Synthetic Versus Biological Mesh in Laparoscopic and Open Ventral Hernia Repair (LAPSIS)

Results of a Multinational, Randomized, Controlled, and Double-blind Trial

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Objective: The aim of this study was to investigate the approach (open or laparoscopic) and mesh type (synthetic or biological) in ventral hernias in a clean setting.

Summary of Background Data: The level of evidence on the optimal surgical approach and type of mesh in ventral hernia repair is still low.

Methods: Patients with a ventral abdominal hernia (diameter 4–10 cm) were included in this double-blind randomized controlled trial across 17 hospitals in 10 European countries. According to a 2 × 2-factorial design, patients were allocated to 4 arms (open retromuscular or laparoscopic intraperitoneal, with synthetic or Surgisis Gold biological mesh). Patients and outcome assessors were blinded to mesh type used. Major postoperative complication rate (hernia recurrence, mesh infection, or reoperation) within 3 years after surgery, was the primary endpoint in the intention-to-treat population.

Results: Between September 1st, 2005, and August 7th, 2009, 253 patients were randomized and 13 excluded. Six of 61 patients (9.8%) in the open synthetic mesh arm, 15 of 66 patients (22.7%) in the open biological mesh arm, 7 of 64 patients (10.9%) in the laparoscopic synthetic mesh arm and 17 of 62 patients (27.4%) in the laparoscopic biological mesh arm had a major complication. The use of biological mesh resulted in significantly more complications ($P = 0.013$), also after adjusting for hernia type, body mass index, and study site. The trial was prematurely stopped due to an unacceptable high recurrence rate in the biological mesh arms.

Conclusions: The use of Surgisis Gold biological mesh is not recommended for noncomplex ventral hernia repair.

Trial Registration: This trial was registered at controlled-trials.com (ISRCTN34532248).

Keywords: biological mesh, clinical randomized controlled trial, incisional hernia, laparoscopic intraperitoneal onlay mesh repair, postoperative complications, primary abdominal wall hernia, recurrence, retromuscular hernia repair, synthetic mesh

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The gold standard for ventral hernia repair (VHR) is the open retromuscular synthetic mesh technique (with anterior fascial closure).[1] Since 1993, laparoscopic VHR with intraperitoneal onlay mesh has been widely adopted because of its less invasive nature.[2] A Cochrane review of randomized controlled trials (RCTs) showed significant advantages of laparoscopy regarding wound infection and hospital stay with comparable recurrence rates.[3] Unfortunately, the included studies were small, highly heterogenic with short follow-up.

The permanent presence of a synthetic foreign body may lead to specific long-term complications such as chronic pain, mesh infection, intestinal adhesions, erosion, and fistula.[4–6] The ideal mesh would; therefore, be a temporary scaffold inducing remodeling

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MM, MH, WHS, GR, FW report personal fees from IFOM, during the conduct of the study (reimbursement of travel expenses during the conduct of the study; administrative fee per patient included and final follow-up accomplished). RL, TM, DS, EN report grants from Cook Medical, Inc., Bloomington, IN, USA, to the IFOM (Witten/Herdecke University), during the conduct of the study. FF, SS, DK, GW, FA, MS, RR, DC, FC, CR, FS, BS, SS, and LN have nothing to disclose.

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of the abdominal wall whereas being resorbed gradually over time, leading to strong, well-organized newly formed collagen. For this reason, biological meshes were introduced. About 20 years later only a few RCTs are available for inguinal and paraesophageal hernia.[7,8] For VHR the evidence available is even lower and mainly limited to surgery in a contaminated environment.[9]

The primary aim of the trial was to identify the optimal surgical approach (laparoscopic or open) and the most suitable mesh (biological or synthetic) in elective, noncontaminated VHR by evaluating major postoperative complications (hernia recurrence, mesh infection, reoperation) within 3 years postoperatively. We proposed that laparoscopic VHR is superior to open surgery and that biological mesh is at least as effective as synthetic material.

METHODS

Design and Ethics

We conducted a double-blind RCT (LAPSIS trial) using a 2 × 2-factorial design involving 17 study sites in 10 European countries, under the auspices of the European Hernia Society.

