SMGroup

How Surgery Can Improve Multimodal Treatment of Gastric Cancer

Elroy Patrick Weledji[1]*

[1]Department of Surgery, Faculty of Health Sciences, University of Buea, Cameroon

***Corresponding author:** Elroy PatrickWeledji, Department of Surgery, Faculty of Health Sciences, University of Buea, Cameroon, Tel: 237699922144; Email: elroypat@yahoo.co.uk

Published Date: June 25, 2016

ABSTRACT

Surgery is the only curative therapy for gastric cancer but most operable gastric cancer presents in a locally advanced stage characterized by tumor infiltration of the serosa or the presence of regional lymph node metastases. Surgery alone is no longer the standard treatment for locally advanced gastric cancer as the prognosis is markedly improved by perioperative chemotherapy. The decisive factor for optimum treatment is the Multidisciplinary Team **(MDT)** specialized in gastric cancer. However, despite multimodal therapy and adequate surgery only 30% of gastric cancer patients are alive at 3 years. This article reviewed how surgical procedures (minimally-invasive or open) may optimize multimodal treatment.

Keywords: Gastric Cancer; Gastrectomy; Laparosopic; Open; Chemotherapy

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

INTRODUCTION

Gastric cancer represents a great challenge and requires a multidisciplinary approach in which surgery plays the main role. This is because gastric adenocarcinoma is a loco-regional disease derived from the lining mucosa and thus commonly presenting late in its natural history as locally-advanced or metastatic disease [1]. As the outcome of treatment of solid malignancy is biologically predetermined by the presence or absence of micro metastases [2]. Peri-operative chemotherapy for gastric cancer is currently the standard of care for localized gastric cancer and type II and III Gastro-Oesophageal Junction **(GOJ)** adenocarcinoma [3]. The overall 5-year survival rate for resected gastric patients remains poor due to loco-regional recurrence.Neoadjuvant/ adjuvant chemotherapy in conjunction with adequate surgery (multimodal therapy) improves outcome in gastric cancer [4]. Pre-operative chemotherapy may, increase the proportion of tumours for whom surgery is possible without surgery all treatment is palliative being directed at improving quality of life [5,6]. This paper reviewed how surgical procedures (minimally- invasive or open) can optimize multimodal therapy.

EPIDEMIOLOGY

Although the incidence has inexplicably been falling for several decades, this advanced cancer is the sixth most common and causes approximately 7,600 deaths per annum in the UK. It is the leading cause of cancer death in Japan (50,562 in 2004) [7]. The incidence of advanced gastric cancer and mortality has decreased in the last decade in Japan because of endoscopic screening and early diagnosis. Gastric adenocarcinoma are divisible into two subtypes which are distinct in their natural history and aetiology. The subtype that remains endemic in Far East, parts of S America and Eastern Europe is principally a disease of the distal stomach associated with chronic gastritis, intestinal metaplasia and atrophy of mucosa. The high incidence rates in these regions is thought to be due to continuing high rate of H. pylori infection, adverse dietary factors (nitrosamines) and genetic predisposition [8]. The increasingly occurring subtype found in Western countries is commonly found near the GOJ and is associated with significant gastritis [9]. Associated with the marked increase in incidence of GOJ cancer over the last 30 years is the downward migration of oesophagealtumours and proximal shift of gastric tumours. GOJ cancer is the fastest increasing solid malignancy of adult life in the West with an increasing incidence of 3-4% per annum [9]. Siewert and Stein proposed a classification system of GOJ cancers in an attempt to simplify the conundrum. (Table 1) [10]. However, only specialist oesophagogastric surgical centers can accurately classify the tumor of GOJ as arising in distal esophagus, gastric cardiac or sub cardinal stomach [11].

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

Table 1: Siewert's classification of GOJ adenocarcinomas[10].

Type 1	Adenocarcinoma of distal esophagus arising in Barrett's segment, which may infiltrate GOJ from above
Type 2	True junctional carcinoma of the cardia
Type 3	Subcardinal carcinoma, which may infiltrate GOJ from below

PATIENT PATHWAY AND SELECTION FOR GASTRIC SURGERY

Only 40% of early gastric cancer are associated with symptoms and 80% of gastric cancer patients present with > T1 disease. 65% patients present as advanced cancers (T3, T4), 85% have lymph node metastases and 40% are metastatic. 25% will require endoscopic, radiological or surgical procedures for haemorrhage, obstruction, pain or perforation [9]. Physical signs develop late and most commonly associated with locally advanced or metastatic disease. Evidence from studies of early gastric cancers from Japan suggests that well-differentiated cancers may metastasize more frequently to the liver and poorly-differentiated tumours to lymph nodes [5]. This may explain the high rate of local recurrence with the poorly-differentiated tumours. In all cases microscopic proof of malignancy is required. Once staging investigations are complete, the patient is discussed at the specialized MDT, to propose an individually tailored management plan [6].The primary objective of surgery is to excise the primary tumor with clear longitudinal and circumferential resection margins (R0 resection), then safely restore intestinal and biliary continuity to allow adequate nutritional intake [5,6]. The final pathological stage, following curative surgery assists in determining prognosis. Survival is significantly poorer among patients with pathological stages II, III and IV [12].

