Notable Grand Rounds
of the
**Michael & Marian Ilitch
Department of Surgery**

Wayne State University
School of Medicine

Detroit, Michigan, USA
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Steve H. Kim, MD, FACS

GASTRIC CANCER

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January 18, 2023

About Notable Grand Rounds

These assembled papers are edited transcripts of didactic lectures given by mainly senior residents, but also some distinguished attending and guests, at the Grand Rounds of the Michael and Marian Ilitch Department of Surgery at the Wayne State University School of Medicine.

Every week, approximately 50 faculty attending surgeons and surgical residents meet to conduct postmortems on cases that did not go well. That "Mortality and Morbidity" conference is followed immediately by Grand Rounds.

This collection is not intended as a scholarly journal, but in a significant way it is a peer reviewed publication by virtue of the fact that every presentation is examined in great detail by those 50 or so surgeons.

It serves to honor the presenters for their effort, to potentially serve as first draft for an article for submission to a medical journal, to let residents and potential residents see the high standard achieved by their peers and expected of them, and by no means least, to contribute to better patient care.

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Gastric Cancer

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January 18, 2023

The talk from which this paper was derived was delivered by Dr. Kim at the Wayne State University School of Medicine Surgical Grand Rounds on January 18, 2023.

Introduction

This paper is primarily about gastric adenocarcinoma but we will touch very briefly on two other gastric tumors often seen by general surgeons, i.e., GI stromal tumors (GIST) and gastric carcinoids.

Types of Gastric Adenocarcinoma

The Lauren classification of gastric cancers (Fig. 1) first described by Finnish pathologist Pekka Lauren divides gastric cancers into two types, intestinal and diffuse, dependent on their histologic and gross appearances.

The intestinal-type is so called because the cancer looks like intestinal mucosa. It tends to be well differentiated and to form glands infiltrating through the desmoplastic stroma.

The diffuse-type, in contrast, tends to be poorly differentiated, with signet ring cells and a less cohesive cellular architecture. It tends to spread more as a diffusely infiltrating tumor throughout the stomach, whereas the intestinal type tends to form large,
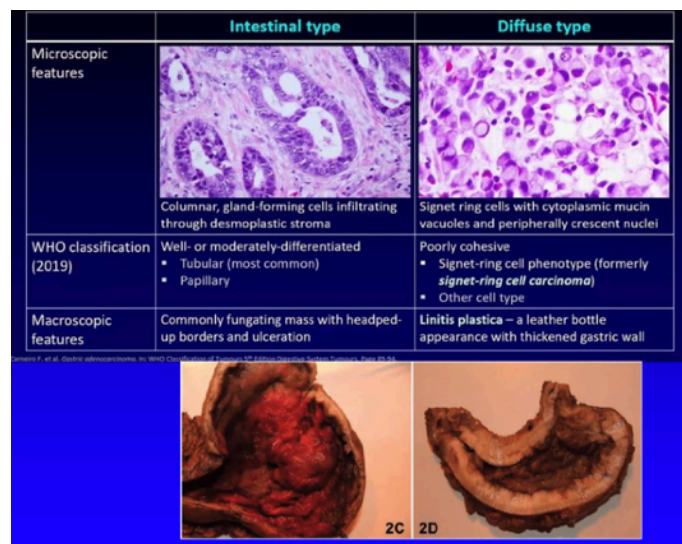

Fig. 1. Lauren classification of gastric adenocarcinoma

fungating masses. Advanced diffuse-type adenocarcinoma can become Linitis plastica which means "leather-bottle" stomach. As the name implies, the completely involved stomach becomes a firm, nondistensible sac. The actor John Wayne died of it.

The intestinal-type tends to be "epidemic," meaning its incidence may go up and down depending on various environmental and acquired risk factors. The diffuse-type tends to be "endemic," meaning it may go up and down slightly but for the most part there is a constant incidence over time. Hereditary gastric cancers are of diffuse-type.

Fig. 2 shows the epidemic areas of gastric cancer—Russia, Eastern Europe, the Asian countries. The United States is a relatively low incidence area of gastric adenocarcinoma so you won't see many gastric cancers in clinic here.
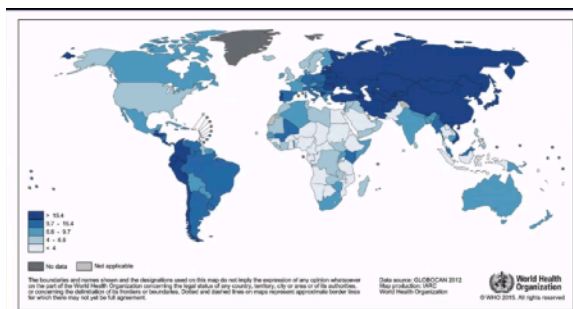

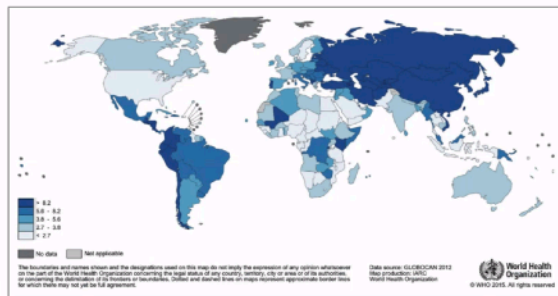**Fig. 2**. Distribution of gastric cancer cases worldwide in 2012.

Risk Factors

Risk-*reducing* factors include a diet rich in raw fruits and vegetables.