Ethical approval of the Lead Ethical Committee (Belgium) was obtained. The Institutional Review Board at each hospital approved the study protocol. Written informed consent was obtained from each patient before enrolment. An Advisory Board Committee supported the preparation of the study protocol. Quality control was performed by on-site monitoring, and data verification. In addition, photo and/or video documentation were performed to ensure protocol compliance and as surgical quality assurance tool.

Participants

Adult patients (≥18 years old) scheduled for elective mesh repair of a ventral primary or incisional hernia (orifice diameter 4–10 cm) without contraindication for laparoscopic repair were eligible. In case of multiple hernia orifices, the total sum of the different orifices was used as hernia diameter. Main criteria for exclusion were: contraindication to general anesthesia, American Society of Anesthesiologists score ≥4, pregnancy, contamination, emergency surgery, previous mesh repair at the same site, hernia orifice within <3 cm from bony edges, lumbar or parastomal hernia, need for more than 1 mesh or a mesh larger than 20 × 20 or 22 × 13 cm, body mass index (BMI) >40, simultaneous participation in another interfering trial, and previous participation in this trial.

Randomization

We used a central web-based preoperative randomization with a variable block length to assign patients, in a 1:1:1:1 ratio. Stratification was performed according to study center and hernia type (primary or incisional). The study was double blinded (patient and final evaluator) for the type of mesh used. The final evaluator was an experienced general surgeon not involved in the trial.

Interventions

Each participating center used local standards concerning pre-, peri- and postoperative, identical in all groups. Surgery was performed by a consultant surgeon with experience in the technique (≥25 procedures performed), including the use of biological mesh in both approaches before the study. The ''best team'' approach was adopted. Single shot antibiotic prophylaxis with a second-generation cephalosporin was performed. The preoperative dimensions of the hernia orifice were reassessed intraoperatively. At least 5 cm circumferential mesh overlap was recommended. Fascial coverage of the whole incision was decided case by case.

The biological mesh used was Surgisis Gold (Cook Medical, Inc., Bloomington, IN), a nonchemically crosslinked acellular resorbable type I collagen glycosaminoglycan scaffold consisting of 8 vacuum-pressed layers derived from extracellular matrix of porcine small intestinal submucosa. During the trial, the manufacturing of the mesh was modified leading to a decreased amount of lipid and DNA fragments in the material (initially Surgisis 8-layer Tissue Graft, C-SAH-8H, later Biodesign Surgisis 8-layer Tissue Graft, C-SAH-8H 2.0). As the synthetic mesh either a composite mesh (Composix E/X, C.R. Bard, Inc, Cranston, NJ) or a ePTFE mesh (GORE DUALMESH PLUS with Holes, W.L. Gore & Associates, Flagstaff, AZ) were used in the laparoscopic group (decision left to the surgeon for each case). A polypropylene mesh (Bard Mesh, Bard, Warwick, RI) was used in the open cases. If there was a medical reason to change the type of allocated mesh, only these materials were approved.

Open surgery was performed using a retromuscular approach. Contact of the bowel with the polypropylene mesh had to be avoided. The mesh was fixed transfascially on the anterior rectus sheath with (non-)resorbable sutures. The anterior rectus sheath was preferably closed (even partially) without tension (mesh augmentation). Relaxing incisions or component separation techniques were not allowed. In laparoscopic repair, there was no attempt to remove the hernia sac or close the fascial defect. Mesh fixation was performed with slowly- or nonresorbable sutures and/or commercially available fixation devices (single or double crown) every 2 cm. Postoperatively, a compressive elastic bandage was compulsory after laparoscopic repair at least until discharge. Patients were recommended not to do sports or lifting for 3 weeks postoperatively.

Data Collection

Patients were clinically assessed at hospital discharge and after 4 weeks (range 3–5), 3 months (range 2–4), 1 year (range 11–13 months), and 3 years (range 35–37 months) postoperatively.