TYPES OF GASTRECTOMY AND EXTENT OF LYMPHADENECTOMY

The type of gastrectomy depends on the site of the primary tumor with the resection margin aimed at a 5cm minimum from the palpable edge of the tumor. Total gastrectomy is for the 'diffuse' (according to the Lauren classification) type tumours which are more prone to lateral spread [5,6,13]. Total gastrectomy may not be necessary for distal tumours as long as adequate staging, mapping biopsies, careful radiological review, on- table Oesophago Gastro Duodeno scopy **(OGD)** with or without frozen section are satisfactory [5,14]. Distal third cancers (tumours of the gastric antrum) will require a subtotal (80%) gastrectomy, including division of the left gastric artery and vein, and excision of regional lymphatic tissue [6]. Total gastrectomy is performed only when there is a large distal third tumor or when sub mucosal tumourin filtration is within 7-8cm of GOJ [5]. Limited gastric resections are suggested only for palliation or in the very elderly [14]. Distal pancreas and spleen is not be resected for a cancer in the distal two-third of stomach as there is no oncological advantage but increased morbidity [14]. The middle third cancers (tumours of the gastric body) often require total gastrectomy as it depends on the proximal margin of the tumor. The amount of stomach remaining below GOJ should be a minimum of 2cm. Serosa negative cancer requires 7cm margin from GOJ and serosa positive cancer requires 8cm from

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

GOJ. Smaller margins are acceptable in elderly patients especially if 'intestinal type' (according to the Lauren classification) [13,14]. Proximal third cancers are tumours of the gastric cardiac. Siewert 3 GOJ tumours may be amenable to total gastrectomy if enough proximal clearance is possible. True junctional tumours (Siewert 2) are treated with extended total gastrectomy or cardio-osophagectomy [10]. The overall aim of surgery is adequate local clearance, appropriate lymphadenectomy (formal D2 and posterior mediastinal, perioesophageal nodes) and an uncomplicated anastomosis with low morbidity [5,6,14]. *Ex vivo* proximal margin of > 3.8cm of normal esophagus (5cm *in vivo*) is associated with minimal risk of anastomotic recurrence and an independent predictor of survival. Intraoperative frozen section is standard. Splenic and hilar node resection should only be considered in patients with tumours of proximal stomach located on greater curvature/ posterior wall of stomach close to splenic hilum where incidence of splenic hilar nodal involvement is likely to be high [5,12,14]. There is marked Health - Related Quality of Life **(HRQL)** deterioration after gastrectomy, and total gastrectomy has greater long-term HRQL deficit than sub-total surgery [15,16]. However, 95% near total gastrectomy which includes complete resection of the gastric fundus and complete cardial lymphadenectomy (groups 1&2) with a little (2cm) gastric pouch has similar oncological outcome but offer best short-term results such as lower anastomotic leak rate and a better quality of life than total gastrectomy. This is because of the limited disruption of the oesophagogastric junction [17].

D1 VERSUS D2 LYMPHADENECTOMY

D1 lymphadenectomy is when all N1 nodes (peri-gastric nodes closest to primary) removed enbloc with the stomach (limited) and D2 is when all N1 and N2 (distant peri-gastric nodes and nodes along main arteries supplying stomach) are systematically removed en bloc with stomach The observation that gastric cancer commonly remained localized to stomach and adjacent lymph node corroborates the Japanese view that radical systemic D2 lymphadenectomy has an increased survival benefit [18]. Excision of the primary lesion with omenta, and N1 and N2lymph nodes can cure patients even in presence of lymph node metastasis [14,15]. Originally, to ensure full nodal clearance along the splenic artery a routine en bloc resection of spleen and distal pancreas was performed. The Western non-radical view is that more radical lymphadenectomy only gives more accurate pathological staging, rather than confer improved survival benefit. The MRC D1 *vs* D2 lymphadenectomy trial concluded in 1999 that the classical Japanese D2 had no survival benefit over D1. However D2 resection without pancreaticosplenectomy may be better than standard D1 [6,15]. The Dutch D1D2 trial 15-year results of 2010 demonstrate an overall survival in 15 years of 21% D1 and 29% D2 group. The gastric cancer-related death rate was significantly higher in the D1 group 48% *vs* D2 group 37%. Local recurrence of 22%D1 group *vs* 12% D2. Operative mortality of D2 was significantly higher 10 *vs* 4%, and complication rate 43% *vs* 25%, D2 *vs* D1. 20% of D2 group with N2 nodes were still alive at 11years; unlikely if D1 alone was performed [14]. Overall D2 has lower loco regional recurrence and gastric cancer-related death rates. It has significantly higher post-operative mortality, morbidity and reoperation rates. Spleen-preserving

