

# Intestinal cell damage, inflammation and wound healing in major gastrointestinal surgery

Citation for published version (APA):

Reisinger, K. W. (2015). *Intestinal cell damage, inflammation and wound healing in major gastrointestinal surgery*. [Doctoral Thesis, Maastricht University]. Datawyse / Universitaire Pers Maastricht. <https://doi.org/10.26481/dis.20150605kr>

## Document status and date:

Published: 01/01/2015

## DOI:

[10.26481/dis.20150605kr](https://doi.org/10.26481/dis.20150605kr)

## Document Version:

Publisher's PDF, also known as Version of record

## Please check the document version of this publication:

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## Valorization

The findings in this thesis are not only relevant from a scientific point of view, but also carry social and economic value. As described in detail in chapter 13, several conclusions drawn from the different studies in this thesis form the basis for improvements in health care strategies. First, we have added to a growing body of evidence that widely used analgesics, the NSAIDs, should be banned from use in the context of gastrointestinal surgery, since this may lead to preventable complications and unnecessarily high health care costs. Patients undergoing major gastrointestinal surgery as well as the community paying health care costs may benefit from this advancement. In the same study, we have shown that administration of prostaglandin E2 may prevent complications in an experimental model of colonic surgery, however this might be mostly applicable to specific subsets of patients. Future research should reveal whether clinical application of prostaglandin E2 indeed decreases complication rates and thereby health care costs and the burden to society.

Next, we aimed at unraveling the phenotype of the vulnerable elderly patient undergoing major gastrointestinal surgery. This population specifically deserves attention as a burden to health care costs. The population of the Netherlands and many other countries is ageing, thereby increasingly demanding health care resources. Furthermore, due to therapeutic improvements over the past decades, high-impact therapies such as major surgery are applied to older, sicker and more vulnerable patients, while complication rates and thus health care costs are high in these patients. Since most research has focused on younger patients, improvements in the elderly are relatively limited. In this thesis, we have presented simple tools to identify patients who are at risk for developing complications. For the first time, we established an association between frailty, sarcopenia and malnutrition on one hand and complication rates after major gastrointestinal cancer surgery on the other. This is important scientific knowledge, which should be explored in further detail. In the near future we will perform a research project that aims to improve the peri-operative physical condition of gastric and colorectal cancer patients, to decrease susceptibility to postoperative complications. A dual modality approach using nutritional supplementation with essential amino acids and physical exercise on physical functioning after gastric and colorectal surgery will be investigated. Essential amino acids and physical exercise elicit the greatest anabolic response. Therefore this is hypothesized to counteract sarcopenia and

malnutrition. To create the greatest societal support, patient associations will be involved to implement patient requests and to resolve practical issues with regard to the nutritional and physical interventions.

Obviously, the target group described in this thesis was comprised of vulnerable patients undergoing major gastrointestinal surgery. However, the results might be applicable to other patient populations as well. A nutritional support and physical exercise program as proposed above could be extrapolated to other vulnerable patient groups, such as patients undergoing chemotherapy and those recovering from severe trauma. The problem of vulnerable elderly patients is not limited to those undergoing surgery.

Another main research theme of this thesis was the accuracy and applicability of biomarkers in plasma, urine and stool. First, we showed interesting results on markers detecting complications after colorectal surgery. As these are observational data, we are aiming to study these markers in a larger, multicenter cohort and eventually to change therapeutic decision making to improve health care. Currently, we have initiated a comparable research project to study the same markers in gastric surgery, to broaden the target group of patients who can benefit from these results. In the second part of this thesis we described non-invasive markers to diagnose necrotizing enterocolitis (NEC) in premature neonates and to guide the decision to perform surgery and to reintroduce enteral feeding. In chapter 13, we presented a decision tree when NEC is clinically suspected. We are aiming to investigate whether clinical implementation in a nationwide study decreases morbidity and mortality in children with NEC.