Tumour debulking for esophageal cancer – Thermal modalities

DAVID FLEISCHER, MD

D FLEISCHER. Tumour debulking for esophageal cancer – Thermal modalities. Can J Gastroenterol 1992;6(5):290-296. Esophageal cancer usually is discovered at a late stage and curative therapy seldom is possible. The prognosis is poor and most therapy is palliative. Endoscopic therapy commonly is employed; two common treatments involve thermal modalities. The Nd:YAG laser has been employed for 10 years and is effective in relieving obstruction in approximately 90% of cases. Re-obstruction usually occurs in two to three months and repeat treatment may be necessary. Limitations to laser use include the fact that equipment is expensive and there are technical restrictions. An alternative thermal modality is the bipolar coagulation tumour probe which employs bipolar electrocoagulation. It is less expensive and, if the tumour is circumferential, tends to be easier to use. (It should not be used if the cancer is noncircumferential.) The advantages and limitations of each modality are addressed.

Key Words: Esophageal cancer, Laser, Tumour probe

Réduction de la tumeur cancéreuse de l’oesophage. Modalités thermiques

RÉSUMÉ: Le cancer de l’oesophage est généralement découvert à une étape tardive et le traitement curatif est rarement possible. Le pronostic est sombre et la plupart des traitements ne sont que palliatifs. Le traitement endoscopique est généralement employé: deux traitements connus utilisent des techniques thermiques. Le laser Nd:YAG est employé depuis 10 ans et il est efficace à réduire l’obstruction dans environ 90% des cas. L’obstruction revient cependant dans les deux à trois mois et le traitement peut devoir être répétée. Parmi les limites du traitement au laser, notons le coût élevé de l’équipement et certaines restrictions au plan technique. Il existe une modalité thermique alternative: il s’agit d’une sonde bipolaire pour la coagulation de la tumeur, qui utilise l’électrocoagulation bipolaire. Elle est moins chère et si la tumeur est circonférentielle, elle tend à être plus facile à utiliser. (Elle ne doit pas être utilisée si le cancer n’est pas circonférentiel.) Les avantages et inconvénients de chaque modalité sont présentés ici.

Georgetown University, Washington, DC, USA
Correspondence and reprints: Dr David Fleischer, Chief, Endoscopy, Professor of Medicine, Georgetown University Hospital, 3800 Reservoir Road NW, Washington, DC 20007, USA

ESOPHAGEAL CARCINOMA IS AN EVOLUTIVE TUMOUR WITH AN EXTREMELY POOR PROGNOSIS. Despite advances in medical technology, survival rates following the diagnosis of esophageal cancer remain dismal. The diagnosis is most often made following the development of symptoms at a time when the disease is usually far advanced. The tumour extends through the submucosal lymphatics of the esophagus with ease and tends to invade contiguous structures readily. Opportunity for cure in this disease is extremely limited.

In 1988, approximately 10,000 new cases of esophageal cancer were diagnosed in the United States and 9400 died from the disease (1-3). The five-year survival rate remains approximately 5% despite decades of curative efforts by surgical resection. Regardless of the dismal prognosis, however, the possibility of a cure must always be considered, using either surgery or radiation. If not possible, then a number of palliative options should be explored. Radiation can often be considered in patients with extensive disease or those unfit for surgery but five-year survival rates are also quite low (4,5). Unfortunately, the main focus of therapy for most cases of symptomatic esophageal cancer is palliative therapy, which provides relief from symptoms but offers no cure.
TABLE 1
Types of lasers

<table>
<thead>
<tr>
<th>Laser type</th>
<th>Wavelength (µ)</th>
<th>Depth of penetration</th>
<th>Visible light?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nd:YAG</td>
<td>1.06</td>
<td>Least superficial</td>
<td>No</td>
</tr>
<tr>
<td>Argon</td>
<td>0.5</td>
<td>Superficial</td>
<td>Yes</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>10.0</td>
<td>Most superficial</td>
<td>No</td>
</tr>
<tr>
<td>Tunable dye</td>
<td>0.5-0.7</td>
<td>Superficial</td>
<td>Yes</td>
</tr>
</tbody>
</table>

