



Original Contribution

COMPARATIVE ANALYSIS OF COLON AND RECTAL CANCERS IN SENTINEL LYMPH NODE MAPPING

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ABSTRACT

The lymphatic status is the most important prognostic factor in patients with colorectal cancer. In our clinic, the intraoperative sentinel lymph node mapping with Patent Blue V is a routine method of choice for better staging of lymph node status and achieving an adequate extent of surgical procedure in patients with colorectal cancer. **Aim:** To compare the results from application of methods of intraoperative sentinel lymph node mapping between patients with colon cancer and patients with rectal cancer. **Results:** There were 136 consecutive patients (65 with colon and 71 with rectum). The sentinel lymph nodes were identified in 100 percent of colon and rectal patients. Skip metastases were found in 3.0 percent of colon vs. 2.81 percent of rectal patients. Occult micrometastases were found in 9 percent of colon vs. 7.0 percent of rectal patients. No other parameters were different between colon and rectum cancers. The sensitivity was comparable between the two cancers and the methods were reliable enough. **Conclusion:** It was required that the surgical approach and the extent of the lymph dissection conformed to the status of lymph node basin to create increased success with surgery in colorectal cancer. Sentinel lymph identification was highly successful for both cancers.

Keywords: Sentinel lymph node mapping, colon and rectum, cancer

INTRODUCTION

The diagnosis, staging and treatment of patients with colorectal cancer involve specialists from many different areas of medicine. Among these the surgeon takes the lead among these specialists. The method of choice is based upon some complex criteria, which include, the data on the stage of differentiation, a presence of extracellular or intracellular mucous secretion, the stage of tumour cell invasion in the lymphatics, arterioles, venules and in perineural space, the angiogenesis of the tumour, the mitotic index, the grade of lymphocytic infiltration in the tumour and the count of T-lymphocytes in the peripheral blood. The molecular and genetic prognostic factors from the primary tumour and metastatic origin, as well as morphological exploration and the ultrastaging of oncological disease are main fields of investigation.

The surgical treatment is at the base of complex medical treatment, which aims to cure definitely the patients with colorectal cancer. Good results from the curative process are obtained by modelling an individual protocol to every single patient, which conforms to the present medical consensus.

The quality of a surgical treatment is defined as well as the choice of appropriate operative approach, but also from the tumour characteristics, the vessels that uptake the lymph flow, and the modalities for preoperative and intraoperative staging.

Undergoing an adequate operation is a premise for precise morphological exploration of the oncological disease and defines the approach in the postoperative treatment. The curative procedures provide the best effect when the patient is diagnosed in the first or second clinical stage of the oncological disease, before the presence of tumour metastasis.

The lymph node status is the most

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important prognostic factor for patients with colorectal cancer. The exact preoperative staging of the lymph node status is an unsolved problem because of the sensitive methods for preoperative diagnosis – PET, CT, MRI and radioimmunoguided detection cannot be used as routine methods in every patient. The clinical examination and intraoperative exploration are not so sensitive; and specific methods could only lead the surgeon in a certain direction. Special intraoperative diagnostic methods were not established for the lymphatic status. Accordingly the surgeon can change his operative behaviour for obtaining a radical treatment. The standard histomorphological intraoperative examination is low-sensitive and cannot define the presence or absence of micrometastasis in lymph nodes. One of the present problems is the inability of exact determination of the lymph node status during the standard morphological examination of resected specimen. The morphologists cannot obtain enough lymph nodes and the ultrastaging techniques are not introduced in the routine practice for the lymph nodes with highest metastatic potential – the sentinel lymph nodes.

The consequences of an imprecise examination of lymph node basin lead to development of recurrence in 1/3 of the patients undergoing curative resections for non – metastatic colorectal cancer.