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

D2-resection is recommended for resectable gastric cancer [15,19]. The current European description of D2 lymphadenectomy involves removal of >15 lymph nodes, irrespective of node stations [5,6]. Extended D3 lymphadenectomy is a more radical en bloc resection including N3 nodes outside normal lymphatic pathways from stomach, involved in advanced stages e.g. station 12 (hepatoduodenal) or by retrograde lymphatic flow due to blockage of normal pathways. There is no advantage of D3 *vs* D2, but D3 *vs* D1 showed improved overall survival [20-22]. Uptake of radical resection remains poor in the West due to relative technical difficulty of achieving nodal clearance, adiposity and lack of formalized training in systematic lymphadenectomy. Practice is likely to change as training is increasingly centralized at high volume centres with lower operative mortality and lower failure to rescue rates due to astute management of complications [11,23]. The future trend is towards lymphadenectomy being tailored to individual preoperative and operative staging, age and fitness [6,15,18].

STRATEGIES TO MINIMIZE LOCO-REGIONAL RECURRENCE

Gastric cancer is a loco-regional disease with 80% recurrence rates in patients with T4 serosal positive disease [1,12]. The majority of recurrences occur locally either in gastric bed, retroperitoneum or anastomosis, rather than distant metastases. The median time to recurrence is 2 years. T1/T2 serosal negative disease as expected show fewer recurrences, but those that recur dos so later. Distant failure (liver metastases) is potentially due to the aggressive sub-set that micro metastasizes early [1,12]. Thus radical surgery in T4 disease produces little benefit. Strategies to prevent gastric bed recurrence include a meticulous surgical technique with en-bloc resection of stomach, affected adjacent organs and intact gastric lymphatic chains to prevent iatrogenic cell spillage and prevent peritoneal dissemination [15]. Two successful strategies are available to improve outcomes in patients with localized gastric cancer [6,24]. The results of a large North American study (Gastrointestinal Cancer Intergroup Trial INT 0116) reported that postoperative chemo radiotherapy conferred a survival advantage compared with surgery alone, which led to the regimen being adopted as a standard of care [25]. More recently the MAGIC/UK Medical Research Council **(MRC)** trial demonstrated that perioperative chemotherapy resulted in an improvement in overall survival and progression free survival. Peri-operative chemotherapy is the standard of care in UK and most of Europe for localized gastric cancer with the accepted regimens of ECF or ECX [3,15]. The MRC MAGIC trial have recommended neoadjuvant/ adjuvant chemotherapy in conjunction with adequate surgery (multimodal therapy) to improve outcomes in gastric cancer. Three cycles ECF chemotherapy before and three cycles after surgery were compared to surgery alone. Peri-operative chemotherapy showed an increased 5-year survival rate from 23 to 36% [3,26]. Similar results were achieved in the French study of perioperative cisplatin and FU [27,28]. Adjuvant chemotherapy alone may confer a survival benefit and should be considered in patients at high risk of recurrence who have not received neo-adjuvant therapy (Japanese ACTS-GC trial) [29,30]. However, despite multimodal therapy and adequate surgery only 30% of gastric cancer patients are alive at 3 years [3,15]. As approximately 15% of gastric and

