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Original research article

Malignant pleural mesothelioma – Pleural cavity irradiation after decortication with helical tomotherapy

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ABSTRACT

Background: Malignant pleural mesothelioma (MPM) is a rare and aggressive disease that poses a treatment challenge in spite of recent technical developments. The aim of this retrospective analysis is to assess the feasibility of administering intensity-modulated radiotherapy (IMRT) to the pleural cavity using helical tomotherapy in patients who had undergone pleurectomy/decortication (P/D) and also the resulting toxicity levels.

Patients and methods: Ten patients who had MPM and had undergone P/D were treated with pleural cavity irradiation that included a median dose of 52.2 Gy using helical tomotherapy. The median age of the patients was 53 years (31–74). In addition to clinical and diagnostic findings from regular follow-up examinations, we evaluated the dose distribution for other organs at risk to assess treatment in relation to toxicity, with special regard for the underlying intact lung.

Results: The mean lung dose on the treatment site was 32.8 Gy (±6.8). The $V_{20\,Gy}$ was 71.7% (±17.2). No treatment-related toxicity that exceeded grade III according to common toxicity criteria (CTC) was observed. Median progression-free survival (PFS) was 13 months with a median overall survival (OAS) of 19 months.

Conclusion: The findings of this analysis provide data indicating that sparing the underlying lung in patients with MPM after P/D is not only feasible with helical tomotherapy, but that this treatment also causes reasonably few side effects.

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1. Background

Malignant pleural mesothelioma (MPM) is a rare disease, and its treatment still poses a clinical challenge. Because of its biological aggressiveness and propensity for local and distant propagation, multimodal treatment approaches are necessary.[1,2] There are two surgical procedures available for patients with MPM. Extrapleural pneumectomy (EPP) involves en bloc resection of the involved lung, parts of the diaphragm, and the parietal pleura and pericardium, while pleurectomy/decortication (P/D) is an alternative surgical option in which the underlying lung can be spared and left in situ.[3] EPP, as the more radical approach,[4] has been used less frequently since comparisons of the two approaches showed a clear advantage with P/D in terms of morbidity and perioperative mortality.[5] Data from the recently published Mesothelioma and Radical Surgery (MARS) Trial substantiate these findings and have even led to the conclusion that EPP, as part of the trimodality treatment, is not only not beneficial but potentially harmful for patients.[6] Therefore, it appears that the choice of surgery that is performed may affect the patient's eligibility for further adjuvant therapy. The increase in the number of P/D treatments performed is of particular importance in terms of the treatment techniques for adjuvant radiotherapy. On the one hand, because there is less extensive resection, the risk for local recurrence might be aggravated and, therefore, no compromises should be made on the dose prescription. However, on the other hand, organ preservation must be taken into account through an improved ability to spare organs at risk (OAR). In general, intensity modulated radiotherapy (IMRT) seems to be a suitable technique for addressing this challenge[7–9] and, as we have already shown, helical tomotherapy in particular allows excellent and homogenous target coverage in patients after EPP.[10] However, the requirements for treating only the pleural cavity while sparing the intact lung as much as possible pose a much greater challenge in terms of both equipment and medical personnel. Recent studies have shown the feasibility and the acceptable toxicity profiles for adjuvant IMRT.[11] While plenty of validated constraints are available for the treatment of central lung tumors, generally accepted constraints for particular dose distribution of pleural cavity irradiation (high doses around the lung) are still missing. This retrospective work investigates the feasibility and clinical outcomes of adjuvant radiotherapy after P/D using helical tomotherapy, with special regard to the dosimetric parameters in terms of the ability to spare OARs.

2. Patients and methods

2.1. Patients' characteristics

Between September 2007 and March 2013, ten patients (seven males; three females) with histological proven MPM (six right-sided; four left sided) were treated adjuvantly after P/D. The median age of the patients was 53 years (31–74 years). All patients received four to six cycles of chemotherapy (a combination of cisplatin and pemetrexed) either neoadjuvantly ($n = 2$) or postoperatively before the initiation of radiotherapy ($n = 8$). Additional patient characteristics are listed in Table 1.

Table 1 – Patient characteristics.

Patient characteristics ($n = 10$)	
Age	53 years (31–74)
Gender	
Male	7
Female	3
Laterality	
Right	6
Left	4
Histology	
Epitheloid	6
Sarcomatoid	2
Biphasic	2
Stage	
I	3
II	1
III	4
IV	2
Gross residual disease	
Yes	4
No	6
Previous treatment with chemotherapy	
Yes	10
No	0

2.2. Treatment planning and radiotherapy

IMRT was conducted as helical tomotherapy with 6 MeV photons. The treatment beam was conformed using a binary multileaf collimator. A median dose of 52.2 Gy (40–54 Gy) was applied in conventional fractionation of 2 Gy single doses five times a week with a median treatment time of 839.8 s (478–1281.4 s). Four patients received an integrated boost to macroscopic residual disease up to 60 Gy. Boost volume was defined as macroscopic tumor as seen on contrast enhanced CT scan expanded by 5 mm resulting in a mean boost volume of 337 cc. Additional boost irradiation had no significant impact on dose distribution for OARs. Patients were immobilized in the supine position with their arms over their heads and using chest boards. For inverse treatment planning, Accuray's tomotherapy treatment planning station was used with a field width of 2.5 cm. The contour of the pleural cavity was isotropically expanded from the apex of the lung to the costophrenic recess by 5 mm; a margin of 1 cm was used inferior of the diaphragm to account for breathing motion. No additional breathing motion management was applied. Mean pleural cavity volume was 2649 cc. Interlobar space was not contoured, to minimize the dose to the lung since it had not been affected in any of the patients.

2.3. Statistics

Overall survival (OAS) and progression-free survival (PFS) were calculated as being from the beginning of radiotherapy until the time of death or the last documented follow-up visit (Kaplan–Meier-estimator, Sigma Plot 12.5, Systat Software). In addition to clinical and diagnostic findings from regular follow-up examinations (every 3 months), we evaluated the