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Laparoscopic repair of incisional hernia in solid organ-transplanted patients: the method of choice?

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Conflicts of interest
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This study is registered in ClinicalTrials.gov with the identifier NCT00455299 and recommended by the Norwegian ethical committee in South Norway with unique protocol ID S-06466b and the Norwegian social science data services with identification number 15731—as well as the participating parties' local science committees.

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Summary

Due to immunosuppressive (IS) therapy, incisional hernias are overrepresented in the organ-transplanted (Tx) population with larger defects, a high rate of recurrence, and a tendency toward more seromas and infectious problems. Thirty-one Tx/IS patients with a control group of 70 non-IS patients with incisional hernia (6/7 recurrences) were included in a prospective interventional study. Both cohorts were treated with laparoscopic ventral hernia repair (LVHR). Follow-up time and rate was 37 months and 95%. One hundred LVHR's were completed as there was one conversion in the Tx/IS group. No late infections or mesh removals occurred. Recurrence rates were 9.7% vs. 4.2% ($P = 0.37$) and the overall complication rates were 19% vs. 27% ($P = 0.80$). The Tx/IS group had a higher mesh-protrusion rate (29% vs. 13%, $P = 0.09$), but also larger hernias. Polycystic kidney disease was overrepresented in the Tx cohort (44% of kidney-Tx). Incisional hernias in Tx/IS patients may be treated by LVHR with the same low complication rate and recurrence rate as non-IS patients. By LVHR, the highly problematic seroma/infection problems encountered in Tx/IS patients treated by conventional open technique seem almost eliminated. The minimally invasive procedure seems particularly rational in the Tx/Is population and should be the method of choice. (ClinicalTrials.gov number: NCT00455299, date: 5 May 2006).

Introduction

Repair of ventral and incisional hernia by laparoscopy (LVHR) has gained widespread acceptance. Especially the smaller and non-loss-of-domain hernias—as well as hernias approximating bony structures seem suitably managed by a minimally invasive technique [1]. Even laparoscopic component separation and sequentially laparoscopic repair have proven to be feasible options—as the hernia surgeons increasingly, in addition to mesh augmentation, find closure of the abdominal wall defect important [2–5]. Questions about hernia approximation in laparoscopic hernia repair are never the less still unresolved with regard to seroma formation, pain, recurrence, and mesh protrusion, as are questions concerning mesh fixation [3,5–7]. The potential benefits of reducing tissue trauma compared with open operation would likely be even greater in immunosuppressed patients [8]. By avoiding the conventional incision above the mesh, troublesome fluid accumulations causing secretion and potential infection may be reduced. This may in return reduce the recurrence rate [9,10].

Incisional hernias are frequent in the normal population after open abdominal surgery and even more frequent in a solid organ-transplanted and immunosuppressed (Tx/IS) population [11–13]. Recurrence rate after open repair with open technique is high, but can be reduced with the use of reinforcing mesh [14,15]. The low risk of infection by laparoscopy makes the method attractive and even more so for the Tx/IS population. Recent studies have proven the feasibility of both open and laparoscopic mesh implantation in immunosuppressed patients [10,16–19]. The literature on outcomes of LVHR in the Tx/IS population is limited [1,9,10,16–18,20]. To our knowledge, no prospective study with a control cohort in a unified protocol is published.

The aim of this study is to assess whether LVHR is a safe and effective solution to incisional hernia in a Tx/IS cohort in comparison with a nonimmunosuppressed (non-IS) cohort by studying how mesh overlap, hernia size, and randomization to closure/not closure of defect is associated with recurrence, protrusion, infection, and seroma.

Patients and methods

Material

The study design was a prospective multicenter interventional study with a cohort of Tx/IS patients and a control cohort with nonimmunosuppressed (non-IS) patients. 101 patients, 31 Tx/IS (liver or kidney) patients and 70 non-IS patients with incisional hernia including recurrences, situated anywhere in the abdominal wall, were enrolled for treatment with LVHR and prospective follow-up for a period of 3 years.

