

# Organ preservation in rectal cancer

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# APPENDICES

Impact



In this chapter, the scientific impact of the results described in this thesis will be outlined, as well as the social impact anticipated or already achieved by discussing the following four aspects:

1. Research
2. Relevance
3. Target group
4. Activity

### **Research**

The main objective of the research described in this thesis was to provide an overview of the challenges in organ preservation in patients with rectal cancer and provide new data regarding patient selection, follow-up and outcomes. The most important results and conclusions of this thesis are: [1] a simplified three-categorized MRI response evaluation system aids radiologists with variable levels of expertise to identify patients who have substantial residual disease who require immediate surgery rather than further response assessment; [2] deep learning based on endoscopy images after chemoradiation (CRT) has a modest accuracy to detect complete responders; [3] the risk of lymph node metastasis increases with increasing depth of residual disease in the tumour wall after CRT, similar to the setting of total mesorectal excision (TME) without neoadjuvant therapy, and the presence of remaining malignant lymph node metastases is a strong predictor for poor outcome, independent from the ypT-stage; [4] the efficiency of the watch-and-wait (W&W) follow-up schedule increases when follow-up is intensified in the first two years and deintensified after two years; [5] the oncological and functional outcomes of older patients who follow a W&W approach are very good; [6] the risk of metastases in W&W patients is low, but there may be a small risk that some metastases originate from local regrowths; and [7] multiple MR imaging techniques are valuable for response prediction and response assessment and more techniques are on the horizon such as AI modelling.

### **Relevance**

This thesis is relevant to clinical practice as it gives tools to finetune the selection and follow-up for W&W in complete responders after CRT. Furthermore, information is provided for counseling of the patient for a W&W policy in the outpatient clinic. Based on the data from this thesis physicians and patients are better informed on the potential risks and benefits of W&W in complete responders (including the elderly). This will facilitate shared decision-making. Last, this thesis guides future research with an emphasis on exploration of new techniques to enable more accurate response prediction and assessment in rectal cancer, with the ultimate goal to increase organ preservation rates without compromising oncological outcomes.

### **Target group**

There are several people who could benefit from the results presented in this thesis. Firstly, in about 20% of locally advanced rectal cancer patients who are treated with neoadjuvant

CRT a clinical complete response is found and in these patients organ preserving treatment could be considered. In addition, patients with a good but not complete response (near complete response) after neoadjuvant treatment or those who are not suitable for surgery due to a high risk of morbidity and mortality might be candidates for organ preservation. Besides, there is a rising interest to aim for organ preservation by neoadjuvant treatment in patients who have a small rectal tumour instead of upfront surgery. These patients all benefit from the results of this thesis. Second, the results in this thesis are also interesting for the multidisciplinary team that deals with rectal cancer, for example physician assistants and clinicians such as surgeons, oncologists, gastroenterologists, radiologists and pathologists, in The Netherlands, but also abroad.

### **Activity**

The website of the Netherlands Cancer Institute provides some more background information about W&W patients that are interested in W&W but who are not familiar with the approach.<sup>1</sup> Also, a former W&W patient created a website specifically about the W&W approach<sup>2</sup> and additionally wrote two books regarding his experience and those of others with W&W.<sup>3,4</sup> This information is specifically interesting for patients with rectal cancer who are potentially eligible or considering to follow a W&W program. Through these channels patients can be informed about the results of this thesis and other results achieved by the W&W group.

The website of the Netherlands Cancer Institute might also be interesting for clinicians who are unfamiliar with W&W. In addition, every two or three years the Netherlands Cancer Institute organizes a national W&W symposium for expert centres and dedicated clinicians from the Netherlands. Every five years an international W&W symposium is being held in Lisbon organized by the International Watch-and-Wait Database (IWWD) in order to discuss the most up-to-date literature and future perspectives regarding organ preserving therapy. The knowledge gained during these meetings should be passed on to the different multidisciplinary teams of W&W expert centres and/or dedicated clinicians.

For a selected group of patients organ preservation has proven to be feasible and oncologically safe, and currently there is a focus on making organ preservation as a treatment option available to an increasing number of patients. At the same time there is a need for more data on functional outcome and quality of life. The current Dutch network originated in Maastricht University and has now been expanded and coordinated by The Netherlands Cancer Institute, with a connection to the IWWD. Maastricht University and The Netherlands Cancer Institute remain close cooperation partners in this network that provides a unique opportunity to set up new studies and provide more data. The Dutch Cancer Society has previously awarded grants to facilitate research in the field of organ preservation in rectal cancer, including the studies in the present thesis. As a result of all these efforts, The Netherlands has at present a leading position in this field, and further funding is required to retain this position.

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