222)	NS	NS	.001 1.583 (1.264–1.983)
Preoperative alcohol drinking (1039)	NS	NS	.013 1.252 (1.049–1.495)
p-stage III–IV (919)	NS	NS	.001 1.879 (1.491–2.367)
Skin invasion (541)	NS	NS	.024 1.354 (1.042–1.761)
Lymphatic invasion (83)	NS	NS	.025 1.384 (1.041–1.839)

Abbreviations: DFS, disease-free survival; HR, hazard ratio; 95% CI, 95% confidence interval; DSS, disease-specific survival; OS, overall survival; NS, not significant; MDTC, multidisciplinary team care; ECS, extracapsular spread.

There were no statistically significant differences between the 1996 to 1999 and 2000 to 2003 no-MDTC subgroups ($p = .4097$). However, the 2008 to 2011 MDTC subgroup showed better OS rates than the 2004 to 2007 MDTC subgroup ($p = .0246$).

Neck treatment and nodal yields

As of 2004, we performed a large number of extended levels I to III neck dissections. The nodal yield obtained in ipsilateral extended levels I to III neck dissection (536 patients; median, 41 nodes [range, 15–128; mean, 42.61) was significantly higher than ipsilateral traditional levels I to III (634 patients; median, 31 nodes [range, 6–94; mean, 31.80]; $p < .001$, non-parametric Mann–Whitney *U* test). Because the number of sampled lymph nodes is higher in extended than in nonextended levels I to III neck dissections, the former were performed increasingly more frequent in the last 10 years; notably, their frequency was markedly higher in the MDTC group than in the no-MDTC group (66.7% vs 0.1%, respectively; $p < .001$; Table 1). The total nodal yield obtained in neck dissection (included bilateral neck dissection) was significantly higher in the MDTC group than in the no-MDTC group (median, 44 [range, 15–154; mean, 48.96] vs median, 32 nodes [range, 6–145; mean, 33.81]; $p < .001$, non-parametric Mann–Whitney *U* test).

Multivariate analyses of factors influencing survival rates

Table 2 depicts the results of multivariate analyses for DFS, DSS, and OS using the presence of MDTC (with vs without) as well as all other parameters listed in Table 1 as covariates. Although MDTC was significantly associated with better DSS and OS rates in univariate analysis, it retained its independent predictive value only for OS after allowance for potential confounders in multivariate analyses.

Subgroup analyses of 5-year overall survival in the multidisciplinary team care and no-multidisciplinary team care groups according to p-staging and treatment modality

The 5-year OS rates in the MDTC and no-MDTC groups according to p-staging were as follows: p-stage I, 92% vs 82%, $p = .0023$; p-stage II, 86% vs 81%, $p = .0623$; p-stage III, 71% vs 64%, $p = .1130$; and p-stage IV, 50% vs 45% ($p = .0194$). The 5-year OS in the MDTC and no-MDTC groups according to the treatment modality were as follows: surgery alone, 87% vs 74%, $p < .0001$; surgery plus RT, 65% vs 59%, $p = .0354$; and surgery plus concurrent CRT, 48% vs 40%, $p = .1245$.

