

Updating advances and controversies on the multidisciplinary therapy of gastric cancer

Fei Shan, Jiafu Ji

Beijing Cancer Hospital, Peking University School of Oncology, Beijing Institute for Cancer Research, Beijing 100142, China

Corresponding to: Jiafu Ji, MD. Department of Surgery, Peking University of School of Oncology, Beijing Cancer Hospital, No. 52, Fu-Cheng Road, Hai-Dian District, Beijing 100142, China. Tel: +86-10-88196048; Fax: +86-10-88196698. Email: jiafuj@hotmail.com.

Abstract: Gastric cancer is one of the most common malignancies. In recent years, the overall treatment modality of gastric cancer has been an integrated mode that combines standardized surgery and perioperative adjuvant therapies based on anatomy, tumor biology and immunology. Reasonable staging of gastric cancer is of great significance in guiding the choice of integrated treatment programs, determination of the efficacy and prognosis. Despite more detailed and accurate staging for gastric cancer and prognosis identification in the updated staging system, more are left to be solved. At the same time, the role of free intraperitoneal cytology and laparoscopy in staging should also be given adequate attention. In terms of operations, after years of extensive debate and exploration, D2 lymph node dissection involving nodes around named branches of the celiac trunk has been considered as a standard treatment. While the development of perioperative adjuvant treatment has substantially improved the outcomes of advanced gastric cancer, altered treatment strategies have also brought new challenges. In recent years, the rapidly developed new treatment technologies and targeted therapy combined with traditional chemotherapy provide a new opportunity for breaking through the existing bottleneck in this field.

Key Words: Gastric cancer; multidisciplinary therapy; advances; controversies



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Introduction

Gastric cancer is one of the most common malignant tumors. Data show a global annual increase of about 934,000 gastric cancer patients and about 734,000 deaths worldwide, with 56% from China and Japan (1). Although surgery is still the primary treatment option for gastric cancer, the treatment model has undergone significant changes: the previously used simple gastrectomy has been replaced by radical approaches aiming at lymph node dissection; and anatomy-based operations are giving their place to an integrated mode that combines standardized surgery and perioperative adjuvant therapies based on anatomy, tumor biology and immunology. This article summarizes the latest research advances and clinical significance of the multidisciplinary management of gastric cancer in recent years as follows.

Staging of gastric cancer

Reasonable staging is the first step in the multidisciplinary management of gastric cancer, a significant link for the choice of treatment programs and determination of the efficacy and prognosis. Since its first edition in 1977, the TNM staging system has been used as a basis for the clinical staging of gastric cancer and a standard staging method in each update of the clinical diagnosis and treatment guidelines of gastric cancer. On January 1, 2010, the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC) promulgated the 7th edition of TNM staging (2), including a new set of TNM staging criteria for gastric cancer. Compared with the 6th edition of TNM staging in 2003, the new system includes major adjustments regarding the identification of tumor invasion, lymph node metastasis and

other aspects of gastric cancer.

These include:

- (I) T stage: (i) The original T1 is divided into T1a (tumor invasion confined to the mucosa) and T1b (invasion of the submucosa); (ii) the original T2 is divided into T2 (tumor invasion of the muscle) and T3 (invasion of serosal connective tissues); and (iii) the original T3 and T4 are respectively changed to T4a [tumor invasion through the serosa (visceral peritoneum) but no invasion of adjacent structures], and T4b (tumor invasion of adjacent structures).
- (II) N stage: Using a cutoff of three metastatic nodes, the original N1 was divided into N1 (metastasis of 1-2 regional lymph nodes) and N2 (3-6 regional lymph nodes); and The original N2 and N3 are combined as N3 (metastasis of 7 or more regional lymph nodes).
- (III) M stage: Mx (distant metastasis unassessable) is removed.

