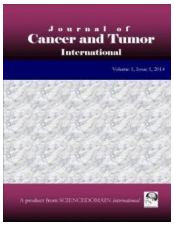

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Do pathologists thoroughly Evaluate the Greater Omentum Following Gastrectomy for Malignancy: an Audit Based on Histopathology Reports

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Authors' contributions

This work was carried out in collaboration between all authors. Author OT designed the study as part of master of surgery degree, did literature search, developed the protocol, collected data, performed the initial data analysis and reviewed the manuscript. Author JK was involved in data analysis, statistical analysis, drafting of the manuscript, review of the manuscript and preparation for submission. Author CJK was involved during protocol development as a co-supervisor, data collection, review of the manuscript. Author MJH was involved during protocol development as a co-supervisor, data collection and review of the manuscript. Author TEL was involved in conception of the idea, protocol development, data collection, writing and review of the manuscript and preparation for submission. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Milky spots in greater omentum are primary sites for seeding of exfoliated cells from intra-abdominal malignancies. Surgery is the mainstay of treatment of gastric adenocarcinoma and the greater omentum is usually resected en-bloc.
Aim: To study the histopathological profile of gastric malignancies and to determine if pathologists routinely analyze the greater omentum submitted following gastrectomy.
Methods: An audit of histopathology records of patients who had gastric malignancies between 2008 and 2012 was undertaken. Data retrieved included patients' demography, tumour site, tumour histology and subtypes, Helicobacter pylori status, associated gastritis, types of gastrectomy and; analysis and finding of omental deposits.
Results: 325 records were found of which 76.6% were adenocarcinomas. The overall male to female ratio of patients was 192:133 and their average age overall was 59.0 years (range: 23102 years). The average age of patients who had adenocarcinoma was 60.2 years. Around 8.8% of patients who had adenocarcinoma were younger than 40 years.
Gastric resection was performed in 23.1% adenocarcinomas of which 9.1% was stage I based on final histology. The greater omentum was part of specimen in 46.6% cases but report regarding cancer deposits was specified in 25.9% of which 11.1% were positive.
Conclusion: Pathologists do not routinely analyze and report findings on the greater omentum of patients who had gastrectomy for cancer. It potentially leads to under-staging. Analysis of the greater omentum for cancer cell deposits should be incorporated into the standard pathology reporting template for gastric cancer following curative gastrectomy.

Keywords: Gastric cancer; greater omentum; milky spots; cancer deposits.

1. INTRODUCTION

Adenocarcinoma, gastrointestinal stromal tumour (GIST) and lymphoma are the three most common malignant tumours of the stomach. Surgical resection is the mainstay of treatment of adenocarcinoma and GIST. The goal of surgery for adenocarcinoma is to obtain cancer free resection margin, which is achieved by performing subtotal or total gastrectomy and appropriate lymphadenectomy; if it is necessary.

Metastases to certain sites in patients with gastric adenocarcinoma are difficult to detect during pre-operative staging investigations [1-11]. These sites include the peritoneum, transverse mesocolon, sub-centimeter liver metastases or metastases near the dome of the diaphragm or in the greater omentum [10].

The greater omentum was erroneously considered a lymph nodes bearing structure until recently [12,13]. Currently however, finding of cancer deposit(s) in the greater omentum implies stage IV disease [10,14,15]. Omentectomy is routinely included during curative resection even if it is not grossly involved to eliminate potential micro-metastases [16,17].

The greater omentum is the first site for trans-peritoneal spread of exfoliated cancer cells from a transmural tumour or cells shed during gastrectomy. Identification of cancer deposits in the greater omentum is reported to be tedious and exceedingly difficult. Pathologists rely on visual inspection and/or palpation of the greater omentum which may only identify deposits when they have reached a size of at least 3-5 mm in diameter or random survey of four quadrants of submitted specimen of greater omentum. Detailed evaluation of the greater omentum such as the use of fat filtration method is rarely practiced as it is tedious [15]. Real time RT-PCR for CEA to detect cancer deposits in early gastric cancers is not freely available and thus infrequently relied on [18]. The aim of the study was to study the histopathological profile of gastric malignancies and to determine if pathologists routinely perform histopathological analysis of the greater omentum submitted following curative gastrectomy.

