
به نام خدایی که در این نزدیکی است

Esophageal cancer panel

Abolghasem Allahyari
Hematologist Oncologist
Associate professor of MUMS
Imam Reza hospital

Panel members:

Dr Soltani oncosurgeon

Dr izadi Radiologist

Dr Aledavod Radiotherapist Oncologist

Dr Rahimi Medical Oncologist

Dr Mohamaddoust Medical Oncologist

The management of patients with esophageal and EGJ cancers requires the expertise of several disciplines, including surgical oncology, medical oncology, gastroenterology, radiation oncology, radiology, and pathology.

- A 63-year-old male patient presented with dysphagia to From 3 months ago
- Weight loss -
- Anorexia -
- Smoking -

همکارمحترم:

باعرض سلام

در بررسی **Upper GI Study** انجام شده:

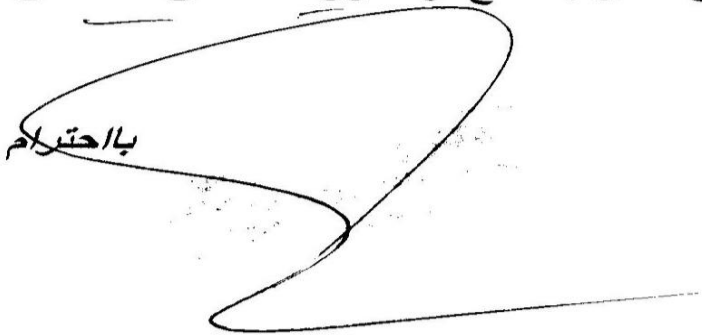
در ارزیابی با انجام گرافی های سریال

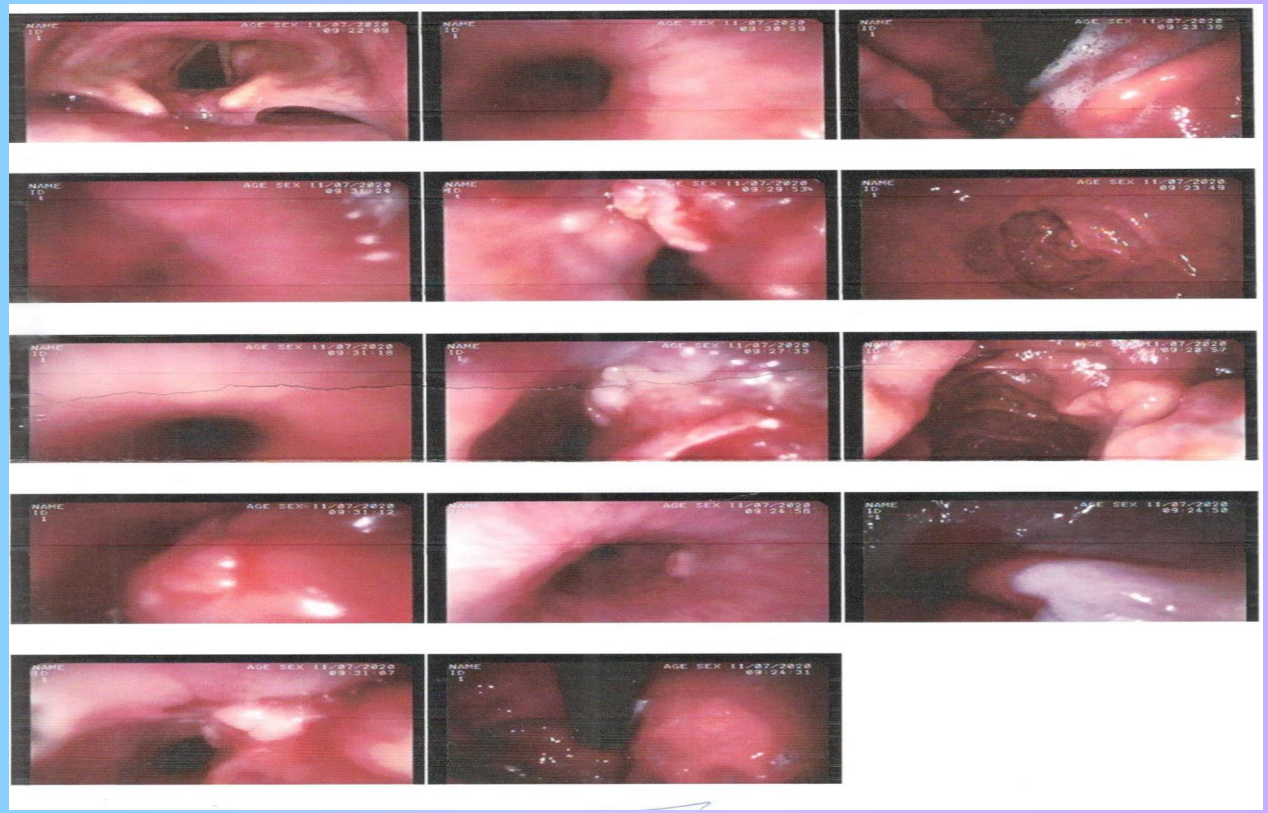
عبور ماده حاجب از مری به خوبی صورت گرفت.

شواهدی به نفع تنگی و نامنظمی مخاطی دیده نمی شود.

در بررسی کادر معده و دئودنوم شواهدی به نفع اولسرونامنظمی مخاطی رویت نگردید.

باحترام





Premedication	:	no medication
Chief complaint	:	Dysphgea and wheigh Loss
Esophagus	:	Normal
Upper	:	Normal
Middle	:	at about 34 cmo to 36 cm from incisor one ulcerovegetative amass was seen with partial stenosis and Biopsy obtained.
Lower	:	at 36 cm from incisor one small Nodule with ulceration was seen and biopsy obtained
EG Junction	:	39CMS.
Stomach	:	Normal
Fundus	:	Normal
Body	:	Normal
Antrum	:	Normal
Pylorus	:	Normal
Duodenum	:	Normal
D1	:	Normal
D2	:	Normal
Biopsy	:	from mass and Nodule of Esophagus
Diagnosis	:	Cancer of Esophagus

Anatomic name	Compartment ICD-O-3	Esophageal location		Anatomic boundaries	Typical esophagectomy (cm)
		ICD-O-3	Name		
Cervical	C15.0	C15.3	Upper	Hypopharynx to sternal notch	15 to <20
Thoracic	C15.1	C15.3	Upper	Sternal notch to azygos vein	20 to <25
		C15.4	Middle	Lower border of azygos vein to inferior pulmonary vein	25 to <30
		C15.5	Lower	Lower border of inferior pulmonary vein to esophagogastric junction	30 to <40
Abdominal	C15.2	C15.5	Lower	Esophagogastric junction to 2 cm below esophagogastric junction	40 to 45
		C16.0	Esophagogastric junction/card	Esophagogastric junction to 2 cm below esophagogastric junction	40 to 45

گزارش آسیب شناسی

نوع نمونه: ۱.بیوپسی قسمت میانی مری ۲. بیوپسی قسمت تحتانی مری

ماکروسکوپی :

۱.نمونه ارسالی شامل ۱ قطعه بافت کرم رنگ به حداکثر قطر ۰٫۲ سانتیمتر است.

۲.نمونه ارسالی شامل ۳ قطعه بافت کرم ر نگ با قوام نرم که بزرگترین به اقطار ۰٫۲ سانتیمتر است.

میکروسکوپی :

در بررسی میکروسکوپی از هر دو نمونه ارسالی مقاطع پوشش اسکواموس با استرومای اندک زیرین در نمونه تحتانی با استرومای کمی بیشتر دیده می شود که در آن ارتشاح سلول های عمدتا متعدد و با دستجات چند سلولی با هیپرکروماز شدید ، پلئومورفیسم متوسط و تصاویر میتوزی در استرومای همبندی پر عروق وجود دارند. پوشش سطحی آکانتوز و پاپیلوماتوز نشان می دهند.

DIAGNOSIS:

BIOPSY OF ESOPHAGOUS (MIDDLE & LOWER):

INVASIVE MALIGNANT TUMOR

MOST COMPATIBLE WITH SQUAMOUS CELL CARCINOMA

همکار محترم با توجه به شرح آندوسکوپی و سطحی بودن بیوپسی انجام بیوپسی عمقی مجدد برای بررسی بیشتر و تشخیص لازم است.

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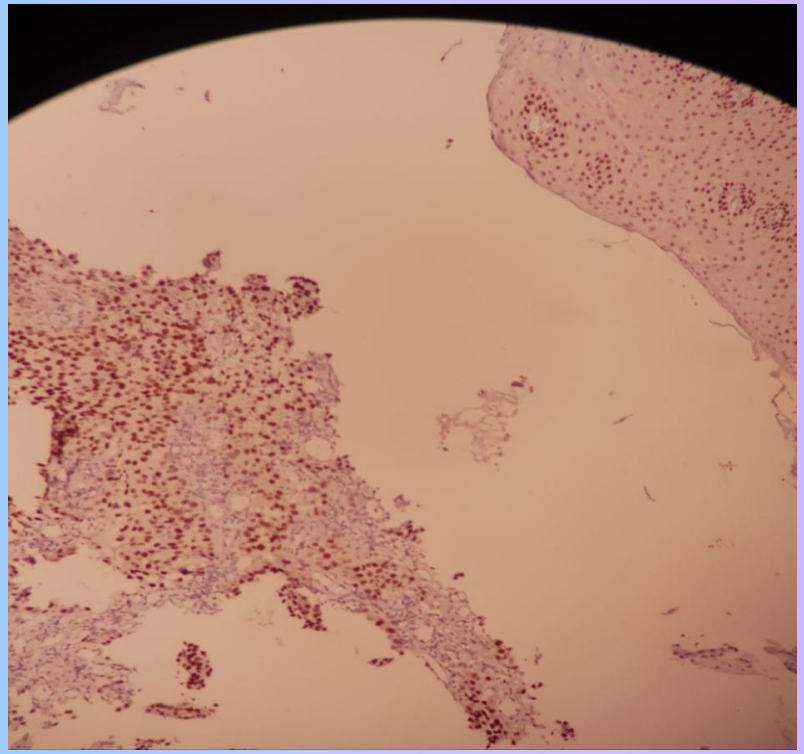
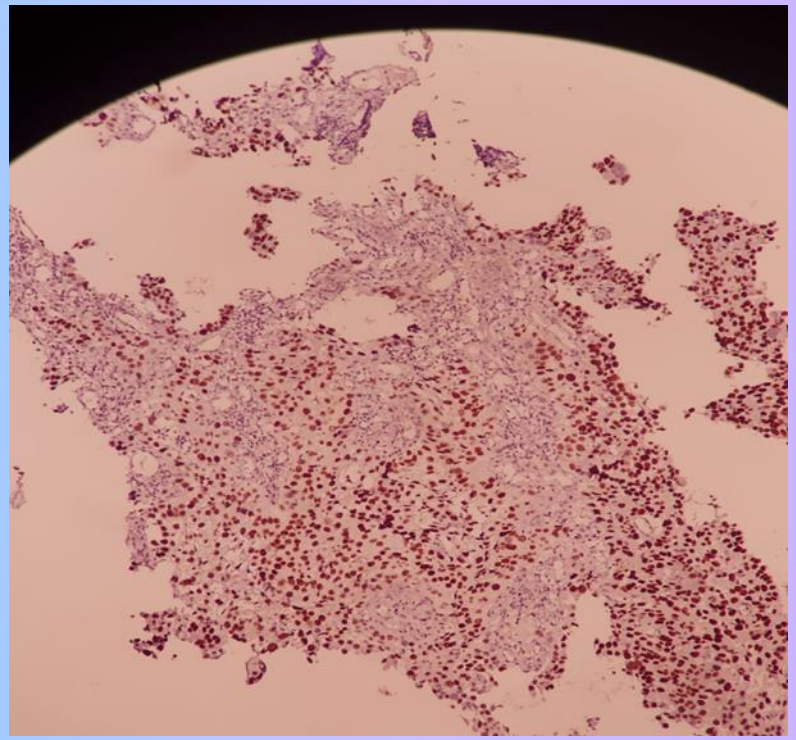


P40+



Which staging investigations would you request?

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2021
Esophageal and Esophagogastric Junction Cancers

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WORKUP

- H&P
- Upper GI endoscopy and biopsy[a]
- Chest/abdominal CT with oral and IV contrast
- Pelvic CT with contrast as clinically indicated
- FDG-PET/CT evaluation (skull base to mid-thigh) if no evidence of M1 disease
- CBC and comprehensive chemistry profile
- Endoscopic ultrasound (EUS), if no evidence of M1 unresectable disease
- Endoscopic resection (ER) is essential for the accurate staging of early-stage cancers (T1a or T1b).[a,b] Early-stage cancers can best be diagnosed by ER
- Biopsy of metastatic disease as clinically indicated
- MSI by PCR/MMR by IHC, and PD-L1 testing if metastatic disease is documented/suspected[c]
- HER2 testing if metastatic adenocarcinoma is documented/suspected[c]
- If sufficient tissue is available after the above testing has been completed, next-generation sequencing (NGS) may be considered[c]
- Bronchoscopy, if tumor is at or above the carina with no evidence of M1 disease
- Assign Siewert category[d]
- Nutritional assessment and counseling
- Smoking cessation advice, counseling, and pharmacotherapy as indicated[e]
- Screen for family history[f]

CLINICAL STAGE[g]

