CLINICAL REVIEW

David W. Eisele, MD, *Section Editor*

SURVIVAL OF PATIENTS WITH NECK RECURRENCE FOLLOWING RADICAL NECK DISSECTION: UTILITY OF A SECOND NECK DISSECTION?

Andrew S. Jones, MD,[1] Sankalap Tandon, MRCS,[1,2] Timothy R. Helliwell, MD,[1,3] David J. Husband, MRCP, FRCR,[4] Terence M. Jones, MD[1,2]

[1] School of Cancer Studies, Division of Surgery and Oncology, University of Liverpool, Liverpool, United Kingdom. E-mail: profasjones@beestoncastle.fsnet.co.uk
[2] Department of Otolaryngology–Head and Neck Surgery, University Hospital Aintree, Liverpool, United Kingdom
[3] Division of Pathology, School of Cancer Studies, University of Liverpool, Liverpool, United Kingdom
[4] Department of Oncology, Clatterbridge Centre for Oncology, Wirral, United Kingdom

Accepted 11 February 2008
Published online 18 July 2008 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/hed.20860

Abstract: Treatment of neck recurrence following radical neck dissection is extremely difficult. Retrospective review of 699 radical neck dissections was performed. Recurrence rates, host, tumor, treatment factors, and survival were analyzed. One hundred nineteen patients who had undergone radical neck dissections had recurrence, 69 were considered candidates for salvage surgery. Factors that increased the risk of neck recurrence were neck node (N) status and no adjuvant radiotherapy. Factors associated with radical salvage treatment were young age, good general condition, and low recurrent N classification. Five-year survival for salvage neck dissection was 31%. Young patients and low T and N classification did well. Low recurrent N classification and salvage surgery were associated with good prognosis for recurrence. In our study, radical neck dissection has a regional failure rate of 20%, a third of recurrence cases were offered curative treatment. Of these, 31% were cured with salvage surgery. ©2008 Wiley Periodicals, Inc. *Head Neck* **30:** 1514–1522, 2008

Correspondence to: A. S. Jones

Keywords: radical neck dissection; recurrence; head and neck; squamous cell carcinoma; salvage surgery

Of all patients presenting with squamous cell carcinoma of the head and neck, approximately one-third will have neck node metastases at that time. This is site-dependent with neck nodes frequently being the cause of presentation in oropharyngeal cancer, while being comparatively rare in laryngeal cancer. Since Crile[1] first described the operation or radical neck dissection, it has remained the "gold standard" method of curing cancer in the regional neck nodes for a century. Recently, there have been many changes in this concept, but until less than a decade ago radical neck dissection was the standard treatment for cancer in the neck. For this reason, the present article deals only with patients seen from 1970 until 1997.

Although standard radical neck dissection needs no introduction to head and neck surgeons, it should be mentioned that it clears almost all lymph node regions of the neck but at considerable expense to both functional and aesthetic recovery.[2]

This radical approach to regional metastases is warranted because of the great risk to mortality that neck node metastases present.[3–5] For similar primary cancers, those associated with neck node have about half the survival of those without a neck node. Despite its relative success, the high cost of the procedure to the patient has led to a more considered approach to the disease. Initially, attempts were made to improve survival. The most obvious and widespread adjuvant treatment was to administer a coarse of radiotherapy (from 40 to 66 Gray [Gy]), particularly in those patients who had extracapsular rupture[3,5] or in those patients who had multiple nodes involved with cancer. Figures from our unit[6] suggest that such adjuvant treatment improves control by around 10% and increases cure rates by a modest 5%. Careful analysis of neck node metastases by primary site[3] has helped to target radical surgery to specific areas. However, this treatment philosophy is more relevant when dealing with the occult neck node metastases rather than frank neck node disease. Although there is little hard statistical evidence to support the concept that controlling occult metastases improves survival,[7] the proponents of this concept make a compelling argument and most head and neck surgeons now will treat high-risk areas in high-risk primary tumors. Examples include levels I and II in mouth cancer and levels II, III, and IV in carcinomas of the piriform fossa, supraglottis, and oropharynx. Such treatment is frequently unilateral, but may need to be bilateral for such structures as the base of tongue, or when the primary tumor straddles the midline.

Most centers report a low recurrence rate in the neck following radical neck dissection, and in our unit it is around 14%.[8,9] Although this appears low, the fact that patients with neck node metastases have a much-reduced survival compared with those without merely demonstrates the tumor's capacity to spread outside the primary site. One must accept that many patients who undergo radical neck dissection may already have occult distant metastases. The implications of this have, until recently, been unclear. It is now evident that the cause-specific survival of patients with micrometastasis in lymph nodes or bone marrow from various primary sites is adversely affected. Interestingly, such metastases frequently appear to be dormant for variable amounts of time before becoming active again.[10] Nevertheless, it is no reason for complacency when dealing with the neck, and while the low regional recurrence rate is very satisfying, it must always be the primary consideration when alternative treatments to radical neck dissection are being considered.

