these editorial questions: is it new, is it true (validity, internal and external and does the evidence support the conclusions) and how will it affect patient care? For rejected manuscripts, read the reviews and consider appealing, but in doing so don't whine or get angry. Remember: every paper will find a home in the right journal!

Friday, 23 March, 14:00–15:30

Session VII. Gastric Cancer

PG 9.01 SPEAKER ABSTRACT

Optimal surgery for gastric cancer: Is more always better?

W. Allum. *Department of Surgery, Royal Marsden NHS Foundation Trust, London, United Kingdom*

The extent of surgical resection for carcinoma of the stomach has been debated for many years. The aims of surgery are to obtain complete histo-pathological clearance of all possible sites of disease based on oncological principles. This has included radical resection of the primary site with combined organ resection as required and resection of associated lymph nodes. Detailed understanding of the natural history of gastric cancer has resulted in the Pichlmayr total gastrectomy "en principe" approach being super-ceded by a tailored approach according to tumour and patient characteristics. Careful tumour staging is fundamental to the selection of surgical intervention. Endoscopic therapy is recommended for well-differentiated, mucosal cancers less than 2 cm in size as the risk of nodal disease is 0–3%. Recently these criteria have been extended to include some larger and ulcerated cancers. Although extended lymphadenectomy has formed the basis of radical surgery, Japanese experience has also confirmed that for early gastric cancer involving the submucosa limited nodal resection can achieve the same outcome as standardized D2 lymphadenectomy. The approach to locally advanced T2, T3 and some T4 cancers has been defined by the Japanese Rules specifying proximal and distal margins as well as extent of lymph node resection. Translation of Japanese results to Western patients has not been straightforward. Two randomized controlled trials have shown limited or no benefit over conventional limited nodal dissection. However these studies have not been without criticism and individual specialist practice in the West now preferentially includes D2 lymphadenectomy in suitable patients. Extending conventional D2 lymphadenectomy has been evaluated but the results are not conclusive. Japanese RCTs have not shown an advantage but in selected cases several groups have reported a benefit. Historically radical gastric surgery in the West was associated with significant morbidity and mortality reflecting the comorbidity of the patient groups. Perioperative approaches have shown that outcome approaching that of radical surgery can be achieved with multimodal therapies for high risk patient groups for whom radical surgery would be contraindicated. Surgery for gastric cancer needs to be determined by a multidisciplinary team to ensure appropriate procedure selection for an individual patient. This allows all relevant information to be considered and to provide the best chance for high quality patient outcome.

PG 9.02 SPEAKER ABSTRACT

Is endosonography and laparoscopy essential before neoadjuvant therapy?

C. Schuhmacher. *Chirurgische Klinik und Poliklinik, TU München, München, Germany*

Clinical assessment of tumour stage is an essential step prior to multimodal therapy in gastric cancer. Based on recent literature indication for neoadjuvant chemotherapy excludes patients with mucosal or sub-mucosal cancer (early gastric cancer) or – in advanced cases – patients with a peritoneal seeding. Different radiological and nuclear imaging techniques are available for staging. Nevertheless, they do not provide sufficient resolution in order to evaluate the depth of infiltration of primary tumour in the hollow organ (T-category) or to accurately assess the peritoneal cavity (M-category). Only advanced clinical situations such as ascites formation or bulky intra-peritoneal masses will be detected by (noninvasive) imaging modalities (without direct inspection of the peritoneum). Thus, endoscopic ultrasound and diagnostic laparoscopy are the only diagnostic tools to address this clinical category with acceptable accuracy.

Several randomized trials are available for multimodal therapy of gastric cancer. Among these the EORTC 40954 trial is the only clinical study including both staging modalities, EUS and diagnostic laparoscopy (DL) into the pre-therapeutic staging process. The recently published French FFCD trial solely involved EUS in the clinical staging modalities and the pivotal MAGIC trial from UK did neither involve endoscopic ultrasound nor diagnostic laparoscopy.

Although EUS is known for high accuracy in discriminating clinical T-categories, the results of the EORTC 40954 trial reported less convincing numbers in this matter. 50% of patients in the surgery alone treatment arm revealed tumours with T-categories less advanced than pT3. This might be attributed to the high incidence of adenocarcinoma of the esophago-gastric-junction (AEG type II and III), a tumour location lacking serosal coverage.

