Proposal for improved staging criteria for carcinoma of the esophagus and cardia

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Abstract

Objective: Current staging for carcinoma of the esophagus and cardia remains imprecise. In an effort to improve on presently accepted staging criteria, new and improved criteria were sought. Methods: A total of 408 specimens resected for carcinoma of the esophagus or cardia between January 1, 1970, and January 1, 1994, were available for analysis. Pathology reports were reviewed, and available histologic slides were examined microscopically. When necessary, paraffin blocks of excised specimens were recut for further pathologic evaluation. On the basis of these findings, tumors were staged according to the criteria of American Joint Committee on Cancer (AJCC). New criteria were established based on the WNM concept and staged accordingly. Survival rates based on these sets of criteria were calculated for each stage, and results were compared. Results: Because our previous studies had shown no advantage provided by the revised AJCC criteria compared with those originally proposed, we modified the WNM system by eliminating the subdivisions of Stage II, reducing the T categories by 1, T3 and T4 having shown no survival differences, and increasing the N categories by 1, depending on the number of nodes involved, e.g. NO = no positive nodes, N1 = 1–4 positive nodes, and N2–5 or more positive nodes. The resulting staging system and 5-year survival rates obtained thereby are as follows: Stage 0 (TO, Tis, NO), 88.2%; Stage I (T1N1, T2N0), 50.3%; Stage II (T2N1, T3N0) 22.5%; Stage III (T3N1, any T N2), 10.7%; and Stage IV (M1) 0%. Conclusions: A new staging scheme for carcinoma of the esophagus and cardia is proposed that provides better prognostic stratification of patients than existing ones. © 1997 Elsevier Science B.V.

Keywords: Staging; Cancer; Esophagus; Cardia

1. Introduction

Current staging criteria for carcinoma of the esophagus and cardia remain imprecise. Until relatively recently, staging systems were unwieldy and of little use to the clinician. With currently available modalities, including the use of laparoscopic and thoracoscopic evaluation, endoscopic ultrasonography, computed to-
which failed to improve on those previously published [4], a modified classification seemed justified. A staging system based on Skinner and associates' [5] WNM system was evaluated whereby tumors limited to the mucosa (Tis) would be equivalent to Skinner's WO designation, T1 and T2 to his W,1, and T3 and T4 to his W2. Nodal status was expanded to include: negative nodes (NO), 1-4 positive nodes (N1), and 5 or more positive nodes (N2). While Skinner and associates' [5] proposal included eight separate categories, our survival data suggested that five of his categories could be combined into two separate groups permitting the establishment of criteria for five stages, each of which was distinct from one another in terms of 5-year survival. However, the need for more data before this conclusion could be confirmed was recognized and is the purpose of the present study.

2. Patients and methods

From January 1, 1970, to January 1, 1994, 454 patients with carcinoma of the esophagus or cardia underwent operation, of which 408 (90%) had an esophagogastrectomy [6]. The resected specimens of these 408 operations had already been reviewed [6], but to evaluate the significance of subdividing T1 tumors into a and b subtypes depending on mucosal involvement only (a) or extension into the submucosa (b) as recommended by the TNM Committee of the UICC [7], the slides of all T1, Tis, and TO tumors were reviewed again. When necessary, specimen blocks were recut and new slides made for reexamination to permit reclassification of these tumors. There were 48 such cases, 31 with Barrett's esophagus, 13 with squamous cell carcinoma, and 4 with adenocarcinoma of the cardia. Eight patients had undergone neoadjuvant therapy. As in our previous studies [8–10], we included carcinomas of the cardia as also favored by others [11].

Because our preliminary modification of the WNM criteria resulted in a disproportionate number of patients with Stage II tumors [1], patients with T3 and T4 tumors with N1 nodes were classified as having Stage III tumors rather than Stage II tumors. In addition, the T4 category has been dropped for, when compared with T3 tumors as independent predictors, there was no difference between the two groups [1]. These staging criteria are depicted in Table 1 and compared with the AJCC criteria [3]. All of the specimens were restaged by the revised modified WNM criteria, and the survival rates compared by stage.