Primary and Secondary Outcomes

The primary endpoint was major complication rate defined as the occurrence of at least one of the following events: hernia recurrence, mesh infection, or reoperation associated with the hernia repair within 3 years postoperatively. This composite endpoint was chosen because a hernia recurrence may be of less concern for the patient than a more severe complication such as mesh infection or reoperation. Hernia recurrence was diagnosed clinically, with ultrasound or CT scan in case of doubt; mesh infection was considered in case of a wound sinus or chronic fistula to the mesh and infiltration and/or abscess around the mesh requiring antibiotics and/or mesh removal; a positive culture of fluid in the vicinity of the mesh was necessary; reoperation was defined as a surgical intervention under general anesthesia related to the earlier VHR.

The secondary endpoints were early (≤30 days postoperatively) and late (>30 days postoperatively) local complications, mortality, and abdominal wall pain (assessed with visual analog scale 0–10 where 0 is best) up to 3 years postoperatively. Additional endpoints were operation time, length of hospital stay (LOS), time of return to work, rate of serious adverse events, and patient satisfaction (visual analog scale 0–10 where 10 is best) up to 3 years postoperatively.

Sample Size

The study was designed to establish noninferiority of the biological mesh compared to synthetic materials and superiority of the laparoscopic versus open surgical approach concerning the primary endpoint in a 2 × 2-factorial design. Given a noninferiority margin of $\Delta = -0.05$ and estimated proportions for major complications based on previous trials (laparoscopic biological: 7%; laparoscopic synthetic: 11%; open biological: 16%; open synthetic: 20%)