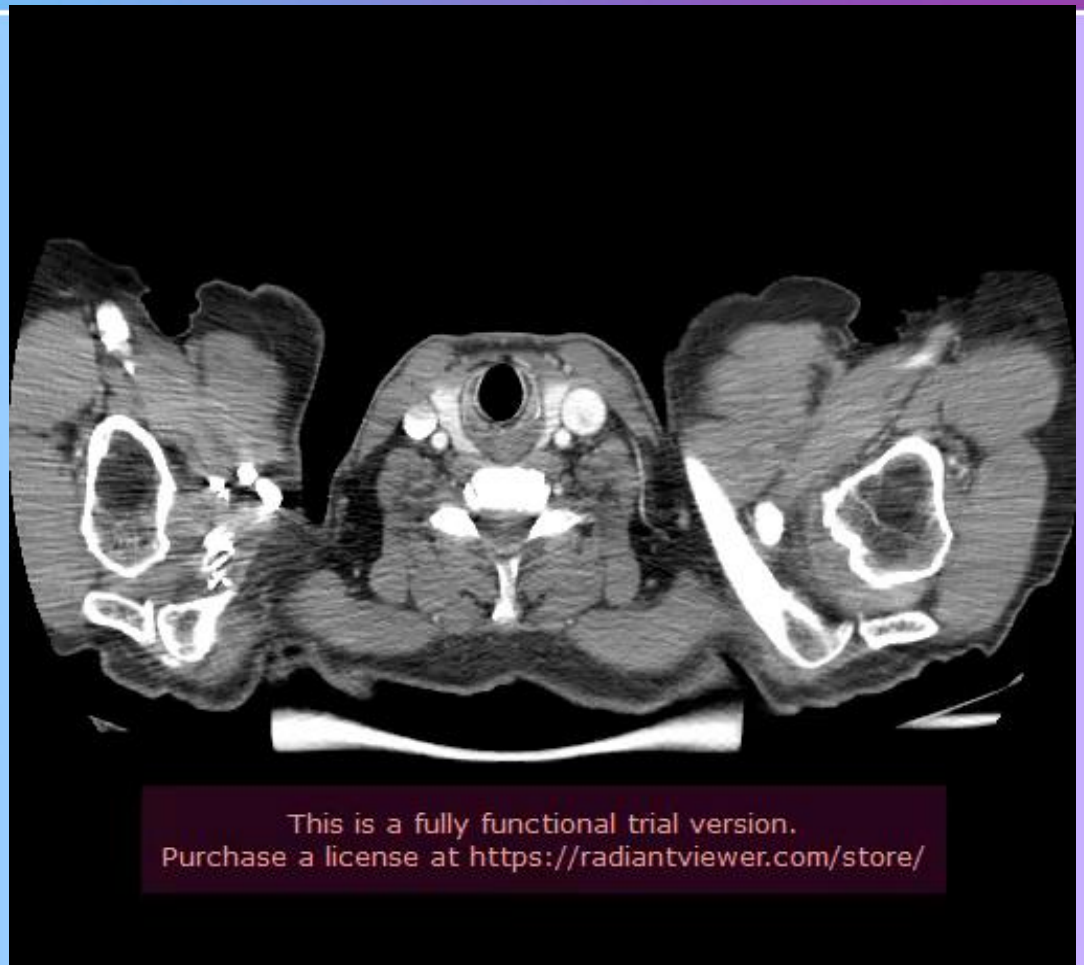
HISTOLOGIC CLASSIFICATION[c]

Stage I–IVA[g,h] (locoregional disease, except T4b or unresectable N3[h])
- Squamous cell carcinoma → See ESOPH-2
- Adenocarcinoma → See ESOPH-11

Stage IVA[g] (includes T4b or unresectable N3 only) and IVB (metastatic disease)
- Squamous cell carcinoma → See ESOPH-10
- Adenocarcinoma → See ESOPH-19

While contrast-enhanced CT is the most widely used modality for detecting distant metastases in esophageal cancer, FDG-PET/CT is more sensitive than CT alone for staging cM disease.[10,49,60,62,71] The addition of FDG-PET improves the detection of distant metastases that may remain occult on CT scan of the chest and abdomen, thereby allowing proper patient selection for surgical resection.[10,49] In a

prospective multicenter trial of 129 esophageal cancer patients without definite distant metastases, PET identified metastatic sites in 41% of cases and altered management in 38% of cases.[72] However, potential pitfalls of FDG-PET/CT include the poor detection of hepatic metastases when the CT component is performed without IV contrast and the high rate of false-positive FDG-PET findings.[58,59,64,65]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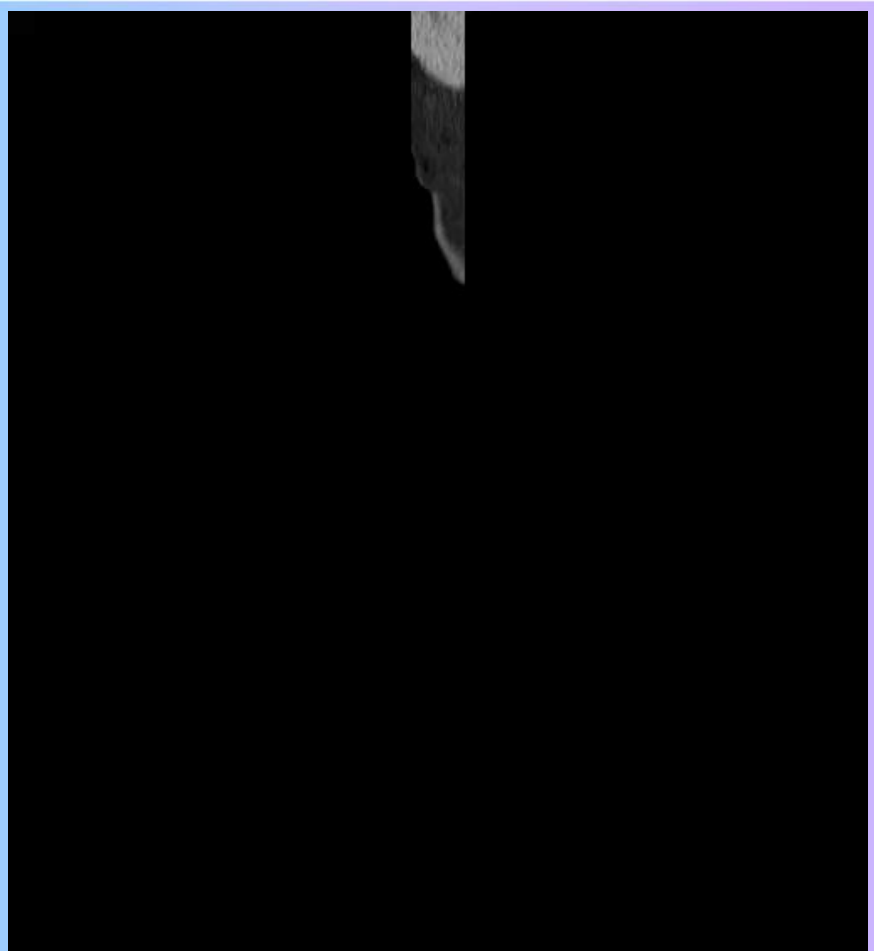


Spiral CT Scan of Thorax With and Without Contrast:

PMH : Case شناخته شده کانسر مری

تیروئید سایز و دانسیته نرمال دارد.

سایز و شکل حفرات قلبی نرمال است.

آدنوپاتی آگزیلاری در دو سمت مشهود نیست.

آدنوپاتی مدیاستینال رویت نمی شود.

کلسیفیکاسیون شرایین کرونری مشهود است.

عروق بزرگ مدیاستن نمای نرمال دارند.

در ناحیه ساب کارینال، افزایش قابل توجه ضخامت دیواره مری خصوصا در دیواره خلفی به شکل ندولی به ابعاد ۱۶*۲۱ م.م و در سگمانی به طول تقریبی ۲۵ م.م از دیواره مری رویت می شود که باعث تنگی خفیف لومن شده است، انوازیون به ارگان های مجاور رویت نمی شود.

GE junction نرمال است.

فاصله لبه تحتانی ضایعه از GE junction حدود ۱۰ سانتیمتر اندازه گیری شد.

دو لنف نود کوچک در مجاورت فوقانی آن در پاراتراکئال چپ رویت می شود که سایز آنها پاتولوژیک به نظر نمی رسد.

در سایر نواحی مری ضایعه پاتولوژیک خاصی مشهود نیست.

شواهدی به نفع پلورال افیوژن و یا thickening رویت نشد.

باند فیبروتیک همراه با دیستورشن نسجی مختصر در لوب تحتانی ریه راست رویت می شود.

در سایر نواحی در فیلد هر دو ریه ضایعه پاتولوژیک مشاهده نگردید.

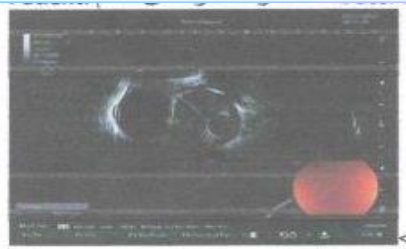
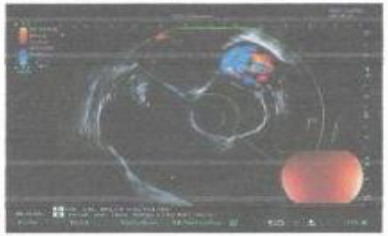
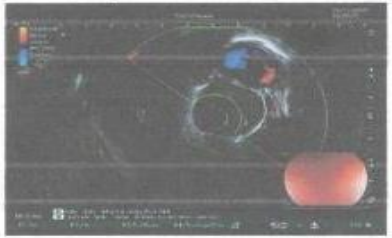
در بررسی نسج نرم و استخوانهای قفسه صدری ضایعه پاتولوژیک مشاهده نمی شود.

یافته ها در مجموع به نفع early stage esophageal cancer می باشد.

Abdominopelvic Spiral CT Scan With And Without IV/Oral Contrast:

کبد سایز نرمال دارد.
کاهش منتشر دانسیته پارانشیم کبد به نفع fatty liver مشهود است.
ضایعه فضاگیر در نسج کبد مشهود نیست.
کبد، طحال، پانکراس، هر دو کلیه و آدرنال دارای ابعاد و دانسیته نسجی نرمال است.
شواهدی به نفع ضایعه فضاگیر در احشاء فوق رویت نگردید.
کیسه صفرا دارای ابعاد و ضخامت جداری نرمال بدون سنگ رویت شد.
اتساع در مجاری صفراوی داخل و خارج کبدی رویت نمی شود.
آدنوپاتی سلیاک و مزانتریک واضحی مشهود نیست.
شواهدی به نفع لنفادنوپاتی در سایر نواحی پاراآئورت رویت نگردید.
سنگی به دیامتر ۳ م.م در کالیس تحتانی کلیه چپ و سنگی به دیامتر ۳/۵ م.م در کالیس تحتانی کلیه راست رویت می شود.
تصویر اتساع در سیستم ادراری دو طرف مشاهده نگردید.
مثانه دارای حجم و ضخامت جداری نرمال است.
پروستات با توجه به سن بیمار سایز و دانسیته نرمال دارد.
دیورتیکول های متعدد در دیواره کولون، خصوصا سیگموئید و کولون نزولی مشهود است که در داخل برخی از آن ها کنتراست بجا مانده از imaging قبلی رویت می شود.
تصویری به نفع دیورتیکولیت مشهود نیست.
در بررسی معده و روده باریک نکته پاتولوژیک رویت نگردید.
در نسج نرم سطحی، در ناحیه باتوک چپ، ضایعه هیپودانس به ابعاد ۲۲*۴۱ م.م با دانسیته high fluid رویت می شود که می تواند به علت تجمع مایع در محل injection قبلی باشد.
مایع آزاد درون حفره شکم و لگن مشاهده نمی شود.
ضایعه لیتیک یا بلاستیک استخوانی مشهود نیست.

Next Step ?

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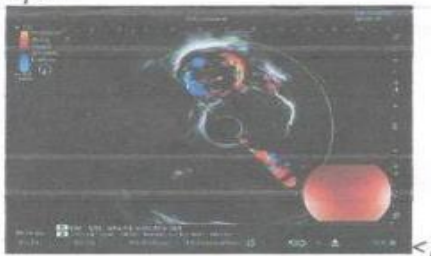
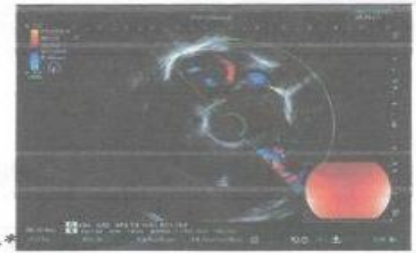

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Code	*Code 400555 = اندوسونو بدون نمونه*
History	*Esophageal SCC reffered for EUS staging*
Lab Data	*Not provided*
Imaging Data	*No distatnt metastasis in CT scan*
Indication	*EUS staging*
Anesthesia	*GA with propofol in lateral position*
EUS Type	*Radial*

Findings: *There was a hypoechoic mass , 15 mm thickness and invaded muscularis propria(T2) at 35 cm from dental arc.At least 3 regional round lymphnode 8-10 mm were seen.Aorta,pericardiumand azygus were intacted.The mass was close contact to pleura.Celiac artery lymphnode was not seen.*

Impression	*Esophageal SCC, T2 N2 ,stage 3*
RECOMMENDATIONS	*Neoadjuvant was recommended*

As with contrast-enhanced CT scanning alone, **PET/CT is of limited value for staging the extent of locoregional tumor, particularly nodal status**

This may be due, at least in part, to **high FDG uptake in the primary esophageal malignancy,** which obscures increased FDG uptake in the regional nodes, and/or **low sensitivity for small involved lymph nodes.**

Furthermore, PET/CT is not consistently able to differentiate the depth of primary tumor invasion.

EUS is more accurate than either PET/CT or contrast-enhanced CT alone. and it is the locoregional tumor staging modality of choice.

Regional nodes

Endosonographic criteria that are suggestive of malignant involvement of the visible **lymph nodes include width >10 mm, round shape, smooth border, and echo-poor pattern**

Of these, **echo-poor pattern and width >10 mm are the most specific for malignancy.**

When all **four features** are present, there is **an 80 to 100** percent chance of metastatic involvement. However, only **25 percent of malignant** nodes will have all of these features.

EUS-guided FNA may improve the accuracy of N staging by providing cytologic confirmation of metastatic disease from accessible nodes,
Sensitivity, specificity, and **accuracy** of **EUS-guided FNA for locoregional lymph nodes are all over 85 percent** when surgical resection specimen or cytology results are considered the gold standard.

EUS is the most accurate technique for loco regional staging of invasive esophageal cancer.

T stage

The **sensitivity and specificity** rates of EUS for the correct **evaluation of T stage are 81 to 92, and 94 to 97 percent**, respectively

in general, EUS performs better with advanced (T4) than with early (T1) disease

The endoscopic finding of a **malignant node in the celiac** area remote from the primary tumor (for **SCCs or for lesions in the upper or middle thoracic esophagus** was **previously** an indicator of unresectability and was **staged as M1a** metastatic disease.

However, **celiac nodal metastases are scored as regional nodal disease in the newest 2017 TNM revision** regardless of the primary tumor location or histology .

