



Retroperitoneal nodal metastases from colorectal cancer: Curable metastases with radical retroperitoneal lymphadenectomy in selected patients

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Abstract

Background: Retroperitoneal nodal metastases (RNM) represent 1–2% of metastases from colorectal cancer (CRC). Non-surgical treatments achieve 5-year overall survival (OS) of 0–12%. Radical retroperitoneal lymphadenectomy (RRL) in this setting remains controversial, but most published series do not distinguish local retroperitoneal recurrences from RNM. We specifically report outcomes after RRL for RNM from CRC.

Methods: We analyzed prospectively recorded data from patients who underwent standardized RRL for RNM from CRC between January 1997 and August 2012 in our institution. Local retroperitoneal recurrences were excluded.

Results: Twenty-five patients underwent RRL for synchronous (n = 19) or metachronous (n = 6) RNM from CRC. Fifteen patients had extra-retroperitoneal metastases. Median hospital stay was 16 [7–23] days. Grade \geq III morbidity was 8% with no perioperative deaths. Median follow-up was 85 [4–142] months. Median OS and progression free survival (PFS) were 60 [4–142] and 14 [1–116] months. One, three- and 5-year OS were 92%, 64% and 47%. One, three- and 5-year PFS were 51%, 26% and 26%. Retroperitoneal nodal metastases from stage III CRC were associated with better median OS compared to those from stage IV CRC (p = 0.02). This variable did not impact on PFS. Subject to substantial risk of type II error on small samples data statistical analysis, survivals were not affected by timing and location of RNM, extra-retroperitoneal metastasis, nodal disruption, neoadjuvant nor adjuvant chemotherapy.

Conclusions: To our knowledge, this is the largest series yet reported which specifically studied outcomes of RRL for RNM from CRC. RRL allows favorable outcomes in selected patients with acceptable morbidity.

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Keywords: Colorectal neoplasms; Lymph nodes; Neoplasm metastasis; Lymph node excision; Long-term survival

Introduction

Colorectal cancer (CRC) is the fourth most frequent cancer worldwide and an estimated 600 000 colorectal cancer deaths occurred in 2008.¹ Over the past twenty years, developments in diagnosis and the adoption of multimodality treatments have improved the prognosis of metastatic CRC. Estimated 5-year overall survival (OS) is now 30–50% after surgery for liver and/or pulmonary metastases^{2,3} and 11–32% in patients with peritoneal metastases.⁴ Surgery for liver and pulmonary metastases from CRC is now the

Abbreviations: RNM, retroperitoneal nodal metastases; CRC, colorectal cancer; RRL, radical retroperitoneal lymphadenectomy; RLR, retroperitoneal local recurrence.

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gold standard and remains the only treatment that allows long-term survival and potential cure.^{5,6}

Compared with the sites mentioned above, retroperitoneal nodal metastases (RNM) from CRC are rare: the estimated incidence of isolated RNM after curative resection is 1–2%.^{7–9} RNM are often accompanied by extra-retroperitoneal metastases.¹⁰ The estimated delay between surgery for the primary CRC and diagnosis of retroperitoneal recurrence is 23–28 months.^{9,11}

Management of RNM from CRC remains controversial.^{12,13} Central localization of the retroperitoneum, neighboring colorectal tumors and related lymphatic systems can lead to the development of both retroperitoneal local recurrences (RLR) and RNM.^{7–9,12,14} Indeed, most published articles do not distinguish between RLR and RNM when reporting the outcomes of surgery but present results globally for retroperitoneal locoregional recurrences associated with poor prognosis. However, RLR and RNM seem not to be the same disease. When lymph node and locoregional retroperitoneal recurrences are distinguished, RLR seems to have a worse prognosis than RNM¹¹ (estimated 3-year OS and progression free survival (PFS) for RLR being 27% and 0% versus 81% and 26% for RNM). Management of these two categories of patients should therefore be different. The better control of nodal metastasis progression permitted by effective chemotherapy is one respect in which treatment might vary.¹¹ Hence, even if distinguishing between RLR and RNM is sometimes difficult,^{11,15} it should be done early so that therapy can be adjusted to the circumstances of individual patients, with the aim of improving their survival.

Several studies have suggested that surgery for RNM is the only potentially curative treatment and can achieve long-term OS in selected patients with an acceptable postoperative morbidity.^{7–9,16–18} Median OS in operated patients was 34–46 months, compared with 3–33 months in those who did not have surgery, and five year OS was 15–53% versus 0–12% respectively. Because RNM is relatively rare, its management is often based on retrospective studies of small groups of CRC patients which (as noted above) often included those with RLR.¹⁷ Even in expert centers, whether to perform radical retroperitoneal lymphadenectomy (RRL) is still discussed on a case by case basis. With the aim of clarifying the role of surgery in RNM from CRC, we studied the outcomes of RRL in, to the best of our knowledge, the largest well-characterized series yet reported.

Patients and methods

Study population

We retrospectively analyzed data from a prospective database of all patients who underwent complete surgical resection of RNM at the Léon Bérard Cancer Center (Lyon, France) between January 1997 and August 2012.

RNM was defined as histologically confirmed retroperitoneal lymph node involvement, without local CRC recurrence, in an area limited laterally by the ureters, the celiac area superiorly and iliac vessels inferiorly.

Preoperative staging included carcinoembryonic antigen (CEA) determination and a thoraco-abdomino-pelvic computed tomography (CT) scan. Positron emission tomography – CT has also been routine since 2005.

All prognostic factors for RNM found in the literature were recorded, including patient characteristics, primary stage according to the 2010 AJCC staging system, timing of metastasis (synchronous vs metachronous), preoperative CEA level, chemotherapy, radiotherapy, the size and number (macroscopically and radiologically) of suspected involved nodes and their location (supra-renal, infra-renal, iliac), nodal disruption, histology, presence of extra-retroperitoneal metastatic sites, postoperative morbidity and mortality, and long-term patient outcomes.

Treatment and follow-up

Therapeutic management was systematically discussed for all patients presenting with retroperitoneal nodal metastases (isolated/not isolated, resectable/unresectable) from CRC in multidisciplinary digestive cancer board meetings at our institution. Surgery, including RRL, was proposed with intent to achieve a R0 resection for all metastatic sites. If indicated, perioperative chemotherapy consisted of infusional fluorouracil and leucovorin (the LV5FU2 regimen) and, more recently, folinic acid plus oxaliplatin or irinotecan with or without the addition of cetuximab or bevacizumab. Standardized RRL, including all nodal tissues in the previously defined retroperitoneal area, was systematically performed. Infra-renal radical lymphadenectomy consisted of the resection of the laterocaval, precaval, retrocaval, lateroaortic, preaortic, retroaortic and interaorticocaval nodal tissues (Fig. 1). A complete resection was defined as no macroscopic residual tumor. Patients with synchronous RNM had them resected at the same time as the primary CRC. When necessary, vascular resection and reconstruction were performed using a vascular prosthesis. Closed-suction abdominal drainage was used routinely. All patients had a postoperative fat-free diet for one month.

Patients were followed up every three months for two years and every six months thereafter. Physical examination, CEA level determination and thoraco-abdomino-pelvic CT-scan were performed at each patient visit.

Statistical analysis

Medians were compared using Wilcoxon non parametric test. Proportions were compared using the Fisher exact test. Survival curves were calculated using the Kaplan–Meier method. The Log-rank test was used for univariate analysis. A p value ≤ 0.05 was considered statistically significant. Hazard ratios were estimated using Cox model and

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