GI Surgical Oncology

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Chapter 1

Overview

1.1 Absences

Please notify Dr Hill, Dr Salo and Dr Squires before the beginning of the rotation if you will be away during the month. This includes vacations, meetings, interview trips, and other absences.

1.2 Communication

Please use Halo for messaging service attendings rather than SMS. Please check our status prior to messaging nights and weekends. If we are listed as unavailable, please contact another Surgical Oncology attending or the CMC "GI MIS Blue Surgery Attending Colorectal Onc" attending on call.

1.3 Inpatients

By in large, service attendings all wish to know about major changes in the status of our own patients. For most of the issues for which you would need to contact an attending at night, we would prefer that you HALO us directly rather than the on-call person. This desire is 24/7 (unless Halo says that attending is "off").

1.4 ER admits

We would ask to use a combination of communication for ER admissions. All patients must be discussed with an attending. • If the patient is stable, does not need surgery, etc. then we would ask you to contact the attending on call

for GI MIS Blue Surgery Attending Colorectal Onc. Please contact them according to that attending's preferences (page, text, call, etc). • If the patient is unstable, may need surgery or will have ongoing and/or have intensive management needs the following day please HALO that patient's surgical oncology attending directly. The difference is that this patient is sick - we would like to know about all of our sick patients. If the Surg Onc attending is listed as "off" within Halo then please contact the GI MIS Blue Surgery Attending Colorectal Onc on-call attending.

1.5 Medical Records

Completing medical records in a timely fashion is critical for patient safety, billing, and compliance. Timeliness also demonstrates an understanding of how the world of surgery for which residents are being prepared functions.

1.6 Operative Logs

Completion of operative logs is critical for board certification of the individual resident but also has implications for the appropriate assignment of residents to surgical rotations AND impacts the ability of the residency to maintain accreditation and recruit resident candidates. Residents who find it difficult to find time to maintain operative logs may find themselves excused from the operating room to complete them. Residents are expected to complete operative logs within two weeks of the end of the rotation.

1.7 Case Assignment

The senior resident will be expected to make case assignments for junior residents and students. It in not necessary split the month by attending - splitting by case is acceptable as well. We also expect that both residents know all the patients rather than just for one attending. This helps with nursing questions, etc.

1.8 Clinic

Clinic is an important part of a surgeon's education, where decisions are made regarding diagnostic workup, patient evaluation, and treatment planning. The expectation is that all residents on the service attend clinic once per week.

1.9 Work Hours

If the service workload jeopardizes your ability to abide by the work hour restrictions, you must notify an attending so that arrangements can be made. The

service attendings are committed to abiding by work hour restrictions.

Chapter 2

Inpatient

Colorectal Surgery (Davis/Kasten) and GI Surgical Oncology (Hill/Salo/Squires) will cover Pineville and CMC. For efficiency, the services at each hospital will merge for patient care. Each patient will continue to have an attending surgeon, but rounding and inpatient care will be provided by the service.

2.1 Admissions

Admitting Provider: "CMC, GI SURGICAL ONCOLOGY"

List Attending Surgeon in addition

Patient List is CMC GI Surgical Oncology

2.2 Rounds

Attending rounds for both services (CR and SurgOnc) start at 6am in STICU or 11T. Dr Salo rounds M-Tu and Drs Squires and Hill round W/Th/F alternate weeks

2.3 Resident Halo teams:

CMC AH Colorectal Surgery 1st Call CMC LCI GI Surgical Oncology 1st Call Residents will be assigned to Halo teams by schedule. It is critical that you notify service attendings before the start of the month to adjust the resident Halo schedule. Each "shift" is 5:50am to 6pm. At 6pm the resident Halo Teams will be forwarded to the night team.

Please append a text block to the bottom of each progress note specifying the Halo Team for that patient to facilitate communication from nursing.

2.4 Attending Halo teams:

CMC AH Colorectal Surgery Attending CMC LCI GI Surgical Oncology Attending Monday through Thursday (24hr), please contact the attending surgeon for each patient. For Surgical Oncology, please use Halo. For Colorectal, please use phone.

Friday and Weekend: Halo "CMC GI MIS Blue Surgery Attending Colorectal Onc" for new admissions. Please keep Surgical Oncology attending informed of inpatient issues.

2.5 Consults

Established patients and directed should be discussed with the attending surgeon.

Unassigned Colorectal: "CMC AH Colorectal Surgery Attending"

Unassigned Surgical Oncology: "CMC LCI GI Surgical Oncology Attending"

In general, benign colorectal consults are staffed by Dr Davis. Colorectal malignancies are staffed as below. Esophageal and GE junction staffed by Dr Salo. Adenocarcinoma of distal stomach: Drs Salo/Squires. Gastric GIST: Drs Hill/Salo/Squires. Squires/Hill alternate weeks.

