Review

Surgical management of advanced gastric cancer: An evolving issue

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Abstract

Worldwide, gastric cancer represents the fifth most common cancer and the third leading cause of cancer deaths. Although the overall 5-year survival for resectable disease was more than 70% in Japan due to the implementation of screening programs resulting in detection of disease at earlier stages, in Western countries more than two thirds of gastric cancers are usually diagnosed in advanced stages reporting a 5-year survival rate of only 25.7%. Anyway surgical resection with extended lymph node dissection remains the only curative therapy for non-metastatic advanced gastric cancer, while neoadjuvant and adjuvant chemotherapies can improve the outcomes aimed at the reduction of recurrence and extension of survival. High-quality research and advances in technologies have contributed to well define the oncological outcomes and have stimulated many clinical studies testing multimodality managements in the advanced disease setting.

This review article aims to outline and discuss open issues in current surgical management of advanced gastric cancer.

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Introduction

Although the incidence of gastric cancer has decreased worldwide, it is still the third most common cause of cancer-related and one of the most common malignancies...
in the world, ranking fifth after lung, breast, colorectal and prostate cancer. These discouraging results are explained mainly by a late diagnosis. However, focusing the global incidence and outcomes of gastric cancer with relation to geography, a significant discrepancy in the data between the Asian and Western Countries was found. While in the United States the incidence is estimated at 21,600 new cases a year, in the South Korea it accounts for 33,000 new cases per year, followed by Mongolia, Japan and China. Nevertheless, Asian gastric cancer patients have a better prognosis than Western patients, probably due to active screening programs resulting in detection of disease at earlier stages, with an overall survival rate more than 70% in Japan for resectable disease. On the contrary, in Europe and the United States, more than two thirds of gastric cancers are usually diagnosed in advanced stages with a locally advanced resectable disease as routine screening for gastric cancer is not recommended owing to cost ineffectiveness. As a result, a 5-year survival rate of only about 25% in locally advanced disease is registered in these countries.

Surgical resection with extended lymph node dissection remains the only curative therapy for non-metastatic gastric cancer, while neoadjuvant and adjuvant chemotherapies, as well as chemoradiation, can improve the outcomes aimed at the reduction of recurrence and extension of survival.

This review article aims to outline and discuss open issues in current surgical management of advanced gastric cancer.

“Advanced gastric cancer” for a surgeon

An accurate categorization of the tumor stage, including the invasive depth and lymph node status, is crucial for prognostic assessment and decision making of the stage-specific therapeutic strategy. The American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) tumor, node, metastasis (TNM) staging system has been used widely for clinical practice and research in determining tumor stage in gastric cancer, representing the most important independent prognostic factor. Several versions of this classification system have been used over the past 30 years and in 2010, the 7th edition of the AJCC/UICC gastric cancer staging manual was introduced, resulting in several changes from the 6th edition, renewing T categories, reducing cutoffs of N status (with a new minimum number of 16 nodes to be removed for an accurate staging), and including a positive peritoneal cytological lavage as M1. In the medical literature there are a large number of studies that examine the difference between the 6th and the 7th AJCC/UICC TNM for GC, however the superiority of the latest edition is still debated worldwide. To this address some Authors support 7th edition as more accurate in overall survival prediction while other did not evidence a better survival discrimination and risk stratification compared with 6th edition, suggesting an hybrid TNM staging system combining T categories from 7th edition and N categories from 6th edition. Further nationwide studies are necessary to evaluate the validity and effectiveness of the new classification from various angles. Finally, the modified staging of gastric cancer to include cancers of the esophagogastric junction (EGJ) arising more than 5 cm distally of the EGJ or within 5 cm of the EGJ but without extension to the esophagus or EGJ generated controversies regarding biological and prognostic considerations, suggesting the Siewert classification would be more adequate in staging these tumors.