Nevertheless, **prognosis is poor in such cases**, even if the primary tumor is located in the distal esophagus or EGJ

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Carcinoma of the Esophagus and Esophagogastric Junction (8th ed., 2017)
Squamous Cell Carcinoma and Adenocarcinoma

Table 1. **Definitions for T, N, M**

T	Primary Tumor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High-grade dysplasia, defined as malignant cells confined to the epithelium by the basement membrane
T1	Tumor invades the lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades the lamina propria or muscularis mucosae
T1b	Tumor invades the submucosa
T2	Tumor invades the muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Tumor invades the pleura, pericardium, azygos vein, diaphragm, or peritoneum
T4b	Tumor invades other adjacent structures, such as the aorta, vertebral body, or airway

N	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in one or two regional lymph nodes
N2	Metastasis in three to six regional lymph nodes
N3	Metastasis in seven or more regional lymph nodes

M	Distant Metastasis
M0	No distant metastasis
M1	Distant metastasis

G	Histologic Grade
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated, undifferentiated

Squamous Cell Carcinoma

Location	Location Criteria
X	Location unknown
Upper	Cervical esophagus to lower border of azygos vein
Middle	Lower border of azygos vein to lower border of inferior pulmonary vein
Lower	Lower border of inferior pulmonary vein to stomach, including gastroesophageal junction

Note: Location is defined by the position of the epicenter of the tumor in the esophagus.

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Carcinoma of the Esophagus and Esophagogastric Junction (8th ed., 2017)

Table 3. **AJCC Prognostic Stage Groups (Adenocarcinoma)**

Clinical Staging (cTNM)

	cT	cN	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T1	N1	M0
Stage IIB	T2	N0	M0
Stage III	T2	N1	M0
	T3	N0-1	M0
	T4a	N0-1	M0
Stage IVA	T1-4a	N2	M0
	T4b	N0-2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

Pathological (pTNM)

	pT	pN	M	G
Stage 0	Tis	N0	M0	N/A
Stage IA	T1a	N0	M0	G1
	T1a	N0	M0	GX
Stage IB	T1a	N0	M0	G2
	T1b	N0	M0	G1-2
	T1b	N0	M0	GX
Stage IC	T1	N0	M0	G3
	T2	N0	M0	G1-2
Stage IIA	T2	N0	M0	G3
	T2	N0	M0	GX
Stage IIB	T1	N1	M0	Any
	T3	N0	M0	Any
Stage IIIA	T1	N2	M0	Any
	T2	N1	M0	Any
Stage IIIB	T2	N2	M0	Any
	T3	N1-2	M0	Any
	T4a	N0-1	M0	Any
Stage IVA	T4a	N2	M0	Any
	T4b	N0-2	M0	Any
	Any T	N3	M0	Any
Stage IVB	Any T	Any N	M1	Any

Postneoadjuvant Therapy (ypTNM)

	ypT	ypN	M
Stage I	T0-2	N0	M0
Stage II	T3	N0	M0
Stage IIIA	T0-2	N1	M0
Stage IIIB	T3	N1	M0
	T0-3	N2	M0
	T4a	N0	M0
Stage IVA	T4a	N1-2	M0
	T4a	NX	M0
	T4b	N0-2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

What treatment do you recommend?

1- up front surgery

2-neoadjuvant chemo RT

3-neoadjuvant chemotherapy

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Esophageal and Esophagogastric Junction Cancers

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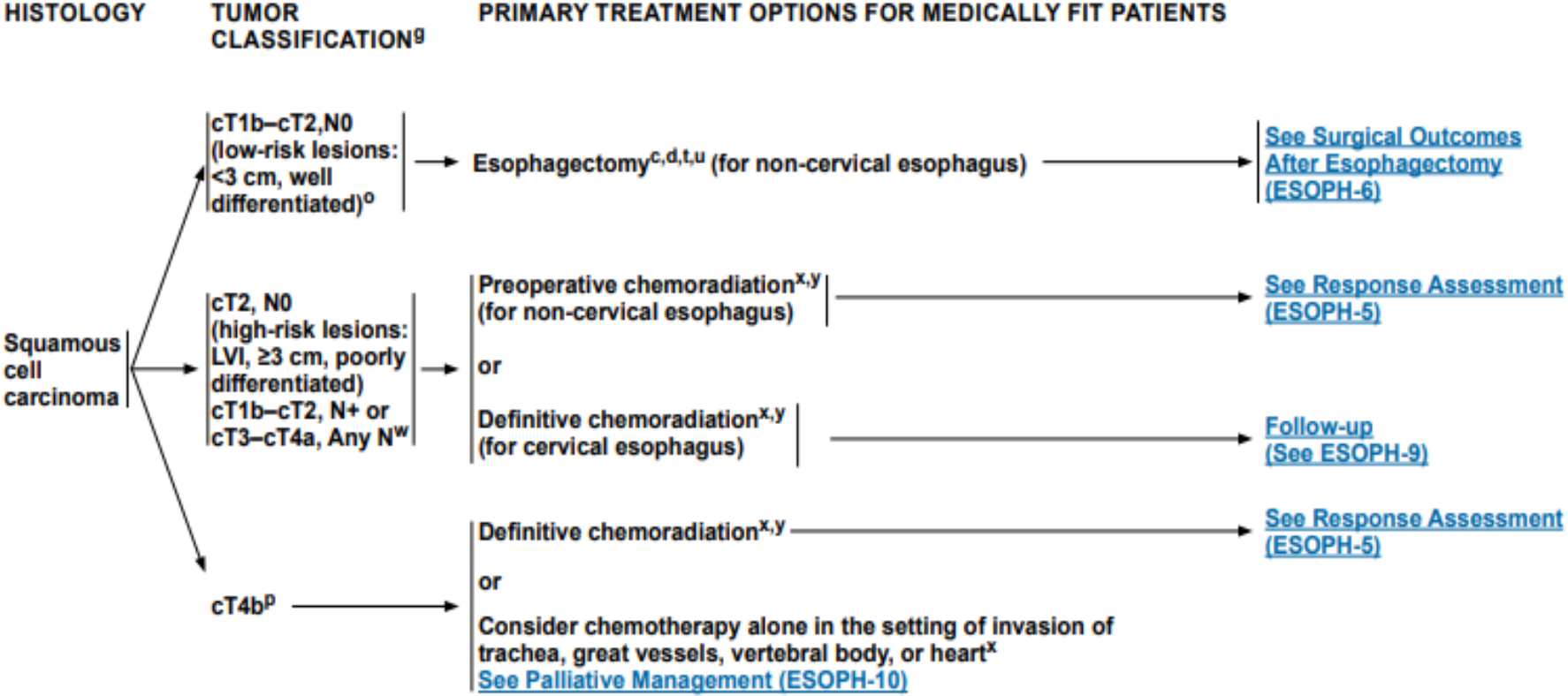


Preoperative chemoradiotherapy

Several trials and meta-analyses have demonstrated **better survival** with **preoperative concurrent chemoradiation as compared with local therapy alone**

Thoracic esophageal cancer

We recommend **combined modality therapy, rather than surgery alone**, for patients with **T3N0, T4aN0, and clinically node-positive thoracic esophageal cancer, regardless of histology .**

We suggest concurrent chemoradiotherapy (CRT) instead of chemotherapy alone for neoadjuvant therapy (**Grade 2B**).

At least **two randomized trials** directly comparing **CRT alone with trimodality therapy (CRT followed by surgery)** have **failed to demonstrate better survival**,

although **both show better locoregional control** and a lesser need for palliative procedures when **surgery** is a component of multimodality treatment

What is the preferrd regimen ?

The optimal type, dose, combination, and schedule of drugs has not been definitively established for neoadjuvant CRT.

For most patients, we suggest low-dose weekly carboplatin plus paclitaxel as was used in the Dutch CROSS trial rather than two courses of cisplatin plus fluorouracil (FU) (Grade 2C)

Preoperative Chemoradiation (Infusional fluorouracil[b] can be replaced with capecitabine)
Preferred Regimens • Paclitaxel and carboplatin (category 1)[1] • Fluorouracil[b] and oxaliplatin (category 1)[2,3]
Other Recommended Regimens • Fluorouracil and cisplatin (category 1)[4,5] • Irinotecan and cisplatin (category 2B)[6] • Paclitaxel and fluoropyrimidine (fluorouracil or capecitabine) (category 2B)[7]

Technique for preoperative RT?

3DRT

IMRT

Adding Intraluminal brachytherapy : yes or no

No trial has compared IMRT plus concurrent chemotherapy with the same chemotherapy regimen plus standard fractionation **3D-CRT,** and thus, **the safety and efficacy of this approach compared with standard 3D-CRT remains undefined.**

Three-dimensional conformal techniques should be used for modern RT treatment planning to minimize toxicities to adjacent vital organs (heart, lung, spinal cord, or liver).

Regardless of the chemotherapy regimen used for concurrent CRT, **the standard preoperative RT dose is 41.4 to 50.4 Gy in once daily fractions**

The **degree of response of a tumor and normal tissues/organs to radiation** depends upon **several radiotherapeutic factors** :

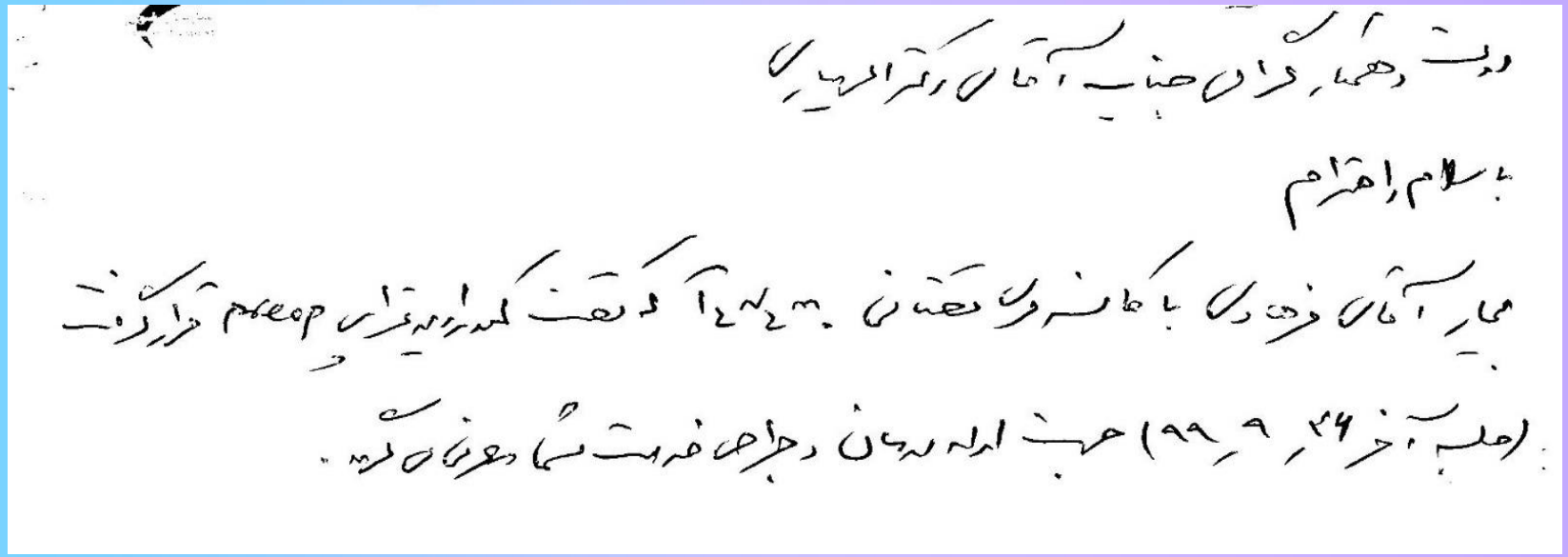
Fraction size (standard fraction size, 1.8 Gy to 2 Gy) and interfractional intervals (standard interval, 24 hours)

Total dose (standard preoperative dose in once daily schedule, **41.4 to 50.4** Gy)

Duration of treatment (**5 to 5.6 weeks** for standard fractionation, **without a rest during treatment)**

Target Volume

The gross tumor volume (GTV) should include the primary tumor and involved regional lymph nodes as identified by pre-treatment diagnostic studies as described above. The CTV includes areas at risk for microscopic disease and is defined as the primary tumor plus a 3- to 4-cm superior and inferior expansion and a 1 cm radial expansion.[288] The nodal CTV includes a 0.5- to 1.5-cm expansion from the nodal GTV. The CTV should also include coverage of elective nodal regions such as the celiac axis; however, this decision depends on the location of the primary tumor.



RESPONSE ASSESMENT ?

Response Assessment and Additional Management

Additional management options are based on the assessment of response to primary treatment. FDG-PET/CT scans are useful for the evaluation of patients after chemoradiation for the detection of distant lymphatic and hematogenous metastases.[57,66] Therefore, assessment with FDG-PET/CT (preferred) or FDG-PET scan should be done ≥5 to 8 weeks after the completion of preoperative therapy and prior to surgery. Chest/abdominal CT scan with contrast is recommended, but is not required if FDG-PET/CT was done. Pelvic CT with contrast can be considered for distal lesions, if clinically indicated. Upper GI endoscopy and biopsy is recommended following definitive chemoradiation, but is optional after preoperative chemoradiation if surgery is planned.