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

oesophageal junctional adenocarcinoma over express Human Epidermal Growth Factor Receptor-2 **(HER2)** on the cell membrane HER2 a tyrosine kinase receptor can be targeted by monoclonal antibody bevacizumab. The MRC ST03 trial compared ECX and bevacizumab with ECX alone for cancer of the stomach, esophagus, or junction of stomach and esophagus (stage 1b (T1N1) II, III or stage IV (T4, N1 or N2MO), Type III GOJ adenocarcinoma). Chemotherapy in three cycles over 9 weeks, 5-6 weeks break then surgery. The safety was marred by perforations at primary tumor, cardiac toxicity, wound healing complications and GI bleeding [31]. Non-randomized studies showed substantial pathological response (down staging of tumor) to preoperative chemo radiation [32,33]. Trials are underway to assess the usefulness of this regime. Recent randomized trials from China revealed a survival benefit with preoperative radiotherapy (30 *vs* 20%) [34]. Currently trials are under way in the west to try and replicate this. Post- operative chemo radiation is the standard of care in the USA and for all patients with positive resection margins. With longer-term (>11years) follow-up, the benefits of both the overall survival (35 *vs* 27 months) and Disease- Free Survival **(DFS)** (27 *vs* 19 months) were maintained [6]. There is less enthusiasm in the UK and in Europe because of the toxicity of abdominal chemo radiotherapy such as nausea and vomiting, myelosuppression including neutropenia, fatigue, mucositis and diarrhea. In addition, the benefit is uncertain post 'optimum' surgery. It may, however, be considered in patients at high risk of recurrence i.e. no neoadjuvant therapy and/or suboptimal surgery, e.g. in emergency context and in selected patients after an R0 resection [15].

OPERATIVE TECHNIQUES

Although perioperative chemotherapy is currently standard treatment for resectable gastric cancers but neoadjuvant and adjuvant therapies are no substitute for inadequate surgery [4,14,15]. For patients whose gastric cancer is diagnosed at a stage that is amenable to surgical treatment, the options include open or laparoscopic gastrectomy. The purposes of laparoscopic surgery for gastric cancer are to minimize surgical insults and to maximize patient's quality of life, while not compromising the oncologic clearance. However, the role of LG remains controversial, because studies of the long-term outcomes of LG are insufficient. Current safety and efficacy evidence suggests adequate support for the use of minimally- invasive surgery for gastric cancer, providing normal arrangements is in place for clinical governance, consent, and audit [35]. A patient who is 'unfit' for an open procedure does not become 'fit' for a laparoscopic procedure. Patient selection and management should be carried out in the context of a MDT with established experience in the treatment of gastric cancer [15].

LAPAROSCOPIC VERSUS OPEN GASTRECTOMY

Indications

Laparoscopic gastrectomy may be considered as a safe procedure with better short-term and comparable long-term oncological results. Compared to open gastrectomy [36]. There is a general agreement that a laparoscopic approach to the treatment of gastric cancer should be chosen

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

only by surgeons already highly skilled in gastric surgery and other advanced laparoscopic interventions. Furthermore, the first procedures should be carried out during a tutoring program. Diagnostic laparoscopy is strongly recommended as the first step of laparoscopic as well as open gastrectomies [37]. The advantage of early recovery because of reduced surgical trauma would allow earlier commencement of adjuvant chemotherapy and the decreased hospital stay and early return to work may offset the financial costs of laparoscopic surgery. The first description of LG was given by Kitano, Korea in 1994 and was initially indicated only for early gastric cancer patients with a low risk lymph node metastasis [36,38]. As laparoscopic experience has accumulated, the indications for Laparoscopic Gastrectomy **(LG)** have been broadened to patients with advanced gastric cancer. However, the role of LG remains controversial, because studies of the long-term outcomes of LG are insufficient [38]. The Japanese Gastric cancer Association guidelines in 2004 suggested EMR or ESD for stage 1a (cT1N0M0) diagnosis; Patients with stage 1b (cT1N1M0) and cT2N0M0) were referred for LG [39]. Totally laparoscopic D2 radical distal gastrectomy using Billroth II anastomosis with laparoscopic linear staplers for early gastric cancer is considered to be safe and feasible. LTG shows better short term outcomes compared with OTG in eligible patients with gastric cancer. There was significant reduction of Intraoperative blood loss, a reduced risk of post-operative complications and shorter hospital stay [40] Western patients are relatively obese and there is an increased risk of bleeding if lymphadenectomy is performed. LG is technically difficult in the obese than in the normal weight due to reduced visibility, difficulty retracting tissues, dissection plane hindered by adipose tissue, and difficulty with anastomosis. Open gastrectomy is thus preferable for the obese [36]. Obesity is not a risk factor for survival of patients but it is independently predictive of post-operative complications. Careful approach is being needed, especially for male patients with high BMI [6,15].

