The Last Word

Mariela A. Blum Murphy, MD
Mariela A. Blum Murphy, MD, is an Assistant Professor of Medicine in the Department of Gastrointestinal Medical Oncology, University of Texas MD Anderson Cancer Center. She earned her medical degree from the Universidad Cátolica de Guayaquil, Ecuador in 2003. She then completed an Internal Medicine Residency program at Jackson Memorial Hospital, University of Miami, Florida, and pursued further training in Hematology and Oncology at the Baylor College of Medicine in Houston, Texas. Her clinical research interests are in patients with gastric and esophageal cancer.

Takashi Taketa, MD
Takashi Taketa, MD, is from the Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas.

Kazuki Sudo, MD
Kazuki Sudo, MD, is from the Department of Gastrointestinal Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas.

Jeffrey H. Lee, MD, MPH
Jeffrey H. Lee, MD, MPH, is Professor, Department of Gastroenterology, Hepatology, and Nutrition, at the University of Texas MD Anderson Cancer Center, Houston, Texas.

The ideas and viewpoints expressed in this editorial are those of the author and do not necessarily represent any policy, position, or program of NCCN.

Journal of the National Comprehensive Cancer Network

Surveillance for Esophageal Cancer: Does it Make Sense?

Mariela A. Blum Murphy, MD; Takashi Taketa, MD; Kazuki Sudo, MD; Jeffrey H. Lee, MD, MPH; and Jaffer A. Ajani, MD

The main objective of screening for high-risk conditions is to diagnose them at an early stage and improve the likelihood of cure. Although this is a seemingly simple concept, it requires navigation through a complex set of circumstances innate in current societies. These complexities include relatively high prevalence of the targeted condition, simplicity with which surveillance can be accomplished, low or absent complication rates, high sensitivity and specificity of the test for screening, and, finally, the perception by the public that it is a cost-effective test coupled with low intrusiveness. In the cancer arena, we can point to relative successes (colorectal and breast cancer screening) and a relative failure (all the debates about the lack of merit for prostate cancer screening).

Additionally, some screening principles can be questioned: Should every adult be considered “at risk”? Can non-genetic test models (based on ethnicity, geographic residence, environment, and lifestyle variables) be developed to enrich a population for targeted surveillance? Is it practical to develop and implement a model that would include genetic susceptibility elements with environmental and lifestyle elements? This commentary discusses the answers to these questions in the context of esophageal cancer (EC).

EC merits this type of discussion because of its high incidence in many regions of the world and its impact on global health. EC is the eighth most common cancer worldwide, with an estimated 407,000 deaths in 2008. EC is often diagnosed at an advanced stage. Therefore, outcomes continue to be dismal. In this setting, one can assume that screening for EC would make sense.

The majority of ECs are squamous cell carcinoma (SCC), but adenocarcinoma (AC) is increasing in incidence. SCC is common in the endemic areas, and AC is more frequently found in the Western world. The highest rates of SCC are seen in the Central Asian “EC belt.” This region includes the countries of the Caspian littoral, the central Asian republics, Mongolia, and northwestern China.

Preneoplastic squamous cell dysplasia is often attributed to tobacco use, alcohol consumption, and decreased intake of fruits and vegetables. Patients with an inactive aldehyde dehydrogenase-2 genotype (present in 20%–30% of the Japanese population) are at a high risk of developing SCC. The identification of susceptibility gene loci related to alcohol and tobacco is important progress in determining the genetic underpinnings of SCC. In the endemic regions of China, balloon cytology was initially used to detect SCC early, but it is no longer a common practice, and no routine screening for SCC is currently performed. This lack of screening is unfortunate, because an aggressive and a strategic approach can save lives in endemic regions.

Survveillance for AC poses unique challenges. The only known premalignant condition for AC is Barrett’s esophagus (BE). BE is defined as specialized intestinal metaplasia of the distal tubular esophagus. In Western societies, where the average adult body mass index is increasing, the prevalence of gastroesophageal reflux disease and consequent BE has increased at an alarming pace. Screening for BE is recommended in white men 50 years of age and older who have frequent (several times per week) and longstanding gastroesophageal reflux disease (> 5 years) along with high body mass index or nocturnal reflux.

However, recent literature confirms that the rate of progression from BE to AC is as low as 0.18% per year. This low rate suggests a need for caution when considering...
surveillance for AC. That the incidence of AC has increased over the past several decades is unquestioned, but this increase may be due to the high prevalence of BE or other undefined factors. Thus, the cost-effectiveness of screening must be questioned, because only a few patients with BE will develop AC.

We acknowledge that patients with BE with high-grade dysplasia (HGD) remain at higher risk of developing AC than those with BE without HGD or those with low-grade dysplasia. Therefore, therapy should be recommended for patients diagnosed with HGD. For localized HGD, endoscopic therapies seem successful, and surgery is rarely needed. However, this situation begs the question, is surveillance warranted in patients with BE without HGD? Current guidelines are based on expert recommendations or retrospective studies; well-designed prospective trials with AC as a primary end point are lacking. For patients with BE without dysplasia, endoscopy every 3 years is suggested, and for patients with low-grade dysplasia, endoscopy every 6 to 12 months is suggested.10,13,14

Furthermore, these recommendations are for patients with BE, but what if an adult has not been diagnosed with BE? We believe the need exists for a model that incorporates genetic susceptibility traits and lifestyle traits to survey targeted populations at high risk for developing AC. If such a model is initially successful, then its efficacy (reduction in AC mortality) and cost-effectiveness must be established before it can be recommended for widespread use.

Assuming a model is developed that can be implemented in high-risk populations, another challenge is implementing it in the target population. This is not a small challenge. We can examine the tools available for surveillance of EC. The gold standard method for diagnosing EC and BE is esophagogastroduodenoscopy. However, this procedure is costly and associated with cardiopulmonary risks, although those risks are small.15,16 An alternative procedure is ultrathin transnasal endoscopy, which is feasible in the office and has low risks and low costs.17–20 Obtaining small biopsies through transnasal endoscopy is a compromise,21 but one that can be equally efficacious as esophagogastroduodenoscopy.22–24

In conclusion, screening is recommended for SCC in endemic areas; however, determining effectiveness and best practices must be accomplished through well-conceived prospective trials. This screening would be worthwhile, because a large number of subjects are at risk. For patients with BE, existing guidelines seem helpful; however, for most adults who have not been diagnosed with BE, surveillance for AC cannot be recommended. Clearly, further research is warranted, and we recommend the goal of creating a model that incorporates genetic susceptibilities and lifestyle elements. This model can then be applied to high-risk populations for targeted surveillance.

Multiple other opportunities lie ahead, including in-depth characterization of genetic susceptibilities; outcome correlation with circulating mRNAs, small RNAs, DNA fragments, and protein/peptide molecules; and molecular studies of the target tissues themselves.

References