National Comprehensive Cancer Network®

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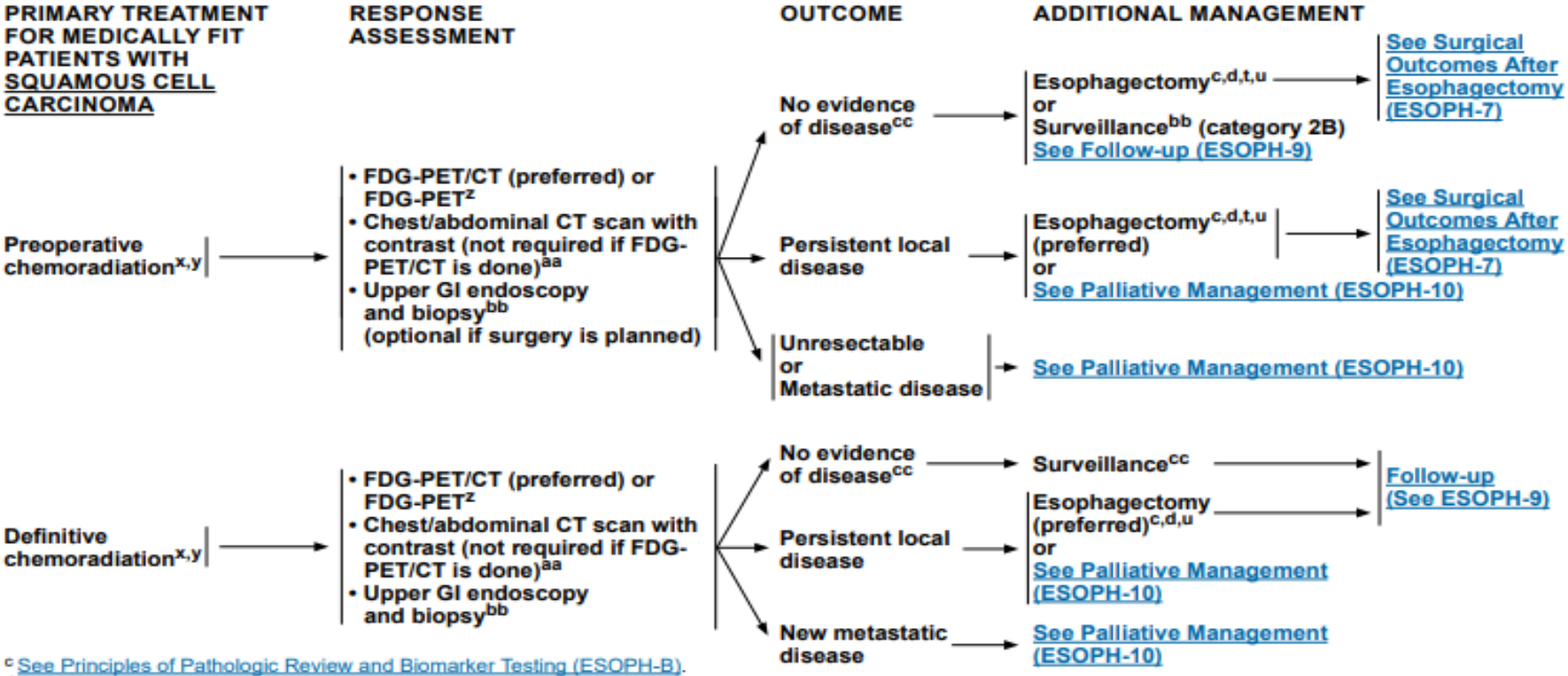


[c] See Principles of Pathologic Review and Biomarker Testing (ESOPH-B).
[d] See Principles of Surgery (ESOPH-C).
[t] Transhiatal or transthoracic, or minimally invasive; gastric reconstruction preferred.
[u] Feeding jejunostomy for postoperative nutritional support, generally preferred.
[x] See Principles of Systemic Therapy (ESOPH-F).
[y] See Principles of Radiation Therapy (ESOPH-G).

PET restaging after induction therapy

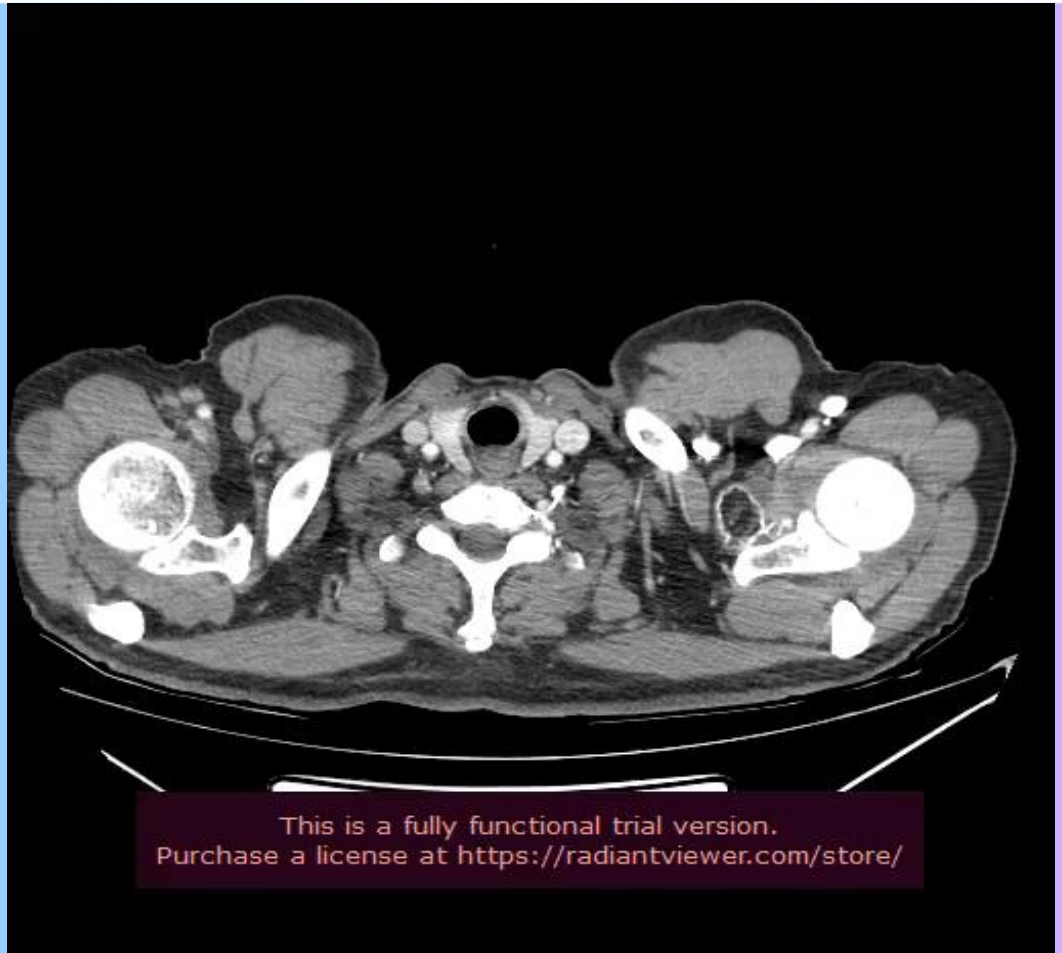
Integrated PET/CT may be also be useful for restaging after preoperative therapy.

Limited experience suggests that **whole-body PET/CT imaging detects distant metastases in approximately 8 percent of patients** following induction chemoradiotherapy with or without induction chemotherapy

In many of these cases, the **metastases were located** in sites (**skeletal muscle, subcutaneous soft tissue, brain, thyroid)** that are not imaged well by conventional radiographic staging techniques.

Utility of postinduction therapy PET scans

Until further data are available, **we do not use postinduction therapy PET scanning** to select patients for nonsurgical therapy.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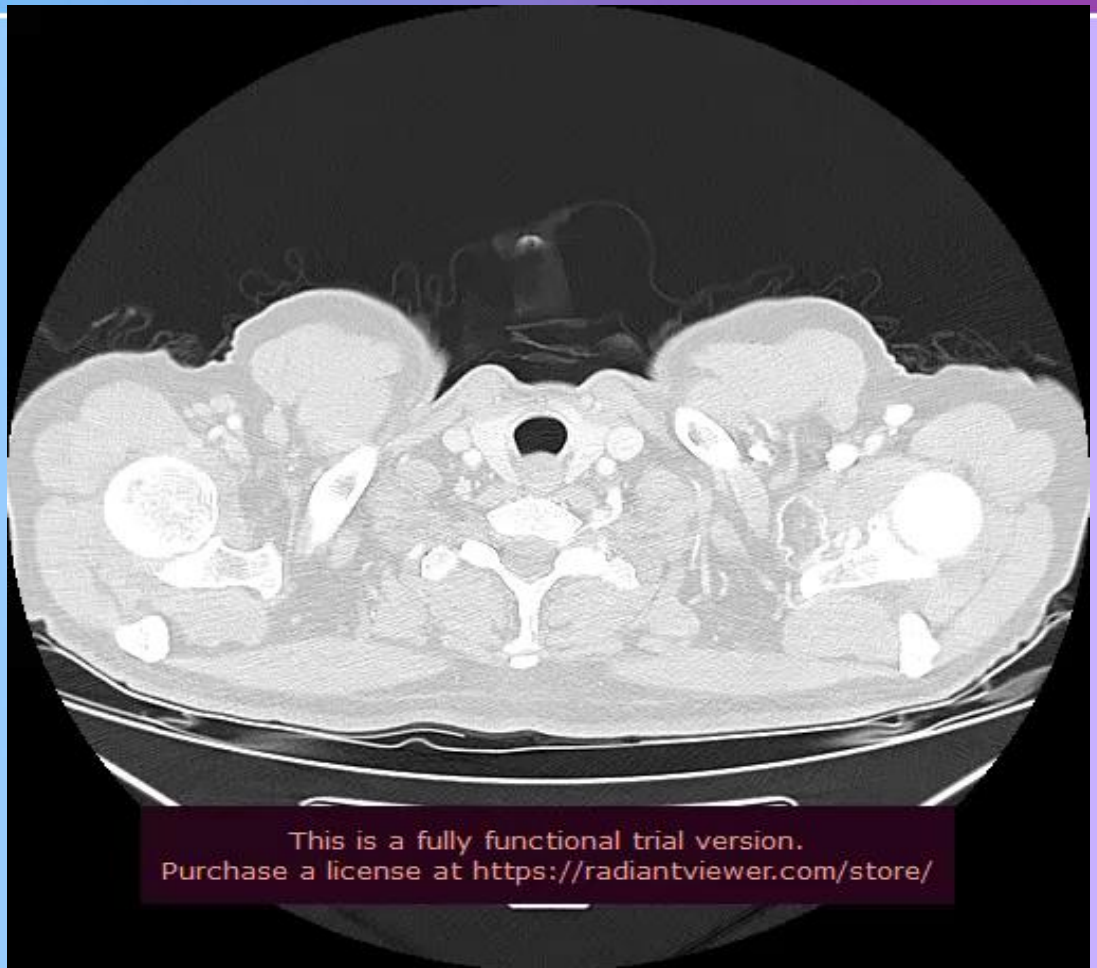
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همکارگرامی جناب آقای دکتر: ابوالقاسم – الهیاری

Spiral CT Scan of Thorax With Contrast:

PMH : Case شناخته شده کانسر مری

تیروئید سایز و دانسیته نرمال دارد.

سایز و شکل حفرات قلبی نرمال است.

آدنوپاتی آگزیلاری در دو سمت مشهود نیست.

آدنوپاتی مدیاستینال رویت نمی شود.

کلسیفیکاسیون شرایین کرونری مشهود است.

عروق بزرگ مدیاستن نمای نرمال دارند.

افزایش ضخامت دیواره مری در ناحیه ساب کارینا رویت می شود، اما توده واضح مشهود نیست.

GE junction نرمال است.

دو لنف نود کوچک در مجاورت چپ کارینا رویت می شود که سایز آنها پاتولوژیک به نظر نمی رسد.

در نواحی مختلف مری ضایعه پاتولوژیک خاصی مشهود نیست.

شواهدی به نفع پلورال افیوژن و یا thickening رویت نشد.

باند فیبروتیک همراه با دیستورشن نسجی مختصر در لوب تحتانی ریه راست رویت می شود.

در سایر نواحی در فیلد هر دو ریه ضایعه پاتولوژیک مشاهده نگردید.

در بررسی نسج نرم و استخوانهای قفسه صدری ضایعه پاتولوژیک مشاهده نمی شود.

همکارگرامی جناب آقای دکتر: ابوالقاسم – الهیاری

Abdominal Spiral CT Scan With IV/Oral Contrast:

کبد سایز نرمال دارد.
کاهش منتشر دانسیته پارانشیم کبد به نفع fatty liver مشهود است.
ضایعه فضاگیر در نسج کبد مشهود نیست.
طحال، پانکراس، هر دو کلیه و آدرنال دارای ابعاد و دانسیته نسجی نرمال است.
شواهدی به نفع ضایعه فضاگیر در احشاء فوق رویت نگردید.
کیسه صفرا دارای ابعاد و ضخامت جداری نرمال بدون سنگ رویت شد.
اتساع در مجاری صفراوی داخل و خارج کبدی رویت نمی شود.
آدنوپاتی سلیاک و مزانتریک واضحی مشهود نیست.
شواهدی به نفع لنفادنوپاتی در سایر نواحی پاراآئورت رویت نگردید.
سنگی به دیامتر ۳ م.م در کالیس تحتانی کلیه چپ و سنگی به دیامتر ۳/۵ م.م در کالیس تحتانی کلیه راست رویت می شود.
تصویر اتساع در سیستم ادراری دو طرف مشاهده نگردید.
مثانه دارای حجم و ضخامت جداری نرمال است.
پروستات قدری حجیم، دانسیته آن قدری هتروژن است.
دیورتیکول های متعدد در دیواره کولون، خصوصا سیگموئید و کولون نزولی مشهود است که در داخل برخی از آن ها کنتراست بجا مانده از imaging قبلی رویت می شود.
تصویری به نفع دیورتیکولیت مشهود نیست.
در بررسی معده و روده باریک نکته پاتولوژیک رویت نگردید.
در نسج نرم سطحی، در ناحیه باتوک چپ، ضایعه هیپودانس به ابعاد ۲۳*۴۳ م.م با دانسیته high fluid رویت می شود که می تواند به علت تجمع مایع در محل injection قبلی باشد.
مایع آزاد درون حفره شکم و لگن مشاهده نمی شود.
ضایعه لیتیک یا بلاستیک استخوانی مشهود نیست.

در مقایسه با سی تی اسکن قبلی بیمار انجام شده در همین مرکز به تاریخ ۹۹/۸/۱۷:

تنها ضایعه **significant**، ضایعه تومورال جدار مری بوده است که بالک آن کاملا از میان رفته و تنها قدری افزایش ضخامت مری باقی مانده است.

آدنوپاتی رژیونال واضح در سی تی اسکن قبلی و اخیر مشهود نیست.

در سایر ارگان های توراکس و شکم و لگن ضایعه پاتولوژیک **significant** در ارتباط با بیماری زمینه ای مشهود نیست و در مجموع یافته ها نشان دهنده **near complete response to treatment** می باشد.

What is the best time for surgery after neoadjuvant chemoradiotherapy?

Timing of surgery after chemoradiotherapy

We prefer that surgery be performed **within five to seven weeks of completing CRT**.

Postoperative complications increase if it is done sooner than four weeks, and the risk for **distant metastasis** from remaining cancer increases as surgery is delayed longer than seven weeks.

The optimal timing between completion of neoadjuvant CRT and resection is not established. The typical interval, **four to seven weeks**, is arbitrary, with the intent of **allowing resolution of acute inflammation** and for **tumor regression** while minimizing chronic fibrotic changes in the surgical field

SURGICAL APPROCHES :

1-Minimally Invasive or open Esophagectomy?

2-Transthoracic or Transhiatal Esophagectomy?

