



Lateral Pelvic Lymph Node Dissection in Locally Advanced Rectal Cancer

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Editorial

Colorectal cancer is the most common of the gastrointestinal system cancers and the fourth most prevalent among all malignancies [1]. Rectal cancer constitutes about one third of all colorectal cancer cases [2]. Rectal cancers, particularly those with lower localizations (located below the peritoneal reflection), show higher local recurrence rates due to their anatomic residence within the pelvis, leading to significant mortality and morbidity. Local recurrence of rectal cancers has devastating consequences in that they often lead to severe pain, and are usually not curable.

Advances in the treatment of rectal cancer have diminished the local recurrence rates, and in some instances, positively contributed to the overall survival. Total mesorectal excision (TME), first described by Heald, has become the gold standard in rectal cancer treatment, since it was shown to provide a dramatic reduction in local recurrence rates [3-5]. However, TME does not involve any approaches for lateral pelvic lymph nodes (LPLN), which may be a source of local recurrences. Tumor containing LPLNs were reported to be found in about 10% - 20% of the rectal cancer patients [6,7]. Eastern and Western countries perform different treatment approaches aiming to achieve lower rates of local recurrence, which occurs through spreading of tumor across the mesorectum. Either extended lymphadenectomy, or lateral pelvic lymph node dissection (LPLND) is performed along with TME in Eastern countries, particularly in Japan. There are a large number of studies demonstrating that LPLND in combination with TME reduces the local recurrence rates and contributes positively to the survival [8-11]. However, LPLND brings about a higher morbidity as means of urinary and sexual dysfunction [12-14]. In Western countries, on the other hand, lateral pelvic lymph node involvement is considered to be metastatic disease, and no surgical intervention is performed on this site during the local treatment [15].

Lymphatic channels accompany the arteries in their course. The upper and the 1/3 middle portion of the rectum drains to the inferior mesenteric lymph nodes; whereas, the 1/3 lower part drains to the inferior mesenteric nodes upwards, and to internal iliac nodes laterally. Perianal lymphatic plexus receives the lymphatic drainage of the anal canal below the dentate line, and further proceeds to the inguinal lymph nodes. The lymphatic spread of the tumors with mid and lower rectal localizations is to the superior and lateral lymph nodes, while upper rectal tumors spread to the superiorly residing nodes only [16].

The lateral lymph nodes include the common iliac lymph nodes, the internal iliac lymph nodes, the obturator artery lymph nodes, and the external iliac lymph nodes.

There are several studies in the literature evaluating the risk factors for LPLN involvement. Tan et al. [17] reported female gender (relative risk for male gender: 0.441; $p < 0.001$), tumor stage above T3 (relative risk: 2.775; $p = 0.003$), tumor differentiation (relative risk: 2.251; $p = 0.002$), status of the pathologic regional lymph nodes (relative risk: 3.101; $p < 0.001$), and lymphatic invasion (relative risk: 1.935; $p = 0.009$) as the risk factors for LPLN metastasis [17]. LPLN involvement rates among the patients with no risk factor and having 1, 2, 3 and >3 of the above were 0.6%, 2.7%, 9.3%, 23%, and 42, 6%, respectively. In the study, the local recurrence rate among the patients having less than 3 of the risk factors mentioned above was calculated to be 4.7%, and the recurrence rate was 7.4 times higher when 3 or more risk factors were present [17]. Fujita et al. [18] identified the risk factors for lymph node involvement as tumor differentiation (relative risk: 4.05; $p = 0.009$), tumor localization (below vs. above the reflection; relative risk 12; $p = 0.009$), status of the pathologic regional lymph nodes (relative risk: 7; $p = 0.002$), and presence of LPLN by CT scan (relative risk: 28; $p < 0.001$).

