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WEIGHT CHANGE POST OESOPHAGECTOMY FOR CARCINOMA OF OESOPHAGUS
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ABSTRACT

Objective: To determine the pattern of weight changes observed in postoperative oesophagectomy patients at the Kenyatta National Hospital and evaluate weight change with selected preoperative variables.
Design: A prospective analysis of post-operative weight change of patients following oesophagectomy utilising body mass index (BMI).
Setting: The cardiothoracic unit, Kenyatta National Hospital, Nairobi.
Subjects: All patients with oesophageal cancer, with a confirmed histological diagnosis of squamous cell carcinoma and discharged post oesophagectomy.
Intervention: Oesophagectomy.
Main outcome measure: Changes observed in the BMI during respective clinic visits.
Results: Fifty nine patients were enrolled into the study with a mean preoperative weight of 50.4 kilograms and mean BMI of 19.4 kg/m^2 (± 4.3). Sixty seven point seven percent of patients preoperatively fell into the underweight category (less than 20kg/m^2); normal were 16 patients (27.1%) and overweight included six patients (10.2%). Postoperatively the majority of patients continued to loose weight and the overall average BMI at the study endpoint was calculated as 18.0 kg/m^2 (± 3.2). This value was significantly lower compared with the preoperative value (p = 0.004). None of the selected variables showed a significant relationship to the postoperative weight change pattern observed, though the patients gaining weight postoperatively had an apparently better survival pattern compared to the others. Analysis of the selected variables versus weight change pattern (gain, stable or weight loss) showed no significant relationships.
Conclusion: This study population presented a lower initial preoperative weight compared to similar studies from the developed world, with the majority being underweight. The majority of patients exhibited a continued postoperative weight loss with only a small number showing any weight gain. The study unfortunately was not able to demonstrate association of weight change with any of the selected variables.

INTRODUCTION

Dysphagia forms the cardinal presenting symptom associated with carcinoma of the oesophagus, unfortunately this symptom occurs in the later stages of the disease (1). With malignant dysphagia there arises a situation of reduced nutritional intake and impairment of associated physiological functions dependant on adequate nutrition. Dehydration and weight loss not uncommonly are the main clinical signs at this late stage of the disease. This clinical association of disease and weight loss on average exhibits a greater correlation for the histological form of squamous cell carcinoma than the adenocarcinomas of the oesophagus (2).

Following oesophagectomy the nutritional intake of these patients is restored and the post operative weight of the patients may be expected to improve in comparison to the preoperative level.

Is it more than just the variable of reduced nutritional intake causing preoperative weight loss and are the effects of these other variable still present in the post operative period? Some studies have attempted to use hyper alimentation preoperatively and shown no improvement in patient operative survival (3,4), could this similarly be reflected in the post-oesophagectomy period with no weight change.

This study looks at the post-operative weight change of the patients at the Kenyatta National Hospital, Nairobi, following oesophagectomy using body mass index (BMI), and attempts to identify some of the preoperative variables that may be associated with postoperative weight change.

MATERIALS AND METHODS

Patient analysis for the study was through retrospective analysis of prospectively collected data. The database used for this study covered the period from January 2001 to February 2005.

Inclusion criteria were all patients who underwent a successful oesophagectomy and in addition fulfilled the following criteria; All those patients who on histology were confirmed to be squamous cell carcinoma, in addition they all had preoperative weights and heights documented and were eventually discharged from the ward after oesophagectomy.

In patient data collected in addition to weight and height included the following variables; age, sex, preoperative haemoglobin values, white cell count, total protein and albumin levels, histological results and the duration of symptoms of dysphagia prior to admission.

No patient had their immunological status determined during the study.

At surgery oesophagectomies were performed using the McEwen, Ivor Lewis or a transhiatal method according to the surgeons' decision in the particular situation.

Pyloroplasty as a drainage procedure in general was not performed in the vast majority of patients in this series and no regional lymph node dissections were performed either.

Weight and height measurements were converted into body mass index (BMI), and this parameter was subsequently used in the follow-up analysis. The weight categories were divided into underweight, normal and overweight using the ranges of BMI <20 kg/m^2, 20- 25 kg/m^2, and >25kg/m^2 respectively.

