The Role of Metastatic Lymph Node Ratio in Cancer Staging

Essay
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Contents

AJCC	American Joint Committee on Cancer
APC	adenomatous polyposis coli
BCSS	breast cancer-specific survival
CIS	Carcinoma in situ
CLND	Complete lymph node dissection
CSS	Cause specific survival.
DFS	Disease free survival.
DSS	Disease specific survival.
EGF	Epidermal growth factor.
EPCs	Endothelial progenitor cells.
EORTC	European Organization for Research and Treatment of Cancer.
FAP	Familial adenomatous polyposis.
HPCs	Bone marrow-derived hematopoietic progenitor cells.
ICAMs	Intercellular adhesion molecule.
JCGC	Japanese Classification of Gastric Carcinoma.
LND	Lymph node dissection.
LNR	Lymph node ratio.
MMPs, TIMPs	Matrix metalloproteineases, and Their tissue inhibitors.
NCAM	Neural cell adhesion molecule.
NCCN	National Comprehensive Cancer Network

OS	Over all survival.
PDGF	Platlet derived growth factor.
PTPs	Protein tyrosine phosphatases.
SEER	Surveillance, Epidemiology, and End Results population-based cancer registry
SNB	Sentinel lymph node biopsy
TNM	Tumor node metastasis
UICC	Union international coter le cancer.
VCAMs	Vascular cell adhesion molecule.
VGEF-A	Vascular endothelial growth factor A.

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Aim of work

This essay aims at highlights the significance of metastatic lymph node ratio as a prognostic factor in tumor staging and management.

Introduction

A clinically useful classification scheme for cancer must encompass the attributes of the tumor that define its behavior. The American Joint Committee on Cancer (AJCC) classification is based on the premise that cancers of the same anatomic site and histology share similar patterns of growth and similar outcomes. This classification is identical to that of the International Union against Cancer (UICC). **(Henson et al., 2001)**

The tumour-node-metastasis (TNM) stage classification of Union Internationale Contre le Cancer (UICC) is the most widely recognized system to classify the spread of cancers and it predicts patient outcome. **(Buonadonna et al., 2003)**

The TNM classification classifies patients into six different groups by the extent of the primary tumour (T), spread of malignant cells to local lymph nodes (N), and the presence or absence of distant metastases (M). A clinical classification (cTNM or TNM) is used to describe the pretreatment TNM status of the patient and a pathological classification (pTNM) to describe the postsurgical histopathological status; both are used clinically. The former is used for selecting the treatment modality, and the latter for evaluation of the patient's prognosis and the need for adjuvant therapy. **(Sobin & Wittekind, 2002)**

Recent literature from many malignancies emphasizes the importance of the number of LNs examined in determining prognosis. In

colon and rectal cancer, staging accuracy and survival are improved with increasing nodal examination and analysis. These analyses have also been borne out in patients with lung, breast, and bladder cancer. **(Gajra et al., 2003)**

The number of metastatic lymph nodes (N stage) and the depth of the primary tumor (Tstage) are currently considered the most reliable prognostic indicators for patients with radically resjected gastric cancer, while T stage can be readily assessed by pathologic examination of the primary tumor, N stage assessment can be affected by the extension of lymph node dissection, which is classically termed D1, D2, and D3. **(Dicken et al., 2005)**

The UICC/AJCC classification suggests that at least 15 lymph nodes for gastric cancer and 12 lymph nodes for colorectal cancer should be examined for a correct assessment of N stage. **(Greene et al., 2002)**

Extended lymphadenectomy may cause a stage migration due to the increase in the number of metastatic lymph nodes. It would thus be useful to establish a corrective method for the number of lymph node metastases based on the total number of resected lymph nodes. The lymph node ratio may give more accurate prognostic information for nodal involvement than the current pN category of the TNM. **(Inoue et al., 2002)**

The ratio between metastatic and examined lymph nodes (N ratio) has been recently proposed as a novel prognostic factor that can identify prognostic subgroups among patients with N1 and N2 disease, and reduce the phenomenon of stage migration. **(Nitti et al., 2003)**

There is recent evidence that the ratio of metastatic to examined LNs (LNR) is an important prognostic factor in malignancies such as gastric cancer, esophageal cancer, breast cancer, and colorectal cancer. **(Berger et al., 2004)**

Chapter one

The Anatomy of Lymphatic System

The lymphatic system is an important component of the immune system. It includes lymphatic fluid, lymphatic vessels, lymph nodes, spleen, tonsils, adenoids, Peyer patches, and the thymus. Lymphatic fluid consists of an ultrafiltrate of blood collected within lymphatic channels, which run throughout the entire body. The fluid is slow-moving and is transported from the head and extremities to larger vessels, which then drain into the venous system. Along these channels reside approximately 600 lymph nodes. ***(Gow KW, 2010)***

Lymph nodes are composed of follicles and contain abundance of lymphocytes. Lymph is filtered through the lymph node sinuses, where particulates and infectious organisms are detected and removed. Because of the exposure to immune challenges, antibody and cell-mediated immunity is mediated. As a result of such normal processes, the lymph nodes can enlarge by proliferation of normal cells or infiltration by abnormal cells.