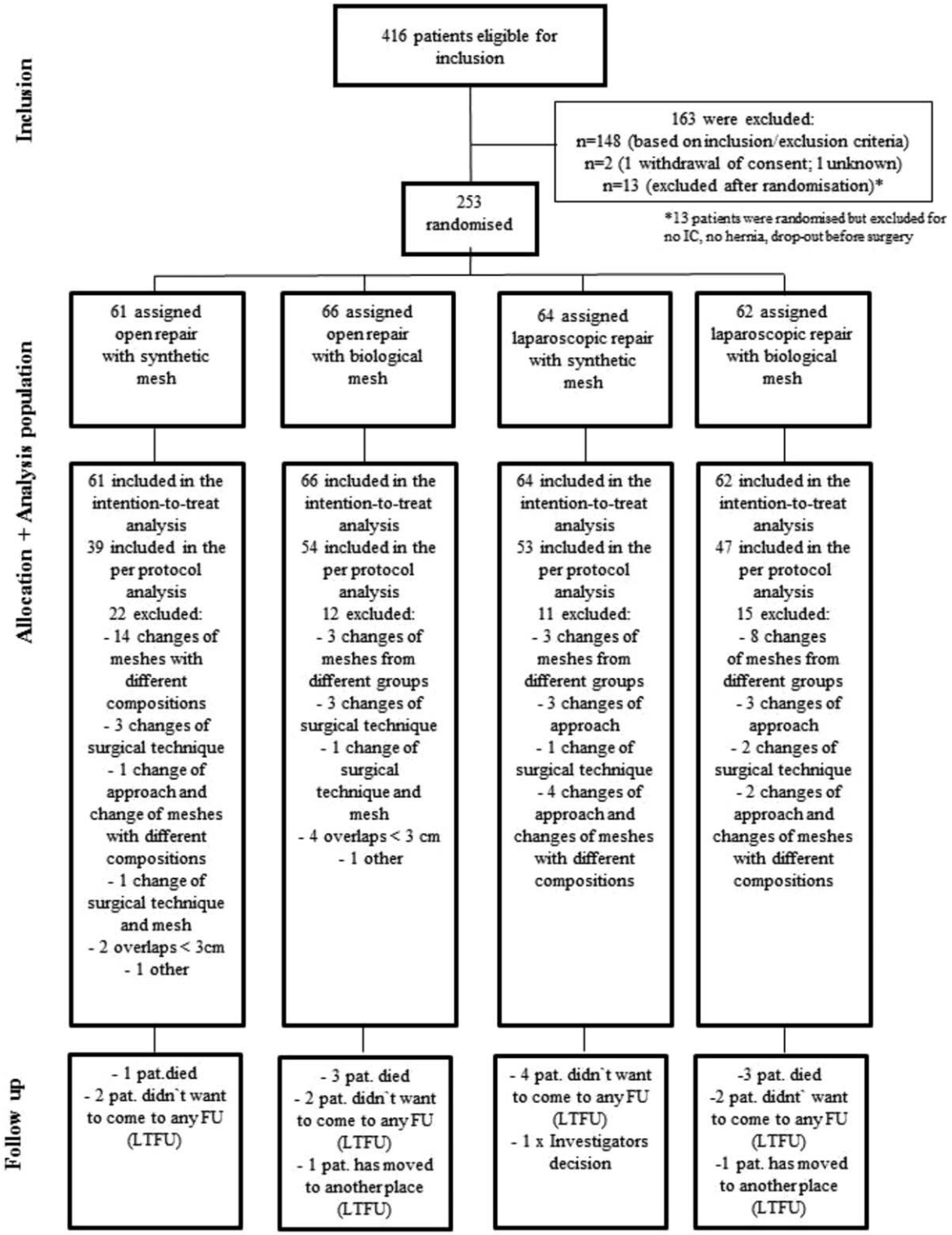


FIGURE 1. Patient inclusion according to CONSORT flow diagram.

TABLE 1. Patient Demographic and Clinical Baseline Characteristics

	Open Synthetic (n = 61)	Open Biological (n = 66)	Lap Synthetic (n = 64)	Lap Biological (n = 62)
Age (yr)	57 (15.4)	63 (13.2)	60 (12.1)	57 (11.3)
Males	29 (47.5%)	36 (54.5%)	35 (54.7%)	29 (46.8%)
Height (cm)	169.7 (9.3)	169.1 (10.1)	169.5 (12.1)	168.2 (9.1)
Weight (kg)	85.2 (18.2)	84.2 (15.6)	83.9 (15.6)	84.6 (16.5)
BMI (kg/m^2)	29.4 (4.8)	29.4 (4.9)	29.2 (4.3)	29.9 (5.1)
Ethnic group				
White	59 (96.7%)	62 (93.9%)	62 (96.9%)	59 (95.2%)
Non-white	2 (3.3%)	4 (6.1%)	2 (3.1%)	3 (4.8%)
Smoking status				
Nonsmoker	38 (62.3%)	44 (66.7%)	41 (64.1%)	38 (61.3%)
Previous smoker	10 (16.4%)	13 (19.7%)	14 (21.9%)	16 (25.8%)
Current smoker	13 (21.3%)	9 (13.6%)	9 (14.1%)	8 (12.9%)
Comorbidity				
Obstructive lung disease	1 (1.6%)	4 (6.1%)	3 (4.7%)	3 (4.8%)
Diabetes mellitus	8 (13.1%)	8 (12.1%)	3 (4.7%)	5 (8.1%)
Hypertension	9 (14.8%)	13 (19.7%)	9 (14.1%)	12 (19.4%)
Cardiac	0	2 (3.0%)	7 (10.9%)	4 (6.5%)
Other	14 (23.0%)	17 (25.8%)	11 (17.2%)	14 (22.6%)
ASA physical status				
I	22 (36.1%)	11 (16.7%)	19 (29.7%)	13 (21.0%)
II	32 (52.5%)	43 (65.2%)	33 (51.6%)	41 (66.1%)
III	7 (11.5%)	12 (18.2%)	12 (18.8%)	8 (12.9%)
Relevant prior abdominal surgery				
Appendectomy	6 (9.8%)	11 (16.7%)	12 (18.8%)	7 (11.3%)
Cholecystectomy	10 (16.4%)	7 (10.6%)	7 (10.9%)	11 (17.7%)
Abdominal aneurysm repair	2 (3.3%)	3 (4.5%)	4 (6.3%)	3 (4.8%)
Inguinal hernia repair	2 (3.3%)	4 (6.1%)	3 (4.7%)	1 (1.6%)
Incisional hernia repair	1 (1.6%)	2 (3.0%)	0	1 (1.6%)
Other abdominal surgery	19 (31.1%)	13 (19.7%)	15 (23.4%)	13 (21%)
Type of hernia				
Primary	14 (23.0%)	17 (25.8%)	16 (25.0%)	13 (21.0%)
Incisional (first)	37 (60.7%)	42 (63.6%)	44 (68.8%)	43 (69.4%)
Incisional (recurrent)	10 (16.4%)	7 (10.6%)	4 (6.3%)	6 (9.7%)
Hernia size				
Hernia length (cm)	6.3 (2.9)	6.6 (2.9)	6.0 (2.4)	6.3 (3.3)
Hernia width (cm)	5.0 (1.8)	5.4 (2.4)	4.9 (1.8)	5.1 (2.1)

