

## Approaches to Perioperative Care for Esophagectomy

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**D**ESPITE ITS LONGSTANDING RECOGNITION, esophageal carcinoma remains a highly lethal disease that affects thousands of patients annually. The United States Centers for Disease Control and Prevention reports heterogeneous development of mortality from esophageal cancer over time (Fig 1).<sup>1</sup> Although improvements over time have been made in the mortality rates of black women and men, the mortality for white men actually has increased in the last decade of the 20th century. In 2010, death rates from esophageal cancer were approximately 40/100,000 for men  $\geq$  65 years of age and about 10/100,000 for women  $\geq$  65 years of age.<sup>1</sup> In 1990, death rates were significantly higher for black than for white patients; in 2010 the death rates were similar (Fig 1).

Perioperative mortality for esophagectomy is the highest among elective procedures, and has been reported from 1% to 3% in contemporary single-center studies<sup>2-4</sup> and between 3.4% high-volume hospitals and 17.3% in low-volume hospitals in a large multicenter retrospective study assessing cancer outcomes from 1984 to 1993 in patients older than 65.<sup>5</sup> A recent study looking at trends and outcomes of esophageal surgery in the United States examined the national inpatient sample database to analyze results for patients with esophageal cancer treated with either total or partial esophagectomy.<sup>6</sup> Between 2001 and 2010 in the United States, 15,190 esophagectomies were performed. Although numbers increased progressively during this period, mortality decreased from 8.3% to 4.2%.

### ANATOMIC PATHOLOGY

The vast majority of esophageal tumors are either squamous cell carcinoma (SCC) or adenocarcinoma. SCC is associated with tobacco and alcohol use and begins as epithelial dysplasia before evolving to carcinoma, and finally becoming invasive. SCC tumors typically are above the tracheal bifurcation in the upper third of the esophagus, which increases its perioperative

mortality.<sup>7</sup> Adenocarcinoma, in contrast, typically arises from sequelae of gastroesophageal reflux disease and the development of Barrett's esophagus; thus, lesions typically are lower, near the gastroesophageal junction, with a concomitant improvement in operative mortality.<sup>7</sup> In the United States, there has been a significant decline in the incidence of squamous cell carcinoma between 1973 and 2002, which was countered by a dramatic increase in the number of patients affected by adenocarcinoma.<sup>8</sup> Whether the increase in adenocarcinoma is related to growing numbers of patients affected by risk factors such as obesity and Barrett's esophagus<sup>9</sup> remains speculative at this time.

### THERAPEUTIC STRATEGIES

Management of esophageal carcinoma is complex. It depends on type and extent of cancer lesions, emphasizing the importance of accurate tissue diagnosis and staging. Current therapy options include chemotherapy, radiation, and surgical resection, which, in many cases, often are combined. Stage IV disease is defined by metastatic spread to other organs or distant lymph nodes. It commonly is approached palliatively with chemotherapy, radiation, and gastrostomy placement. Preceding surgery with neoadjuvant treatment using chemotherapy or more often combined chemoradiotherapy has been shown to provide a survival benefit in several large meta-analyses.<sup>10-13</sup> The anesthesiologist carefully should review individual chemotherapeutic regimens and have a high level of suspicion for specific toxic sequelae such as cardiotoxicity from radiation or after epirubicin treatment.

### SURGICAL APPROACHES

#### Traditional: Ivor Lewis and McKeown Esophagectomy

Ivor Lewis described his work on resection of the middle third of the esophagus in 1946.<sup>14</sup> His approach using a laparotomy to assess tumor extent and mobilize the stomach, followed by a resection through a right-sided thoracotomy, formed the basis for future generations of thoracic surgeons around the world.<sup>15,16</sup>

A tri-incisional, or McKeown technique<sup>17</sup> uses the advantages of the Ivor Lewis approach along with a cervical incision for the esophagogastric anastomosis. The anastomosis then lies outside of any potential area of adjuvant radiation. Also, in case of an anastomotic leak, the cervical location can be drained more easily.

#### Transhiatal Esophagectomy

Esophagectomy without thoracotomy originally was proposed in 1913 by a German physician named Denk. This technique was not used widely until the late 1970s but since