Although much has been written on salvage treatment for recurrence in head and neck patients and also on terminal care, little has been concentrated on recurrence of cancer in the neck following a radical neck dissection.

The present article addresses the problem of those patients developing a recurrence in a neck already treated with primary radical neck dissection. In the present study, the term "second (radical) neck dissection" implies salvage radical surgery to the neck, with curative intent, with or without adjuvant therapy. A patient who has already had a radical neck dissection obviously cannot have a second one.

PATIENTS AND METHODS

For over 40 years, the University Department of Head Neck Surgery in Liverpool has collected data on all patients seen with head and neck neoplasms. Data were collected on structured cards in a prospective manner in the clinic and subsequently entered onto an electronic database. All data were stored securely for future analysis.

The stage of the tumor and regional neck nodes at presentation were classified and reclassified according to the latest Union Internationale Contre le Cancer (UICC) method.[11] The general condition of the patient was coded using the method of the Eastern Corporative Oncology Group.[12] Histological grade was assigned as well, moderate, or poorly differentiated squamous carcinoma on the basis of the most-differentiated area seen within the tumor on histopathological examination. In a number of cases, no grade was assigned. Follow-up times; dates of recurrences, and date and cause of death if this occurred were recorded from clinic visits, General Practitioner records, the Merseyside and Cheshire Cancer Registry, and the National Statistics Office.

This study includes 708 patients with involved neck nodes at the time of presentation of a head and neck mucosal squamous cell carcinoma. Patients with skin cancers were excluded, as were

Table 1. Host and tumor factors (n = 708) (groups 1 and 2).

Factor	Group 1: Primary RND (n = 589)	Group 2: Neck recurrence postprimary RND (n = 119)	X^2/p
Age, mean y	61.3	66.1	p = .0811
Sex, M/F	401/188 (68%/32%)	73/46 (61%/39%)	p = .1874
ECOG			p = .0792
0	313 (53%)	51 (43%)	
1–4	141 (24%)	36 (30%)	
Not graded	135 (23%)	32 (27%)	
Site			p = .0382
Larynx	163 (28%)	44 (37%)	
Hypopharynx	148 (25%)	21 (18%)	
Oropharynx	107 (18%)	14 (11%)	
Oral cavity	111 (19%)	27 (23%)	
Other	60 (10%)	13 (11%)	
Histology			p = .1388
Well Diff SCC	124 (21%)	19 (16%)	
Mod Diff SCC	261 (44%)	43 (26%)	
Poorly Diff SCC	183 (31%)	45 (38%)	
Not graded	21 (4%)	12 (10%)	
T classification			p = .5965
1	155 (26%)	30 (25%)	
2	105 (18%)	24 (20%)	
3	169 (29%)	26 (22%)	
4	160 (27%)	27 (23%)	
Not staged	0	12 (10%)	
Treatment of 1°			p = .7866
Radical RT	98 (17%)	18 (15%)	
Radical surgery	491 (83%)	101 (85%)	

Abbreviations: RND, radical neck dissection; ECOG, Eastern Cooperative Oncology Group Coding; Diff SCC, differentiated squamous cell carcinoma; 1°, primary tumor; RT, radiotherapy.

those patients with an undetectable primary.[13] Twenty percent of patients presented with an enlarged cervical lymph node with the primary tumor subsequently identified either on clinical examination, panendoscopy, or radiology—such patients were included in the study.[13] The details of host and tumor factors with their associated chi-square and p values are given in Tables 1–4.

Of the 708 patients, the primary tumor was treated by radical irradiation in 116 and by surgery in the remainder (n = 592). Of these, 239 patients had both surgery and radiotherapy. After 1988, it became routine practice to irradiate the primary site if the margins were suspect, <0.5 cm or in the case of T4 tumors. Similarly, the neck was irradiated if extracapsular rupture had occurred in the involved lymph node or if multiple lymph nodes were involved. Early in the series, irradiation was delivered as photons by a 4 or 5 mega-electron volt (MeV) linear accelerator, but more recently a 6-MeV machine was used. Photons were delivered following immobilization of the head in a plastic shell, using the appropriate fields for the primary site and the neck. Radiation was given in 2 Gy fractions, 1 fraction being given each weekday. Radiation was delivered to a total dose of 66 Gy in almost all cases. First echelon nodal areas were included since 1980.

