General discussion and future perspectives
Inguinal hernia repair is the most frequently performed general surgical procedure worldwide. The incidence of inguinal hernias is positively correlated with the patients’ age. With advancing age, there is a disbalance in collagen synthesis towards more collagen degradation and less collagen formation and cross-linking. On the other side of the age spectrum, very young patients are also at risk for developing an inguinal hernia. The reason for this increased risk is the presence of a patent processus vaginalis which seems not only associated with congenital inguinal hernias in premature born infants, but also associated with indirect inguinal hernias which are acquired later in life. Other factors that are found to be associated with the incidence of inguinal hernias are male sex, smoking, diabetes mellitus, physical activities, and a positive family history. In a post-hoc analysis of a large population based cohort study, we focussed on incidence and risk factors for inguinal hernias in men aged 45 years and older. The hazard ratio was approximately 2 in men aged 75 years and older compared to men aged under 65 years. Literature suggests that excess body weight is associated with an increased risk of inguinal hernias, because it is believed to affect the intra-abdominal pressure. Interestingly, subgroup analysis in our study showed that a BMI over 30 kg/m² was associated with a lower incidence of inguinal hernia compared to participants with a BMI under 25 kg/m². These results were supported by data of two earlier published large population based cohort studies.

As mentioned before the incidence of an inguinal hernia increases with age, especially in men from the fifth to the seventh decade of life. Interestingly, in this population more than one-third of inguinal hernias are reported to be mildly symptomatic or asymptomatic at first presentation. Two randomized trial already focussed on the role of a watchful waiting strategy compared to elective surgery in treatment of men with minimally symptomatic inguinal hernias. These trials, however, could not show superiority of one treatment over the other with respect to inguinal hernia pain or discomfort. We decided to perform a non-inferiority trial comparing watchful waiting and elective repair of mildly symptomatic or asymptomatic inguinal hernias with special focus on men aged 50 years and older. This specific group was chosen because they particularly have more concomitant diseases and usually tend to have less physical constraints in their daily activities compared to their younger and more mobile counterparts. It can be imagined that especially at this age the risk of complications due to the procedure may not outweigh the benefits of surgery if an inguinal hernia is asymptomatic at first presentation. Using a 0.20-point difference as a clinically relevant margin, it was hypothesized that watchful waiting was non-inferior to elective repair. The results of our trial showed that the mean pain/discomfort score over 24 months is on average 0.23 points lower in the elective repair group (95% CI -0.32 to -0.14). As such, our data could not rule out a relevant difference in favor of elective repair with
regard to the primary endpoint. Because the 95 percent confidence interval of the difference of means ranged from -0.32 to -0.14, a difference of the pre-defined margin of 0.20 points or greater cannot be excluded and, therefore our trial is inconclusive in this respect. Secondary endpoints included quality of life questionnaires which were slightly in favor of elective repair. These differences, however, were too small to be clinically relevant. About one-third of the patients, initially assigned to watchful waiting, crossed over to surgery. This was mostly driven by an increase in pain or discomfort and in only 2.3 percent of the patients an emergent repair had to be performed due to an incarceration. The long-term results of the earlier mentioned randomized trial reported crossover rates up to 80 percent in men aged over 65 years old after 10 years of follow-up. It recommended surgical repair of asymptomatic inguinal hernias in medically fit men as most men will develop symptoms over time. However, subgroup analyses of our data found no differences in crossover rates between men aged 50-65 or 65 years and older. Although our data could not rule out a relevant difference in favor of elective repair with regard to the primary endpoint, we conclude, in view of all other findings, that our results justify watchful waiting as a reasonable alternative compared to surgery in frail patients.

The risk of an inguinal hernia is not only increased in middle-aged and elderly individuals, but also in the youngest amongst us. Factors that are associated with an increased risk of inguinal hernias in premature born infants include a patent processus vaginalis, male sex, gestational age, low birth weight, and prolonged mechanical ventilation. Many paediatric surgeons prefer to perform a herniotomy when the prematurely born infant reach a certain weight or age. Although this somewhat conservative approach may minimize the risk of surgical and anaesthetic complications, it might also increase the risk of incarceration forcing an emergency procedure with a potential risk of ischemia of the bowel or testicular atrophy. In literature very little is known on timing of inguinal hernia repair in prematurely born infants. In our retrospective study we showed an association between very low birth weight (birth weight under 1500g) and risk of incarceration. Prematurely born infants of 1500 grams or less had a 3-fold greater risk of incarceration with subsequent emergent repair compared to prematurely born infants over 1500 grams.