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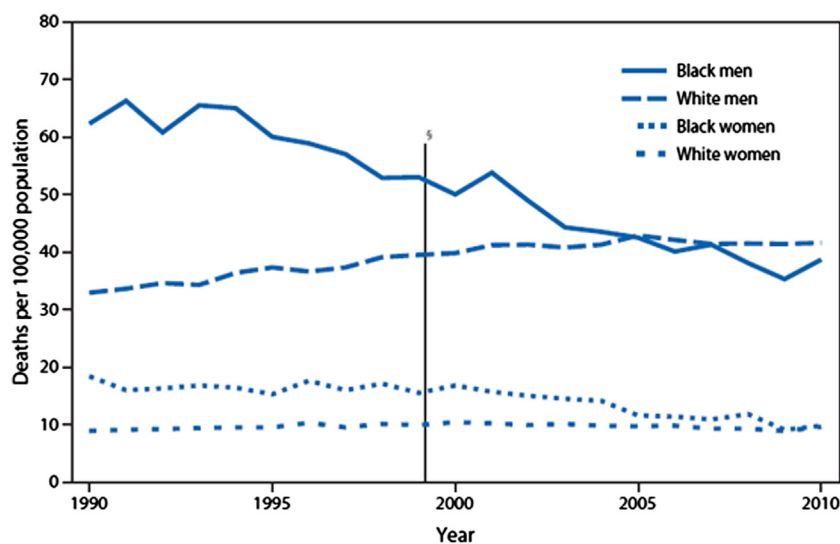
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**Fig 1.** Age-adjusted death rates from esophageal cancer for persons aged  $\geq 65$  years, by race and sex in the United States during 1990-2010. During 1990-2010, the age-adjusted esophageal cancer death rate decreased 38% for black men and 47% for black women aged  $\geq 65$  years. For white men in this age group, the rates increased 26% during 1990-2002 and stabilized during the rest of the decade; for white women the rates stayed nearly the same. In 2010, esophageal cancer death rates were nearly 40 per 100,000 population for white and black men aged  $\geq 65$  years and nearly 10 per 100,000 population for white and black women in the same age group. **Figure 1** reproduced from MMWR, 2013<sup>1</sup> as reported by Yelena Gorina, MS, MPH.

has become an accepted method that has been reported to substantially reduce morbidity and mortality. In this procedure, classically described by Orringer,<sup>3</sup> the lower mediastinal and esophageal dissection is performed through a widened diaphragmatic hiatus. Paraesophageal and mediastinal nodes then are resected as far as visualization allows. Next, a left cervical incision is made, and the remainder of the esophagus is dissected inferiorly and delivered through this cervical incision. Lastly, an esophagogastric anastomosis is fashioned. Of note and concern to the treating anesthesiologist, the blunt dissection of the middle third of the esophagus can induce both arrhythmias as well as impair ventricular filling causing transient hypotension. Malhotra et al found that more than half of patients suffered intraoperative arrhythmias during mediastinal manipulation, and that degree of hypotension was correlated linearly with duration of manipulation.<sup>18</sup>

Much controversy exists as to the overall reduction in patient morbidity and mortality using the transhiatal esophagectomy (THE) approach. A variety of single-center studies have shown reductions in respiratory morbidity and mortality.<sup>19</sup> A 2014 study by Papenfuss et al analyzed National Surgical Quality Improvement Program data from 1,428 patients between 2005 and 2011. A total of 52.5% of patients underwent THE procedures and 47.5% underwent a transthoracic esophagectomy (TTE). Their results showed no difference in 30-day mortality (THE = 2.9%, TTE = 4.7%,  $p = 0.095$ ); however, a trend favored the THE group. Serious morbidity was high in both groups (THE = 39.6%, TTE = 43.5%,  $p = 0.146$ ). The THE group had a significantly higher superficial wound infection rate (11.6% v 6.2%,  $p < 0.001$ ) while the TTE group required more perioperative blood transfusions (12.5% v 8.9%,  $p = 0.032$ ) and returns to the operating room (14.5% v 10.9%,  $p = 0.046$ ).<sup>20</sup>

The potential reductions in patient morbidity and mortality undergoing the THE approach also must be weighed against the concerns that the transhiatal approach compromises cancer outcomes. With the transhiatal approach, it is not possible to perform extensive lymphadenectomy, and the technique has the potential of compromising establishment of the deep or circumferential cancer margin. To date, there are no randomized trials that are able to answer this question.

### Minimally Invasive Esophagectomy

Since the 1990s, laparoscopic techniques have allowed esophagectomy to be performed by a minimally invasive approach. Minimally invasive approaches exist for transhiatal techniques as well as for the Ivor Lewis procedure, and the tri-incisional version combining thoracoscopic/laparoscopic mobilization with the cervical incision/anastomosis. Laparoscopic and robotic techniques aim to reduce the thoracotomy/abdominal incision size, reduce blood loss, minimize inflammatory response, and, finally, improve postoperative outcomes. The most common approach for minimally invasive esophagectomy allows for completion of the classic Ivor Lewis surgery through the use of multiple port sites (can be as many as 9-10) in the thoracic and abdominal regions. The thoracic portion of the procedure is performed using a video-assisted thoracoscopic surgery (VATS) approach with the patient in the left lateral decubitus position.

Two recent database-related outcomes publications from the UK and Japan indicated that 15% to 20% of esophagectomies performed from 2005 to 2010 used minimally invasive esophagectomy (MIE) (>14,000 total surgeries / >2000 MIE).<sup>21,22</sup> The majority of studies published examined surgical outcomes in single-center studies only, and to date no randomized multicenter trials exist that compare open esophagectomy to MIE. However, the traditional invasive versus minimally invasive esophagectomy trial currently is underway.<sup>23</sup>

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