The first report of SLNM (sentinel lymph node mapping) in colorectal cancer was a feasibility study presented in 1997 at the Society of Surgical Oncology's 50th Annual Cancer Symposium in Chicago [1]. This series of 10 patients was followed by a series of 56 patients presented at the 17th International Cancer Congress in Brazil in 1998 [2]. This report confirmed the high (98%) feasibility of the technique and demonstrated its high (95%) degree of accuracy for predicting the status of the nodal basin. In 1999, Joosten et al. [3] in the Netherlands published a report of SLNM in 50 patients with colorectal cancer. On the basis of a feasibility rate of 70% and a false-negative rate of 60%, they concluded that SLNM was not a reliable method of staging colorectal cancer. However, their injection method and especially the timing of pathological examination differed from those described by us. Their results underscored the importance of adhering to strict technical details of the procedure and following a specific protocol for handling and processing of the specimen by the pathologist. A

subsequent publication in the *Annals of Surgical Oncology* outlined the technical details associated with excellent feasibility (99%) and accuracy (96%) rates as reported in our original studies [4]

In December 2000, Saha et al. [5] included co-author Wong's technique of ex vivo lymphatic mapping in colorectal cancer. Kitagawa's group focused on the use of SLMN in oesophageal, gastric, and colorectal cancers, and for the first time described the use of radio-labelled tracers and a hand-held gamma probe for successful lymphatic mapping in colorectal cancer [6].

Thorn [7] in 2000 and Merrie et al. [8] in 2001 combined blue dye and radioactive tracer for mapping, as previously described in breast and melanoma. The success rates of dual-agent mapping were 100% [7] and 88% [8]. In 2001, Wood et al. [9] reported a series of 75 patients who underwent lymphatic mapping by in vivo, ex vivo and laparoscopic techniques [9]. The overall success rate of mapping was 96%, and the rate of occult micrometastasis was 17%.

The first large series of ex vivo SLNM in colon and rectal cancers was published by Wong et al. in 2001 [10]. Laparoscopic SLNM has been attempted at a few centres for colorectal and gastric cancers, with high success rates [9, 11] comparable to those associated with mapping performed during open laparotomy. Also in 2001, Bilchik et al. [12] first reported molecular profiling of colon cancer with use of the RT-PCR technique for multiple markers in 40 patients. This study showed a high correlation between the expression of p53, beta-HCG, c-Met, and uMAGE in a primary tumour and the presence of micrometastases in regional lymph nodes.

AIM

To compare the results from application of methods of intraoperative sentinel lymph node mapping in patients with colon cancer vs. patients with rectal cancer.

MATERIAL

We made a prospective study for a period of 2004 – 2006, in 242 patients, operated for colorectal cancer. The investigation was conducted in the clinic of general and operative surgery in the University Hospital "St. Marina", Varna.

In 136 of the cases we applied the method of intraoperative sentinel lymph node mapping.

METHODS

We applied the next modes of lymphatic mapping:

1. Intraoperative sentinel lymph node mapping in 71 patients with rectal cancer.
2. Intraoperative sentinel lymph node mapping in 65 patients with colon cancer.

STATISTICS

In the statistical processing of our data we used the following methods:

1. Estimating the indexes for the relative share.
2. Estimating of the average values.
3. Tables
4. Charts

We developed and suggest the following algorithm for intraoperative sentinel lymph node mapping in patients of colon and rectal cancer **Figs..1, 2, 3, 4, 5, 6 and 7.**