All patients referred with primary (i.e. nonincisional) or incisional hernia in the inclusion period from 2007 to 2010 were invited—and no patients were excluded due to surgical strategy. Primary nonincisional ventral hernias were considered as a different entity and not presented in this paper. All patients were Caucasian and have submitted verbal and written informed consent certified by the Norwegian Ethical Committee before inclusion. Data handling was approved by the Norwegian Data Inspectorate.

The Mercedes incision had been used in all liver recipients in the present study. The kidney recipients had been accessed by an extraperitoneal oblique incision, or (in a few cases) a midline intraperitoneal incision.

Three surgical centers in Norway participated: Two university hospitals and one community teaching hospital with emphasis on advanced laparoscopic procedures. One center (Oslo University Hospital Rikshospitalet) treated all—and only—the Tx/IS patients. In the Tx-center, LVHR had only been practiced for about a year, prior to the study. Of the non-IS patients, 20% were operated at the other university hospital and 80% at the rural community teaching hospital —and, there, operated or supervised by eight different senior surgeons. There was a close collaboration between the hospitals with mutual visits/meetings through the study period, and the details of the operative procedure was firmly standardized in the protocol, both regarding type of mesh, anchoring material, sutures, and overlap. There were only 3–4 transplant surgeons involved in treating the IS/Tx group.

The study was planned and completed as a randomized controlled multicenter study powered on results from a nonpublished retrospective clinically controlled study on LVHR regarding pain duration after different mesh fixation techniques. A shift of focus toward the cohort substudy was made as it became clear that the needed number of patients for the randomized study would not be reached.

Surgery

All patients were operated with laparoscopic technique: Open access or Verres' needle for creation of pneumoperitoneum, three trocars—and, in a few patients, one or two trocars were added for dissection or to accomplish secure mesh fixation. The hernia sac contents were completely reduced, and the mesh-receiving abdominal wall was stripped of preperitoneal fat. A polyester-based mesh with collagen barrier for intraperitoneal use (Parietex Composite, Covidien, Mansfield, MA, USA) was introduced—targeted in size for a minimum of 5 cm overlap of the hernia in primary hernia or the whole previous incision in incisional hernia—and fixated to the abdominal wall. To preserve the integrity of the inner antiadhesion membrane, no mesh was down-sized—according to manufacturer's rec-

ommendation. Half of the patients were to have approximated the defect before mesh placement. The sample was also split in a cross-design for two fixation techniques: four nonabsorbable corner stay-sutures and one ring of nonabsorbable tackers (ProTack, Covidien) and the other half with only tack fixation with an outer and an inner ring of tackers [21]. Patients were blindly randomized for fixation technique to the four groups: suture-raphe, suture-nonraphe, double crown-raphe, double crown-nonraphe. Defect closure was achieved by intracorporeal suture in a figure of eight and extrafascial knotting [22].

Immunosuppression

The Kidney-Tx recipients of the Tx/IS group received quadruple immunosuppression with calcineurine inhibitor (CNI) or mammalian target of rapamycin inhibitor (mTOR), basiliximab, mycophenolate mofetil (MMF) and corticosteroids. The triple immunosuppressive protocol of the liver-Tx recipients consisted of CNI or mTOR, MMF, and corticosteroids. At transplantation, both liver and kidney recipients received a 500 mg methylprednisolone bolus, which was tapered to 20–30 mg prednisolone after 8 days, and further weaned to 5 mg prednisolone after 6–12 months.

At the time of LVHR, the recipients received 2.5–15 mg prednisolone, while in two liver recipients, steroids had been withdrawn. Nine of the 31 in the Tx/IS group were on mTOR.

Collection of data

Patients were invited to nonblinded clinical control at their respective hospitals 2 months and 3 years after the operation. Patient- or clinician-observed adverse reactions were recorded and suspicion of recurrence or protrusion of mesh through hernia defect were examined by sonographic specialist with ultrasound including Valsalva maneuver and in some patients a CT scan was supplementary. Recorded information in addition to the variables presented in Table 1 include heart disease, type and topography of hernia, previous hernia treatment, access method for laparoscopy, number and size of used trocars, pain level (VAS score), pain duration, time to normal activity, and duration of sick-leave. In the Tx/IS group also, previous transplantation and reason for transplantation were registered.