Factors associated with increased risk of gastric adenocarcinoma include:

- Smoking
- Salted and/or smoked foods
- Nitrate and nitrosamine preservatives.
- Previous gastrectomy for benign disease (e.g., peptic ulcer disease). These operations were commonly used to treat PUD in the 70s, before proton pump inhibitors came along. There is usually a long latency period. The mechanism is thought to be related to chronic bile reflux gastritis.
- Pernicious anemia and atrophic gastritis.
- Infection with *Helicobacter pylori*. As with hepatitis B infection and hepatocellular cancer, the rate of infection with the organism is much higher than the actual rate of the cancer with which it is associated. It's thought that chronic infection and inflammation acts as a tumor promoter in the stomach. It has been theorized that treating the infection may decrease the risk of cancer. Data from a program conducted in the Matsu Islands off the coast of Taiwan between 2004 and 2018 found that mass eradication of *H. pylori* significantly re-duced gastric cancer incidence within this population (**Fig. 3**) (1).
- The increasing incidence of GERD appears to correlate with an increased risk of cancer in the proximal part of the stomach, again likely due to tumor promotion caused by chronic inflammation.

Intestinal-type gastric adenocarcinoma, which is mainly associated with the above environmental and acquired risk factors,
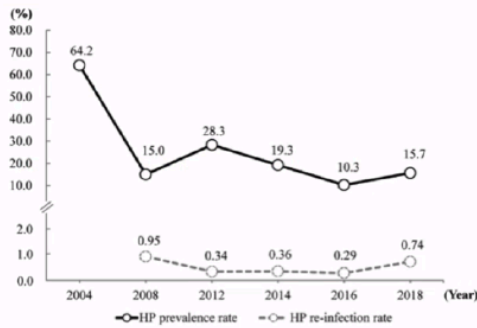
Figure 2   Prevalence rates and reinfection rates of *Helicobacter pylori* (HP).
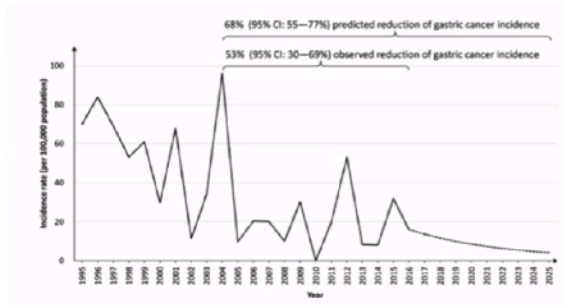
Figure 4   Incidence rates of gastric cancer between 1995 and 2016, correlated with the start of the mass eradication programme in 2004.

***Fig. 3**. Reduction in H. pylori infection associated with a reduction in gastric cancers. Source: See note 2.*

is somewhat decreasing in incidence globally, and tends to have a more distal predominance anatomically in the stomach. On the other hand, diffuse-type gastric adenocarcinoma appears to be slightly increasing in incidence. These also have a strong genetic component and a tendency to have tumor epicenter more frequently in the proximal stomach.

In further regard to proximal gastric cancers, it is useful to classify their specific location, because this may affect treatment. The Siewert classification divides proximal gastric cancer into three types - I, II, and III.

Type I is basically an adenocarcinoma in the distal esophagus that is impinging on the most proximal aspect of the stomach. Siewert Type II is adenocarcinoma originating at the GE junction. Siewert Type III is a true proximal gastric cancer arising in the fundus or the cardia of the stomach (**Fig. 4**).

Staging

Gastric cancer patients usually come to clinic with an endoscopy report and a pathology report showing adenocarcinoma. The tumor markers associated with the gastric cancer are CEA and CA 19-9. As with all tumor markers, these are only

helpful in diagnosis and treatment if they are elevated. A normal tumor marker does not rule out the diagnosis of a cancer with which it is associated.

If a tumor marker is elevated at the time of diagnosis, it is useful for monitoring treatment response, e.g., after potentially curative surgery, the levels may normalize. If so, then it can be used in post-operative surveillance, as a rising level suggests tumor recurrence, often before symptoms occur.
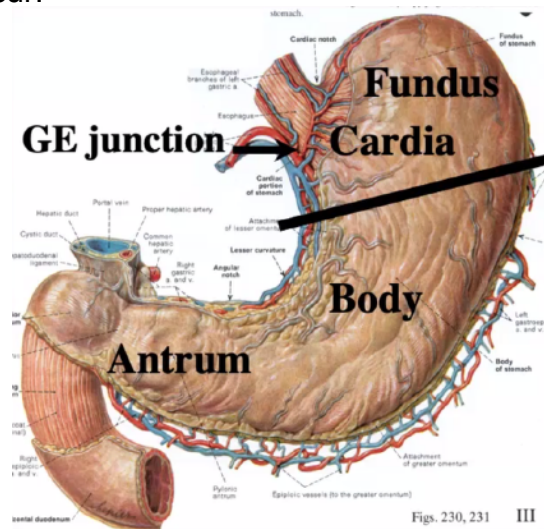

Fig. 4. Stomach anatomy

Initial staging is usually done with a CT scan of the chest, abdomen, and pelvis (see **Fig. 5**). PET scans are sometimes used but some insurance companies do not like to reimburse for them.
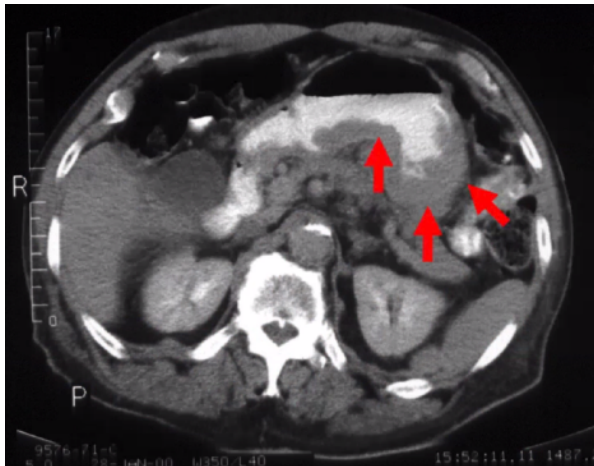

Fig. 5. CT scan showing a fairly obvious cancer in the posterior aspect of the stomach, as a large fungating lesion.

