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Review

In patients with radiologically-staged resectable oesophago-gastric junctional tumours, is diagnostic laparoscopy useful as an additional staging procedure?

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ABSTRACT

A best evidence topic in surgery was written according to a structured protocol. The question addressed was in patients with oesophago-gastric junctional tumours which have been radiologically-staged as potentially resectable, is diagnostic laparoscopy useful as an additional staging procedure. 292 papers were found using the reported search, of which 5 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group, study type, relevant outcomes and results of these papers are tabulated. We conclude that as an additional tool following radiological staging of oesophago-gastric junctional tumours, diagnostic laparoscopy does appear to detect previously occult peritoneal metastases as well as liver metastases and lymph nodes and these findings do in turn lead to changes in management in over ten percent of patients. The procedure is however associated with some morbidity and its efficacy in changing management in the era of routine PET scanning remains to be evaluated.

1. Introduction

A best evidence topic was constructed according to a structured protocol as described in a previous publication.[1]

2. Clinical scenario

You are at a multi-disciplinary team meeting discussing a patient with a biopsy-proven oesophago-gastric junctional (OGJ) tumour. He has undergone computed tomography (CT) of the chest and abdomen and endoscopic ultrasound (EUS) which have staged him as a T3N1M0 adenocarcinoma. He is physiological fit for oesophagectomy however it is suggested that he undergo diagnostic laparoscopy prior to consideration for resection. You resolve to check the literature to ascertain whether diagnostic laparoscopy after radiological staging of OGJ tumours adds useful staging information prior to resection?

3. Three-part question

In patients with radiologically-staged resectable disease undergoing an oesophagectomy for an OGJ tumour, does laparoscopy provide useful additional staging information?

4. Search strategy

Medline 1966 to January 2011 using the OVID interface for the terms:

[staging] AND [laparoscopy] AND [oesophago-gastric] OR [oesophageal] AND [cancer].

5. Search outcome

292 abstracts were found using the reported search. Using the criteria outlined in a previous publication,[1] we selected only those papers which to directly assess the impact of laparoscopy on staging and operative management. This yielded five papers which provided the best evidence to answer the clinical question.

6. Results

The results of the five papers that provided the best evidence to answer the question are summarised in Table 1.

7. Discussion

Despite improvements in the management of oesophageal cancer long-term survival following surgical resection remains poor. Part of the reason for this lies in the fact that many of the patients undergoing resection have occult advanced disease at the

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Table 1
Best evidence papers.

Author, date and country	Patient group	Study type and level of evidence	Outcomes	Key results	Comments
Heath et al, (2000), [5] USA	59 patients with biopsy-proven oesophageal cancer over a 54 month period All had good performance status and were fit to undergo oesophagectomy All patients who were candidates for curative treatment after EUS and CT staging and then underwent diagnostic laparoscopy and lymph node biopsy	Level IV Retrospective Study	Changes to Staging	**9 of 59 (15%)** **Liver Metastases:** 2 liver metastases detected **Regional Lymph Nodes:** 1 patient with radiologically diagnosed node negative disease was in fact positive for tumour and upstaged. 2 patients with radiologically diagnosed node-positive disease were in fact negative for tumour and downstaged. **Non-Regional Lymph Nodes:** 2 patients with radiologically diagnosed coeliac node disease were tumour negative and were downstaged. No patient was upstaged **Peritoneal Metastases:** 3 peritoneal metastases detected (1also had a liver metastases)	This was a small, well-conducted study looking only at patients radiologically staged using EUS and CT undergoing a diagnostic laparoscopy and where technically possible lymph node biopsy (achieved in 75% of cases). It demonstrated a change in management in 17% of cases. In the majority this was due to laparoscopy detecting serosal spread into the stomach, necessitating a change in operative strategy as opposed to changes in TNM stage. In addition 7% had occult peritoneal or liver metastases detected by DL alone. With respect to lymph nodes, DL and biopsy resulted in downstaging of non-regional lymph nodes in 2 patients and upstaging of 1 patient with regional lymph nodes.
			Change to management	**10 of 59 (17%)** 6 of 10 diagnosed with extension to the gastric serosa and therefore did not undergo oesophageal resection. 4 of 10 diagnosed with M1 disease and did not undergo resection (as detailed above)	It should be noted that staging laparoscopy was associated with significant morbidity.
			Complications	**Mortality: 0 of 59 (0%)** **Morbidity: 2 of 59 (3%)** 1 case of small bowel perforation requiring laparotomy and small bowel resection 1case of intra-operative pulmonary oedema from previously undiagnosed aortic valve stenosis.	
Bonavina et al. (1997), [6] Italy	50 patients consecutively enrolled with distal oesophageal and gastric cardia tumours over a 13 month period 36 patients with biopsy proven adenocarcinoma of the cardia 14 patients with squamous cell carcinoma of the lower third of the oesophagus All patients had been investigated with CT scan and US and underwent diagnostic laparoscopy at the same sitting as planned surgical resection	Level IV Retrospective Study	Changes to Staging	**5 of 50 (10%)** **Liver Metastases:** 1 patient with a liver metastases detected on CT/US in fact had a haemangioma detected at DL and subsequently underwent resection **Regional Lymph Nodes:** Not commented on **Non-Regional Lymph Nodes:** 2 patients with node negative coeliac disease on imaging were upstaged at DL (however in 1 of these patients it did not affect management) **Peritoneal Metastases:** 3 patients had previously undetected peritoneal carcinosis (1 of whom also had a non-regional lymph node involvement diagnosed at DL)	This study included both distal oesophageal and gastric cardia tumours. As part of their pre-operative radiological staging this study used both CT and ultrasound of the abdomen (but not EUS). 5 patients underwent changes in staging due to DL- 1 was downstaged, 1 was upstaged to M1a disease, 2 was upstaged to M1b and 1 was upstaged to both M1a and M1b disease Management was changed in a total of 5 patients- 4 for oncological reasons and in 1 for case non-oncological reasons In addition to evaluating the role of DL as an adjunct to radiological staging, this study also looked at DL in isolation. In comparison to CT or US, DL was: 1) more sensitive and specific for the detection of lymph node metastases 2) more sensitive for the detection of peritoneal and liver metastases
			Change to Management	**5 of 50 (10%)** 4 patients underwent changes in management due to changes in staging; 1 was diagnosed with advanced liver cirrhosis and deemed unfit for resection	
			Complications	Mortality: 0 of 50 (0%) Morbidity: 1 of 50 (0%)	