2. MATERIALS AND METHODS

2.1 Methods

The study was based on an audit of histopathology records of the National Health Laboratory Services of the Republic of South Africa of all patients who were diagnosed with

gastric malignancies at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Academic Hospital (CHBAH) from January 2008 to December 2012. Data retrieved included patients' demography, tumour site, tumour histology and subtypes, Helicobacter pylori status, associated gastritis, type of gastrectomy and presence of cancer deposits in the greater omentum. The Lauren classification and TNM staging system were used to classify and to stage the tumour.

Data were entered into Microsoft Excel spreadsheet and imported into STATA vs 11 (statistical software) for analysis purposes. For summary of categorical variables data were reported as frequency and percentages whereas the mean with standard deviation or median with range was used to summarize continuous data. Frequency tables, pie charts and bar graphs were used when appropriate.

3. RESULTS

Records of 325 patients who had gastric malignancies were found and majority were adenocarcinomas (249/325) 76.6% (Fig. 1). The overall male to female ratio of patients was 192:133 and the average age was 59.0 years (range: 23-102 years). The average age of patients who had adenocarcinoma was 60.2 years (Fig. 2). The intestinal and diffuse subtypes of adenocarcinoma were diagnosed in 35.3% (88/249) and 21.3% (53/249), respectively (Fig. 3). The median age of patients who had diffuse gastric carcinoma, signet ring and intestinal types were 50.5 years (range: 26-84 years), 63 years (range: 27-90 years) and 64 years (range: 24-88 years), respectively. Around 8.8% (22/249) of patients who had adenocarcinoma were younger than 40 years. Chronic gastritis was a concurrent finding in 53.0% (132/249) and 12.0% (30/249) were histologically positive for Helicobacter pylori (*H. pylori*) (Table 1).

Gastric resection was performed in 62 of the patients of which 58 were adenocarcinomas. Only 23.1% (58/249) of adenocarcinomas therefore had some form of gastrectomy. Around 9.1% (5/58) of resected adenocarcinoma cases were stage I disease and 30.9% (17/58) had stage IV cancer (Table 2).

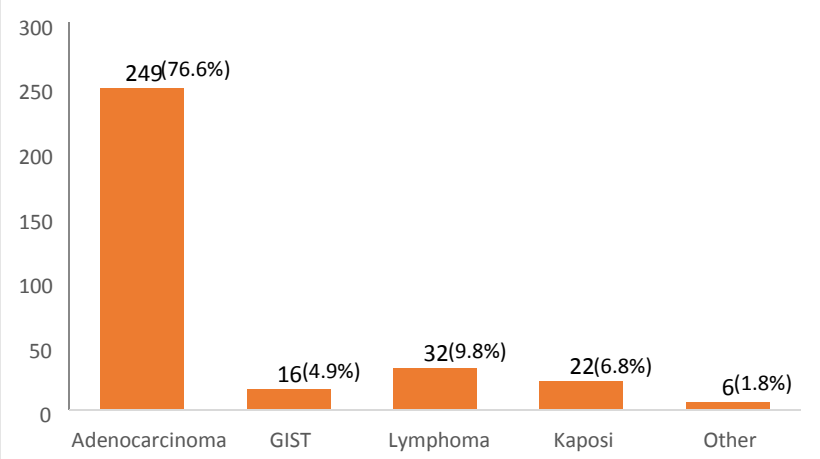

Fig. 1. Number of patients with various gastric malignancies, N (Total) = 325

Table 1. Comparison of clinical, treatment and histological findings in gastric malignancies (N=325)