For your board exams, it is important to remember endoscopic ultrasound (EUS) as a means of preoperatively determining the T and the N stages of a cancer. The T stage is determined by how far into the wall the cancer has invaded (depicted graphically in **Fig. 6**). The N stage is determined by the number of lymph nodes that are clinically positive for metastatic disease, as follows:

N0:   0 nodes (+)
N1:   1-6 nodes (+)
N2:   7-15 modes (+)
N3:   >15 nodes (+)

Fig. 7 (opposite page) shows the EUS of a patient with very early gastric cancer. She was being followed for peptic ulcer disease, and EGD and EUS revealed a tiny T1N0 lesion, for which she underwent a gastrectomy. The final pathology was indeed T1aN0.

EUS, in my opinion, is more helpful in countries that conduct routine mass screenings to identify small cancers prior to their becoming large and symptomatic. This study may identify loco-regionally advanced tumors that might benefit from preoperative chemotherapy (more on this later).

In the United States, a presentation like the one in the CT scan shown in **Fig. 5** is much more common. Patients often present already symptomatic and large lesions are visible on CT. At this point an EUS is not going to change the management of the case because it is likely T3 just by CT scan.

Staging laparoscopy is also very important in staging patients with gastric cancer. This is done to look for evidence of metastatic disease not revealed on the initial CT. In the 1990s, before staging laparoscopy was introduced, only CT scans were used to determine operability. If they revealed metastatic disease, treatment was usually non-operative, unless the patient was obstructed or had significant bleeding and thus required palliative gastrectomy. However, if the CT revealed no metastatic disease, the patient usually went straight
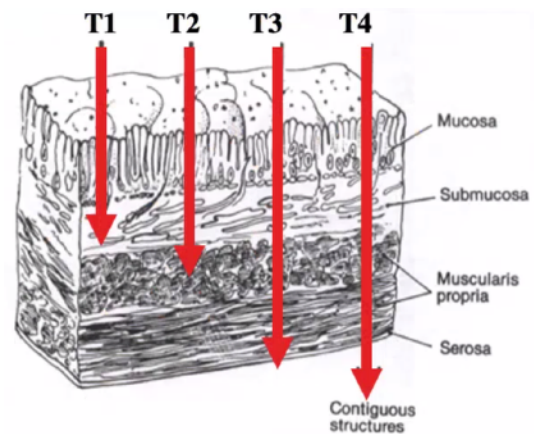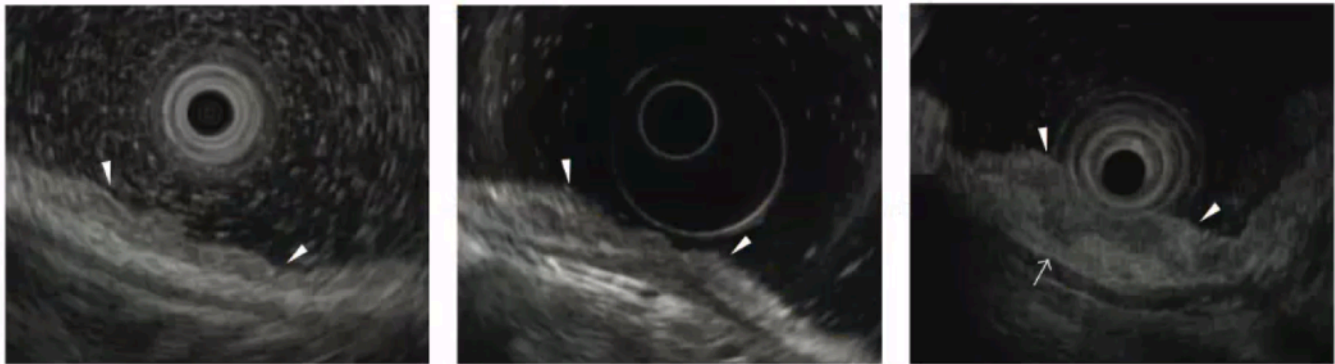

Fig. 6. Gastric Cancer T Staging

Fig. 7. Endoscopic Ultrasound (EUS) revealing an early gastric cancer

to laparotomy for attempted resection.

The problem was that up to 20-40% of the patients were found to have occult metastases discovered at laparotomy that were not seen on the CT, precluding any attempt at curative resection. So the laparotomy and the associated inpatient hospital stay was unnecessary.

Memorial Sloan-Kettering (2) and MD Anderson Cancer Centers (3) were the first in the USA to re-port their initial experiences with staging laparoscopy (**Fig. 8**). All patients in both studies had preoperative CT scans showing no metastatic disease.
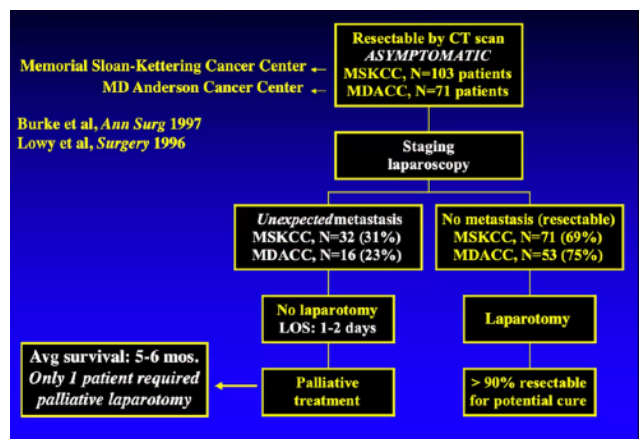

Fig. 8. Staging laparoscopy for gastric cancer

They were also not significantly symptomatic (e.g., no gastric outlet obstruction). At laparoscopy, occult metastasis was found in 23% of the MSK study cohort and 31% of the MDA study cohort and therefore, they were spared needless laparotomy. Their length of stay was 1-2 days but nowadays, the laparoscopy would be an ambulatory procedure.

