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PROCEEDINGS

STANDARDIZED OR PERSONALIZED LYMPH NODE DISSECTION VOLUME IN RIGHT-SIDED COLON CARCINOMA

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ABSTRACT

INTRODUCTION: Colorectal carcinoma is among the leading oncological diseases in frequency and mortality. There is no standard technique for right-sided colon carcinoma, and the length of the resection and the extent of the lymphadenectomy remain a matter of debate. Complete mesocolic excision (CME) and D3 lymphadenectomy could potentially become a standard approach for right-sided carcinoma in the future. With the rapid development of new technologies entering surgery, similar results can be achieved using personalized approach concerning the length of the resection and the extent of the lymphadenectomy.

AIM: The aim of this review is to compare current techniques, approaches, and technologies in right-sided colon resection for carcinoma, to discuss their advantages and disadvantages, as well as obstacles to their widespread implementation.

MATERIALS AND METHODS: We conducted a literature review after 2019 using the PubMed and Google Scholar databases. The keywords used were: "right colon", "cancer", "lymph node staging", "intraoperative", "surgery", "sentinel lymph node". Based on the results and after reviewing, we performed additional searches.

RESULTS: We did a comparison of a standard technique—CME and D3, and personalized intra-operative staging approaches using novel technologies—sentinel lymph node biopsy, indocyanine green lymph node mapping, optical coherence tomography, near infrared imaging, and fluorescence.

CONCLUSION: Complete mesocolic excision/D3 lymphadenectomy offers a standard method with good long-term results, but has a long learning curve and potentially serious intra-operative complications. Randomized controlled trials in personalized approaches need to be performed in order to prove their feasibility over the standard method. Some of them come at high cost, but offer limited resections and potentially rapid recovery and fewer complications.

Keywords: *right-sided colon cancer, CME, personalized surgery, lymphadenectomy*

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INTRODUCTION

Colorectal carcinoma is among the leading oncological diseases in terms of frequency and mortality with right-sided colon carcinoma being a prevalent subtype. Surgical resection remains the cornerstone of curative treatment. However, the extent of lymph node dissection in right-sided colon carcinoma has been a subject of ongoing debate. Lymph node

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involvement plays a critical role in staging and treatment planning for patients with right-sided colon carcinoma (1). Traditionally, the number of lymph nodes harvested during surgical resection has been considered an important marker for the adequacy of dissection. However, recent studies have suggested that the number alone does not necessarily reflect the quality of the dissection or accurately predict the patient's outcome (2).

There is a growing body of evidence, focusing on the significance of lymph node dissection volume, rather than just on the number of nodes examined (2). The concept of lymph node dissection volume includes various factors, such as the total number of lymph nodes examined, the ratio of positive to negative nodes, and the presence of high-grade tumor involvement within the nodes (3).

An adequate lymph node yield is important because it helps ensure that all potential areas of cancer spread are assessed. If only a few lymph nodes are examined, there is a risk of underestimating the stage of cancer and potentially missing areas of metastasis (3). On the other hand, a high lymph node yield indicates a more thorough examination, providing a more accurate assessment of the cancer's stage.

The introduction of national screening programs for bowel cancer has resulted in a higher number of early-stage tumors being detected. However, current imaging techniques are not effective enough to identify patients with nodal involvement before surgery, even though it is estimated that 10 to 20% of patients with stage T1 and T2 disease have nodal involvement. As a result, all patients with stage T1 and T2 colon cancer undergo major surgery, but en-bloc mesenteric resection does not offer significant therapeutic benefits for patients without nodal involvement.

There is no standard operative technique for right-sided colon carcinoma, and the length of resection and the extent of lymphadenectomy remain a matter of debate (4–6). Complete mesocolic excision (CME) and D3 lymphadenectomy could potentially become a standard approach for right-sided carcinoma in the future. With the rapid development of new technologies entering surgery, similar results can be achieved using personalized approach concerning the length of the resection and the extent of the lymphadenectomy (7,8).

