Original Article

ILIAC LYMPH NODES FLOW AND METASTASES IN MIDDLE AND LOWER RECTAL CANCER

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Summary

There are controversial views regarding the role of iliac lymph flow and metastases in middle and lower rectal cancer. We defined the role of lymph flow and metastases in middle and lower rectal cancer (MLRC) in iliac lymph nodes. Over a period of two years, 40 patients were operated on for MLRC. Two combinations of techniques (radionuclide imaging and staining) of sentinel lymph node (SLN) mapping and biopsy were applied. Iliac radioactive and stained lymph nodes were found in four of the patients, using the first combination. Four cases with iliac SLNs were found, using the second combination. In one case (2.5%), iliac lymph node metastasis was detected. The three lymph node biopsy methods for detecting metastases in the iliac lymph pool (macromorphological, sampling and lymph mapping) lead to results controversial with the theory that lateral lymph node metastases are relatively common.
Key words: rectal cancer, iliac lymph node, metastasis, sentinel biopsy

Introduction

There is no consensus concerning the direction of lymphatic drainage and metastasis in rectal cancer, and this lack is attributable to the peculiarities of rectal lymph flow whose course tends to follow the course of the respective vascular system (mesenteric, iliac). Based on these peculiarities, results reported from clinical studies on the problem also vary. Against this background, there is a variety of approaches in determining the extent of lymph node dissection which is deemed appropriate in radical surgery for rectal cancer.

Two opposing views on the issue are held in the surgical oncology scientific community. Japanese surgeons mostly recommend mandatory iliac dissection as a stage of surgical treatment in middle and lower rectal cancer. To support this view, they have reported both anatomically normal iliac lymphatic drainage and high rates (15-20%) of detected iliac lymph metastases after extended lymph node dissection [1, 2, 3, 4]. According to Takahashi [5], there are three anatomical spaces around the rectum: the internal space between visceral pelvic fascia on the posterior side and the Denonvilliers' fascia anterior to the rectum, the intermediate space limited by the parietal pelvic

fascia on the posterior side and the internal iliac arteries and their branches on both lateral pelvic sides and on the anterior side, and the external space located outside the internal iliac arteries and their branches. This is the reason why Japanese authors believe that lateral lymphatic drainage is anatomically reasonable, yet they note the major role of the lymph drainage along the inferior mesenteric artery.

In a nation-wide clinical study on rectal cancer incidence, involving 9 296 patients in Japan, Mori (1998) found lateral lymph metastases in 9.2% of them [2]. N. Ueno and al. (2001) established lateral metastases in 21.2% of the patients with T3 tumors [6]. In patients with tumors of the lower rectum, lateral metastases accounted for 13% of metastases for all stages, and for 25.5% of the cases in Dukes stage C. The presence of metastases in the early stages confirms the theory of the natural course of lymphatic drainage and metastases in the pelvic lymph nodes. In a number of studies, Japanese specialists have reported long-term clinical studies, demonstrating better local disease control and longer survival after extended lymph node dissection [2, 3].

European surgeons express an opposite viewpoint, claiming that there is usually no iliac lymphatic drainage in the middle and lower rectal thirds. F. Stelzner and al. (2001) have found that in the colon and rectum, as part of the visceral compartment of the body, the lymphatic drainage and metastases are only in mesorectum and only on the cranial side, never crossing into the lateral pelvic-iliac system [7]. The lateral lymph flow is described as a non-anatomical pathway. In the presence of a rectal cancer, infiltrating the mesorectum laterally, T3 and T4 tumors or a blockage in the mesenteric lymph drainage, an alternative iliac lymphatic drainage route is seen [8]. The conception that the rectum and the mesorectum, both enveloped by the visceral pelvic fascia, is as a single embryonic and anatomic unit, in which the initial spread of the tumor process begins and remains within it for a long time, has served as a ground to accept the idea that removal of this structure by total mesorectal excision (TME) is needed for optimal surgical treatment of rectal cancer. After TME, the frequency of local recurrence is less than 10% [9, 10]. This has made surgeons ignore the iliac lymph nodes and their surgical removal. According to the 6th TNM edition, metastases in the lymph along the internal iliac artery are classified as regional ones. This implies that it is necessary to pay attention to their local treatment [11].

Based on these conflicting claims, the aim of this study was to establish the presence or absence of lymphatic drainage and metastases in iliac lymph nodes in cases of middle and lower rectal cancer, using the methods of sentinel lymph nodes (SLN) biopsy.

Materials and Methods

The two-year study included 40 patients, operated on for middle or lower rectal cancer according to staging and localization. Prior to surgery, all patients had been diagnosed with middle and lower rectal cancer clinically, endoscopically and histologically. None of the patients had undergone previous surgery in the recto-anal area. Standard operative interventions according to staging and localization were performed: low anterior resection with TME (28 patients), abdomino-perineal extirpation after Miles (9 patients), and resection after Hartman (3 patients). Stages of disease were as follows: $pT_{1-2}N_{0,}T_{3-4}N_0$ - 25 patients, and $T_{3-4}N_{1-2}$ - 15 patients.