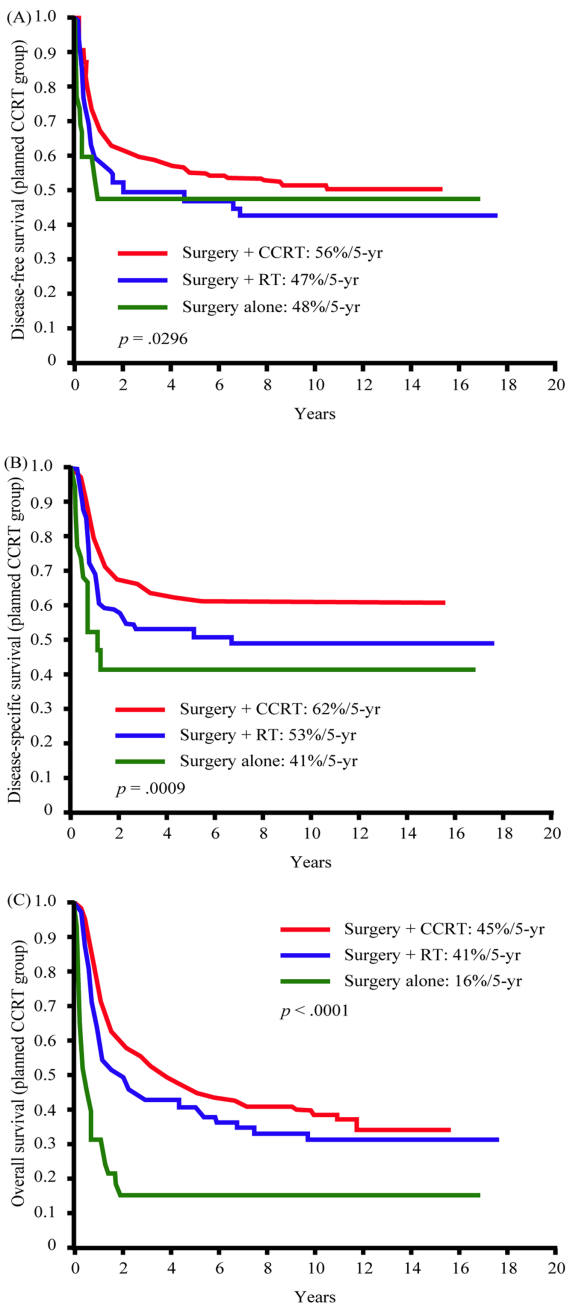

FIGURE 2. Kaplan–Meier plots of 5-year outcomes in the planned concurrent chemoradiotherapy (CRT) patients stratified with surgery alone (green line), surgery plus radiotherapy (RT; blue line), and surgery plus concurrent CRT (red line). (A) disease-free survival, (B) disease-specific survival, and (C) overall survival.

Planned adjuvant therapy and actual adjuvant treatment

In the entire study cohort ($n = 1616$), postoperative adjuvant RT and concurrent CRT were planned in 498 patients (31%) and 471 patients (29%), respectively. However, only 78% of the patients (387 of 498) who were scheduled to receive adjuvant RT and 77% (363 of 471) of those who were scheduled to be treated with concurrent CRT actually completed their treatment plans accordingly. In the planned RT group, patients who received adjuvant RT did not have significant survival benefit than surgery alone (data not shown). In the planned concurrent CRT group, patients who received adjuvant RT/concurrent CRT had better DSS or OS than surgery alone (Figures 2A–2C).

Notably, approximately 90% of the patients in the MDTC group actually underwent their adjuvant RT or concurrent CRT treatment as originally planned, a percentage that was significantly higher than that observed in the no-MDTC group (60% to 70%, $p < .001$; Table 3).

DISCUSSION

Recent studies have suggested that MDTC may improve clinical outcomes in patients with cancer, but the question as to whether this approach can increase survival rates remains open.[5–7,9,10] In a previous multicenter study focusing on 16,991 patients with oral cavity SCC, Tsai et al[9] found a statistically significant benefit of MDTC for OS in patients with stage IV disease ($p < .001$) but not in those with stage I to III disease. In a single-center study conducted in 726 patients with head and neck cancer (including 141 patients with oral cavity SCC), Friedland et al[10] demonstrated significant benefits of MDTC for OS in the entire study cohort ($p = .024$), and especially in patients with stage IV disease ($p = .004$). However, no survival benefits were observed in the subgroup of patients with oral cavity SCC, possibly because of the small sample size (Supplementary Table S2, online only). However, in our study, we observed a significant association of MDTC with improved survival rates across all p-stages, especially in p-stages I and IV. Although definitive evidence is still lacking, MDTC has the potential to ameliorate management strategies through an integrated and team advocate approach.[6] Over the past years, individual cooperation with surgeons, radiation oncologists, and medical oncologists was the main strategy used for oral cavity SCC management in our institution. As of 2004, MDTC (extensively involving pathologists, radiologists, nuclear medicine physicians, dentists, supportive care providers, psychologists, nurses, nutritionists, social workers, and case managers) has been formally introduced for comprehensive care of patients with oral cavity SCC. In our weekly MDTC tumor board meeting, all of the potential diagnostic and treatment options of every oral cavity SCC case are thoroughly discussed in order to develop an individually tailored management program. In addition, each patient is assigned to a case manager who is in charge of supervising the treatment course and the follow-up schedule. Although MDTC is publicly funded by our hospital and the Taiwanese government, the potential benefits of such an approach in patients with oral cavity SCC have not been reported yet.

In this study, we demonstrate that the 5-year survival rates were significantly higher in the MDTC group as compared with those of patients who did not receive MDTC. Of note, the largest difference in tumor control was observed in the neck site. Importantly, OS rates in the late MDTC subgroup (2008–2011) were better than in the early MDTC subgroup (2004–2007; Figure 1H). Although the reasons behind these observations may be multifactorial in nature, this phenomenon may be

TABLE 3. Planned and actual adjuvant therapy in the no-multidisciplinary team care (1996–2003) and multidisciplinary team care (2004–2011) groups.