	Mon	Tues	Weds	Thu	Fri
CR Malig	JSH	MHS	MHSJSH	JCS	MHSJSH
GI Surg Onc	JSH	MHS	MHSJSH	JCS	MHSJSH

2.6 Conferences

- GI Tumor Planning Conference Monday 7-8am
- Resident Teaching Conference Tuesday 7-8am 5th floor LCI II. Please review the upcoming clinic schedule and choose a case to present.
- Bone and Soft Tissue Conference Friday 7-8am

Chapter 3

Rounds

Please plan to update the attending of record about their patients in the morning.

The following format will help speed communication on rounds.

ID: One line description: "Mr Glenn: PostOp day 3 after low anterior resection"

24 hour events: Summary of important events in prior 24 hrs

Systems-oriented Presentation:

Neuro: Pain control, level of alertness, psychotropic meds, sedatives, and pain meds.

CardioVascular: Vital signs (normal OR cite the range of systolic blood pressures and range of heart rate). Heart rhythm. Cardiac meds. Most recent recommendations of cardiology consult.

Respiratory: Pulmonary exam, oxygen saturation, supplied oxygen, ventilator setting. Results of CXR.

GI: Diet, bowel function, NG output. Drain outputs can often be summarized unless they are unusually high or low (and ready to be removed. New finding of bile in any abdominal drain needs special emphasis. GI meds (eg protonix, Entereg). Tube feed formula, rate and duration (continuous or nocturnal). Status of C Diff tests. Results of JP drain amylase levels (gastroesophageal patients). Results of JP triglycerides or creatinine, if sent,

Renal: Urine output in 24 hours AND in most recent 8 hour shift. Presence (or absence) of Foley catheter and plans for removal, if present. Most recent creatinine. If diuretics administered, dosage and amount of urine output during the shift when it was administered. Most recent potassium in any patient receiving (or about to receive) furosemide (Lasix). Results of Mg and Phos if abnormal.

Heme: Hemoglobin, platelets, DVT prophylaxis. PLEASE CHECK THE MAR SUMMARY DAILY to be certain that the ordered DVT prophylaxis has been given.

ID: WBC, Tmax in past 24 hours, culture results.

Endo: Diabetic regimen, blood sugar range, and amount of sliding scale insulin administered in the prior 24 hours.

Problem-Oriented Plan:

Each of the patients problems are addressed with an assessment and plan. Pre-existing medical problems and postoperative complications need to be addressed in the plan

Chapter 4

Progress Notes

Progress notes should include a comprehensive summary of pertinent information for the patient's medical care.

A running summary of events is recorded in the Shared Hospital Course under Inpatient Workflow

Each day, this section is carried from note to note so that each progress note contains the cancer history and the daily events.

The Progress Note then includes the date and a one-line summary of the operation performed and any intraoperative complications or events which impact the post-operative care.

Each day, an additional line is added to the Shared Hospital Course which summarizes events for that day. This makes it possible to see within each Progress Note the pertinent events for the hospitalization. These events would include extubation, re-intubation, positive cultures, dates lines are inserted or removed, dates of removal of NG tubes and drains, and transfer to ward or re-admission to ICU. This chronology assists in treatment decisions ("how old is the IJ line" or "when did we start antibiotics?" or "when is the planned antibiotic stop date"?) but also makes the discharge summary much easier to prepare.

Assessment/Plan The medical problems currently being managed are addressed in the assessment.

Esophagectomy Events to be Documented (in Shared Hospital Course):

- Extubation date/time
- NG Removal date
- Chest tube removal date
- MBS date(s) and results (aspiration | penetration)

- ICU DC orders written
- ICU discharge (transfer to ward)

Esophagectomy Complications to be Documented (in Shared Hospital Course):

N	Delirium
	Stroke
CV	New arrhythmia req Rx
	MI
R	Pneumonia (3 of fever | WBC | infiltrate | abx | sputum cx)
	Effusion req drainage
	Reintubation
	Atelectasis req bronchoscopy
	ARDS
	PE
	Ventilation >48 hours after leaving OR
GI	Anastomotic leak (medical rx | stent | surgery)
	Delayed gastric emptying req botox or NG >7d
	C Diff
GU	Urinary Retention
	Discharge with foley catheter
H	DVT req treatment
	Return to OR
	Return to ICU

Communication

Please add an addendum at the BOTTOM of each progress note which includes a means for contacting the team:

Please message "CMC LCI GI Surgical 1st Call" via Halo 24/7. Messages are automatically forwarded to the General Surgery Resident on Call evenings and weekends.

#Signout

Evening Signout

The Handoff Tool should be completed for all inpatients, and the responsible attending designated. This tool is critical for the safe care of patients by the nigh team. If there are studies which are pending at the time of signout (CT scan, follow-up Hb), it is critical that a plan be in place for whom to notify with an abnormal or critical study. In general, Drs Hill and Salo are always available until 10pm. Attending notification plans (service attending vs covering attending) for unstable patients should be negotiated before nightfall.

