



## Samenvatting van het proefschrift

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*"Beneficial effects of calorie restriction"*

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In the beginning of the twentieth century a non-invasive way to prolong the life-, and health span of various animal species, including non-human primates was found: dietary restriction (DR). The aim of this thesis was to investigate whether the beneficial effects of long-term dietary restriction could be induced by short-term nutritional interventions, and tapped for clinically relevant situations. In chapter 2 we reviewed the literature on short-term dietary restriction interventions and protection against ischemia-reperfusion (I/R) injury in animal models. In chapter 3, 4 and 5 we sought to elucidate the mechanisms of protection induced by fasting against hepatic I/R injury in mice. We conclude that upregulation of antioxidant enzymes and the stress response gene HO-1, and a better response following reperfusion likely underlie the protection by short-term fasting against hepatic I/R injury. Increased levels of corticosterone and ghrelin are unlikely to play a pivotal role. In chapter 6 the therapeutic use of dietary restriction is extended. There is emerging evidence suggesting that surgery induced processes facilitate tumor metastases. Postoperative inflammatory responses facilitate metastasis formation of circulating tumorcells by increasing the expression of adhesion molecules. We have shown that two weeks of dietary restriction reduces the expression of adhesion molecules and protects against surgically induced inflammation. We found that preoperative DR beneficially interferes with surgery-induced inflammation and subsequent adhesion of circulating tumorcells as DR reduces hepatic tumor load. In chapter 7 and 8 we describe a study which investigates whether preoperative DR regimen is feasible in the clinical setting and explored the effects of DR in surgical patients. In conclusion, preoperative DR is a promising non-invasive strategy with therapeutic benefits in various settings. Future research is needed to specify the role of DR in the clinical setting. ◀