Surgery was carried out as appropriate with ablative surgery generally following the guidelines laid down by Stell and Maran.[2] Reconstruction depended on the primary site and the size of the tumor and ranged from primary closure through pedicle flaps to microvascular free flaps, the latter being used almost universally from 1990 onwards. Details of those treatments adjuvant to radical neck dissection administered to patients who had recurrent neck disease (including those who had a second neck dissection) are given in Table 4. Seven patients had skin breakdown following reirradiation and were treated with a radial forearm free revascularized flap. The internal carotid artery was sacrificed in 8 patients, and in the last 4 patients of the series the artery was reconstructed using a long saphenous vein graft. In none of the grafted patients did

Table 2. Regional metastases factors (n = 708).

Factor	Group 1: Primary RND (n = 589)	Group 2: Neck recurrence postprimary RND (n = 119)	X^2/p
N classification			p <.0001
N1	186 (32%)	26 (22%)	
N2a	133 (23%)	20 (17%)	
N2b	119 (20%)	27 (23%)	
N2c	61 (10%)	25 (21%)	
N3	19 (3%)	18 (15%)	
Not staged	71 (12%)	3 (2%)	
N level			p = .0128
1	63 (11%)	9 (8%)	
2	404 (68%)	73 (61%)	
3	69 (12%)	18 (15%)	
4	7 (1%)	6 (5%)	
Not staged	46 (8%)	13 (11%)	
Histology of ND			p <.0001
1 node positive	195 (33%)	14 (12%)	
2 nodes positive	40 (7%)	6 (5%)	
3 nodes positive	20 (3%)	8 (7%)	
4 + nodes positive	36 (6%)	13 (11%)	
1 node with ECR	44 (7%)	14 (12%)	
2 nodes with ECR	41 (7%)	16 (13%)	
3 nodes with ECR	36 (6%)	15 (12%)	
4 nodes with ECR	121 (21%)	19 (16%)	
Free tumor in neck	56 (10%)	14 (12%)	

Abbreviations: RND, radical neck dissection; ND, neck dissection.

neurological sequellae occur although in those not grafted 2 suffered an ipsilateral cerebrovascular accident and one of these died.

Statistical Analysis. All data were transferred to a Microsoft Excel spreadsheet, organized, and then transferred to the SAS statistical package.[14] This was used for all statistical calculations. Categorical data are displayed in contingency tables (Tables 1–4) and analyzed by chi-square with the Yates correction. Differences between groups were further analyzed using categorical modeling.[14] Multiple logistic models were constructed using host, tumor, and treatment factors. The following parameters were investigated: age, sex, performance status,[11] histological grade, site, T classification, N classification, and recurrence at the primary site, the neck, or both. Both forward and backward elimination was performed, and the model checked for stability. The aim was to develop a stable model to ascertain which parameters reliably explain the dependent variable. For significant parameters, the estimates were converted to odds ratios.

Survival curves were calculated using the method of Kaplan and Meier[14,15] and differences in survival curves analyzed using the log rank test.[15] Both cause-specific and observed survival were calculated together with confidence intervals estimated using a modification of the method due to Greenwood.[15] Factors associated with survival were further analyzed using Cox proportional hazard's model.[16] Here, a multivariate model was constructed in a similar fashion as described for categorical modeling but with survival or recurrence as the dependent variable. Stepwise elimination was carried out as for categorical modeling.

The appropriate ethical committees and authorities granted approval for this study.

RESULTS

Host and tumor factors for the whole group of 708 patients are given in Tables 1–4 and analyzed by chi-square with Yates correction. Cause-specific survival for the 3 groups of patients is shown in Figure 1. The overall failure rate of primary radical neck dissection was 20% and for a radical neck dissection for recurrence was 69%.

Chi-Square Analysis. Carcinoma of the larynx was mildly associated with an increased risk of developing a neck node recurrence. There was also a slight excess risk with oral cavity cancer and with hypopharyngeal cancer and a slightly reduced risk

Table 3. Neck node recurrence following initial primary radical neck dissection ($n = 119$).

