Preoperative blood management in colorectal cancer surgery: the controversial role of iron

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Chapter 9 // **Summary and conclusions**

In **chapter 1** a general outline of this thesis is given and the topic of perioperative blood management is introduced with a special focus on the detrimental effects of anti-anemic therapies and the role of iron in colorectal cancer patients.

Anemia is a common finding in cancer patients and is observed in up to 40 percent of the patients diagnosed with colorectal cancer. It has been hypothesized that anemia impairs long-term prognosis via worsening of tumor hypoxia, which is linked to radiotherapy and chemotherapy resistance. In **chapter 2** the results of a systematic review and meta-analysis assessing the long-term prognostic value of preoperative anemia in colorectal cancer patients are presented. In meta-analyses including both colon and rectal cancer patients, preoperative anemia was significantly associated with decreased overall survival (HR 1.56, 95% CI 1.30 to 1.88) and disease-free survival (HR 1.34, 95% CI 1.11 to 1.61). However, when restricted to studies exclusively on colon or rectal cancer patients, analyses demonstrated that preoperative anemia is only significantly associated with decreased long-term overall and disease-free survival in rectal cancer patients, and not in colon cancer patients.

In **chapter 3** an overview of the prevalence and treatment of preoperative iron deficiency in colorectal cancer patients is provided. In approximately 50 percent of all colorectal cancer patients, and 80 percent of anemic colorectal cancer patients, iron deficiency is observed. In regard of the type of iron deficiency, the vast majority was a combination of absolute and functional iron deficiency (81.0%); only 3.7% and 15.3% was an isolated absolute and isolated functional iron deficiency, respectively. The clinical relevance of iron deficiency in our patient cohort, however, was disputable, as only severe iron deficiency was significantly associated with increased postoperative complication rate in a univariate analysis.

Results of a survey among surgeons, gastroenterologists and anesthesiologists to assess the preoperative blood management strategy in colorectal cancer patients in Dutch hospitals are presented in **chapter 4**. A distinct variability in preoperative blood management practices was demonstrated. Strikingly, this variability was not only seen between, but also within Dutch hospitals, as indicated by the varying responses from surgeons, gastroenterologists and anesthesiologists. In general, poor compliance with the recommendations in international guidelines on the management of anemia in cancer patients was observed. This was for example illustrated by the low number of hospitals in which iron status was measured during screening for colorectal cancer (i.e. less than 40 percent), crucial to identify the type of anemia and to determine the optimal treatment.

In **chapter 5** the short-term effect of preoperative intravenous iron therapy is studied in a cohort study. Preoperative intravenous iron therapy is most effective in patients presenting with more severe anemia, and with higher transferrin and lower ferritin levels. The results failed

to demonstrate that the distinct hemoglobin increase after iron infusion leads to a decreased proportion of patients with a postoperative complication and/or blood transfusion.

In **chapter 6** the long-term safety of preoperative intravenous iron therapy is being questioned. The hypothesis that iron therapy as treatment of anemia could be a potentially detrimental and hazardous strategy in colorectal cancer patients is elaborated.

Supported by the hypothesis in chapter 6, the effect of preoperative intravenous iron therapy on long-term survival in anemic colorectal cancer patients is studied in a matched cohort study in **chapter 7.** The study failed to demonstrate that preoperative intravenous iron therapy has a profound effect on long-term overall and disease-free survival in anemic colorectal cancer patients. However, it should be stressed that the results were derived from a small-sized retrospective study, and therefore should be interpreted with caution.