Accurate staging of cancer is essential for determining the extent of the disease and guiding treatment decisions. Traditionally, staging has relied on pre-operative imaging and clinical assessment, but these methods have limitations in accurately characterizing the tumor stage. Approximately 15–25% of patients with colorectal cancer are initially diagnosed with lymph node metastases. Intra-operative staging plays a crucial role in determining the extent of resection needed. Having a reliable method of intra-operative staging is essential to ensure that the appropriate level of resection is performed. Undertreating the disease by opting for a less radical resection in a more advanced stage could increase the risk of recurrence and negatively impact overall survival. Conversely, overtreatment by opting for a more radical resection in an early-stage tumor may lead to unnecessary morbidity and decreased quality of life for the patient (6).

Personalizing the resection volume based on individual tumor stage, guided by reliable intra-operative staging methods, is crucial for optimizing outcomes in colorectal cancer surgery. This personalized approach can help tailor the extent of the resection to each patient's specific disease characteristics, maximizing the chances of complete tumor removal while minimizing the risk of overtreatment.

AIM

The aim of this review is to critically evaluate the importance of lymph node dissection volume in right-sided colon carcinoma by comparing current techniques, approaches, and technologies and to discuss their advantages and disadvantages, as well as obstacles to their widespread implementation.

MATERIALS AND METHODS

We conducted a literature review after 2019 using the PubMed and Google Scholar databases. The initial keywords used were: "right colon", "cancer", "lymph node staging", "intraoperative", "surgery", "sentinel lymph node". Only relevant literature in English was reviewed. Based on the results and the references in the articles, additional searches were performed.

RESULTS

Complete mesocolic excision with D3 lymphadenectomy are considered to be more extensive and radical surgical procedures compared to traditional colectomy techniques. They are associated with improved oncological outcomes. However, they require advanced surgical skills and expertise. The decision to perform CME and D3 lymphadenectomy is made based on several factors, including the stage of the cancer, the patient's overall health, and the surgeon's experience and judgment (5,6).

We performed a comparison of a standard technique—CME and D3, and personalized intra-operative staging approaches using novel technologies—sentinel lymph node (SLN) mapping, indocyanine green (ICG) lymph node mapping, radioisotope-guided SLN mapping, dual tracer method, carbon nanoparticles, real-time near-infrared imaging, and optical coherence tomography.

Indocyanine Green

Indocyanine green fluorescence imaging: ICG binds to lymphatic vessels and enables the visualization of the lymphatic drainage pathways and SLNs under near-infrared imaging. This technique helps identify the precise location of SLNs during the surgery (9–13).

Table 1 presents the advantages and disadvantages of the method.

Studies have reported detection rates using ICG mapping ranging from 82% to 95% for right colon resection, accuracy rates above 90%, demonstrating the reliability of ICG mapping in identifying metastatic lymph nodes and sensitivity rates ranging from 65% to 94% (13–15).

It is important to note that these rates can vary depending on various factors, such as the experience of the surgeon and the specific technique used for ICG mapping.

Tumor-Specific Imaging Methods

Tumor-specific imaging methods actively aim at tumor cells using a specialized probe that is designed to detect a molecule associated with the tumor or passively accumulate in the tumor due to its structural properties. The most basic system involves connecting a fluorescent substance to a ligand that specifically targets tumors. This probe usually is a fluorophore so this method is somehow similar to ICG mapping but tumor deposits could be visualized in addition to lymph nodes. Successful targeting of colorectal cancer was achieved in preclinical studies using near-infrared fluorescent antibodies, showing promising outcomes (10,16).

Radioisotope-Guided Intraoperative (RIGS) Sentinel Lymph Node Mapping

Various antibodies, usually anti-carcinoembryonic antigen (CEA) or anti-tumor-associated glycoproteins are commonly used as radioactive tracers.

Table 1. Advantages and disadvantages of ICG fluorescence imaging.