Primary endpoints were hernia recurrence and mesh protrusion. Mesh protrusion was defined as a bulge at the previous hernia defect, but the whole defect is still completely covered and abdominal content retained by the implanted mesh. Any perceivable bulging not classified as recurrence after clinical and sonographic evaluation was recorded as protrusion in this study. Protrusion was documented as small (≤2.5 cm), medium (2.6–5.0 cm), or large (>5 cm) in prominence above the abdominal wall during Valsalva maneuver in supine position. Secondary endpoints were complications as enterotomy, mesh infection, wound infection, reoperation, seroma formation, and long-term pain.

Table 1. Laparoscopic incisional hernia repair: demographic data and disease/medication characteristics in a solid organ-transplanted and immunosuppressed (Tx/IS) cohort and a nonimmunosuppressed (non-IS) cohort.

	Tx/IS, # = 31	Non-IS, # = 70	Fisher exact test, *P*-value
Age, years, mean (range)	56 (37–69)	57 (32–81)	0.758
Body mass index, kg/m^2, mean (range)	28 (19–33)	30 (20–50)	0.549
ASA physical score, 0-E, mean (range)	2.2 (1–3)	1.8 (1–3)	0.001
Chronic obstructive pulmonary disease, # (%)	6 (19)	9 (13)	0.287
Female/Male sex, #:#	9:22	55:15	<0.001
Primary (nonrecurrent) incisional hernias, # (%)	25 (81)	63 (90)	0.165
Recurrent incisional hernias, # (%)	6 (19)	7 (10)	0.165
Liver-Tx/Renal-Tx, #:#	15:16		
mTor immunosuppression Liver-Tx/Renal-Tx, #:#	4:5		
Polycystic kidney disease, # (%)	7 (23)		

mTOR, mammalian target of rapamycin inhibitor.

Data calculations and analysis

A one-dimensional overlap coefficient defined as the least difference between mesh size and hernia size in two directions, divided by the double of the targeted mesh overlap of 5 cm in any direction, was calculated. Hernia size in quadratic area (multiplication of hernia length and hernia width, for comparison with other studies) as well as a more geometrically sound ellipsoid area calculation (area calculation by ellipsoid formula: $\pi/4$* A * B, where A and B are the two diagonals), and the area for in-growth derived by subtracting ellipsoid area hernia size from mesh area, was also calculated [23].

The six studied endpoints were all dichotomous variables. The following study factors were categorized into ordinal variables with three categories: hernia area ellipsoid (≤20 cm^2, >20 and ≤100 cm^2, and >100 cm^2), ingrowth area (≤200 cm^2, >200 and <301 cm^{2,} and ≥ 301 cm^2) and overlap coefficient (≥1, <1 and ≥0.8, and <0.8). The

treatment group was dichotomous (Tx/IS vs. non-IS patients) as was defect closure. Four possible confounding variables were considered for adjustment: BMI was divided into three categories (≤25 kg/m^2, >25, and <30 kg/m^2, and ≥30 kg/m^2) and age in years (<50, ≥50 and <60, and ≥60), while sex and chronic obstructive pulmonary disease (COPD) were dichotomous.

The associations between treatment group and hematoma and re-operation, respectively, were analyzed bivariate using Fisher's exact test. The other endpoints were analyzed in four multiple regression models. The adjusted odds of recurrence and protrusion, respectively, were estimated for randomization to defect closure, hernia area ellipsoid, overlap coefficient, and treatment group, adjusted for BMI, age, chronic obstructive pulmonary disease (COPD), and sex. The same study factors were included in the analysis with seroma as the endpoint, but without adjustment for additional factors. The odds of infection in the Tx/IS treatment group compared with the non-IS group was adjusted for BMI.

The significance level was set at five percent in all tests. Odds ratios (OR) with 95% confidence intervals (CI) are reported for all study factors included in each regression model, and the *P*-values from the Fisher's exact tests.

