

# Minimally invasive surgery for gastric cancer in UK: current status and future perspectives

Muhammad Shafique Sajid<sup>1</sup>, Madhusoodhana Hebbar<sup>2</sup>, Mazin E. Sayegh<sup>2</sup>

<sup>1</sup>Department of Gastrointestinal Surgery, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK; <sup>2</sup>Department of General and Laparoscopic Surgery, Western Sussex Hospitals Foundation NHS Trust, Worthing Hospital, Worthing, UK

*Contributions:* (I) Conception and design: MS Sajid, ME Sayegh; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: ME Sayegh, MS Sajid; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Mr Mazin E. Sayegh, MBChB, MSc, FRCS. Consultant Gastrointestinal & Laparoscopic Surgeon, Department of General and Laparoscopic Surgery, Western Sussex Hospitals Foundation NHS Trust, Worthing Hospital, Worthing, West Sussex, BN11 2DH, UK. Email: mazinsayegh@nhs.net.

**Abstract:** The aim of this study is to review the literature and report the various minimally invasive methods used to treat gastric cancer in the UK and compare it with worldwide practice. Published randomised studies, non-randomised studies and case series reporting the use of minimal invasive approach to treat gastric cancer were retrieved from the search of standard medical electronic databases and their outcomes were highlighted suggesting their effectiveness. Several randomised, controlled trials and meta-analyses have proven the clinical and oncological safety of the laparoscopic gastrectomy for gastric cancer. Similarly, robot-assisted gastrectomy, EMR (endoscopic mucosal resection) and ESD (endoscopic sub-mucosal dissection) have also been proven feasible and safe to treat gastric cancer of various stages in prospective and retrospective comparative studies. However, UK based studies on minimally invasive surgery to treat gastric cancer is scarce and the paucity of trials led to uncertain outcomes. Laparoscopic gastrectomy, robot-assisted gastrectomy, EMR and ESD are feasible procedures in terms of clinical and oncological safety but mainly being practiced in Asian countries with high prevalence of stomach cancer. The UK based practice is still small and limited but the introduction of MIGOCS and STOMACH trial might help to widen the application of this technique.

**Keywords:** Gastric cancer; laparoscopic gastrectomy; endoscopic mucosal resection (EMR)

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## Introduction

Gastric carcinoma is relatively prevalent malignancy and has been rated the 16<sup>th</sup> most common cancer in the United Kingdom (UK), with 2% of all new cases reported annually. Its incidence (1-6) is slightly higher in males (13<sup>th</sup> most common cancer) compared to females (15<sup>th</sup> most common cancer). The statistics of 2014 indicates that 6,682 new patients were diagnosed with gastric carcinoma with peak rate of incidence between the ages of 85-89 years (1-4). The gender based distribution of gastric cancer as per European

age-standardised incidence rate is suggestively lower for men in England compared to Wales, Scotland and Northern Ireland. As for women, the rates are significantly lower in England compared with Scotland and Northern Ireland. Female rates are also lower in Wales than Northern Ireland (1-7). Gastric cancer is the 8<sup>th</sup> and 13<sup>th</sup> most common cause of death in men and women respectively in the UK. As expected the mortality rate is higher in population with age more than 90 years. Due to the development of new diagnostic and therapeutic modalities, the mortality resulting from the gastric cancer in the UK is decreased by

the 30% in last decade (7). The overall survival from the gastric cancer is poor in the UK as well in the rest of the world. Forty-four percent males survive stomach cancer for at least one year which is projected to reduce further (20%) after five years or more (7). The overall survival rate for females is relatively lower at one year (38%) but similar at five years (18%).