Post discharge clinic visit data collected consisted of the weight and the date of clinic visit.

The weights and heights of patients were measured using "health-O-meter" weight scales both in the ward and clinic. The weights in kilograms were recorded to the nearest 100 gms while height to the nearest centimetre.

A change in BMI of greater than ± 0.5 units between clinic visits was empirically used to signify a significant change in weight of the patient.

Analysis included variation in body mass index values between clinic visits; the determination of the association between the change in BMI and preoperative variables. Students t-test and the Chi square test was used where appropriate and level of significance taken as a p-value of less than 0.05. Kaplan Mayer curves were used to evaluate the survival pattern of the different body mass index groups. Significance of the difference between curves was calculated using the Log Rank method, again with significance being taken as a p-value of less than 0.05.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS), version 11.5 and Microsoft Excel 2003.

RESULTS

During the study period, 59 patients fulfilled the inclusion criteria. All of these 59 patients fell within the time period from February 2001 to February 2005 of the database.

Males formed 54% of the patient population. The mean age for the study population was 53.8 years (±14.8).

For all patients the mean preoperative weight was 50.4 kilograms (range 30-88 kilograms) and the BMI mean was 19.4$kg/m^2 \pm 4.3$ (with a median of 18.6 kg/m^2). The preoperative distribution of the various categories for the BMI was as follows. The majority of patients, 37, fell into the underweight category (62.7%), normal BMI range were 16 patients (27.1%) and overweight included six patients (10.2%).

Postoperatively these patients were reviewed at various clinic visits, however, irrespective of how many visits some of the patients might have made to the clinic during the study period only the first four postoperative clinic visits were included into the analysis. This was the case as the numbers of patients still attending follow up after the fourth visit fell to very low levels.

During the postoperative visits the duration between the visits from the time of discharge showed a wide variation and the average durations from the time of discharge to the various clinic visits were as shown in Table 1.

On the first postoperative visit the changes for the body mass index (relative to the preoperative BMI), were recorded and these were as follows; a loss in BMI was observed in 21 patients (52.5%), the BMI remained stable in 11 patients (27.5%), while eight patients (20%) demonstrated a gain in BMI.

No records were documented for 14 patients on this first visit as they failed to attend. In addition four patients attended but their weight readings were missed on this clinic visit for various reasons. Of these four, only three attended subsequent visits.

The various changes observed in the BMI values compared with the various time periods from the time of discharge to the first clinic visit are summarised in Table 2.

As of the time of the first clinic visit the re-distribution of the various categories for body mass index compared to the preoperative distribution were underweight in 31 (77.5%) patients, normal BMI in six (15%) patients and overweight in three (7.5%) patients.

Thirty patients were weighed on the second postoperative clinic visit. Again the majority, 16 (53.3%) patients, lost weight, five (16.7%) patients, remained stable while nine (30%) patients exhibited a weight gain. Two patients who attended a second clinic visit were not weighed.

The various BMI changes during the second visit when distributed according to the interval since the time of hospital discharge are shown in Table 3.

Similar to the analysis during the first visit, on analysis of the redistribution of the various BMI classes following the second visit; the re-distribution of the various groups compared to the preoperative groups were as follows; underweight 22 (73.3%) patients, normal eight (26.6%) with no patients observed overweight.

Table 1

Mean duration from time of patient discharge at respective clinic visits

Visit	Mean duration (months)	Median duration (months)	No. of patients
First	4.8 ± 7.4	1.45	40
Second	10.1 ± 8.9	7.0	30
Third	16.4 ± 12.5	12.3	11
Fourth	25.7 ± 16.8	28.8	7

Table 2

BMI change compared to various time periods to the first clinic visit

Duration to first clinic visit	Gain in BMI	Stable BMI	Loss in BMI	Total
≤3 months to visit	4	8	15	27
3-6 months	1	1	3	4
> 6 months	3	2	3	9
Total	8	11	21	40

Table 3

BMI change compared to various time periods to the second clinic visit

Duration to second clinic visit	Gain in BMI	Stable BMI	Loss in BMI	Total
≤3 months to visit	0	0	4	4
3-6 months	3	3	3	9
>6 months	6	2	9	17
Total	9	5	16	30

For the third and fourth clinic visits, 11 and seven patients respectively had data recorded. For the third visit one patient was not weighed and on the forth visit, for one patient the date was not recorded. The changes in the BMI are collectively represented in Table 4.

