GENERAL SUMMARY AND DISCUSSION

In the last 30 years, abdominal surgery has progressed from the standard open approach to less invasive techniques such as laparoscopy and natural orifice translumenal endoscopic surgery. This thesis describes the progress and implementation of new minimally invasive techniques such as single port surgery and NOTES for the treatment of rectal cancer.

**Single-port surgery**

Several randomized studies showed clear benefits of laparoscopic colon surgery over open surgery regarding short-term outcomes and equal results regarding long-term (oncological) outcomes. Single-port surgery is the result of a growing interest in further reducing the amount of surgical trauma by reducing the size and number of port sites.

**Chapter 2** displays the initial results of single-incision laparoscopic right colectomy in comparison to the multiport procedures. The study shows that the technique can be introduced safely in experienced centres. Short-term results and oncological specimen characteristics were similar between both groups.

Single-incision laparoscopy is still considered technically challenging due to loss of triangulation and clashing of the instruments, which alters the posture of surgeons. To evaluate a possible difference in physical workload to the surgeon between single-incision laparoscopy and multiport laparoscopy we designed an ergonomics study (**chapter 3**). Surface electromyography was recorded from 8 muscles bilaterally during simulated single-port and multiport laparoscopic tasks. Furthermore, questionnaires were used to measure perceived workload. Especially the back, neck and shoulder muscles showed high activity during single-incision laparoscopy when compared to multiport procedures.
NOTES

Our hospital was the first in The Netherlands to perform hybrid NOTES (transvaginal) cholecystectomy (TVC) in women with uncomplicated symptomatic cholecystolithiasis on a regular basis. It was introduced as a new scarless technique in which the posterior wall of the vagina is used as the entry point. Our studies (chapters 4 and 5) demonstrated safety and feasibility, and a superior cosmetic result of TVC when compared to single-incision and multiport laparoscopic cholecystectomy. No transvaginal-specific complications occurred.

TAMIS

In chapter 6 we describe our experience with transanal endoscopic microsurgery (TEM) with a single-port system and regular endoscopic instruments (TAMIS) instead of more expensive specialized TEM instruments. We showed that the excision of polyps with TAMIS is a save technique with results which are comparable to the classic TEM. The reduced costs of TAMIS compared to TEM makes the technique more accessible for hospitals. With the expected increase of patients due to the colon cancer screening programs, increased capacity for local excision might be necessary.

TaTME

Our experience with TAMIS and rectal cancer surgery led to the development and introduction of transanal total mesorectal excision (taTME), the main objective of this thesis. TaTME is a NOTES procedure in which rectal carcinomas are approached both through laparoscopy and transanal endoscopy. In The Netherlands, we were the first to perform this procedure. Chapters 7 and 8 display our first experience with taTME and illustrate that this new technique can be performed safely. We demonstrated a lower conversion rate and better oncological specimen characteristics, such as an improved quality of the mesorectum, when compared to multiport laparoscopic TME.

These observations prompted us to initiate a prospective study on the pathological quality of the specimen after taTME compared to multiport TME (chapter 9). We found a complete mesorectum in 96 per cent of the total of 25 specimens after taTME. Our short-term outcomes of our first 80 taTME cases showed a complete or nearly complete mesorectal excision in 97 per cent of all patients (chapter 11).
The importance of completeness of the mesorectum was pointed out by the Dutch TME trial in 2002. The trial reported an increased overall recurrence rate after two-year follow-up in case of an incomplete mesorectal excision, despite a negative resection margin (28.6 per cent versus 14.9 per cent after (nearly) complete mesorectal excision; p = 0.03). Furthermore, survival rates were significantly higher in patients with a (nearly) complete mesorectum in comparison with patients with an incomplete resection (90.5 per cent versus 76.9 per cent; p < 0.05).¹

The transrectal route has generally been seen as the least appropriate NOTES route, because of fear of bacterial translocation and related infections. Chapter 10 describes the results of a prospective study on the presence and clinical significance of peritoneal bacterial contamination during taTME. The study shows a relatively low contamination rate after taTME. However, when contamination occurs, a higher infection rate is seen. Further research is needed for the optimal rectal disinfectant procedure.

These chapters represent the development of a new surgical technique; taTME. The initial short-term results are promising. However, after the performance of different small taTME cohort studies by various surgeons over the world, we think it is time to combine this knowledge. We would like to achieve this by setting up an international randomized controlled trial: the COLOR III trial. A summary of its study protocol is written in chapter 12.

