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Review

Percutaneous management of pulmonary metastases arising from colorectal cancer; a systematic review

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Abstract

Background: Radiofrequency ablation (RFA) is a well-established treatment modality for colorectal hepatic metastases, the success of which has prompted its use to treat other lesions such as colorectal pulmonary metastases (CRPM). Our aim was to perform a systematic review of the evidence and to assess the safety and effectiveness of ablative techniques in the management of CRPM.

Method: A literature search was performed using PubMed, Embase, Cochrane Library, CINAHL and Google scholar databases to identify studies, which analysed ablative techniques and their effectiveness in the management of CRPM. The primary outcome measures were overall survival, local recurrence rates and disease free survival. Secondary outcome measures were complication (major/minor), chest drain insertion rates and follow up duration.

Results: Eight studies were included in the review with a total of 903 patients and all of which used RFA for ablation. Mortality from ablation was <1% with overall survival ranging from 31 to 67 months. 1, 3 and 5 year survival ranges of 84–95%, 35–72% and 20–54% respectively. Local progression following ablation ranged from 9 to 21%. Major complication rates were noted in 0.5%–8% of patients with minor complications ranging between 7% and 33%. 23% of patients required chest drain insertion post procedure.

Conclusion: s: RFA is a safe and effective technique for the management of CRPM. However, in the absence of large randomised controlled trials it is unclear where RFA should sit in the treatment algorithm for patients with CRPM.

Keywords: Radiofrequency ablation; Colorectal cancer; Pulmonary metastases

Introduction

There are approximately 41,000 cases of colorectal cancer (CRC) diagnosed in the UK each year resulting in over 16,000[1] deaths. The lungs and liver are the most common sites of metastatic spread with 10–30% of cases having metastatic pulmonary disease at presentation and significant rates of metastases following resection of the primary lesion.[2–5]

Pulmonary metastases from colorectal cancer (CRPM) are the second most common area for metastatic spread with the majority of patients having coexisting hepatic metastases.[2] Whilst we have seen significant improvement in the 5 year survival rate for these patients following improvements to chemotherapy regimens,[6] there has been increasing interest in the use of metastasectomy for these patients with curative intent. There are many published studies demonstrating 5 year survivals as high as 71.2%, but more typically 32–45% and with several good quality systematic reviews summarising their outcomes.[7–10]

Superficially these figures look encouraging, however, only a small percentage of patients with CRPM are suitable for surgical intervention due to tumour site, histology, comorbidities and extra pulmonary disease.[11] For those patients who are eligible for resection, management of recurrences is limited given the technical difficulties associated with repeat thoracotomy and loss of lung volume.

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Inevitably this results in a large population of patients with inoperable disease and as such there is significant interest in alternative treatment options such as percutaneous techniques.

RFA causes focal coagulative necrosis by generating high frequency alternating electrical current (460–500 kHz) in the tissue, which results in ionic oscillation and subsequent heat leading to tumourlysis.[12] Whilst cytotoxicity may occur <50 °C the aim of RFA is to achieve temperatures of 60–90 °C to ensure cell death. It typically takes 3–4 min for the RFA probe to reach its target temperature and large tumours may require treatments at several locations to cover the target area effectively. Treatment sessions are thus limited by time constraints, patient comfort as well as by the location of the lesion. Other limitations include the proximity of large vessels (>3 mm) that act as "heat sinks" and dissipate the energy.[13] As with all treatment, RFA is susceptible to treatment failure (TF) either due to technical failure (inability to effectively ablation lesion due to the aforementioned heat sink effect, tumour size of anatomical location) or due to the underlying cancer biology.[14]

Whilst there is a large body of published evidence for the use of RFA colorectal hepatic metastases, there is comparatively little regarding the use of RFA for CRPM.[15–18] Therefore, the aim of this systematic review is to determine the effectiveness and safety of ablative techniques for patients with CRPM.

Materials and method

A literature search was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) protocol.[19] MeSH search terms used were "*Colorectal*", "*Colorectal Cancer*", "*CRC*", "*Pulmonary Metastases*", "*Lung Metastases*", "*Ablation*", "*Radiofrequency*", "*Microwave*", "*Outcome*" and "*Survival*"; terms were combined using "and/or" as appropriate. These terms were then applied to Medline (since 1952), EMBASE (since 1980), the Cochrane library (since 1995), CINAHL (since 1982) and Google Scholar and the search conducted independently by authors NL and PS. MeSH terms were exploded to identify additional studies.

Inclusion criteria

Included studies assessed the effectiveness of the intervention by reporting disease free survival (DFS, patients who are alive and cancer free at a prescribed end point), rates of local progression (LP, an increase in size of lesion after ablation[20]) and overall survival (OS, number of patients alive with or without disease) of patients who underwent percutaneous management of CRPM. Observational and comparative studies were considered provided that outcomes for management of CRPM managed percutaneously were discernible from other data. Studies were carefully evaluated for duplication or overlapping data and where institutions had published two studies either the most recent or best quality data set was included.

Exclusion criteria

Studies were excluded if they were non-English language failed to provide discrete data on CRPM when non-colorectal primaries were considered, or on the outcome of percutaneous management.[21] Animal studies, letters, reports, conference abstracts or abstract only reports were similarly excluded. Studies with duplicated or overlapping data sets were rationalised and the largest/most recent data set was taken forwards.

Outcome measures

Outcomes were classified into primary and secondary outcome measures. Primary outcome measures were OS, LP and DFS. Secondary outcome measures were categorised as complications (major vs minor), chest drain insertion rate and average follow up duration.

Study selection

Two authors (NL and SP) independently performed the search strategy initially undertaking a title screen followed by abstract review, then full text review of appropriate studies. Publications satisfying the exclusion criteria were discarded at each stage. Publications without abstracts moved straight to full text review. Discrepancies between author searches were resolved by consensus following discussion. Failure to reach agreement resulted in review by the senior author (NJS) whose decision was considered final.

Data extraction

Data extraction was undertaken independently by NL and SP using a standardised proforma. Any discrepancies were discussed between the authors and escalated to the senior author for adjudication when necessary. The following demographic and clinical parameters were extracted from each study; study characteristics (year of publication, first author) population characteristics (number and demographics, mean tumour size and number of tumours, follow up duration), type of intervention (radiofrequency, microwave or laser ablation), complications (major, minor and chest drain insertion rate) and outcomes of interest.

Quality assessment

The quality of all studies was analysed using the methodological index for non-randomized studies (MINORS) to establish quality of the study and risk of bias.[22] Each study