Results

Two patients in the Tx/IS cohort and three patients in the non-IS cohort with incisional hernia died of causes unrelated to hernia surgery before 3 years follow-up but with updated status at their time of death, leaving 96 patients (95%) for the full-time follow-up period of 3 years. The studied cohorts are well matched regarding age, body mass index and American Society of Anestesiologists physical classification score (ASA), but not in sex (Table 1). There was no difference in operating time (median 110 min vs. 90 min) or time to normal activity. Of significance was male majority, longer admission time, larger hernias, less mesh overlap, and a smaller Zuhlke adhesion classification score [24] in the Tx/IS group (Table 2).

As shown in Table 3, there were no differences in hematoma, reoperation or infection rate. Treatment group and the study factors were not associated with the adjusted risk of recurrence or seroma, but there was a tendency toward less seroma incidence in the Tx/IS cohort (OR = 0.23; CI: 0.02–2.27). No difference was seen in percentage of patients with pain recorded at 2 months ($P = 0.318$), but five patients in the non-IS group have had fixation devices removed: three with removal of suture and two with tacker removal. None of the transplant patients had long-term fixation device-related pain.

As shown in Table 4, the recurrence rates in the studied cohorts were similar (9.7% vs. 4.2%, $P = 0.368$) in univariate comparison. The three patients with recurrences in the Tx/IS group were leaner [mean BMI 27 (25–29) vs. 32 (28–38)] and younger (mean age 54 vs. 62) than the three patients with recurrences in the non-IS cohort. Both sexes (two male and one female) were represented in the Tx/IS group with recurrence—in the non-IS group, there were only female patients [25]. There was no correlation between

Table 2. Laparoscopic incisional hernia repair: perioperative data and events in a solid organ-transplanted and immunosuppressed (Tx/IS) cohort and a nonimmunosuppressed (non-IS) cohort.

	Tx/IS, mean (range)	Non-IS, mean (range)	Fischer exact test, *P*-value
Hernia length, cm	11.0 (3–25)	7.9 (1.0–28)	0.029
Hernia width, cm	8.5 (3–18)	4.8 (1.0–15)	<0.001
Mesh length, cm	19.9 (9–35)	21.6 (15–37)	0.249
Mesh width, cm	16.2 (9–30)	16.4 (10–28)	0.878
Hernia area—quadratic, cm^2	117 (6–450)	50 (1–405)	<0.001
Hernia area—ellipsoid, cm^2	92 (5–353)	40 (1–318)	<0.001
Ingrowth area*, cm^2	260 (76–761)	334 (131–794)	0.004
Overlap coefficient†	0.7 (0.3–1.2)	1.1 (0.5–1.8)	<0.001
Zuhlke adhesion score, 0–4	1.8 (0–3)	2.7 (0–4)	0.013
Operating time, min	114 (45–220)	98 (26–235)	0.869
Admission time, days	4.7 (1–9)	2.8 (0–30)	<0.001
Intestinal serosal damage repaired, # (%)	1 (3.2)	6 (8.3)	0.582
Conversions, # (%)	1 (3.2)	0‡	0.674

*Ellipsoid hernia area subtracted from mesh area.
†Coefficient of ideal overlap, 1.0 equals 5 cm overlap (ref. Methods).
‡One open adhesiolysis but laparoscopic hernia repair.

Table 3. Laparoscopic incisional hernia repair: complications in a solid organ-transplanted and immunosuppressed (Tx/IS) cohort and a nonimmunosuppressed (non-IS) cohort.

	Tx/IS, # (%)	non-IS, # (%)	Fischer exact test, *P*-value
Intestinal perforation	*0*	*1 (1.4)*	*0.504*
Omental bleeding	*0*	*1 (1.4)*	*0.504*
Bladder perforation	*1 (3.2)*	*0*	*0.674*
Reoperations total	1 (3.2)	2 (2.8)	0.757
Trocar wound cellulitis	2 (6.5)	5 (7.1)	0.633
Trocar wound hematoma	0	2 (2.9)	0.126
Hernia sac seroma	1 (3.2)	9 (12.9)	0.285
Pneumonia/atelectasis	2 (6.5)	1 (1.4)	0.462
Urinary tract infection	0	0	1.000
Thromboembolic event	0	0	1.000
Mortality	0	0	1.000
Total	6 (19.4)	19 (27.1)	0.801

Causes for reoperation in italic typography.