Factor	Stage of disease at recurrence: Neck recurrence postprimary RND ($n = 119$)	Node recurrence not treated ($n = 50$)	Node recurrence treated by second RND ($n = 69$)	X^2/p
Age, mean y	66.1	69.2	56.4	$p = .0156$
Sex, M/F	73/46 (61%/39%)	28/22 (56%/44%)	45/24 (65%/35%)	$p = .4074$
ECOG				$p < .0001$
0	51 (43%)	4 (8%)	47 (68%)	
1–4	36 (30%)	17 (34%)	19 (28%)	
Not graded	32 (27%)	29 (58%)	3 (4%)	
Site				$p = .3472$
Larynx	44 (36%)	23 (46%)	22 (32%)	
Hypopharynx	21 (18%)	10 (20%)	13 (19%)	
Oropharynx	14 (12%)	6 (12%)	7 (10%)	
Oral cavity	27 (23%)	9 (19%)	19 (27%)	
Other	13 (11%)	2 (4%)	8 (12%)	
Histology				$p = .7471$
Well diff SCC	19 (16%)	8 (16%)	11 (16%)	
Mod diff SCC	43 (36%)	22 (44%)	21 (30%)	
Poorly diff SCC	45 (38%)	18 (36%)	27 (39%)	
Not graded	12 (10%)	2 (4%)	10 (15%)	
T classification				$p < .0001$
1	30 (25%)	9 (18%)	21 (30%)	
2	24 (20%)	7 (14%)	17 (25%)	
3	26 (24%)	13 (26%)	13 (19%)	
4	28 (24%)	19 (38%)	9 (13%)	
Not classified	11 (9%)	2 (4%)	9 (13%)	
N classification				$p < .0001$
N1	26 (22%)	10 (20%)	16 (23%)	
N2a	20 (17%)	4 (8%)	16 (23%)	
N2b	27 (23%)	4 (8%)	23 (34%)	
N2c	15 (13%)	13 (26%)	12 (17%)	
N3	18 (15%)	16 (32%)	2 (3%)	
Not classified	13 (10%)	3 (6%)	0 (0%)	

Abbreviations: RND, radical neck dissection; ECOG, Eastern Cooperative Oncology Group Coding; diff SCC, differentiated squamous cell carcinoma.

with oropharyngeal cancer ($p = .0382$) (Table 1). Advanced neck node stage and histology at presentation was also associated with a later recurrence in the neck ($p < .0001$) (Table 2).

Several factors influenced which patients underwent a second radical neck dissection and which had palliation only. Young and fitter patients were more likely to receive a salvage neck dissection ($p = .0156$ and $p < .0001$ respectively), while late-stage disease of the primary and neck at recurrence militated against ($p < .001$ and $p < .0001$ respectively) (Table 3). Details of the primary and recurrence radical neck dissections are given in Table 4. Recurrent neck disease was more advanced histologically than primary neck disease ($p < .0001$).

Categorical Modeling. Patients who had advanced neck disease at primary surgery to the neck as assessed clinically or by histology had an increased risk of developing recurrent neck disease ($p = .0485$, odds ratio = 1.2) and ($p < .0001$, odds ratio = 2.1) respectively. Patients whose index tumor and first echelon nodes were treated with irradiation had a reduced risk of recurrence in the neck ($p = .0064$, odds ratio = 1.6). Categorical modeling failed to confirm that T classification had any effect on the risk of recurrence in the neck.

The decision as to which patients with recurrent disease in the neck were treated radically and those who were not was studied by categorical modeling. Young patients were more likely to have radical neck surgery ($p = .0093$, odds ratio = 1.2), as were patients in good general condition ($p = .0136$, odds ratio 1.4). Patients with advanced recurrent disease in the neck were less likely to undergo a second radical neck dissection ($p = .0013$, odds ratio = 1.7). Categorical modeling

Table 4. Details of neck dissections.

Factor	Neck recurrence postprimary RND (n = 119)	Neck dissection for recurrence (n = 69)	X^2/p
Histology at 1° ND			$p < .0001$
1 node positive	56 (47%)	12 (17%)	
2 nodes positive	19 (16%)	8 (12%)	
3 nodes positive	13 (11%)	25 (36%)	
4 + nodes positive	31 (26%)	24 (35%)	
ECS	56 (47%)	44 (64%)	
No ECS	63 (53%)	25 (36%)	
Neck treatment			Not applicable
RND	45 (37%)	27 (39%)	
RND + BT	2 (2%)	8 (12%)	
RND + repeat RT	Not applicable	3 (4%)	
RND + flap	7 (6%)	20 (29%)	
Bilateral ND	9 (8%)	3 (4%)	
RND + RT	56 (47%)	8 (12%)	

Abbreviations: RND, radical neck dissection; ND, neck dissection; ECS, extracapsular spread; BT, brachytherapy; RT, radiotherapy.

failed to confirm that the stage of primary disease had any effect.