Principles

The same principles that govern open surgery are applied to laparoscopic surgery. In order to ensure the same effectiveness of LG as conventional open gastrectomy, all the basic principles such as properly selected patients, sufficient surgical margins, standardized D2 lymphadenectomy, no-touch technique etc, should be followed [36-40]. As laparoscopic experience has accumulated, the indications for Laparoscopic Gastrectomy **(LG)** have been broadened to patients with advanced gastric cancer. Commonly, five operative ports are used in Laparoscopic Gastrectomy **(LG):** one 10-12mm ports in the right periumbilically, three 10mm ports in the right and left flank, and wide left flank, with further 5mm port at epigastric level. Positions and sizes are open to local preference. Commonly five operative ports are used: one 10-12mm portperi-umbilically, three 10 -12mm ports in the right and left flank, and wide left flank, with a further 5-mm port at epigastric level. The positions and sizes are open to local preference [41].

The series of steps described in open gastrectomy are identical in LG, except performed through much smaller incisions with specialized and expensive laparoscopic equipment [36,42].

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

These include a liver retractor, e.g. Nathanson's, gastric retraction maintained by combination of elevation with atraumatic prospers e.g. Johan's and 'tenting' the stomach from the lesser sac. Vascular pedicles are divided using vascular haemostatic staplers, ligaclips, haemolocks, or laparoscopic ligation. Laparoscopic anastomosis following total gastrectomy utilizes the Orvill anvil introduced orally and laparoscopic linear staplers used in partial gastrectomy [43]. A larger incision may facilitate a hand being introduced into the peritoneal cavity for hand-assisted gastrectomy or laparoscopically assisted subtotal gastrectomy depending on the size of the tumor. Removal of the draining lymph nodes is an integral part of the procedure. A slightly larger incision (3.5cm) may be required in order to remove diseased stomach (through wound protector), but the location should be cosmetic and less likely to cause pain or respiratory complications [36]. Laparoscopic pylorus preserving gastrectomy is advocated in Korea and Japan for early tumours with minimal risk of station 5 lymph node metastasis i.e. minimally 6cm from pylorus [16].

Robotic Surgery

Robotic surgery will become additional options in Minimally Invasive Surgery **(MIS)** involving LG. The importance of performing effective extended lymph node dissection may provide the advantage of using robotic systems. Such developments will improve the quality of life of patients following gastric cancer surgery. A multicenter study with a large number of patients is needed to further investigate the safety and efficacy as well as long-term outcomes of robotic surgery, traditional laparoscopy and the open approach [36,44].

Efficacy

Multicentre case series have reported 5-year disease-free survival rates for early gastric cancer treated with LG as 99.8, 98.7 and 85.7% for stage 1A, 1B and II, respectively. For advanced disease the 5-year overall survival is 59% and disease-free survival of 57%. The conversion rate from laparoscopic to open surgery is 2-3% and the reasons include anatomical constraints, bleeding, and mechanical problems. The key efficacy outcomes include 30-day mortality, cancer-free survival rates, adequate surgical margins, and number of lymph nodes removed. Early results had suggested lower lymph node harvest particularly in laparascopic subtotal gastrectomy group compared with open surgery [36,37]. Laparoscopy- Assisted Distal Gastrectomy **(LADG)** for EGC reduced surgical trauma, improved nutrition, reduced post-operative pain, rapid return of GI function, shorter hospital stays, and no reduction in curability [45]. Kim et al demonstrated an improved QOL in the LADG group followed for up to 3 months as compared to the open procedure [16]. LADG for patients with clinical stage I gastric cancer is safe and has a benefit of lower occurrence of wound complication compared with conventional ODG. Although Laparoscopically Assisted Distal Gastrectomy **(LADG)** has several advantages over open distal gastrectomy, there is also safety, feasibility and advantages of Totally Laparoscopic Distal Gastrectomy **(TLDG)** [46-48]. Usui et al reported Laparoscopy -Assisted Total Gastrectomy **(LATG)** successful in 20 patients, with equal operating time, reduced blood loss and time to ambulatory status, first flatus,

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

and first oral intake significantly shorter as was the length of the post-operative hospital stay [49]. The frequency of analgesics given in LATG group was lower than that on OTG group. KLASS phase II multicenter prospective RCT trial (Korea) showed no significant differences between LADG and ODG. Post-operative complications were 10.5% and 14.7% respectively. There were three reoperations in each group and post-operative mortality was 1.1% and 0% respectively. TLDG is safe and feasible compared with LADG. However, it was difficult to identify the clinical advantages of TLDG over LADG based on the study [50]. Thus, the choice of surgical approach mainly depends on the patient conditions and the preference of the patients or surgeons [51].