Table 4. Laparoscopic incisional hernia repair: long-term outcomes in a solid organ-transplanted and immunosuppressed (Tx/IS) cohort and a nonimmunosuppressed (non-IS) cohort. Protrusion size defined by prominence above abdominal wall at Valsalva maneuver in supine position.

	Tx/IS, # (%)	non-IS, # (%)	Fischer exact test, *P*-value	Odds ratio (95% confidence interval) binary logistic regression
Observation time (months)	36 (8–46)	38 (12–73)	0.235	
Recurrence	3 (9.7)	3 (4.2)	0.264	
Protrusion/Eventration	9 (29.0)	9 (12.7)	0.088	
Large (>5 cm)	6	5	0.088	
Medium (2.6–5 cm)	2	2	0.584	
Small (0.1–2.5 cm)	1	2	1.000	
Protrusion, Female:Male	0:9		0.032	Not applicable
Protrusion, Female:Male		4:5	0.018	0.16 (0.04–0.69)
Protrusion, PKD in Tx cohort	3:7		0.358	2.75 (0.36–21.30)
Trocar hernia	0	0	1.000	
Hernia reoperations	3	2	0.167	
Pain at 2 months	3 (9.7)	11 (15.3)	0.319	
Removal of fixation material	0	5 (7.1)	0.320	
Local repair of protrusion	1	0	0.674	

PKD, Polycystic Kidney Disease.

mTOR immunosuppressive therapy at the time of LVHR and recurrence. The mean hernia area size in the Tx/IS cohort was higher ($P < 0.001$), but the mean mesh size used was equal to the control cohort. This is reflected by the mean overlap coefficient, which in the Tx/IS cohort was 0.7 (i.e. mean overlap 3.5 cm), and the targeted overlap of 5 cm was reached in only five of 31 patients (16%). 14 patients (45%) had a coefficient of 0.8 or higher (i.e. ≥4 cm overlap). In the non-IS cohort, the mean overlap coefficient was 1.1 (i.e. mean overlap 5.5 cm) and the target was reached in 47 of 70 patients (67%), and 66 patients (94%) had an overlap coefficient of 0.8 or more.

Table 5. Laparoscopic incisional hernia repair: multiple logistic regression on combined organ transplant and immunosuppressed (Tx/IS) and nonimmunosuppressed cohorts: the adjusted odds ratios (with 95% Wald confidence intervals) for recurrence, protrusion, seroma, and infection for study factors in the multivariate models.

	Recurrence*	Protrusion†	Protrusion† men only	Seroma	Infection
Tx/IS cohort *belonging to*	1.35 (0.11–17.24)	3.69 (0.70–19.47)‡	3.63 (0.42–31.30)	0.23 (0.02–2.27)	1.11 (0.19–6.36)
Hernia size (ellipsoid) *increasing*	2.53 (0.45–14.18)	0.98 (0.39–2.51)	0.61 (0.12–3.04)	1.30 (0.46–3.64)	Not applicable (NA)
Ingrowth area§ *increasing*	0.69 (0.12–3.96)	**3.46** (1.16–10.35)¶	**6.14** (1.19–31.68)	1.34 (0.46–3.66)	NA
Defect closure *Intended (randomized)*	1.04 (0.18–6.05)	0.51 (0.15–1.71)	0.16 (0.02–1.18)	0.42 (0.10–1.77)	NA
Overlap coefficient** *decreasing*	1.75 (0.39–7.90)	1.33 (0.50–3.52)	1.24 (0.38–4.05)	NA	NA
COPD†† *present*	2.98 (0.38–23.62)	0.82 (0.18–3.75)	0.46 (0.06–3.56)	NA	NA
Body mass index (BMI) *increasing*	1.00 (0.31–3.18)	**0.46** (0.22–0.98)	0.58 (0.18–1.54)	NA	2.35 (0.73–7.52)