Lymph nodes are organized in groups that drain specific regions of the body. This knowledge guides the clinician to inspect particular areas of anatomy when lymphadenopathy occurs.

Lymphatic drainage of the head and neck is traditionally divided into 6 regions. The most important nodes in this grouping are around the internal jugular lymph nodes. The superior aspect is termed region II; it receives lymph from the supraglottic larynx, anterior nasopharynx, and oropharynx via submental and submandibular lymph nodes (region I). The middle portion of the internal jugular chain is region III; it collects drainage from the superior hypopharynx and superior larynx via direct drainage through lymphatic capillaries. ***(Standring S, et al, 2005)***

The inferior part of the internal jugular chain is region IV; it collects drainage from the inferior hypopharynx, inferior larynx, and thyroid and supraclavicular regions. Region VI sits in the anterior aspect of the neck; it contains supraclavicular, pretracheal, and thyroid nodes, which drain into region IV. Region IV of the internal jugular chain is the common collecting point for regions I-III and VI. Region V collects lymph from the scalp and posterior nasopharynx. All lymphatic drainage from region V and region IV on the internal jugular chain collect into the jugular trunk and then subsequently into the thoracic duct on the left or directly into the brachiocephalic vein on the right. ***(Standring S, et al, 2005)***

The thoracic cavity contains a distinct collection of lymph nodes, with a slightly complex drainage route that parallels bronchi,

arteries, and veins. Each major bronchi division has a collection of nodes called the intrapulmonary lymph nodes, which lie within the lungs and drain each of the lung's corresponding segments. The intrapulmonary nodes drain into a set of nodes, the left and right bronchopulmonary (hilar) lymph nodes, which are located at the junction of each lung and its main bronchi. These nodes collect the lymphatic drainage from the segments of their respective lung. ***(Gow KW, 2010)***

At the bifurcation of the trachea and beginning of each bronchus, 3 sets of nodes reside, the right and left tracheobronchial lymph nodes and the inferior tracheobronchial lymph nodes. An unusual feature of this anatomy is that the inferior tracheobronchial nodes, also known as the carinal nodes, collect lymph from the left lower lobe but drain that fluid into the right tracheobronchial lymph nodes. This is significant because a suspicious-appearing lymph node in the right hilar region should prompt evaluation of the left lower lobe and the right lung. ***(Standring S, et al, 2005)***

Aligned with the sides of the trachea are groups of nodes known as the right and left paratracheal lymph nodes, which collect lymphatic fluid from the right and left tracheobronchial nodes, respectively. The posterior thoracic cavity is drained via the intercostal lymph nodes and into the posterior mediastinal lymph

nodes. The anterior thoracic cavity is drained through the parasternal lymph nodes, which are located next to the sternum in the intercostal space. The parasternal lymph nodes collect lymph from the anterior mediastinum and communicate with the medial aspect of the anterior chest wall. The common drainage site for all of the aforementioned lymph nodes is into the jugular trunk and then into the thoracic duct on the left or directly into the brachiocephalic vein on the right. ***(Gow KW, 2010)***

The thoracic duct is the final common lymphatic drainage system for the lower extremities, pelvis, mesentery, most of the thoracic cavity, left upper extremity, and left head and neck. The thoracic duct is positioned on the right side of the aorta in the abdomen and receives lymph from the cisterna chyli. It ascends up through the thorax in the posterior mediastinum while receiving lymphatic drainage from the intercostal nodes. It crosses over to the left just below the carina and ascends to the level of the junction of the left internal jugular and left subclavian vein, where it connects into the venous system. The upper intercostal nodes and right apical axillary nodes drain directly into the right brachiocephalic vein via the right bronchomediastinal trunk, and lymphatic drainage from the right side of the head and neck drain directly into the right brachiocephalic vein via the right jugular trunk. ***(Standring S, et al, 2005)***