Safety

Meta-analysis has shown fewer complications overall following laparoscopic subtotal gastrectomy compared with open gastrectomy. However, there were no differences between groups with respect to mortality, anastomotic leak, stricture or wound infection. Pulmonary complications were surprisingly non- significantly higher in the open gastrectomy group. Post-operative ileus was significantly reduced following laparoscopic gastric resection [36-38]. Expected mortality/ major morbidity should be < 5% and 5-10% respectively in high volume specialist centers [15,35,36]. 'Failure to rescue' is a significant cause of mortality but critical complications are recognized early and managed proactively in these specialist centers [52,53]. Over signs of sepsis, failure to progress as expected, or subtle signs such as new onset cardiac arrhythmias should heighten suspicion of complication and require investigation in first instance with contrast-enhanced CT (oral contrast) [23,54]. Close multidisciplinary follow-up for late complications with surgeons, specialist nurse and dietitians is crucial.

CONCLUSION

Gastric cancer is a loco regional disease. Adequate surgery is for loco regional control which is 'treatment' only. 'Cure' requires neoadjuvant/adjuvant chemotherapy to attack the putative micrometastases and prevent local recurrence. Perioperative chemotherapy is currently standard treatment for resectable gastric cancers but neoadjuvant and adjuvant therapies are no substitute for inadequate surgery. Minimally-invasive surgery (laparoscopic gastrectomy) has the advantage over open gastrectomy in reducing surgical trauma, improved nutrition, and reduced post-operative pain, rapid return of GI function, shorter hospital stays with no reduction in curability. Optimization of multimodal therapy by adequate surgery is based on the decision of the specialist oesophagogastric Multidisciplinary Team **(MDT)** following the discussion of the diagnosis, stage and assessment of fitness for treatment or palliation.

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

References

1. Fuchs CS, Mayer RJ. Gastric carcinoma. N Engl J Med. 1995; 333: 32-41.
2. Fisher B. Laboratory and clinical research in breast cancer-a personal adventure: the David A. Karnofsky memorial lecture. Cancer Res. 1980; 40: 3863-3874.
3. Mongan AM, Kalachand R, King S, O'Farrell NJ, Power D, et al. Outcomes in gastric and junctional cancer using neoadjuvant and adjuvant chemotherapy (epirubicin, oxaliplatin and capecitabine) and radical surgery. Ir J Med Sci. 2015; 184: 417-423.
4. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med. 2006; 355: 11-20.
5. Roukos DH, Kappas AM. Perspectives in the treatment of gastric cancer. Nat Clin Pract Oncol. 2005; 2: 98-107.
6. Rajdev L. Treatment options for surgically resectable gastric cancer. Curr Treat Options Oncol. 2010; 11: 14-23.
7. Ferlay J, Shin HR, Bray F, David Forman, Colin Mathers, et al. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No.10. Lyon, France: International Agency for Research on Cancer. 2010.
8. Forman D, Burley VJ. Gastric cancer: global pattern of the disease and an overview of environmental risk factors. Best Pract Res Clin Gastroenterol. 2006; 20: 633-649.
9. Jemal A, Siegel R, Ward E, Murray T, Xu J. Cancer statistics, 2006. CA Cancer J Clin. 2006; 56: 106-130.
10. Siewert JR, Feith M, Werner M, Stein HJ. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. Ann. Surg. 2000; 232: 353-361.
11. Pal N, Axisa B, Yusof S, Newcombe RG, Wemyss-Holden S. Volume and outcome for major upper GI surgery in England. J Gastrointest Surg. 2008; 12: 353-357.
12. Barchi LC, Yagi OK, Jacob CE, Mucerino DR, Ribeiro U, et al. Predicting recurrence after curative resection for gastric cancer: External validation of the Italian Research Group for Gastric Cancer (GIRCG) prognostic scoring system.Eur J SurgOncol. 2016; 42: 123-131.
13. Lauren P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. An attempt at a histo-clinical classification. Acta Pathol Microbiol Scand 1965; 64:31-49.
14. Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ, et al. Surgical treatment of gastric cancer: 15 -year follow follow-up results of the randomized nationwide Dutch D1D2 trial. Lancet Oncol 2010; 11: 439-449
15. Allum WH, Blazeby JM, Griffin SM, Cunningham D, Jankowski JA. Association of Upper Gastrointestinal Surgeons - Guidelines for the management of esophageal and gastric cancer. Gut. 2011; 60: 1449-1472.
16. Kim YW, Baik YH, Yun YH, Nam BH, Kim DH, Choi IJ, Bae JM. Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial. Ann Surg. 2008; 248: 721-727.
17. Arru L, Azagra JS, Facy O, Makkai-Popa ST, Poulain V. Totally laparoscopic 95% gastrectomy for cancer: technical considerations. Langenbecks Arch Surg. 2015; 400: 387-393.
18. Xu YY, Huang BJ, Sun Z, Lu C, Liu YP. Risk factors for lymph node metastasis and evaluation of reasonable surgery for early gastric cancer. World J Gastroenterol. 2007; 13: 5133-5138.
19. Vasilescu C, Herlea V, Tidor S, Ivanov B, StÄƒnciulea O. [D2 lymph node dissection in gastric cancer surgery: long term results--analysis of an experience with 227 patients]. Chirurgia (Bucur). 2006; 101: 375-384.
20. Cho BC, Jeung HC, Choi HJ, Rha SY, Hyung WJ, et al. Prognostic impact of resection margin involvement after extended (D2/D3) gastrectomy for advanced gastric cancer: a 15-year experience at a single institute. J SurgOncol. 2007; 95: 461-468.
21. Yonemura Y, Wu CC, Fukushima N, Honda I, Bandou E, et al. East Asia Surgical Oncology Group. Operative morbidity and mortality after D2 and D4 extended dissection for advanced gastric cancer: a prospective randomized trial conducted by Asian surgeons. Hepato gastroenterology. 2006; 53: 389-394.
22. Sasako M, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. N Engl J Med. 2008; 359: 453-462.
23. Weledji EP, Verla V. Failure to rescue patients from early critical complications of oesophagogastric cancer surgery. Ann Med Surg (Lond). 2016; 7: 34-41.
24. Sano T. Adjuvant and neoadjuvant therapy of gastric cancer: a comparison of three pivotal studies. Curr Oncol Rep. 2008; 10: 191-198.