PALLIATIVE THERAPY

The goal of palliation in esophageal cancer is to relieve symptoms. For dysphagia, numerous options exist. Blood loss may also be treated. Relief of pain is an important supportive measure. The currently available methods of esophageal cancer palliation include surgery, radiation, bougienage, stent placement, gastrostomy with pharyngostomy and, more recently, laser and bipolar coagulation tumour probe therapy. Each method may be beneficial in selected cases but individual limitations exist. Surgical palliation may not always be possible for technical reasons. Moderately high morbidity and mortality also render it less desirable. Radiation therapy may provide symptomatic relief but often takes several weeks before benefit is achieved. Patients who then develop recurrent symptoms cannot receive repeat radiation treatments.

Bougienage with or without stent placement may be effective in providing palliation but is highly dependent upon anatomical location and characteristics of the tumour itself (6-8). In some patients for example, the malignant stricture is too small to allow dilatation which will clinically benefit the patient.

The benefit derived from dilation alone is often extremely short-lived and frequent repeated dilations are necessary to maintain palliation. An editorial by Tytgat and den Hartog (9) lager remarks that dilation alone becomes extremely burdensome to the patient because it must be performed at shorter intervals and may be technically more difficult and painful. Esophageal prosthesis placement offers satisfactory palliation but tumour anatomy and location may limit benefit. Gastrostomy with pharyngostomy is another option that rarely offers an acceptable outcome. This procedure does not address one of the primary goals in the palliation of esophageal cancer which is to provide some comfortable means of swallowing by restoring the patency of the esophageal lumen.

ENDOSCOPIC TECHNIQUES

Developments and improvements in endoscopic techniques have broadened the range of available palliative techniques for esophageal cancer. Endoscopic laser therapy and bipolar coagulation tumour probe therapy have gained popularity in the palliative treatment of esophageal cancer. Both techniques offer effective means of re-establishing a patent esophageal lumen which is crucial to allow improvement in swallowing. It is important in palliation of esophageal cancer to consider the differences between the technical and functional success of the applied treatment modalities.

Technical success reflects the effectiveness of establishing a patent esophageal lumen, whereas functional success is defined as the ability not only to achieve lumen patency but also to restore an oral means for the patient to maintain caloric intake. Both endoscopic laser therapy and bipolar coagulation tumour probe therapy provide a high percentage of technical success in the range of 95% and 80 to 90%, respectively. Their respective rates of functional success are 75% and 70%.

Specific characteristics of the esophageal tumour itself may dictate which modality would provide the most effective palliation in the safest manner. When an endoscopist is confronted with the issue of choosing between different treatment modalities a number of factors must be considered. Efficacy, safety (to the patient and physician), ease of use, patient tolerance, duration of benefit, expense and versatility are all important considerations. The focus of the rest of this discussion will be to describe these methods individually and to allow for some basis for comparison of their unique advantages and disadvantages when applied to the palliative treatment of esophageal cancer.

ENDOSCOPIC LASER THERAPY

Endoscopic laser therapy was first applied in the treatment of gastrointestinal disease for hemostasis in patients with upper gastrointestinal bleeding (10). Early in the 1980s it became apparent that laser could be applied to treat gastrointestinal neoplasms (11-13). Fleischer and Kessler (14) first described its use in the palliative treatment of esophageal cancer patients. All five patients described experienced relief from symptoms and were able to eat solid foods after therapy was completed. Endoscopic laser treatment of esophageal cancer has many appealing aspects: it averts the need for surgery and the risks of general anesthesia; it diminishes the likelihood of systemic side effects since treatment is limited to the esophageal lumen; it is performed under direct vision; and retreatment is possible if symptoms recur.