Chief Complaint of the Patient History & Primary Diagnosis: ..... شکایت اصلی بیمار و تشخیص اولیه:

Final Diagnosis: تشخیص نهایی:

Medical & Surgical Procedures: Esophagectomy ..... اقدامات درمانی و اعمال جراحی:

Mckown procedure

Results of ParaClinical Examination: ..... نتایج آزمایشات پاراکلینیکی:

Disease Progress (Cause of Death): ..... سیر بیماری(درصورت فوت،علت مرگ):

Pathology report

Source of specimen:

1-Esophagus

Gross Examination:

1-SRF labeled as esophagus, consist of esophagus with M: 11 cm in length and upto M: 3 cm in diameter and proximal part of stomach, cardia, with M: 7.5*3.5*3.5 cm. On opening in middle part, a scar like lesion with M: 0.8 cm in diameter was seen. The mucosal layers in other areas were intact, GEJ was not involved by tumor (M: 3.5 cm far from scar). Some lymph nodes were found in perigastric fatty tissue which the biggest was M: 1.4*1*0.7 cm and the smallest was M: 0.4 cm.
SOS: M/14 E: 10%

Microscopic Examination:

1-Sections reveal esophageal wall with remnant of malignant neoplastic lesion composed of undifferentiated cells with round to oval nuclei with nuclear groove and atypia arranged as single cells or small clusters invaded into submucosa and upper part of muscle layer. No perineural or lymph-vascular invasion was seen. GE junction, distal and proximal and radial margins were free from tumor. 14 perigastric lymph nodes were not involved by malignancy.

Diagnosis/Impression:

1-Esophagus – Known case of esophageal cancer, Esophagectomy after neoadjuvant chemotherapy:
-Undifferentiated carcinoma.
-Treatment effect: Single cells or rare small groups of cancer cells (near complete response, score 1)
-Tumor location: Middle part
-Microscopic extension: Tumor invaded into muscularis layer (upper part).
-No lymph-vascular invasion.
-No perineural infiltration.
-All surgical margins, GE junction were free from tumor.
-None of 14 perigastric lymph nodes were involved by malignancy or show tumoral effect.

Pathology report

Source of specimen:

2-Lung

Gross Examination:

2-SRF labeled as pulmonary nodule, consist of a piece of greenish to dark soft tissue with M: 1*0.6*0.5 cm.
SOS: 1/1 E: Total

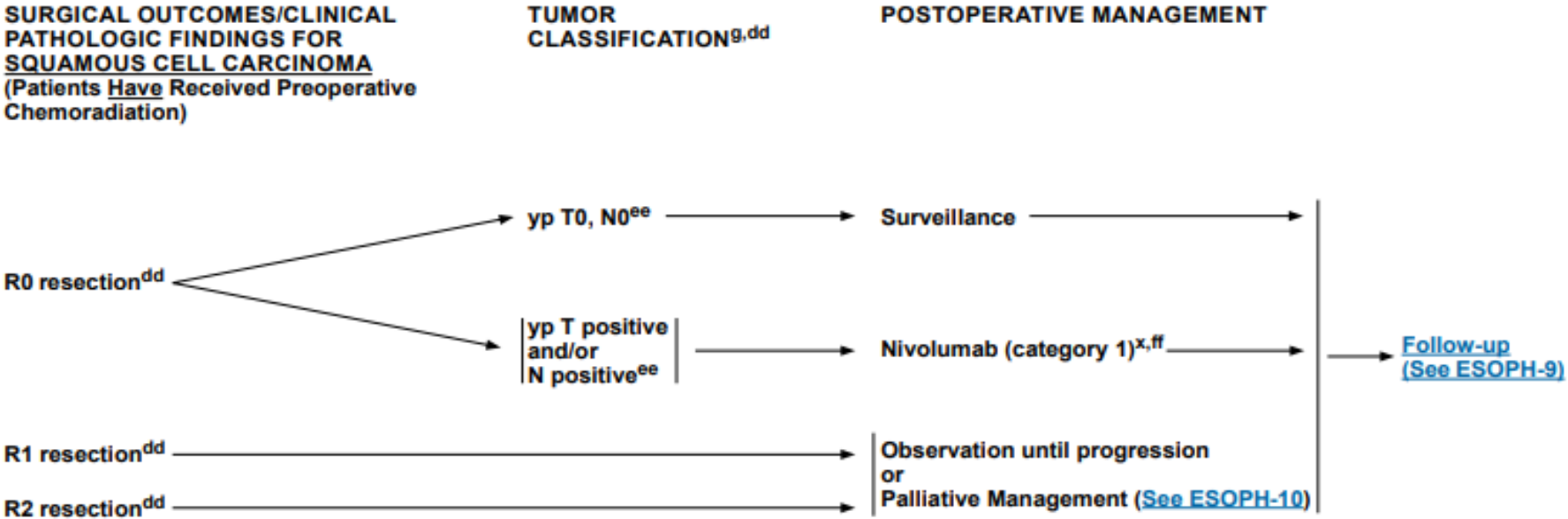
Microscopic Examination:

2-Sections reveal pulmonary parenchyma with alveolar spaces lined by septa that show mild interstitial fibrosis with no inflammation. The alveoli filled by scattered alveolar macrophages. Pleural surface shows non-reactive monolayer of mesothelial cells.
No malignancy was found.

Diagnosis/Impression:

2-Lung – Nodule – Biopsy:
-Pulmonary parenchyma with no specific pathologic changes.
-No malignancy.

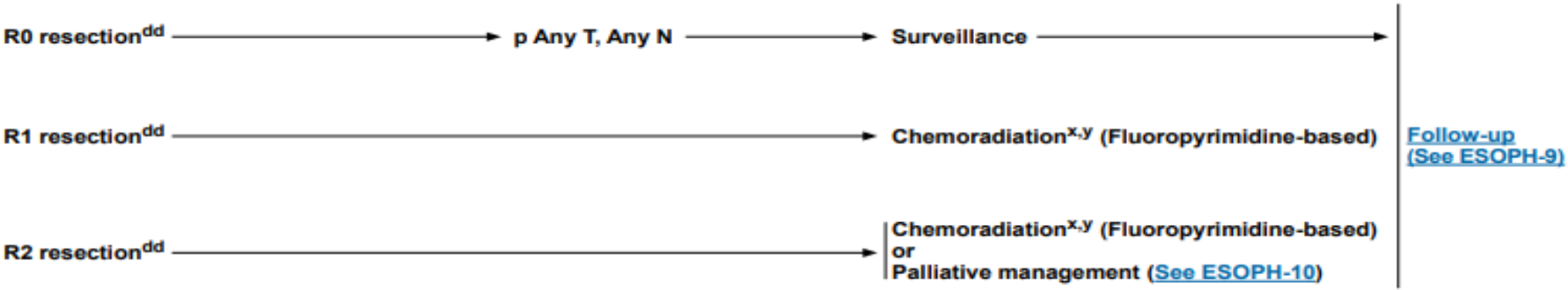
Post operative management ?



For patients with residual disease after preoperative CRT we suggest nivolumab for **up to one year** (**Grade 2B**).

For patients with **residual nodal disease** after neoadjuvant CRT who **lack access to nivolumab, treatment must be individualized**.

One approach is to administer adjuvant chemotherapy with **different agents than those given preoperatively** (FOLFOX if the initial CRT regimen included only paclitaxel and carboplatin).



[g] See Staging (ST-1) for tumor classification.
[x] See Principles of Systemic Therapy (ESOPH-F).

surveillance ?

Since the majority of recurrences (90%) occur within 3 years of surgery, routine surveillance for at least 36 months is recommended for patients with T2–T4b, any N tumors following trimodality therapy. However, since locoregional recurrence is relatively uncommon after trimodality therapy and most luminal recurrences can be detected by routine imaging studies, EGD surveillance should only be performed as clinically indicated.[308,436,437] Imaging studies (chest/abdominal CT with contrast, unless contraindicated) should be considered every 6 months for at least 2 years,

PRINCIPLES OF SURVEILLANCE

Stage II or III (T2–T4,N0–N+,T4b) treated with bimodality therapy (definitive chemoradiation)
Literature suggests that locoregional relapses are common after bimodality therapy.[3] Therefore, EGD is a valuable surveillance tool in these patients. Most relapses (95%) occur within 24 months. Thus, surveillance for at least 24 months is recommended for these patients.[3]

Stage II or III (T2–T4,N0–N+,T4b) treated with trimodality therapy
Literature suggests that local/regional relapses are uncommon; therefore, EGD surveillance is not recommended.[1,2,4] The risk and rate of relapse have been correlated with surgical pathology (yp) stage. For example, yp stage III patients have a much higher rate of relapse (and relapses occurring early during surveillance) than patients with yp stage 0 (relapses are not frequent in these patients). Literature also suggests that 90% of relapses occur within 36 months of surgery; therefore, surveillance for at least 36 months is recommended.

See Table 2 for specific surveillance recommendations.

Table 2

Tumor Classification	Type of Therapy Rendered	Surveillance Recommendations
T2–T4,N0–N+,T4b	Bimodality therapy (definitive chemoradiation)	• Imaging studies (CT chest/abdomen with contrast unless contraindicated) should be considered every 6 months for up to 2 years if the patient is likely to tolerate additional curative-intent therapy for recurrence. • EGD every 3–6 months for the first 2 years, every 6 months for the third year, then as clinically indicated. • The value of carcinoembryonic antigen (CEA) and other tumor markers is unknown.
T2–T4,N0–N+,T4b	Trimodality therapy	• Imaging studies (CT chest/abdomen with contrast unless contraindicated) should be considered every 6 months for up to 2 years if the patient is likely to tolerate additional curative-intent therapy for recurrence. Unscheduled evaluation is recommended if a patient becomes symptomatic. • The value of CEA and other tumor markers is unknown. • EGD surveillance as clinically indicated.

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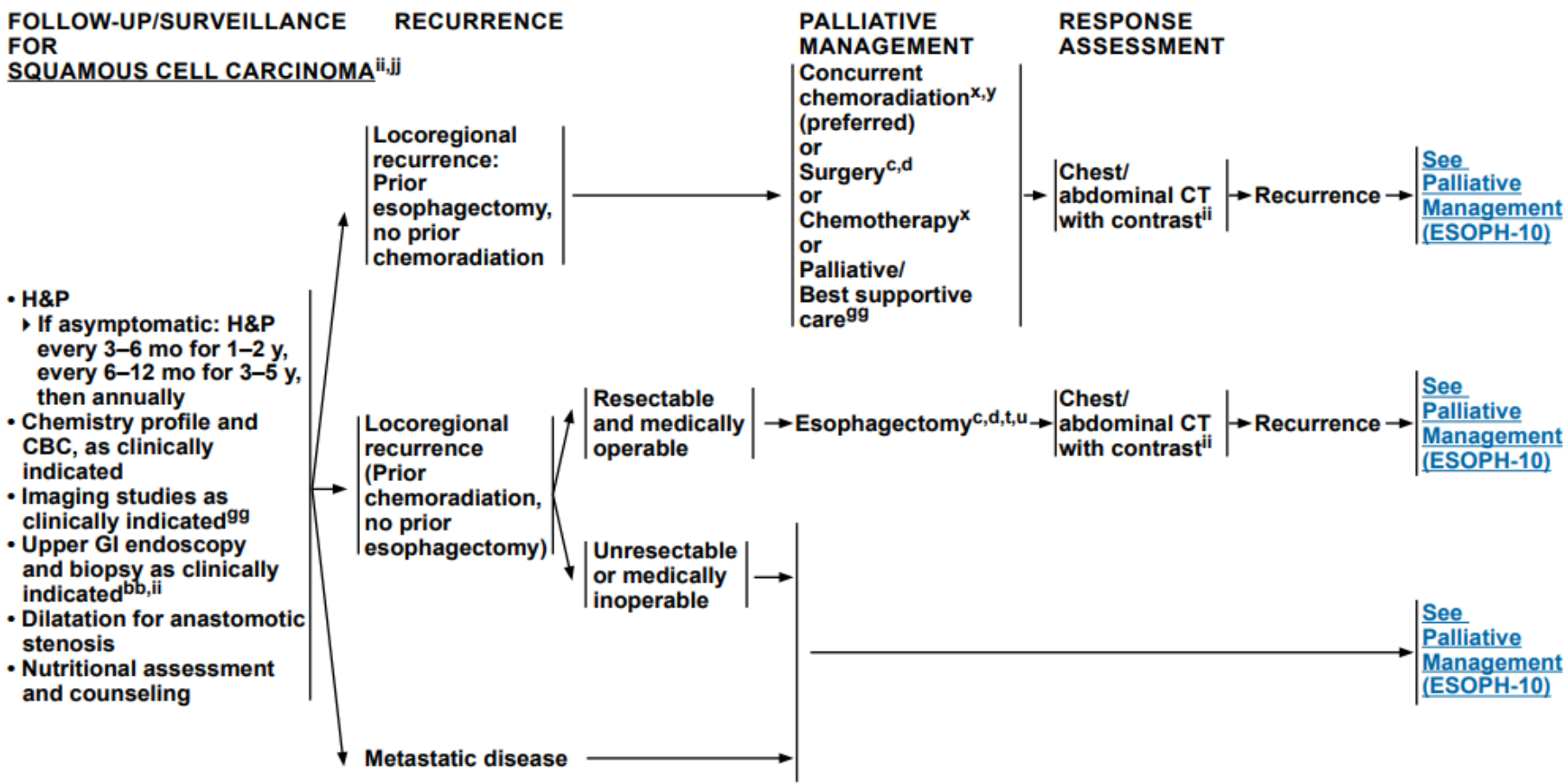