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

25. Kozak KR, Moody JS. The survival impact of the intergroup 0116 trial on patients with gastric cancer. Int J Radiat Oncol Biol Phys. 2008; 72: 517-521.

26. Yoshikawa T, Omura K, Kobayashi O, Nashimoto A, Takabayashi A, et al. A phase II study of preoperative chemotherapy with S-1 plus cisplatin followed by D2/D3gastrectomy for clinically serosa-positive gastric cancer (JACCRO GC-01 study). Eur J SurgOncol. 2010; 36: 546-551.

27. Messager M, Lefevre JH, Pichot-Delahaye V, Souadka A, Piessen G, et al. The impact of perioperative chemotherapy on survival in patients with gastric signet ring cell adenocarcinoma: a multicenter comparative study. Ann Surg. 2011; 254: 684-693.

28. Robb WB, Messager M, Goere D, Pichot-Delahaye V, Lefevre JH, et al. FREGAT Working Group-Predictive factors of postoperative mortality after junctional and gastric adenocarcinoma resection. JAMA Surg. 2013; 148: 624-631.

29. Sasako M, Saka M, Fukagawa T, Katai H, Sano T. Adjuvant chemotherapy using S-1 for curatively resected gastric cancer-the nationwide clinical trial. GanTo Kagaku Ryoho. 2006; 110-116.

30. Shitara K, Chin K, Yoshikawa T, Katai H, Terashima M. Phase II study of adjuvant chemotherapy of S-1 plus oxaliplatin for patients with stage III gastric cancer after D2 gastrectomy. Gastric Cancer. 2015.

31. Bouché O, Penault-Llorca F. [HER2 and gastric cancer: a novel therapeutic target for trastuzumab]. Bull Cancer. 2010; 97: 1429-1440.

32. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC. Chemo radiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med. 2001; 345: 725-730.

33. Jackson C, Mochlinski K, Cunningham D. Therapeutic options in gastric cancer: neoadjuvant chemotherapy *vs* postoperative chemo radiotherapy. Oncology (Williston Park). 2007 Aug; 21: 1084-1087.

34. Zhang ZX, Gu XZ, Yin WB, Huang GJ, Zhang DW, Zhang RG. Randomized clinical trial on the combination of preoperative irradiation and surgery in the treatment of Adenocarcinoma of Gastric Cardia (AGC)--report on 370 patients. Int J RadiatOncolBiolPhys. 1998; 42: 929-934.

35. National Institute for Health and Clinical Excellence (NICE). Laparoscopic gastrectomy for cancer: National institute for health and clinical excellence. 2008.

36. Parisi A, Nguyen NT, Reim D, Zhang S, Jiang ZW, Brower ST, et al. Current status of minimally invasive surgery for gastric cancer: A literature review to highlight studies limits. Int J Surg. 2015; 17: 34-40

37. Bracale U, Pignata G, Lirici MM, Hüscher CG, Pugliese R, et al. Guideline Committee Of The Italian Society Of Hospital Surgeons-ACOI and Italian Hi-Tech Surgical Club-IHTSC. Laparoscopic gastrectomies for cancer: The ACOI-IHTSC national guidelines. Minim Invasive Ther Allied. Technol. 2012; 21: 313-319.