Table 4

BMI changes observed during the third and fourth clinic visits

Visit	Gain in BMI	Stable BMI	Loss in BMI	Total
3	3	0	8	11
4	2	1	4	7
Total	5	1	12	18

As a result of the varying durations for follow up of the patients during the various clinic visits, in an effort to standardise the follow up durations, the last clinic visit, or the fourth visit if more than four visits were made, was selected as the end point of the study for each patient. All weight changes at this point were used to analyse weight change per duration since discharge, (irrespective of the number of visits made).

Using this end point, the weight change for all patients (single entry), for the three periods, less than three months, three to six months and greater than six months follow up, were determined (Figure 1).

The overall average BMI at the study end point calculated as 18.0 kg/m^2 ± 3.2. This value was significantly lower compared with the preoperative value, (Paired sample t-test, $p = 0.004$).

The distribution for the average BMI's within the different time periods at their end points were as follows; for less than three months follow up 19.4 kg/m^2 ± 6.0, for follow up between three and six months 17.7 kg/m^2 ± 2.3 and 17.9 kg/m^2 ± 2.1 for greater than six months. This difference was not statistically significant.

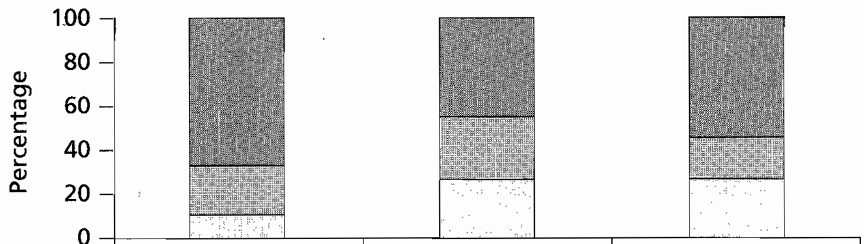
Looking at the pattern graphically it appears that in all three groups the number of patients exhibiting weight loss is greater than the two other categories. For those patients who gain weight this gain seems to be proportionately more in the longer follow up periods (more than three to six months and over), compared to those patients who have short term follow up.

The mean follow up period for the study group averaged approximately just less than ten months. Patients showing a weight gain postoperatively were associated with an apparently better follow up, ($p = 0.076$). The group of patients who maintained a stable BMI relative to their preoperative BMI at the end point of the study had a slightly shorter follow up compared to those either loosing or gaining weight ($p = 0.0401$). For this group who maintained a stable BMI, only one patient fell within the normal BMI range, while all the others were underweight, (average 18.6 kg/m^2). This compares with 18.2 kg/m^2 for those patients who gained weight and 17.7 kg/m^2 for those loosing weight (Figure 2).

Univariate analysis of the various preoperative parameters against this final weight change pattern using the chi square test is as shown in Table 4. Chi square analysis of variable versus weight change (gain, stable or weight loss).

Figure 1

Weight change observed as per the different follow-up periods at the study end point



	< 3 months	3–6 months	>6 months
Weight loss	6	5	12
Stable	2	3	4
Weight gain	1	3	6

