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Percutaneous lung ablation of pulmonary recurrence may improve survival in selected patients undergoing cytoreductive surgery for colorectal cancer with peritoneal carcinomatosis

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Abstract

Purpose: To analyze the outcomes of patients developing pulmonary metastases (PM) following cytoreductive surgery (CRS) and perioperative intra-peritoneal chemotherapy (IPC) for colorectal cancer (CRC) with peritoneal carcinomatosis.
Patients and methods: A retrospective analysis of patients undergoing CRS/IPC for CRC from 1996 to 2016 was performed. Lung-specific disease-free and patient overall survival was analyzed. Patients undergoing percutaneous lung ablative therapy (PLAT) for PM were compared to patients receiving systemic chemotherapy alone.
Results: 273 patients underwent CRS/IPC for CRC. Of these, 61 (22%) developed PM. Median time to development of PM was 8 months (range 0–52 months) and 41 patients (67%) had metachronous lesions. Twenty-one PM patients underwent PLAT, either by radio-frequency or micro-wave ablation, for an average of 3 lesions (range 1–12) and 13 (62%) had bilobar disease. The most common post-interventional complication was the development of pneumothorax (71%). Overall survival following development of PM was 18 months and higher in patients undergoing PLAT compared to those treated with systemic chemotherapy (26 vs. 14 months, $p = 0.03$). In eight cases (38%) local tumor recurrence developed post-PLAT. A peritoneal carcinomatosis index >10 (HR 3.48, 95% CI 1.69–7.19), presence of liver metastases (HR 2.49, 95% CI 1.24–5.03) and PLAT (HR 0.43, 95% CI 0.20–0.93) were identified as significant predictors of overall survival following diagnosis of PM.
Conclusion: PM develop in approximately a fourth of patients undergoing CRS/IPC for CRC. Of these, about 1/3 may be eligible for PLAT. PLAT is a valuable treatment option providing good local control and potentially prolongation of overall survival.

Keywords: Colorectal cancer; Cytoreductive surgery; Heated intraperitoneal chemotherapy; Lung metastasis; Percutaneous lung ablation therapy; Radiofrequency & microwave ablation

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths in the Western world [1,2] with survival outcomes inversely correlated to its stage at the time of diagnosis [3]. Less than half of patients present with localized disease and over 50% will die of

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metastases [2,4]. Peritoneal carcinomatosis (PC) as a site disease spread occurs in approximately 40% of patients with CRC and is a frequent site of primary presentation as well as disease recurrence [5,6]. The success of systemic chemotherapy for CRC with PC is moderate with median survival rates ranging from 7 to 20 months and 5-year survival rates as low as 4% [7–9]. On the other hand, cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy (IPC) results in a significant survival benefit compared to systemic chemotherapy alone with median survival rates of up to 60 months [10]. Because of numerous encouraging reports, including three randomized controlled trials; CRS/IPC now has an established role in the treatment of selected patients with CRC and peritoneal surface disease [11–14].

Pulmonary metastases (PM) are the most common extra-abdominal metastatic site of CRC and present in up to 10–20% of patients following attempted curative surgical therapy [15,16]. However, the incidence and management of PM in patients being evaluated for and/or having undergone CRS/IPC for CRC is not as well documented. Two studies have reported that approximately 3–4% of patients with CRC undergoing CRS/IPC have synchronous PM [17,18]. Whereas a study from Sweden documented a 6.6% (10/151) isolated pulmonary recurrence rate following CRS/IPC for CRC [19], another recent two-institution study reported that up to 50% of patients undergoing this treatment may develop lung recurrence [20].

Whilst high level evidence for the removal pulmonary CRC deposits is still awaited [21–23], some large retrospective series suggest that pulmonary metastasectomy provides loco-regional control and may result in improved disease-free and overall survival when compared to chemotherapy alone [16,24–27]. However, only a few patients meeting strict selection criteria are eligible for this treatment strategy. Percutaneous lung ablative therapies (PLAT) such as radiofrequency (RFA) and microwave ablation (MWA) represent alternatives for patients deemed to have inoperable pulmonary disease. RFA offers a relatively safe and effective means of treating PM with retrospective data suggesting that the combination of RFA with systemic chemotherapy offers a survival advantage over chemotherapy alone [28]. Moreover, one-, three- and five-year survival outcomes of RFA treated patients have been reported to be as high as 84–96%, 46–57% and 30–35% respectively [29–37].

Whilst data on patients receiving ablative therapies of PM following treatment of their primary tumor or liver metastases are readily available, the outcomes of patients developing PM following CRS/IPC have, to our knowledge, not yet been reported. The aim of this study was to analyze the outcomes of patients developing PM following CRS/IPC for colorectal cancer with peritoneal metastases as a whole. Furthermore, the outcomes of patients developing PM amenable to PLAT were analyzed.

Methods

Treatment setting and patients

From February 1996 to September 2016, 273 CRC patients were treated with CRS/IPC by a single surgical team at St George Hospital, Sydney, Australia. Patient demographic, tumor-related, treatment and perioperative outcome features were collected in a prospectively maintained database. Equally, all patients undergoing percutaneous ablative therapy for PM (RFA and/or MWA) were simultaneously collected prospectively as previously described [38]. All patients consented to inclusion of information into these databases and institutional ethics board approval for this study was obtained. Staging and assessment of treatment eligibility of patients undergoing CRS/IPC at our unit has been previously described [14]. Postoperative complications were recorded according to the Clavien-Dindo classification [39].

Cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC)

The extent of abdominal disease was recorded during laparotomy by calculation of the peritoneal cancer index (PCI) [40]. CRS was performed as described by Sugarbaker [41]. Completeness of cytoreduction (CC-score) was recorded as an indication of residual disease [40]. IPC was administered as described previously by our unit [42].

Patient selection criteria for percutaneous lung ablation therapy (PLAT)

Offering PLAT in patients deemed as falling outside of regular criteria for surgery is based on the current opinion, that macroscopic tumor eradication may help achieve better local control, reduce overall tumor burden and potentially enhance the effect of systemic therapies [43].

Surgical pulmonary colorectal cancer metastasectomy (either as open or as video-assisted thoracoscopic surgery) was not regularly performed at our hospital for the included patients due to institution specific preferences, as many patients presented with bilateral disease as well in most cases PM developed within one year of CRS/HIPEC.

Thus, the selection of patients for PLAT was based on the following factors: patient age between 18 and 85 years; complete resection of primary colorectal tumor and other sites of tumor deposits either already achieved or deemed achievable (in cases of pre-CRS ablation) as well as signed informed consent. In patients with a history of pulmonary disease, pre-treatment lung function tests were performed to assess suitability of the patients for PLAT.

Exclusion criteria for PLAT included more than 10 lesions per hemithorax, a metastasis diameter >5 cm, lesions with major venous, bronchus or hilar involvement and patients with marked coagulopathy (international normalized

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