Long-term quality of life after treatment for locally advanced oropharyngeal carcinoma: surgery and postoperative radiotherapy versus concurrent chemoradiation.

Oral Oncology 45 (2009) 953–957

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Long-term quality of life after treatment for locally advanced oropharyngeal carcinoma: Surgery and postoperative radiotherapy versus concurrent chemoradiation

Paolo Boscolo-Rizzo [a,*], Marco Stellin [a], Roberto Fuson [a], Carlo Marchiori [a], Alessandro Gava [b], Maria Cristina Da Mosto [a]

[a] Department of Medical and Surgical Specialities, Otolaryngology Clinic – Regional Center for Head and Neck Cancer, University of Padua, School of Medicine, Treviso Regional Hospital, Italy
[b] Department of Radiation Oncology – Treviso Regional Hospital, Treviso, Italy

ARTICLE INFO

Article history:
Received 11 May 2009
Received in revised form 12 June 2009
Accepted 12 June 2009
Available online 8 August 2009

Keywords:
Quality of life
Oropharyngeal cancer
Head and neck cancer
Chemoradiotherapy
Surgery

SUMMARY

The aim of this study was to evaluate the long-term quality of life (QoL) in survivors with oropharyngeal carcinoma (OC) treated with surgery and postoperative radiotherapy (PORT) versus concurrent chemoradiation (CRT) using the European Organization for Research and Treatment of Cancer QoL Questionnaires. The study group consisted of 57 patients. The scores for physical ($P = 0.043$) and social ($P = 0.036$) functioning were significantly more favorable in the chemoradiation group. Surgical patients showed statistically higher problems with fatigue ($P = 0.047$), pain ($P = 0.027$), swallowing ($P = 0.042$), social eating ($P = 0.038$) and social contact ($P = 0.002$). CRT group reported significantly greater problems with teeth ($P = 0.049$), open mouth ($P = 0.036$), dry mouth ($P = 0.022$) and sticky saliva ($P = 0.044$). The global QoL score was higher in CRT group ($P = 0.027$). These results support an organ preservation approach with CRT in patients with advanced OC. However, considering the absence of randomized trial comparing outcomes after surgical versus nonsurgical approaches, severe xerostomia following CRT, the higher postoperative morbidity in the setting of salvage surgery, future prospective clinical trials on greater samples of patients are needed to confirm our conclusions.

Introduction

Oropharyngeal carcinoma (OC) is one of the most common cancers of the head and neck region.[1,2] Surgery or radiation alone are equally successful in early stage OC. Conversely, considerable controversy surrounds the appropriate combined treatment of advanced OC. Although no prospective randomized trials are available evaluating the outcomes after surgical versus nonsurgical treatment of OC, the focus of treatment has recently shifted away from surgical approach toward chemoradiation protocols.[3,4] Actually, surgical treatment of advanced OC may profoundly impact crucial activities such respiration, speech, chewing and swallowing as well as facial cosmesis with consequent emotional and social disabilities. Chemoradiation is perceived by patients and physicians to be a more effective function preservation strategy compared with surgery. In addition, RT is generally recommended as adjuvant treatment also after surgical resection of advanced OC.[5] However, major concerns remain over the toxicity of concurrent chemoradiation (CRT), sometimes requiring hospitalization and nutritional support.[4] Furthermore, surgical management of persistent or recurrent OC after failure of chemoradiation therapy is associated with higher complication rates because of wound-healing difficulties.[6]

In this scenario, quality of life (QoL) is receiving increasing attention as a criterion for the assessment of different treatment modalities. Post-treatment QoL should be a decisive factor to choose between different therapies giving similar results. To date, only few studies have compared QoL outcomes between patients undergoing surgical and PORT and patients receiving CRT for advanced OC.

The aim of this cross-sectional study is to evaluate the long-term QoL in survivors with OC and to compare the results of patients treated with surgery and PORT with those undergoing CRT using the European Organization for Research and Treatment of Cancer QoL Questionnaires (EORTC-QLQ).