Survival—Kaplan–Meier Method. The 5-year cause-specific survival for all 589 patients not developing a neck recurrence was 56% (95% confidence interval, 48% to 62%). For those 69 patients with a regional recurrence undergoing a second neck dissection, 31% survived 5 years and were considered cured (95% confidence interval, 25% to 37%, log rank p = .0011). Young patients lived considerably longer than older patients (log rank p = .0012). Patients with early primary site and neck disease at presentation faired better than those

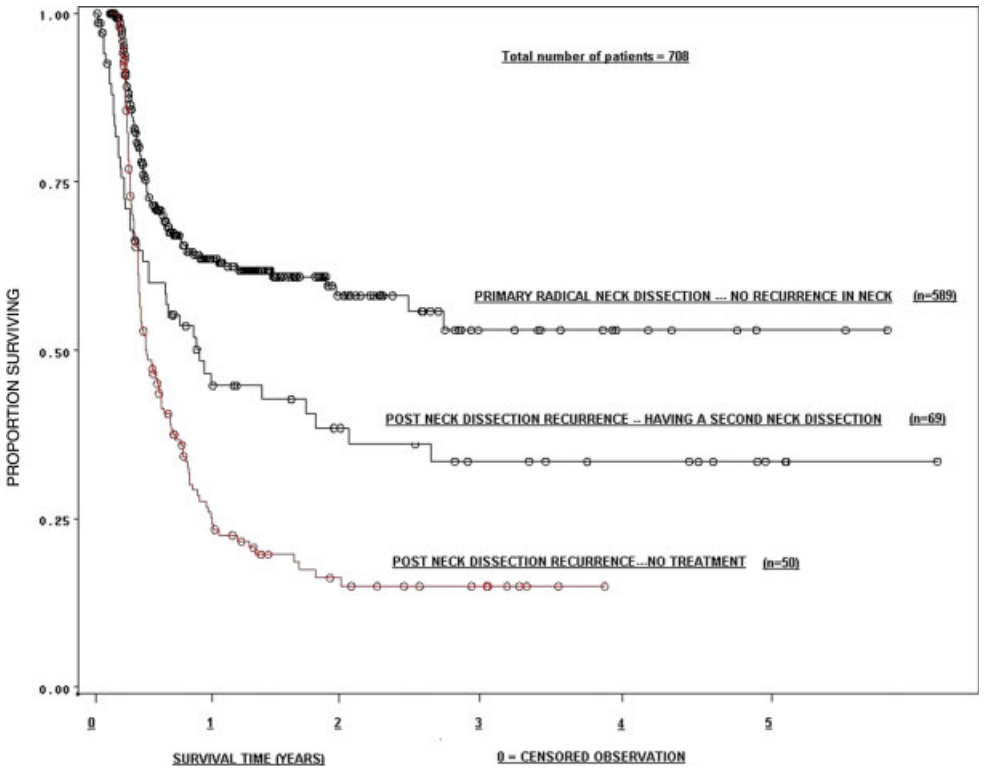

FIGURE 1. Cause-specific survival of those having a radical neck dissection with no recurrence versus those developing a recurrence. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

with advanced disease (log rank $p = .0165$ and $p = .0012$), respectively.

The 50 patients with a regional recurrence not receiving treatment with curative intent had a dismal prognosis with none surviving 5 years and a 3-year survival of only 12% (95% confidence intervals, 6% to 18%). The difference in survival of patients whose regional recurrence was treated versus those, which were not, was highly significant (log rank $p = .0003$).

Cox Proportional Hazards Model. Of the patients developing a regional recurrence, those who did well were young patients ($p = .0049$) and patients with a low T classification and low N classification at primary presentation ($p = .0411$ and $p > .0001$, respectively).

Cox's model confirmed that low recurrent N classification ($p < .0001$) and radical neck surgery with curative intent to the recurrence was also associated with relatively good prognosis ($p < .0001$).

Taken from the time of presentation of recurrent neck disease, only good general condition ($p = .0153$) and a low recurrent N classification ($p = .0011$) were associated with a good prognosis.

Subgroup analysis was carried out on those patients who developed a synchronous primary site and regional recurrence. The results were not significantly different from those given above and for the sake of clarity, are not quoted. In addition, not enough patients were available for a statistical assessment of the effect of treatments adjuvant to salvage radical neck surgery.