The new staging system was subject to academic verification from different angles after its release. Qiu *et al.* (3) conducted a retrospective analysis of 1,000 patients with gastric cancer, and found that the 7th version was not as efficient as the 6th version in predicting the 5-year survival. Ahn *et al.* (4) compared the two staging criteria in 9,998 cases of gastric cancer, however, suggested that the new one better reflected the difference in survival between patient groups. Nevertheless, these changes signify more active and meticulous treatment strategies for gastric cancer patients with regional lymph node metastasis as developed by the international academic community, which is consistent with China's past experience in this regard. In this revision, however, the original IV stage regarding non-distant metastases has been moved forward. Whether this adjustment is reasonable remains subject to further discussion, and the relevant verification and analysis is underway. Moreover, in light of the lacking of sufficient data on individualized treatment, the modification of treatment strategies in line with the updated staging also needs to be further studied.

In Japan, anatomic classification of lymph nodes based on the location of primary lesions has been used to determine the degree of metastasis (N1-N3, M1) and staging and define the corresponding dissection scope (D1-D3) until the provision of the 13th edition. However, in view of the complexity and lacking of objective identification of the location of primary lesions and metastatic lymph nodes,

these staging criteria have not been accepted by non-oncologists as well as investigators in other countries. Meanwhile, a growing number of studies have shown that classification based on the number of metastases is a better indicator of prognosis than the anatomic one. Therefore, the anatomic N stage staging has been abolished and replaced by the lymph node-based methodology in the new Japanese guidelines and management protocols. The current revision fully reflects the general applicability and objectivity of tumor staging valued by both Eastern and Western scholars.

At present, the primary means for diagnosing gastric cancer include endoscopy, endoscopic ultrasound, CT, PET-CT and MRI, where pathological diagnosis is still the gold standard. Difficulty in determining the depth of invasion and lacking the ability to identify metastases to lymph nodes and distant tissues make traditional endoscopy only a qualitative diagnostic tool, which can not be used for staging. Endoscopic ultrasound has an accuracy up to 80.3% in preoperative staging of gastric cancer, and has particularly great clinical significance in determining levels of tumor invasion. CT and MRI have a higher sensitivity for lymph node metastasis and distant metastasis. In addition, preoperative diagnostic laparoscopy enables accurate observation of the location and extent of the primary tumor, lymph nodes, peritoneal metastasis and invasion of adjacent tissues, and is thereby gaining more and more attention in recent years. Muntean *et al.* (5) conducted staging laparoscopy (SL) for 45 patients with gastric cancer and found that the tool had an overall sensitivity of 89%, specificity of 100% and diagnostic accuracy of 95.5%. It also showed 54.5% sensitivity, 100% specificity and 64.3% accuracy for lymph node metastases. On the other hand, PET/CT has been more and more valued in the assessment of resectable gastric cancer. Hur *et al.* (6) suggested in a study that a higher ¹⁸FDG uptake of the primary tumor and regional lymph nodes may indicate a higher degree of local progression and lower chance for radical treatment, hence reducing the possibility of a simple laparotomy.

Treatment options for early gastric cancer

The Japan Gastrointestinal Endoscopy Society first introduced the concept of early gastric cancer (EGC) in 1962 (7). EGC is confined to the intramucosal lesion, regardless of its size or lymph node metastasis. It is generally believed that lymph node metastasis may occur even in early gastric cancer, and thus D2 resection has

been regarded as the standard surgery for early gastric cancer. With deepened studies on the molecular biology and clinical pathology of EGC and gradual understanding of the pattern and biological behavior of lymph node metastasis, the treatment model has undergone great changes. Surgeries with narrowed scope of gastrectomy and lymph node dissection are introduced, including endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), laparoscopic wedge resection (LWR), intragastric mucosal resection, (IGMR), laparoscopic-assisted radical gastrectomy and other surgical procedures. Many long-term follow-up results show that with appropriate surgical indications, minimally invasive surgery has benefits of less postoperative pain, faster recovery of gastrointestinal function and less blood loss without increasing postoperative recurrence of cancer.