Data are n (%) or mean (SD).
ASA indicates American Society of Anesthesiologists; BMI, body-mass index.

a total of 660 patients was needed to allow decisions with a power ≥80%, preserving a family-wise error of $\alpha = 0.05$, including a 10% increase to account for losses to follow-up.

Statistical Analysis

Comparison concerning superiority of the laparoscopic approach was planned using a stratified Cochran-Mantel-Haenszel-test. In case of a significant association, it was to be repeated separately for each mesh type. Due to the inferior performance of the biological mesh after 1-year,[10] the initially planned noninferiority analysis for the mesh type comparison would be futile. Therefore, we switched the analysis to show superiority of synthetic mesh, also using a Cochran-Mantel-Haenszel-test stratified according to hernia type, BMI, and study center.[11] According to the protocol stratified odds ratios (OR) were calculated for the primary endpoint and its components with 95% confidence interval (CI). Primary efficacy and safety analyses were based on the intention-to-treat population (ITT, all randomized patients except patients that did not undergo hernia repair). Except for the survival analysis, missing data for the ITT analysis were imputed using multiple imputations. For analysis of sensitivity and noninferiority analysis a per-protocol population approach was used. Patients were excluded from this analysis, if the approach/mesh used were not according to the randomization, the surgical technique did not follow the protocol and/or the mesh overlap was <3 cm. The analysis of the per-protocol population did not show relevant differences, hence only data of the ITT population are presented. All analyses were performed using the SPSS statistical software package (IBM, version 21; Armonk, NY). An Independent Data Monitoring Committee (IDMC) was designated to monitor cumulative safety data. No interim analyses were planned. This trial has been registered at http://www.controlled-trials.com (ISRCTN34532248).

RESULTS

Between September 1, 2005 and August 7, 2009, 253 of 416 screened patients were randomly assigned to either open VHR with a synthetic (n = 61) or a biological mesh (n = 66), or laparoscopic VHR with a synthetic (n = 64) or a biological mesh (n = 62). On 7 August 2009, patient recruitment was stopped prematurely due to a recommendation of the IDMC because of serious concerns for the unexpected higher preliminary recurrence rate in the biological vs the synthetic mesh groups (as treated), the low rate of patient recruitment and the incompleteness of study data.[10] Of the 253 randomized patients, 60 patients were not treated according to protocol. One patient randomized to the open approach was operated

TABLE 2. Intra- and Postoperative Data

	Open Synthetic (n = 61)	Open Biological (n = 66)	Lap Synthetic (n = 64)	Lap Biological (n = 62)
Operation time (min)	85 (60–105)	87 (68–102.5)	85 (63–115)	95 (68–117.5)
Mesh size				
Mesh length (cm)	18.7 (5.7)	18.6 (3.6)	18.8 (3.5)	19.8 (4.4)
Mesh width (cm)	16.6 (4.4)	15.9 (3.4)	16.4 (3.2)	16.9 (3.6)
Mesh fixation				
Resorbable sutures	24 (39.3%)	42 (63.6%)	3 (4.7%)	5 (8.1%)
Nonresorbable sutures	36 (59.0%)	24 (36.4%)	4 (6.3%)	0
Fixation devices	1 (1.6%)	0	13 (20.3%)	16 (25.8%)
Fixation devices with nonresorbable sutures	0	0	19 (29.7%)	24 (38.7%)
Fixation devices with resorbable sutures	0	0	25 (39.1%)	16 (25.8%)
Other	0	0	0	1 (1.6%)
Concomitant surgery				
Adhesiolysis (unrelated to hernia)	1 (1.6%)	0	4 (6.3%)	1 (1.6%)
Cholecystectomy	0	0	0	1 (1.6%)
Gynecological intervention	0	0	0	2 (3.2%)
Other	1 (1.6%)	1 (1.5%)	3 (4.7%)	2 (3.2%)
Elastic bandage				
No	20 (32.8%)	22 (33.3%)	5 (7.8%)	8 (12.9%)
Yes	41 (67.2%)	43 (65.2%)	59 (92.2%)	54 (87.1%)
Length of stay in hospital (d)	5 (4–6)	5 (3.75–7)	4 (2.25–6)	4 (3–6)
Return to work				
Answers available	37 (60.7%)	44 (66.7%)	41 (64.1%)	37 (59.7%)
Time until return to work (d)	34 (25.5–59.5)	29 (22–42)	28 (19–38)	24 (24–42)