Various techniques for SLN mapping were applied.

Tc^{99} Nanocoll marker (1.5 ml) was injected through the anus with a rigid rectoscope submucosally 1 cm below and round the tumor under direct vision at 3, 6 and 9 o'clock, 17-20 hours before the operation after informed consent from the patient. Submucosal injection was verified by visible protrusion of the mucosa. The activity of radio-colloid solution was 110-140 Mbq. For better visualization of the field, we used optical glasses with a small magnification and a large focal length (Fig. 1). Early (up to hour 1) and late (up to hour 4) lymphoscintigraphy was performed with a double-head rotating gamma camera SPECT, Toshiba (Fig. 2).

Intraoperatively, Patent Blue V was injected submucosally in the same manner around the tumor at 3, 6 and 9 o'clock. The injected volume was 0.5 ml for each site.

The green dye (Indocyanine green) was injected intraoperatively in the mesorectum at the level of the so-called lateral ligaments of the rectum. The amount of dye injected was 1 ml in both sites.

When the posterior side of rectum had been mobilized, the pelvic walls and mesorectum were inspected to detect stained and radioactive lymph nodes. The radioactively labeled lymph nodes

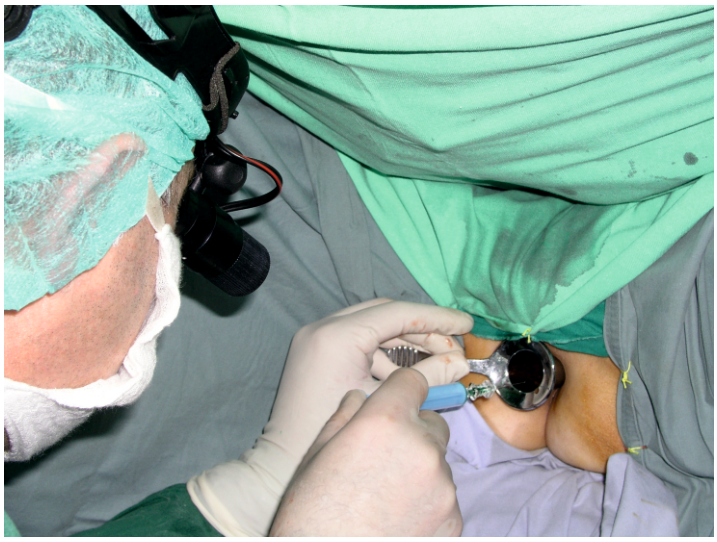

Fig. 1. Tc^{99} Nanocoll marker injected with a rigid rectoscope.

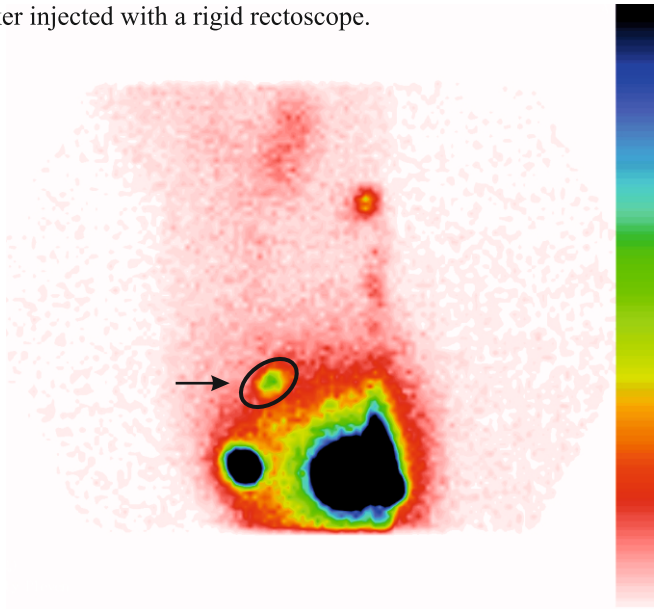

Fig. 2. Lymphoscintigram obtained with double-head rotating gamma camera SPECT, Toshiba (anteroposterior aspect), with a labeled lateral SLN.

were located manually using a gamma probe (Gamma Finder System, Silicone instruments).

The lymphoscintigraphic data was used as a reference. Radioactive and stained nodes stitched (Fig. 3 and 4). Removed SLN were investigated immunohystochemically.