Weekend Signout

The chief resident is responsible for making certain that the weekend rounding resident is familiar with the patients, their problems, and the plan of care. A signout email should be prepared Friday afternoon and forwarded to the service attendings by 6pm for their review. This signout can then be edited with the attendings' notes and forwarded to the weekend rounding attending.

Chapter 5

Discharges

Discharge Prescriptions

Prescriptions should be ideally be prepared the day prior to anticipated discharge and left in the patient's 'soft chart.' According to North Carolina STOP guidelines, opioid prescriptions for postoperative patients should be for no more than a 7 day supply.

Postop Clinic Appts

Postoperative patients are generally seen for a Transition of Care visit within the first week

Discharge appointments are made by sending a message in Canopy the evening prior (preferred) OR the morning of discharge before 8am to:

LCI CMC GI, Clerical Verona Jordan (Hill) OR Marsha Sukhdeo (Salo and Squires) Stefanie Olson (Hill) OR Kendra Zacharias (Salo and Squires)

Please include the following information in the Canopy Message:

- Ward from which the patient is being discharged
- Desired date for appointment
- Need for Wound Ostomy RN appointment at same time (essential for new stomas)
- Need for bloodwork at first visit
- Other studies to be done same-day
  - Upper GI
  - Chest X-ray
  - Modified Barium Swallow

If messages cannot be sent in time, clinic schedulers can be reached at: Marsha Sukhdeo (Salo and Squires): 980-442-6110 or Verona Jordan (Hill): 980-442-6183.

If schedulers are not available, clinic RNs can be reached at: Stefanie Olson (Hill) 980-442-6146 or Kendra Zacharias (Salo and Squires) 980-442-6143.

For patients likely to go home over the weekend or holidays, please plan to send a canopy message before 3pm on Friday or the day prior.

The scheduler will respond with a message to the discharging resident AND to the ward CNL with the appointment time, which can be included within the discharge summary. Copies of the message will also be sent to clinical nurse leaders:

- 11Tower: Sharon Hood
- 6Tower: Amy Peterson

Additional Appointments

If followup appointments in additional to surgical followup are needed, these should be designated on the discharge orders. Particularly:

- Primary Care Physician
- Cardiologist (if new cardiac medicines)
- Co-surgeons (Urology, Thoracic Surgery, GYN)

Discharge Summary

The discharge summary documents important events and complications in the postoperative course and serves to inform the referring physician and primary physician about these events, but also serves as a blueprint for post-discharge treatment planning. Please recognize that the first post-operative visit may be with a resident who may be meeting the patient for the first time. Key items to include:

N	Followup plan for chronic pain management
	Stroke
CV	Complications: (Arrhythmia | MI | CHF)
	If new cardiac meds: Who is managing medications
	If afib: CHADS score and anticoagulation plan
R	Complications (Pneumonia | ARDS | TRACH)
	Need for home oxygen?
	CXR needed at first postop visit?
GI	Complications: (delayed gastric emptying | leak | ileus)
	Tube feed regimen
	Diet at discharge (Low residue | Full liquds | Meds with thickened water |NPO)
	New stoma (ileostomy | colostomy)
	Wound care needs (VAc | Prevena)
GU	Urinary Retention
	Discharge with foley catheter
H	Complications: DVT | PE
	Anticoagulation Plan

Endo	Insulin regimen at discharge (dose will be in med rec)
ID	Antibiotics at DC
	Return to ICU

Communication

It is essential that discharge summaries be sent to the patient's primary MD and referring physician. Please review the initial consultation note for the names of providers involved in a patient's care.

In order to easily access the patient's providers, please prepare a "]Providers" autotext:

Click the AutoText icon on a document Add new AutoText by clicking the blue + sign Create a name for the new AutoText (such as "]Providers") Select a smart template by clicking the second icon from the right of the buttons Search for "Transition" and select "Transition Clinic Header" Save the AutoText Please paste the]Providers AutoText in the body of the discharge summary to easily access who should receive copies of the discharge summary

Esophageal Cancer

Chapter 6

Esophageal Overview

Esophageal cancers can be grouped into 4 treatment categories:

- Superficial → Endoscopic therapy
- Localized → Primary surgery
- Locally Advanced → Trimodality therapy
- Metastatic → Systemic therapy

Patients with minimal dysphagia, no weight loss, and small (<3cm length) tumors are evaluated with endoscopic ultrasound:

- If uT1 on EUS and <2cm in size, endoscopic mucosal resection yields more information and may be therapeutic for tumors with negative margins and without high-risk features.
- If uT2N0 on EUS, and PET scan shows a small tumor (MTV <10cm^3), primary surgery is preferred in patients who are good surgical risks
- If T3 or N+ on EUS, if PET shows no metastatic disease, trimodality therapy is optimal)

Patients with dysphagia to solids or weight loss or tumor length >3cm are unlikely to have T1-2 tumors and can be evaluated with PET scan.