The actual cost of the treatment of gastric cancer in the UK and worldwide is variable depending upon the stage of the disease and the modality of treatment such as neo-adjuvant therapies, surgical resection and adjuvant therapies. According to a study published in the *Journal of Gastrointestinal Cancer Research* (8), it costs about US \$20,100 to add chemo-radiotherapy, a combination of chemotherapy and radiation, after surgery for localized gastric cancer. According to the *American Society of Clinical Oncology* (9), the total mean monthly cost of care for a newly diagnosed gastric cancer patient, for the first year, including hospitalization, doctor visits, lab fees, radiology and drugs, was more than US \$10,600 per month. This could total almost US \$130,000 for a year. The multi-disciplinary approach of managing gastric cancer in the UK involve the utilization of services of upper gastrointestinal surgeon, gastric cancer medical oncologist, gastric histo-pathologist, radiation oncologist, nutritionist, gastric cancer care nurse specialist, palliative care team and sometimes psychiatrist/psychologist. Understandably, true cost of the treatment of gastric cancer depends upon the stage of the disease and can be immensely diverse and economically huge.

The minimally invasive surgical (MIS) procedures to treat gastric carcinoma are laparoscopic or robot-assisted partial or total gastrectomy as well as endoscopic resections in the form of endoscopic mucosal resection (EMR) and sub-mucosal dissection (ESD). MIS for gastric cancer resections is associated with multiple advantages over open resection, including reduced risk of intraoperative bleeding, quicker recovery, reduced post-operative pain, shorter hospital length of stay and quicker return to work. Numerous trials have proven that the laparoscopic and robotic-assisted gastrectomy provides equivalent surgical and oncologic outcomes to open approaches. The objective this study is to review the literature and report the use of minimally invasive surgery to treat gastric carcinoma in the UK and compare it with the worldwide practice.

## Methods

All published articles on MIS i.e., laparoscopic surgery,

endoscopic surgery and robotic surgery were identified through searches of MEDLINE, EMBASE, CINAHL, Cochrane library and PubMed databases. The search terms “minimally invasive surgery”, “laparoscopic surgery”, “key-hole surgery”, “hand-assisted laparoscopic surgery”, “robotic surgery”, “robot assisted laparoscopic surgery”, “endoscopic surgery”, “endoscopic mucosal resection”, and “endoscopic submucosal dissection” were used in combination with the medical subject headings “gastric cancer”, “gastric carcinoma”, and “stomach cancer”. The bibliography of the published relevant articles was hand searched. The “related article” function was also used to widen the search results. All abstracts, case reports, case series and published single centre or multicentre audits were retrieved and searched comprehensively. The website of AUGIS (Association of Upper Gastrointestinal Surgeons of Great Britain & Ireland) and EAES (European Association of Endoscopic Surgery) was searched to find the registries related to the gastric cancer treatment and to find if any novel MIS approach is being used to treat gastric cancer.

## Results

MIS techniques are emerging and evolving options in the management of gastric carcinoma in Europe and the UK. Although most of the existing knowledge about these MIS and its outcomes has been reported from the far eastern countries such as Japan, China and the Korean peninsula. The experience from the UK is limited and just started growing. The outcome of the standard electronic medical databases resulted in several randomised, control trials, non-randomised controlled trials, and comparative studies originating mainly from the Far Eastern world probably due to higher incidence of gastric cancer.

### *Laparoscopic surgery for gastric cancer outside UK*

Twelve randomized controlled trials (10-21) have reported clinical as well as oncological outcomes of gastric carcinoma resection comparing open technique to MIS. These trials extensively investigated the various surgical procedures depending upon the location of the gastric carcinoma such as partial gastrectomy, total gastrectomy, sub-total gastrectomy and various levels of nodal dissection. Based upon the findings of these trials, the laparoscopic gastrectomy for gastric carcinoma performed by experienced surgeons resulted in the reduction of postoperative pain. In addition, the laparoscopic gastrectomy significantly reduced

Peri-operative blood loss, analgesia requirement, post-operative morbidity, expedited recovery and shortened the length of hospital stay. However, it was at the cost of longer operative time and reduced number of harvested lymph nodes. Collectively, the survival outcome of laparoscopic gastrectomy was excellent and the procedure was found to be feasible and routinely acceptable provided the resources as well as the expertise are available. The same outcome was reported in the published systematic reviews and non-randomized as well as control studies (22-32).