Materials and methods

Patients

In our institution, treatment planning of OC is decided by a multidisciplinary team mainly on the basis of TNM staging. Most T1

* Corresponding author. Address: Viale Umbria 6, IT-30019 Chioggia, Venezia, Italy. Tel.: +39 0422 322320; fax: +39 0422 322374.
E-mail address: paolo.boscolorizzo@unipd.it (P. Boscolo-Rizzo).

1368-8375/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.oraloncology.2009.06.005

and T2 carcinomas are treated with conservative surgery or definitive RT. On the other hand, most patients with T3 or T4 cancer undergo radical surgery often followed by PORT or CRT. In the last decade, after popularization of nonsurgical treatment as the front-line method of treating advanced OC, a trend of shifting treatment from surgery toward CRT was observed in our institution. Surgery is generally preferred in presence of bone invasion. In other cases, the decision to choose between these two reasonable alternatives is commonly based on patient preferences. However, we cannot exclude the possibility that patients may be influenced by the way in which treatment alternatives are presented during informed consent.

Surgery involved resection of the primary tumor via transoral, transcervical, or combined approach with an elective neck dissection in the N0 neck (selective neck dissection or type III radical modified neck dissection) or a therapeutic neck dissection in the N+ neck (radical or radical modified neck dissection depending on N-stage). Regional myocutaneous or microvascular free flaps were used for reconstruction. PORT was performed in patients with more than one positive lymph node, extracapsular extension, perineural tumor invasion, lymphovascular invasion, positive tumor margins, and in patients with T4 tumors.

RT was performed using 4–6 MV photons from a linear accelerator administrated in 2 Gy daily fractions applied five times weekly. A volume encompassing the primary site and all draining lymph nodes at risk was prescribed to receive a dose of 60 Gy in 30 fractions over a period of 6 weeks in postoperative setting, and a dose of 70 Gy in 35 fractions over a period of 7 weeks in nonsurgical group, respectively. Both sides of the neck were prescribed to receive a boost of electrons with a dose of 4 Gy in N0 and 14 Gy in N+ cases. Concurrently with radiation therapy, patients were administered at least two cycles of chemotherapy using cis-platinum 100 mg/m^2 on day 1, 5-fluorouracil 1000 mg/m^2 as a continuous infusion on days 1–5.

In patients treated with nonsurgical approach, a neck dissection was planned for patients with node metastasis larger than 3 cm regardless of the response to therapy and for patients who had suspected persistent neck disease 8–12 weeks after completing treatment.

The criteria of inclusion were: (1) patients with previously untreated T3–T4 OC, (2) complete remission after surgery plus PORT or CRT, (3) treatment completed at least 24 months prior to inclusion in the study.

The EORTC QoL Questionnaire-Core 30 (QLQ-C30) and the EORTC QoL Questionnaire-Head and Neck 35 (QLQ-H&N35)[7] were submitted to the patients at the time of a surveillance visit. Few patients were invited to participate in the study by telephone. All patients voluntarily filled out the questionnaires at the hospital. The questionnaires were labeled with the patient's non-descriptive letter identifier and were auto-administered so that patients were not influenced by the clinic's presence. The institutional review board approved the protocol of this study.

Statistical analysis

Statistical analyses were conducted using the SPSS/PC statistical program (version 15.0 for Windows; SPSS, Inc., Chicago, IL).

Survival was calculated from the date of the end of treatment and was analyzed using the standard Kaplan–Meier method. Tests of significance were based on log rank statistic. Hazard ratios were calculated with the use of the Cox proportional-hazards model. Chi-square test, Fisher's exact test, Student *t* test were used to assess group differences on clinical data.

The scores of the QoL were calculated according to the EORTC QLQ scoring manual. Nonparametric Wilcoxon rank sum analysis was used to test for differences between groups on the EORTC scales. Tests were two tailed and levels of statistical significance have been calculated at the 5% level of probability ($P < 0.05$).

Results

Demographics and survival

Between January 1998 and April 2006, 151 patients with T3–T4 OC were treated with curative intent using either surgery plus PORT (66 patients) or platinum-based CRT (85 patients) at University of Padua, Treviso Regional Hospital.

