

East African Medical Journal Vol. 78 No. 12 December 2001

FOLLOW UP OF OESOPHAGEAL CANCER THERAPY AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI

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ABSTRACT

Objective: To determine the pattern of follow-up for oesophageal cancer patients following hospital discharge and reviewing followup results of the different treatment modalities with emphasis on oesophagectomies.

Design: A retrospective hospital based study covering the period January 1987 to January 2001.

Setting: Surgical outpatient clinic, Kenyatta National Hospital, Nairobi.

Main outcome measures: Determination and the comparison of the one, two and three-year followup rates for the different treatment modalities and their median follow-up period in addition to reviewing the common variables associated with follow-up.

Results: The median followup for patients managed by oesophagectomy was 9.5 months with a 43%, 22% and 10% one-, two- and three-year followup rates respectively. This compared to a median of two months and a 7% and 3% one-, and two- year follow-up rate for patients managed by intubation, and a 3-month median followup with a one- and two- year follow-up rate of 12% and 4% respectively for radiotherapy treated patients. Oesophagectomy patients had a better followup compared to intubations and radiotherapy ($p < .00001$). Oesophagectomy for stage T4 tumours had an apparently better follow-up compared to both stage T1-3 tumours and patients managed with intubations ($p = .002$ and $.02$ respectively).

INTRODUCTION

Carcinoma of the oesophagus is a very common problem in this country and accounts for about 30% of the workload within the cardiothoracic unit in this hospital. As a result of the late presentation of our patients the resectability rate of the tumours for our unit is low(1). Carcinoma of the oesophagus is a disease associated with a very poor prognosis and a relatively low postoperative survival outcome. Currently there is no local data available on the post discharge outcome of this group of patients in our setting. This study attempts to form a starting point in the understanding of the follow-up of our patients and compares the follow-up results of the various treatment modalities offered. Though the follow-up data in this type of study is an underestimation of the true post discharge survival pattern, there may be a strong correlation between the two.

MATERIALS AND METHODS

This is a retrospective study reviewing the follow-up of inpatients admitted to the KNH with a diagnosis of carcinoma of the oesophagus or cardia over a fourteen-year (January 1987 to January 2001) period.

A data base was compiled from various sources. These sources consisted initially of the admission books from the

various wards and the operating theatre register for the cardiothoracic and general surgical theaters. With this information the files of all patients with a diagnosis of oesophageal carcinoma admitted at the KNH within the last fourteen years were requested from the records office and the radiotherapy unit.

Data relating to this study collected from the various sources included, the type of treatment given and their dates, the age of the patients, patient discharge dates and subsequent clinic visits. In addition, data relating to endoscopic and histological data was collected. Intra-operative information relating to tumour spread was also compiled for patients undergoing surgery. This was predominantly a macroscopic description of tumour spread with additional microscopic information where lymph node specimens were taken. Further information of contacts was collected to aid in contact tracing to facilitate follow up information through friends or relatives. For patients who had an admission diagnosis of dysphagia but no barium swallow or endoscopy done, they were excluded from the study.

Data of follow-up through patient files and contact tracing was used to construct follow-up curves using the Kaplan Meyer method. The follow-up curves were analysed to determine one-two- and three- year follow-up rates. Median follow-up times were derived from the resultant graphs. The end point of follow-up is defined as having been reached when any patient died or failed to attend follow-up for a period of three months or more (and could not be traced at the contact address provided). For patients whose definite dates of death were known these were used as the end points. In the event that the relative(s) or other sources were unable to give the exact date of death but remembered

the month, the mid-month was used as the end point. For patients for whom no date of discharge was documented and it was confirmed the patient was discharged, the discharge date was estimated using the average duration of hospital stay for all the patients with complete data on their dates of surgery and discharge. Comparison of differences between patient ages was performed by the use of box and whisker charts (mean \pm 2 standard errors). The Gehan's Wilcoxon test was used to determine the statistical difference between cures ($p < 0.05$).

RESULTS

During the study period 1,742 patients were admitted with a diagnosis of carcinoma of the oesophagus or cardia who fulfilled the inclusion criteria. Two hundred and sixty one oesophagectomies, 260 explorations and 222 intubations (209 Mousseau-Barbin tubes, 2 Celestine tubes and 11 endoscopic intubations) were performed. Radiotherapy as the sole modality of therapy was administered to 225 patients, these having been either patients found inoperable on exploration or direct admissions into the radiotherapy unit. A large number of patients either had no interventions during their admission or only a diagnostic endoscopy. From the records office and radiotherapy unit a total of 930 patient files were retrieved.