In a prospective analysis of patients with locally advanced gastric cancer undergoing a diagnostic laparoscopy at the TU Munich, in 24% of all cases the diagnostic laparoscopy revealed findings, which beyond the standard imaging modalities, changed the initial stage of the disease.

In addition, detection of peritoneal seeding of gastric cancer will avoid unnecessary laparotomy and protect patients from a prognostically problematic tumour resection.

Retrieving peritoneal fluid for cytological assessment during the staging laparoscopy is an additional and highly useful diagnostic tool to rule out potential sources of therapy failure. Disseminated tumour cells result in a significant upstaging of the disease with dismal prognostic consequences even if no intra-peritoneal tumour growth is visible. These patients should rather be treated with a less toxic and yet lasting chemotherapy regimen including modern targeted antibody components.

Endoscopic ultrasound and diagnostic laparoscopy are essential in clinical staging of gastric cancer, especially in the context of multimodal therapy. Tomographic imaging modalities lack accuracy to detect both, early gastric cancer within the stomach wall and incipient peritoneal seeding.

Reference(s)

Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectablegastroesophageal cancer. N Engl J Med 355:11–20, 2006.

Feussner H, Omote K, Fink U, et al. Pretherapeutic laparoscopic staging inadvanced gastric carcinoma. Endoscopy 31(5):342–347, 1999.

Kelly S, Harris KM, Berry E, et al. A systematic review of the staging performance of endoscopic ultrasound in gastro-oesophageal carcinoma. Gut 49:534–539, 2001.

Schuhmacher C, Gretschel S, Lordick F, et al. Neoadjuvant chemotherapy compared with surgery alone for locally advanced cancer of the stomach and cardia: European Organisation for Research and Treatment of Cancer randomized trial 40954. J Clin Oncol. 2010 Dec 10;28(35):5210–8.

PG 9.03 SPEAKER ABSTRACT

Can adjuvant radiochemothrapy replace extended lymph node dissection?

E.P.M. Jansen. *Department of Radiation Oncology, Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands*

Surgical resection remains an essential part in the curative treatment of gastric cancer [1]. However, with surgery only, long-term survival is poor (5-year survival <25% in Europe). Randomized studies that compared limited (D1) lymph node dissection with more extended (D2) resections in the Western world, failed to show a survival benefit for more extensive surgery. 15-year follow-up of the Dutch D1D2 trial showed that D2 surgery was associated with lower locoregional recurrence rates and gastric-cancer related death rates than D1 surgery [2]. Centralization of gastric cancer surgery in Denmark increased the percentage of patients with at least 15 lymph nodes removed from 19 to 76 [3]. A substantial increase in survival was found with peri-operative chemotherapy in the MAGIC study [4]. In addition, the SWOG/Intergroup 0116 study showed that postoperative chemoradiotherapy prolonged 5 year overall survival compared to surgery only.[5] Since 54% of patients in this study had a D0 dissection, many judged chemoradiotherapy (CRT) to compensate for suboptimal surgery. Investigators from the SWOG concluded that surgical undertreatment undermined survival in their trial, but subgroup analysis did not have enough power to detect an association between D-level and outcome [6]. However, in a Korean study with almost 1000 patients who all underwent a D2 dissection, 544 patients received postoperative CRT accordingly to the SWOG regimen [7]. Although patients were not compared in a randomized trial, the study demonstrated a survival benefit with postoperative CRT (5 year OS 57.1% vs. 51%, $p = 0.02$). The percentage of patients that had >15 lymph nodes removed was >98% in both groups. Results of the already completed ARTIST trial from Korea (clinicaltrials.gov NCT 00323830), where 458 patients are randomized between postoperative capecitabine/cisplatin and capecitabine plus 45 Gy radiotherapy after D2 dissection, are eagerly awaited. At our institute phase I–II studies with adjuvant cisplatin and capecitabine based CRT have been performed in over 120 patients with resected gastric cancer. These studies demonstrated that intensive postoperative concurrent CRT has manageable toxicity [8–10]. Retrospective comparison of patients treated in these studies with those that had surgery only in the D1D2 study, demonstrated that postoperative CRT was associated with better outcome, especially after D1 or a R1 resection [11]. For daily practice it remains unclear whether patients with operable gastric cancer should have pre- (and post-) operative chemotherapy or postoperative CRT. To resolve this dilemma the CRITICS (ChemoRadiotherapy after Induction chemotherapy In Cancer of the Stomach) study was developed. The CRITICS study is a randomized phase III trial (clinicaltrials.gov NCT 00407186) in which all patients receive 3 courses of ECC chemotherapy and then have D1+ gastric resection. After surgery

patients receive either another 3 courses of ECC chemotherapy or CRT. Currently, over 400 patients have been entered in the study. In conclusion, there is no evidence that CRT can replace D2 dissection. More importantly, it seems that CRT will have its best effect after optimal surgery.