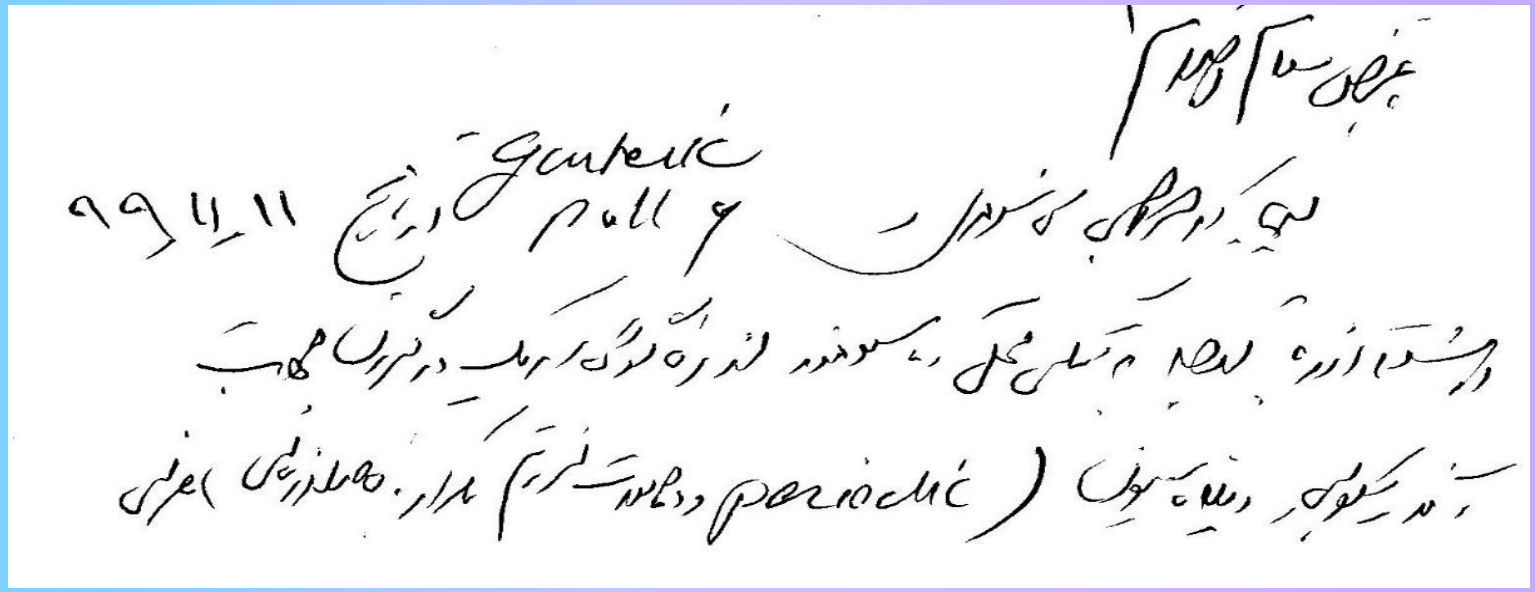
Post-treatment surveillance

There are **no randomized trials** to **guide** the **postoperative surveillance** strategy and **no data that demonstrate improvement in quality of life or longevity** from earlier detection of asymptomatic recurrences.

We perform history, physical examination, targeted blood work, and **CT of the chest and abdomen every four months for the first three years**.

We **do not carry out surveillance endoscopy** unless there was a preoperative history of Barrett's esophagus, a questionable margin at the time of surgery, or if the patient has a recalcitrant stricture that is worrisome for an occult local recurrence.

By contrast, consensus-based guidelines from the **ESMO** emphasize the lack of evidence that **regular follow-up after initial therapy has an impact on survival outcomes**, with the **possible exception** of patients who might be potential candidates for early "**salvage surgery" after failing definitive CRT**



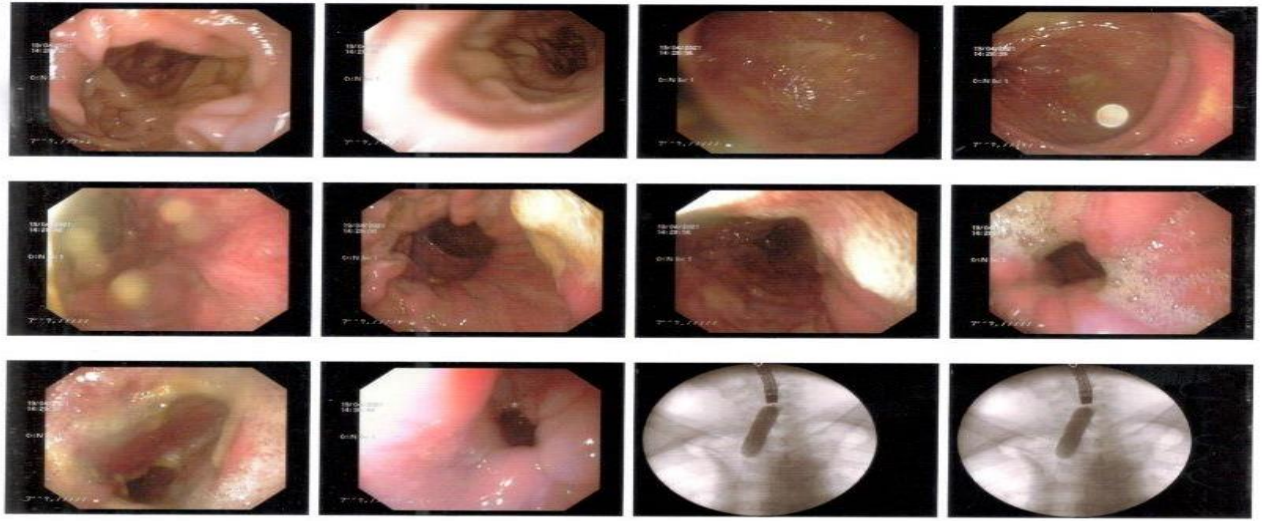
در بررسی باریم سوالو:

با بلع باریم مری حاجب گردید، تغییرات مربوط به جراحی (بالاکشیدن معده) دیده می‌شود.

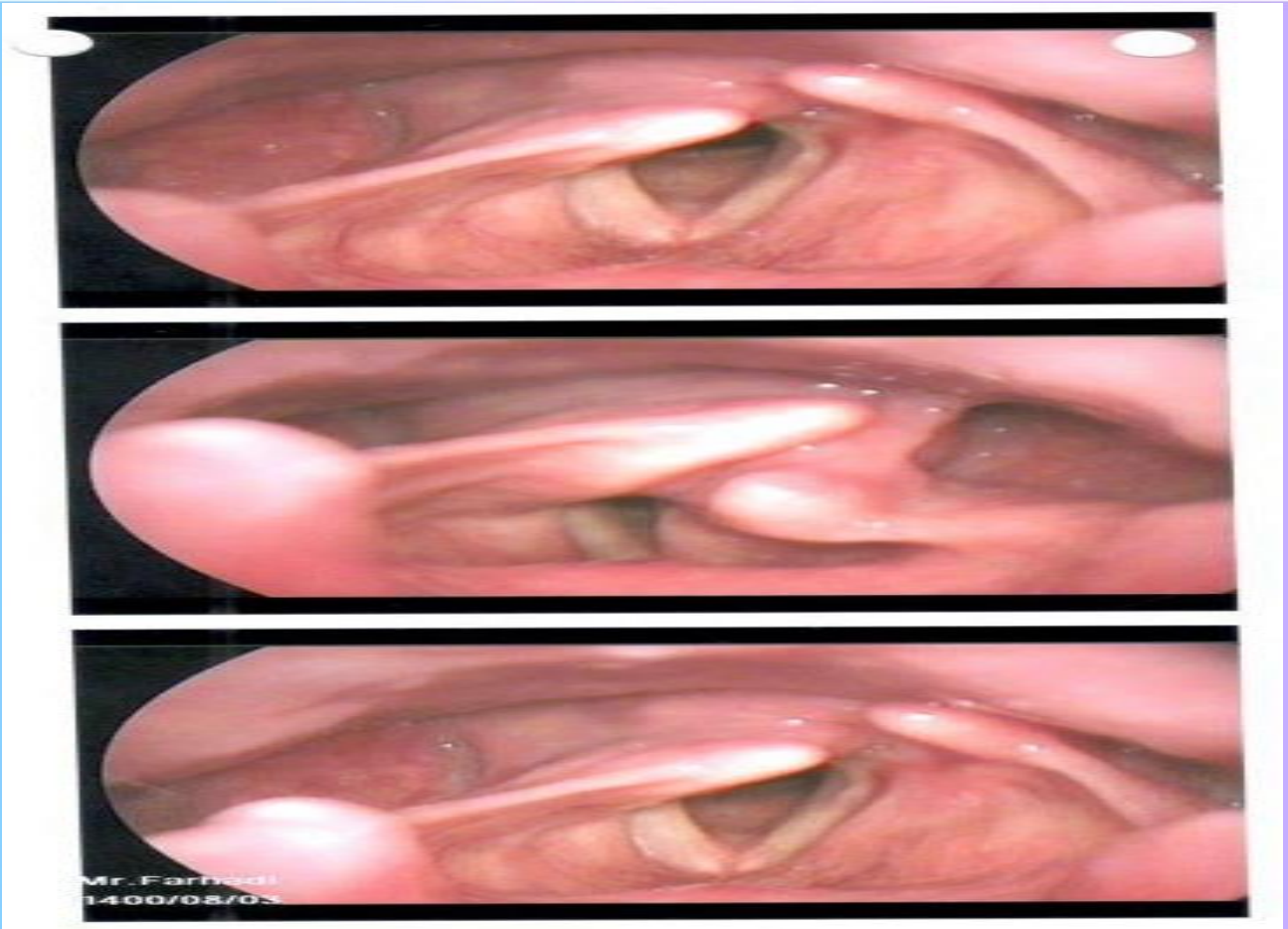
کاهش دیامتر در محل آناستوموز مری به معده دیده می‌شود.

Report Description: H-Pylori: None

- **Chief Complaint**: Dysphagia
- **Premedication**: Propofol
- **Esophagus**: At anastomosis site partial narrowing was seen, passing was done, guidewire inserted and a dilation with 18MM size balloon under fluroscopic guide was performed.
- **Stomach**: Cardia, fundus and body were normal, mucosal redness at antrum was seen.
- **Duodenum**: D1-D2 were normal.



6 months after surgery the patient came to me because of the hoarsness


Mr.Farhadi
1400/08/0

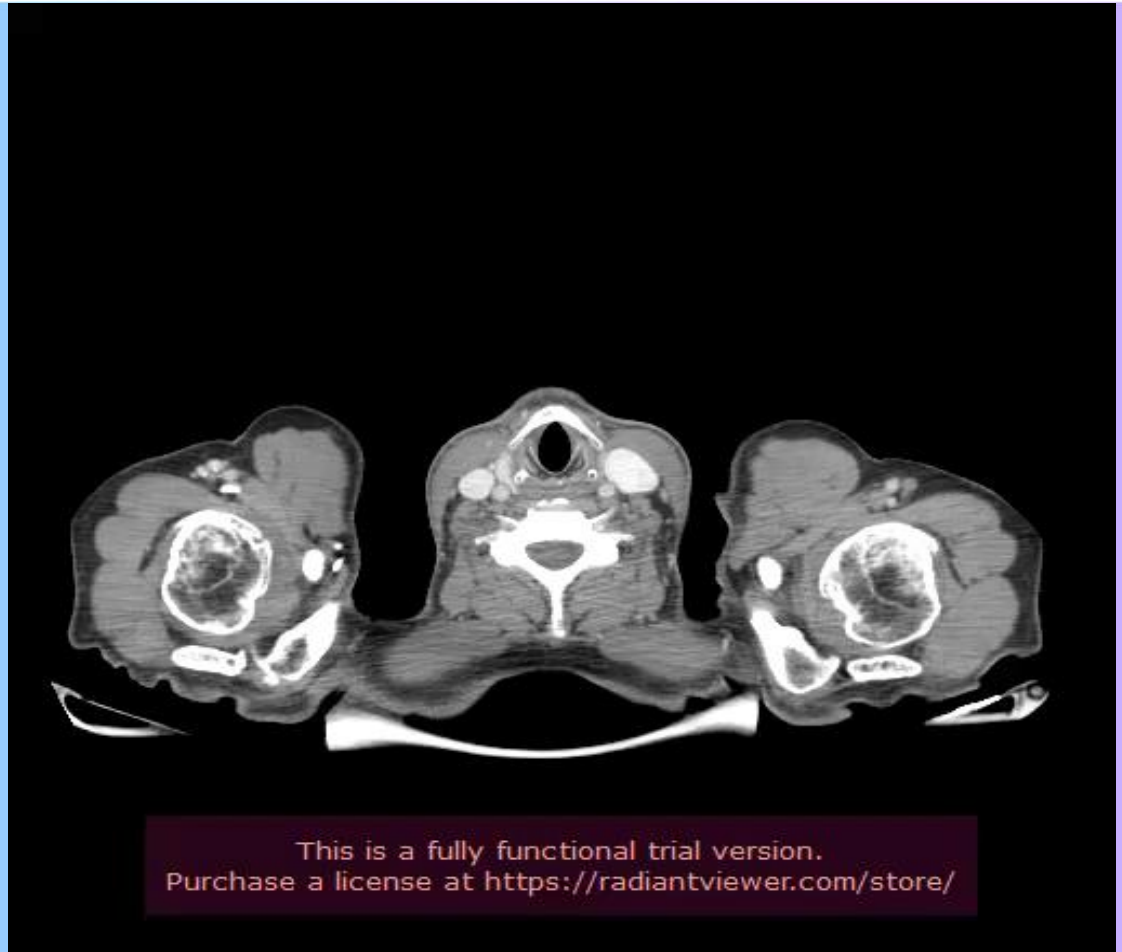
با سلام و احترام

بدینوسیله عکس و فیلم ثبت شده از حنجره بیمار در وضعیت phonation و respiration جهت معاینه و درمان به حضور ارسال می گردد.

موبیلیتی در Rtvc مشاهده نشد .

The most common sites of **distant metastases** in patients with esophageal cancer are the **liver, lungs, bones, and adrenal glands .**

Adenocarcinomas most frequently metastasize to intraabdominal sites (liver, peritoneum), while **metastases from SCCs are typically intrathoracic.**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همکارگرامی جناب آقای دکتر: ابوالقاسم- الهیاری

Spiral CT Scan of Thorax With and Without Contrast:

Case : PMH شناخته شده کانسر مری

تیروئید سایز و دانسیته نرمال دارد.

شواهد ازوفاژکتومی قبلی، gastric pull up و آناستوموز ازوفاگوگاستریک در ورودی توراکس مشهود است.

در سمت راست محل آناستوموز، مجاور دیواره تراشه، توده نسج نرمی به ابعاد ۱۹*۲۳ م.م رویت می شود که با شریان innominate و پروگزیمال شریان های کاروتید مشترک و ساب کلاوین چپ مجاورت نزدیک دارد و با توجه به محل و شکل ضایعه، قویا به نفع عود موضعی مجاور محل آناستوموز است.

ضایعه مذکور به دیواره مری، تراشه و همچنین قسمت فوقانی pull up چسبندگی دارد و پس از تزریق کنتراست انهنسمنت نشان می دهد (افزایش دانسیته از حدود 40HU به حدود 70HU).