Laser principles: The word LASER is an acronym for ‘Light Amplification by Stimulated Emission of Radiation’. This phenomenon occurs when a substance is excited to a higher energy state and emits light energy when it returns to its ground or resting state. Amplification occurs when the photons interact between two mirrors, one 100% reflective and the other only partially reflective. This allows for the release of a high energy beam of laser light which is coherent, monochromatic and easily focused. The wavelength of laser light is dependent on the medium used to produce the laser beam. The individual properties of the different available lasers are in turn the result of the individual wavelength (15-17). The Nd:YAG laser is produced from a solid medium which receives energy from an intense lamp light. Several different lasers have been developed and used for therapeutic purposes in medicine.
TABLE 2
Temperature and tissue reaction in laser light

<table>
<thead>
<tr>
<th>°C</th>
<th>Histological event</th>
<th>Endoscopic manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>Cell death, edema, endothelial</td>
<td>Erythema</td>
</tr>
<tr>
<td>60</td>
<td>Protein coagulates</td>
<td>Tissue turns white, blood turns black</td>
</tr>
<tr>
<td>80</td>
<td>Denatured collagen contracts</td>
<td>Tissue &quot;puckers&quot;</td>
</tr>
<tr>
<td>100</td>
<td>Tissue water boils</td>
<td>Vaporization causes a divot</td>
</tr>
<tr>
<td>210</td>
<td>Dehydrated tissue burns</td>
<td>Blackened tissue disappears or glowing embers appear</td>
</tr>
</tbody>
</table>

(Tables 1). The level of tissue absorption and depth of tissue penetration are dependent upon laser wavelength. The tissue effects produced by lasers involve interaction with water and hemoglobin which depends upon individual laser wavelengths.

Laser light consists of light energy which is converted to heat energy when it interacts with tissue. Laser light creates a molecular agitation in biological tissue which in turn creates heat. The level of molecular agitation induced reflects the amount of light absorbed into the tissue. The depth of tissue penetration is dependent upon the amount of light absorbed versus that which is scattered.

Laser irradiation has several effects on tissue which can lead to hemostasis and tissue ablation. These tissue effects rely upon the temperature achieved in particular layers of tissue. When a critical temperature of 80°C is reached in a particular layer of tissue, histological evaluation would reveal the presence of denatured collagen, contraction and blood vessel constriction. As the temperature reaches 100°C, tissue water boils resulting in tissue vaporization (or 'divot' formation). As tissue is heated different critical temperatures are reached which lead to endothelial damage, cell death, protein denaturation, blood vessel constriction and tissue vaporization (Table 2) (15,16).

These principles become important when laser therapy is applied in the palliation of esophageal cancer. The goal is to achieve tumour tissue destruction. This may be accomplished most rapidly by tissue vaporization or more slowly by coagulation. The former is more commonly employed but each has its advantages and disadvantages.

The application of laser to the treatment of esophageal cancer and other gastrointestinal neoplasms has been made possible by the development of endoscopy and a reliable laser delivery system. The development of flexible endoscopes allows the endoscopist to reach the tumour in the lumen of the gut and to apply therapy directly. The laser delivery system enables one to apply the laser light energy in close proximity to the tissue surface. The emergence of the flexible quartz waveguide has enhanced the role of the laser delivery systems. The quartz waveguide carries the laser light beam from the laser source to the treatment site via the endoscope. This waveguide is usually housed in a 'plastic' catheter and is designed to allow gas to flow through a small space between the actual fibre and the catheter. This coaxial gas flow keeps the fibre clean by blowing away blood or debris at the treatment surface. It also serves to cool the temperature of the fibre tip. Currently, only the Nd:YAG, argon and dye lasers have suitable waveguides available which allow application to treatment of gastrointestinal lesions via the endoscope. The availability of the flexible waveguide has led to widespread endoscopic use of lasers in the treatment of various gastrointestinal tumours.

Patient selection: Endoscopic laser treatment is used primarily as a method of palliation in patients with esophageal cancer. Patients selected for treatment are generally not surgical candidates. Patients who have recurrent tumour following surgical resection and radiation therapy are also good candidates. Laser therapy may also be used in patients with severe obstructive symptoms before the initiation of radiation and/or chemotherapy in order to establish a patent esophageal lumen so that oral caloric intake and nutrition may improve.