Statistically significant values ($P < 0.05$) in bold typography.
*Adjusted for age and sex.
†Adjusted for age.
‡4.81 (0.87–26.69) when ingrowth area was included as dichotomous variables.
§Ellipsoid hernia area subtracted from mesh area.
¶16.32 (1.36–196.40) in the middle category with the lowest category as reference; 25.33 (1.69–380.20) in the highest category with the lowest category as reference.
**Coefficient of ideal overlap (ref. Methods).
††Chronic obstructive pulmonary disease.

One recurrence occurred in a patient who previously had radiotherapy for treatment of malignant lymphatic abdominal disease. She got an unattended iatrogenic colonic perforation and consequently had her mesh explanted and thus regained her hernia. She also developed enteric fistulae and had a long hospital stay. No other mesh-related infection or explantation has been observed. Another recurrence was a technical failure as the mesh positioned at primary repair was found to be fixated only just tangential to the defect and therefore not augmenting the defect. These recurrences were in the non-IS group.

The adjusted odds ratio for protrusion was 3.69 (CI: 0.70–19.47) in the Tx/IS group compared with the non-IS group. As there were no women with protrusion in the Tx/IS cohort, sex was removed from the model. However, the association for the Tx/IS group was also observed when including only men in the analysis (OR = 3.63; CI: 0.42–31.30). Male sex was significantly associated with protrusion in a bivariate analysis ($P < 0.001$; Fisher's exact test). In either cohort, there were no differences in overlap between subgroups with or without protrusion. The hernias in the respective protrusion subgroups were larger. However, hernia size was not associated with an increased risk of protrusion, but larger mesh ingrowth area was (OR = 3.46; CI: 1.16–10.35), with additional accentuation in the men-only analysis (OR 6.14; CI: 1.19–31.68). The estimated ORs for seroma, recurrence, and protrusion were independent of how the patients were randomized, as randomization to defect closure was adjusted for in the regression models. However, we found a protective tendency of defect closure in regard to protrusion when including only men in the regression analysis (OR = 0.16; CI: 0.02–1.18). There were no missing values for any of the variables included in the analysis. The detailed results of the regression analyses are presented in Table 5. One patient became pregnant during the follow-up period and completed her pregnancy without adversities [26].

Discussion

The Tx/IS population

The *solid organ transplant population* is obviously prone to more wound complications and recurrences, due to delayed and incomplete wound healing, involving severely affected fibroblast proliferation and fibrous repair. Previous studies have shown the hernia defects in the Tx/IS population to be distinctly larger [13,27,28]. Our data support these findings.

The impact of these immunosuppressive effects may be demonstrated/exemplified by the fact that lymphocele/lymph leakage is a major problem after allograft kidney transplantation (KTx) (3–18% requiring re-interventions) [29], while in renal auto-transplantation, this problem is almost nonexistent [30]. During recent years, the immunosuppressive treatments have been increased and optimized, resulting in fewer rejection episodes, but probably with more severe adverse effects also regarding wound healing.

Polycystic kidney disease (PKD) is a congenital, systemic disorder affecting fibrous tissue development and structure [31]. Interestingly, PKD is distinctly overrepresented in our material constituting seven of 16 KTx (44%), while the PKD proportion in our KTx population is only 10–12% [32]. The debilitating effect of PKD on fibrous healing seem to potentiate the immunosuppressive antiproliferative effect.

The Mercedes incision used in all liver recipients in the present study is probably a major risk factor for hernia due to simple vascular reasons. The now preferred L-shaped incision [33] will probably give rise to a lower hernia incidence in the future.

The likely explanation of the distinct preponderance of men (71%) in the Tx/IS group is that more men suffer from both kidney and liver failure [28]. We are not able to explain the predominance of women (71%) in the non-IS group—but cosmetic reasons, in conjunction with distinctively smaller hernia, may be a reasonable factor.