Interestingly, in the literature, the definition of early gastric cancer (EGC) is well codified, even there is considerable heterogeneity in the definition of advanced gastric cancer (AGC). De Sol et al. individually analyzed all parameters of the 6th TNM classification for AGC reported in each previous selected study providing a summary of babel-like definitions. Only few Authors considered as AGC the T3 or T4 neoplasms, whereas the remaining studies accounted as AGC all neoplasms with parietal invasion initiating from stage T2. As regard the N parameter, most of Authors defined gastric cancers as “advanced” even in the absence of regional lymph nodes involvement (N0), others required at least one metastatic lymph node (N1 or more) and only few did not consider the N parameter. Furthermore gastric cancers were defined advanced irrespective of the presence or absence of distant metastasis (M1 or M0).

Currently the tendency of surgeons is to consider as AGC a non-early/non-metastatic gastric cancer infiltrating deeper than submucosal layer with or without nodal involvement (T2-4b/N0-3b/M0, 7th AJCC/UICC TNM), for which the surgical therapy alone, while not always providing any advantage, still remains the central curative modality at present.

Optimal surgery

Extension of gastric resection

Although a surgical R0 resection and a retrieval of a minimum of 16 lymph nodes represent the well ascertained mandatory surgical principles, there is still some controversies and opinions about the extent of surgical resection and lymphadenectomy. The primary tumor excision is based on the location, extension and histologic subtype of gastric cancer. Proximal gastric cancers are generally treated with total gastrectomy since the anastomosis between the esophagus and distal stomach is burdened with a significant rate of postoperative complications as well as intractable postoperative reflux esophagitis. Total gastrectomy is also required for large tumors or tumors of the lesser curve/gastric body. Conversely, antral cancers may be adequately resected with a distal gastrectomy if a 5 cm margin can be achieved. As regard the importance of histologic subtype (intestinal or diffuse...
spread were believed to be independent prognostic factors. Lymph node metastasis, depth of invasion and peritoneal cancers after multiorgan resection were largely investigated. More interestingly, many prognostic factors for T4 gastric cancer were hypothesized to offer oncological advantages over subtotal distal resection (for cancers of the antrum) entailing a wider lymphadenectomy and effective removal of multicenter neoplastic foci for diffuse subtype carcinomas. Nevertheless, two European trials reported no differences in overall survival rates between total and subtotal distal gastrectomy to this address. Currently, there is general agreement that “a proximal margin of at least 3 cm is recommended for T2 or deeper tumors with an expansive growth pattern and 5 cm is recommended for those with infiltrative growth pattern”, thus finally ending a long-term debate.

In T4 cases, however, a multivisceral resection (MVR), or gastrectomy with resection of adjacent organs, may be required to provide patients with advanced gastric cancer the best chance at survival with a curative R0 resection, but the price to pay seems to be very high in terms of postoperative morbidity and the prognostic benefit of MVR in patients with locally advanced disease is still debated. Furthermore, the true microscopic invasion into adjacent organ is hard to identify with pre-operative imaging or even during an operation, making the decision to proceed with MVR a surgical challenge. Kasaku et al. reported a higher complication rate in multivisceral resection group compared to gastrectomy alone group, with no survival difference, while Pacelli et al., in an Italian multicenter observational study, found no significant differences in postoperative morbidity and mortality rates. Other retrospective studies investigating this issue evidenced a survival disadvantage for gastrectomy with additional organ resection. Contrarily, most studies registered an overall 5-year survival improvement (19.9%–38%) for patients who underwent gastrectomy with multivisceral resections when compared with patients who underwent gastrectomy alone or palliative surgery. More interestingly many prognostic factors for T4 gastric cancers after multiorgan resection were largely investigated and R0 resection, number and type of resected organs, lymph node metastasis, depth of invasion and peritoneal spreading were believed to be independent prognostic factors with a state of uncertainty still. Almost all published studies confirm that R0 resection represent the most powerful prognostic factor. The 5-year survival rate in patients with T4 gastric cancer undergoing curative R0 resection ranges from 23% to 46%, and this rate decreases in cases of R+ resection, ranging from 17.5% to 0%. As regard the number of resected organs, it has been found a negative prognostic index by several authors while other studies reported no statistically significant difference in the survival of patients who underwent en bloc resection of 1 organ when compared with those who had 2 or more resected organs, showing that the involvement of several organs should not be a contraindication for surgery. Splenectomy, pancreatecosplenectomy, colectomy, or any other organ resection did not result as predictors of poor survival, while positive peritoneal washing cytology as well as the depth of invasion and the presence and extent of lymph node metastasis were reported as the most powerful independent poor prognostic factor for patients with T4 gastric cancer treated with potentially curative resection.

