



OESOPHAGEAL CANCER

Gail E Darling MD FRCSC

Professor of Surgery, Division of Thoracic Surgery University of Toronto; Kress Family Chair in Esophageal Cancer; Editor in Chief Pearson's Textbook of Thoracic Surgery

The purpose of staging is to guide treatment and estimate prognosis. Treatment decisions are based on clinical staging, whereas prognosis is based on pathological staging. In contrast to many cancers, clinical staging for esophageal cancer is imprecise even if all staging modalities are utilized. Globally, while most patients are staged with CT, the use of PET-CT or EUS is variable. The previous iteration of the staging system was data driven using the WECC database. This was a major advance in that the database was large, and complete. The question is whether further changes in the staging system are required now.

Research in esophageal cancer is limited as it is a relatively rare cancer, large scale clinical trials are few in number and the number of patients in those trials is small compared to breast cancer trials. As long term survival is uncommon, there are few advocates. As a result, what we know about esophageal cancer is limited, as are treatment options. This is in complete contrast to breast cancer. Most patients are treated in a similar fashion unless they have distant metastatic disease or very early (T1a) cancer. Given the current state of our knowledge and treatment options, clinical staging should be simple and easily applied. Complex algorithms are not useful at this time.

The practising clinician faced with an esophageal cancer patient needs to know: 1) is it localized or metastatic? 2) is there lymph node involvement? Secondary questions include: 1) Is it resectable? 2) Is radiation feasible and safe? 3) Is chemotherapy safe? At present even our ability to accurately identify lymph node involvement is less than optimal. We can use all available tests including FNA but many times we guess betting the odds that lymph nodes will be involved based on depth or length of tumor.

Currently tumors are classified as cT1, T2, T3, T4a, T4b. However, patients with T3, T4a and T4b are treated in similar fashion as are T2N+ tumours. N1, N2 and N3 are all N+ and are treated with similar protocols. Unless we have new treatment options, there is no need for a system as complex as the one we currently use. If we are going to change the staging system, perhaps it should be simplified : T1-3, N negative or positive, M0-1?

There are other factors which may be considered in making treatment decisions: Her 2 expression, PDL-1 expression, signet ring cell morphology, cancer stem cells, tumour length, circumference, SUV max and other PET parameters. Other than Her 2 expression, data to

support inclusion of such factors in staging is lacking. These are clearly areas for research. These factors are relatively easy to identify and readily available to most centers.

Proposals for inclusion going forward include molecular markers and genomic signatures. These are certainly appealing but to date, researchers have not identified anything that is clinically useful. Undoubtedly such research is needed and may yet yield fruit.

Pathological staging is more precise and granular. As adjuvant therapy is increasingly utilized, pathologic staging will become even more relevant for treatment decisions. Once molecular markers are identified, and found to be clinically relevant, pathological staging will become more complex. However, changes must be driven by data. For the present, we rely on our pathology colleagues to examine all resected lymph nodes. Surgeons must deliver those nodes. Previous studies have shown that the more nodes resected, the more accurate the staging will be particularly for pN0.

In the future, staging will go beyond TNM. At present we do not have the data to support such changes.

It is important that we evaluate our current staging system in a contemporary and global patient dataset to determine if changes are required. That dataset should also include other factors known to influence prognosis to determine if these factors should be included in staging. It is essential we prepare for the future by collecting molecular and genetic data where available. For the present, no changes are required until we have the data to support change.

Key References

1. Rice TW, Gress DM, Patil DT, Hofstetter WL, Kelsen DP, Blackstone EH. Cancer of the esophagus and esophagogastric junction-Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin.* 2017;67(4):304-317. doi:10.3322/caac.21399, 10.3322/caac.21399
2. Rice TW, Ishwaran H, Ferguson MK, Blackstone EH, Goldstraw P. Cancer of the Esophagus and Esophagogastric Junction: An Eighth Edition Staging Primer. *J Thorac Oncol.* 2017;12(1):36-42. doi:10.1016/j.jtho.2016.10.016, 10.1016/j.jtho.2016.10.016
3. Rice TW, Apperson-Hansen C, DiPaola LM, et al. Worldwide Esophageal Cancer Collaboration: clinical staging data. *Dis Esophagus.* 2016;29(7):707-714. doi:10.1111/dote.12493, 10.1111/dote.12493
4. Rizk NP, Ishwaran H, Rice TW, et al. Optimum lymphadenectomy for esophageal cancer. *Ann Surg.* 2010;251(1):46-50. doi:10.1097/SLA.0b013e3181b2f6ee, 10.1097/SLA.0b013e3181b2f6ee
5. Zuccaro G Jr, Rice TW, Vargo JJ, et al. Endoscopic ultrasound errors in esophageal cancer. *Am J Gastroenterol.* 2005;100(3):601-6. doi:10.1111/j.1572-0241.2005.41167.x
6. Rice TW, Ishwaran H, Hofstetter WL, et al. Esophageal Cancer: Associations With (pN+) Lymph Node Metastases. *Ann Surg.* 2017;265(1):122-129. doi:10.1097/SLA.0000000000001594, 10.1097/SLA.0000000000001594