- If PET shows disease confined to the esophagus and regional nodes, trimodality therapy (chemoradiation followed by surgery) is optimal.
- If PET shows metastatic disease, patients are eligible for palliative chemotherapy with radiation for treatment of symptoms of dysphagia.
- If PET shows extra-regional lymph node disease, patient is at high risk for distant disease and can be treated with induction chemotherapy followed by chemoradiation and surgical evaluation.

Chapter 7

Staging

The staging workup begins once a diagnosis is made on endoscopy.

The first step is to make a preliminary determination whether the tumor is early stage (and can be treated with endoscopy or primary surgery) or later stage (and treated with chemoradiation followed by surgery or with)

The diagnostic studies needed for these treatment groups are different, so the workup can be make more efficient by sorting patients at presentation in to two groups:

Patients with minimal dysphagia, no weight loss, and tumors with less than 3cm cranio-caudal extent have a reasonable change of being T1 or T2 tumors. Tumors <3cm in length are much more likely to represent T1-2 lesions than those $\geq$ 3cm(Hollis et al., 2017)

Superficial and Localized tumors generally present with minimal dysphagia or weight loss. These tumors may present with bleeding, or dysphagia without weight loss. For these patients, determining the precise T stage is important in their workup, so **endoscopic ultrasound** is the most frequent staging study after diagnosis.

Locally-advanced or metastatic tumors tend to present with dysphagia and weight loss. At first approximation, these tumors are usually clinical T3 lesions, and the important bifurcation in their treatment is the presence or absence of metastatic disease. For patients with dysphagia and weight loss, **PET** is the most frequent initial staging study after diagnosis.

Patients who present with dysphagia are likely to have T3 or T4 disease, which is generally treated with neoadjuvant chemoradiation followed by surgery. Data from Memorial Sloan Kettering [Ripley 226] among 61 patients with esophageal cancer who presented with dysphagia, 54 (89%) were found on EUS to have uT3-4 tumors. On the other hand, among 53 patients without dysphagia, 25

(47%) were uT1-2, and were potentially candidates for primary surgery. Their conclusion was that EUS could be omitted from the workup of patients with dysphagia, but is useful in patients without dysphagia.

PET can be helpful in evaluating patients who may have T1-2 disease, and might be candidates for primary surgical therapy. A comparison of PET and EUS [malik,claxton,1] showed that uT1-2 tumors had median metabolic tumor volume (MTV) of 6.7cm^3, compared with uT3-4 tumors, with a median SUV of 35.7cm^3.

Chapter 8

Superficial Esophageal Cancer

Superficial esophageal cancer is usually asymptomatic, which means that the diagnosis is generally made in the context of surveillance for Barrett's esophagus.

Nodular Barrett's esophagus can be best evaluation with endoscopic mucosal resection, which can provide further staging information if an adenocarcinoma is found, such as depth of invasion, differentiation, and lymphovascular invasion.

Larger lesions should first be evaluated with endoscopic ultrasound (EUS)?

EUS is less sensitive for T1 lesions (Bergeron et al., 2014) -> use EMR for diagnosis (Maish and DeMeester, 2004)

(Should nodular Barrett's be evaluated with EUS prior to EMR?)

T1a tumors have a low risk of nodal metastasis (Dunbar and Spechler, 2012)

8.1 Endscopic Mucosal Resection (EMR)

For patients with nodular Barrett's esophagus or small tumors judged to be T1 by endoscopic ultrasound, endoscopic mucosal resection (EMR) can be diagnostic and potentially curative.(Thomas et al., 2009)

EMR also helps establish the difference between T1a and T1b compared with pathology (Worrell et al., 2018)

EMR is likely sufficient for small tumors with favorable patholgic factors(Pech et al., 2014) (Nurkin et al., 2014):

- Size less than 2cm
- Lateral and deep margins clear

- Absence of lymphovascular invasion
- Well- or moderately- differentiated

EMR: (Soetikno et al., 2005)

See MOlina JTCVS 153:1206

EMR for high-grade dysplasia (Shaheen et al., 2009)

EMR for low-grade dysplasia (Phoa et al., 2014) resulted in 25% riskd reduction in progression go HGD.

Endoscopic submucosal dissection is a technique for deeper endoscopic removal of esophageal lesions using endoscopic cautery, which dissects through the submucosa. ESD has a higher rate of curative resection (Cao et al., 2009) albiet at the cost of prolonged operative times and increased risk of complications such a bleeding. (Repici et al., 2010)

ESD takes more time and has higher R0 resection rate but similar recurrence erate at 2 eyars (Terheggen et al., 2017)

Need for RFA of Barrett's after EMR: (Haidry et al., 2013) Combination therapy with EMR and RFA results in lower rate of recurence than EMR alone.(Pech et al., 2008)

RFA for Barrett's national registry (Ganz et al., 2008)

Chapter 9

Localized Tumors

9.1 T1b Tumors

9.2 T2N0 Tumors

Multiple studies have failed to show the additional benefit of chemotherapy or chemoradiation for pT2N0M0 esophageal cancer patients treated with radiation.