Survival was calculated using the product-limit method of Kaplan and Meier [12]. Tarone-Ware [13] analysis was used to determine the significance of survival distribution among groups.

3. Results

The division of T1 tumors into a and b subdivisions, as described earlier, disclosed that 9 of the tumors involved only the mucosa (T1a and Tis), whereas an additional 9 patients, 5 of whom had undergone neoadjuvant therapy, were classified as having TO tumors. A total of 30 tumors were classified as T1b. Comparison of 5-year survival rates between T1a and T1b tumors did not reveal a statistically significant difference (87.5 versus 74.8%; P = 0.6394). However, no T1a tumors were associated with positive nodes. On the other hand, 10 of the 30 T1b tumors (33.3%) had positive nodes, and a comparison of 5-year survival rates between patients with and without positive nodes revealed a significant difference (60.0 versus 83.6%; P = 0.0389). Accordingly our new staging proposal takes these findings into account, with T1NO staged as Stage 0 and T1N1 tumors staged as Stage 1 (Table 1).

The adjusted actuarial survival curves are pictured in Fig. 1 and Fig. 2. The curves are compared statistically in Table 2. By employing the newly proposed staging criteria, not only is the number of patients more evenly divided among the five stages but the comparison between stages of 5-year survival rates is highly significant statistically with almost a 50% reduction in survival rates for each increasing stage. The current AJCC criteria for staging results in only two of the comparative analyses between stages as being significantly different. The remaining three show no statistically significant difference in 5-year survival rates.

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM Categories</th>
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<tbody>
<tr>
<td>0</td>
<td>TO, is 1 NO MO</td>
</tr>
<tr>
<td>I</td>
<td>T1 N1 MO</td>
</tr>
<tr>
<td>II</td>
<td>T2 NO MO</td>
</tr>
<tr>
<td>III</td>
<td>T3 N1 MO</td>
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<td>T3 N1 MO</td>
</tr>
<tr>
<td>IV</td>
<td>T4 Any N MO</td>
</tr>
</tbody>
</table>

Table 1:
The new staging system (above) compared with the AJCC system (below)
4. Discussion

The need for improved staging criteria for carcinoma of the esophagus became evident to us while comparing the revised AJCC criteria with those previously proposed. The ‘improved’ criteria did not provide more satisfactory prognostic stratification of patients. It occurred to us that by reducing the number of T categories and increasing the N categories according to the number of nodes involved, a modification of Skinner and associates’ [5] WNM system might be converted to a better staging system. This proved to be the case, yet in so doing the bulk of cases became classified as Stage II [1]. This was corrected by switching patients with T3,4 N1 tumors (Skinner’s W2 N1) from Stage II to III [6].

A more controversial change from the traditional AJCC criteria has been our inclusion of carcinomas of the cardia in our esophageal staging system. We have included carcinomas of the cardia because the surgical approach to such lesions is similar to that for carcinomas of the lower esophagus and the prognosis is the same. Furthermore, a comparison of staging results using esophageal criteria with those obtained using gastric criteria showed no difference in the resulting stages [1]. Increasing evidence suggests that up to 50% of carcinomas of the cardia may actually arise from tongues or short segments of Barrett’s esophagus, implying an esophageal rather than a gastric origin [14–16], all of which suggests that these tumors behave more like esophageal carcinomas than gastric carcinomas [11].

The present study embodies these proposals. However, our analysis of T1 tumors does not support the TNM Committee’s suggestion of differentiating superficial tumors into those limited to the mucosa (T1a) and those involving the submucosa (T1b) [7]. Although none of the T1a tumors was associated with positive nodes, one third of the T1b tumors were. Perhaps larger numbers might support this distinction, which has been stressed by Sabik and associates [17]. Interestingly, in the initial proposal of Skinner and associates [5] mucosal tumors (W0) were separated from tumors penetrating into the submucosa and the muscularis propria (W1).