The resectability rate for the carcinomas for the period was calculated at 35.0%. Of the patients who had an oesophagectomy the files of 93 patients discharged were retrieved out of the 104 recorded as discharged. While for patients managed with intubations and radiotherapy alone, 130 and 214 patients were discharged respectively.

Only 62 of the oesophagectomy patients discharged opted to attend follow-up at the KNH. The median follow-up for the combined group was 9.5 months with a 43%, 22% and 10% one- two- and three-year follow-up rates respectively. For the patients intubated, 61 patients attended follow-up at KNH with a median follow-up of two months and a 7% and 3% one- and two- year follow-up rates.

The median follow-up for 92 patients managed with radiotherapy alone who attended KNH outpatients for follow-up was three months, while the one- and two- year follow-up rates were 12% and 4% respectively. There was a shift towards more upper third tumours for the radiotherapy group compared to the others (Table 1). There was a significant difference in the follow-up between the oesophagectomy patients and the other two, ($p < .00001$) while the radiotherapy patients had a better follow-up compared to the intubation patients ($p = .011$) (Figure 1).

Table 1

Percentage distribution of tumour location

	Upper	Middle	Lower
Radiotherapy	12.5	44.1	43.4
Intubation	0.9	15.8	83.3
Oesophagectomy	0	46.8	53.6

Figure 1

Comparison of treatments at KNH

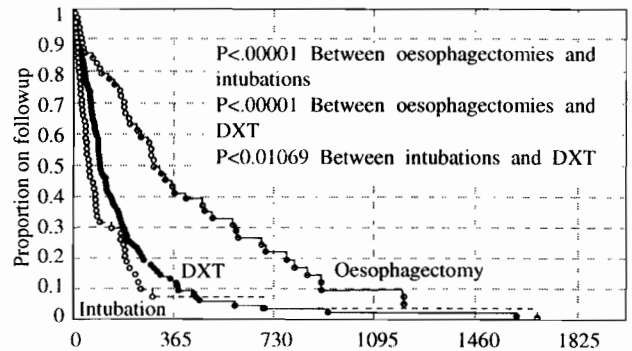


Figure 2

Follow up for tumour \leq 35 CM and $>$ 35 cm

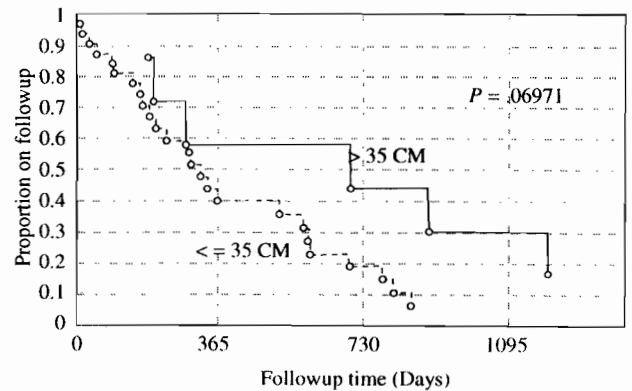


Figure 3

Follow up of differentiation (squamous)

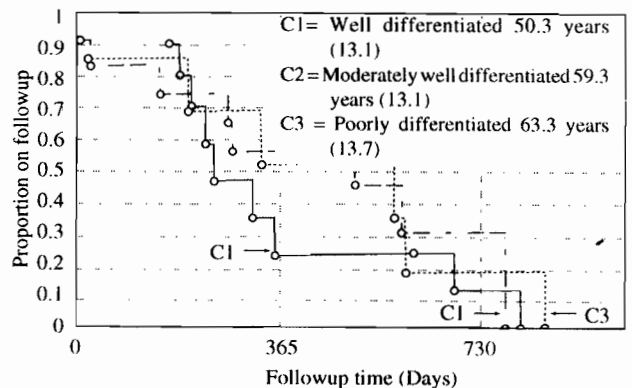


Figure 4

Box and whisker plot (mean age versus tumour differentiation)
(Mean plus/minus 1.96 standard errors)