When sentinel lymph nodes were not detected after removing the specimen, the iliac area, the obturator fossa and the pelvic wall were thoroughly examined for suspected macroscopic metastatic lymph nodes. In case such nodes were detected, they were also analysed. When macroscopic data for suspected metastatic iliac lymph nodes were not found, biopsy samples of bilateral internal iliac artery region and bilateral obturator fossa region were studied histologically and morphologically.

Two combinations of methods for SLN mapping were used. The first combination included preoperative radionuclide mapping combined with intraoperative injection of Patent BlueV and Indocyanine green, and was applied in 20 patients. If no evidence for SLNs was found, a careful inspection of pelvic walls and sampling biopsy were performed. The second combination included intraoperative injection of Patent BlueV and Indocyanine green, and was applied in 20 patients. If no evidence of SLNs was found, the pelvic walls were thoroughly examined, followed by sampling biopsy.

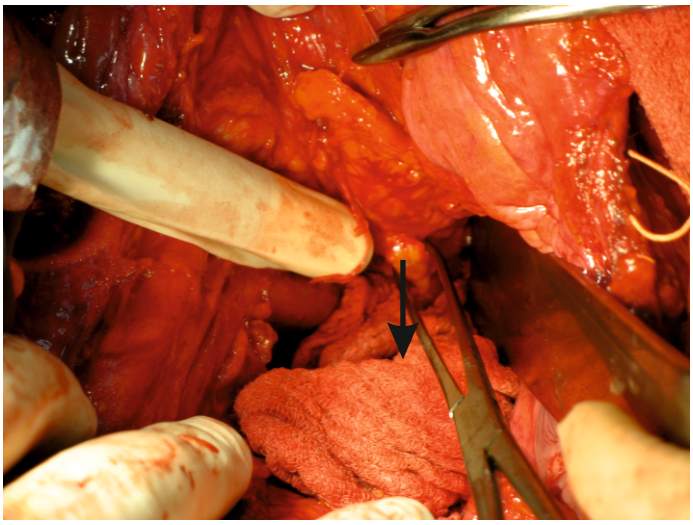

Fig. 3. Iliac radioactive SLN detected with a manual Gamma Probe (Gamma Finder System, Silicone instruments).

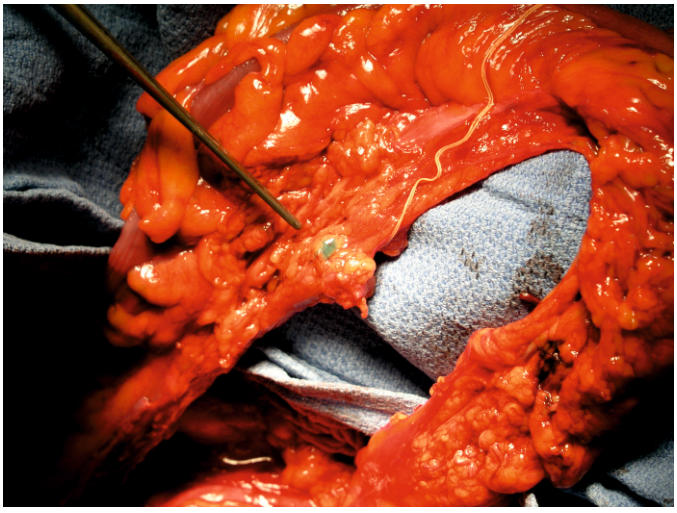

Fig. 4. Blue stained mesorectal SLN.

Results

In four of the patients, the application of first combination of methods revealed iliac sentinel lymph nodes. (Table 1) In one of these patients, the radioactive lymph node was located in the left common iliac artery. In another, the radioactive node was in the left internal iliac artery. Two radioactive SLNs, located around the left external iliac artery were found in the third patient. A blue-stained and radioactive lymph node around the right external iliac artery was detected in the fourth patient. According to the lymphoscintigrams, all mapped SLNs were identified using a manual gamma probe. Lymph node metastases were not proved by immunohistopathological analyses.

Of the 20 patients, in whom the second combination of methods was applied, four were found with iliac SLNs. (Table 2). The location of the SLNs in three patients was around the left internal iliac artery, and in the fourth patient the SLN was located at the right iliac artery bifurcation. Blue-stained lymph nodes were detected and defined as sentinel. In one of the patient with SLN around the left internal iliac artery, two green-stained SLNs were found along the right internal iliac artery. Immunohistopathological analyses did not confirm lymph node metastases.