Since May 2008, 60 disease-free survivors were identified as eligible to participate in the study. Eight patients were loss to follow-up, 69 were death, 14 were alive with disease. Overall, median follow-up for surviving patients was 56 months (range, 11–124). Overall survival at 4 years was 61.4% (95% CI, 43.7–79.1%) and 58.5% (95% CI, 42.2–74.8%) in surgery group and in chemoradiation group, respectively ($P = 0.280$, logrank test). Disease-free survival at 4 years was 55.2% (95% CI, 36.1–74.3%) and 54.2% (95% CI, 37.0–71.5%) in surgery group and in chemoradiation group, respectively ($P = 0.406$, logrank test). As compared with the surgical group, the chemoradiation group had not a significant higher risk of disease progression or death (hazard ratio, 1.20; 95% CI, 0.77–1.87; $P = 0.409$).

The study group consisted of 57 patients as three patients refused to perform the questionnaire. Median age at diagnosis was 61 years (range, 42–77 years), and the majority of patients were male (84.2%). Twenty-six patients (45.6%) were treated with surgery plus PORT, 31 (54.4%) with CRT. The median dose of RT was 60 and 66 Gy in surgical and nonsurgical group, respectively. The mean time of QoL evaluation from the end of treatment was 56 months (range, 25–124).

Clinical data and treatment are shown in Table 1. The two groups did not differ significantly with respect to age, sex, tumor stage, comorbidities, and average time of QoL assessment. The pharynx was reconstructed using a local plasty in 13 patients, a pectoralis major flap in 10 patients, and a radial forearm free flap in three cases. A type III modified radical neck dissection was

Table 1
Clinical data and treatment.

	Surgery + PORT ($n = 26$)	Chemoradiotherapy ($n = 31$)	*P*-value
Sex			
Male	22 (84.6%)	26 (83.9%)	1.000
Female	4 (15.4%)	5 (16.1%)	
Mean age in years (range) at time of QoL evaluation	57 (45–77)	62 (42–73)	0.269
Subsite			
Tonsil	18 (69.2%)	14 (45.2%)	0.151
Base of the tongue	6 (23.1%)	10 (32.3%)	
Soft palate	2 (7.7%)	3 (9.7%)	
Posterior wall	0 (0.0%)	4 (12.9%)	
Stage			
III	14 (53.8%)	15 (48.4%)	0.681
IV	12 (46.2%)	16 (51.6%)	
Comorbidities			
None	20 (76.9%)	23 (74.2%)	0.812
One or more	6 (23.1%)	8 (25.8%)	
Neck dissection			
Yes	21 (80.8%)	6 (19.4%)	0.000
No	5 (19.2%)	25 (80.6%)	
Mean time of QoL evaluation from the end of treatment in months (range)	72 (34–123)	56 (25–124)	0.095

PORT: postoperative radiotherapy.

performed in six cases after chemoradiation (with controlateral selective neck dissection in one case). In surgical group a monolateral selective neck dissection was performed in four patients, a radical neck dissection in four patients (with controlateral selective neck dissection in three cases), and a type III radical modified neck dissection in 13 patients (with controlateral selective neck dissection in five cases). At the time of data collection one patient who underwent chemoradiotherapy depended on tracheostomy; furthermore, one patient of surgery group and one patient of chemoradiotherapy group still had gastrostomy feeding tubes.

EORTC QLQ-C30

The results from QLQ-C30 are shown in Table 2. The global QoL score was higher in the nonsurgical group ($P = 0.027$, mean difference 11.2). The scores for physical ($P = 0.043$, mean difference 8.5) and social ($P = 0.036$, mean difference 8.9) functioning were significantly more favorable in the chemoradiation group. Moreover, patients who underwent surgery had more problems with fatigue ($P = 0.047$, mean difference 10.0) and pain ($P = 0.027$, mean difference 13.2).

EORTC QLQ-H&N35

The results from the QLQ-H&N35 are shown in Table 3. Surgical patients showed statistically higher problems with swallowing ($P = 0.042$, mean difference 16.9), social eating ($P = 0.038$, mean difference 12.6) and social contact ($P = 0.002$, mean difference 10.2). A trend of significance was found with speech ($P = 0.056$, mean difference 13.5), reporting more difficulties in surgical patients. On the other hand, chemoradiation group reported significantly greater problems with teeth ($P = 0.049$, mean difference 19.3), open mouth ($P = 0.036$, mean difference 18.1), dry mouth ($P = 0.022$, mean difference 19.6) and sticky saliva ($P = 0.044$, mean difference 16.8).