ضایعه مذکور با توجه به مجاورت های عروقی، unresectable به نظر می رسد، جهت اثبات تشخیص، بیوپسی پرکوتانه تحت هدایت سونوگرافی امکان پذیر به نظر می رسد.

ضخامت دیواره pull up در نواحی مختلف طبیعی به نظر می رسد.

سایز و شکل حفرات قلبی نرمال است.

آدنوپاتی آگزیلاری در دو سمت مشهود نیست.

آدنوپاتی مدیاستینال رویت نمی شود.

کلسیفیکاسیون شرایین کرونری مشهود است.

عروق بزرگ مدیاستن نمای نرمال دارند.

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در سایر نواحی در فیلد هر دو ریه ضایعه پاتولوژیک مشاهده نگردید.

ضایعه اوسیفیه در قدام اسکاپولای چپ به نفع ossified hematoma رویت می شود که significant به نظر نمی رسد.

در بررسی نسج نرم و استخوانهای قفسه صدری ضایعه پاتولوژیک مشاهده نمی شود.

Abdominopelvic Spiral CT Scan with and without IV/Oral Contrast:

کبد، طحال، پانکراس، هر دو کلیه و آدرنال دارای ابعاد و دانسیته نسجی نرمال است.
شواهدی به نفع ضایعه فضاگیر در احشاء فوق رویت نگردید.
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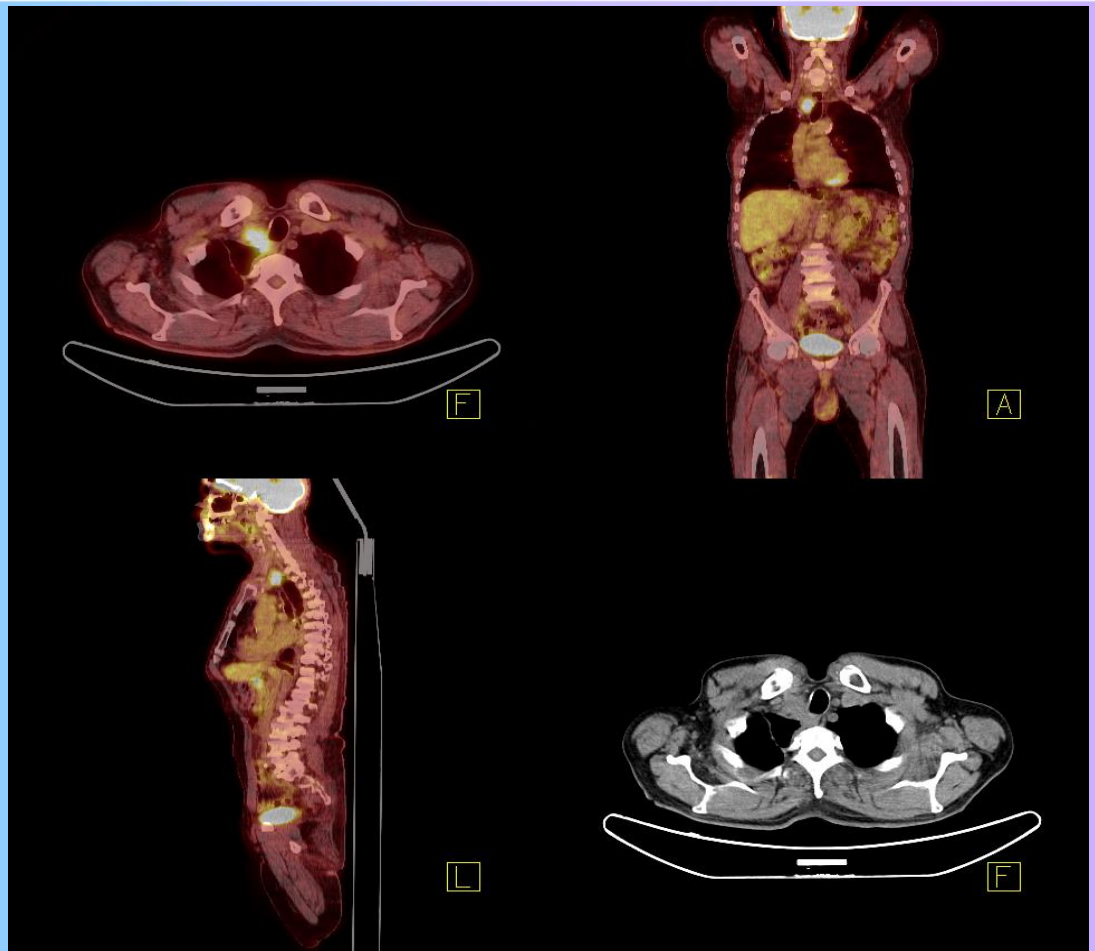
آدنوپاتی سلیاک و مزانتریک واضحی مشهود نیست.
شواهدی به نفع لنفادنوپاتی پاراآئورت رویت نگردید.
سنگی به دیامتر ۳ م.م در کالیس تحتانی کلیه چپ و سنگی به دیامتر ۳/۵ م.م در کالیس تحتانی کلیه راست رویت می شود.
تصویر اتساع در سیستم ادراری دو طرف مشاهده نگردید.
مثانه دارای حجم و ضخامت جداری نرمال است.
پروستات قدری حجیم، دانسیته آن قدری هتروژن است.
دیورتیکول های متعدد در دیواره کولون، خصوصا سیگموئید و کولون نزولی مشهود است که در داخل برخی از آن ها کنتراست بجامانده از imaging قبلی رویت می شود.
تصویری به نفع دیورتیکولیت مشهود نیست.
در بررسی معده و روده باریک نکته پاتولوژیک رویت نگردید.
در نسج نرم سطحی، در ناحیه باتوک چپ، ضایعه هیپودانس به ابعاد ۲۳*۴۳ م.م با دانسیته high fluid رویت می شود که می تواند به علت تجمع مایع در محل injection قبلی باشد.
(بدون تغییر significant نسبت به سی تی اسکن قبلی)
مایع آزاد درون حفره شکم و لگن مشاهده نمی شود.
ضایعه لیتیک یا بلاستیک استخوانی مشهود نیست.

What is your openion about continuing the treatment of this patient ?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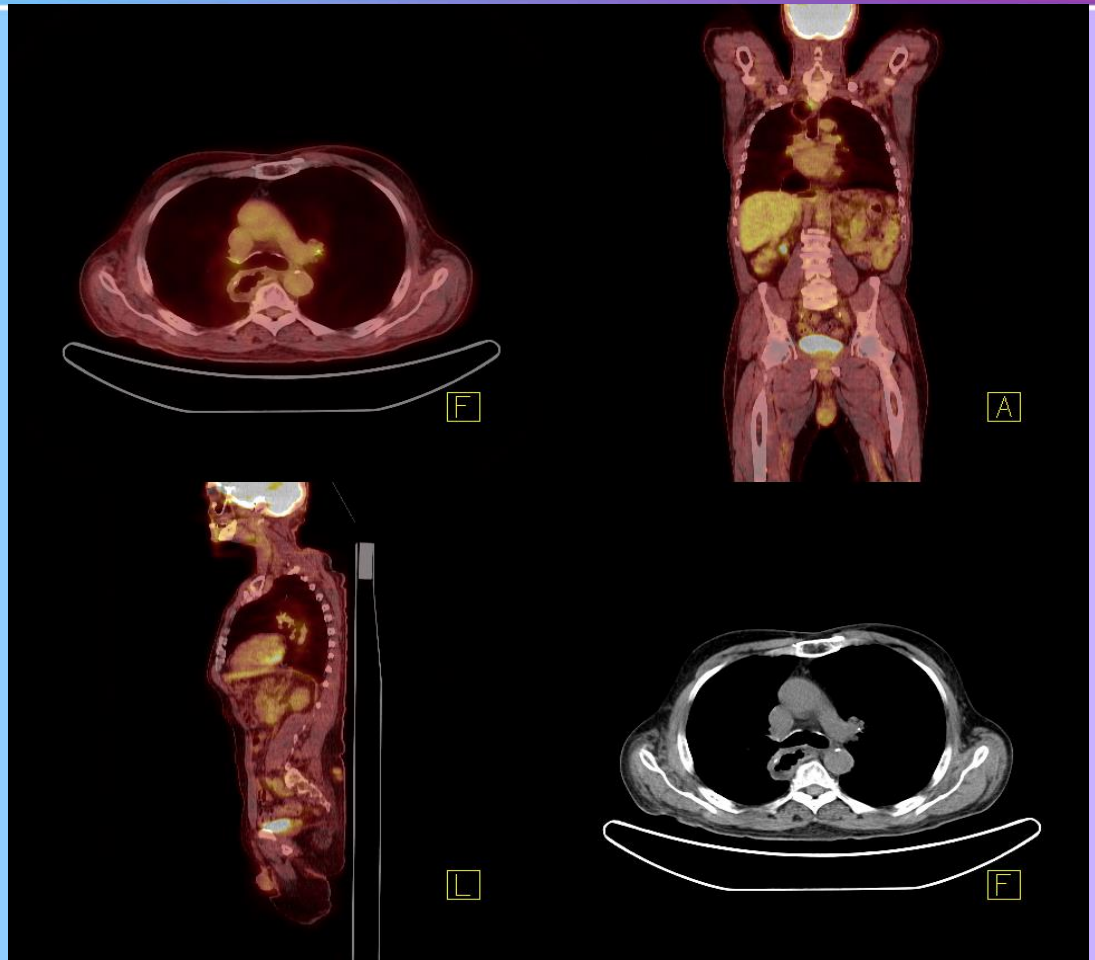
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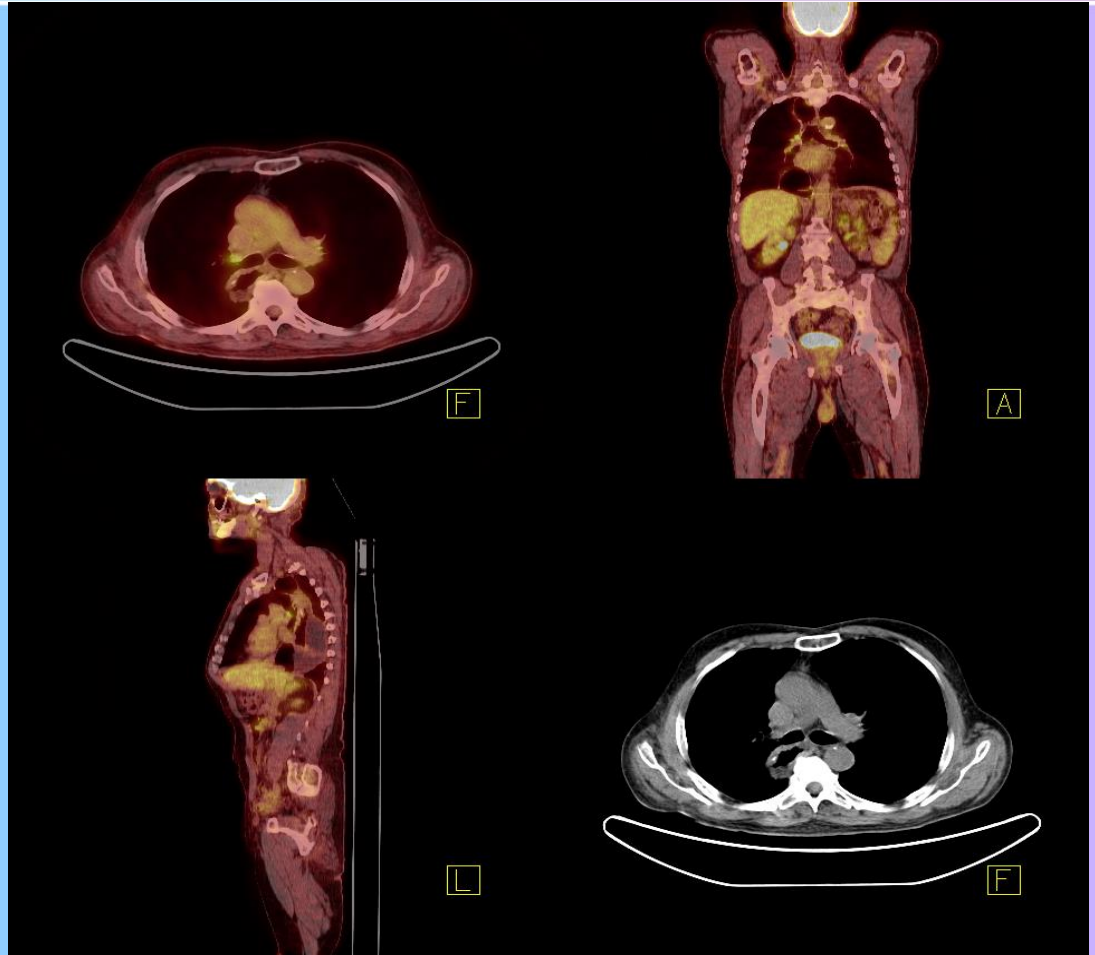
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EXAMINATION: ^{18}F-FDG PET/CT scan, Skull base to Mid-Thigh

CLINICAL HISTORY: A 65 y/o man with history of esophageal cancer , underwent esophagectomy and gastric pull-up; referred for residual disease evaluation

Status: residual disease evaluation

PROCEDURE:
7.52 mCi (18F)-fluorodeoxyglucose was administered intravenously via the dorsal vein of the left hand. To allow for distribution and uptake of radiotracer, the patient was allowed to rest quietly for 50 minutes in a shielded room. Imaging was performed on an integrated 6-slice PET/CT scanner, with scanning from the skull base to the mid-thigh. Serum blood glucose at the time of the injection was measured at 121 mg/dL. CT scanning was performed without oral or intravenous contrast material.

FINDINGS: Mean SUV of the right hepatic lobe is 3.

Head and Neck:
Paranasal sinuses are within normal limits.
There is no nodal hypermetabolism in the neck.
The visualized portions of the brain are normal in appearance on CT.
Major salivary glands are normal.
Thyroid is of normal size and texture.

Chest:
There is a zone of hypermetabolism in the region of previous esophago-gastric anastomosis, in the right side of thoracic inlet.(SUVmax=9.96, 2.5*2 cm)
There is a hypermetabolic lymph node in the subcarinal region (SUVmax=5.14).
Bilateral hypermetabolism is noted in hilar regions (SUV max up to 4.3)
There is no hypermetabolism in the axillary region.
There are no hypermetabolic pulmonary nodules.
Major bronchi and great vessels are normal.