DISCUSSION

A discussion of the mechanism by which recurrent regional metastases develop is not the subject of this article, but there are a number of theories and in particular the biological aggressiveness of the primary tumor is crucial. An aggressive histological picture is also correlated with the extent of both primary regional disease and recurrent regional disease.[17] A number of patients will have micrometastases present either in the tissues of the neck or within lymph nodes that have been missed during the original radical neck dissection, and these have been implicated as the source of a recurrence in a number of patients.[18] Although it should be remembered that most patients with head and neck cancer will die of locoregional disease, it is becoming increasingly recognized that distant metastases are important, and as locoregional disease becomes better controlled, more and more patients are dying of distant spread.[17]

If the regional nodes are controlled at the time of primary surgery, it should be noted that metastases can occur in other juxtaposed lymph nodes such as the infraclavicular fossa[19] and the axilla.[20,21] Other noncervical lymph node metastases can occur in the mediastinum and indeed in patients with subglottic, hypopharyngeal, and thyroid carcinomas upper mediastinal lymph nodes should be treated at the time of primary tumor ablation.[22]

In the present series, most patients who had primary radical neck dissection suffered no recurrence in the neck, with a cure rate of 56%, significantly higher than usually quoted. Of those who had recurrence and had a second neck dissection, 31% were cured. Of those that had no curative treatment to their neck, there are no long-term survivors and a median survival of 7 months.

The literature dealing with recurrent regional disease is not extensive, perhaps because it has been considered an unrewarding area of study. Nevertheless, our figures show that a third of patients can be saved if they are suitable for radical retreatment. As lymph node metastases and particularly recurrent lymph node metastases are the most important prognostic factor in head and neck cancer, recurrent regional disease is worthy of more study, and a recent review by Layland et al emphasizes this point.[23]

In a study by Stoeckli et al,[24] in patients who underwent radical irradiation for carcinoma of the larynx and hypopharynx, the disease-specific 5-year survival was only 20% for salvage neck dissection. This is a disappointing figure, as the results of a salvage neck dissection in a patient with radiotherapy can usually be expected to be much higher than this, and certainly much better than salvage surgery following radical neck dissection.[9] In an article on recurrent neck disease and oral cancer, Godden et al[25] noted a particularly poor survival in the treatment of patients with recurrent neck disease, with a median survival time of only 18 months. Koo et al,[26] in a further article on oral cavity cancer, underlined the importance of radical neck dissection, and emphasized the importance of aggressive treatment with surgery and adjuvant therapy in patients with recurrent neck disease. They point out that chemotherapy with or without radiation therapy is far inferior at controlling the disease.

In a recent study by Kim et al,[27] they point out the usefulness of free flap reconstruction in this

type of case, and our series includes 20 such patients. Although not specifically analyzed in our series, we did use brachytherapy in a number of patients, and its efficacy is underlined by Stafford and Dearnaley.[28]

In a very recent article (2007), Jeong et al[29] studying the role of surgical salvage for regional recurrence following treatment of laryngeal cancer noted a 61% surgical salvage rate. This is an intriguingly good result—nearly double our rate and very high compared with the rest of the literature. It should be remembered that regional neck disease even at the time of presentation is only associated with an overall cause-specific 5-year survival of between 30% and 45%. How such a high cure rate in recurrent disease was achieved is difficult to understand.

In the present study, locoregional recurrence was only diagnosed using routine clinical method up until 1988. After that time, CT scanning and then MRI scanning has been routinely employed and has greatly improved our early detection of locoregional disease. Although not proven, common sense dictates that recurrence should be identified as soon as possible to offer the best chance of cure.[7] Various techniques for diagnosing early disease have appeared recently in the literature including the identification of T lymphocyte subsets,[30] the expression of matrix metaloproteinases[31] and studies on squamous cell carcinoma antigen, carcinoembryonic antigen, and CA19.1 and CA125.[32] Such biochemical and molecular biological techniques are very likely to be important in the future, but at present their performance is disappointing.

In most units, including our own, MRI scanning is still the most often used investigation in following up these patients in search for early recurrence,[33] particularly where disease may be hidden under flaps of 1 type or another. Single photon emission computed tomography (SPECT) imaging uses Technetium 99m attached to a substance taken up by metabolizing cells. In a recent study[34] of 200 patients with a clinical suspicion of head and neck tumors, the overall sensitivity/specificity was around 90%/78% for the detection of tumor at the primary site and 90%/95% for malignant lymph node involvement. Although the results are not quite as good for recurrent disease, they demonstrate that SPECT is a very useful technique.

However, in most units the technique of choice for identification of the unknown primary and the early detection of recurrent disease is positron emission tomography (PET). Using this technique, Schmidt et al[35] studied 55 patients with suspected recurrent head and neck cancer. PET showed a sensitivity of 79% and a specificity of 97% for local recurrence and was even more impressive for detecting metastatic lymph nodes, with a sensitivity of 100% and a specificity of 95%. Certainly, this is the technique of choice in our unit, and for improved localization of the recurrence a PET CT is ideal.