European trials such as LOGICA which is a multicentre prospectively randomized controlled trial comparing Laparoscopic versus open gastrectomy for gastric cancer, aiming to randomise 210 patients from 10 Dutch centres with a similar primary outcome of postoperative hospital stay (days) and secondary outcome which include postoperative morbidity and mortality, oncologic outcomes, readmissions, quality of life and cost-effectiveness. The study started in December 2014 and will take 3 and 5 years for inclusion and follow-up respectively. It will of course be some time before the final outcome is revealed but it will be interesting to see whether results of Asian studies can be extrapolated to the western population (33). Prior to this Brenkman *et al.* looked at 277 patients who underwent minimally invasive gastrectomy between 2010 and 2014 from Netherlands Cancer Registry and concluded that with a proctoring program, the introduction of minimally invasive gastrectomy in Western countries is feasible and can be performed safely (34).

#### *Laparoscopic surgery for gastric cancer within the UK*

Most of the published studies on the MIS for gastric cancer were predominantly conducted in Asian countries (35,36), where the occurrence of gastric carcinoma is higher in comparison to the UK and other Western countries (37). The gastric cancer screening program in Japan which started more than three decades ago had led to significant improvement in the early diagnosis and more effective treatment of gastric carcinoma. Therefore, the tumour is diagnosed at a much earlier stage in Japan compared to the UK. It is challenging to translate the results of Asian studies to a Western population whereby there is no screening program, and gastric cancer is diagnosed late and at an advanced stage (38).

Minimally Invasive Gastro-Oesophageal Cancer Surgery (MIGOCS) registry which is a co-operative database for the study of MIS gastroesophageal cancer in

the UK which was set up in 2005 amongst UK surgeons. An online database was developed for data collection which included demographics, pre-operative staging and assessment, surgical intervention, post-operative course, as well as pathology and clinical outcome. The Association of Laparoscopic Surgeons (ALS), decided to sponsor the registry as part of a suite of prospective databases for MIS procedures. An agreement in principle has been reached with Covidien to fund a Registry Office. Upon establishment of the office, MIGOCS will officially change its name to the ALS Minimally Invasive Upper GI Cancer Registry, although the acronym will be retained for a transitional period (39). Fully trained UK based specialist surgeons performing laparoscopic gastrectomy were encouraged to submit their data to the registry. This was the first ever UK based multicentre registry which was also endorsed by the National Institute for Health and Clinical Excellence NICE in 2008 whereby a full guidance to the National Health Service NHS in England, Wales, Scotland, and Northern Ireland on laparoscopic gastrectomy for cancer was issued (40). NICE advised clinicians wishing to undertake the procedure to submit data to the MIGOCS database supported by the Association of Upper Gastrointestinal Surgeons (AUGIS) & ALS.

There were two studies, the first was retrospective collecting data from 1996 up to December 2006 while the second study was prospective with data obtained from December 2006 to July 2008 from centres around the UK using the MIGOCS database (41). The results of the systematic review of minimally invasive gastro-oesophageal surgery consisted in the majority of case reports, with no randomised controlled trials of oesophagectomies and 4 (low quality) randomised controlled trials of gastrectomies. It demonstrated a mortality and morbidity of 2.3% and 46.2% respectively for oesophagectomies; 0.1% and 12.7% respectively for gastrectomies.

There were 60 MIGOCS member consultant surgeons from over 40 UK centres but the retrospective study data were obtained from 7 UK centres with an overall mortality and morbidity of 6.0% and 57% respectively for oesophagectomies and 7.7% and 13% respectively for gastrectomies. While the prospective study collected data from 7 UK centres, comprising a total of 258 minimally invasive oesophagectomies and 33 minimally invasive gastrectomies. Overall mortality and morbidity were 2.5% and 56.6% respectively for oesophagectomies and 10.8% and 27.3% respectively for gastrectomies. There was a considerable variation in the CUSUM (continuous

surveillance monitoring) analysis between the centres which studied the operative time at each centre. The two larger volume centres however demonstrated an improvement in their operative time with experience, with a possible plateau at around 30 procedures.