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD)

The currently accepted indications for EMR treatment of EGC include visible mucosal carcinoma (cT1a) with a size <2 cm, differentiated histological type and no formed ulcers. Studies have confirmed that lymph node metastasis is rare among cases with those indications. If pathological results confirm invasion of the superficial submucosa without involvement of vessels, gastrectomy or close follow-up may be applied. If SM1 is invaded with vascular and lymphatic involvement or infiltration of deep submucosal SM2, D2 gastric resection should be added. Introduced since 2000, ESD has the following advantages compared with EMR: (I) Resection with controllable scope and size, enabling complete removal of even large tumors; and (II) Ulcer lesions are no longer a contraindication for ESD. Therefore, ESD can achieve complete removal of larger even ulcer lesions. EMR or ESD currently facing the biggest problem is how to improve the accuracy of preoperative staging.

Laparoscopic assisted gastrectomy

In recent years, Japanese scholars put forward that laparoscopic gastrectomy is suitable for about 20% of candidates of gastric cancer surgery (8,9). So far, however, randomized controlled trials with a large sample comparing laparoscopic (assisted) surgery and open surgery are still lacking, and there are only a few small-scale controlled trials available (10,11). No high-level evidence was derived

from these results to demonstrate the superiority of laparoscopic surgery, as a minimally invasive treatment, in the intraoperative bleeding volume, respiratory dysfunction, narcotic dosage, and length of hospital stay or other indicators (12). Hence, laparoscopic surgery is still considered only for IA, IB patients and as an experimental option. The recommendation grade of laparoscopic surgery for gastric cancer is merely “C” in the Japan Society of Laparoscopic Surgery Clinical Guidelines. Therefore, although it is technically feasible to perform laparoscopic surgery for a strict selection of gastric patients to achieve as effective D2 resection as open surgery, this modality needs to be further explored due to the lacking of clinical trial results with a large sample and evidence-based design.

Function-preserving minimally invasive surgery

This mainly includes the following types: (I) Laparoscopic assisted vagus-preserving radical surgery; (II) Pylorus-preserving gastrectomy (PPG); (III) Laparoscopic assisted vagus sparing segmental gastrectomy (LAVSSG). These approaches improve the quality of life by preserving the hepatic and celiac branches of the pyloric vagus and thus effectively improving postoperative digestive function and reducing the incidence of gallstones (13) and diarrhea. However, due to overlapping indications with endoscopic surgery, it is not commonly used in conventional therapy. Careful consideration should be given to older patients and those with poor body conditions. However, since function-preserving local excision provides better quality of life (14) after operation, renewed assessment may be possible as diagnostic techniques (such as sentinel lymph node detection technology) advance and standard options change.

Multidisciplinary management of advanced gastric cancer

Surgical treatment

The long-term survival in patients with advanced gastric cancer is less than 30%. Surgery has dominated in the combined treatment for long. Two preliminary consensus are present in gastric cancer surgery: Surgery alone can not provide biologically radical treatment even with extended resection and lymph node dissection; and palliative resection enables better outcomes in patients without distant metastasis than those untreated. For advanced gastric cancer, a commonly accepted practice is standard surgery for the purpose of radical resection,

which requires removal of 2/3 or more of the stomach and D2 lymph node dissection to ensure R0 resection of the primary tumor (distance between gross margin and the original lesion >5 cm and microscopic negative margins). Correspondingly, non-standard operations may also be available with varying resection and dissection extents based on disease progression.

Scope of lymph node dissection

The scope of lymph node dissection has been a highly controversial topic in studies of gastric cancer. Most investigators from Japan, China, Korea and some from Europe and the US suggest extended lymph node dissection (ELND), which is advised against by most European and American investigators. In recent years, however, they have accepted most of the Asian opinions with the release of a series of large-scale randomized controlled trial results. A retrospective analysis of the data of 1,377 patients undergoing gastric cancer resection from the US-SEER database showed that the longest survival period of advanced patients was among those with 15 or more N2 lymph nodes or 20 or more N3 lymph nodes (15). A 15-year follow-up of the Dutch study also revealed increased survival after D2 dissection. A further analysis of the cause of death pointed out that the mortality related to gastric cancer after D2 operation was obviously lower than those undergoing D1 dissection (37% versus 48%, $P=0.01$), whereas higher perioperative mortality as a result of the combined splenectomy or pancreatectomy was a major cause of bias in the study (16). The Italian gastric cancer study group reported the results of pancreas-preserving D2 dissection, which confirmed that the perioperative morbidity and mortality of D2 was comparable to D1 surgery (17). Australia and Spanish studies also demonstrated that D2 surgery improved patients' quality of life without increasing their risk of perioperative mortality (18,19). Enzinger *et al.* conducted a subgroup analysis of the highly controversial INT0116, showing that D1 or D2 surgery tended to improve survival in centers with a relatively large number of gastric cancer patients (20).