Table 2
Results from the EORT QLQ-C30[a].

	Surgery + PORT Mean (95% CI)	Chemoradiotherapy Mean (95% CI)	*P*-value
Physical functioning	79.2 (70.9–87.5)	87.7 (80.7–94.8)	0.043
Role functioning	85.2 (74.9–95.6)	91.0 (83.8–98.1)	0.357
Social functioning	84.6 (74.2–95.0)	93.5 (86.4–100.0)	0.036
Emotional functioning	76.2 (66.0–86.3)	84.7 (78.0–91.4)	0.210
Cognitive functioning	85.9 (77.2–94.6)	90.3 (84.2–96.4)	0.392
Global QoL	68.6 (60.11–77.0)	79.8 (72.8.9–86.9)	0.027
Fatigue	22.9 (13.9–31.9)	12.9 (5.9–19.8)	0.047
Nausea and vomiting	6.4 (0.7–13.5)	2.1 (1.3–5.6)	0.152
Pain	21.8 (12.3–31.3)	8.6 (3.6–13.6)	0.027
Dyspnea	10.3 (1.9–18.6)	14.0 (6.4–21.6)	0.368
Sleep disturbance	9.0 (2.9–15.1)	10.7 (1.6–19.9)	0.661
Appetite loss	12.8 (3.4–22.2)	11.8 (5.1–18.6)	0.842
Diarrhea	5.1 (1.1–11.4)	2.1 (0.9–5.2)	0.482
Constipation	16.7 (5.7–27.6)	14.0 (4.6–23.3)	0.660
Financial impact	15.4 (5.1–25.6)	14.0 (4.1–23.8)	0.598

CI: confidence interval; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; PORT: postoperative radiotherapy.

[a] Note. The EORTC Quality of Life Questionnaire-Core 30 (QLQ-C30) incorporates 30 items and consists of five functional scales (physical, role, cognitive, emotional and social functioning), three symptom scales (fatigue, pain and nausea/vomiting), a global QoL scale and six single items (dyspnea, insomnia, appetite, constipation, diarrhea and financial impact). All scales pertaining to the EORTC QLQ-C30 range from 0 to 100. A high score for a functional or global QoL scale represents a relatively high/healthy level of functioning or global QoL, whereas a high score for a symptom scale indicates a higher level of symptoms or problems.

Table 3
Results from the EORT QLQ-H&N35[a].

	Surgery + PORT Mean (95% CI)	Chemoradiotherapy Mean (95% CI)	*P*-value
Pain	9.0 (3.2–14.7)	10.7 (4.8–16.7)	0.810
Swallowing	36.2 (24.1–48.3)	19.3 (11.3–27.4)	0.042
Senses	25.6 (14.7–36.6)	22.0 (13.5–30.6)	0.715
Speech	30.3 (18.6–42.0)	16.8 (10.8–22.7)	0.056
Social eating	26.6 (16.1–37.1)	14.0 (7.2–20.7)	0.038
Social contact	14.9 (5.4–24.3)	4.7 (0.89–10.3)	0.002
Sexuality	23.7 (9.7–37.7)	15.6 (5.5–25.7)	0.462
Teeth	20.5 (8.4–32.6)	39.8 (27.4–52.2)	0.049
Open mouth	14.1 (5.4–22.8)	32.2 (19.8–44.7)	0.036
Dry mouth	38.5 (24.9–52.0)	58.1 (47.6–68.5)	0.022
Sticky saliva	35.9 (21.7–50.1)	52.7 (41.4–64.0)	0.044
Coughing	15.4 (3.8–26.9)	24.7 (13.8–35.6)	0.123
Felt ill	6.4 (2.9–15.7)	0.0 (0.0–0.0)	0.119
Painkillers	38.5 (18.4–58.5)	19.3 (4.6–34.1)	0.113
Nutritional supplements	23.1 (5.7–40.4)	22.6 (7.0–38.2)	0.965
Feeding tube	3.8 (0.1–11.8)	6.4 (2.7–15.6)	0.664
Weight loss	23.1 (5.7–40.4)	16.1 (2.4–29.8)	0.512
Weight gain	11.5 (1.6–24.7)	25.8 (9.5–42.1)	0.178

CI: confidence interval; EORTC QLQ-H&N35: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Head and Neck 35; PORT: postoperative radiotherapy.