Advantages	Disadvantages
Real-time visualization: ICG emits a near-infrared fluorescent signal that can be detected and imaged in real-time using a specialized camera system	*Limited tissue penetration:* The fluorescent signal emitted by ICG has limited tissue penetration, usually up to 1–2 centimeters, which means that deeper lymph nodes may not be detected.
Enhanced lymph node identification: ICG provides high sensitivity and a great number of detected lymph nodes	*Variability in lymphatic drainage:* The lymphatic drainage patterns may differ between individuals, causing variation in the location and number of sentinel lymph nodes. This can affect the accuracy and detection rate of ICG mapping.
Non-radioactive	*Lack of standardized protocol:* There is currently no standardized protocol for the use of ICG in sentinel lymph node mapping, leading to variations in technique and interpretation across different centers.
Availability and cost: ICG is widely available and relatively inexpensive	

They are injected near the tumor site and their migration to the regional lymph nodes can be traced using a gamma probe during surgery. This technique allows real-time identification and removal of SLNs. Only case series have been published on RIGS for colon cancer (17,18).

Table 2 presents the advantages and disadvantages of the method.

The detection and accuracy rates using radioisotope-guided mapping are generally high, ranging from 90–95% in studies. The reported sensitivity of radioisotope-guided mapping ranges from 85–95%.

Table 2. Advantages and disadvantages of RIGS.

Advantages	Disadvantages
Accurate identification of sentinel lymph nodes: The use of radioisotopes allows for precise identification and mapping of the sentinel lymph nodes	Radiation exposure
Real-time guidance during surgery: Radioisotope-guided mapping provides real-time information about the location of the sentinel lymph nodes during surgery	*Additional cost and complexity:* Radioisotope-guided mapping adds an extra step and associated costs to the surgical procedure. It requires the availability of specialized equipment and trained personnel, which may not be readily available in all hospitals
Improved staging and prognostic information	

The Dual Tracer Method

The dual tracer method involves the use of two different tracers to identify and map the SLNs. Generally, a combination of both ICG fluorescence imaging and radioisotope-guided SLN mapping is used. The dual tracer method is particularly helpful when one of the techniques fails to detect SLNs due to technical limitations or anatomical variations (16,19,20).

Table 3 presents the advantages and disadvantages of the method.

The detection rate, accuracy rate, sensitivity and specificity are generally higher compared to using just one tracer.

Nanoparticles

Bionanotechnology is a rapidly developing field that is expanding into different areas of medicine. Because they are small, nanoparticles delivered through the bloodstream tend to build up in solid tumors passively, thanks to leaky blood vessels and ineffective drainage. Recent experiments with nanoparticles combined with a near-infrared cyanine fluorophore have shown promising results in targeting colorectal cancer, as well (21,22).

Carbon nanoparticles can be injected around the tumor site. They are taken up by the lymphatic

Table 3. Advantages and disadvantages of the dual tracer method.

Advantages	Disadvantages
Increased detection rate	*Increased complexity:* Using two tracers instead of one increases the complexity of the procedure, including the logistics of providing and administering two different tracers simultaneously
Enhanced accuracy: The dual tracer method helps to reduce false-negative results, as using two different tracers increases the chances of identifying and mapping all SLNs accurately	*Potential for technical difficulties:* Coordinating the timing and administration of two tracers may be challenging, and there might be technical difficulties associated with using both tracers intraoperatively
Improved sensitivity and specificity	*Higher cost:* Using dual tracers adds to the overall cost of the procedure
Comprehensive lymphatic mapping	

system and accumulate in the SLNs, making them visible. This technique provides high accuracy in SLN mapping and is especially useful in cases where other techniques fail (23).

Table 4 presents the advantages and disadvantages of the method.

Table 4. Advantages and disadvantages of nanoparticles.

Advantages	Disadvantages
Improved visualization	Limited availability
Higher detection rate	Higher costs
Improved accuracy	Lack of long-term data
Reduced false-negative results	
Simplified surgical procedure	

Studies have reported high detection rates—between 92% and 100%, using carbon nanoparticles. The accuracy rate can vary but is generally reported to be above 90%. Studies have reported sensitivity and specificity rates above 90%.