What of those patients who were not suitable for radical surgery with or without adjuvant treatment? They are left with either radiotherapy or chemotherapy or chemoradiation. Chemoradiation is a relatively new treatment modality in recurrent regional disease, and we have not included it in this study. Certainly, it is an option, particularly if the patient has not been previously irradiated and is reasonably fit. However, treatment is toxic and from our experience so far it would help only a few patients. Thus, chemotherapy or radiotherapy may give control of symptoms and disease for a period of time. Radiotherapy is, of course, particularly useful if the patient has not been irradiated before. The danger is skin breakdown if the patient is being reirradiated, and chemotherapy may offer better alternatives. Three cycles of cisplatin alone can be effective if the patient is fit. If the patient is not particularly well, they may respond to 50 mg of methotrexate given intramuscularly every fortnight. If they respond, it is a most useful technique. A recent study by Johnson et al[36] showed adjuvant chemotherapy to be disappointing even when dealing with advanced regional disease at presentation.

What of newer techniques? The Turin Group[37] has used interleukin 2 injected perilymphatically and found that the technique may induce temporary regression of the tumor. Immunotherapy has long been the recourse for desperate oncologists. However, over the last decade, clinical immunology has emerged as a potentially powerful tool in the treatment of disease, including cancer. Systemic adoptive T-cell immunotherapy has been administered in recurrent squamous cancer of the head and neck,[38] and has the advantage of low toxicity. In a relatively recent publication, CD4+ and CD8+ cells were infused in 17 patients with recurrent and metastatic cancer. Some modest results were observed in that 6 patients had a useful response.[38]

Obviously, new therapies are required and the perfection of new treatments such as described above may be 1 way forward. However, it is our

group's view that only modest improvements in survival will be made until a basic understanding of cancer in terms of information theory and operating systems using complex self-learning algorithms is obtained.