These patients who had a positive staging laparoscopy then underwent palliative treat-ment, and their average survival was only 5-6 months. Only *one* of these 174 stage IV study patients required an invasive surgical procedure at some point due to a complication from the primary gastric tumor. This would obviously argue against doing "prophylactic" gastrectomy in asymptomatic or mildly symptomatic patients with stage IV gastric cancer.

On the other hand, if patients had no evi-dence of metastatic disease on a staging la-paroscopy, they then underwent laparotomy and greater than 90% of patients in both studies had a potentially curative resection.

Here is a good example of what we are talk-ing about. The PET scan (**Fig. 9**) on this gastric cancer patient shows no evi-dence of metastatic disease. Unfortunately,
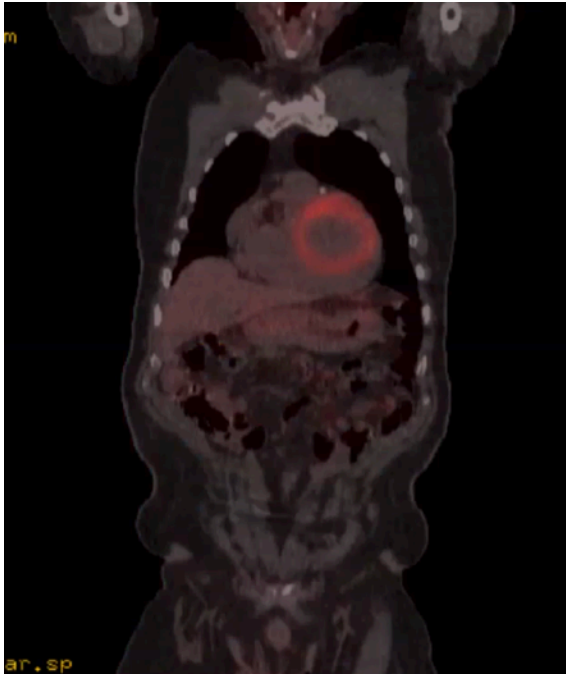
Fig. 9. PET scan showing no evidence of malignancy despite its presence.

his staging laparoscopy revealed small white plaques on the undersurface of the right and left hemidiaphragms (**Fig 10**). Pathology showed peritoneal metastasis and carcinomatosis. These are too small to be picked up by CT and PET. This patient went home the same day and underwent

chemotherapy as the primary treatment.

In a more recent study from MD Anderson, Allen et al (4) found that even patients with relatively early stage gastric adenocarcinoma, i.e. T1 or T2 and N0 by EUS, have a significant risk of having occult metastatic disease as this was found in 18% of these "early" stage patients!

In sum, staging laparoscopy is a critical part of the workup for gastric adenocarcinoma and not to be forgotten when evaluating patients and taking board exams.

Surgical Issues

Modes of Gastrectomy

Lesions in the proximal stomach are usually treated either by total gastrectomy or by proximal gastrectomy with or without a thoracotomy. Proximal gastrectomy (where the GE junction is resected and the distal stomach is anastomosed to the distal esophagus) may result in significant risk of gastroesophageal reflux disease (GERD), though Japanese surgeons have devised a number of ingenious operations to try to obviate this (5).
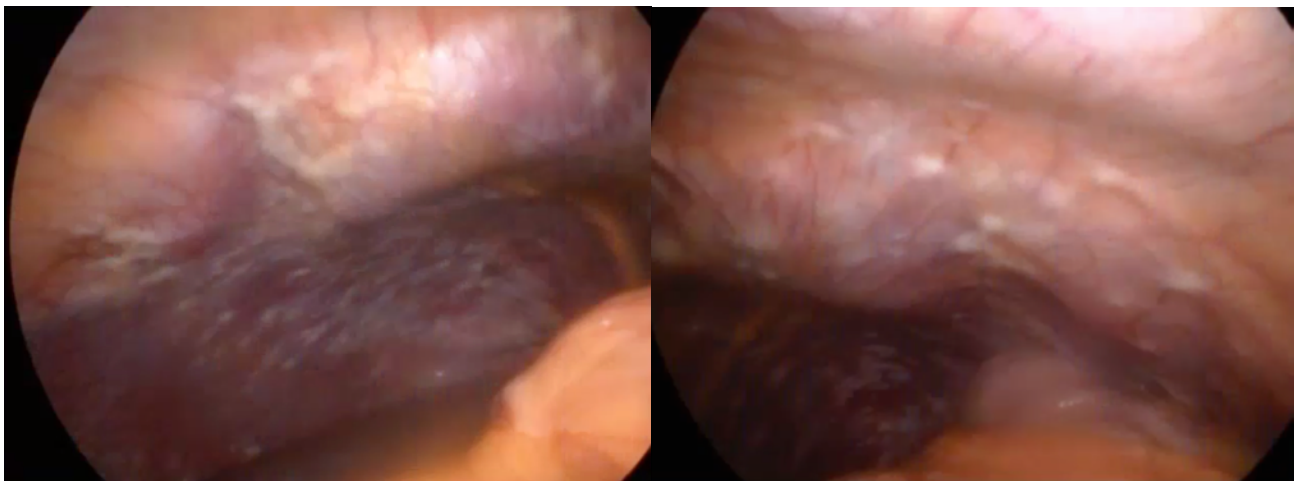