(*continued on next page*)

Table 1 (*continued*)

Author, date and country	Patient group	Study type and level of evidence	Outcomes	Key results	Comments
				This patient had moderate bleeding from manipulation of a liver haemangioma	
Romijn el al., (1998), [7] Netherlands	60 consecutive patients with biopsy- proven cancer of the oesophagus (40) or gastric cardia (20) over a 27 month period were included All patients had been staged using: US of abdomen and supraclavicular region; CT chest and abdomen and EUS Those with curative disease were put forward for DL and staging laparoscopic ultrasound	Level IV Retrospective Study	Changes to Staging	**5 of 60 (8%)** **Liver Metastases:** 1 in 60 **Regional Lymph Nodes:** Not commented on **Non-Regional Lymph Nodes:** None found on diagnostic laparoscopy but 5 patients with radiologically staged node negative disease were shown to have node positive disease using laparoscopic ultrasonography **Peritoneal Metastases:** 4 in 60	This study concluded that diagnostic laparoscopy had a minor effect on the staging of oesophageal cancer but was more effective in staging of gastric cardia tumours. The paper also looked at the role of laparoscopic ultrasonography in conjunction with DL and concluded that the addition of LUS resulted in an increased detection of coeliac lymph nodes and liver metastases.
			Change to Management	5 of 60 (8%) DL itself led to upstaging and hence the abandonment of resection in five cases as detailed above. All of these cases were in gastric cardia tumours. As a consequence of laparoscopic ultrasound as opposed to DL itself, an additional five cases of coeliac lymph node involvement and two cases of liver metastases were detected.	
			Complications	Mortality: 0 of 60 (0%) Morbidity: 0 of 60 (0%)	
Heath et al, (2000), [5] USA	59 patients with biopsy-proven oesophageal cancer over a 54 month period All had good performance status and were fit to undergo oesophagectomy All patients who were candidates for curative treatment after EUS and CT staging and then underwent diagnostic laparoscopy and lymph node biopsy	Level IV Retrospective Study	Changes to Staging	**9 of 59 (15%)** **Liver Metastases:** 2 liver metastases detected **Regional Lymph Nodes:** 1 patient with radiologically diagnosed node negative disease was in fact positive for tumour and upstaged. 2 patients with radiologically diagnosed node-positive disease were in fact negative for tumour and downstaged. **Non-Regional Lymph Nodes:** 2 patients with radiologically diagnosed coeliac node disease were tumour negative and were downstaged. No patient was upstaged **Peritoneal Metastases:** 3 peritoneal metastases detected (1also had a liver metastases)	This was a small, well-conducted study looking only at patients radiologically staged using EUS and CT undergoing a diagnostic laparoscopy and where technically possible lymph node biopsy (achieved in 75% of cases). It demonstrated a change in management in 17% of cases. In the majority this was due to laparoscopy detecting serosal spread into the stomach, necessitating a change in operative strategy as opposed to changes in TNM stage. In addition 7% had occult peritoneal or liver metastases detected by DL alone. With respect to lymph nodes, DL and biopsy resulted in downstaging of non-regional lymph nodes in 2 patients and upstaging of 1 patient with regional lymph nodes. It should be noted that staging laparoscopy was associated with significant morbidity.
Krasna et al., (2002), [8] USA	111 patients with pathologically proven oesophageal cancer over a 96 month period 53 Squamous Cell Carcinomas, 54 adenocarcinoma, 2 small cell carcinoma, 2 poorly differentiated carcinoma All had been radiologically staged using USS and CT. In addition 85 had EUS and 59 underwent chest and abdominal MRI. A total of 76 patients underwent DL (67 had DL and Thoracoscopy, 9 had DL alone) 35 had Thoracoscopy alone	Level IV Retrospective Study	Changes to Staging	**21 of 76 (28%)** **Liver Metastases:** 2 of 76 **Regional Lymph Nodes:** 3 patients with node-negative regional disease on imaging were upstaged at DL **Non-Regional Lymph Nodes:** 16 patients with node-negative coeliac disease on imaging were upstaged at DL **Peritoneal Metastases** Not discussed in this paper	This study uses a bi-modal minimally-invasive approach to surgical staging. With reference to the findings on laparoscopy alone, it demonstrates the value in DL as far as re-staging cancers and discusses the usefulness of visualising the peritoneum directly in the detection of metastases. The study does not specify the site at which the unexpected lymph nodes were found The paper also discusses the relative sensitivities and specificities of thoracoscopy and laparoscopy.