Another group of frail individuals who are generally advised to refrain from surgery unless it is absolutely necessary are patients with liver cirrhosis and ascites. Patients with liver cirrhosis and refractory ascites have a 20 percent risk of developing an umbilical hernia during the course of their disease. Possible factors that contribute to umbilical hernia formation in this group of patients include increased intra-abdominal pressure due to ascites, weakening of the abdominal wall due to muscle wasting as a
result of poor nutritional status and dilatation of the umbilical vein that enlarges the preexistent umbilical opening in patients with portal hypertension. Currently there are no guidelines for umbilical hernia management and timing of repair in patients with liver cirrhosis and ascites. Again, surgical dogma dictates not to perform umbilical hernia repair in these patients. However, refraining from umbilical hernia repair in patients with liver cirrhosis could lead to complications such as incarceration or strangulation of the bowel leading to emergency surgery. Even a relative simple procedure such as the repair of an umbilical hernia could have deleterious effects on the remaining liver function. In these patients the timing of the umbilical hernia repair is also essential, because concordant progression of the cirrhosis could hamper the possibility of future surgery. Currently a randomized controlled trial is managed comparing watchful waiting and elective repair, which will provide evidence that will help to create guidelines for management of umbilical hernias in patients with liver cirrhosis and ascites.

In contrast to inguinal and umbilical hernias, incisional hernias are postoperative complications after abdominal surgery with incidences between 11 and 20 percent and even up to 35 percent in several high risk groups. With improved long-term survival after liver transplantation, an incisional hernia has become a frequently diagnosed and clinically more relevant complication with reported incidences as high as 34 percent. Factors that are found to be associated with incisional hernias after liver transplantation include age, male sex, body mass index, pulmonary complications, wound infections, immunosuppressive regimen and incision type. Traditionally the classic ‘chevron’ incision (a bilateral subcostal laparotomy with medial extension) was the incision of choice to enter the abdominal cavity. More recently smaller incisions like a subcostal incision with or without a mediocranial extension (J-shaped incision) are preferred. The J-shaped incision still provides sufficient access to the abdominal cavity but with less abdominal wall trauma, which should theoretically reduce the incidence of incisional hernias. Despite promising results of the J-shaped incision reported in an earlier published retrospective study, the incidence of incisional hernias found in our prospective study was unexpectedly high. An incidence of 43 percent was reported, while only 7 percent was found in the previous published retrospective study. In contrast to prospective studies, it should be mentioned that retrospective studies on incisional hernias after surgery tend to underestimate the incidence of incisional hernias as most of the asymptomatic hernias are often not diagnosed and therefore not reported by those studies. Surgical site infections and age were found to be associated with the presence of an incisional hernia. Except for these factors, a clear explanation for the high incidence in this study could not be given. It was hypothesized that the increased mechanical strain on the laparotomy wound due
to wound retractors, which were used to provide adequate access to the abdominal activity, could have compromised vascularization and subsequent wound healing. The well vascularized abdominal wall, however, should provide sufficient wound healing in contrast to the aponeurotic closure in midline laparotomies. Recently, a randomized controlled trial focusing on the optimal suture technique after midline laparotomies showed that the small bites suture technique is more effective than the traditional large bites technique for prevention of incisional hernias in midline incisions.\textsuperscript{52} In liver transplantation meticulous closure of the fascia is recommended to further reduce the incidence of incisional hernias.

To conclude, surgical repair of abdominal wall hernias such as the inguinal hernia, umbilical hernia and incisional hernia are the most frequently performed general surgical procedures worldwide and considered the ideal learning procedures for young residents. In a generally healthy population, the odds of serious complications due to the procedure are fairly low. However, there are groups of frail individuals who are more prone to complications and morbidity, even if it involves a procedure such as the one at hand. Refraining from surgery in these individuals however, could also lead to complications such as incarceration or strangulation of the bowel, which subsequently could result in emergency surgery with an even higher risk of serious complications. In these individuals, timing of the surgical procedure is essential, because concordant progression of the underlying disease (such as liver cirrhosis) could hamper the possibility of future surgery. As an example, even a relatively simple procedure such as the repair of an umbilical hernia could have deleterious effects on the remaining liver function in patients suffering from liver cirrhosis.