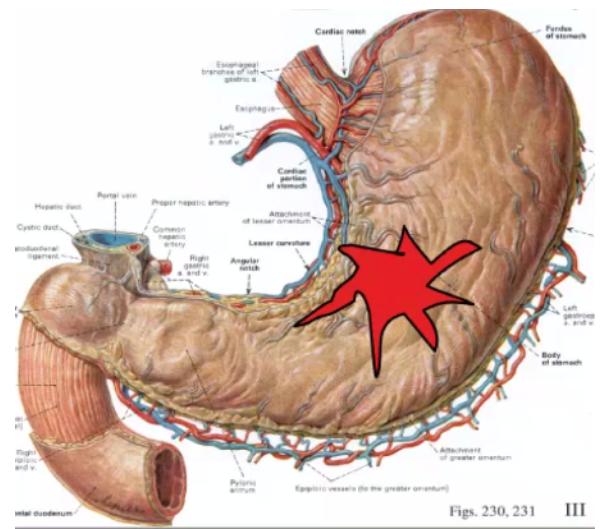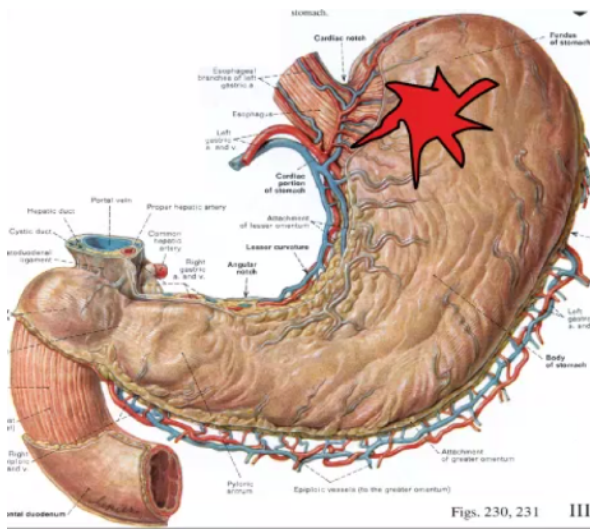**Fig. 10**. Plaques missed by PET/CT.

Fig. 11. Lesions in proximal stomach (L) and in body or antrum ®.

Lesions that significantly encroach on the esophagus (Fig. 11, left) may call for an Ivor Lewis operation (esophago-gastrectomy via laparotomy and right thoracotomy). Lesions in the body or the antrum (Fig. 11, right) usually are treated with either totalgastrectomy or a distal subtotal gastrectomy.

There are no differences in oncologic metrics between open, laparoscopic, and robotic modes of gastrectomy. In the short term, the lymph node harvest and the margin positivity rate are about the same, and so are long- term recurrence rates and overall survival.

The major advantage of robotic and laparoscopic gastrectomy is that there is a shorter length of stay. In most studies, it is approximately a day or so.

Margins
The NCCN (National Comprehensive Cancer Network) does not specify a specific margin width but says every effort should be made to try to get an R0 resection. The dogma has been the "5 cm rule," i.e, at least 5 cm of normal gastric tissue should be obtained at both the proximal and distal margins in the gastrectomy specimen. Often, for proximal gastric cancers, esophago-gastrectomy may be required in order to comply with this rule.

In 2015, the US Gastric Cancer Collaborative studied 162 patients operated on for proximal gastric cancer at multiple institutions in the United States (6).

Median margin width was 2.6 cm at the proximal margin - about half the 5 cm rule. Margins greater than this were not associated with increased rates of local recurrence or poor overall survival. Thus, in cases where it is easy to apply the 5 cm rule either proximally or distally, it is recommended to comply with the 5 cm rule, but *not* at the cost of esophagectomy or the cost of having to convert to duodenectomy and Whipple in order to get a 5 cm margin distally.

In regards to patients with R1 disease (having microscopically positive margins), this is often associated with patients who have loco-regionally advanced disease, meaning big, extensive tumors and nodal metastases.

Advanced nodal disease often nullifies any effect of the positive margin on overall survival. In other words, the survival of a patient with a microscopically positive margin but whose pathology shows multiple positive nodes is going to depend more on the advanced nodal disease than on the positive margin (7-9).

Extended (D2) Lymphadenectomy for Gastric CA

Extent of lymphadenectomy that should be done for gastric cancer has been a long-standing controversial issue. D1 perigastric nodes are found along the lesser and the greater curvature, and are usually routinely removed at gastrectomy for cancer. D2 nodes run along the vessels off the celiac trunk—the hepatic artery, the splenic artery, the left gastric artery and the celiac trunk itself. **Fig. 12** illustrates both (D1-green and D2-black.
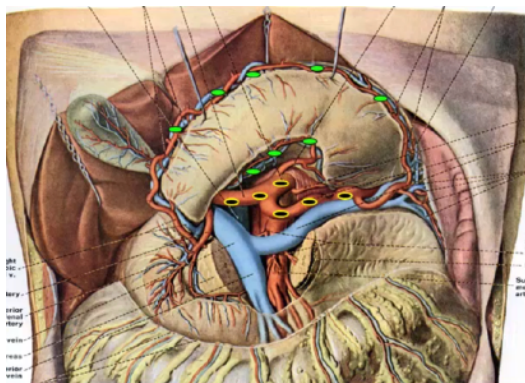

Fig. 12. D1 and D2 nodes

Fig. 13, from a review by Degiuli *et al* (10), shows the portal vein looped by the blue vessel loop on the left, to the left
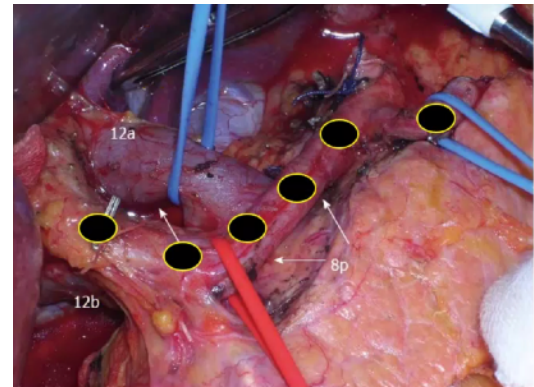
Fig. 13. D2 nodes

of that is the hepatic artery, and then there is the celiac trunk and splenic artery. The vessels have been skeletonized in order to remove the D2 nodes that sit along them.