Parameter	Adenocarcinoma (n=249)	GIST (n=16)	Lymphoma (n= 32)	Kaposi (n=22)
M:F Ratio	158:91	5:11	14:18	13:9
Average age	60.2 years	62.6 years	46.6 years	39.7 years
HIV positive (%)	4 (1.6%)	0 (0%)	12 (37.5%)	18/22 (81.8%)
Gastrectomy	58 (23.1%)	2 (12.5%)	0 (0%)	0 (0%)
Gastritis	132 (53.0%)	5 (31.3%)	5 (15.6%)	14 (63.6%)
H-pylori	30 (12.0%)	0 (0%)	4 (12.5)	0 (0%)

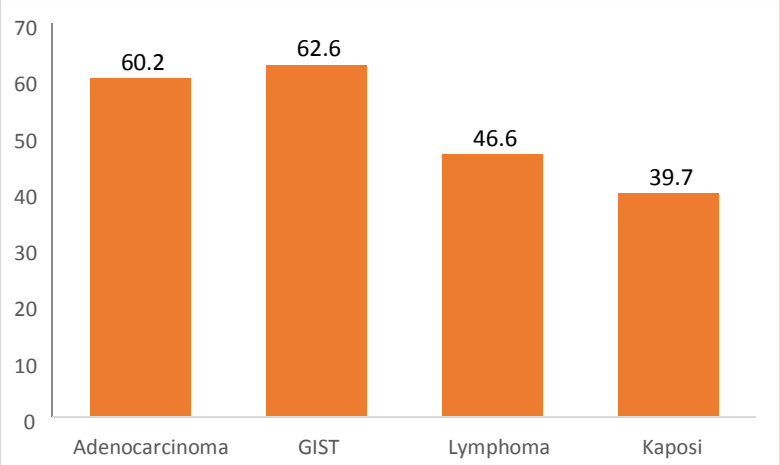

Fig. 2. Average age of patients with various gastric malignancies in years

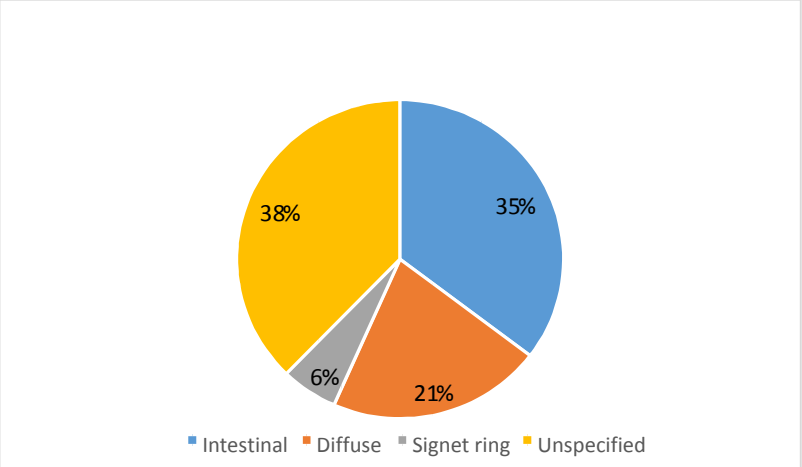

Fig. 3. Breakdown of adenocarcinomas according to histological subtypes

Table 2. Breakdown of adenocarcinomas which were resected according to stage (n=58)

Stage	Number (%)
Stage I	5 (8.6%)
Stage II	16 (27.6%)
Stage III	16 (27.6%)
Stage IV	18 (31.0%)
Unspecified	4 (6.9%)
Total	**58 (100%)**

The greater omentum was noted to have been submitted as part of tissue block and evaluated by the pathologists in (27/58) 46.6% of the specimens. However report regarding cancer deposits in the greater omentum was only recorded in (7/27) 25.9% of which (3/27) 11.1% had cancer deposits. For details of patients who had status of greater omentum reported see Table 3.