On the basis of these results, actually, the gastrectomy with multivisceral resection should be the therapeutic choice in locally advanced gastric cancer patients where a complete resection could be realistically obtained and when lymph node metastatic involvement is not evident, with an acceptable postoperative morbidity and mortality rates.

Lymphadenectomy

Controversy over the extent of lymph node dissection in the gastric cancer treatment has been a topic of debate for decades. In D1 dissections, only the perigastric nodes directly attached along the lesser curvature and greater curvatures of the stomach are removed (stations 1–6: right and left pericardial, lesser curvature, greater curvature, supra and infrapyloric). D2 dissections add the removal of nodes along the left gastric artery (station 7), common hepatic artery (antero-superior group, station 8a), celiac trunk (station 9), splenic hilus and splenic artery (station 10 and 11), hepatoduodenal ligament (along the proper hepatic artery, station 12a). Even though the D2 lymphadenectomy has been traditionally recommended in Japan as standard practice since the 1960s on the basis of long-term results and overall survival rates improvement, in Western countries the majority of surgeons still perform a D1 dissection. This incongruity was based on the results of two large European randomized clinical trials that failed to prove a survival benefit of D2 lymphadenectomy compared to D1. Furthermore these studies were harshly criticized mainly for the lack of experience of many participating surgeons as well as the inclusion of splenectomy and/or pancreatectomy as part of a D2 resection, with subsequently confounding results of post-operative morbidity and mortality rates. By contrast, a randomized trial in Taiwan proved a significant benefit in overall survival (OS) and recurrence free survival (RFS) for a D2 dissection as compared with D1 lymphadenectomy, with no increase in operative mortality, which also indicate that adequate local control is essential for the treatment of gastric cancer. Recently, in Dutch trial, a 15-year follow-up showed a lower rate of local recurrence and gastric cancer-related mortality in the D2 lymphadenectomy group compared to the D1 group.

A recent meta-analysis including eight Eastern and Western randomized controlled trials over 2000 patients, showed no significant differences in overall survival between D1 and D2. Subgroup analysis of patients without spleen and pancreas resection had a clear trend for OS.
and RFS much more benefiting D2 compared to D1 patients, highlighting the spleen and pancreas-sparring D2 lymphadenectomy as the standard surgical approach to resectable gastric cancer. Indeed, using a RAND Corporation/University of California Los Angeles (UCLA) Appropriateness Methodology (RAM), an expert panel considered D2 lymphadenectomy in all patients with tumors > T1N0.41 The panel also found the use of total gastrectomy for all patients and distal gastrectomies for patients with distal gastric cancers, in expert hands, as the optimal surgical standard.

Another debated issue concerns the clinical value of systematic para-aortic nodal dissection (PAND) in addition to D2 gastrectomy in resectable advanced gastric cancer. In 2008 the Japan Clinical Oncology Group (JCOG), in a randomized controlled trial comparing D2 lymphadenectomy alone with D2 lymphadenectomy plus PAND in patients undergoing gastrectomy for curable advanced gastric cancer, did not find improvement in overall or recurrence free survival with the super-extended lymphadenectomy.32 There were no significant differences between the two groups in the surgery-related complication rates, even if the D2 lymphadenectomy plus PAND was associated with a longer intervention time, greater blood loss, and a significant increase in minor complications.32 After these results the prophylactic D2 lymphadenectomy plus PAND is no longer recommended in patients undergoing gastrectomy for curable gastric cancer.30

Recently the Italian Research Group for Gastric Cancer (GIARGC), in a retrospective study on 568 patients undergoing curative gastrectomy for advanced gastric cancer found that D2 lymphadenectomy plus PAND reverses the negative impact of diffuse histotype on relapses, especially on locoregional recurrences.33 Therefore the super-extended nodal dissection could be considered a valid therapeutic option in histotype-oriented tailored treatment of advanced GC.