Table 1 (*continued*)

Author, date and country	Patient group	Study type and level of evidence	Outcomes	Key results	Comments
de Graff et al., (2007) [4], UK	416 patients with oesophago-gastric cancer referred to two UK hospitals over a 60 month period were included. All patients had been assessed as fit for surgery with curative intent based on staging CT and EUS in 48 patients, CT alone in 337 patients and abdominal USS only in 31 patients. Diagnostic laparoscopy was then performed to assess resectability of the tumour.	Level IV Retrospective Study	Change to Management	**18 of 76 (24%)** As detailed above	This was a retrospective study analysing patients with oesophageal and gastric cancers. undergoing DL following radiological staging. They showed that DL led to changes in management in 20% of cases. In addition, of those deemed resectable at DL, 27 (8.1%) were subsequently found to be unresectable at laparotomy based on locally advanced disease (16) or undetected metastases (11). Although this was a large scale study, it should be noted that the cohort had undergone non-standardised radiological staging for their tumours.
			Complications	Mortality: 0 of 76 (0%) Morbidity: 0 of 76 (0%) 1 laparoscopy was aborted due to peritoneal adhesions	
			Changes to Staging	**89 of 416 (21%)** **Liver Metastases:** 18 patients were found to have liver metastases not diagnosed radiologically. **Regional Lymph Nodes:** Not stated in the paper **Non-Regional Lymph Node Involvement:** 4 patients were upstaged based on previously undiagnosed non-regional lymph node involvement. **Peritoneal Metastases:** 50 patients were found to have undiagnosed peritoneal metastases	
			Changes to Management	**84 of 416 (20%)** 63 patients had metastases (13 with liver metastases, 45 with peritoneal disease and 5with both); 4 had non-regional lymph node involvement and 17 had locally advanced disease	
			Complications	Mortality: 0 of 416 (0%) Morbidity: 0 of 416 (0%)	

time of surgery. As a consequence of this there has been increased focus on accurate pre-operative staging of oesophageal cancers to detect non-regional lymph node involvement, peritoneal disease and distant metastases in order to prevent futile surgery on patients with non-surgically curable disease. Over the last twenty years there has been increasing use of CT and EUS as routine pre-operative staging modalities for oesophageal cancer.[2] Diagnostic laparoscopy (DL) is a well-established procedure in its own right for staging a number of intra-abdominal cancers and has been shown to be useful in detecting lymphadenopathy, peritoneal and liver metastases.[3]

With respect to the efficacy of DL as an adjuvant staging therapy following radiological staging of tumours, the earliest study was performed by Bonavina et al.[6] who analysed a cohort of patients with distal oesophageal and gastric cardia tumours who had been staged radiologically using CT and ultrasound. These patients underwent a staging laparoscopy and if this was clear proceeded to oesophagectomy at the same sitting. In this study, DL changed the treatment plan in 10% of patients. In addition to evaluating the role of DL as an adjunct to radiological staging, this study also looked at DL in isolation and concluded it was a more sensitive staging test than either CT or US. It should be noted however that the study did not compare DL against the combined information obtained from both CT and US and as such does not comment on the relative efficacy of DL as compared to the synergistic information from all radiological scanning.