FUTURE PERSPECTIVES

Personalised surgery
In this thesis various new surgical techniques have been described. Currently, for cholecystectomy we can choose between an open, a multiport laparoscopic, a mini-laparoscopic, a single-incision laparoscopic, a transvaginal and a robotic cholecystectomy. In surgical research we are keen to develop the best surgical technique, which we can perform in all patients. The question however is, whether this is a realistic goal in an era in which there are multiple modern therapeutic surgical
options and well self-informed patients with a strong opinion. Patients differ in gender, age, morbidity, body measurements, stage of current disease, and preference. Perhaps the technique that is used should be tailored to the preference of the patient and the stage of disease.

Personalised medicine is a model that is already being successfully applied in other medical specialties. It proposes to customize healthcare with therapy tailored to the individual patient, sometimes through multidisciplinary meetings.

Regarding the different laparoscopic techniques for cholecystectomy, there is no clear clinical advantage of one approach over the other in uncomplicated disease. Surgeons preference and patient’s demands are therefore essential in decision-making. Some patients will be highly motivated to travel to hospitals where they provide single-incision or NOTES cholecystectomy, just to avoid abdominal scars. Whereas other patients are less worried about the cosmetic results and just want a safe procedure nearby.

**Options in rectal cancer**

Treatment of rectal cancer has evolved during the last few decades. Treatment is determined by many factors with tumour stage as the most important one. However, the type of treatment is also influenced by the height of the tumour, comorbidity and age of the patient. Furthermore preoperative and expected postoperative functional outcomes may also play a role. Often there are various options in which the patient plays a central role in the decision-making. Preoperative diagnostics are therefore essential, for both patients and surgeons to make a well-balanced decision.

Traditional radical rectal cancer surgery, which includes a low anterior resection (LAR) or abdominoperineal resection (APR), is associated with high morbidity rates of 36%\(^2\) and faecal and/or urinary incontinence, sexual dysfunction and (temporary) stomas, resulting in a diminished quality of life.\(^3-5\) In the elderly and patients with comorbidities it leads to high mortality rates.\(^6-8\)

The interest in less invasive treatment than radical surgery has therefore grown, especially after the observation of a complete pathological response of the primary tumour in 8-24 per cent of
patients after chemoradiotherapy.\textsuperscript{9-10} Chemoradiotherapy in combination with watchful waiting can be preferable in patients with an increased operative risk due to age and comorbidities. In these patients, a watchful waiting policy resulted in an improved survival at 1 year after treatment with a similar disease free survival and quality of life when compared to surgical resection.\textsuperscript{5} Another rectal preserving option is the performance of local endoluminal resection instead of watchful waiting after downsizing the tumour through chemoradiotherapy. Transanal local excision techniques comprises TEM, TAMIS and flexible endoscopy, including snare polypectomy, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). These techniques are more frequently seen as an adequate monotherapy in case of low risk T1 rectal cancer, defined as well to moderately differentiated adenocarcinoma without lymphatic or vascular invasion and an excision margin of at least 1 mm.\textsuperscript{12} The CARTS Study Group demonstrated the possibility of organ preservation in one-half of the patients who underwent chemoradiation followed by TEM because of cT1-3N0 rectal cancer. One out of nine patients with an ypT1 tumour after TEM developed a local recurrence after 9 months. None of the patients with an ypT0 tumour after TEM developed a local recurrence after a median follow-up of 17 months.\textsuperscript{11} In case of a pT1-2 rectum carcinoma without evidence of lymph node involvement or distant metastases, the guideline still recommends a completion TME after local excision.\textsuperscript{12} It is questionable if all patients with intermediate risk tumours should undergo completion TME surgery after neoadjuvant therapy.

The soon to start STAR-TREC study is designed to gain clarity regarding the possibilities of rectum preserving therapy by randomizing patients to one of three treatments: standard radical surgery, short-course radiotherapy followed by a TEM or chemoradiotherapy followed by a TEM. Another future study, the TESAR study, will compare the local recurrence rate after three years between adjuvant chemoradiotherapy and completion TME after local excision in case of intermediate risk early rectal cancer.

For intermediate risk resectable rectal cancer (cT1-3N1 or cT3N0 with extramural invasion of more than 5mm and a distance to the mesorectal fascia of more than 1mm) organ-sparing surgery is currently no realistic option. These patients are treated by preoperative radiotherapy and TME surgery according to the Dutch guidelines.\textsuperscript{12}
In case of indication for TME surgery, we can currently choose between open, multiport laparoscopic, combined laparoscopic with transanal, pure transanal and robotic TME.

Because of the variety of possibilities in the treatment of rectal cancer, we should be able to define the most adequate surgical technique for our individual patient. And perhaps, we should even leave our surgical skills at home when it comes to the treatment of the elderly with comorbidities. Different strategies for the treatment of rectal cancer will have different risk profiles for individual patient (morbidity of procedures versus oncologic risk). All options should be discussed with the patient so that the patient can make a well-informed decision. The therapy should be tailored to the individual patient.
REFERENCES