Therefore, starting from the 2010 version, NCCN guidelines for surgical treatment of gastric cancer have particularly provided that "modified" D2 surgery (not combined with pancreatectomy or splenectomy) performed by experienced surgeons in larger-scale cancer centers could actually provide lower mortality and better survival benefits. Hence, "radical surgery for gastric cancer should be completed by experienced surgeons in a large cancer

center, which should include dissection of regional lymph nodes-perigastric lymph nodes (D1) and lymph nodes along the named vessels accompanying the celiac trunk for the purpose of examining at least 15 or more lymph nodes". D2 lymph node dissection involving nodes around named branches of the celiac trunk has been considered as a standard treatment.

Extensive surgery

Extended radical resection is performed for primary gastric cancer or metastases that directly invade perigastric organs (T4) or those with lymph node metastasis of N2 where radical resection is still available (*Table 1*). This includes: Extensive resection combined with removal of other organs; and D2 or above level lymph node dissection, such as surgeries targeted at IIIa, IIIb and some IV lesions involving the number 16 lymph nodes.

(I) Extended resection combined with removal of the pancreas and the spleen

Since dissection of numbers 10 and 11 lymph nodes is required for D2 dissection in upper gastric cancer, some investigators suggested combined resection of the left pancreas, the splenic artery and vein and the spleen. However, this brought to a high incidence of severe postoperative complications such as pancreatic fistula, intra-abdominal infections and diabetes. Wang *et al.* (27) randomly assigned 84 patients with advanced gastric cancer to receive pancreas-preserving radical resection (38 cases) and combined pancreatic resection (46 cases). As a result, postoperative complication rates were 23.7% and 52.2%; respectively, while the postoperative 5-year survival rates were the opposite -- 42.4% and 35.6%, suggesting that routine combined resection of the head and tail of the pancreas should be avoided in upper and medium advanced gastric cancer. Therefore, combined pancreatectomy is often not recommended when the lesion is not invading this organ and only metastasis of the lymph nodes around the splenic artery or splenic hilum is suspected. Left pancreatic resection combined with splenectomy is only indicated for patients whose gastric cancer has directly invaded the pancreas.

For advanced gastric cancer of the upper stomach, it has been controversial as to whether splenectomy should be combined for complete dissection of numbers 10 and 11d lymph nodes. In particular, European and American investigators have regarded this combination as a high-risk modality. Recent studies have found that

Table 1 Randomised trials comparing the extent of lymphadenectomy

	Arm	N	Morbidity (%)	Mortality (%)	5-year Survival (%)	10-year Survival (%)	15-year Survival (%)
Cuschieri <i>et al.</i> (1999) (21)	D1	200	28	6.5	35	-	-
	D2	200	46	13	33	-	-
Bonenkamp <i>et al.</i> (1995) (22); Hartgrink <i>et al.</i> (2004) (23); Songun <i>et al.</i> (2010) (16)	D1	380	25	4	45	30	21
	D2	331	43	10	47	35	29
Degiuli <i>et al.</i> (2004) (24)	D1	76	10.5	1.3	-	-	-
	D2	86	16.3	0	-	-	-
Wu <i>et al.</i> (2006) (25)	D1	110	7.3	0	53.6	-	-
	D3	111	17.1	0	59.5	-	-
Sasako <i>et al.</i> (2008) (26)	D2	263	20.9	0.8	69.2	-	-
	D2+PAND	260	28.1	0.8	70.3	-	-