**FUTURE DIRECTIONS AND POLICY IMPLICATIONS**

History has taught us that knowledge of anatomy is the cornerstone of abdominal wall surgery and treatment of abdominal wall hernias. Abdominal wall surgery with all its anatomical complexities is still mostly practised by general surgeons and residents. But there is a growing tendency to perform abdominal wall and hernia surgery in dedicated hernia centers. Experts in the field of hernia surgery tend to have less complications compared to general surgeons and residents.\textsuperscript{53} As this is still at an early stage, more extensive anatomical training by cadaver dissections and personal tuition for residents should be incorporated – especially in the beginning of their training, in order to lay a solid foundation, and later, further reduce preventable complications such as recurrent inguinal hernias and chronic pain as this is no longer acceptable in modern hernia surgery. As such, training modules for abdominal wall surgery for
residents should be designed and incorporated by these dedicated hernia surgeons. To improve knowledge and technical skills, abdominal wall hernia registration systems should be implemented to centralize data of patients with complex hernias from hernia centers, as these patients are currently operated by a few dedicated hernia experts with a tailor-made approach for each individual patient. Together we can further standardize care with regard to the numerous and still rising amount of techniques and materials. In modern times like these abdominal wall hernias with all its complexity should be considered and treated as a separate surgical entity and performed in hernia centers by dedicated experts in the field to further improve care of patients with (complex) abdominal wall hernias.

This thesis addresses some of the questions raised by the European Hernia Society in the latest draft of the upcoming guidelines on management of asymptomatic individuals with inguinal hernias. Our data conforms that the risk of complications – incarceration or strangulation of the bowel, following a watchful waiting strategy is low in asymptomatic individuals with inguinal hernias and, therefore, could be recommended safely. It provides information on the crossover rate from watchful waiting to surgery, which is mostly driven by an increase in pain or discomfort and not due to an emergent repair. The question then arises if most asymptomatic individuals with inguinal hernias will indeed develop symptoms over time and, will they also require hernia surgery in the future? This is a more difficult question to answer. One could argue that a substantial part of the asymptomatic or mildly symptomatic individuals with inguinal hernias are treated conservatively by their general practitioners and only a fraction of these patients are eventually referred to a hospital. The supposedly asymptomatic individuals that were included in our trial could therefore be more symptomatic compared to the population visiting their general practitioners. This could result in higher crossover rates as observed in our study. Nevertheless, our data still showed that the majority of patients randomized to watchful waiting remained asymptomatic and did not need surgery after 3 years of follow-up. One could argue that with more statistical power and the pre-defined margin of 0.20 points for the 4-point pain scale, we might be able to prove that elective repair is ‘superior’ compared to watchful waiting. Instead of just concluding this thesis with a standardized statement such as ‘more extensive trials are needed to replicate our results’, our methodology and results could be translated and add to the discussion on treatment of asymptomatic individuals with inguinal hernias. This should involve information on development on pain and discomfort and quality of life over time, which can be used for a more tailor-made approach in this group of patients in light of personalized medicine. Not only patient’s health-related quality of life, but also life style and social factors should be incorporated in this shared decision-making process leading
up to the optimal decision in hernia management on the individual level – instead of focusing solely on group level results, which are likely to be small given our results, and more likely to be close to our cut off value of 0.2. For shared decision making, physicians need to communicate to the patient personalized information about the possible outcomes of their inguinal hernia management. Whether the magnitude of the expected benefit (e.g. the risk of incarceration or strangulation of the bowel leading to emergency repair) would outweigh the disadvantages of immediate inguinal hernia surgery (e.g. co-morbidities, risk of postoperative complications, recurrence, and chronic pain) can be discussed with the individual patient sitting in front of the physician in order to reach agreement on the inguinal hernia management.
REFERENCES