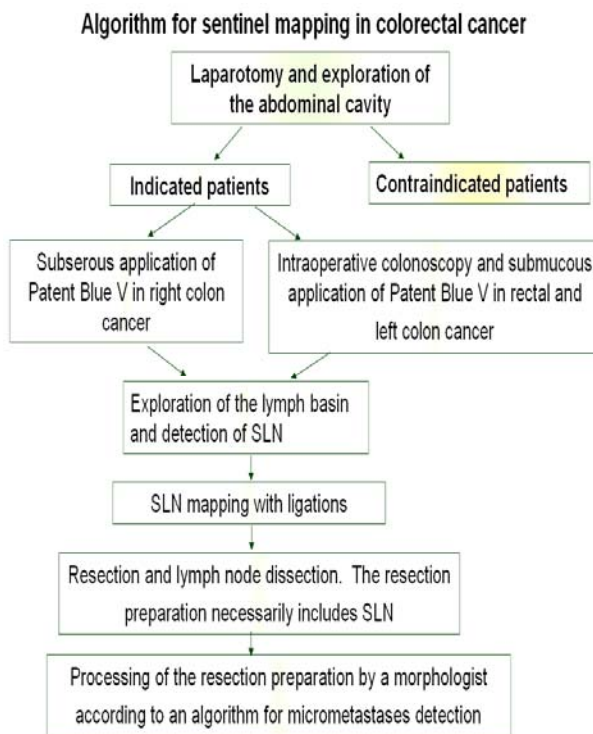


Figure 1. Algorithm for sentinel mapping in colorectal cancer



Figure 2. Intraoperative colonoscopy

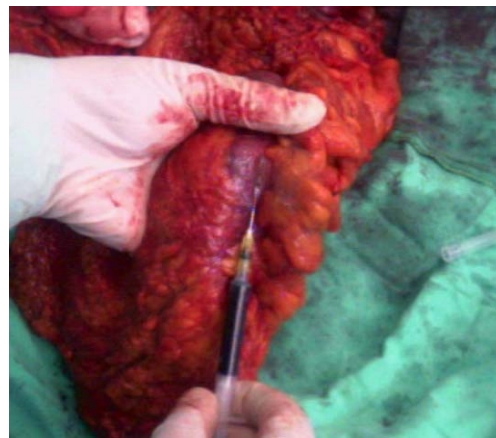


Figure 3. Subserosal application of Patent Blue dye

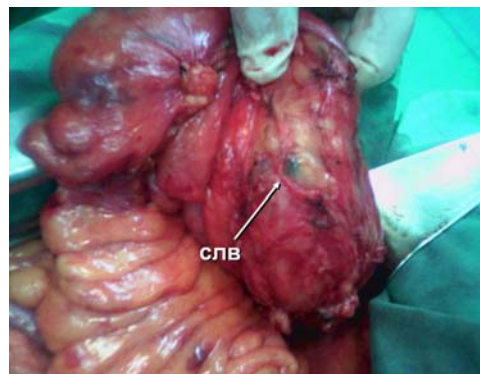


Figure 4. Sentinel Lymph Node – mesorectum-laparotomy

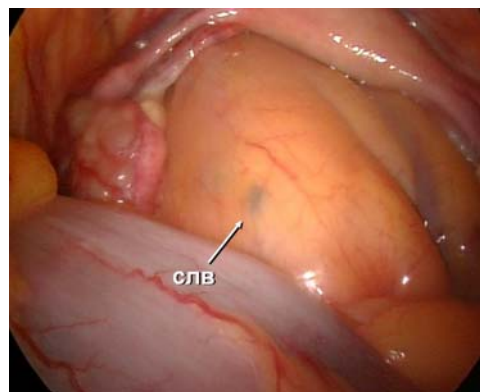


Figure 5. Laparoscopic view of sentinel lymph node of mesorectum

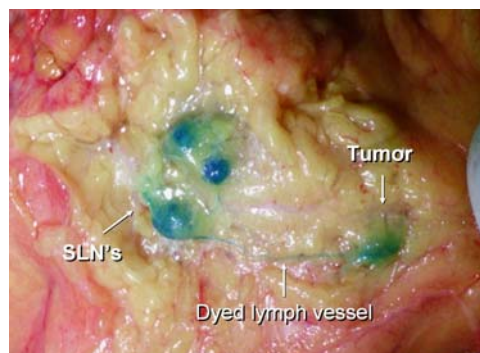


Figure 6. Tumour of the colon, peritumoral injecting of Patent Blue V dye. Gained direct visualization of the lymphatic, draining the primary tumour to tree sentinel lymph nodes

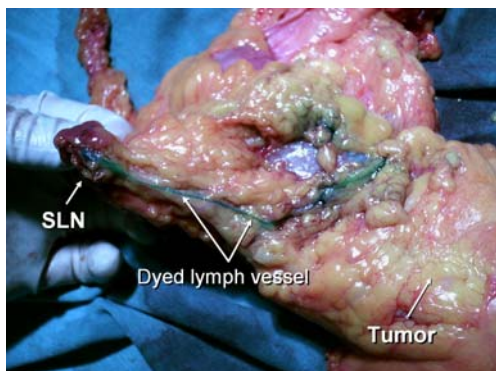


Figure 7. Dyed with Patent Blue V is demonstrated on the figure connecting the tumour with a sentinel lymph node from third level

RESULTS

We present the distribution of the patients in localization, sex and age in the following **Tables 8, 9, and 10.**

Table 8. Distribution of the patients

| Localization Groups of patients | Colon cancer | Rectal cancer | Total |
|------------------------------------|--------------|---------------|------------|
| Patients (n) | 65 | 71 | 136 |
| Male (n) | 30 | 33 | 63 |
| Female (n) | 35 | 38 | 73 |
| Average age (years) | 63 | 66 | 65 |

