A multidisciplinary approach to improve treatment strategies for patients with hepatic or pancreatic cancer

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Summary

Part I–Hepatic perfusion for the treatment of unresectable liver metastases
Because the majority of metastasized uveal melanoma (UM) patients have unresectable liver only metastases, locoregional therapy was developed. In this thesis percutaneous hepatic perfusion (PHP) is described as a treatment for these patients. Previous to PHP, patients were treated with isolated hepatic perfusion (IHP) during an open surgical procedure (***Chapter 1***). To determine the most effective therapeutic agent used in IHP, several drugs have been investigated. It was hypothesised that IHP treatment with a combination of drugs would improve the treatment effect and hopefully improve survival of patients with liver metastases of colorectal cancer or uveal melanoma. Contrary to the hypothesis it did not, because of hepatotoxicity and therefore, the combination of two chemotherapeutic agents has not been investigated further (***Chapter 2***). In more recent trials, melphalan alone was used in IHP. After successful in vivo studies, clinical trials for UM patients were initiated (***Chapter 3***). In two centers, 30 patients with UM liver only metastases were treated with IHP using melphalan in a clinical trial setting. Progression-free survival was 6 months (1–16) and median overall survival was 10 months (3–50). Compared to survival with no treatment (2-6 months [45]) or best supportive care treatment (OS 5.2 months) [46] this seems to be quite an improvement. Because of the considerable peri-operative morbidity, the complexity and duration of the procedure, IHP did not become standard of care. First, the procedure had to be adjusted and simplified. With advances in surgical techniques, imaging modalities and the emergence of interventional-radiology, percutaneous hepatic perfusion (PHP) was developed, as described in this thesis. During the 3-4 hours PHP procedure, the chemotherapeutic agent is infused in the hepatic artery and thereby delivered to the liver and metastases directly. Via a veno-venous filtration system, the chemotherapeutic agent is filtered before it reaches the systemic circulation. (***Chapter 4***) As described in ***Chapter 5*** a clinical study was conducted treating 20 UM patients with metastases confined to the liver with repeated PHP procedures (up to four procedures, 38 in total). In this study, pharmacokinetic analysis showed an overall filter efficiency of 86% (range 71.1–95.5%) with the Delcath Second Generation hemofiltration system, which is higher compared to earlier generation filters. Median overall survival was 29 months (range 7-40). Partial responses were achieved in 75% of patients and one-year overall survival was 80%. Median hepatic progression-free survival was 10 months (range 2-29). The side-effects were as expected, transient and well manageable. It was concluded that the results PHP outbalanced the (minimal) toxicity for patients with uveal melanoma metastases. (***Chapter 6***)

Part II - Tailored care for patients with pancreatic cancer

The poor prognosis of pancreatic cancer did not change much over the last decades, despite the improvements in treatment modalities. Previous studies have reported variations in incidence and mortality in pancreatic cancer between countries worldwide and European countries. [45, 46] A 2013 EUROCHIP survey (European Cancer Health Indicators Project) showed that cancer registry data are a reliable source for evaluation and strategy planning, but not all data is available in every registry, impeding a complete comparison. EURECCA aims to augment quality assurance by investigating differences in data registry, sharing knowledge in treatment strategies and science and thus improve cancer care throughout Europe. (***Chapter 7***) Previously, these international comparisons were performed for colon cancer, upper GI cancer, breast cancer and rectal cancer. [47-50] This data was collected by audit and registry structures, based on the assumption that an international comparison of population-based data will represent the actual patterns of care. Based on the experience gained by the researchers of this previous consortia, a collaboration was initiated across Europe to compare patterns of care and identify best practices for pancreatic cancer care. A core dataset was identified to identificate differences in age, gender, incidence, tumour stage and differences in treatment strategies.

At Moffitt Cancer Centre (Tampa, U.S.A.) a 'Senior Adult Oncology Program' was specially designed. [51] It was developed for patients aged 70 and older with all types and stages of cancer and offers a complete range of diagnostic, educational, therapeutic and preventative services, all tailored to meet the needs of the elderly population. For instance, a geriatric oncologist is included in the multidisciplinary tumour board. To identify any differences in treatment and/or survival a comparison was performed of data on geriatric pancreatic cancer care and survival at Moffitt and elderly patients in The Netherlands. (***Chapter 8***). We reported that patients treated at Moffitt more often received chemotherapy, also without surgery or as palliative treatment. For patients with locally advanced pancreatic cancer, a higher percentage underwent surgery in The Netherlands. One- and three-year overall survival was higher for patients treated at Moffitt, this difference seems to be largely explained by differences in treatment strategy. Given the associated survival benefit, this indicates that there might be a need for a reconsideration of the used therapies for elderly Dutch patients.

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