Abdomen and Pelvis:
There is no nodal hypermetabolism in retroperitoneal or pelvic chains.
The spleen is normal in size and FDG avidity.
Liver is of normal size and texture and no hypermetabolism is noted.
Kidneys are normal in size axis and cortical thickness.
Adrenal glands can be seen in normal manner on both sides.

Musculoskeletal: Marrow uptake is within normal range.
There is a well defined cyst-like lesion in the left subscapular region, medial to the left acromio-clavicular joint, without significant hypermetabolism, representing a benign lesion.
There is well defined soft tissue mass in the left gluteal region, with mean HU of 30 (SUVmax= 3.67).

IMPRESSION:

1-Hypermetabolic tumoral recurrence in the region of previous esophago-gastric anastomosis, located in the right side of thoracic inlet.
2-Hypermetabolic metastatic subcarinal lymph node.
3-Mild bilateral hilar hypermetabolism is most likely due to inflammatory processes.

- The well defined soft tissue mass in the medial part of left gluteal region, with mild hypermetabolism, warrants further evaluation and tissue sampling.

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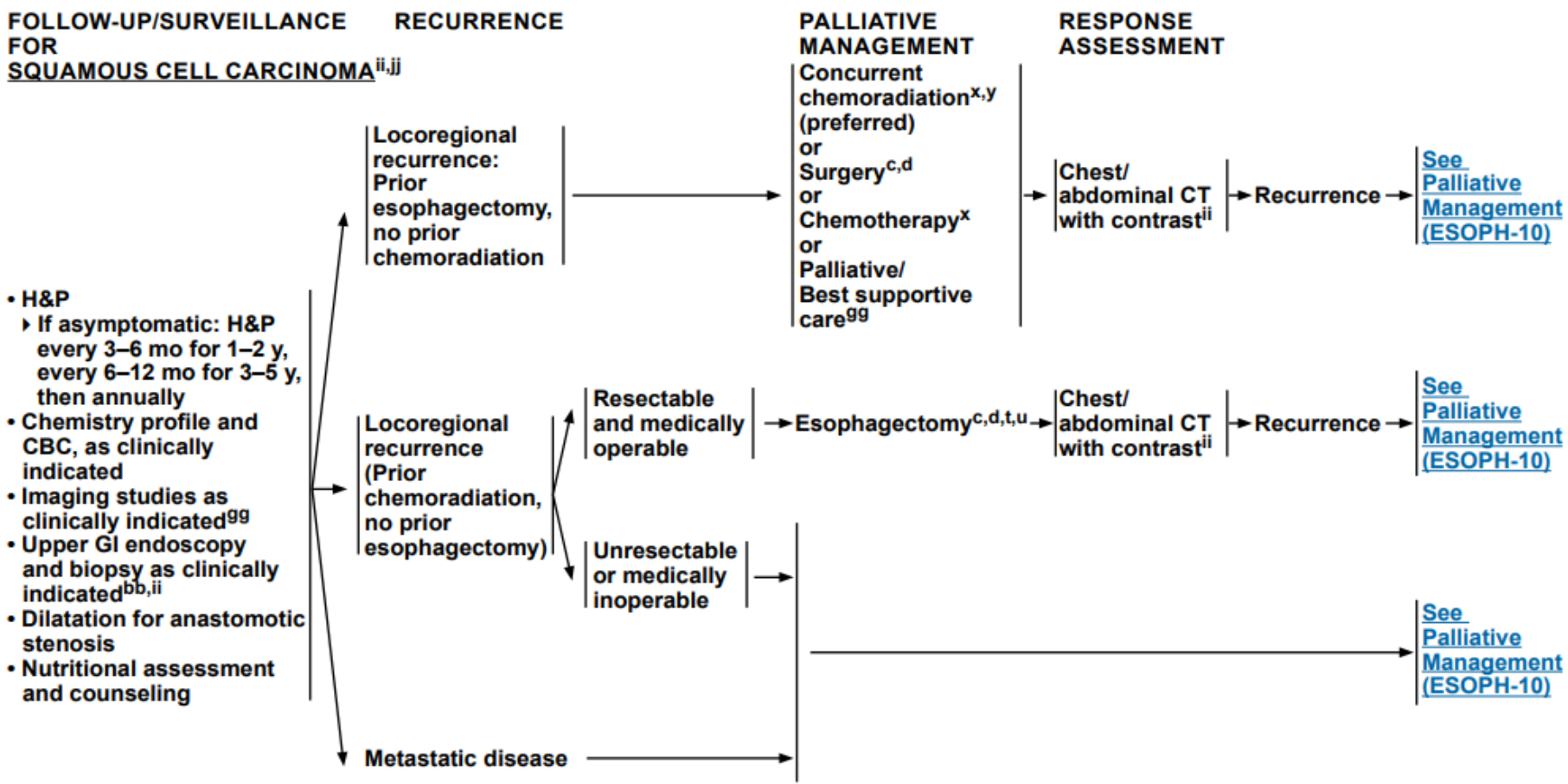

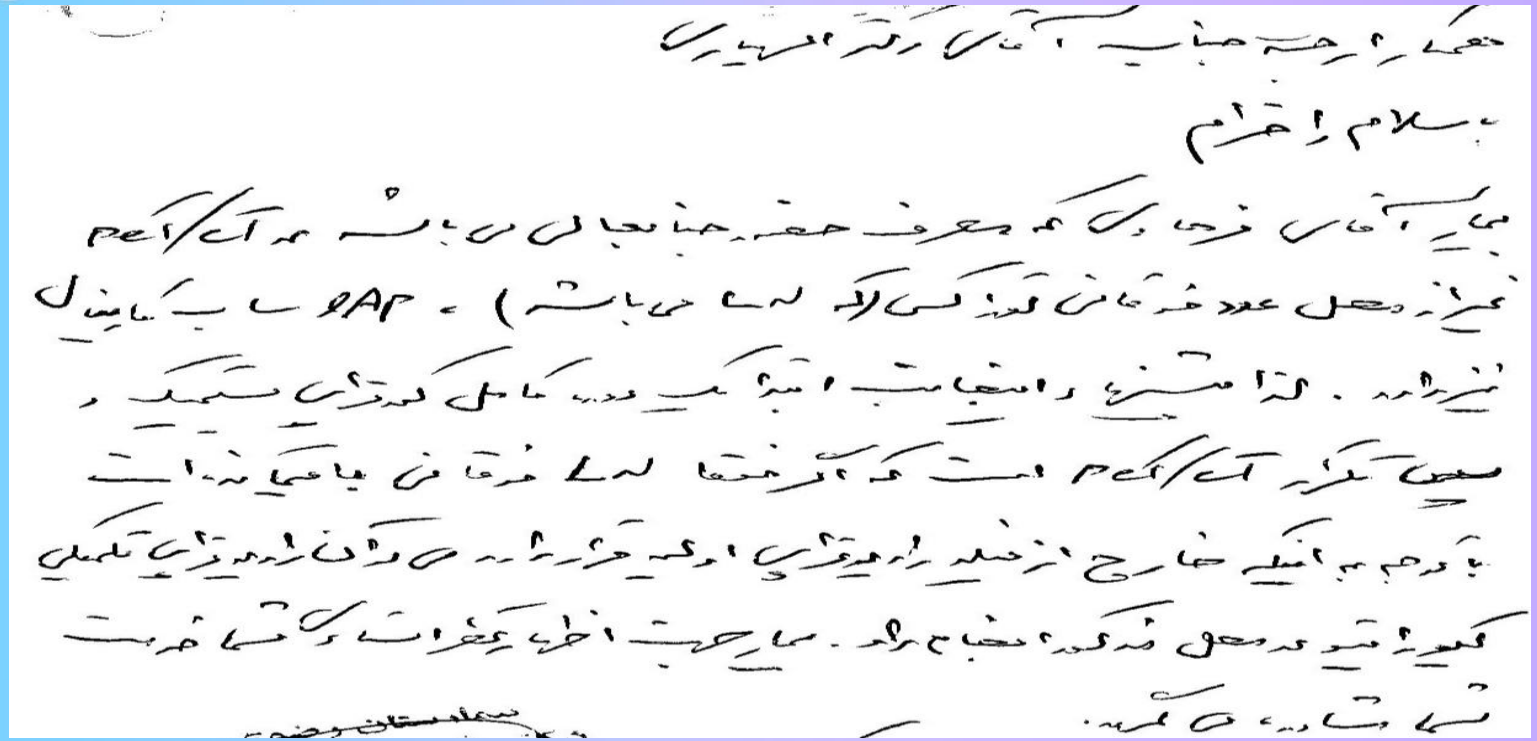

Nivolumab

Nivolumab is a monoclonal PD-1 antibody that was approved by the FDA in June 2020 for the treatment of patients with unresectable advanced, recurrent or metastatic esophageal SCC after prior fluoropyrimidine- and platinum-based chemotherapy.[409] This approval was based on results from the international phase III ATTRACTION-3 trial, which compared

In 2019, the FDA approved pembrolizumab for the second-line treatment of esophageal SCC with PD-L1 expression levels by CPS of ≥10 based on the results of the KEYNOTE-180 and KEYNOTE-181 trials.[167] In the

For patients whose tumors are **dMMR or overexpress PD-L1** and who did not receive first-line immune checkpoint inhibitor immunotherapy, there is disagreement about the optimal timing of immune checkpoint inhibitors.

In the United States, pembrolizumab is approved for third-line treatment in patients with PD-L1-expressing gastric or esophagogastric junction (EGJ) adenocarcinoma (**combined positive score [CPS] 1 or higher**) after **failure of two separate** chemotherapy regimens.

It is also approved for recurrent locally advanced or metastatic SCC of the esophagus that expresses high levels of **PD-L1 (CPS ≥10)** and has progressed **after one or more** prior lines of systemic therapy.

Treatment selection

•**Squamous cell cancer (SCC)** – Regardless of PD-L1 overexpression, we suggest -chemotherapy plus immunotherapy rather than chemotherapy alone (**Grade 2B**).

Although the chemotherapy backbone in the CheckMate and KEYNOTE studies was cisplatin plus fluorouracil(FU), many clinicians, including some of the authors and editors associated with this topic review, prefer pembrolizumab or nivolumab in combination with an oxaliplatin-based regimen such as oxaliplatin plus leucovorin with bolus plus short-term FU (FOLFOX),

Leucovorin Shortage

Leucovorin is indicated with certain fluorouracil-based regimens. However, there is currently a shortage of leucovorin in the United States.[449] There are no specific data to guide management under these circumstances, and all proposed strategies are empiric. One is the use of levoleucovorin, which is commonly used in Europe. A levoleucovorin dose of 200 mg/m^2 is equivalent to 400 mg/m^2 of standard leucovorin. Another option is to use lower doses of leucovorin in all patients, since lower doses are likely to be as efficacious as higher doses based on several studies in patients with colorectal cancer.[450-452] However, the panel recommends use of these regimens without leucovorin in situations where leucovorin is not available.

THANKS FOR YOUR ATTENTION

Nivolumab – Benefit for nivolumab was shown in the CheckMate 577 trial, in which 794 patients who had received neoadjuvant CRT for esophageal or EGJ cancer (70 percent AC) and had residual pathologic disease at the time of surgery were randomly assigned to nivolumab (240 mg) or placebo every 2 weeks for 16 weeks followed by nivolumab 480 mg or placebo every 4 weeks; the maximum treatment duration was one year [150]. Enrollment was irrespective of programmed death receptor-1 ligand 1 (PD-L1) overexpression. Tumor site was esophagus in 60 percent and EGJ in 40 percent; histology was AC in 71 percent and SCC in 29 percent. At a median follow-up of 24.4 months, median disease-free survival, the primary endpoint, was twice as long with nivolumab (22.4 versus 11 months, HR for disease progression or death was 0.69, 95% CI 0.56-0.86), and the benefits were seen across all patient subgroups (histology, location, initial and post-treatment disease stage, PD-L1 overexpression or not). Overall survival data were not mature. Although treatment-related adverse effects were frequent, most were grade 1 or 2 and only 9 percent of patients discontinued adjuvant nivolumab because of adverse effects. The benefits were gained without any significant decline in patient-reported health-related quality of life over the year of nivolumab treatment.

Post-treatment cancer surveillance
Patterns of failure
The majority of recurrences develop **within one year**, and **recurrences tend to develop earlier in patients treated with neoadjuvant therapy as compared with surgery alone**.

This was illustrated in a series of **590 patients** who underwent esophagectomy for AC .The **peak interval for recurrence after esophagectomy alone** was **six to nine months**, and **more than 90 percent** of the disease recurrences occurred by **three years**.

By contrast, among patients treated with **neoadjuvant CRT** (trimodality therapy), the peak time frame for recurrence was the **first three months**, and **>90 percent** of recurrences were evident by **21 months**.
The pattern of recurrence was distant, locoregional, or both in 60, 30, and 10 percent of patients, respectively, and did not differ in patients treated with surgery alone.
Of note, these results may be impacted by selection bias, as patients with more advanced tumors likely had an increased likelihood of receiving neoadjuvant therapy. A similar distribution of recurrences (distant, locoregional, or both in 55, 28, and 17 percent) have been reported by others following trimodality therapy

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On the other hand, **isolated local recurrences** are more frequent after definitive CRT, and salvage surgery may benefit a greater number of these patients.

This was shown in a retrospective analysis of 276 patients with esophageal cancer (78 percent AC) who were treated with definitive CRT at MD Anderson Cancer Center over a nine-year period (2002 to 2011) .
The site of first failure was local only in 64 (23 percent); and 23 (36 percent, 8 percent of the entire cohort) of these were amenable to salvage surgery. At a median follow-up of 54 months for the entire cohort, the estimated three- and five-year overall survival rates for those undergoing salvage surgery were 61 and 45 percent, respectively. Ninety-one percent of the local recurrences developed within two years, suggesting that vigilant surveillance is more important in this time frame.

Leucovorin Shortage

Leucovorin is indicated with certain fluorouracil-based regimens. However, there is currently a shortage of leucovorin in the United States.[449] There are no specific data to guide management under these circumstances, and all proposed strategies are empiric. One is the use of levoleucovorin, which is commonly used in Europe. A levoleucovorin dose of 200 mg/m^2 is equivalent to 400 mg/m^2 of standard leucovorin. Another option is to use lower doses of leucovorin in all patients, since lower doses are likely to be as efficacious as higher doses based on several studies in patients with colorectal cancer.[450-452] However, the panel recommends use of these regimens without leucovorin in situations where leucovorin is not available.

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