Data are n (%) or median (IQR), apart from mesh size which is mean (SD).

laparoscopically, whereas12 cases from the laparoscopic group received open surgery (pre- or intraoperative conversion). Details are given in the CONSORT flow diagram (Fig. 1). Patient and surgical baseline characteristics of the ITT population are presented in Table 1. The 4 treatment arms were also comparable with regard to intraoperative data (Table 2).

Primary Endpoint

Overall, 6 patients (9.8%) in the open synthetic, 15 patients (22.7%) in the open biological, 7 patients (10.9%) in the laparoscopic synthetic, and 17 patients (27.4%) in the laparoscopic biological mesh group, respectively, had a major complication (Table 3). Thirty-one reoperations, 30 hernia recurrences, and 4 mesh infections were observed. The biological mesh ($P = 0.01$) but not the surgical approach ($P = 0.37$) had a significant effect on the occurrence of the primary endpoint (Table 4). The mesh type remained a significant determinant after adjusting for hernia type, BMI, and study center (stratified OR for mesh type: 2.902; 95% CI 1.316–6.398; stratified OR for surgical approach: 1.524; 95% CI 0.726–3.196).

Five patients (8.2%) in the open synthetic, 9 patients (13.6%) in the open biological, 2 patients (3.1%) in the laparoscopic synthetic and 14 patients (22.6%) in the laparoscopic biological mesh group, respectively, developed a hernia recurrence (Table 3). The stratified OR for biological versus synthetic mesh regarding recurrence and reoperation were 3.150 (95% CI 1.275–7.783; $P = 0.02$) and 2.594 (95% CI 1.005–6.696; $P = 0.09$), respectively. Wound complications were the main indication for reoperation. A mesh infection was observed once in each study group. Fig. 2 shows the development of the primary endpoint over time.

Secondary and Additional Endpoints

Operation time was not related to the type of surgical approach ($P = 0.15$) or type of mesh used ($P = 0.52$), but LOS was 1 day shorter for the laparoscopic approach ($P = 0.001$), whereas the type of mesh used did not influence LOS ($P = 0.13$) (Table 4).

The rate of postoperative morbidity other than the endpoints stated above is illustrated in Table 5. Most seromas were seen in the open biological mesh group and more patients in the biological mesh groups developed postoperative bulging. The number of serious adverse events probably or definitely related to the mesh was 8 in the biological versus 3 in the synthetic mesh group. Seven patients died during follow-up because of cancer (n = 2), cardiac disease (n = 1), or unknown (n = 4). The evolution of abdominal wall pain and patient satisfaction over time is illustrated in Figs. 3 and 4,