Complications/seroma/infection

One of the most prominent features regarding the Tx/IS patients in this study, is the low rate of major *postoperative complications* (19%). The problem of seroma formation and thereby increased infection hazard above the mesh, seem almost eliminated with the LVHR approach, quite obviously caused by omitting the incision above the mesh. The tendency toward a lower incidence of seromas in the Tx/IS group may also be explained by a reduced inflammatory response caused by the immunosuppressive drugs, in particular, corticosteroids and mycophenolate mofetil [34]. Prior to the minimally invasive era, the open procedure—with a large incision above the mesh—gave rise to huge problems, often involving a seroma with communication to mesh and cutaneous incision.

All detected seromas (predominantly in the non-IS group) regressed spontaneously prior to 3 months without treatment.

This study indicates that the low rates of complications in the non-IS population when using LVHR, compared with open methods [32,35], can indeed be conveyed to the Tx/IS patient population. The previous reluctance with using synthetic mesh in immunosuppressed patients seems a surpassed stage.

Recurrence; causes

A *recurrence rate* of about 10% in the Tx/IS population must be considered satisfactory and comparable to non-IS

patients. Previous studies have also been able to show an equally low recurrence rate with LVHR [8–10,13]. However, methodologically, we do consider our 3-year observation period with almost 100% complete follow-up as a strength. The inherently larger hernias and immunosuppression (and PKD incidence) in the Tx/IS group would be suspected to cause more recurrences [11,12,19,25,27,28, 36,37].

Furthermore, the regression analysis (Table 5; on both groups collected) revealed a possible association between the factors 'Hernia size (ellipsoid)' and COPD with recurrence. The factor 'Overlap coefficient' only gave rise to an insignificant OR of 1.75. Several authors emphasize the importance of sufficient overlap in LVHR to compensate for mesh shift, positioning, and shrinkage, but no randomized study has to our knowledge substantiated these claims [38].

Recurrences may also be related to awkward hernia localizations, particularly with larger defects in the Tx/IS group extending toward the iliac crest or ribs/sternum [39,40]. The single conversion in the Tx/Is group and one of the three recurrences were caused by a potentially insufficient mesh overlap in-between the kidney graft and the iliac crest. In these cases, an open approach should be considered. Furthermore, in other locations with osseous proximity, in particular toward the ribs—the exact placement of transfascial sutures and tackers—should be deliberate.

Protrusion

The Tx/IS hernias seemed distinctly more prone to *mesh protrusion* (Table 5: OR 3.69; CI: 0.70–19.47), probably due to larger defects and inferior wound healing, with retarded scar formation and diminished mesh shrinking. These relationships have been depicted in Fig. 1. From obvious physical reasons, we consider a larger mesh to be subjected to more peripheral tension and thus protrusion, further accentuated with immunosuppression. Even though we did not find any association between hernia size and protrusion in the combined cohorts (Table 5: OR 0.98; CI: 0.39–2.51), we think the basic data and theoretical considerations are consistent [41].

In our study, male sex was associated with protrusion overall and within each cohort (Table 4). The great baseline discrepancy regarding sex distribution (71% males in Tx/IS vs. 71% females in non-IS) does represent a methodological weakness. However, by segregating 'Men only' in the regression analysis, the same observed elevated risk for protrusion is sustained. Furthermore, there is no support from the literature, nor from basic physio-pathological considerations, to favor a sex difference regarding protrusion.

Increased 'mesh ingrowth area' was also associated with development of protrusion (Table 5: OR 3.46; CI: 1.16–10.35), which may be explained by the fact that a larger hernia, from simple mathematical reasons, will require a larger