Characteristics (no. of patients; %)	No-MDTC No. of patients (%)	MDTC No. of patients (%)	*p* value
Planned adjuvant RT and actual RT			<.001
No (111; 22.3)	95 (28.4)	16 (9.8)	
Yes (387; 77.7)	240 (71.6)	147 (90.2)	
Planned adjuvant concurrent CRT and actual RT/concurrent CRT			<.001
No (32; 6.8)	22 (12.0)	10 (3.5)	
Yes, RT (76; 16.1)	56 (30.4)	20 (7.0)	
Yes, concurrent CRT (363; 77.1)	106 (57.6)	257 (89.5)	

Abbreviations: MDTC, multidisciplinary team care; RT, radiotherapy; concurrent CRT, chemoradiotherapy.

explained, at least in part, by the MDTC learning curve. Interestingly, the total lymph node yields from neck dissection were significantly higher in ipsilateral extended levels I to III neck dissection than ipsilateral classical levels I to III neck dissection (median, 41 vs 31 nodes, respectively), as well as in the MDTC group than in the no-MDTC group (median, 44 vs 32 nodes, respectively). This phenomenon can be a result of the learning curve improvement occurring during the study rather than MDTC itself. Moreover, it can also be explained by the higher number of extended neck dissections performed in the MDTC group. Previous studies demonstrated that both the total lymph node yield in patients with oral cavity SCC and node density in patients with pN+ oral cavity SCC are significant prognostic factors.[16–18] Herein, we have shown that such factors are associated with neck control and survival rates. In this scenario, an adequate neck dissection should be achieved for removing all of the risky regional nodes. Of note, the percentage of patients with pathologically close or positive margins ($\leq$4 mm) — a factor that may be surgeon-dependent — was similar in the MDTC and no-MDTC groups (9.8% vs 9.4%, respectively; $p = .800$). It is also noteworthy that the use of free flap reconstructions was relatively high in both the MDTC and no-MDTC groups (>80% for both), resulting in the possibility for the surgeon to perform a radical tumor excision with adequate margins.

Subgroups analyses revealed that, in patients who received adjuvant therapy, the rates of completion of RT or concurrent CRT were significantly higher in the MDTC group than in the no-MDTC groups ($p < .001$; Table 3). This observation may explain, at least in part, the survival benefit observed at 5 years in patients who received MDTC compared with those who did not (Figures 2B and 2C). The lack of an individually tailored thorough multidisciplinary discussion, as well as the absence of universally accepted treatment guidelines and suboptimal follow-up schedules, may have resulted in a reduced number of patients receiving adjuvant therapy in the no-MDTC group. The improved RT and concurrent CRT completion rates in the MDTC group are likely to be multifactorial and may be due to: (1) a cogently planned treatment schedule reached by consensus of the MDTC tumor board; (2) the presence of a case manager in charge of supervising the treatment course and the patient follow-up; (3) a better therapeutic alliance between the patient and the MDTC personnel; and (4) an improved supportive care system that can be ascribed to optimal clinical, mental, and financial support.[4,19] All of the above-mentioned reasons may explain the significantly better outcomes obtained in the MDTC group.

We recognize that the use of different chemotherapy regimens in the no-MDTC and MDTC groups may represent a potential source of confounding both because of their different distribution and their effect on the radiation doses. A previous review and Meta-Analyses of Chemotherapy in Head and Neck Cancer did not demonstrate significant differences ($p = .19$) between monochemotherapy (hazard ratio [HR] = 0.84) and polychemotherapy (HR = 0.78).[20] The effect of monochemotherapy in patients with head and neck cancer is greater when platin-based regimens are used (as compared with other forms of monochemotherapy; $p = .006$). Notably, we have previously shown that no significant differences in time-to-event outcomes were noted between patients with oral cavity SCC who received high-dose versus low-dose cisplatin.[21] Therefore, the published literature suggests that different combination protocols should not have a major impact on outcomes when cisplatin-based regimens are used. The subgroups analyses of treatment modality demonstrated a trend toward better OS rates in MDTC patients treated with surgery plus concurrent CRT. However, the MDTC and no-MDTC groups did not differ in terms of OS ($p = .1245$, plots not shown).