In all other patients with absent lymphatic iliac flow (32 cases), inspection of the pelvic wall and sampling biopsies were performed. Macroscopic metastatic iliac lymph nodes were suspected in three of them. Following histopathological analysis, peri- and intraneural invasion of a lymph node was found in one of the cases (Fig. 5). Macroscopically suspected

Table 1. Cases with iliac mapping lymph nodes – first combination of methods

Patient	T	N	M	Middle third	Lower third	Left iliac Region	Right iliac Region
1	4	1	1		+	1 SLN	
2	3	1	0		+	2 SLNs	
3	2	0	0	+		1 SLN	
4	3	0	0		+		1 SLN

Table 2. Cases with iliac mapping lymph nodes –

Patient	T	N	M	Middle third	Lower third	Left iliac Region	Right iliac Region
1	2	0	0		+	1. SLN *	
2	3	0	0		+		1. SLN *
3	4	1	0		+	1. SLN *	
4	3	1	0		+	1. SLN *	2 SLNs**

*Blue-stained lymph nodes, ** Green-stained lymph nodes

metastasis in the second case was not confirmed histologically. Lymph metastasis of adenocarcinoma was histologically confirmed only in the third case. Forty-one lymph nodes were harvested by sampling biopsies. Lymph node metastases were not identified after histopathological investigation.

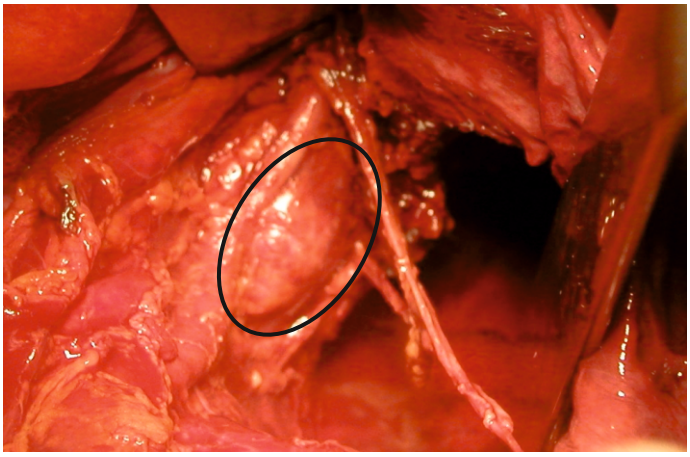

Fig. 5. Lateral lymph node with macroscopically suspected metastasis after exploration of left lateral pelvic wall.

Discussions

We investigated the iliac lymph status by inspecting mapped nodes and labeled them as sentinel, in accordance with the modern theory of SLN biopsy. After injecting a radionuclide or Patent Blue submucosally, we detected lymphatic iliac flow in 20% of the cases. Similar results have been reported by other authors. Quadros et al. (2006) used the method of sentinel biopsy in rectal cancer in 30 patients, injecting technetium and, immediately after that, Patent Blue submucosally or subserosally under anesthesia [12]. They detected radioactive lateral lymph node in seven cases (23%), and blue-stained lateral lymph nodes in only three patients (10%). Cutini et al. (2001) mapped 11 patients with Tc ^{99sh} human albumin colloids preoperatively, and detected iliac lymph nodes only in two cases [13]. They had difficulties applying the method of sentinel biopsy in anorectal tumors because there was more than one possible area for lymphatic drainage, unlike in malignant melanoma and breast cancer.

In 87.5% of the cases in our study with lateral lymphatic flow, localization of the tumor was in the lower third of the rectum, occurring mainly in locally advanced pT_3 and T_4 tumors (75% of cases).

Sterk et al. have suggested that lateral lymph flow in SLN mapping might be attributed to deeper application of the radiocolloid [8]. To ensure precise submucous application, we made sure that the injector could not go deeper by placing a stop 4 mm from the tip of the injector.

In four out of eight cases with mapped non-metastatic iliac lymph nodes, metastatic mesorectal lymph nodes were found. This indicates a high rate of false-negative cases, but a conclusive assessment of the sensitivity of the

method can be made after studying a larger mumber of patients. In the cases we studied, lymph node metastases were not found in any of the biopsied and immunihistochemically analysed SNLs.

Immunohistochemical examination of the biopsied lymph nodes provides maximum accuracy in determining the lymph node status. Some studies indicate that this provides upstaging of 13%-15% of patients [12, 14].

Sampling biopsy targets in the iliac area are described as the most common metastatic lateral lymph nodes in middle and lower rectal cancer [15]. Although sampling biopsy of metastasis lymph nodes does not yield reliable information about the status of the whole basin, not finding metastasis supports the theory of the minor importance of this lymphatic flow and metastases. Only in one case (2.5%) iliac lymph node metastasis was found.

Using SLN mapping in middle and lower rectal cancer for preoperative and intraoperative detection of extramesorectal lymph nodes metastases could improve the quality of staging [12, 13]. In case iliac lymph flow is detected, a more extensive lymph node dissection is possible. This is manageable, without any additional risk of postoperative complications, and does not affect life quality of patients.

Conclusion

The three lymph node biopsy methods for detecting metastases in the iliac lymph pool (macromorphological, sampling and lymph mapping) lead to results controversial with the theory that lateral lymph node metastases are relatively common.

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