Neoadjuvant chemo not likey to be helpful for early stage disease - FFCD 9901 [Mariette 2416] enrolled patients with T1-2 or T3N0 tumors to chemoradiation followed by surgery versus surgery alone. The majority of the tumors (72%) were squamous cell carcinoma.Postoperative mortality was significaly increased in the chemoradiation arm (11.1% vs 3.4%).

Meta-analysis of 5265 patients in 10 studies showed that while neoadjuvant therapy was associated with a reduction in positive margin rate, there was no difference in terms of recurrence or survival.[MOta 176]

French trial FREGAT(Markar et al., 2016)

Retrospective review of the National Cancer DataBase failed to demonstrate a difference in survival of cT2N0M0 esophageal cancer with or without preoperative chemoradiation.(Speicher et al., 2014)

A retrospective report from Johns Hopkins examined outcomes of T2N0 squamous cell carcinoma patients and showed equivalent outcomes for primary surgery vs neoadjuvant chemoradiation followed by surgery (Zhang et al., 2012)

9.3 Staging of T2N0 Tumors

The challenge for treatment decision-making is the limited sensitivity of endoscopic ultrasound in ruling out pT3 or pN+ disease. In other words, if a patient

who is thought to have cT2N0 disease undergoes resection, and is found on pathology to have pT3 or pN^+ disease, this would dictate the need for post-operative chemoradiation. In general, chemoradiation after esophagectomy is difficult for patients to tolerate, with a _____ % chance of failure to complete therapy.

Data from the Cleveland Clinic looked at 53 patients judged to be T2N0 by endoscopic ultrasound (uT2N0) were treated with primary surgery. Pathologic examination showed that 17 (37%) were understaged by endoscopic ultrasound, and were pathologic (pT3) in 4 or node positive (pN^+) in 13 cases. These patients were treated with postoperative adjuvant chemoradiation.(Rice et al., 2007)

It is critical, therefore, in patients for whom primary surgery is contemplated, to attempt to identify those with occult T3 or N+ disease.

Patients who appear to have limited stage disease benefit from evaluation with a combination of

See also PMID:25047477

(MTV)

(Tumor Length)

(dysphagia)

##Primary Surgery {#primary_surgery}

NCCN recommends PET scanS

Most common sites of metastasis are liver, lung, bones, adrenal.

PET detects occult metastasis in 10-20% of cases (Kato et al., 2002, Kim et al. (Apr)). Among 129 patients with esophageal cancer, PET detected additional sites of disease in 41% and changed management in 38% (Chatterton et al., 2009)

PET for restaging detects interval development of metastatic disease in 8-17% of cases (van Vliet et al., 2008)

Chapter 10

Locally Advanced Cancer

Tumors that are T2N$^+$M0 or T3NxM0 are considered locally-advanced. The high rate of failure with surgery alone has led to development of adjunctive therapies.

10.1 Trimodality Therapy

Trimodality therapy consists of chemoradiation followed by surgery.

CROSS trial randomized 364 patients with resectable esophageal and gastroesophageal junction tumors (75% adenocarcinoma) to neoadjuvant chemoradiation consisting of 4,140 cGy of radiation with concurrent carboplatin and paclitaxel or surgery alone.(van Hagen et al., 2012) Clinical node-positive disease was present in 16%. Pathologic complete response was seen in 23% of adenocarcinoma and 49% of squamous cell carcinomas. Median overall survival was 49 months after trimodality vs 24 months after surgery alone (p=0.003). Squamous cell carcinomas appeared to have particular benefit, with a hazard ratio of 0.42 for squamous cell vs 0.74 for adenocarcinoma. Median survival was improved for adenocarcinoma from 27.1 months to 43.2 months, but the median survival for squamous cell increased from 27.1months to 81.6 months for squamous cell. Rate of R0 resection was higher with chemoradiation (92% vs 69% p<0.001) andlocal recurrence rates lower (14% vs 34% P<0.001), and peritoneal recurrence lower (4% vs 14% P<0.001). Despite the relatively low dose of radiation, in-field recurrences were less than 5%. The primary cause of failure was distant disease (31%) and local/regional failure (14%).(Oppedijk et al., 2014)

Alternative to carbotaxol is FOLFOX (SOG trial (Leichman et al., 2011))

Ogoing PROTECT trial ompares FOLFOX to paclitaxel and carbo (Messager et al., 2016)

10.1.1 Neoadjuvant chemoRT for SCCA

NeoCRTEC5010 (Yang et al., 2018)

Meta-abalysis of chemoRT vs chemo (Zhao et al., 2018)

10.2 ChemoRT vs Trimodality therapy

The sensitivity of squamous cell carcinoma of the esophagus to chemoradiation has raised the question whether