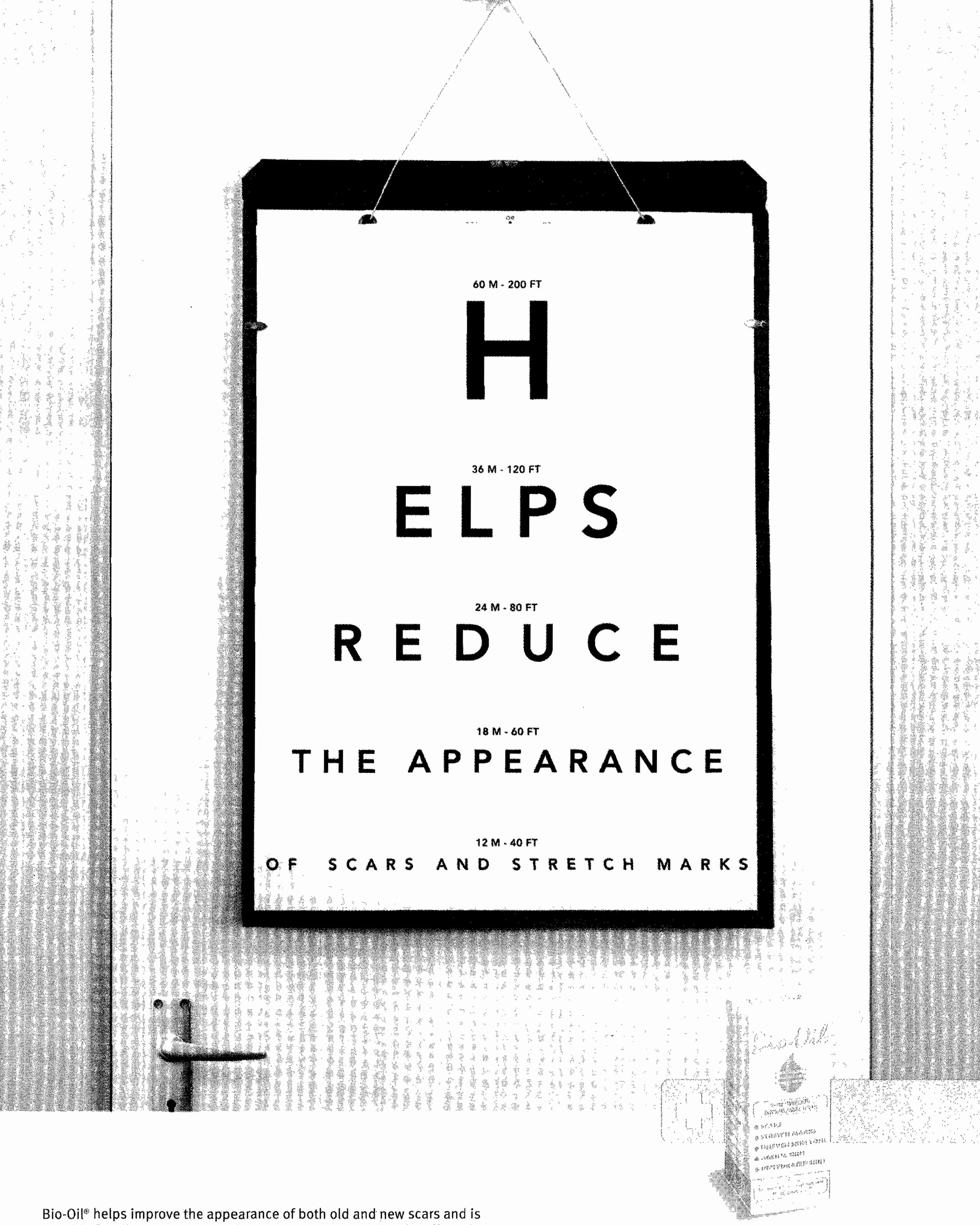

60 M - 200 FT
H
36 M - 120 FT
ELPS
24 M - 80 FT
REDUCE
18 M - 60 FT
THE APPEARANCE
12 M - 40 FT
OF SCARS AND STRETCH MARKS