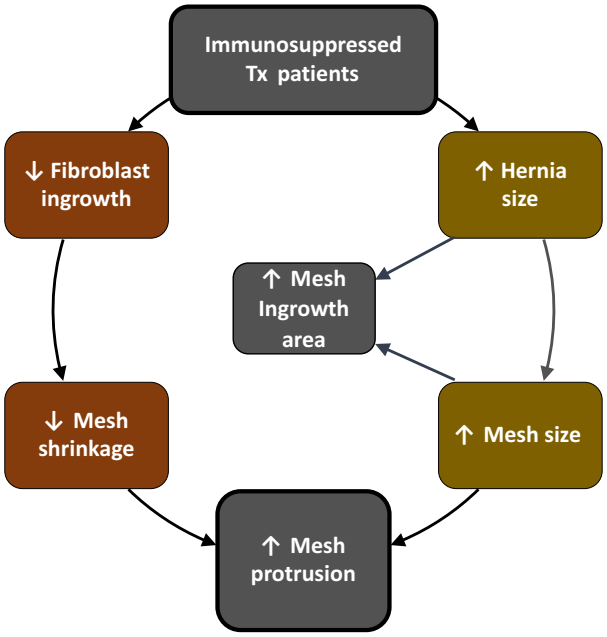

Figure 1 Factors/Relationships favoring net-protrusion in immunosuppressed/Tx patients.

mesh size/area, to secure a 5 cm overlap all around the perimeter.

The increased protrusion rate in the Tx/Is group with significantly larger defects and the potential protective effect of raphe suggested by the men-only regression analysis does support defect closure. Thus, we would consider an open, laparoscopic, or hybrid procedure in the Tx/IS population with larger defects (> 8–12 cm); attempting total fascial closure above the mesh, by layer separation/mobilization [42,43]. This is also proposed in the recently published European Hernia Society guidelines [2].

One patient in the Tx/IS population required a successful tightening of the mesh by an open procedure by splitting the mesh and overlapping the mesh edges for sufficient tension. Many small and medium bulges (<5 cm) are indolent and even unrecognized by the patients. In our experience, slender patients seem to be less compliant to a bulge and are more perceptive to its presence. This may explain the protective association of increasing BMI (OR 0.46; CI: 0.22–0.98).

Type of mesh/fixation devices

In this study, a mesh made of polyester with a good ingrowth ability [44] and antiadhesive absorbable inside layer was used. Superior ingrowth ability is a key feature in the choice of mesh [31,38,45] and probably even more so in the immunosuppressed population [46]. Proposing the use of biological meshes in the Tx/IS population seems

rational. In future (disregarding the economic aspects), biological 'decellularized', 'scaffold' meshes may be the chosen material in Tx/IS patients, even in uncontaminated circumstances. However, the performance of a disintegrating scaffolding mesh in a fibroblast-retarded population still needs to be investigated [38,47]. This study supports the feasibility of synthetic mesh implantation in the intraperitoneal space.

Though not statistically significant, it is remarkable that no fixation device was found related to long-term pain in the Tx/IS group, as opposed to the non-IS cohort, with five cases in need of fixation material removal. The immunosuppressive medication (involving corticosteroids) may have exerted an anti-inflammatory—and thereby analgesic—response [48]. As no undesired effects were observed from permanent fixation devices and impaired inflammation/fibrous repair required for ingrowth of mesh is expected, a permanent (non-absorbable) fixation method may still seem advisable in the Tx/IS group. After this study—numerous absorbable tacker devices have been marketed and reported to have less long-term pain problems. However, no firm evidence has been presented, and particularly not any concerning the Tx/IS population.

The minimally invasive procedure seems particularly justified in the immunosuppressed population and should be the method of choice. These considerations are further accentuated by the introduction of more potent antiproliferative drugs (mTOR/MMF).

Conclusions

We found no difference between an immunosuppressed cohort and a nonimmunosuppressed cohort regarding recurrence or complications after laparoscopic incisional hernia repair. We observed a higher rate of protrusion in the Tx/IS group. We conclude that solid organ transplant and immunosuppressed patients can be treated with laparoscopic hernia repair with similar results as in nonimmunosuppressed patients—omitting the troublesome seromas/infections above the mesh—and thus qualify as the favored procedure.

Authorship

JRL: designed and performed study, collected data, analyzed data, writer. MS: collected data, evaluated data, co-writer. ET: Collaborated in study design, collected data, co-writer. AV: Analyzed data, co-writer. OMØ: Collaborated in study design, collected data, evaluated data, co-writer.

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