The conclusion of the review data suggested that the minimally invasive approach is beneficial compared to open surgery in terms of reduced mortality, respiratory complications, blood loss and early return to usual activities and providing good quality of life (but not reduced hospital stay as expected.) However, the data presented in this thesis was weakened by the number of operations recorded and centres involved in the studies (41).

At the Stockholm EAES meeting in June 2008 the MIGOCS registry was offered to EU-surgeons performing minimally invasive resections and the data was supposed to be held separately but joint analysis would be possible.

Based upon the outcomes of literature search, the UK based publications and experience of laparoscopic gastric carcinoma resection are scarce but the trend towards a registry of the laparoscopic procedures, guidelines development and randomized trials comparing the outcomes between laparoscopic versus open gastrectomy is developing. A multicentre combined UK & European trial comparing surgical and oncological outcomes of patients undergoing laparoscopic versus open gastrectomy for gastric cancer (STOMACH trial) is recruiting patients at present (42) but UK based recruitment has not started yet.

#### ***Robotic surgery for gastric cancer within and outside the UK***

Although MIS for gastric carcinoma resection is a well-established technique in Asia, it needed to demonstrate at least equal clinical efficacy as well as oncological safety worldwide before wider applicability and acceptance. The lymphadenectomy associated with the gastrectomy can pose significant technical challenge to surgeons who endeavour to perform a proper and oncologically sound Laparoscopic D2 lymphadenectomy. The anatomical complexity of the vascular structures and the technical limitations of the conventional laparoscopic instrumentation can make the procedure more complex even for a well-trained laparoscopic surgeon, and can be associated with significant bleeding particularly during the dissection around the hepatic, coeliac, and splenic arteries (43). On the background of these technical challenges, the idea of using robotics seems potentially feasible. The robotic surgical system can overcome some of the inherent

drawbacks of conventional laparoscopic surgery, improving manoeuvrability and vision (43). Robot-assisted gastrectomy and D2 lymphadenectomy has been shown to be safe and promising in several prospective and retrospective studies endorsing its oncological safety. But there is paucity of a high quality randomised control trials investigating the technical advantages of robot assisted gastrectomy for gastric cancer (43-51). The UK based experience of robot assisted gastrectomy is still lacking and not reported in the medical literature yet. It is still in the early stages of infancy as the clinical commissioning policy on robotic assisted surgery for oesophago-gastric cancers was issued in July 2016 (NHS England: 16006/P).

#### ***Endoscopic approaches for the management for gastric cancer within and outside UK***

Early stage mucosal gastric carcinomas can be treated endoscopically by EMR and ESD. The value of EMR and ESD has been proven effective in the management of early gastric cancer in several retrospective and prospective cohort studies but lack of high quality randomized controlled trial remains a challenge before routine use of this approach worldwide (52-57). Considering that bleeding risk does not differ between ESD and EMR and that the perforation risk does not usually lead to life-threatening disease, therefore the benefit of ESD can outweigh the overall harm when compared with EMR with the proviso that that the ESD is performed by experienced practitioners (58). Unfortunately, the UK experience for both EMR and ESD is limited and although few endoscopists have carried out these procedures effectively and with success, they were mainly for oesophageal lesions. There is very limited published data in the medical literature regarding a wide and extensive UK practice. The author has some experience with EMR and ESD for stomach and duodenal benign and malignant lesions but the numbers are small and have not yet been published.

#### **Summary**

MIS for gastric cancer is still not widely adapted and variations in practice between continents continue to exist. Laparoscopic gastrectomy is mostly performed in Far Eastern countries such as Japan, Korea and China due to higher prevalence of gastric cancer and the presence of screening program. Laparoscopic gastrectomy for gastric adenocarcinoma is evolving in the rest of the world due to

the advent of new diagnostic and laparoscopic technologies and with improved surgical techniques and training.

Although inconsistencies exist in performing MIS for gastric cancer between the high- and low-incidence countries which undoubtedly hamper its wider application at least in the UK. There is very limited reporting and practice of MIS of gastric cancer in the UK but the basic principles of its wider and safe practice has been laid out in the form of NICE guidelines, MIGCOS registry and clinical commissioning policy for robot-assisted gastrectomy.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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