The prevalence of lateral pelvic lymph node involvement in lower rectal cancers is between 10% - 20% [19,20]. Total mesorectal excision procedure doesn't involve the dissection of lateral pelvic

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lymph nodes, therefore the lateral nodes left resident may become niches for local recurrences and severe morbidity (e.g. severe pain, difficulties in respectability) [19,21,22]. LPLN involvement is reported to lead to a significant recurrence rate of 58.1% [23]. The recurrence patterns emerge as intrapelvic (17.5%), hematogenous metastasis (25.3%), and both intrapelvic and hematogenous metastasis (5.1%) [23]. There are several treatment modalities in rectal cancers, aiming to reduce the local recurrences emerging from involved LPLNs. In the East, especially in Japan, LPLN dissection is performed in addition to TME to treat the potentially involved LPLNs. Numerous studies are available [21,24] reporting that this approach has a success rate of 45%-55% [23] in diminishing the postoperative local recurrences in the patients with locally advanced rectal cancer. On the other hand, LPLND gives rise to higher morbidity rates, particularly due to sexual and urinary dysfunction [11,22]. Rates of urinary and sexual dysfunction after LPLND are reported to be between 50% - 75% [22]. Therefore, in Western countries, neoadjuvant radiotherapy is chosen in combination with TME, in order to sterilize the lateral pelvic nodes and decrease the local recurrence rates. Neoadjuvant radiotherapy (NRT) has been reported both to be an effective modality in reducing the local recurrence rates [25,26], and to cause a lower morbidity compared with LPLND, in several studies [22]. However, the efficacy of NRT on the diseased lateral pelvic lymph nodes has not yet been shown clearly; and contradicting literature are also available, presenting cases with persistent lateral pelvic node involvement despite NRT administration, and suggesting that NRT deteriorates the prognosis [27]. Kim et al. [28] detected pelvic recurrence rates of 12.5% (6/48) and 68.8% (11/16) among the patients with LPLNs of 5-10mm and >10 mm transverse diameters by pre-NRT MRI imaging, respectively. Akiyoshi et al. [27], in their prospective series of 127 cases, described the positive effects of selective LPLND performance on the local recurrence rates (0/38 in LPLND+TME, and 3/89 in TME only) among the cases with positive LPLNs detected by pre-NRT imaging studies.

There are a number of studies from Japan demonstrating that TME+LPLND approach decreases the local recurrence rates and positively effects the survival in lower rectal cancer cases [21,29]. The patients included in those studies did not undergo NRT, which brings obstacles to compare the results with the ones from Western countries which include NRT administration. Watanabe et al. [30] has not found any significant differences between the patients underwent NRT + TME and TME + LPLND regarding local recurrence and survival rates, in their retrospective series of 115 patients. Nagawa et al. [31] studied 51 patients in their prospective randomized series, and compared the patients underwent NRT only and underwent NRT with TME + LPLND, revealing no difference in local recurrence and survival rates between the groups; however, they reported that sexual and urinary dysfunction rates were significantly higher in the LPLND group (92% and 45%, $p=0.02$ vs. 65% and 27%, $p=0.02$). In the study by Kim et al. [28], the effects of postoperative chemoradiotherapy (CRT) and LPLND were compared in 485 patients, and the local recurrence rates in LPLND group were found to be 2.2 times higher than those in the postoperative CRT group (16.7% vs. 7.5%, $p=0.044$). Finally, Kusters et al. [32] compared the results of the Netherlands series of 379 cases in which NRT and TME were performed, with the results of the Japanese series of 324 patients who underwent TME + LPLND without NRT; and they have not found any significant differences between the two series regarding the local recurrence rates and disease-free survival.

There are several reports demonstrating that LPLND procedure increases the duration of operation and bleeding volume. The preliminary results of an ongoing study by The Japanese Colorectal Cancer Group demonstrate longer operation time and increased intraoperative bleeding volume with LPLND [11,33].

The approaches to lateral pelvic lymph nodes in lower rectal cancers differ between Japan and the Western countries. In Western countries, lateral pelvic node involvement is considered as metastatic disease, therefore the standard treatment is total mesorectal excision combined with neoadjuvant chemoradiotherapy. Whereas in Japan, lateral pelvic node metastasis is accepted to be curable with excision, and dissection of lateral pelvic lymph nodes is performed along with total mesorectal excision for the treatment of locally advanced rectal cancers [34].

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