Reference(s)

[1] Hartgrink HH, Jansen EP, van Grieken NC, et al: Lancet 374:477–490, 2009.
[2] Songun I, Putter H, Kranenbarg EM, et al: Lancet Oncol 11:439–449, 2010.
[3] Jensen LS, Nielsen H, Mortensen PB, et al: Eur J Surg Oncol, 2010.
[4] Cunningham D, Allum WH, Stenning SP, et al: N Engl J Med 355:11−20, 2006.
[5] Macdonald JS, Smalley SR, Benedetti J, et al: N Engl J Med 345:725–730, 2001.
[6] Hundahl SA, Macdonald JS, Benedetti J, et al: Ann Surg Oncol 9:278–286, 2002.
[7] Kim S, Lim do H, Lee J, et al: Int J Radiat Oncol Biol Phys 63:1279–1285, 2005.
[8] Jansen EP, Boot H, Dubbelman R, et al: Br J Cancer 97:712–716, 2007.
[9] Jansen EP, Boot H, Saunders MP, et al: Int J Radiat Oncol Biol Phys 69:1424–1428, 2007.
[10] Jansen EP, Boot H, Dubbelman R, et al: Ann Oncol 21:530–534, 2010.
[11] Dikken JL, Jansen EP, Cats A, et al: J Clin Oncol 28:2430–2436, 2010.

PG 9.04 SPEAKER ABSTRACT

Oesophagogastric cancer: A case for perioperative chemotherapy

M. Ychou. *Medical Oncology, Centre Régional de Lutte Contre le Cancer Val d'Aurelle, Montpellier Cedex 05, France*

Although the global incidence of gastric adenocarcinoma is declining in western countries, the incidence of gastroesophageal junction (GEJ) tumors has risen faster than other GI adenocarcinoma over the last quarter century [1].

For resectable desease, the use of adjuvant chemotherapy has been disappointing and has never been adopted as a standard of care. In 2001, Macdonald reported a positive phase III trial for a post operative radiochemotherapy regimen, but associated to a high digestive toxicity and a low quality of surgical procedures.

After several phase II trials of Neoadjuvant chemotherapy, the results of a large phase III study (MAGIC) were published in 2006 [2]. Five hundred and three patients with resectable stomach (74%), lower oesophagus or GEJ adenocarcinoma were randomized between surgery alone and perioperative chemotherapy using ECF regimen. A significant improvement of TN stage and R0 resection was obtained in the chemotherapy group and resulted in a better Progression Free Survival (HR 0.66) and a better 5 year overall Survival (36%versus 23%). The surgical mortality was not affected by pre-operative chemotherapy but only 55% of operated patients could initiate post-operative chemotherapy.

More recently, a French trial published in 2011 [3] confirms these results using another chemotherapy regimen with 5-Fu (800 mg/m^2/day day 1−4 in CI) and Cisplatin (100 mg/m^2 day 1 or 2) every 4 weeks. Two hundred and twenty four patients were randomized between surgery alone (n = 111) and perioperative chemotherapy (n = 113). At the opposite of the MAGIC trial, a majority of patients (75%) had a tumor located to lower oesophagus or GEJ.

No significant difference was obtained in pathological T or N staging but the neoadjuvant chemotherapy improved the R0 resection rate (84% versus 74%). The post operative fatal complications were similar in the two groups and only 50% of the patients could receive at least one cycle of postoperative chemotherapy.

The 5-year Disease Free Survival and Overall Survival were significantly improved in the chemotherapy arm, respectively 34% vs 19% and 38% vs 24%.

These two randomized trials support the use of peri-operative chemotherapy as a standard of care for resectable Oesophagogastric adenocarcinoma.

Some questions are still pending for the chemotherapy regimen: the role of Epirubicin, the possibility to replace Cisplatin by Oxaliplatin and intravenous 5FU by Capecitabine, the place of Taxanes.

Other questions have to be adressed in future trials: the early selection of good candidates to neoadjuvant chemotherapy (PET, Biomarkers, . . .), the place of Biologic drugs (Trastuzumab in HER-2 positive tumors, c-met inhibitors, . . .) or the role of pre-operative radiotherapy.