Obviously, many factors as patient comorbidities, tumor extension and surgical expertise can affect the choice of surgical decision since the more aggressive surgical strategy can affect the outcomes as regard survival, treatment-related mortality and morbidity, and postoperative quality of life.

An accurate preoperative prognostic assessment as well as remarkable clinical experience are essential to establish the best tailored approach for individual patients.

**Multimodality management**

**Neoadjuvant chemotherapy**

Neoadjuvant chemotherapy (CHT) for AGC aims at disease downstaging, increasing the rate of curative resection, and reducing the incidence of systemic metastases by means of undetectable micrometastasis eradication. Overall, pre-surgical patients usually can tolerate treatments better due to a higher performance, with no postoperative morbidity and mortality increased rates. On this basis, all guidelines actually recommend this treatment for patients with locally advanced gastric cancer.

The first randomized controlled trial of pre-operative chemotherapy (FAMTX - 5-Fluorouracil, doxorubicin and methotrexate) versus surgery alone on 56 patients with apparently operable gastric cancer, did not show a beneficial effect of neoadjuvant treatment.44 Two years later the MAGIC trial45 evaluated the efficacy of a preoperative and postoperative cisplatin, epirubicin and 5-FU (ECF) CHT versus surgery alone on 503 potentially resectable gastric, esophagogastric junction or lower esophagus cancer patients. As compared with the surgery group, the perioperative-chemotherapy group had a higher likelihood of overall survival (HR for death = 0.75; 95% CI: 0.60–0.93, P = 0.009; 5-year survival rate: 36% vs 23%) and progression-free survival (HR for progression = 0.66; 95% CI: 0.53–0.81, P < 0.001). Of note there was a greater proportion of T1 and T2 tumors and less advanced nodal disease in the perioperative group. Similar benefit emerged from the French FFCD 9703 trial, in which 224 patients with resectable adenocarcinoma of the EGJ or lower esophagus (75% of all patients), and of the stomach (25% of all patients), were randomly assigned to either perioperative chemotherapy with infusional 5-fluorouracil plus cisplatin (CF) followed by surgery and adjuvant CF chemotherapy, or surgery alone.46 The neoadjuvant treatment significantly increased the curative resection (84% vs 74%; P = 0.04), 5-year disease-free survival (34% vs 19%; P = 0.003) and 5-year overall survival (38% vs 24%; P = 0.02) rates.

Recently, the European EORTC 40954 phase III trial47 examined the efficacy of preoperative cisplatin, 5-fluorouracil, and leucovorin chemotherapy in gastric and EGJ cancer patients compared to surgery alone. This trial was stopped for poor accrual after 144 patients were randomly assigned (72:72). The curative resection rate was 81.9% after neoadjuvant chemotherapy as compared with 66.7% with surgery alone (P = 0.036). The surgery-only group had more lymph node metastases than the neoadjuvant group (76.5% vs 61.4%; P = 0.018). Postoperative complications were more frequent in the neoadjuvant arm (27.1% vs 16.2%; P = 0.09). After a median follow-up of 4.4 years and 67 deaths, a survival benefit could not be shown (hazard ratio, 0.84; 95% CI, 0.52 to 1.35; P = 0.466).

This trial showed a significantly increased R0 resection rate but failed to demonstrate a survival benefit. Possible explanations are low statistical power, a high rate of proximal gastric cancer including EGJ cancer and/or a better outcome than expected after radical surgery alone due to the high quality of surgery with resections of regional lymph nodes outside the perigastric area (D2 dissection).

It seems clear that tumor downstaging and R0 resection rates increase after neoadjuvant chemotherapy. However, there are still debates about survival after preoperative
treatment, since that the MAGIC and the French FFCD 9703 trials are affected by a lot of staging and surgical drawbacks. Similarly, the EORTC trial failed to confirm this advantage.

The optimal patient selection in the clinical trials setting, by means of appropriate pretreatment staging as well as prediction of response to therapy, could be the cornerstone for correctly evaluating the survival benefit of neoadjuvant therapy in advance gastric cancer. Further data will be provided by expected results from the ongoing MAGIC B, CRITICS and JCOG 0501 prospective trials based on the neoadjuvant modality approach.

Cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC)

Gastrectomy for gastric cancer with positive peritoneal cytological lavage or peritoneal carcinosis (PC), classified as metastatic disease according to current TNM, has no benefit role except as a palliative surgery to reduce symptoms such as bleeding and stricture, resulting in extremely poor prognosis after surgery. However, recent data suggests that in selected patients the surgical resection may have a role. According to the recent recommendations, cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy are highly suggested for the treatment of peritoneal pseudomyxoma, peritoneal mesothelioma, and peritoneal carcinosis from colorectal and ovarian cancer. Treatment of peritoneal malignancies from gastric cancer represents a new attracting topic in the management of GC but it is still to be validated.

Yang et al., in a randomized phase III study evaluating the efficacy and safety of CRS and HIPEC (Cisplatin and Mitomycin C) versus CRS alone for the treatment of peritoneal carcinosis from gastric cancer, reported a survival improvement with acceptable morbidity in CRS and HIPEC group (median survival rate: 6.5 months; 95% CI, 4.8–8.2 months in CRS vs 11 months; 95% CI, 10–11.9 months in CRS and HIPEC, p = 0.046). Similarly, Magge et al. prospectively analyzed 23 patients with peritoneal carcinosis from gastric cancer undergoing CRS and HIPEC, reporting a median overall survival (OS) of 9.5 months (95% CI: 4.7–17.3), with 1- and 3-year OS rates of 50 and 18% respectively. A multivariate Cox regression model showed that male gender, lymph node involvement, residual tumor nodules and 2 anastomoses were joint significant predictors of poor OS, while signet ring cells histological subtype, male gender and 2 anastomoses were joint significant predictors of poor progression, suggesting that CRS with HIPEC may offer survival benefit in a carefully selected population.

In 2006, the combination of bidirectional chemotherapy [intraperitoneal and intravenous or bidirectional intraperitoneal and systemic induction chemotherapy (BIPSC)] prior to CRS and HIPEC was described as a new therapeutic strategy for patients with peritoneal carcinosis from gastric cancer. Canbay et al. recently published results from a single Japanese specialized center in peritoneal malignancy evaluating the outcome of bidirectional induction chemotherapy (intraperitoneal docetaxel and cisplatin followed by four cycles of oral S-1) in patients with PC arising from GC. After BIPSC, 152 of 194 (78.3%) patients who showed negative results on peritoneal cytology underwent CRS plus HIPEC. Major complications occurred in 23.6% of patients, with treatment-related mortality of 3.9%. The median survival rate was 15.8 months, with 1-, 2-, and 5-year survival rates of 66, 32 and 10.7%, respectively. Furthermore, a meta-analysis of 20 randomized controlled trials including a total of 2145 patients (1152 randomized to receive radical resection and HIPEC and 993 randomized to receive radical resection alone) also reported an improvement in 1-, 2- and 3-year overall survival in CRS and HIPEC treatment.

In light of such evidences, while CRS and HIPEC is not commonly recommended in peritoneal carcinosis from GC, selected patients may benefit of this more aggressive treatment for a long-term survival but it should be performed in clinical trial in specialized high volume centers only.

Surgery of liver metastasis

The new challenge in the treatment of gastric cancer is represented by liver metastases, considered as a systemic disease with no indication for surgery with curative intent. Synchronous or metachronous liver metastases are found in 3.5%–9.9% of patients diagnosed as gastric cancer and only 4%–20% of these metastatic patients underwent hepatectomy for cure, since such metastases are found as clinically resectable disease, and can represent exceptions to either palliative chemotherapy or supportive care. Mortality is reported to be 1.1% and morbidity ranged from 19% to 47%. Mainly, a 5-year survival rate ranged from 0% to 37% and a median survival time ranged from 9 to 38.8 months.