Treatment technique: Endoscopic laser therapy can be applied in a prograde or retrograde fashion. When Fleischer originally described the technique (14), it was performed in the prograde fashion. The two channel therapeutic endoscope was advanced to the proximal margin of the tumour after the patient was sedated with meperidine, a benzodiazepine, and a topical anesthetic. The quartz waveguide was then passed out through the biopsy channel of the endoscope. The Nd:YAG laser was set at 90 to 100 W for 2 s pulses. The tip of the fibre was positioned at 1 cm from the tissue surface as treatment was applied. The proximal margin of the tumour was treated first with the beam aimed at the portion of the lesion closest to the lumen. The treatment progresses in increasingly larger concentric circles towards the wall of the esophagus. The treatment session is complete when the cross-section of the tumour has been treated. If the lumen of the esophagus is wide enough to allow safe passage of the endoscope, treatment may be carried out at various levels during the initial session.

A period of 48 h elapses between treatments. This period allows for maximal tissue necrosis. When the treatment area is examined 48 h following treatment it appears as a whitish yellow, soft, necrotic mass. This portion of destroyed tumour tissue can be removed in various ways with forceps, polyp graspers or large bore tube suction. Following the removal of the necrotic debris, treatment is begun on the underlying previously untreated tumour. This approach is continued until the lumen is opened sufficiently to allow passage of the endoscope freely into the stomach. This method offers successful palliation, as several subsequent investigators have observed (18-28). Symptoms of dysphagia were relieved in virtually all patients treated in this fashion in the initial study.

Pietrafitta and Dwyer (29-31) later described a technique using tumour dilatation which enabled initiation of treatment at the distal margin of the tumour. This particular technique in-
wolved the insertion of a stainless steel guidewire with a flexible tip through the narrowed lumen of the tumour. Savary-Guillard dilators were then passed with progressively larger sizes until a 15 mm dilator had been passed successfully. With the guidewire in position a small calibre endoscope could be passed to the distal margin of the tumour. Treatment of the tumour would then begin at the distal margin and continue in a retrograde fashion until the entire tumour was treated. Repeat endoscopy was typically performed within 48 to 72 h to evaluate the results of treatment and to assess the luminal diameter of the esophagus. The goal of therapy was to achieve a luminal diameter of at least 1.2 cm. The advantage of this particular technique was that it allowed most patients to receive treatment in a single session. Palliation was comparable to the prograde method. This technique allowed more rapid relief of obstruction without compromising safety.

Pietrafitta (29) compared prograde and retrograde techniques in palliating esophageal obstruction head to head. He reported that patients achieved palliation after undergoing fewer treatments (mean 1.6) over a shorter time interval when the retrograde technique was used. Both treatment techniques were similar with regards to technical and functional success. The post treatment lumen diameters were similar and all patients in both groups were able to tolerate regular diets at the completion of therapy. The retrograde (single session) technique was regarded as preferable because it allowed more rapid treatment without complications which ultimately results in a shorter hospital stay and fewer hospital costs.

**Efficacy and safety:** Important efficacy and safety considerations must be addressed when using endoscopic modalities in the palliation of cancer. Experience supports the high percentage of successful palliation with the use of endoscopic laser therapy (14,19, 20, 25, 27-37). Technical success in restoring lumen patency is fairly consistent at greater than 90%. Functional palliation tends to be less, ranging from 70 to 85% of individual patient characteristics probably contribute to the situation where functional palliation is not achieved. The extent of disease, the anatomical location of the tumour and the patient's general performance status all contribute to the lack of successful palliation.

The average number of treatment sessions needed to achieve technical success using the prograde or retrograde technique are three and one to two, respectively. The duration of benefit when technical and functional success is achieved averages between two and three months. If recurrent symptoms develop retreatment is often beneficial.

The issue of safety has been examined closely and it appears that laser therapy is a relatively safe method of palliation. Minor complications which may occur include transient fevers, mild transient chest pain during the procedure, a transient initial worsening of dysphagia due to tissue edema and mild leukocytosis which often resolves.

Major complications include tracheoesophageal fistulae, perforation, bleeding and stricture formation. Tracheoesophageal fistulae may be managed with the endoscopic placement of an esophageal prosthesis. Perforation may also be managed successfully in a conservative fashion. Occasionally a pseudostricture or pneumomediastinum occur without demonstrable perforation. This entity is thought to be due to the transmission of the coxial carbon dioxide gas which flows through the laser fibre during treatment. Its course is usually benign and without consequence. Overall, laser therapy appears to be an effective and safe means of palliation.

