



Anti-Tumour Treatment

What to choose as radical local treatment for lung metastases from colo-rectal cancer: Surgery or radiofrequency ablation?



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SUMMARY

Background: Long-term survival can be obtained with local treatment of lung metastases from colorectal cancer. However, it is unclear as to what the optimal local therapy is: surgery, radiofrequency ablation (RFA) or stereotactic radiotherapy (SBRT).

Methods: A systematic review included 27 studies matching with the a priori selection criteria, the most important being ≥ 50 patients and a follow-up period of ≥ 24 months. No SBRT studies were eligible. The review was therefore conducted on 4 RFA and 23 surgical series.

Results: Four of the surgical studies were prospective, all others were retrospective. No randomized trial was found. The reporting of data differed between the studies, which led to difficulties in the analyses. Treatment-related mortality rates for RFA and surgery were 0% and 1.4–2.4%, respectively, whereas morbidity rates were reported inconsistently but seemed the lowest for surgery.

Conclusion: Due to the lack of phase III trials, no firm conclusions can be drawn, although most evidence supports surgery as the most effective treatment option. High-quality trials comparing currently used treatment modalities such as SBRT, RFA and surgery are needed to inform treatment decisions.

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Introduction

Colorectal cancer is the third most common tumor type in males, and the second in females, with in 2008 an incidence of 1.2 million new cases and a mortality rate of over 600,000 world-wide.¹ In the Netherlands, approximately 20% of colorectal cancer patients have synchronic metastatic disease at time of diagnosis.²

Although the cure rate of patients with colorectal cancer has improved over the last decades, distant metastases are still of concern. Temporary remissions with systemic treatment can be obtained, but most of the time, cure remains elusive once distant

metastases have occurred. In 1995, Hellman and colleagues proposed an intermediate state between localized cancer and distant metastases, called “oligo-metastases”.³ In this concept, treatment of a few distant metastases with curative intent may still be possible, if all visible cancer can be eradicated with local treatments such as radiotherapy, surgery or radiofrequency ablation (RFA).

The observation that long-term survival may be achieved with surgical resection of liver metastases from colorectal cancer⁴ has been used as an argument supporting the oligo-metastases concept. Besides liver, also lung metastases from colorectal cancer have been treated with curative or radical intent. Most series deal with surgery, although RFA and Stereotactic Body Radiation Therapy or SBRT⁵ (also called SABR, Stereotactic Ablative RadioTherapy) are used as well. Most studies included patients with several types of primary tumors, whilst few studies reported outcomes on lung metastases from primary colorectal cancer, only. To the best of our knowledge, most series are retrospective or observational

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and no randomized series investigating survival outcome of these treatment modalities have been published. This was the reason for Treasure et al.⁶ to perform an ongoing phase III trial that investigates whether or not pulmonary metastasectomy in colorectal cancer influences survival.

Several systematic reviews regarding one or more of the three local treatment methods have been published.^{7–9} However, to the best of our knowledge, no systematic review has been reported comparing the outcome of surgery, RFA and SBRT specifically in the treatment of lung metastases of colorectal cancer. This was the aim of the current review.

Methods

Search strategy and selection criteria

The literature search was performed by using a broad strategy which was composed by following the PICO method^{10,11} (Supplementary Material 1). The complete search strategy is shown in Appendix 1 and was used to identify studies in Pub Med, EMBASE, Web of Science and the Cochrane Library from 2001 until the search date in October 2011.

For this review a priori selection criteria were established prior to the search and selection of articles. These included a minimal follow-up period of 24 months, a minimum of 50 patients included in the study with pulmonary metastases from colorectal cancer without constraint on previous therapies. Only original articles were included. Another limitation used was language, in which only English, German and Dutch articles were included. All inclusion- and exclusion criteria are summarized in Table 1.

In order to complete the search and to identify all relevant studies, the references of all eligible articles were manually searched for other potentially relevant studies.

Outcomes

One researcher conducted the search and selection of eligible studies. All articles were then evaluated by two independent reviewers. When available, the following data were obtained from the trials: patient and tumor characteristics, inclusion- and exclusion criteria, disease-free interval, treatment technique, follow-up, complications, tumor progression, recurrence rate, survival and prognostic factors.