38. Koeda K, Nishizuka S, Wakabayashi G. Minimally invasive surgery for gastric cancer: the future standard of care. World J Surg. 2011; 35: 1469-1477.

39. Japanese gastric cancer treatment guidelines 2010 (V3) gastric cancer. 2011; 14: 313-323.

40. Haverkamp L, Weijs TJ, van der Sluis PC, van der Tweel I, Ruurda JP. Laparoscopic total gastrectomy versus open total gastrectomy for cancer: a systematic review and meta-analysis. Surg Endosc. 2013; 27: 1509-1520.

41. Tanimura S, Higashino M, Fukunaga Y, Kishida S, Nishikawa M, et al. Laparoscopic distal gastrectomy with regional lymph node dissection for gastric cancer. SurgEndosc. 2005; 19: 1177-1181

42. Su XQ, Yang H. Never ignore the therapeutic principles during the procedure of laparoscopic gastrectomy for gastric cancer. Zhonghua Wei Chang WaiKe ZaZhi. 2013; 16: 118-1120.

43. Nunobe S, Hiki N, Tanimura S, Kubota T, Kumagai K, et al. Three-step esophago jejunal anastomosis with atraumatic anvil insertion technique after laparoscopic total gastrectomy. J Gastrointest Surg. 2011; 15: 1520-1525.

44. Huang KH, Lan YT, Fang WL, Chen JH, Lo SS, et al. Initial experience of robotic gastrectomy and comparison with open and laparoscopic gastrectomy for gastric cancer. J Gastrointest Surg. 2012; 16: 1303-1310.

45. Kitano S, Shiraishi N, Fujii K, Yasuda K, Inomata M. A randomized controlled trial comparing open vs laparoscopy-assisted distal gastrectomy for the treatment of early gastric cancer: an interim report. Surgery. 2002; 131: S306-311.

46. Ikeda O1, Sakaguchi Y, Aoki Y, Harimoto N, Taomoto J. Advantages of totally laparoscopic distal gastrectomy over laparoscopically assisted distal gastrectomy for gastric cancer. Surg Endosc. 2009; 23: 2374-2379.

47. Jin K, Lan H, Tao F, Zhang R. Totally laparoscopic D2 radical distal gastrectomy using Billroth II anastomosis: A case report. Oncol Lett. 2016; 11: 1855-1858.

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.

48. Kim W, Kim HH, Han SU, Kim MC, Hyung WJ, et al. Korean Laparo-endoscopic Gastrointestinal Surgery Study (KLASS) Group. Decreased Morbidity of Laparoscopic Distal Gastrectomy Compared With Open Distal Gastrectomy for Stage I Gastric Cancer: Short-term Outcomes From a Multicenter Randomized Controlled Trial (KLASS-01). Ann Surg. 2016; 263: 28-35.

49. Usui S, Yoshida T, Ito K, Hiranuma S, Kudo SE. Laparoscopy-assisted total gastrectomy for early gastric cancer: comparison with conventional open total gastrectomy. Surg Laparosc Endosc Percutan Tech. 2005; 15: 309-314.

50. Kim HH, Hyung WJ, Cho GS, Kim MC, Han SU, et al. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). Ann Surg 2010; 251: 417-420.

51. Chen K, Mou YP, Xu XW, Pan Y, Zhou YC, et al. Comparison of short-term surgical outcomes between totally laparoscopic and laparoscopic-assisted distal gastrectomy for gastric cancer: a 10-y single-center experience with meta-analysis. J SurgRes. 2015; 194: 367-374.

52. Ghaferi AA, Birkmeyer JD, Dimick JB. Hospital volume and failure to rescue with high-risk surgery. Med Care. 2011; 49: 1076-1081.

53. Skip worth RJ, Parks RW, Stephens NA, Graham C, Brewster DH, et al. The relationship between hospital volume and post-operative mortality rates for upper gastrointestinal cancer resections: Scotland 1982-2003. Eur. J. Surg. Oncol. 2010; 36: 141-147.

54. Facy O, Goergen M, Poulain V, Heieck F, Lens V, et al. Minimally invasive management of postoperative esophagojejunal anastomotic leak. Surg Laparosc Endosc Percutan Tech. 2014; 24: 183-186.

Copyright © Weledji EP.This book chapter is open access distributed under the Creative Commons Attribution 4.0 International License, which allows users to download, copy and build upon published articles even for commercial purposes, as long as the author and publisher are properly credited.