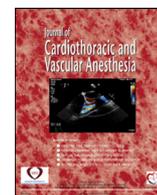Contents lists available at ScienceDirect

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Editorial

Optimal Surveillance Regimen to Identify Cancer Recurrence after Esophagectomy: Surveillance Imaging or History and Physical Examination? An Anesthesiologist's Point of View

ESOPHAGEAL CANCER is the seventh leading cause of cancer-related mortality for men in the United States, with a death rate of 3.9 per 100,000 for men and women, claiming >18,000 lives annually. Esophagectomy is the mainstay in curative treatment for local and locoregional disease. It is often combined with neoadjuvant or perioperative chemotherapy with or without radiotherapy.[1] Trimodality therapy with neoadjuvant chemoradiation followed by surgery has become the standard of care for many patients.[2]

Surgical treatment of esophageal cancer can be done through an open transhiatal, transthoracic (2-stage or Ivor-Lewis) or 3-stage (McKeon) procedure.[3] In addition, with the advances in minimally invasive esophagectomy,[4] it has shown improvement in postoperative outcomes by reducing postoperative pulmonary complications.[5,6] Other interventions in the early stage of the disease include endoscopic mucosal resection and radiofrequency ablation.[7] Interestingly, the effects of regional anesthesia and general anesthesia compared with general anesthesia alone and outcomes after minimally invasive Ivor Lewis esophagectomy have not shown significant differences in reduction in postoperative pulmonary and cardiovascular complications.[8] Although there are multiple interventions to treat this cancer, the surgical approach is dictated by the location of the cancer or histologic type. However, the type of esophageal resection performed, to some degree, is one of personal preference, and different surgical approaches are used among surgeons.[9]

Despite these advances, esophageal cancer frequently reoccurs with local-regional or distant disease, highlighting the importance of long-term surveillance.[10-12] Esophageal cancer recurrence is common after esophagectomy, developing in approximately 40% of patients within 1-to-3 years after surgical treatment. The recurrence of this cancer often is associated with poor prognosis; according to Chang et al.,[10] the recurrence of esophageal cancer is defined as (1) a local recurrence if recurrence occurred at or near the anastomosis, is intraluminal, or is within the stomach; (2) regional recurrence (ie, nodal recurrence in the neck, mediastinum, or abdomen); or (3) distant recurrence if the recurrence occurs outside the esophagus or periesophageal or perigastric lymph nodes.

Two modality regimens are used as follow-up surveillance after esophagectomy, including history and physical examination (HPE), which in general may show suspicious symptoms such as weight loss, dysphagia, shortness of breath, and neurologic symptoms, or findings during physical examination such as cervical or supraclavicular adenopathy.[13] The National Comprehensive Cancer Network guidelines recommend that asymptomatic patients be evaluated by HPE every 3-to-6 months for up to 1-to-2 years.[14] The other regimen used includes surveillance imaging (SI) with different techniques and invasive diagnostic procedures such as contrast computed tomography (CT) of chest and abdomen, positron emission tomography (PET) scan, magnetic resonance imaging, and endoscopy and/or endoscopic ultrasonography.[1] The efficacy of each surveillance modality has not been assessed systematically in large-cohort studies.

Monitoring and surveillance after esophagectomy represent a challenge for the thoracic surgeon. Currently there is no consensus regarding the frequency, duration, or method of follow-up SI for patients after esophagectomy. An interesting study by Chang et al.[10] included a retrospective review of 225 patients with esophageal cancer who underwent esophagectomy. Their retrospective review was aimed to determine if SI would identify patients with cancer recurrence earlier and improve long-term survival. In their study, patients were categorized as those with recurrence detected through SI or those with recurrence detected with HPE alone. The hypothesis from Chang et al.[10] is important for addressing the recurrence after esophagectomy because this is often associated with a poor prognosis. The optimal follow-up surveillance regimen (HPE vs SI) should be directed to detect new lesions (nodes or

cancer) early after esophagectomy and to have an impact on outcomes and survival.

