110. Percutaneous hepatic perfusion with melphalan in treating unresectable liver metastases of colorectal cancer and uveal melanoma: A phase I/II trial

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Background: Irresectable liver metastases can be treated with systemic therapy, which aims to limit the disease, extend survival or turn the metastases into resectable ones. Some patients however suffer from systemic therapy and its side effects or the disease is progressive under these therapies. For these patients, with metastases confined to the liver, isolated liver perfusion may be an alternative because it has the advantage of controlling liver disease and decreasing treatment related symptoms and complications. In the past this was performed during an extensive surgical procedure, with satisfying results but an increased morbidity and mortality related to the open procedure prohibited wide clinical acceptance. Recently, a new fully percutaneous procedure in which hepatic infusion with simultaneous chemofiltration was developed. Besides decreased morbidity and mortality, this procedure can be performed several times, expectedly leading to a higher percentage of patients that might qualify for a radical resection after perfusion.

Material and methods: A prospective phase II trial is started in the Leiden University Medical Center and Erasmus Medical Center investigating the effects of percutaneous hepatic perfusion (PHP) with melphalan. We aim to include 34 patients with irresectable liver metastases of colorectal carcinoma and 20 patients with uveal melanoma. The primary end points are the response rate expressed as the RECIST 1.1 criteria after two procedures and the percentage of patients whose metastases turned into resectable. Secondary endpoints are safety, overall survival, progression free survival and hepatic progression free survival, duration of stable disease and quality of life, according to EORTC questionnaires.

Results: Seven procedures have been performed in five patients up to now. All procedures were uncomplicated. Post procedural recovery was fast with a mean length of hospital stay of 2.7 days.

On CT scans 5 weeks after the first treatment all target lesions decreased in size and were more hypodense. No new lesions were found in the liver. According to the analyses of the pharmacokinetic sampling, the filter removes up to 93% of the melphalan. The small systemic leakage of melphalan lead to a decrease in white blood cell count and thrombocytes after the first procedure. One severe adverse event, febrile neutropenia, was reported. Anticipating to this, hematopoietic growth factors were administered routinely in further patients.

Conclusion: Up to now, percutaneous hepatic perfusion appears to be an effective and safe procedure in selected patients with irresectable liver metastases of colorectal cancer or uveal melanoma. Moreover, pharmacokinetic analysis showed indeed low systemic exposure to melphalan.

No conflict of interest.

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111. Prehabilitation before liver surgery

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Background: Following surgery fitter patients have shorter hospital length of stay and fewer complications. Prehabilitation programs aim to improve preoperative fitness. No successful prehabilitation program has been delivered in just 4 weeks and none in patients with metastatic cancer. This prospective trial sought to establish the feasibility of a four-week prehabilitation program in patients with colorectal liver metastasis prior to hepatectomy.

Methods: This prospective randomised controlled trial sought to improve the cardiopulmonary exercise test (CPET) assessed anaerobic threshold (AT) by 1.5 ml/kg/min. Patients prior to hepatectomy for colorectal liver metastasis were recruited and randomised to either a 4-week supervised cycle interval training program or standard care. A CPET was conducted at baseline and prior to surgery. Secondary outcome measures included quality of life (SF-36, EORTC), and Dukes activity questionnaire. The study was not powered for perioperative outcomes but data was collected to power future studies.

Results: 38 patients were recruited (20 Prehab, 18 Standard Care). 3 (8%) patients withdrew prior to study completion (2 Standard Care, 1 Prehab). Adherence to the exercise program was high at 98.7%. There was no significant difference in baseline characteristics between the cohorts including CPET values, age, sex distribution, BMI, comorbidities, smoking status, medication and prior chemotherapy treatment. Patients in Standard Care had a drop in AT from 11.4 ml/kg/min to 11.0 ml/kg/min (p=0.09), with no change in VO2peak (18.7 ml/kg/min) (p=0.96). Patients in the prehabilitation program had an increase in the AT from 11.2 ml/kg/min to 12.2 ml/kg/min (p<0.09), and an increase in VO2peak from 17.6 ml/kg/min to 19.4 ml/kg/min (p=0.02). When compared to standard care patients on the prehabilitation study arm had a 1.5 ml/kg/min higher AT (p=0.03), and a 2.0 ml/kg/min higher VO2peak (p=0.05) following prehabilitation. There was an improvement in overall SF-36 score by 11 points (17%) in the prehabilitation program (p<0.01).

Conclusions: A four-week prehabilitation program can deliver clinically relevant improvements in patient fitness, and improved preoperative quality of life. A larger prospective study is needed to evaluate the effect of prehabilitation on perioperative outcomes, and the economic cost of delivering care.

No conflict of interest.

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113. Small intestinal neuroendocrine tumours with liver metastases and resection of the primary: Prognostic factors for decision making

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Background: Patients with small intestine neuroendocrine tumors (SI-NETs) present with liver metastases in 50-75% of cases at diagnosis. The aim of this study was to assess prognostic factors in patients with SI-NET liver metastases after primary tumor surgical removal with or without liver surgery or radiofrequency ablation (RFA). The primary endpoint was disease-specific survival (DSS).

Material and methods: Seventy-eight consecutive SI-NET patients with liver metastases who undergone primary tumor surgical removal between 1996 and 2011 were extracted from the institutional tumor registry.

Results: Liver tumor burden was < 25% in 43 (55.1%) 25-50% in 30 (38.5%) and >50% in 5 (6.4%) patients. For the whole cohort of patients DSS at 3, 5 and 8 years was 93.2%, 83.6% and 77.3%, respectively. Fifteen patients who underwent radical liver surgery were all alive with a median survival of 106 months (range 18-152 months). In multivariate analysis the Ki-67 index in a continuous fashion significantly correlate with prognosis.