**BIPOLAR COAGULATION TUMOUR PROBE THERAPY**

The bipolar coagulation tumour probe is a recently developed endoscopic device which has been applied to the palliative treatment of obstructing gastrointestinal cancer. This technique uses the principles of bipolar (multipolar) electrocoagulation. It is particularly useful when tumour anatomy may not be ideally suited for laser therapy.

Bipolar electrocoagulation is dependent upon the principles of thermal tissue effects (33). The applied electrical density is concentrated at the bipolar electrode tips. The tissue completes the circuit between two wires that are positioned only a few millimetres apart. The depth of coagulation effect can vary by changing the generator power settings and the appositional force. As the targeted tissue is heated and dries out, the electrical resistance increases and the current flow drops. This limits the duration and degree of thermal effect.

Johnston et al (34) used these principles to develop a large tumour probe in conjunction with the manufacturer (American Cystoscope Manufacturing, Inc, Connecticut). The first probe comprised a cylindrical active element which was 15 mm in diameter, 15 mm in length and incorporated six pairs of bipolar electrodes oriented longitudinally on the surface. Its overall design is similar to an Eder-Puestow olive-shaped dilator which can be passed over a guidewire under fluoroscopic guidance. The olive-shaped tip is connected permanently to a flexible shaft which is 60 cm in length. The shaft is marked with 1 cm increments denoting the distance from the electrode. The shaft, olive and spring-tip which serves as the leading edge all have a central lumen which allows for passage of the device over a guidewire. Five separate probes have been developed. Four of these probes have a 360° treatment surface located on the olive-shaped portion. Each probe has a different diameter (6, 9, 12 and 15 mm). In addition, there is a probe with a 180° treatment surface with a 15 mm diameter. The whole instrument consisting of spring tip, olive-shaped probe and flexible shaft are connected to a 50 W ACMI/ Circon Bipolar Electrocoagulating Generator via a Y-shaped electrical connection.

**Patient selection:** All patients considered for the bipolar coagulation tumour probe treatment should have undergone certain preliminary studies which include a contrast x-ray of the esophagus and stomach; a screening endoscopy and an imaging study (i.e., computed tomography scan with oral
TABLE 3
Factors favouring one form of thermal therapy

<table>
<thead>
<tr>
<th></th>
<th>Nd:YAG laser</th>
<th>Tumour probe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exophytic tumour</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Submucosal tumour</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Circumferential</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Noncircumferential</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>&gt; 6 cm long</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>&lt; 6 cm long</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Technique: The procedure begins after the patient receives topical oropharyngeal anesthesia followed by intravenous sedation with meperidine. A small caliber endoscope is used initially, proceeding in the usual manner and taking note of the proximal margin of the tumour. If the endoscope can be passed through the entire tumour, precise recordings of the proximal and distal margins are made.

It is optional at this point to have the radiologist put markers on the skin denoting tumour margins while the patient is in the left lateral decubitus position. Although helpful, it is not always a reliable means of defining treatment limits, since the patient can move during the procedure and the markings would then be in a different plane.

The endoscope may then be advanced into the stomach to evaluate the patency of the pylorus. Once this is established, a marked spring-tip guidewire is inserted through the endoscope and into the stomach antrum. The endoscope is carefully withdrawn in a coordinated fashion which allows the guidewire tip to remain in optimal position in the antrum. The tumour is then dilated with polyvinyl dilators to the largest diameter possible (usually 12 to 15 mm). The bipolar coagulation tumour probe is passed over the guidewire to the level of the proximal margin of the tumour. Treatment may begin at this level and proceed in an antegrade fashion or the probe may be advanced to the distal margin of the tumour and then proceed in a retrograde or cephalad fashion. Treatment in retrograde fashion must be guided by fluoroscopic observation. A small calibre endoscope may be passed alongside the probe to allow the olive tip to be seen directly as it reaches the proximal portion of the tumour. This enables the endoscopist to position the probe properly so that normal tissue located above the tumour is not inadvertently burned. The tumour probe and guidewire are removed and the endoscope is again passed to evaluate the treatment site. The treatment site usually shows a combination of a circumferential, white exudative area along with areas of black eschar which result from treatment of tumour tissue in which blood may have been present. Once the procedure has been completed, the patient is observed for any immediate complications.