In the Chang et al. study,[10] it was reported that 88 patients had cancer recurrences (39.1%). In addition, when the subjects were divided into 2 groups according to their surveillance method used, in 41 of 101 patients (40.6%) recurrences were detected by SI, in comparison to 47 recurrences of 124 (37.9%) by HPE; overall, the rate of recurrence of esophageal cancer was quite similar in both groups. Interestingly, additional treatment after diagnosis showed similar results: 36 of 41 patients in the SI group (87.8%) and 34 of 47 patients in the HPE group (72.3%) had recurrence; this was not significantly different. The only remarkable difference in their study was the survival rate. The median overall survival was significantly longer in the SI group, at a median of 23 months, compared with those in the HPE group, who had a median survival of 16 months. Although SI did not improve the detection of recurrence, the data supported that the survival rate improved by 7 months (median value) in the SI group, and these findings were clinically significant.

Previous studies by Lou et al.[12] and Abate et al.[15] have shown different alternatives to follow-up with surveillance regimens. The Lou et al. study[12] was a retrospective cohort study involving 1,147 patients who had esophagectomy. Recurrence of cancer occurred in 435 patients (38%); among those, 217 patients had recurrence determined by HPE and CT scan of the chest and abdomen. In addition, upper endoscopy detected recurrence in only 6 patients. Overall, 50% of recurrences were detected because of the HPE + CT scan of the chest and abdomen; also, they reported that surveillance with upper endoscopy had very limited value. In Abate et al.[15] a retrospective study was conducted including 590 patients who had esophagectomy. Their objective was to determine the optimal follow-up strategy after esophagectomy, specifically evaluating the timing of the recurrence and the method that first detected the recurrence. Their results showed that recurrence of the cancer occurred in 233 patients (40%). However, the methods to detect recurrence first suspected by symptoms and/or physical examination were variable, and some were chosen by surgeon preference. Recurrence by HPE was detected only in 29 patients (17%); in comparison, recurrence by CT scan was detected in 105 patients (60%), PET scan in 32 patients (18%), and elevated carcinoembryonic antigen in 8 patients (5%). Their conclusion from the study was that early follow-up after esophagectomy is appropriate, and the best test to identify both systemic and locoregional recurrence is a contrast-enhanced CT scan of the chest and abdomen. The retrospective studies by Lou et al.[12] and Abate et al.,[15] although valuable, lacked specific guidelines and recommendations to be used as a surveillance regimen to detect early recurrences after esophagectomy.

To consider SI as a viable alternative as a follow-up after esophagectomy, the clinical tools available to detect new lesions must be safe, efficient, and reliable surveillance protocols. Currently, among the multiple imaging studies, such as PET/CT, CT with intravenous contrast of the chest and abdomen, magnetic resonance imaging, or upper endoscopy,

none of these modalities has been found to be reliable to independently predict pathologic complete response. Among the limitations and personal preferences by the treating physician when using SI (ie, CT of the chest or abdomen radiology studies), the cost and continuous radiation exposure to the patient must be taken into consideration.[14] Previous studies of HPE versus SI alone have shown conflicting results. Although PET appears to be superior to contrast CT for detection of cancer recurrence, integrated PET/CT seems to be a more accurate method for detection of recurrent esophageal cancer. The advantage of PET/CT is seeing the whole body and the ability to detect small lymph node metastases up to 0.9 mm in diameter, as well as recurrent tumors outside the esophagus.[10]

Based upon current studies, the optimal surveillance regimen remains undefined; also, there is limited information published regarding follow-up surveillance protocols for esophageal cancer after esophagectomy. Differences in the detection of recurrences may be attributed to several factors including the retrospective nature of the studies, the differences in follow-up protocols, and the lack of definitions of symptomatic recurrence, in addition to a lack of information in how long the SI will be used, as it is known that after 6 years only 4% of patients are at risk of developing recurrence.