the occurrence of splenic lymph node metastasis is mostly associated with gastric cancer at the cardia area, with an incidence of 9.8-14%, and is mainly observed in advanced tumors that have invaded into or beyond the serosa (T4). Since direct violation of the spleen is clinically rare, prophylactic splenectomy does not provide better outcome for the treatment of gastric cancer than spleen-preserving approaches and it is therefore not routinely advised. A number of clinical trials, including the (28) Japanese JCOG0110, are underway to explore this practice. Nonetheless, the preliminary consensus for now is that splenectomy should be performed as long as the spleen is directly invaded by IIIb and IV gastric cancer at the cardia or greater curvature, or circulation metastasis and splenic lymph node metastasis is present.

In short, for gastric cancer of the upper and medium part of stomach that invades the tail and head of pancreas, total gastrectomy should be combined with spleen and pancreatic resection; in the case of metastasis of the numbers 10 and 11 lymph nodes, combined splenectomy should be considered. Prophylactic splenectomy should not be performed when there is no metastasis to numbers 10 and 11 lymph nodes.

(II) Lymph node dissection at the level of D2 or above

The significance of extended dissection is unclear. The significance of prophylactic number 16 lymph node dissection has been denied by a Japanese randomized controlled trial (JCOG9501) (26). For metastasis to the number 16 lymph nodes without other non-radical curable factors, although R0 could be achieved by D2+No. 16

dissection, the outcomes remain poor. Whether D2 or D2+No.16 should be the choice following downstaging by preoperative chemotherapy is still under study.

Perioperative treatment

Perioperative chemotherapy

Changes in the trend of managing solid tumors such as breast cancer and lung cancer have in large part triggered a revolution in the field of tumor treatment. It is recognized that tumor is a systemic disease even in the early stages, which entails systemic management such as chemotherapy. Tumor recurrence and metastasis are associated with not only the completion of surgical resection and lymph node dissection, but also the presence of micrometastases and its further growth and proliferation, which play a more important role. For a long time, attempts have been made with adjuvant chemotherapy to control relapse and metastasis, though no satisfying, definite results have been produced. Adjuvant chemotherapy after the resection of primary lesions does not achieve individualized effects even applied according to the specific staging. Therefore, the concept of preoperative adjuvant therapy (also known as neoadjuvant therapy) has been introduced based on the experience of adjuvant therapy, which includes neoadjuvant chemotherapy, neoadjuvant radiotherapy and neoadjuvant chemotherapy. The introduction and application of preoperative neoadjuvant treatment has been a challenge of the new century to both cancer surgeons and physicians (*Figure 1*).