[a] Note. The head and neck-specific questionnaire EORTC QLQH&N35 consists of seven multiple-item scales and six symptom items with a total of 35 questions that assess pain, swallowing, senses (taste and smell), speech, social eating, social contact, sexuality, teeth problems, trismus, dry mouth, sticky saliva, cough and feeling ill. A high score for a symptom scale indicates a higher level of symptoms or problems.

Discussion

QoL is a global construct that emerges from several, overlapping aspects or 'domains' of life. In the last three decades, this construct has been developed quite extensively in medical research in order to assess the individual's perception of overall well-being revolving around four core domains: physical and psychological functioning, social interaction, and disease and treatment related symptoms. Therefore, despite the term "QoL" is usually used, the term "Health Related QoL" (HRQoL) appears more appropriate because only the quality of few expressions of life is measured. In the last few years, several valid HRQoL tools have become available to measure HRQoL in cancer patients.

Nonsurgical approaches have been increasingly integrated into first-line therapy of advanced OC. In these series, patients undergoing chemoradiation treatment did not experience a significant decreased in disease free and overall survival. However, considering the absence of direct randomized comparisons and taking into account the toxicity of chemoradiation protocols, HRQoL assessment has become a key objective in evaluating the efficacy of a given treatment. Unfortunately, only few studies comparing QoL after surgical and nonsurgical treatment of specific head and neck cancers are available.

In this study, the QLQ-C30 together with the head and neck cancer-specific QLQ-H&N35 module were chosen to evaluate long-term HRQoL in patients with advanced OC treated using either surgery plus PORT or platinum-based CRT. QLQ-C30 is among the most used HRQoL instruments because of its high specificity, reliability, and validity.

We hypothesized that, after the resolution of acute side effects of chemoradiation, a better HRQoL would be observed in nonsurgical group. The results of the present analysis show some differences in HRQoL outcomes between the groups. Although emotional functioning was quite impaired in both groups, patients who underwent surgical treatment plus PORT for advanced OC have demonstrated significantly more impaired physical and social scores than nonsurgical patients. Furthermore, nonsurgical

patients had better global HRQoL score. This was not an unexpected result. Extended surgical excision of advanced OC may affect both function and cosmesis with profound psychological and emotional impact.[4,8] On the other hand, organ preservation strategies are considered to minimize functional and social impairment. Consequently, conservative management is now the standard of care in numerous patients with upper aerodigestive tract cancer including OC.[8] The uncorrelation between global HRQoL score and most of domains evaluated with QLQ-C30 may partially be explained by the fact that QLQ-C30 measures generic domains of QL and may not address all factors constituting HRQL in patients with head and neck cancer. Actually, major differences in QoL domains between the two groups manifested themselves in the head and neck-specific EORTC QLQ-H&N35 module (Table 3).

Furthermore, negative findings in some domains may be related to the small sample size.

When comparing HRQoL after surgical versus nonsurgical approach, not all authors found similar results. Mowry et al. found a similar perception of QoL in their series. In this study, the mean time from treatment to questionnaire was about 25 months (range: 3–73).[9] Therefore, acute adverse effects of CRT may have had a greater impact on QoL. Although, Pourel et al. observed an impaired QoL in long-term survivors of OC, particularly in psychosocial domains, QoL was similar, whatever the initial treatment approach (brachytherapy, external beam RT, and surgery plus RT). However, more than two-third of the patients presenting with T1–T2 tumor and patients with T4 tumor were not included in the study.[7] Conversely, in their series of patients evaluated at least 12 months after treatment, Allal et al. found a trend to significantly better score for physical, role, emotional, and social functions favoring patients treated with RT or chemoradiotherapy for T3 and T4 OC.[10]

Recently, Suarez-Cunqueiro et al. in population of 1334 patients treated for oral and OC found that patients undergoing RT associated with the surgical removal of tumor and having advanced stage tumors were at greater risk of persistent severe speech and swallowing problems.[11] Swallowing problem should be properly identified in order to rehabilitate and nutritionally support patients, and improve their HRQoL. In this sense, a nutritionist and a rehabilitation therapist should be part of the multidisciplinary team planning the care of these patients.