Randomized controlled trials are needed to evaluate survival benefits of surveillance regimens. Routine postoperative surveillance of patients can help clinicians detect recurrence and initiate intervention early to improve outcomes. Currently, there is no controlled trial that has investigated the impact of intensive routine surveillance versus symptom-triggered surveillance.[16,17] The vast majority of studies on the topic are observational in design, have small sample sizes, and are underpowered, such as the Chang et al. study.[10]

Despite significant progress in the diagnosis and staging of esophageal cancer after esophagectomy, there is no single modality that reliably can detect local recurrence or residual disease with clinical acceptable degree of accuracy; therefore, multiple imaging methods need to be used to detect recurrences.[1,17] It is possible that a prospective, randomized study of subjects after esophagectomy in order to monitor surveillance could include 3 groups of patients: (1) an HPE group; (2) an SI group; and (3) an HPE + SI group, along with the timing, intervals, and duration of this surveillance in order to determine the best surveillance regimen and the survival in this challenging disease after surgery. In addition, including multiple cancer centers would be ideal. Table 1 displays studies that compare outcomes with different regimens and follow-up surveillance after esophagectomy.

The Chang et al. study[10] brought a new perspective on a follow-up surveillance regimen after esophagectomy by using HPE and/or SI as a surveillance modality to improve outcomes. Without question, prospective studies are needed to assess the effects of early diagnosis on survival treatment outcomes defined by the best regimen and quality of life after esophagectomy, considering the different alternatives that are available at the current time,[17] including surgery versus active surveillance in esophageal cancer patients.[18]

Table 1
Studies of Different Regimens to Diagnose Recurrence After Esophagectomy

Authors	Surgery	Study Design	Outcomes	Key Results	Limitations
Abate et al.[15]	Esophagectomy −Transthoracic −Transhiatal −Minimally invasive esophagectomy	Retrospective cohort study	590 patients had esophagectomy Cancer recurrence occurred in 233 (40%) Recommendation: frequent, early follow-up is appropriate	Recurrence first suspected by HPE in 29 patients (17%) CT scan in 105 (60%) was the best method to detect recurrences PET in 32 (18%) Recurrence was detected at a median 11 mo (range, 3-72)	Retrospective review Follow-up surveillance by the surgeons was variable: HPE, CT, CEA levels, PET scan yearly recommended by some surgeons Single institution
Lou et al.[12]	Esophagectomy	Retrospective cohort study	1,147 patients had		

esophagectomyRecurrence occurred in 435 (38%)217 patients' recurrence was determined by HPE and CT scan chest and abdomenIn 6 patients their recurrence was detected by upper endoscopy

- Conclusion: surveillance endoscopy had limited value50% of recurrences were detected with HPE and CT scans

  CT scans of chest and abdomen are effective in identifying subclinical recurrenceRetrospective review

  Study not designed to evaluate the effect of intensive follow-up on survival

  Not a comparative group (HPE *vs* SI)

  Single institutionChang et al.[10]Esophagectomy

  −McKeown

  −Ivor Lewis

  −Transhiatal esophagectomyRetrospective review of a prospectively maintained databaseComparison recurrence detection within 2 methods

    −HPE group

    −SI Group

225 patients had esophagectomy88 patients had recurrences (39.1%)Rate of recurrence

  −HPE: 47 of 124 (37.96%)

  −SI: 41 of 101 (40.6%)

Rate of recurrence was similar based on screening method

  SI group was not associated with improved detection but was associated with improved overall survival by (median value) average 7 moRetrospective review

  Relatively small sample size

  The regimen of selection HPE versus SI was based on surgeon preference

  Single institution

Abbreviations: CEA, carcinoembryonic antigen; CT, computed tomography; HPE, history and physical examination; PET, positron emission tomography; SI, surveillance imaging.

Conflict of Interest

None.

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