REFERENCES

1. Crile GW. Excision of cancer of the head and neck with special reference to the plan of dissection based on 132 patients. J Am Med Assoc 1906;47:1780–1786.
2. Stell PM, Maran AGD. Head and neck surgery. London: William Heinemann Medical Books Ltd; 1980. 456 p.
3. Jones AS, Roland NJ, Field JK, Phillips DE. The level of cervical lymph node metastases: their prognostic relevance and relationship with head and neck squamous carcinoma primary sites. Clin Otolaryngol 1994;19:63–69.
4. Gamel JW, Jones AS. Squamous carcinoma of the head and neck: cured fraction and survival times as functions of age, sex, histologic type and node status. Br J Cancer 1993;67:1071–1075.
5. Violaris NS, O'Neill D, Helliwell TR, Caslin AW, Roland NJ, Jones AS. Soft tissue cervical metastases of squamous carcinoma of the head and neck. Clin Otolaryngol 1994;19:394–399.
6. Jones AS, Houghton DJ, Beasley NJ, Husband DJ. Improved survival in patients with head and neck cancer in the 1990s. Clin Otolaryngol 1998;23:319–325.
7. Jones AS, Phillips DE, Helliwell TR, Roland NJ. Occult node metastases in head and neck squamous carcinoma. Eur Arch Otorhinolaryngol 1993;250:446–449.
8. Jones AS. Prognosis in mouth cancer: tumour factors. Eur J Cancer B Oral Oncol 1994;30B:8–15.
9. Jones AS, Husband D, Rowley H. Radical radiotherapy for squamous cell carcinoma of the larynx, oropharynx and hypopharynx: patterns of recurrence, treatment and survival. Clin Otolaryngol 1998;23:496–511.
10. Braun S, Pantel K, Muller P, et al. Cytokeratin-positive cells in the bone marrow and survival of patients with stage I, II, or III breast cancer. N Engl J Med 2000;342:525–533.
11. Hermanek P, Sobin LH. UICC TNM classification in malignant tumours. Berlin: Springer-Verlag; 1992.
12. Beahrs OH, Henson DE, Hutter RVP, Myers MH. General rules for cancer staging: Eastern Co-operative Oncology Group Scale. Manual for staging of cancer (AJCC). Philadelphia: Lippincott; 1988. p 9.
13. Jones AS, Cook JA, Phillips DE, Roland NJ. Squamous carcinoma presenting as an enlarged cervical lymph node. Cancer 1993;72:1756–1761.
14. SAS Institute Inc. Users guide: statistics version, 5th ed. North Carolina: SAS Institute; 1985.
15. Armitage P, Berry G. Survival analysis. In: Armitage P, Berry G, editors. Statistical methods in medical research. Oxford: Blackwell; 1987. pp 421–439.
16. Cox DR. Regression models and life-tables (with discussion). J R Stat Soc B 1972;4:187–220.
17. Petruzzelli GJ, Benefield J, Yong S. Mechanism of lymph node metastases: current concepts. Otolaryngol Clin North A 1998;31:585–599.
18. Quabain SW, Natsugoe S, Matsumoto M, et al. Micrometastases in the cervical lymph nodes in oesophageal squamous cell carcinoma. Dis Oesophagus 2001;14:143–148.
19. Erdamar B, Süogiu Y, Kiyak E, Güven M, Hafiz G, Asian I. Metastasis to infraclavicular lymph nodes in head and neck cancer: a report of three cases. Kulak Burun Bogaz Ihtis Derg 2002;9:368–371.
20. Koch WM. Axillary nodal metastases in head and neck cancer. Head Neck 1999;21:269–272.
21. Rayatt SS, Dancey AL, Fagan J, Srivastava S. Axillary metastases from recurrent oral carcinoma. Br J Oral Maxillofac Surg 2004;42:264–266.
22. Kowaiski LP. Noncervical lymph node metastasis from head and neck cancer. ORL J Otorhinolaryngol Relat Spec 2001;63:252–255.
23. Layland MK, Sessions DG, Lenox J. The influence of lymph node metastasis in the treatment of squamous cell carcinoma of the oral cavity, oropharynx, larynx, and hypopharynx: N0 versus N+. Laryngoscope 2005;115:629–639.
24. Stoeckli SJ, Pawlik AB, Lipp M, Huber A, Schmid S. Salvage surgery after failure of nonsurgical therapy for carcinoma of the larynx and hypopharynx. Arch Otolaryngol Head Neck Surg 2000;126:1473–1477.
25. Godden DR, Ribeiro NF, Hassanein K, Langton SG. Recurrent neck disease in oral cancer. J Oral Maxillofac Surg 2002;60:748–753; discussion 753–755.
26. Koo BS, Lim YC, Lee JS, Choi EC. Recurrence and salvage treatment of squamous cell carcinoma of the oral cavity. Oral Oncol 2006;42:789–794.
27. Kim AJ, Suh JD, Sercarz JA, et al. Salvage surgery with free flap reconstruction: factors affecting outcome after treatment of recurrent head and neck squamous carcinoma. Laryngoscope 2007;117:1019–1023.
28. Stafford N, Dearnaley D. Treatment of 'inoperable' neck nodes using surgical clearance and postoperative interstitial irradiation. Br J Surg 1988;75:62–64.
29. Jeong WJ, Jung YH, Kwon SK, et al. Role of surgical salvage for regional recurrence in laryngeal cancer. Laryngoscope 2007;117:74–77.
30. Kuss I, Hathaway B, Ferris RL, Gooding W, Whiteside TL. Decreased absolute counts of T lymphocyte subsets and their relation to disease in squamous cell carcinoma of the head and neck. Clin Cancer Res 2004;10:3755–3762.
31. Katayma A, Bandoh N, Kishibe K, et al. Expressions of matrix metalloproteinases in early-stage oral squamous cell carcinoma as predictive indicators for tumour metastases and prognosis. Clin Cancer Res 2004;10:634–640.
32. Krimmel M, Hoffmann J, Krimmel C, Cornelius CP, Schwenzer N. Relevance of SSC-Ag, CEA, CA 125 for diagnosis and follow up in oral cancer. J Craniomaxillofac Surg 1998;26:243–248.
33. Tomura N, Watanabe O, Hirona Y, Kato K, Takahashi S, Watarai J. MR imaging of recurrent had and neck tumours following flap reconstructive surgery. Clin Radiol 2002;57:109–113.
34. Leitha T, Glaser C, Prukmayer M, et al. Technetium-99m-MIBI in primary and recurrent head and neck tumours: contribution of bone SPECT image fusion. J Nucl Med 1998;39:1166–1171.
35. Schmidt M, Schmalenbach M, Jungehulsing M, et al. 18F-FDG PET for detecting recurrent head and neck cancer, local lymph node involvement and distant metastases. Comparison of qualitative visual and semiquantitative analysis. Nuklearmedizin 2004;43:102–104.
36. Johnson JT, Wagner RL, Myers EN. A long-term assessment of adjuvant chemotherapy on outcome of patients with extracapsular spread of cervical metastases from squamous carcinoma of the head and neck. Cancer 1996;77:181–185.
37. Cortesina G, De Stefani A, Glovarelli M, et al. Treatment of recurrent squamous cell carcinoma of the head and neck with low doses of interleukin-2 injected perilymphatically. Cancer 1988;62:2483–2485.
38. To WC, Wood BG, Krauss JC, et al. Systemic adoptive T-cell immunotherapy in recurrent and metastatic carcinoma of the head and neck: a phase 1 study. Arch Otolaryngol Head Neck Surg 2000;126:1225–1231.