# Watch-and-Wait in Rectal Cancer

# IMPACT PARAGRAPH

**Main aims and outcomes of this thesis**

The main aims of this thesis are: (1) to explore how to better select patients for organ preservation with the tools currently used, (2) to investigate the quality of life and the functional outcomes in patients undergoing a watch-and-wait approach, (3) to explore the patients' perspective on organ preservation and rectal cancer treatment outcomes and (4) to evaluate treatment and outcome of local regrowth.

In Chapter 2 of this thesis we identified distinct features that may form pitfalls for clinicians in the assessment of tumor response with MRI and endoscopy. These included residual mucosal abnormalities on endoscopy, along with full thickness or irregular shaped fibrosis and mixed signal intensity on T2W-MRI, and focal diffusion restriction on DWI. These pitfalls may lead to an underestimation of patients that are eligible for organ preservation. In our diagnostic study in Chapter 3 we found that endoscopy had a moderate accuracy for the prediction of a complete response. While a white scar was most predictive of a complete response, we concluded that patients who show a small flat ulcer in the rectal mucosa surgery may also be selected for an extended observation interval. The results of Chapter 4 and 5 showed that watch-and-wait patients had good long-term quality of life, although bowel and sexual dysfunction were observed after treatment with (chemo)radiotherapy. Patients who did not have local regrowth had better quality of life and less bowel and sexual dysfunction compared to patients who had rectal surgery for local regrowth. The results of our studies can be used to counsel patients on the watch-and-wait approach and make informed treatment decisions on organ preservation. Making the right treatment decision for the individual patient is an increasingly difficult task for clinicians and patients. The results of Chapter 6 showed that patients and clinicians value treatment outcomes different and therefore have different treatment preferences. It showed that patients do value being free of cancer very high, but not at the cost of functional outcomes after treatment. The last part of this thesis, Chapter 7, showed that having a local regrowth did not compromise the outcome for patients undergoing a watch-and-wait approach. Almost all patients were still able to undergo treatment and there seemed to be no increased risk for complications after delaying the surgery.

**Relevance**

Colorectal cancer has a major impact on society, as it is a major cause of morbidity and mortality. In the Netherlands, it's the fourth most common type of cancer in men and women and approximately 4000 patients are newly diagnosed with rectal

cancer each year. The treatment of rectal cancer has tremendously evolved over the past decades and is moving towards a personalized approach for each rectal cancer patient. Organ preservation will play a major part in future treatment decisions, but it is still in a transitional phase. In 2020, the watch-and-wait approach has been included in the Dutch national guidelines on colorectal cancer as a treatment option that can be discussed with patients with a clinical complete response. While organ preservation should be performed in centers with a certain level of experience, clinicians in all colorectal multidisciplinary teams should be aware of organ preserving alternatives and should discuss these with the patient when a clinical complete response is encountered. This thesis gives clinicians more insight into the different MRI and endoscopic features that can be found at restaging and what they mean for the clinical prediction of treatment response. This could aid the standardization of the definitions of clinical complete and near clinical complete response and may be used in response-based decision algorithms. This thesis also provides valuable information on treatment outcomes regarding quality of life, functional outcome and regrowth after a watch-and-wait approach and on patient preferences. This can be used to counsel future patients on the watch-and-wait approach and to make better shared and informed treatment decisions.

**Target population**

The results of this thesis are relevant for several target groups. The relevance for clinicians has been described above. Including organ preservation as a treatment option multidisciplinary team will also affect rectal cancer patients. The results of this thesis give a clear overview of patient outcomes that can be used to counsel patients on what to expect following a watch-and-wait approach, including when regrowth occurs. Patients can therefore be better informed with the results of this thesis. If surgery can be omitted, significantly less morbidity and better functional outcomes and quality of life are expected for these patients. While this thesis was mostly focused on patients with locally advanced rectal cancer who have an indication for treatment with (chemo)radiotherapy before surgery, organ preservation could potentially also benefit patients with other stages of rectal cancer. Ongoing studies such as the TESAR and STAR-TREC trial will show the of organ preservation in patients with early stage rectal cancer. This thesis is also relevant for other researchers, as the data on outcome provided in this thesis be used as reference standard in new organ preserving strategies.

**Activities**

The research presented in this thesis has been shared with the medical community in peer reviewed papers and at national and international conferences. Research

has also been shared among the Dutch Watch-and-Wait consortium, consisting of the participating clinicians of the prospective multicenter study on the watch-and-wait approach. Newsletters are shared and a watch-and-wait symposium has been organized at the Antoni van Leeuwenhoek for the consortium for training and updates on recent study results. Future meetings could continue to provide a platform for scientists and clinicians to share results and new ideas for organ preservation in rectal cancer. The data registry that was initially build for our multicenter study, now continues to serve as a registry for patients following a watch-and-wait approach in rectal cancer in the Netherlands, which can be a source of data for any future research.