Figure 2

Follow-up pattern for the various BMI categories

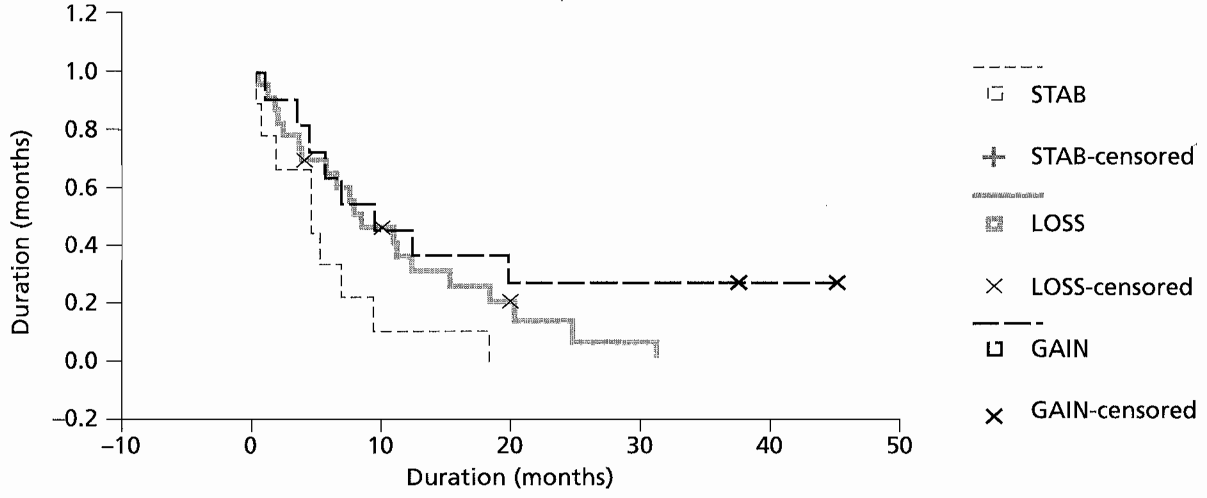


Table 5

Univariate analysis of pre-operative variables and BMI changes

Variable	P-value	Significance
Preoperative age group (<60 years>)	0.5161	N/S
Sex	0.8201	N/S
Symptom duration <six months, 6-12 months, >12 months	0.5612	N/S
Initial BMI (underweight, normal and overweight)	0.0413	Significant
Haemoglobin range <10 gm%, 10-15 gm% and >15 gm%	0.587	N/S
Histology. Squamous cell carcinoma (well vs. moderately and poorly differentiated)	0.7734	N/S
Serum albumin high(>52), normal (51-32) and low (<32)	0.4859	N/S
Serum protein high (>82), normal (81-63) and low (<63)	0.3778	N/S
Resected margins free of tumour. Resected margins free vs. not free of tumour	0.8449	N/S

NS = Not Significant

All the selected variables with the exception of preoperative BMI, showed no statistically significant relationship with the weight change pattern for this study population. Like for the student t-test, the BMI showed a significant difference using the Chi square test (Table 5).

DISCUSSION

Late presentation of patients with oesophageal carcinoma is a big problem within the developing world where the infrastructure is not supportive to immediate medical attention, consequently a significant number of patients are first seen when the disease is already advanced and frank cachexia has set in.

The multiple factors of nutritional, endocrine, immunological and metabolic factors mediated through the pro-inflammatory cytokines as well as other mediator components differentially contribute to the aetiology of the malignant cachexia (5,6). A suggestion that an increase in resting metabolic rate (BMR), is also a contributory factor for the cachexia has not been born out in caloric tests (7). These tests show the BMR to be the same for patients with oesophageal malignancy and normal subjects when expressed as energy per kilogram of fat free mass.

This study population presented with a low mean initial preoperative weight of 50.4 kilograms, (BMI of 19.4kg/m²), compared to similar studies from the developed world, with examples of preoperative weights of 70kg or more in some studies or a preoperative BMI of 24.2 + 2.8 kg/m² from one Australian study (8- 11). Sixty three percent of the study patients were underweight preoperatively.

From The World Health Organisation Global InfoBase, the mean BMI for males and females above 15 years of age in Kenya in 2002 were 20.5 and 22.1 kg/m² respectively (12).

Poverty, late presentation for treatment, and a low national BMI each have some contribution to play towards the low comparative preoperative weight pattern observed.

It has been demonstrated that obesity is associated with the subsequent development of oesophageal adenocarcinoma; hence patients with adenocarcinoma will tend to have a higher initial body mass compared to their squamous cell carcinoma counterparts' (2). This may also contribute towards explaining the fact that in the developed world where adenocarcinoma predominates, their average weight at initial presentation is more than would be anticipated in this part of the world (13).