Real-Time Near-Infrared Imaging

Advanced imaging systems allow real-time visualization of the lymphatic drainage pathways and SLNs using near-infrared technology. The surgeon can directly observe the SLN mapping during the surgery, aiding in targeted lymph node dissection and minimizing the risk of missed SLNs (20).

Table 5 presents the advantages and disadvantages of the method.

The accuracy of near-infrared imaging in SLN mapping depends on various factors, including the surgical technique, experience of the surgeon, and quality of the imaging system used. However, studies have reported high accuracy rates, ranging from 90% to 99%. High sensitivity and specificity rates have been reported, ranging from 90% to 100%.

Optical Coherence Tomography

Optical coherence tomography (OCT) is an imaging technique that uses light waves to create detailed, cross-sectional images of tissue. It is commonly used in ophthalmology to visualize the retina and is now being explored for other applications, including intraoperative imaging. OCT can offer subsurface tissue visualization, enabling identification of cancerous infiltration beyond the lymph node capsule. However, OCT is still a relatively novel technique for SLN mapping in colorectal surgery, and further research is needed to evaluate its efficacy, accuracy, and potential impact on patient outcomes (24,25).

Table 6 presents the advantages and disadvantages of the method.

The detection rate, accuracy rate, sensitivity, and specificity of OCT vary across studies due to various factors, such as patient selection, operator expertise, and the OCT system used. However, several studies have reported promising results with OCT in SLN mapping for various cancers, suggesting its potential utility in right colon resection as well.

Table 5. Advantages and disadvantages of real-time near-infrared imaging.

Advantages	Disadvantages
Real-time imaging: Near-infrared imaging allows for immediate visualization of the lymphatic drainage in real-time during surgery	Cost
Improved detection rate	Learning curve
Enhanced accuracy	Contrast agents may be needed
Increased sensitivity	Limited depth of penetration
Minimal invasiveness	Lack of long-term data

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Table 6. Advantages and disadvantages of OCT.

Advantages	Disadvantages
Real-time imaging	*Limited field of view:* It is challenging to image larger areas
Non-invasive: It does not require the use of contrast agents or ionizing radiation	Operator-dependent
High resolution	Cost
Depth penetration: It can visualize tissue structures up to several millimeters deep	Lack of long-term data

DISCUSSION

Standardized lymph node dissection involves removing a predetermined number of lymph nodes regardless of the individual patient's characteristics or tumor characteristics. This approach ensures uniformity and allows for comparison of outcomes across different studies. However, it may result in unnecessary removal of lymph nodes in some patients, leading to increased surgical morbidity without significant clinical benefit. Complete mesocolic excision/D3 lymphadenectomy offers a standard method with good long-term results, but has a long learning curve and potentially serious intra-operative complications.

On the other hand, personalized lymph node dissection volume involves tailoring the extent of lymph node removal to individual patients based on various factors, such as tumor size, location, depth of invasion, and histologic grade. This approach aims to maximize therapeutic benefit by removing all potentially involved lymph nodes while minimizing unnecessary surgery. However, it lacks standardization and may lead to variability in practice patterns and difficulty in comparing outcomes between different studies.

The described techniques and technologies are constantly evolving, and newer approaches continue to emerge. The choice of technique or technology depends on various factors such as the surgeon's expertise, availability of resources, patient factors, and specific institutional protocols.

Randomized controlled trials in personalized approaches need to be performed in order to prove their feasibility over the standard method. Some of them come at high cost, but can offer limited resections and potentially rapid recovery with lower complication rates.

CONCLUSION

There is currently no consensus on whether lymph node dissection volume should be standardized or personalized in right colon carcinoma. Both approaches have their advantages and disadvantages, and further research is needed to determine the optimal strategy for lymph node dissection in this specific setting.

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