Whether or not going after these D2 nodes is oncologically worthwhile has always been controversial. Surgeons in Japan and Korea strongly advocate for it whereas western surgeons usually just take out the cancer along with just the perigastric D1 nodes. In a randomized prospective trial to examine the issue - the Dutch Gastric Cancer Group Trial (11) - patients with resectable gastric cancer were divided into two arms: limited (D1) lymph node dissection vs extended (D2)

Fig. 14. Dutch Gastric Cancer Group Trial

lymph node dissection (**Fig. 14**).

The extended lymph node dissection was monitored by surgeons familiar with the procedure to make sure it was done appropriately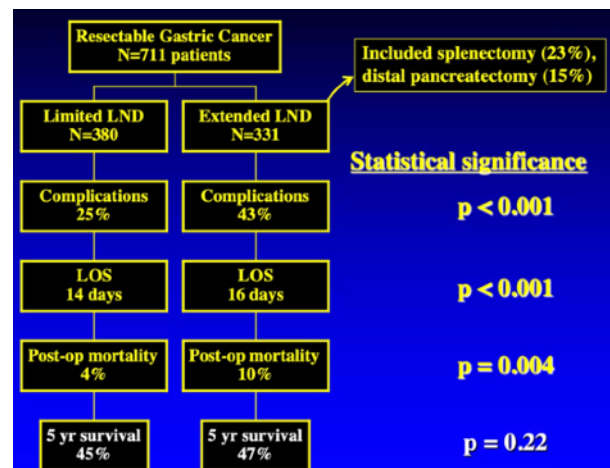. An important aspect of this trial was that in the 1980s and '90s extended D2 lymph node dissection meant not only taking out those lymph nodes along the celiac trunk vessels but also oftentimes the spleen and distal pancreas as well. The study found a significant increased rate of complications in patients who had D2 dissections—longer length of stay and almost double post-operative mortality. However, 5-year survival was essentially the same for both arms in the initial report of this study.

However, at 15 year follow-up, statistically significant oncologic differences emerged. Cancer specific survival was better and the local recurrence rate was lower in patients who had D2 vs D1 (see **Fig. 15**).
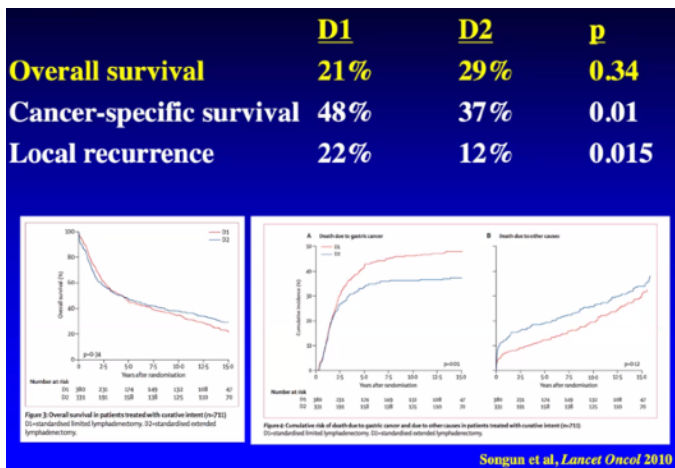

	D1	D2	p
Overall survival	21%	29%	0.34
Cancer-specific survival	48%	37%	0.01
Local recurrence	22%	12%	0.015

Songun et al, *Lancet Oncol 2010*

Fig. 15. Gastric Cancer Group Trial: 15-year follow up

The sticking point always has been the high operative mortality in patients who have D2 dissection. Japanese investigators looked into this further by re-examining the data

from the Dutch trial and found the factors most associated with morbidity and mortality were age greater than 65, male gender, splenectomy, and pancreatectomy. They suggested that the latter two procedures should be undertaken with caution during D2 lymphadenectomy (12).

In support of this, a 15-year follow-up of the Italian Gastric Cancer Study Group Trial of D1 *vs*. D2 dissection (in which no routine splenectomy or pancreatectomy was done) showed that the operative mortality was about the same between the two arms, but cancer-specific survival was significantly improved with D2 for "locally advanced" patients (pT2N1 or higher) (13). D2 lymph node dissection is clearly the oncologic operation of choice for these patients and splenectomy and distal pancreatectomy should only be done if it is required due to tumor involvement, and not done on a routine basis during lymphadenectomy.

Stage Migration and Lymph Node Number
It is not only the location of the lymph nodes that matter but also the total number of lymph nodes removed. The greater the node harvest - positive plus negative - the better the prognosis. An important metric that looks at the quality of gastric cancer resections is >15 total lymph nodes removed, and this is associated with improved survival. Much of this is due to a phenomenon called stage migration. An example of this is shown graphically in **Fig. 16**, which represents a patient with gastric cancer.
In this example, some D1 lymph nodes (green) can be seen along the lesser and greater curvature. They are free of cancer. Some D2 lymph nodes along the celiac ves-sels are also free of cancer (black). However, there are a couple of D2 lymph nodes that are positive - one along the
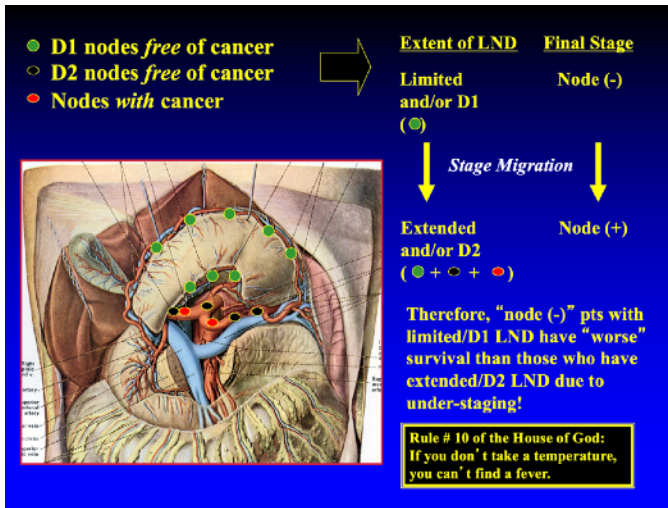
Fig. 16. Stage migration