Repeat endoscopy is performed 48 h later and usually reveals yellow-white, necrotic debris in the middle of the treatment site. This debris is usually easily removed by advancing the endoscope into the stomach. Debridement can also be accomplished with the passage of dilators over a guidewire. Ideally, an 11 mm endoscope should pass through the treatment site and into the stomach. Once the patency of the esophageal lumen is established, the patient may undergo radiation therapy and/or chemotherapy. Subsequent treatment may be done if necessary depending upon the clinical circumstances.

Efficacy and safety: The bipolar coagulation tumour probe has been effective in the palliation of esophageal cancer. Although not used as extensively as the laser, investigation has demonstrated successful results in palliation. Post treatment assessment has shown significant improvement in the grade of dysphagia and an increase in lumen channel size (35,36). A satisfactory lumen channel could be established in a relatively few number (mean 1.7) of treatment sessions. The mean duration of benefit before symptoms recurred and retreatment became necessary was approximately seven weeks (36).

Early experience with the bipolar coagulation probe has shown it to be safe — minor complications include transient fevers and chest pain (35). The major complications described have been delayed hemorrhage and tracheoesophageal fistula. The formation of delayed strictures have also been described as a consequence of bipolar coagulation tumour probe therapy (37). In one series, it was described in two of 16 patients at the proximal margin of the tumour treatment site. Investigation using a canine model led to the conclusion that esophageal injury and subsequent stricture formation can occur when normal tissue is treated with a 30° tumour probe (36). Direct viewing of the proximal treatment margin with an endoscope could potentially minimize this hazard.
COMPARISON OF TECHNIQUES

Investigation has concluded that effective and safe endoscopic palliation of obstructive circumferential esophageal cancer is similarly achieved with laser or bipolar coagulation tumour probe therapy. There are advantages and disadvantages to each method. The morphological and anatomical characteristics of the tumour may dictate which method is preferable.

If, for instance, an exophytic, non-circumferential tumour is located in the mid to distal portion of the esophagus, use of the Nd:YAG laser would be preferred. If the tumour is a long, circumferential stricture which is predominantly submucosal, treatment with the bipolar coagulation tumour probe will offer a quicker and safer means of palliation (Table 3). A long stricture may require frequent laser treatment sessions before benefit is achieved whereas the bipolar coagulation tumour probe therapy may be accomplished in a single treatment session. Laser treatment of a submucosal tumour may be rather difficult from a technical standpoint and may also result in treatment of a normal layer of superficial tissue which could result in pain. Stricture formation and possible perforation could also occur as a consequence of this form of treatment.

Treatment of a proximal or cervical esophageal lesion with the laser has been difficult due to the technical difficulties involved. These lesions can be treated with the bipolar coagulation tumour probe more easily. Both techniques are generally well tolerated by the patient. Laser treatments may lead to transient gaseous distension of the bowel, however, which may lead to some discomfort. This results from the slow but continuous flow of gas through the waveguide catheter. Palliation with the tumour probe may require fewer sessions to complete, particularly in patients with long strictures.

Duration of benefit on the average is equivalent with both methods. Another important issue concerns the cost considerations. The laser unit and accessories tend to be initially more expensive than the bipolar coagulation tumour probe apparatus but tends to offer more versatility. The laser may be used to treat other gastrointestinal tumours as well as gastrointestinal bleeding. The bipolar coagulation tumour probe, on the other hand, has only been used in the palliative treatment of esophageal and rectal cancer. Both methods may be used in a complementary fashion, thereby allowing treatment of lesions which may not be ideally suited for the other.

Laser therapy and bipolar coagulation tumour probe therapy offer effective and safe means for palliating obstructive esophageal cancer. Future developments may allow more precise application of these techniques based on more sensitive means of identifying abnormal tumour tissue. The development of endoscopic ultrasonography and the use of tissue sensitizing agents (such as hematoporphyrin derivatives) may allow more accurate means of differentiating normal from abnormal tissue. This could lead conceivably to more precise and extensive tumour destruction, less injury to normal tissue and even less potential for complications. As the use of both these modalities becomes more widespread, their role in the treatment of esophageal cancer will continue to grow.

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