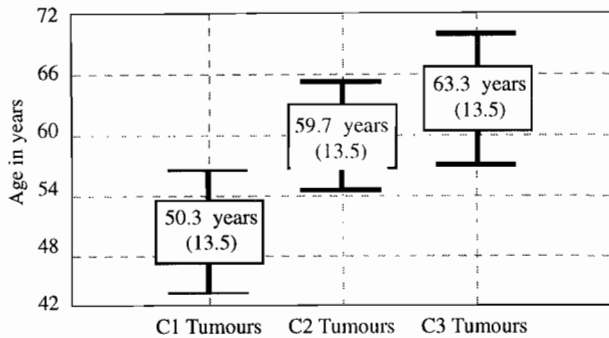
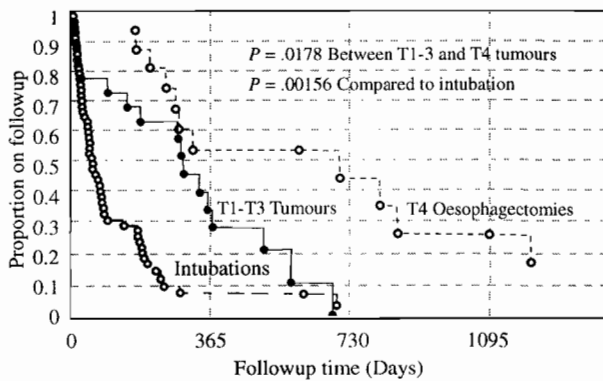


Figure 5

Followup T1-4 squamous cell vs intubation



For the oesophagectomy patients who had an endoscopic measurement for the tumour level, lower third tumours had a better follow-up compared to middle third tumours. These tumours had a 57% and 44% one- and two-year follow-up, with a median follow-up of 23 months. This is compared with 39% one-year, 16% two-year follow-up and a median of 11 months for middle third tumours (Figure 2).

Though not statistically significant, the poorly differentiated tumours and moderately well differentiated tumours had an apparently better follow-up compared to the well-differentiated tumours. In addition the average age of the patients increased with a corresponding deterioration in the degree of tumour differentiation (Figure 3). Patients with poorly differentiated tumours had a statistically significant older age (95% confidence interval) (Figure 4). Finally, oesophagectomies for stage T4 tumours (TNM classification), had a better follow-up compared to both stage T1-3 tumours and patients managed with intubations ($p = .002$ and $.02$) (Figure 5). It was assumed that all intubations were T4 tumours.

Most of the T4 tumours were classified macroscopically at surgery among which were added those with positive nodal involvement on histology.

DISCUSSION

Survival following oesophageal cancer surgery is associated with many variables including the stage of the tumour, duration of symptoms, types of treatment modality offered and age of the patient amongst others. Most of these are, however, a direct reflection of the extent of the disease at presentation. At the KNH, patients tend to present late for surgery, on average six months after the onset of symptoms(1). By this time the disease is likely to have spread and the prognosis is likely to be very poor.

Over the years, though the operative mortality for oesophageal resection has fallen, the overall postoperative survival has remained fairly constant, the average survival time being about 6 months once metastasis is present(2). It has been well documented that the two significant independent prognostic factors following oesophagectomy that influence survival are the spread of tumour through the oesophageal wall and the presence of lymph node metastasis(3). The presence of metastasis to the nodes is a fairly common occurrence. Isono *et al*(4) in their series found node metastasis present in up to 32% of neck nodes and about half of the nodes in the four chest and abdomen at surgery. The major problem at the KNH is the difficulty of accurate staging of the disease and of assessing intrathoracic or abdominal nodal extension at surgery.

Apart from the preceding two factors, other factors that may influence survival but are not significant independent prognostic factors, include patient age, size of the tumour, duration of symptoms, nutritional status and postoperative complications(3,5).

Data on patient survival post oesophagectomy from different centres vary widely. The 5-year survival rates from different series range from about 7% to 86% with an average cumulative 5-year survival rate of 21%(2,6,7). This wide variation results from the inclusion of both early and late stages of cancer in the different reports. In his study King *et al*(8) demonstrated that the survival of stage I tumour patients is up to six times better than stage III tumour. For this study the overall 5-year follow-up (survival) for all the patients combined is below the average quoted above and falls to 10% at three years, with a median follow up of 9.5 months.

Late presentation and thus advanced disease at presentation is one factor related to this poor survival. This hospital is one of the only centres offering surgery for this condition and the only one at the moment with an operational radiotherapy unit in the country. As a result of the normal referral system there is some delay from the time of onset of symptoms to surgery or radiotherapy(1).