splenic artery and one along the hepatic artery (red). If this patient gets a limited D1 lymph node dissection, where only a limited number of the green nodes are removed and the red lymph nodes are missed since these are D2 nodes that were not removed, how would that patient have been staged pathologically? The pathologist can only look at the lymph nodes that the surgeon takes out, so with a limited or D1 lymph node dissection, this patient will be staged as "node negative."

However, if the patient had undergone an extended D2 lymph node dissection - removing the green, black, and red nodes - the patient is going to be staged as node positive. It's the *same* patient, but *different* operations. This phenomenon is called *stage migration*, in which node-positive patients are erroneously staged as node negative because they have undergone limited node dissection and not enough lymph nodes have been removed and assessed. As a result, "node-negative" patients like in this example who have had too few lymph nodes removed (D1 dissection) will be perceived to have a worse survival than other *truly* node-negative patients who have undergone extended D2 lymph node dissection and hence have been more accurately staged. The greater the number of lymph nodes removed and examined, the less chance there is of this phenomenon.

Gholami *et al* (14) looked at the total number of lymph nodes removed in patients diagnosed with stage 1 (N0) cancer (the first survival curve in **Fig. 17**). All lymph nodes were negative, yet patients who had more than 15 lymph nodes removed had a better survival rate than those who had fewer than 15 lymph nodes removed. The reason probably had to do with stage migration.
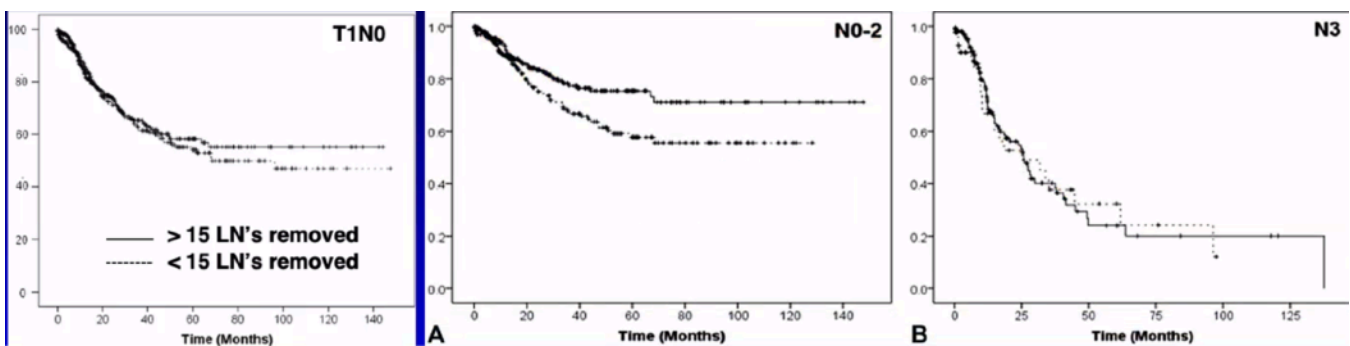

Fig. 17. The number of LNs removed vs. risk of occult N1 disease

In **Fig. 17A**, there is still a survival benefit for removing > 15 nodes in node-positive patients with limited nodal metastatic disease (N1 and N2). However, as the number of *positive* lymph nodes increases to N3 stage (**Fig. 17B**), the total number of lymph nodes removed seems to make no difference to outcomes in these more advanced patients. That makes sense because N3 patients have a significantly increased risk of having occult *distant metastatic* disease (M1) so more extensive *loco-regional* therapy (i.e., surgery) is unlikely to make much difference in these patients.

Adjuvant Therapy

Adjuvant therapy for gastric adenocarcinoma includes post-operative chemoradiation, post-operative chemotherapy, perioperative (neoadjuvant) chemotherapy (*i.e.*, chemo followed by surgery followed by chemo) and possibly immunotherapy, which is being used more and more for colorectal as well as gastric cancer. Unfortunately, this treatment is usually only reserved for patients with these cancers who have microsatellite instability (MSI-high tumors). This finding appears to be a marker for susceptibility/ sensitivity to immunotherapy. They are a relatively small fraction of both gastric and colorectal cancer patients.

Radiation Therapy

For a long time, post-operative chemoradiation was the standard of care for gastric cancer. In a trial reported more than 20 years ago in the New England Journal of Medicine, Macdonald *et al*. (15) randomized gastric cancer patients after surgery to either observation or post-operative chemotherapy with an oral form of 5-fluorouracil and 45 Gy of radiation therapy. They found significant improvement in median survival in the

treatment arm, hence this became the standard of care.

However, the quality of the surgery in this trial has been questioned, with very few patients having had what would be considered an adequate lymphadenectomy. Only 10% of the 556 total patients in both arms of the study had a D2 lymph node dissection. Many had D1 and some of them had D0 (no lymph nodes at all found in the specimen). The criticism was that the postop chemoradiation was just making up for inadequate surgery, thus resulting in the improved survival in that arm.