Stahl Locally advanced squamous cell carcinoma randomized to induction chemotherapy (cisplatin, etopiside, 5FU with leuocovrin) followed by chemoradiation (4000cGy with concurrent ciplatin and etopiside) followed by surgery compared with induction chemotherapy followed by chemoradiation (6400cGy with concurrent cisplatin and etopiside).(Stahl et al., 2005) progression-free survival was better in the trimodality group (64.3% vs 40.7%) Treatment-related morality was substantial in the surgery arm (13% vs 4%). This would be considered an excessive rate of operative mortality by modern standards. Unsurprisingly, there was no difference in overall survival between groups, in part because the surgical group had an excess 9% mortality rate from treatment. Two-year survival in the surgery arm was 40% vs 35% in the definitive chemoradiation arm. (**?**)

In the French FFCD trial, 444 patients with carcinoma of the esophagus (90% squamous cell) were treated with two cycles of 5-FU and cisplatin with concurrent radiation.(Bedenne et al., 2007) Patients with a partial or complete clinical response to chemoradiation were randomized to either surgery or a boost of radiation. Patients who did not respond to chemoradiation were treated with surgery and were eliminated from the study. Only 259 of the original 444 patients (59%) went on to randomization, with the remainder (those not responding to chemoradiation) treated with surgery. Of the randomized group, median survival was 17.7months in the surgery arm versus 19.3months in the definitive chemoradiation arm. Like the Stahl study, treatment-related mortality in the surgical arm was high (9% versus 1%).

10.2.1 Neoadjuvant chemotheraphy followed by surgery

POET Trial (Pre-Operative therapy in Esophageal adenocarcinoma Trial) treated patients with adenocarcinoma of the gastroesophageal junction with either neoadjuvant chemotherapy (5-FU, leucovorin, cisplatin) followed by surgery or induction chemotherapy with the same agents, followed by chemoradiation (4000cGy with concurrent cisplatin and etoposide). The study failed to meet its accrual goal, but there was a suggestion of improved 3-year survival with preoperative chemoradiation (47.4% vs 27.7% p=0.07) as well as improved local control (76.5% vs 59%). In addition, chemoradiation was associated with a higher pathologic complete response rate (15.6% vs 2%)(Stahl et al.,

2009). A meta-analysis of 33 randomized trials further suggested a greater benefit from neoadjuvant chemoradiation followed by surgery compared with neoadjuvant chemotherapy followed by surgery(Pasquali et al., 2017) and a similar meta-analysis (Sjoquist et al., 2011)

#Active Surveillance

EGD is poor predictor of pCR (Sarkaria et al., 2009)

10.3 GE Junction

(Siewert et al., 2006)

10.4 Induction chemotherapy followed by chemoRT

See NCCN pages M-25 and M-26

Stahl (Stahl et al., 2009) randomized patients to preoperative chemotherapy (A) vs preoperative chemotherapy followed by preoperative chemoradiation (B). Higher pcR rate in arm B (15.6% vs 2%) and ypN0 resection (64.4% vs 37.7%).

10.5 Postoperative chemoradiation

Intergroup-0116 (Macdonald et al., 2001) (Smalley et al., 2012) treated 556 patients with adenocarcinoma of the stomach or GE junction with surgery along vs surgery followed by postoperative chemoradiation. After a median followup of over 5 years, median overall survival iin the surgery alone group was 27 months vs 36 months in the postoperative chemoradiation group (p=0.005) Decrease in local failure as the first site of failure in the chemoradiation group (19% versus 29%).

Chemoradiation afte resectdion of GE junction tumors (Kofoed et al., 2012) among a group of 211 patients with GE junction adenocarcinoma with positive lymph nodes with improved 3-year disease-free survival (37% s 24%).

Chapter 11

Definitive ChemoRT

11.1 Phase II Studies

Experience with patients who refuse surgery or are medically unfit:

(Taketa et al., 2012) (**?**) (**?**)

Castoro(Castoro et al., 2013)

preSANO(**?**) Clinical Response evaluation after chemoRT for esophageal cancer with PET and EGD.

11.2 ChemoRT vs Trimodality therapy

The sensitivity of squamous cell carcinoma of the esophagus to chemoradiation has raised the question whether

Stahl Locally advanced squamous cell carcinoma randomized to induction chemotherapy (cisplatin, etopiside, 5FU with leuocovrin) followed by chemoradiation (4000cGy with concurrent ciplatin and etopiside) followed by surgery compared with induction chemotherapy followed by chemoradiation (6400cGy with concurrent cisplatin and etopiside).(Stahl et al., 2005) progression-free survival was better in the trimodality group (64.3% vs 40.7%) Treatment-related morality was substantial in the surgery arm (13% vs 4%). This would be considered an excessive rate of operative mortality by modern standards. Unsurprisingly, there was no difference in overall survival between groups, in part because the surgical group had an excess 9% mortality rate from treatment. Two-year survival in the surgery arm was 40% vs 35% in the definitive chemoradiation arm. (**?**)

In the French FFCD trial, 444 patients with carcinoma of the esophagus (90% squamous cell) were treated with two cycles of 5-FU and cisplatin with concur-

rent radiation.(Bedenne et al., 2007) Patients with a partial or complete clinical response to chemoradiation were randomized to either surgery or a boost of radiation. Patients who did not respond to chemoradiation were treated with surgery and were eliminated from the study. Only 259 of the original 444 patients (59%) went on to randomization, with the remainder (those not responding to chemoradiation) treated with surgery. Of the randomized group, median survival was 17.7months in the surgery arm versus 19.3months in the definitive chemoradiation arm. Like the Stahl study, treatment-related mortality in the surgical arm was high (9% versus 1%).