Within the international literature there is a scarcity of literature on weight change patterns post oesophagectomy. However the general pattern of weight loss seen in this study was noted to be similar to a few studies available. In these papers similarly, the majority of the weight loss occurred within the first few months and thereafter the rate of weight loss ceases and even reversed with gains noted after one to three years postoperatively but rarely exceeds preoperative weight (8,10,14,15). This latter pattern was not however noted in this study and the majority of our patients showed a general continued loss of weight. Poor prognostic signs associated with the pattern of postoperative weight change include a continued weight loss after six months (16). A very small number of the patients within our study developed recurrent dysphagia secondary to either benign or malignant stricture.

So why is there a continued weight loss post operatively in our patients despite restored nutritional intake?

Postoperative stress associated with surgical trauma is a major contributory factor to the immediate postoperative weight loss with associated increased cytokines, heightened metabolic and immune responses. This effect on weight change is more severe the greater the trauma, as demonstrated through comparison of thoracoscopic oesophagectomy (less trauma), over standard transthoracic oesophagectomy (17).

After three months the effects associated with surgical stress should have worn off allowing the commencement of restoration of preoperative body weight. Yu *et al* (16) demonstrated that post gastrectomy weight loss in the first six months had no correlation with the prognostic outcome; while weight loss continuing into the second six months had a poor prognostic impact on survival. This poor prognostic outcome was however a direct result of variables like serosal tumour invasion and nodal metastasis being present. For all our patients no preoperative staging of the disease was performed however, on average patients at this institution tend to present late and on average are operated six months after they are first seen in the clinic where the majority have dysphagia of grade three to four (18). By this stage most patients are likely to have stage three and four tumour.

Another possible explanation is the preoperative chemical mediators of weight loss may still be present or changes in other mediators come into play. For example, a reduction in the level of serum ghrelin and lectine levels following oesophageal surgery affect the postoperative weight pattern. These hormones work through reduction of appetite amongst other mechanisms (14,19). Indeed, this complaint of lack of appetite in the postoperative patient population within this study was very common requiring nutritional education. Return to normal levels took up to three years postoperatively. Similar post oesophagectomy loss of appetite has been documented in other studies with up to 50–70% of patients reporting appetite loss (9). Dumping and diarrhoea are an added complication compromising adequate nutritional intake; we however noted these complications in very few patients.

Whether the gastric absorption rate is affected post oesophagectomy in the same way as occurs in partial gastrectomy is not clear. In relation to maintaining near normal gastric function, the vagal sparing oesophagectomy seems to show promising results in terms of maintenance of postoperative weight (20). Not only are the anatomical relationships maintained but gastric reservoir functions and production of digestive juices are as normal. However the role of this procedure in advanced disease with significant preoperative weight changes like in our patients will still need to be evaluated.

The main assumption to the above argument assumes for all patients the daily caloric requirements are restored to normal. Unfortunately adequacy of nutritional intake was not quantified in this study as in other studies which documented the adequacy of caloric intake. Assessment of the caloric intake compared to the daily requirements and the effects this may have on the study results is an important factor that was omitted and needs to be evaluated.

Patients who exhibited an increase in BMI through the study period showed the best survival pattern. This is probably consistent with restoration of adequate nutritional intake and removal of factors related to malignant cachexia. An interesting observation derived from our study suggests that patients maintaining a stable post operative weight on the other hand fell off faster to follow up. What is not clear is if these represent true deaths or if they are composed of patients who just felt better and therefore ceased to come for follow up compared to those loosing weight as they, the latter, did not improve and tended to have a reason to come for follow up.

Analysis of the various selected preoperative variables showed no variable to be significantly associated with eventual weight change. For gastric resection where more data is available, stage of the disease and extent of gastric resection were significantly associated with the postoperative weight pattern (16). Clinical staging and biochemical variables are probably more relevant in the evaluation of postoperative weight change than the selected variables.

In addition to patient selection, the role of medical management through drug intervention of the inflammatory response has shown some promising results in various human and animal studies in maintaining a stable weight postoperatively (21). The role of this mode of intervention may play a role in improving weight gain and collaboration with clinical biochemists is a useful first line of approach. However it should be pointed out not all such interventions produce equally good results and the selection of medication is important, however some studies demonstrated no benefit in using anabolic steroids for example (15).

As the overall prognosis of oesophageal cancer is poor, identification of variables relevant to improved postoperative quality of life would be useful in the selection and planning of surgery as well as identifying postoperative patients at risk.

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