Although the Japanese Gastric Cancer Treatment Guidelines recommend only chemotherapy, radiation, palliative surgery, and best supportive care for treatment of Stage IV or metastatic gastric cancer, recently the guidelines committee of the Japan Gastric Cancer Association decided to revisit the treatment of potentially resectable metastatic disease. Patients diagnosed to have single liver metastasis or a small number of metastatic nodules (<=3), less than 5 cm in size, could be indicated for surgery.

Radiofrequency ablation (RFA), conducted either percutaneously under ultrasonic imaging guidance, laparoscopically, or by the open surgery approach, may represent a valid alternative to surgical resection to treat selected patients with liver metastasis, including metastasis with less than 3 cm in diameter or patients unfit for major hepatic surgery. Unfortunately reports on RFA applied to liver metastases from gastric cancer remain scarce and further prospective studies are needed to establish its real efficacy compared to surgical resection alone.
Technical issues

Staging laparoscopy

The efficacy of staging laparoscopy (SL) in detecting occult intra-abdominal metastasis, also by means of cytological examination of peritoneal aspirate or washing, has been assessed only in prospective and retrospective observational studies over the last 20 years.50,61 Although it represents a recommended tool able to identify patients who may benefit from chemotherapeutic approaches, its employment in the gastric cancer patients setting is still modest.62,63 Coburn et al.62 reported staging laparoscopy in only 8.8% of 3666 gastric cancer patients. Similarly, in a large cohort of 11,759 patients who underwent surgery for gastric cancer by Karanicolas et al.63 only 8% had staging laparoscopy. Recently the application of SL is becoming more used routinely. Tourani et al.64 performed SL in 74.3% of patients, while Convie et al.65 reported a routinely use of SL in all gastric cancer patients. Interestingly, unsuspected metastatic distant disease was detected in 18–40% of cases65–67 while unexpected peritoneal metastasis in 22–40%,67–69 leading to a high rate of unnecessary laparotomies or gastrectomies with change in the treatment intent.70

On the other hand, in the multimodal therapeutic setting the laparoscopy also represents an accurate “second staging” tool in patients receiving intensive chemotherapy for carcinosis GC in all cases in which the lesions cannot be detected by CT or US helping make decisions regarding R0 gastrectomy.71 Yano et al.71 showed that a second staging laparoscopy accurately assessed the response to neoadjuvant chemotherapy, improving make decisions regarding R0 gastrectomy. Furthermore, Ajani et al.63 highlighted that clinical staging by laparoscopy and endoscopic ultrasonography improved R0 resection rates after chemotherapy in patients with potentially resectable gastric cancer.

The ultrasonographic tool added to SL (laparoscopic ultrasonography) represents a new fascinating challenge that showed further improvement in diagnostic accuracy for detecting small liver metastases, lymph node metastases and for the assessment of the local extension of gastric cancer.72

It is clearer now that the role of staging laparoscopy in the treatment decision and multidisciplinary therapy of gastric cancers is emerging; due to major advantage in preventing unnecessary laparotomies associated with an unobtrusive morbidity rate as well as the effectiveness in response assessment after neoadjuvant chemotherapy, staging laparoscopy should be routinely performed in the staging of gastric cancer.

Laparoscopic gastrectomy

The first laparoscopic distal gastrectomy (LDG) for early gastric cancer was described by Kitano et al.73 in 1994 while the first laparoscopic total gastrectomy with a D2 lymphadenectomy for advanced gastric cancer was reported in 2000 by Uyama et al.74 To date, laparoscopic approach is considered effective and feasible for the treatment of EGC due to low postoperative pain, earlier return to normal bowel function and resumption of oral intake, faster recovery, shorter hospital stay, better cosmetic outcome and lower financial costs, compared with the open approach.75–77 Moreover controversies about the lower lymph node sampling following laparoscopic resection compared with the open one have also been clarified since no significant differences have been found when less than D2 lymphadenectomy was performed.