Romijn et al.[7] conducted a study in which biopsy-proven oesophageal or gastric cardia cancer patients who had been radiologically staged using ultrasound, CT and EUS underwent DL together with laparoscopic ultrasonography (LUS). DL resulted in a change in management in 13% of their population- in all cases due to the detection of peritoneal or liver metastases. This study did not evaluate the role of DL in the detection of occult lymph node involvement; instead preferring to use LUS for this purpose. Interestingly they found that LUS was useful in the detection of occult coeliac lymph node involvement. Their overall conclusion was that DL is of little benefit in oesophageal carcinoma but had more of a role in the staging of gastric cardia tumours.

Heath et al.[5] performed a small retrospective study on patients with biopsy-proven oesophageal cancers, all of whom had undergone staging using CT and EUS. This study demonstrated that DL led to a change in treatment in 17% of their population. In the majority this was due to laparoscopy detecting serosal spread into the stomach, necessitating a change in operative strategy as opposed to changes in oncological stage- however 7% of patients had occult peritoneal or liver metastases detected by DL alone. In addition Heath et al[2] utilised DL to attempt to perform routine lymph node biopsies although this was only technically achievable in 75% of cases. This strategy of lymph node biopsy did but did lead to changes in the status of regional lymph nodes but did not lead to any change in management of the cancers. With respect to the operative procedure itself, the mean hospital stay was 2 days and there were significant complications in 2 patients. The authors did however note that DL could be used a therapeutic procedure to insert a feeding jejenostomy in the cases where the tumours were discovered to be unresectable.

Krasna et al.[8] examined 111 patients with pathologically proven oesophageal cancer; all of whom had been pre-operatively radiologically staged using CT and USS and in some cases EUS and MRI. These patients then underwent minimally-invasive staging using combined thoracoscopy and laparoscopy (in 67 patients), thoracoscopy alone (in 35 patients) or laparoscopy alone (in 9 patients). With respect to the 76 patients who underwent DL, this procedure resulted in upstaging in 21 patients- the majority being due to the diagnosis of previously occult coeliac lymph node involvement.

Although this paper does not specifically differentiate between changes in management made as a result of thoracoscopy or laparoscopy it does appear from analysing the data that DL led to changes in management in 24% of cases. They also concluded that DL itself has a higher sensitivity and specificity for the detection of lymph node involvement as compared to combined radiological staging. Although the study has a large number of patients it should be noted that the cohort was heterogeneous with regard to histological cell type and as previously discussed there was no uniform radiological staging for all patients.

The largest and most recent study on this topic was undertaken by de Graaf et al.[4] This retrospective study was conducted on 416 patients with oesophago-gastric cancer who were staged preoperatively based on CT and/or EUS or abdominal ultrasound. Diagnostic laparoscopy resulted in changes to staging 21% of the patients with 20% becoming non-operable mainly due to the diagnosis of previously undetected peritoneal carcinomatosis. It should be noted however that although this was a large- scale study, patients did not undergo standardised radiological staging and this study failed to distinguish between oesophageal, junctional and gastric tumours, choosing instead to treat them as a single cohort. In addition, there is a paucity of information on the exact findings on laparoscopy- for example 17 patients were deemed unresectable due to the presence of "locally advanced disease" but there is not information as to exactly what this term entailed.

On reviewing all of these studies, it is striking that there are that no randomised-controlled trials on the role of DL and most of the studies involved relatively small populations with significant heterogeneity with regard to the tumour location and the radiological techniques used to stage the cancers. In addition, the majority of these studies are include patients operated over a decade ago and as such pre-date the publication of the MRC study[9] on the efficacy of pre-operative chemotherapy and the introduction of routine positron emission tomography (PET) as a staging modality. Given the documented efficacy of this radiological tool in detecting occult disseminated disease,[10] it is unclear, in the era of routine neoadjuvant chemotherapy and PET, whether the finding that DL provides useful additional staging information is still applicable. Finally it should be noted that although the addition of DL does appear to be superior to radiological imaging alone in detecting occult disseminated disease, it is still associated in these studies with a false negative rate of approximately 5%.

8. Clinical bottom line

As an additional staging tool following radiological staging of OGJ tumours, diagnostic laparoscopy does appear to detect previously occult peritoneal metastases as well as liver metastases and lymph nodes. These findings in turn lead to changes in management in over ten percent of patients. The procedure is however associated with some morbidity and its efficacy in changing management in the era of routine PET scanning remains to be evaluated.

Conflict of interest
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Author contribution

Richardson- Literature search, analysis, writing.
Khan- Analysis and editing of manuscript.

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