One researcher (R.S.) reviewed all eligible studies, whereas the second extraction was performed by three reviewers (R.H., J.G. and D.D.R.). Data were extracted and tabulated independently in order to reach validity of the data (appendix 2 for extraction table). If outcomes differed, there was discussion between the reviewers until consensus was reached.

Results

Search results

The initial search in the four databases included 4727 articles in total, which were searched for duplicates using Endnote by which 453 duplicates were excluded.

Table 1
Inclusion and exclusion criteria for the literature search.

Follow-up period	≥ 24 months
Site of primary tumor	Colorectal carcinoma
Number of patients	≥ n = 50
Previous treatment	All therapies
Tumor stage	Stage IV
Type of metastasis	Recurrence or first secondary tumor
Study type	Reviews excluded

The remaining studies were manually evaluated and 226 more duplicates were excluded. Another 3250 studies were then excluded based on titles that were not relevant for this study (Fig. 1) leaving a total of 798 studies for further analysis.

Abstracts of all remaining 798 studies were then compared to the a priori selection criteria. Studies not matching these criteria were excluded as well. After this first selection, 27 relevant studies were identified and included in this review. Of these 27, the majority (23) focused on surgery, four examined RFA and none regarded SBRT.

Description of the studies

Of the twenty-seven studies that matched the selection criteria and were included in this review, four studies investigated RFA, all of which were retrospective.^{12–15} Three of these studies were performed in the same institute in Sydney, Australia^{13–15} with two of these papers^{13,14} investigating the same patient population. In our analysis, we used this population only once. All twenty-three remaining studies reviewed surgical metastasectomy, of which four prospective studies and the remaining retrospective studies. Study and patient characteristics are found in Table 2.

Despite the known importance according to the “oligo-metastases hypothesis”,³ only six studies reported on the median or mean number of the pulmonary lesions. Yan et al.^{13,14} reported a median of 2 lesions per patient (range, 1–6), whilst Kanemitsu et al.¹⁶ and Pfannschmidt et al.¹⁷ found a median of 1 lesion per patient (ranges, 1–8 and 1–35 lesions, respectively). Two series only reported mean values of 2.3 ± 2.1 lesions¹⁸ and 1.6 ± 0.8 lesions.¹⁹

Other study and patient characteristics such as tumor diameter and follow-up durations are listed in Table 2.

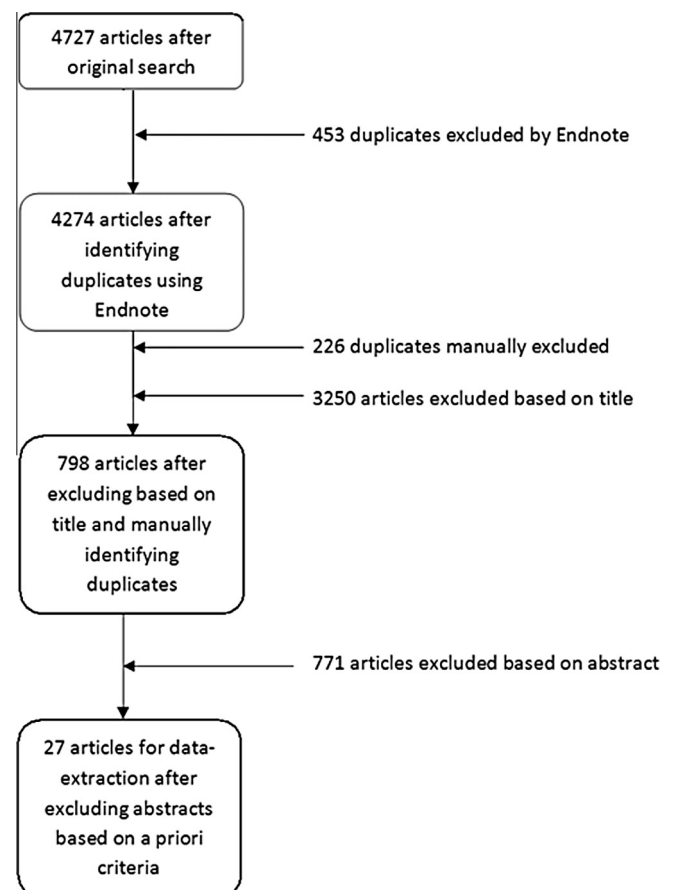


Fig. 1. Flowchart of selection process.

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