Table 9 Average numbers of lymph nodes and sentinel lymph nodes in the resected specimen.

| Localization Lymph nodes | Colon cancer | Rectal cancer |
|-----------------------------|--------------|---------------|
| Lymph nodes (n) | 15,2 | 13,6 |
| Sentinel LN (n) | 1,9 | 1,6 |

Table 11 Summarized results from the application of intraoperative sentinel lymph node mapping in cases of colorectal cancer

| Cases | Colon cancer | | Rectal cancer | | Total | |
|---------------------------|--------------|-----|---------------|-----|------------|------------|
| | n | % | n | % | n | % |
| Patients | 65 | 48 | 71 | 52 | 136 | 100 |
| Successful SLNM | 65 | 100 | 71 | 100 | 136 | 100 |
| Presence of LN metastases | 34 | 52 | 38 | 54 | 72 | 53 |
| False-negative | - | - | 3 | 4 | 3 | 2 |
| Metastases only in SLNs | 8 | 12 | 9 | 13 | 17 | 13 |
| micrometastases | 6 | 9 | 8 | 11 | 14 | 10 |

Table 10 Distribution of the patients depending on sentinel lymph nodes

| Patients (n) Lymph Nodes | n | % |
|-----------------------------|----|----|
| 1 | 54 | 40 |
| 2 | 53 | 39 |
| 3 | 26 | 19 |
| 4 | 3 | 2 |

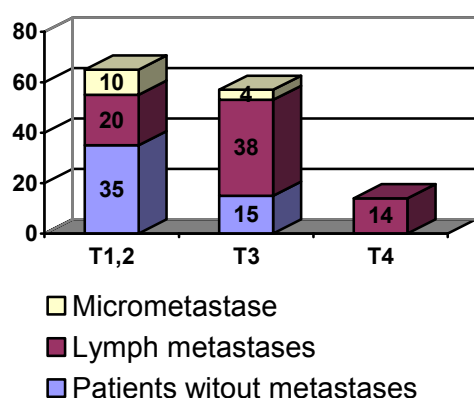
We found metastases and micrometastases in 57% (112 of 196) of the SLNs, compared to 9% (198 of 2208) in non-SLNs.

In case of absence of metastases in SLNs, the possibility for presence of non-SLNs is only 0.6% (4 of 658), **Tables 11, 12, and Figure 13.**

From the group of 136 patients, 65 (48%) of them were with T_{1,2} – stage of the primary tumour; 57 (42%) of them were with T₃ – stage of the primary tumour; 14 (10%) of them were with T₄ – stage of the primary tumour. It is underlined that from the T_{1,2} group of 65 patients, 20 (31%) of them were with presence of LN’s metastases and 10 (15%) of them were with micrometases. From the T₃ group of 57 patients, 38 (66%) of them were with presence of LN’s metastases and 4 (7%) of them were with micrometases. From the T₄ group of 14 patients, 14 (100%) of them were with presence of LN’s metastases and 0 (0%) of them were with micrometastases. It is demonstrated that the micrometastases were more often present in cases of lower T-stage of the primary tumour.

Table 12 Ratio between T-stage of the primary tumor and the presence of lymph node metastases after application of SLNM

| <i>T stage</i> | <i>T1,2</i> | | <i>T3</i> | | <i>T4</i> | |
|-----------------------------|-------------|----------|-----------|----------|-----------|----------|
| | <i>n</i> | <i>%</i> | <i>n</i> | <i>%</i> | <i>n</i> | <i>%</i> |
| <i>Metastases in LN</i> | | | | | | |
| Patients | 65 | 48 | 57 | 42 | 14 | 10 |
| Presence of LN's metastases | 20 | 31 | 38 | 66 | 14 | 100 |
| Micrometastases | 10 | 15 | 4 | 7 | - | - |

**Figure 13.** Ratio between T-stage of the primary tumour and the presence of lymph node metastases after application of SLNM

CONCLUSION

1. The method of intraoperative sentinel lymph node mapping with Patent Blue V is an accurate and objective diagnostic method for evaluating of lymph basin status in patients with colorectal cancer. The method is an objective intraoperative criterion for determination of surgical decision making. .
2. The method of intraoperative sentinel lymph node mapping is feasible and has a high success in patients with colorectal cancer. The method is high successful and sensitive, respectively 100% and 98%.

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