4. DISCUSSION

Adenocarcinoma is the commonest malignant tumour of the stomach and it affects patients above the age of 60 years unlike in Nigeria [19] and Iran [20] where it is commonly diagnosed in individuals in their 5th decade of life. Similar to what has been reported, majority of patients affected by gastric adenocarcinoma in the current study were males and the intestinal subtype was the most prevalent subtype of gastric adenocarcinoma [21,22]. Although GIST

Table 3. Details of patients who had histological status of the greater omentum reported

Case	Gender	Age	Subtype	Differentiation	T status	Deposit
1	M	49	Diffuse	Moderate	T3	Yes
2	F	66	NS	Poor	T4	Yes
3	M	40	Diffuse	Poor	T4	Yes
4	M	80	Intestinal	Moderate	T3	No
5	M	52	Intestinal	Moderate	T1	No
6	M	66	Intestinal	Moderate	T4	No
7	F	64	Intestinal	Moderate	T2	No

NB: In one record omental deposit was reported as representing lymph node metastasis

and lymphoma are supposed to be the next most common malignancies of the stomach [21,23], in this study cases of Kaposi's sarcoma were almost twice more common than GISTs.

Close to 10% of gastric adenorcarcinomas were in patients who were less than 40 years old, the so called early onset cancer. Matley et al. [24] in a study of patients with gastric cancer at Groote Schuur Hospital in South Africa found that 5% of their patients were younger than 35 years. An even higher incidence (23.2%) of gastric cancer in young patients was reported by Pishbijari et al. [20] in a study of gastric cancer in Tehran. The aggressive variants of adenocarcinoma i.e. poorly differentiated, diffuse and signet ring adenocarcinomas were reported in 81.8% of patients younger than 40 years in the current Study [24].

Different cut-off ages, ranging from less than 30 years to less than 45 years are used to define early onset gastric carcinoma [24,25]. A cut-off age of 40 years was preferred in the current study as it is presently used to recommend evaluation for possibility of hereditary gastric carcinoma [25,26]. We did not set the ceiling age for early onset gastric cancer at 50 years as in certain countries majority of patients are diagnosed in their fifties. Diffuse gastric adenocarcinoma as compared to intestinal type is more likely to be hereditary. Other potential causative factors of early onset gastric cancer such as H-pylori [27] in the current cohort of young patients cannot be ruled out. Another finding which mirrors previous reports is that gastric adenocarcinoma in young patients in this study was more prevalent in females [24].

Unfortunately HIV test result was not available for all patients. Patients who had Kaposi's sarcoma and lymphoma of the stomach were younger than 50 years. Both Kaposi's and lymphoma are linked with HIV infection and it is not surprising as South Africa is in the epicentre of HIV/AIDS pandemic. HIV in sub-Saharan Africa is predominately a disease of individuals who are younger than 50 years. All patients who had Kaposi's sarcoma and had traceable record of HIV test results tested positive. The above is understandable as the stomach is most commonly affected extra-cutaneous organ in patients with Kaposi's sarcoma [28]. Gastritis was an associated finding in majority of patients (63.6%) who had Kaposi's sarcoma.

Although around 23% of adenocarcinomas had gastrectomy majority of them already had advanced disease including stage IVcancer. Similar to findings elsewhere other than in East Asia where close to 70% of patients present with early gastric carcinoma, the majority of patients in the current study either had advanced or metastatic gastric carcinoma . Less than 10% of patients in this study had early gastric carcinoma. Pishbijari et al. [20] also reported low levels of early gastric cancer at presentation in Iran.

Although the greater omentum was mentioned as part of the block of tissue submitted for evaluation in 46.6% of the records, finding following histopathological analysis included the omentum in only 25.9% of cases. And, in the four cases (including a case which was reported as lymph node metastases) in which there were cancer deposits in the greater omentum the cancer was either locally advanced (T3 or T4) or stage IV.

