



ORIGINAL ARTICLE

The significance of extended lymphadenectomy for colorectal cancer with isolated synchronous extraregional lymph node metastasis



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KEYWORDS

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Summary *Background/Objective:* The significance of extended lymphadenectomy for colorectal cancer with extraregional lymph node metastasis, such as para-aortic lymph node metastasis, has not been established. The purpose of this study was to evaluate the significance of extended lymphadenectomy for colorectal cancer with synchronous isolated extraregional lymph node metastasis.

Methods: Between July 2004 and December 2013, 16 patients with synchronous extraregional lymph node metastasis without other organ metastases underwent curative resection and extended lymphadenectomy (R0 group). The clinical characteristics and survival outcomes of the R0 group were compared with those of 12 patients with extraregional lymph node metastasis who underwent palliative surgery (control group).

Results: In the R0 group, the 5-year cancer-specific survival (CSS) rate was 70.3% and the 5-year relapse-free survival (RFS) rate was 60.5%. The 5-year CSS differed significantly between the R0 and control groups (70.3% vs. 12.5%; $p = 0.0003$). Univariate analyses revealed that the total numbers of metastatic lymph nodes and metastatic regional lymph nodes present were significantly associated with RFS ($p = 0.019$ for both).

Conflicts of interest: All authors declare that they have no conflicts of interest.

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Conclusion: Findings from our study suggest that extended lymphadenectomy for colorectal cancer with synchronous isolated extraregional lymph node metastasis might be effective in carefully selected patients.

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1. Introduction

Approximately 20% of patients with colorectal cancer are diagnosed with Stage IV cancer.¹ With recent advances in systemic chemotherapy and improvement in the survival of patients with stage IV colorectal cancer,^{2,3} more aggressive hepatic or pulmonary resection has become a standard strategy for liver or lung metastasis when R0 resection can be achieved.^{4–7} However, the clinical significance of extended lymphadenectomy for synchronous extraregional lymph node metastasis, such as para-aortic lymph node (PALN) metastasis in colorectal cancer, remains highly controversial. Generally, extraregional lymph node metastasis is considered a systemic disease that is not amenable to surgical cure. There are very few studies on the benefit of extended lymphadenectomy for synchronous isolated extraregional lymph node metastasis in colorectal cancer, and most of these studies were conducted before the modern concept of the multimodal approach or they were case reports.^{8–10} The purpose of the current study was to evaluate the clinical significance of extended lymphadenectomy for colorectal cancer with synchronous isolated extraregional lymph node metastasis.

2. Methods

Between July 2004 and December 2013, 4166 patients with primary colorectal cancer underwent surgery including noncurative surgery at the Cancer Institute Hospital of the Japanese Foundation for Cancer Research. Among 668 patients with Stage IV colorectal cancer who underwent surgery, 36 had isolated synchronous extraregional lymph node metastasis without other organ metastases such as to the liver, lungs or peritoneum (Figures 1 and 2). Extraregional lymph node metastasis was defined as metastasis to lymph nodes other than the regional mesenteric or mesorectal lymph nodes. In accordance with the Japanese guidelines, we considered the lateral pelvic lymph nodes involved in lower rectal cancer as being regional lymph nodes.^{11–13} Furthermore, inguinal lymph node metastasis in lower rectal cancer involving the anal canal was excluded from the definition of extraregional lymph node metastasis in the current study.¹⁴ Among the 36 patients evaluated in our study, eight with PALN metastasis located above the renal vein were excluded because they were not candidates for curative surgery. Finally, 28 patients with isolated synchronous extraregional lymph node metastasis situated below the renal vein were included in the current study. The indications of extended lymphadenectomy for synchronous isolated extraregional lymph node metastasis were discussed and determined at our multidisciplinary

team meetings. Sixteen patients underwent curative resection with extended lymphadenectomy (R0 group), and 12 patients underwent noncurative palliative surgery including stoma construction or exploratory laparotomy (control group). The clinical characteristics and survival outcomes were compared between these two groups. All of the patients in the current study provided informed consent.

Initial staging included complete physical examination, chest radiography, chest/abdominal/pelvic computed tomography (CT), and colonoscopy. Positron emission tomography (PET) was performed in 14 patients (50%); all patients had radiologic evidence of extraregional lymph node metastasis with hot uptake detected in PET scans. Extraregional lymph node metastasis was histologically confirmed in 15 patients in the R0 group. One patient with ypT0N0M0 cecal cancer and inguinal lymph node metastasis who underwent preoperative chemotherapy (6 courses of 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) plus bevacizumab) was included in the R0 group; this was because the inguinal lymph node showed clear strong uptake on PET–CT scans prior to preoperative chemotherapy (Figure 3). Extraregional lymph node metastasis in the control group was histologically confirmed in only two patients; however, the growth and progression of extraregional lymph node metastasis during the clinical course were confirmed in all patients.

In colon cancer, complete mesocolic excision and D3 lymph node dissection with main feeding artery ligation at the level of origin was performed. In rectal cancer, total mesorectal excision with high ligation of the inferior mesenteric artery was undertaken. With regard to the extended lymphadenectomy of extraregional lymph node metastasis, we generally targeted and widely dissected the region in which the metastasis was observed on radiological examinations. Follow up of all patients usually consisted of the following: physical examination (including digital examination) and blood tests (including measurement of carcinoembryonic antigen levels) every 3 months; chest/abdominal/pelvic CT or PET–CT every 6 months; and surveillance colonoscopy 1 year after surgery and every 2 years thereafter.

Quantitative data are expressed as the median (range). Survival analysis was performed using the Kaplan–Meier method with the log-rank test using JMP software V11.0 (SAS Institute, Cary, NC, USA) for Windows. Patients who died from other causes, and those who were living at the most recent follow up, were censored in the analysis of cancer-specific survival (CSS). Relapse-free survival (RFS) was defined as the time from surgery to any type of recurrence. A *p* value of <0.05 was considered to indicate a statistically significant difference.

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