For the KNH group of patients offered oesophagectomy, the T4 tumours appear to have a better survival compared to T1-3 tumours. This is the opposite of what is expected. One of the possible explanations may be due to the fact that T1-3 tumours are associated with less morbidity and a lower mortality postoperatively, and these patients will tend to stop coming for follow-up. This usually results from their feeling better than patients with

T4 tumours and hence may see no need to continue with follow-up. The same argument could also explain the apparent reversal in the follow-up associated with poorly differentiated tumours compared to the well-differentiated group. This is further confirmed through a few post oesophagectomy patients traced by telephone contact. The other cause of this discrepancy may be the difficulty in assessing the tumour spread, as this study relied mainly on intra-operative macroscopic spread, which would be less reliable in assessing tumour spread than microscopic evaluation. Better tumour assessment, possibly with frozen sections, at the microscopic level would result in more patients being assigned to their correct TNM group.

In order to better predict the post treatment survival of T4 patients there is a need for a more critical assessment of the tumour stage. Survival is directly related not only to nodal spread, but also to the number of nodes involved and their distribution pattern. The nodal distribution pattern that has been found to be significant prognostically is that around the recurrent laryngeal nerve chain. In addition to the nodal involvement the extent of penetration of the nodal serosa by tumour also independently relates to survival(9,10). This prognostic disadvantage associated with the upper third tumour spread may be related to the better survival associated with the lower third tumours compared to middle and upper third tumours as seen in this study.

For patients who are not suitable candidates for oesophagectomy some form of palliation is provided. At the KNH the modalities which are offered are intubation, radiotherapy and tumour dilatation. More recently the use of chemotherapy combined with radiotherapy has increased. The Mousseau-Barbin tube is currently the most favoured method of intubation at the KNH. The internationally accepted median survival time with intubation by all modes is about six months(2,11,12). Inoperable tumours, poor surgical risk patients and patients with tracheo-oesophageal fistulae (TOF) are the main candidates offered this form of therapy.

For this study the median survival with intubation was found to have been much lower at only two months with a 7% one-year follow-up. This group of patients tend to do fairly poorly and this author feels that, not only is the tumour stage related to the survival in this group of patients but more importantly, dehydration and malnutrition also play a significant role in survival. A significant number of the intubated patients are indeed re-admitted subsequent to discharge for re-hydration. Probably with more aggressive management of dehydration the median survival of this group could be improved.

The cure rate with radiation alone as the only modality of treatment is estimated to be about 5%. In part this outcome is as a result of the fact that about 30% of patients presenting for radiotherapy have non-metastatic disease(13). The median survival with radiotherapy alone is about 8-10 months and approximately 5% of patients surviving for five years(2,14). As for patients managed with surgery alone, the tumour stage at the time of therapy has an influence on the post treatment survival.

Despite the use of radiotherapy most surgical series report better survival results than radiotherapy series(2). This is indeed the case in this study. However, care is needed in interpreting these results as surgical results are based on resected tumours while for radiotherapy the tumor mass remains in situ. Secondly the resected patients have the advantage of improved nutritional and fluid intake not available to all radiotherapy treated patients.

Similar to the surgical results, our radiotherapy figures are below the average quoted with a median survival of only three months and a 4% two-year follow-up. Advanced tumour at presentation and a greater number of upper third tumours, associated with a worse prognosis(10), probably contribute to these poor follow-up results. Most patients referred from the surgical wards for radiotherapy are already confirmed inoperable either through clinical examination or exploration. As a result there are a high number of cases of advanced disease in this group of patients.

The use of radiotherapy in addition to chemotherapy has an increasing usage in the management of oesophageal carcinoma while the use of radiotherapy alone is declining(2). In theory combined chemotherapy and radiotherapy provide treatment of loco-regional disease and distant spread. Analysing the results of several studies the survival with combined chemo-radiotherapy has a median of 12 - 20 months and a 2-year survival rate of 35% - 40%(2). In the Radiation Therapy Oncology Group (RTOG) study the median survival with dual therapy was significantly better than radiation therapy alone from a median of 8.9 months to 12.5 months, similar results have been reported elsewhere(17,18).

For a more accurate assessment of the true survival pattern of our patients following discharge a prospective follow-up is required. Retrospective follow-up data will always give, not only less accurate results, but even with the most accurate review, the results will be an underestimation of the true survival picture. Currently such a study reviewing a five-year period is in progress and the unit hopes to have a more accurate post discharge survival picture after this study.

ACKNOWLEDGEMENTS

Director of the Kenyatta National Hospital for permission to review patient notes and the radiotherapy unit for access to patient treatment cards.

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ACKNOWLEDGEMENT

The Editor-in-Chief wishes to thank the authors, reviewers, advertisers, readers and subscribers for the support rendered to EAMJ in the year 2001. He looks forward to continued support and co-operation in future.

Have a merry Christmas
and a prosperous year 2002