#Active Surveillance

EGD is poor predictor of pCR (Sarkaria et al., 2009)

Chapter 12

Radiation for esophageal cancer

RTOG 94-05 clinical trial (Minsky et al., 2002)

12.1 Salvage esophagectomy

(Markar et al., 2014)

(Swisher et al., 2002)

Chapter 13

Surgery

Three general approaches exist for surgical therapy.

Trans-thoracic or Ivor Lewis esophagectomy(Visbal et al., 2001) removes the intrathoracic portion of the esophagus and constructs an anastomosis within the chest. The approach include an abdominal phase, during which an esophageal substitute is constructed (usually from stomach). A thoracic phase then removes the intrathoracic esophagus and constructs an anastomosis within the chest cavity.

A McKeown esophagectomy utilizes three surgical fields: abdomen, right chest, and neck. The right chest approach allows dissection of peri-esophageal lymph nodes, and the cervical incision allows removal of the total esophagus.(McKeown, 1976) This approach is useful for tumors which involve the proximal thoracic esophagus, to ensure a negative margin. The cervical anastomosis carries a higher risk of anastomotic leak than a thoracic anastomosis, although the morbidity of a cervical anastomosis leak is less serious than that of a leak of a thoracic anastomosis.

A transhiatal esohpagectomy approaches the esophagus from the abdomen through the hiatus and from neck. By blunt dissection the esophagus is freed up without the need for thoracotomy. An esophageal substute is then brought from the abdomen to the neck through the mediastinum(Orringer and Sloan, 1978) (Orringer et al., 2007)<! – Orringer Ann Surg 2007 –> The operation is designed to avoid the pulmonary toxicity of the right chest approach. On the other hand, the blunt nature of the mediastinal dissection means that fewer lymph nodes are harvested than with a trans-thoracic approach.

Randomized trial of transthoracic esophagectomy with extended lymph node dissection versus transhiatal esohpagectomy showed fewer pulmonary complications with the transhiatal approach. (Hulscher et al., 2002) Fewer lymph nodes were havested with a transhiatal appraoch. A post-hoc analysis showed that

among patients with 1-8 positive lymph nodes, survival with improved with the extended lymph node dissection.(Omloo et al., 2007)

Minimally-invasive approaches to esophagectomy are now common, with evidence for less perioperative morbidity than an open approach (Biere et al., 2012) (Zhou et al., 2015)

Randomized trial of a hybrid MIE (with laparoscopy and thoracotomy) was associated with lower postoperative complications than open esophagectomy (Mariette et al., 2019)

High volume (Birkmeyer et al., 2003) (Wouters et al., 2009)

Siwert III lesions are considered gastric cancers (Rusch, 2004) (Siewert et al., 2006)

Laparoscopy may be helpful in Siewert III tumors (de Graaf et al., 2007)

13.0.1 Preoperative Evaluation

Dysphagia can be scored accordgin to Mellow et al (Mellow and Pinkas, 1985):

- 0 No dysphagia
- 1 Dysphagia to normal solids
- 2 Dysphagia to soft solids (ground beef, poultry,fish)
- 3 Dysphagia to solids and liquids
- 4 Inability to swallow saliva

13.1 Minimally-invasive Esophagectomy

Higher lymph node yield with MIE vs open approach [Kalff]

13.2 Transthoracic

13.3 Transhiatal

13.4 Three-hole

13.5 Extended lymphadenectomy

Chapter 14

Metastatic

14.1 Palliative radiation

Palliative radiation vs chemoradiation (Penniment et al., 2018)

Radiation along favored over chemoradiation in the palliaitve setting (Penniment et al., 2018)

14.2 Chemoradiation vs chemotherapy in Stage IV

(Guttmann et al., 2017)

Chapter 15

Stents for malignant disease

(Vakil et al., 2001)

Review of guidelines 2010 Am Society GI (Sharma et al., 2010)

Chapter 16

Surveillance

16.1 T1a treated with endoscopic resection

EGD every 3 mo for first year, then every 6 months for second year, then annually(Shaheen et al., 2016)

16.2 Tib treated with endoscoic resection

EGD every 3 mon for first year, then every 4-6 months for seond year, then annually CT chest/abdomen every 12 months for up to 3 years (as clinically indicated)

16.3 T1b treated with esophagectomy

EGD every 3-6 months for first 2 years, then annually for 3 more years. CT every 6-9 months for first 2 years, then annually up to 5 years.