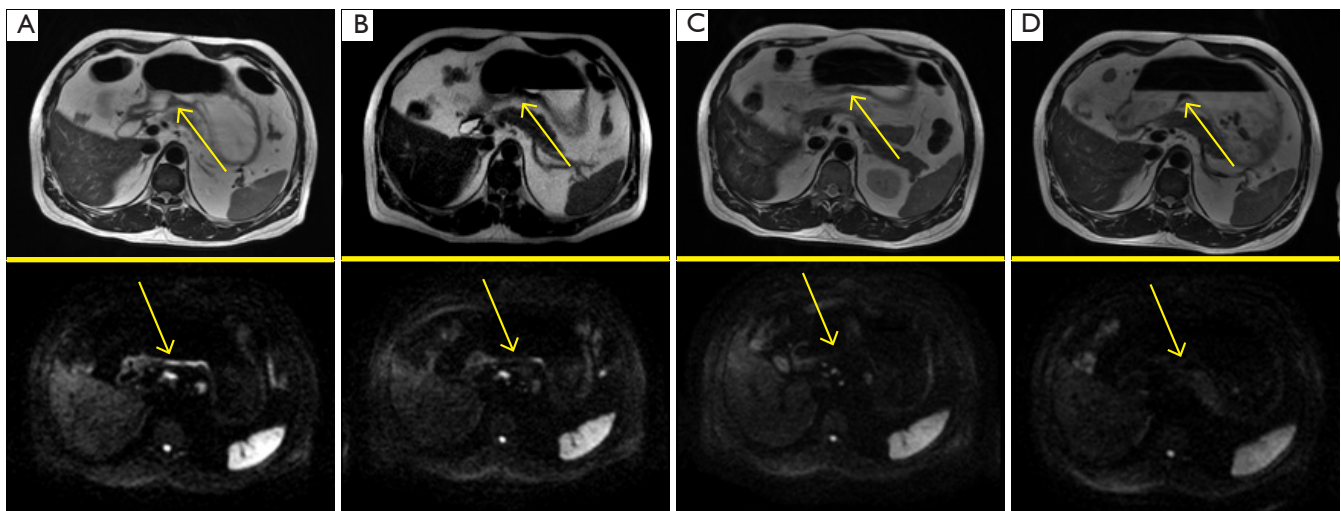


Figure 1 Metabolic response to chemotherapy. Patient with CT and EUS staged T4aN2 disease underwent laparoscopy with peritoneal washings, which was negative for M1 disease. Combined PET/CT was performed prior to the initiation of chemotherapy in the form of Oxaliplatin and TS-1 (Panel A). Repeat imaging was obtained after 2-cycles intervals. Note, the decreased metabolic uptake within the primary tumor which corresponded to a decrease in tumor size seen on CT. The patient underwent radical D2 gastrectomy and was found to have pathological complete response

The most representative clinical trial regarding perioperative chemotherapy is the UK MAGIC study (29). In the study, three cycles of epirubicin combined with cisplatin and 5-FU (ECF regimen) chemotherapy were given respectively before and after surgery, and were well tolerated in the 86% patients who completed the preoperative chemotherapy. In the combination therapy group, 229 patients (92%) received surgical exploration, of which 69% received radical surgery, while only 66% patients received radical treatment in the surgery alone group. There was no significant difference in the postoperative mortality and surgically related mortality between the two groups. Pathological tumor size was used to evaluate the efficacy of treatment, and the results showed a significantly lower value in the combination therapy group than in the surgery alone group ($P < 0.001$). The disease-free survival and 5-year survival rate in the combined treatment group were significantly prolonged, with a 25% decrease in the risk of recurrence and metastasis ($HR = 0.75$, $P = 0.009$). The results suggested that perioperative chemotherapy might improve long-term survival in patients with advanced gastric cancer, where neoadjuvant chemotherapy could downstage the T, N staging of locally advanced gastric cancer and improve the surgical cure rate.

Currently accepted principles of neoadjuvant chemotherapy necessitate control of micrometastasis

in high-risk groups with locally advanced yet radically resectable cancer. The specific indications include clinical stage II-IIIb ($cT3-4$, $cN1-2$) with the use of following regimens: EEP (30), ECF (29), OLF (Oxaliplatin, leucovorin, 5FU) and so on. For cases whose lesions are not radically resectable, the objective will be downstaging III and IV advanced tumors with a larger size and extensive lymph node metastasis. The specific indications include $cT3-4$, $cN2-$, M1 (LYM) with the use of following programs: P-ELF (CDDP, etoposide, leucovorin, 5-FU), EAP (etoposide, ADR, CDDP), CPT-11 + CDDP (31), PLF (32), S-1 + CDDP, OLF (Oxaliplatin, leucovorin, 5-FU), DCF (Docetaxel, CDDP, 5-FU) and so on. Phase III clinical trial results have confirmed that radiotherapy is effective against tumors of the gastroesophageal junction (33). In addition, although there are reports that potent chemotherapy may achieve a higher negative conversion rate for patients with positive peritoneal free cells, a high level of clinical evidence is still lacking.