We have not followed the suggestion of the TNM Committee of the UICC to expand the N categories to include three categories of involved lymph nodes; 1–3 positive nodes (N1a), 4–7 nodes involved (N1b), and greater than 7 nodes involved (N1c). In fact, their example used to support this proposal shows no difference in 5-year survival rates between N1b and N1c tumors. We have not altered the existing M criteria to comply with the Committee’s suggestion that metastases to nodes beyond regional lymph nodes be considered as a subgroup of M1 tumors. Doing so, in our opinion, would convert tumors of the esophageal body with metastases to celiac nodes and tumors of the esophagogastric junction with metastases to mediastinal nodes into Stage IV tumors. Some of these patients can be cured by resection of the tumor and all of the involved nodes at the time of esophagectomy and should not, therefore, be classified as having Stage IV tumors because a 5-year survival rate of 10 + % can be expected after esophagectomy in such patients [11].

Although, to be sure, the data we are presenting are based on a relatively small number of cases, the proposals we are making are worthy of serious consideration, for their incorporation in a revised staging system for carcinomas of the esophagus and cardia appears to provide better prognostic stratification of patients. However, confirmation by other studies involving larger patient populations is necessary.
Table 2
Comparisons of two staging systems

<table>
<thead>
<tr>
<th>Stage No.</th>
<th>AJCC Patients</th>
<th>5-year survival (%)</th>
<th>P value</th>
<th>Modified WNM Patients</th>
<th>5 year survival (%)</th>
<th>P value</th>
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<td>37.9</td>
<td>NS</td>
<td>II</td>
<td>95</td>
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<td>NS</td>
<td>III</td>
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</table>

Acknowledgements

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References


Appendix A. Conference discussion

Dr Skinner (New York, USA): Congratulations to Dr Ellis. We appreciate his efforts on this and agree fundamentally with what he is proposing. Staging is getting to be more important because we are getting so many options in therapy these days. The two parts of this paper that are particularly significant are the fact that the tumors located only in the mucosa as stage 0 cases have not had any lymph node metastases. And this is the same finding that Kato found in Tokyo and has led the Japanese to be able to do mucosectomy. The other is the confirmation, Dr Ellis, of our earlier finding that patients with a few lymph nodes subjected to a total resection of the lymph nodes have a quite good prognosis, whereas those with four or five or more nodes generally have a very poor prognosis. So the fact that you discovered a positive lymph node on a CAT scan or an ultrasound does not mean that the patient has a terrible prognosis if you do a thorough removal of all those lymph...
nodes. I greatly enjoyed reading the manuscript and appreciate the opportunity to discuss the paper. Thank you.

**Mr Moghissi (Hull, UK):** I think that to reduce the number of T is very reasonable. In my large series of patients, I have been through the various classifications. At first I used the original classification and then I used the classification proposed by Dr Skinner. My problem about increasing the N number is that by the time the cancer is so advanced, it is extremely difficult to separate all these nodes and say that, look, we have got node 1, 2, 3, 4 and 5. Do you not find that increase in N numbers would bring a new burden?

**Dr Ellis:** Thank you Dr Skinner and Mr Moghissi for your comments. In answer to your question Mr Moghissi, unfortunately I have to rely on our pathologists to determine the number of lymph nodes that are positive, though I agree with you that in the presence of matted nodes, an accurate number may be difficult to determine, but in such cases there are usually five or more nodes involved.

Interestingly enough, the TNM Committee of the UICC has recently suggested an additional N category, so there would be 4N categories, (N0, N1a, N1b and N1c) reflecting the number of involved nodes. However, the example they use in support of this suggestion indicates no difference in survival of patients with N1b (4-7 nodes involved) and N1c (7 or more nodes involved), so I think that what we are proposing, which is the same as what Dr Skinner reported originally, is less complicated and does, in fact, show a significant difference in 5-year survival rate between N1 (1-4 nodes involved) and N2 (5 or more nodes involved). However, transhiatal resections present a problem, since the resulting specimens don't provide as complete a sampling of the mediastinal nodes as would be the case after an Ivor Lewis type resection. As a result, the numbers of nodes involved may be underestimated in patients who have a transhiatal resection. Thank you again for your comments and questions.