With the continuing improvements in cancer care, we are constantly implementing novel strategies for reducing morbidity and mortality, albeit with varying degrees of success (see Figure 3). For example, the introduction of intensity-modulated RT (IMRT; as of 2001), better tumor coverage, and reduced radiation doses are expected to improve disease control with a lower incidence of adverse side effects. Unfortunately, such an approach did not result in a significant survival benefit in our patients with oral cavity SCC.[13] As of 2010, dose escalation to high-risk areas with simultaneously integrated boost techniques was selectively offered to patients with oral cavity SCC with suspicious residual and/or recurring lesions. Concurrently, a postoperative fluorodeoxyglucose positron emission tomography/CT scan within 1 week before starting adjuvant RT/concurrent CRT was performed in patients with oral cavity SCC with ECS for detecting the presence of any residual, recurring, or distant lesion occurring between radical surgery and adjuvant RT.[22] This approach resulted in the modification of adjuvant treatment plans in

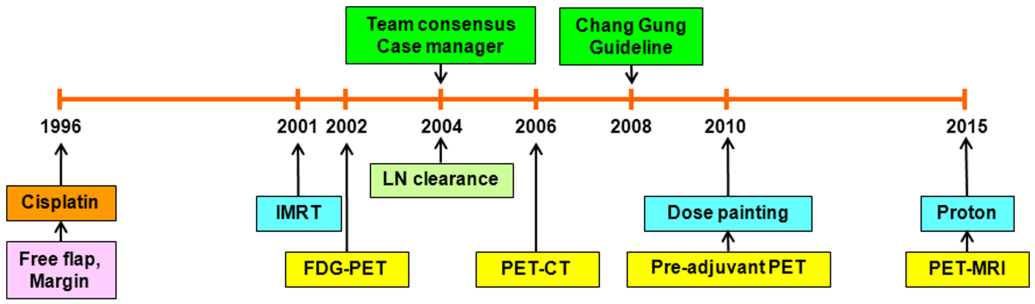

FIGURE 3. Major progress in oral cavity squamous cell carcinoma (SCC) treatment observed at the Chang Gung Memorial Hospital. IMRT, intensity-modulated radiotherapy; FDG-PET, fluorodeoxyglucose positron emission tomography; LN, lymph node.

some patients and produced obvious OS improvement.[23] Finally, case managers have a paramount role in summarizing treatment plans and recovery progress, even though they have not always enjoyed the same stature accorded to other specialists involved in MDTC.[24,25]

Several caveats of our research merit comment. The retrospective nature of our study did not allow making strong causal inferences between the use of MDTC and improved survival in each subgroup. Better clinical outcomes in the MDTC group might be multifactorial in nature and do not necessarily imply that MDTC per se is the unique cause. In this regard, potential confounders include but are not limited to changes that occurred in oral cavity SCC treatment over time, the effect of human papillomavirus infections on survival,[26] the presence of nodal disease, the emergence of concurrent CRT and RT as adjuvant treatments, the clarity for indications for RT after surgery, the emergence of IMRT radiation techniques for postoperative adjuvant RT, improve surgical techniques resulting from surgeon training, and improved reconstructive modalities. Besides MDTC, all of these factors may have contributed, at least in part, to the improvement in survival observed over the study period. In particular, we cannot exclude that secular trends in surgical techniques and pathological specimen management may be, at least in part, responsible for the observed improvements. For example, the surgeon's learning curve might be responsible for the improved nodal yields obtained in the MDTC group. Although an improved surgical care may have resulted in better survival figures, we did not observe significant differences in terms of perioperative mortality between the no-MDTC and MDTC groups (0.5% vs 0.4%; Table 1). In addition, disease upstaging based on more extensive neck dissection and pathological nodal examinations may have similar beneficial effects on outcomes, although actually only 0.4% of the study patients (2 of 553) had their disease upstaged. We recognize that the effects of improved care over time were not accounted for, ultimately representing a potential bias inherent in our study. We are also aware that the available evidence indicating that MDTC can enhance patient adherence is weak. Finally, data on several potential confounders (eg, comorbidities, well-being, support from nurse specialists, and nutritional status) were not available in our study.

CONCLUSION

To our knowledge, this is the first article to indicate that MDTC may serve as an independent predictor for survival in patients with oral cavity SCC (Table 2). The survival benefit associated with MDTC might be explained by a higher nodal clearance, the identification of high-risk patients, the selection of the optimal supportive care approaches, and the reduction of treatment-related morbidity. All of these factors may contribute to a more comprehensive treatment strategy that can ultimately improve clinical outcomes. Finally, case managers may strengthen the therapeutic alliance between the patient and the tumor board and/or ensure a greater thoroughness in the patient clinical management.

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