Reference(s)

[1] Botterweck AA, Schouten LJ, Volovics A, et al: Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. Int J Epidemiol 29:645–654, 2000.
[2] Cunningham D, Allum WH, Stenning SP, et al: Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 355:11−20, 2006.
[3] Ychou M, Boige V, Pignon JP, et al: Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: an FNCLCC and FFCD multicenter phase III trial. J Clin Oncol 29:1715–1721, 2011

Friday, 23 March, 16:00−17:30

Session VIII. Gastric Cancer

PG 10.01 SPEAKER ABSTRACT

Predicting the response to neoadjuvant chemotherapy I (Who profits from neoadjuvant chemotherapy)

C. Mariette. *Service De Chirurgie Digestive Et Générale Hôpital Claude Huriez, University Hospital of Lille, Lille, France*

Despite a decline in the overall incidence, gastric adenocarcinoma remains the second most common cause of cancer death worldwide and thus a significant global health problem. Even in early-stage locoregional confined disease the 5-year survival rarely exceeds 25−35%. Randomized trials have demonstrated a benefit from neoadjuvant and perioperative chemotherapy. However the optimal approach in individual patients is not clear and remains controversial. A consistent finding is that patients who have a histopathological response to neoadjuvant therapy are more likely to receive a survival benefit. These clinical data provide a strong argument for the urgent development of methods to predict histopathological response to neoadjuvant therapies for gastric adenocarcinomas. Published data demonstrate that clinino-pathological features (tumour histology and location), imaging through metabolic response by FDG-PET and tissue/molecular biomarkers may have all a predictive value for neoadjuvant therapies. However it is still uncertain from published data whether or not they will be useful for clinical decision making in individual patients. Existing candidate biomarkers need to be properly qualified and validated and novel biomarkers are required and an optimal approach should involve the combination and integration of clinical, imaging, pathological and molecular biomarkers.

PG 10.02 SPEAKER ABSTRACT

Predicting the response to neoadjuvant chemotherapy II (Ability of pretherapeutic parameters to predict response and prognosis early in patients with locally advanced gastric cancer)

S. Lorenzen. *NCT Nationales Centrum für Tumorerkrankungen, UNI-Klinikum Heidelberg, Heidelberg, Germany*

Introduction: Response to neoadjuvant chemotherapy is an independent prognostic factor in locally advanced gastric cancer. However, no prospectively tested pretherapeutic parameters predicting response and/or survival in gastric cancer are available in clinical routine.

Patients and Methods: We evaluated the prognostic significance of various clinicopathologic parameters in 410 patients who were treated with neoadjuvant chemotherapy followed by gastrectomy. Clinical and histopathological response evaluation was performed using standardized criteria. A prognostic score was created on the basis of the variables identified in the multivariate analysis.

Results: Three pretherapeutic parameters were identified as positive predictive factors for response and prognosis: tumor localization in the middle third of the stomach ($p = 0.001$), well differentiated tumors ($p = 0.001$) and intestinal tumor type according to Laurén's classification ($p = 0.03$). A prognostic index was constructed, dividing the patients into three risk groups: low (n = 73), intermediate (n = 274) and poor (n = 63). The three groups had significantly different clinical ($p = 0.007$) and histopathological response rates ($p = 0.001$) and survival times, with a median survival time that was not reached in the low risk group, 39.2 months in the intermediate risk group and 20.5 months in the poor risk group. The corresponding 5 year survival rates were 65.3%, 41.2%, and 21.2% ($p < 0.001$), respectively.

Conclusion: A simple scoring system based on three clinicopathologic parameters, accurately predicts response and prognosis in neoadjuvant treated gastric cancer. This system provides additional useful information that could be applied to select gastric cancer patients pretherapeutically for different treatment approaches. However, prospective testing of the score in an independent patient cohort is warranted.

PG 10.03 SPEAKER ABSTRACT

Lessons from the GASTRIC metaanalysis of adjuvant treatment

P. Rougier. *Digestive Oncology, Hopital Ambroise Paré, Boulogne Billancourt, France*

Background: Despite potentially curative resection of stomach cancer, 50−90% of patients die of disease relapse. Numerous encouraging phase II and phase III trials compared surgery alone to adjuvant chemotherapy, but definitive evidence is lacking. These trials generally used the overall survival at 5 years as the primary endpoint leading to long and costly trials. Our group has