Hammerlid et al. reported that QoL of head and neck cancer patients can benefit from psychological group therapy.[12] In addiction, Allison et al. reported that providing a psycho-educational coping strategies intervention for patients with head and neck cancer improve physical, social and global QoL.[13] Therefore, assessment of psychological distress and facial disfigurement should be routinely performed in patients treated for head and neck cancer.

Pain may increase during or shortly after treatment of head and neck squamous cell carcinomas and decrease over time. However, long-term head and neck pain has been reported in about to 60% of patients.[14] Considering the long-term nature of this study, we were not able to capture pain symptoms attributable to acute adverse effects of CRT. Pain score as evaluated by QLQ-C30 was significantly worse in surgical patients. However, this result was not confirmed by QLQ-H&N35 evaluation of pain. Pain in patients surgically treated for head and neck squamous cell carcinoma is usually a consequence of neck dissection. Chronic pain and shoulder dysfunction are common after radical and radical modified neck dissection.[15] Recently, Terrell et al. have found neck dissection to be associated with significant decrements in QoL domains.[16] Therefore, pain is mainly localized to the neck and shoulder rather than to the mouth, jaw, and throat as evaluated by QLQ-H&N35. Postoperative rehabilitation is still not incorporated in the standard management of patients undergoing neck dissection. Data about the efficacy of physical therapy in the literature are inconsistent.[17] Recently, a significant reduction in pain and dysfunction was observed in patients undergoing neck dissection who were randomized to receive weekly acupuncture versus usual care.[18]

In our series, chemoradiation patients reported significantly greater problems with dry mouth, opening mouth, teeth, and sticky saliva than surgical patients. Considering that all patients underwent irradiation, these results should be interpreted as indicative of radiation-sensitizing effects by concurrent chemotherapy causing more severe decreased salivation, xerostomia, and mucosal fibrosis, as well as a consequence of a more extended radiation field and a higher dose of radiation therapy used in nonsurgical group. The use of amifostine has been suggested in order to decrease the incidence of acute and late xerostomia in patients undergoing upper aerodigestive tract irradiation. However, recent guidelines do not support the routine use of amifostine in patients undergoing RT with platinum-based CRT.[19]

Recently, Gurney and colleagues found advanced stage of disease as predictor of low QoL in patients treated for oropharyngeal cancer.[20] In our series, subsite and stage distribution between groups was not statistically different. Therefore, our results should not be biased by different stage and subsite distribution.

The design of the current study has some limitations. The cross-sectional fashion of this study may limit the applicability of our results. Therapy was not standardized and treatment preferences could have biased the results. However, all patients were evaluated as regards QoL at least 24 months after treatment, and there were no significant differences in the timing of the analysis, age, and comorbidities between groups. Finally, although not statistically significant, chemoradiation group experienced a higher risk of death and disease progression. Subject dropping out because of death or not selected because of progression may represent a cohort that may have had a decreased QoL.

Conclusion

A better long-term QoL was observed in patients undergoing CRT for advanced OC. Surgical resection of advanced OC impacts more adversely physical and social functioning than organ preservation strategies. Furthermore, surgical patients are more troubled by pain. These results support an organ preservation approach with CRT in patients with advanced OC. However, considering the absence of randomized trial comparing outcomes after surgical versus nonsurgical approaches, severe xerostomia following CRT, the higher postoperative morbidity in the setting of salvage surgery, future prospective clinical trials are needed to confirm our conclusions.

Conflicts of Interest Statement

None declared.