Two trials, one in Korea (16) and one in Europe (17), sought to replicate the Macdonald trial but with the condition that all patients had D2 lymph node dissection prior to being randomized to observation or chemoradiation. Both trials showed that when D2 lymphadenectomy was performed, the addition of post-operative radiation therapy did not seem to add any benefit in terms of loco-regional recurrence or overall survival. For this reason, radiation has mostly fallen out of favor as postop adjuvant therapy for gastric cancer, except for patients who have had incompletely resected disease, i.e., a positive margin or extensive regional lymph node metastases that could not all be removed.

Chemotherapy

Chemotherapy is beneficial in gastric cancer and may be administered either postoperatively or perioperatively (neoadjuvant). The Korean CLASSIC trial showed a benefit with surgery *first* followed by post-operative adjuvant chemotherapy (18). The European MAGIC trial showed a benefit to perioperative chemotherapy - chemotherapy followed by surgery followed by more

chemotherapy (19). Either of these approaches are appropriate. The question then is: How to choose?

The essential first step is to discuss the case in the multidisciplinary tumor board. These are the general indications for neoadjuvant therapy that we use in our tumor board:
1) Patients with tumors that look locally advanced on the CT scans, i.e., very large +/- signs of gross lymph node metastases but no obvious evidence of distant metastatic disease. Even if staging laparoscopy is negative, these patients have a significant risk of developing metastatic disease in the near future. Those that progress on the neoadjuvant chemo will be spared unnecessary gastrectomy.

2) Another indication for initial chemotherapy would be patients who have signs suggestive of but not definitive for metastatic disease on initial imaging. They would be treated with chemo until the imaging could be repeated to re-assess these findings.
3) Patients who have equivocal pathologic/cytologic findings on staging laparoscopy, for instance, peritoneal washing cytology re veals some suspicious atypical cells that are not definitive for cancer but also are clearly not reactive mesothelial cells. These patients should be treated with neoadjuvant chemotherapy to see if more definitive signs of metastatic disease are found down the line.
4) Another indication would include current comorbidities that might preclude safe surgery as the initial treatment. Neoadjuvant chemotherapy might serve to gain time to get the patient medically cleared or at least in better shape for surgery.

Who should have surgery as the first treatment? Patients who are relatively fit, with early stage disease based upon CT scan and EUS, and a negative staging

laparoscopy could go straight to resection. So should patients who are symptomatic, for example with gastric outlet obstruction, for which chemotherapy would be contraindicated. However, there have been some promising preliminary studies at using endoscopic stents to palliate the obstruction so that initial surgery could be avoided and the patient can still get neoadjuvant chemo (20).

**A Very Brief Synopsis
on Other Tumors of the Stomach**
Gastrointestinal stromal tumors
Gastrointestinal stromal tumors are found most commonly in the stomach followed by the small intestine. c-Kit mutations are found in about 80% of GI stromal tumors while another 5-10% have mutations in the PDGFRA (platelet-derived growth factor receptor A) gene. These tumors are resected like sarcomas. The operations for these are frequently very different than for adenocarcinomas in that the extent of gastrectomy is only to obtain negative margins. For example, a large fungating tumor hanging off the greater curvature, say 10 cm in size but attached to the stomach by only a 2 cm stalk, does not require a radical gastrectomy, only enough partial gastrectomy to obtain a negative margin.

It is important to remember also that no lymphadenectomy is done for GI stromal tumors which like other sarcomas, very rarely metastasize to lymph nodes. The only indication for doing a lymphadenectomy in GI stromal tumors is evidence of clinical nodal metastases on a CT or PET scan or if obvious lymph node mets are found at the time of surgery. Otherwise, unlike adenocarcinomas, there is no routine lymphadenectomy done for GISTs.

The prognosis of GISTs is based on their size and histologic grade. The pathologic features of the cancer—size, number of mitotic figures, degree of necrosis—can be input into nomograms published by Memorial Sloan Kettering to generate a prognosis for 5 and 10 year survival. Medical oncologists often use these nomograms to determine whether a patient should get adjuvant therapy. This is usually with the oral drug imatinib (Gleevec®). The indications for giving this would be large size, high grade with a lot of mitotic figures, and significant necrosis.

Gastric carcinoids

Finally, a few words on *gastric carcinoids*. These are neuroendocrine tumors, and there are three types. Type I is the most common, making up about 80% of all gastric carcinoids. Type II, associated with Zollinger-Ellison Syndrome and Multiple Endocrine Neoplasia (MEN I), make up about 5%, and these are pretty rare. Type III, making up about 15%, tend to be large, aggressive, and often metastatic at the time of diagnosis. For these reasons, they are clearly discernible from Type I.

Type I patients usually start out with atrophic gastritis. The atrophic gastritis leads to achlorhydria. The lack of acid in the stomach leads to G-cell hyperplasia as a positive feedback loop, i.e., the increased G-cell population tries to pump out more gastrin in order to increase acid formation and correct the achlorhydria. This hypergastrinemia chronically stimulates neuroendocrine cells in the stomach, which subsequently become hyperplastic and in some cases become transformed into Type I gastric carcinoids. These tend to be small and multifocal.

An appropriate history of gastritis can help with the diagnosis. If type I gastric carcinoids are discovered on endoscopy, a serum gastrin level should be obtained - it is likely to be very elevated. Type I is also often associated with a positive anti-parietal cell antibody titer, so this should also be ordered.

Radical surgery is not indicated for Type I carcinoids. I have one longstanding patient with multiple small Type I gastric carcinoids. A previous opinion recommended that she have total gastrectomy to remove all of the disease. Instead, we have been doing routine annual endoscopic surveillance. She still has small persistent Type I carcinoids, and the larger ones are plucked out by her endo-scopist. After over seven years of follow up, there has been no progression to anything more significant. It is very rare for Type I to progress to the point where they become endoscopically uncontrollable. If they become so, a distal gastrectomy (antrectomy) can be contemplated, so as to remove the area where the G-cells reside. This eliminates the cells causing the hyper-gastrinemia and hence decreases the impetus to formation of these tumors.

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