Regarding adjuvant chemotherapy after surgery, the INT0116 (34) study and MAGIC study (29) from the US have respectively proved the effectiveness of postoperative 5-FU/LV combined with radiotherapy and ECF (Epirubicin + CDDP + 5-FU) for preoperative/postoperative chemotherapy, though neither of them is not as effective as the overall result in the Japanese trial. The

Table 2 Randomized trials of surgery only versus surgery combined with chemotherapy or chemoradiotherapy

	Arm	N	RFS	OS
MacDonald <i>et al.</i> (2001) (34)	Surgery only	275	31% (3-year)	41% (3-year)
	CRT	281	48% (3-year)	50% (3-year)
Cunningham <i>et al.</i> (2006) (29)	Surgery only	253	-	23% (5-year)
	ECF	250	-	36% (5-year)
Sasako <i>et al.</i> (2011) (35)	Surgery only	530	53.1% (5-year)	61.1% (5-year)
	S-1	529	65.4% (5-year)	71.7% (5-year)
Boige <i>et al.</i> (2007) (38)	Surgery only	111	21% (5-year)	24% (5-year)
	FP	113	34% (5-year)	38% (5-year)

CRT=postoperative chemoradiotherapy (fluorouracil plus leucovorin followed by 45 Gy radiotherapy); ECF=Three preoperative and three postoperative cycles of epirubicin, cisplatin, and fluorouracil; S-1=cycles of S-1 (orally active combination of tegafur, gimeracil, and oteracil) for 1 year postoperatively; FP=2–3 cycles of preoperative fluorouracil and cisplatin; postoperative FP was recommended for patients with a response or stable disease with pN+

latest ACTS-GC trial has (35) confirmed that one-year TS-1 adjuvant chemotherapy after D2 radical treatment for stage II and III gastric cancer is associated with increased survival (71.7% *vs.* 61.1%, HR=0.669, 95% CI 0.540–0.828) and decreased risk of recurrence and metastasis by 34.7% (HR=0.653, 95% CI 0.537–0.793). The SPIRITS (36) study compared TS-1 combined with cisplatin and TS-1 single-drug treatment in 305 patients with gastric cancer from 38 centers in Japan. The results showed that the combined treatment group had significantly better overall and progression-free survival than the single-agent S-1 group. Therefore, for the initial treatment of gastric cancer patients with standard chemotherapy, Japanese investigators recommend TS-1 + CDDP36 (36), while the ECF program is still the traditional treatment recommended by western countries. Since 2009, NCCN guidelines have included paclitaxel-based chemotherapy (2B evidence level) in systemic gastric cancer chemotherapy and valued sorafenib and other targeted agents in combination with conventional chemotherapy. With the announcement of the ToGA study results (37), the therapeutic value of chemotherapy combined with trastuzumab for HER2-positive advanced gastric cancer patients has been confirmed by investigators from various countries, and this therapy has been included in the standard program for metastatic or locally advanced gastric cancer treatment (2A evidence level). Throughout the recent years, targeted drugs may have been playing an increasingly important role in the non-surgical treatment of gastric cancer, a trend shown in relevant clinical trials.

Perioperative radiotherapy

Preoperative induction chemotherapy followed by chemoradiotherapy can produce significant pathological remission and prolong the survival of gastric cancer patients (Table 2). MacDonald *et al.* (34) conducted a randomized controlled study (INT0116) on 556 patients undergoing surgery alone or combination of postoperative radiotherapy and chemotherapy (5-FU/LV +45 Gy radiotherapy), which showed that postoperative radiotherapy and chemotherapy was associated with prolonged survival. Since then, the program became the standard treatment in the United States. At present the CALGB80101 study is comparing it with the ECF program. However, in view of the 10-year follow-up results from the INT0116 study, the efficacy was limited in all subgroups except for poorly differentiated adenocarcinoma. The Korean randomized controlled study using capecitabine/cisplatin (XP) as a control group is also in progress.