Findings in this study suggest that pathologists do not routinely assess the greater omentum even if it is submitted following gastrectomy for gastric malignancies. It was not possible to determine predictors of omental deposits in the current study as pathologists did not report pathological findings in majority of specimens submitted; even in T4 cancers from which shedding-off of malignant cells is more likely. It is highly likely that not analyzing and reporting findings in some cases where the greater

omentum was provided might have led to under-staging of the cancer. Results following analysis of the greater omentum would potentially be of therapeutic value such as leading to consideration of hyperthermic intraperitoneal chemotherapy (HIPEC) if cancer deposits were found, and is also of prognostic value [15].

Although removing the greater omentum has been proven not to be beneficial and actually harmful in early gastric cancer, the same cannot be said in cases where the cancer is transmural i.e. T3 and T4 [16]. The greater omentum acts like a magnet for spontaneously exfoliating cancer cells or cells which broke loose during resection [29,31,32]. One of the reasons why the greater omentum is attractive to exfoliated cancer cells in the peritoneal cavity is its reach blood supply, especially in the areas where there are aggregates of immune cells, the so called milky spots [30,32]. The milky spots are able to sustain viability of exfoliated cancer cells until implantation. The homing phenomenon is enhanced by caloric rich environment provided by abundant adipocytes found in the greater omentum and vascular endothelial growth factor (VEGF) elaborated by its mesothelial cells [33].

The greater omentum of patients who have gastric cancer of Stage 1B or greater is likely to be harboring cancer cells and therefore necessitate a thorough histopathological evaluation. Unfortunately targeted histological assessment of greater omentum is not part of standard reporting format of post gastrectomy specimen of gastric cancer [35]. If the greater omentum is not thoroughly assessed it is highly probable that metastases could be missed which would lead to under-staging of the cancer and thus wrong prognostication [34]. The reported difficulties regarding histological assessment of greater omentum evaluation may be ameliorated by focusing on the milky spots where cancer deposits are likely to be found.

The major limitation of this study is that it was a retrospective study. Some records regarding histological subtypes of adenocarcinoma, HIV and H.pylori status, associated gastritis and definitive treatment were not found. It is therefore not possible to reach a definitive conclusion regarding the stage and resectability of gastric malignancies at presentation. Neither is it possible to provide a robust comment on the association between H.pylori infection, gastritis and HIV with adenocarcinoma of the stomach in South Africa.

5. CONCLUSION

Adenocarcinoma is the commonest malignant tumour of the stomach and is a disease of individuals above the age of 60 years. Kaposi's sarcoma should be considered in HIV positive individuals presenting with gastric tumour and are younger than 50 years. Majority of patients with gastric malignancies do not undergo gastrectomy. Pathologists do not routinely assess and/or report pathological findings in the greater omentum following gastrectomy which potentially leads to under-staging. As the greater omentum is a magnet for exfoliated malignant cells, its thorough assessment should be incorporated into the standard pathology reporting template following curative gastrectomy.

6. RECOMMENDATION

Assessment of greater omentum should be incorporated into the standard pathology reporting format following gastrectomy. Omentum preserving gastrectomy should not be offered to patients who have potentially curable gastric adenocarcinoma in a setting where majority of patients present with advanced disease.

CONSENT

Receiving informed consent from each patient was waived as the study was retrospective and based on histopathology records.

ETHICAL APPROVAL

The study was conducted as part of partial requirement of a Master of Medicine in Surgery (MMed degree) for the first author. Approval to conduct the study was received from the Human Ethics Committee of University of the Witwatersrand (M121104) and, Research Review Boards of Charlotte Maxeke Johannesburg Academic and Chris Hani Baragwanath Academic Hospitals. Permission to access histopathology records was obtained from the Head of Department of Anatomical Pathology of the National Health Laboratory Services of the Republic of South Africa. All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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