References

1. Gillison ML. Current topics in the epidemiology of oral cavity and OCs. *Head Neck* 2007;**29**(8):779–92.
2. Chaturvedi AK, Engels EA, Anderson WF, Gillison ML. Incidence trends for human papillomavirus-related and -unrelated oral squamous cell carcinomas in the United States. *J Clin Oncol* 2008;**26**(4):612–9.
3. Parsons JT, Mendenhall WM, Stringer SP, Amdur RJ, Hinerman RW, Villaret DB, et al. Squamous cell carcinoma of the oropharynx surgery, radiation therapy, or both. *Cancer* 2002;**94**(11):2967–80.
4. Duvvuri U, Myers JN. Contemporary management of OC: anatomy and physiology of the oropharynx. *Curr Probl Surg* 2009;**46**(2):119–84.
5. Lundahl RE, Foote RL, Bonner JA, Suman VJ, Lewis JE, Kasperbauer JL, et al. Combined neck dissection and postoperative radiation therapy in the management of the high-risk neck: a matched-pair analysis. *Int J Radiat Oncol Biol Phys* 1998;**40**(3):529–34.

6. Bumpous JM. Surgical salvage of cancer of the oropharynx after chemoradiation. *Curr Oncol Rep* 2009;**11**(2):151–5.
7. Pourel N, Peiffert D, Lartigau E, Desandes E, Luporsi E, Conroy T. Quality of life in long-term survivors of oropharynx carcinoma. *Int J Radiat Oncol Biol Phys* 2002;**54**(3):742–51.
8. Cognetti DM, Weber RS, Lai SY. Head and neck cancer: an evolving treatment paradigm. *Cancer* 2008;**113**:1911–32.
9. Mowry SE, Ho A, Lotempio MM, Sadeghi A, Blackwell KE, Wang MB. Quality of life in advanced oropharyngeal carcinoma after chemoradiation versus surgery and radiation. *Laryngoscope* 2006;**116**(9):1589–93.
10. Allal AS, Nicoucar K, Mach N, Dulguerov P. Quality of life in patients with oropharynx carcinomas: assessment after accelerated radiotherapy with or without chemotherapy versus radical surgery and postoperative radiotherapy. *Head Neck* 2003;**25**(10):833–9.
11. Suarez-Cunqueiro MM, Schramm A, Schoen R, Seoane-Lestón J, Otero-Cepeda KH, Bormann KH, et al. Speech and swallowing impairment after treatment for oral and OC. *Arch Otolaryngol Head Neck Surg* 2008;**134**(12):1299–304.
12. Hammerlid E, Persson LO, Sullivan M, Westin T. Quality-of-life effects of psychosocial intervention in patients with head and neck cancer. *Otolaryngol Head Neck Surg* 1999;**120**(4):507–16.
13. Allison PJ, Nicolau B, Edgar L, Archer J, Black M, Hier M. Teaching head and neck cancer patients coping strategies: results of a feasibility study. *Oral Oncol* 2004;**40**(5):538–44.
14. Rogers SN, Hannah L, Lowe D, Magennis P. Quality of life 5–10 years after primary surgery for oral and oro-pharyngeal cancer. *J Craniomaxillofac Surg* 1999;**27**(3):187–91.
15. Talmi YP, Horowitz Z, Pfeffer MR, Stolik-Dollberg OC, Shoshani Y, Peleg M, et al. Pain in the neck after neck dissection. *Otolaryngol Head Neck Surg* 2000;**123**(3):302–6.
16. Terrell JE, Ronis DL, Fowler KE, Bradford CR, Chepeha DB, Prince ME, et al. Clinical predictors of quality of life in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg* 2004;**130**(4):401–8.
17. Lauchlan DT, McCaul JA, McCarron T. Neck dissection and the clinical appearance of post-operative shoulder disability: the post-operative role of physiotherapy. *Eur J Cancer Care (Engl)* 2008;**17**(6):542–8.
18. Pfister D, Vickers A, Deng G, Lee JS, Garrity D, Lee N, et al. Acupuncture for pain and dysfunction after neck dissection: preliminary results of a randomized controlled trial. *J Clin Oncol* 2008;**26**. (May 20 suppl; abstr 6016).
19. Hensley ML, Hagerty KL, Kewalramani T, Green DM, Meropol NJ, Wasserman TH, et al. American society of clinical oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants. *J Clin Oncol* 2009;**27**(1):127–45.
20. Gurney TA, Eisele DW, Orloff LA, Wang SJ. Predictors of quality of life after treatment for oral cavity and oropharyngeal carcinoma. *Otolaryngol Head Neck Surg* 2008;**139**(2):262–7.