As regard to the AGC, however, only a few surgeons worldwide have performed laparoscopic gastric resections.78–83 However, the role of minimally invasive treatment in this setting still remains unclear due to its technical difficulty and the lack of long-term results. Furthermore some issues are debated so far: dissection of lymph-node stations 12a or 10 is considered technically challenging due to the serious risks of organ injury, bleeding, and/or bile and pancreatic leakage from a major vessel78–84; lymphadenectomy results in morbidity and mortality rates similar to those of open resections23,38; a peritoneal seeding of malignant cells as well as port-site recurrence have been proposed as potential complications of the serosal infiltrated tumors by the laparoscopic approach; long-term oncological outcomes are still poor.81,84

Recently Zou et al.85 conducted an interesting meta-analysis of 14 trials (1 RCT, 13 non-RCTs) comparing laparoscopic and open D2 gastrectomies for the treatment of advanced gastric cancer. Laparoscopic and open approach resulted in comparable numbers of sampled lymph nodes, tumor recurrence and metastasis rates as well as disease-free and overall survival rates. Laparoscopic approach provides better short-term prognoses with lower postoperative pain, faster recovery, and shorter hospital stays, without differences in morbidity and mortality were found. A longer operative time was registered for the minimally invasive technique only.

Despite these encouraging results indicating that the laparoscopic technique represents an acceptable alternative to open surgery for AGC, additional clinical trials are needed for further evaluation of this procedure. Seven RCTs comparing the laparoscopic gastrectomy and open gastrectomy to treat AGC in East Asia (three in China, three in South Korea, and one in Japan)86–92 are currently ongoing and the results will help researchers to further clarify this matter.

Robotic surgery

The da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) is characterized by a three-dimensional, ten-fold magnified vivid view of the operating field, instruments with articulating end-effectors and 7 degrees of freedom, tremor filtering, and motion scaling.
Application of the da Vinci robotic surgical system has opened up a new era of minimally invasive approaches in gastric cancer overcoming intrinsic limitations of a traditional laparoscopy experienced during the D2 lymph node dissection and reconstruction of bowel continuity.13 The first series of robot-assisted gastrectomy (RAG) were published by Giulianotti et al.94 and Hashizume et al.95 in 2003. Since then, many available reports highlight how robotic gastrectomy is a safe and feasible option for the treatment of gastric cancer93–97; unfortunately these published studies are small and limited to perioperative outcomes, with no oncological long-term results. Similarly, a published meta-analysis evaluated eight retrospective studies comparing RAG with laparoscopic gastrectomy98 reporting RAG is as acceptable as laparoscopic gastrectomy in terms of safety and oncological effectiveness, highlighting a lack of oncological long-term outcomes. Recently, Coratti et al.99 reported an unique retrospective study providing long-term survival data following 98 robot-assisted gastrectomies for cancer, suggesting that the robotic platform can produce oncological outcomes similar to open or conventional laparoscopic surgery.

Currently, although there is a lack of specific studies investigating the role of robotic surgery in the AGC settings, the accepted indications for RAG are similar to those in laparoscopic surgery. However, the robotic approach for treatment of AGC should be performed only in the context of controlled studies and in dedicated centers.

Conclusion

In 2015, several controversial issues and open questions as regard the optimal surgical treatment of advanced GC surgical treatment still exist. Depending on the site and extent of cancer, surgery remains the only potentially curative treatment for AGC, and a spleen and pancreas-sparing D2 lymphadenectomy should be recommended as standard of care in resectable neoplasms. Anyway, a multimodal approach is mandatory to achieve better survival results. Perioperative and adjuvant chemotherapy can improve outcome of resectable advanced gastric cancer treated with standard of care surgical approach. Nevertheless results of neoadjuvant therapy trials are controversial, and further data related to the open problems will be provided by expected results of the ongoing randomized studies. Furthermore, more aggressive approaches to surgical resection including cytoreductive surgery plus HIPEC for peritoneal carcinosis as well as surgical treatment of liver-limited metastases, may also be considered for the treatment of selected patients. In the same way, minimally invasive gastrectomy, either laparoscopic or robotic, is currently under extensive consideration as possible approached that should be offered by experienced surgeons in dedicated centers. Although more studies are needed to adequately assess the indications and oncological effectiveness of minimally invasive techniques in advanced gastric cancer treatment, their surgical potentiality in continuous quality improvement of gastric cancer treatment cannot be overlooked.

Conflict of interest statement

The Authors have no conflict of interest or financial ties to disclose.

References


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