Intraperitoneal hyperthermic chemotherapy

The postoperative recurrence rate gastric cancer is high and peritoneal recurrence is the most common form with an overall incidence up to 50% for patients with advanced gastric cancer postoperatively. Developed in recent years, the intraperitoneal chemo-hyperthermia (IPCH) is one of the highly valued therapeutic tools, which combines the anti-cancer effects of synergies from regional chemotherapy and hyperthermia. This easy-to-operate technology, showing significant effects both in the prevention and treatment of peritoneal metastasis or postoperative

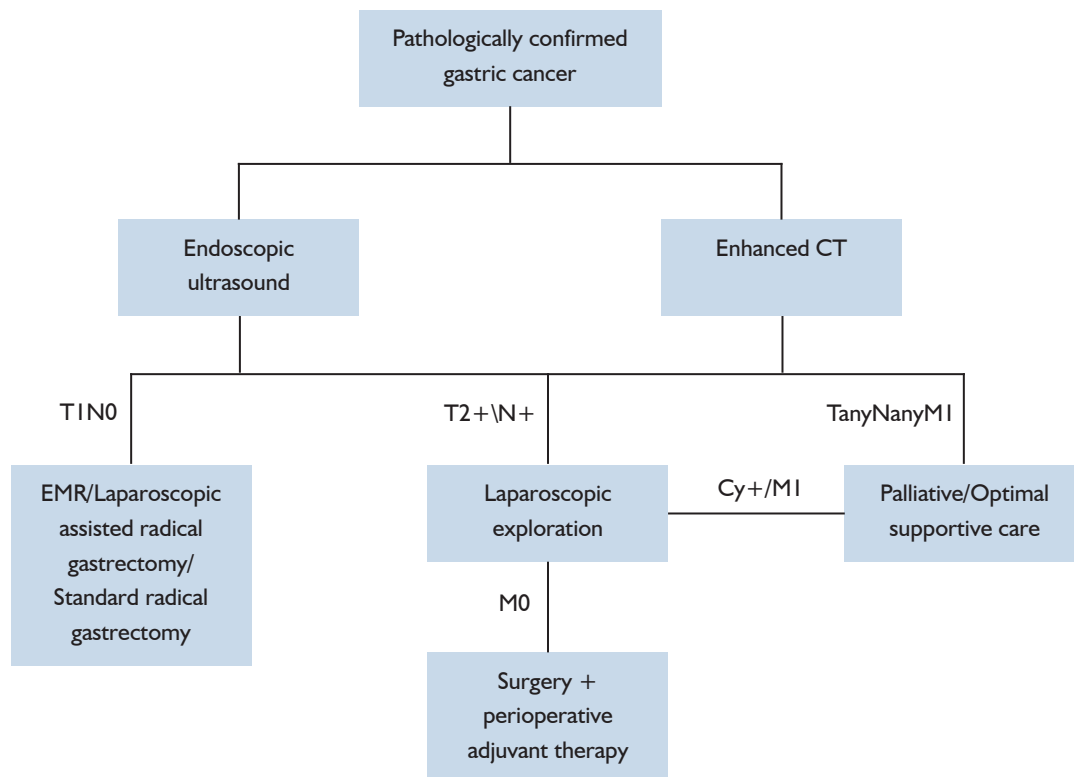


Figure 2 The multidisciplinary therapy of gastric cancer

recurrence of advanced gastrointestinal cancer with small toxicity, has become an ideal surgical adjuvant therapy.

Gastric cancer patients with no distant metastasis that involves the liver, lung, brain or bone and no serious organic complication of the heart, lung, liver, kidney and other vital organs, who have had the primary foci cured or palliatively resected and have one of the following conditions, are eligible for IPCH treatment: (I) Positive for intraperitoneal free cancer cells (FCC); (II) Tumor invasion into or beyond the serosa, or peritoneal metastasis; and (III) Postoperative scattered peritoneal recurrence or small or moderate malignant ascites, for whom radical cytoreductive surgery is possible, i.e. surgical removal of as much visible metastases as possible, particularly nodules on the peritoneal surface. Relevant articles have noted that hyperthermic perfusion chemotherapy is only effective on nodules of 3-5 mm. Therefore, to achieve satisfying outcomes, it is recommended to perform IPCH therapy following minimization of the intra-abdominal tumor burden.

In summary, the new mode of 'surgery + perioperative therapy' has come on the stage of gastric cancer treatment (Figure 2). With the development of medical technology and wide application of more and more novel

technologies, evidence-based approaches in combination with the strengths of various treatments will be the key to multidisciplinary management of gastric cancer for ultimately improving the outcomes and quality of life of these patients.

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