16.4 Stage II or III treated with chemoradiation.

These patients are at risk for local recurrence (Sudo et al., 2014) and some may be candidates for salvage esophagectomy. Most relapses (95%) occur within 24 months. See also (Taketa et al., 2014)

16.5 Locally-advanced treated with trimodality therapy

Local/regional relapses are uncommon. (Dorth et al., 2014) (Oppedijk et al., 2014) (Sudo et al., 2013) => NCCN does not recommend EGD. 90% of relapses occur within 36 months of surgery.

CT every 6 months up to 2 years (if patient is a candidate for additional curative-intent therapy)

Chapter 17

Survivorship

17.1 Nutritional consequences

(Baker et al., 2016)

Weight loss (Martin and Lagergren, 2009) (Ouattara et al., 2012)

17.2 Cardiac toxicity of radiation

(Beukema et al., 2015) (Frandsen et al., 2015) (Gharzai et al., 2016)

Gastric Cancer

Chapter 18

Gastric Overview

Chapter 19

Superficial

Chapter 20

Locally-Advanced Gastric

Locally-advanced gastric cancer (T3 or N^+) is generally treated with some form of adjuvant therapy, which has been shown to improve upon the outcomes with surgery alone.

20.1 Preoperative Chemotherapy

FLOT chemotherapy (Al-Batran et al., 2019)

MAGIC study randomized 503 patients to perioperative 'sandwich' therapy consisting of epirubicin, cisplatin, and 5-FU versus surgery alone. In the perioperative chemotherapy group, 4 cycles were administered prior to surgery, and 4 cycles afterwards. Tumors of the esophagus or gastroesophageal junction comprised 26% of the study population. While over 90% of patients assigned to the chemotherapy arm completed their preoperative chemotherapy, only 66% completed their postoperative therapy. Survival at 5 years was 36% in the perioperative chemotherapy group, compared with 24% in the surgery group ($p<0.001$).(Cunningham et al., 2006)

CLASSIC clinical trial randomized 1033 patients with stage II or III gastric cancer after D2 gastrectomy to 6 months of adjuvant chemotherapy versus surgery alone. Three-year survival was improved in the chemotherapy group (74% *v* 59%).(Bang et al., 2012)

The FFCD trial randomized patients to preoperative chemotherapy with 2 or 3 yccles of cisplatin and 5-FU versus surgery alone. Tumors of the lower esophagus or gastroesophageal junction comprised 75% of the study population. Survival at 5 years was longer in the chemotherapy group (38%) versus 24% in the surgery alone group ($p=0.02$).(Ychou et al., 2011)

20.2 Postoperative chemotherapy

CLAASIC trial (Noh et al., 2014) (Bang et al., 2012) patients with II or IIIB gastric cancer received gastrectomy with D2 node dissection randomized to postoperative chemotherapy with capecitabine and oxaliplatin. Chemotherapy group had improved 3-year DFS (74% vs 59% P<.0001)

Chapter 21

Locally Advanced Gastric Ca

21.1 Postoperative chemoradiation

Intergroup 0116 trial (Macdonald et al., 2001) Surgical quality control was poor, as 90% were treated a limited lymph node dissection. Long-term followup, however (Smalley et al., 2012) showed a persistent benefit of postoperative chemoradiation.

ARTIST trial 450 patients treated with a D1 α gastrectomy were randomized to adjuvant capcitibine and cisplatin versus chemoradiation consisting of two cycles of capcitabine/oxalipaltin followed by chemoradiation followed by chemotherapy. Overall 3- year survival did differ between groups (78.2% vs 74.2% p =0.86). A post-hoc analysis of patients with positive nodes showed a beneficial effect of chemoradiation (77.5% v 72.3% p=0.365).(Lee et al., 2012)

CRITICS trial treated all patients with preoperative chemoterhapy followed by surgery. Postoperative patients were then randomized between additional chemotherapy versus chemoradiation.

21.2 Preoperative chemoradiation

(Ajani et al., 2006)

Chapter 22

Neoadjuvant Chemotherapy for colon cancer

Seymour MT, Morton D. FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer. J Clin Oncol. 2019 May;37(15 Suppl):3504-3504.

Chapter 23

Extended Node dissection for colon cancer

Short-term outcomes of complete mesocolic excision versus D2 dissection in patients undergoing laparoscopic colectomy for right colon cancer (RELARC): a randomised, controlled, phase 3, superiority tria

Short-term outcomes of a multicentre randomized clinical trial comparing D2 versus D3 lymph node dissection for colonic cancer (COLD trial). Karachun A, Panaiotti L, Chernikovskiy I, Achkasov S, Gevorkyan Y, Savanovich N, Sharygin G, Markushin L, Sushkov O, Aleshin D, Shakhmatov D, Nazarov I, Muratov I, Maynovskaya O, Olkina A, Lankov T, Ovchinnikova T, Kharagezov D, Kaymakchi D, Milakin A, Petrov A. Br J Surg. 2020 Apr;107(5):499-508. doi: 10.1002/bjs.11387. Epub 2019 Dec 24. PMID: 31872869 Clinical Trial.

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