TABLE 3. Primary Endpoint and Individual Components

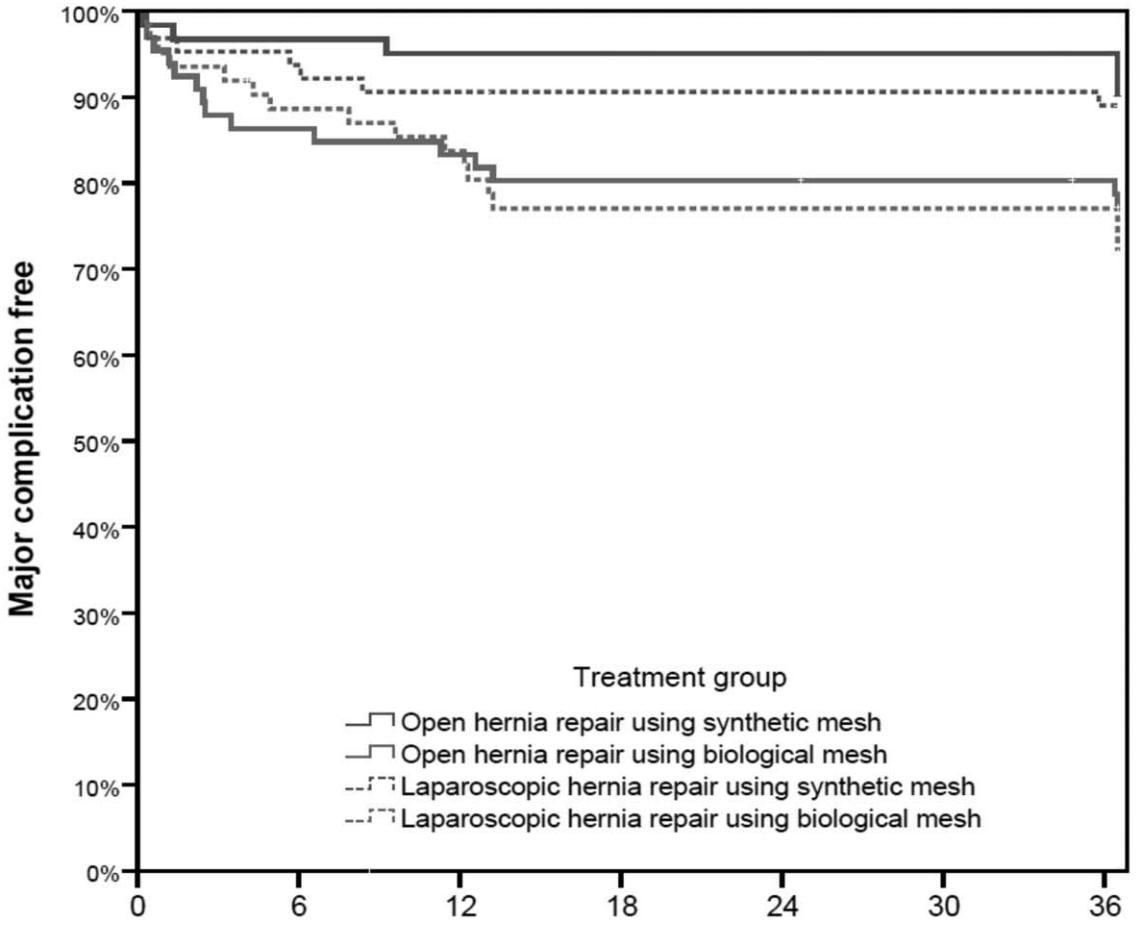
	Open Synthetic (n = 61)	Open Biological (n = 66)	Lap Synthetic (n = 64)	Lap Biological (n = 62)
Major complications				
Recurrence	5 (8.2%)	9 (13.6%)	2 (3.1%)	14 (22.6%)
Mesh infection	1 (1.6%)	1 (1.5%)	1 (1.6%)	1 (1.6%)
Reoperation	3 (4.9%)	12 (18.2%)	6 (9.4%)	10 (16.1%)
Primary endpoint: at least one of these major complications	6 (9.8%)	15 (22.7%)	7 (10.9%)	17 (27.4%)

Data are n (%).

TABLE 4. Operation Time, Length of Hospital Stay, and Primary Outcome in the Factor Subgroups

	Open Approach (n = 127)	Lap Approach (n = 126)	*P*-value
Operation time (min)	87 (63.5–105)	90 (65–166.5)	0.15
Length of stay in hospital (d)	5 (4–7)	4 (3–6)	0.001
Primary endpoint: at least 1 major complication	21 (16.5%)	24 (19.0%)	0.37
	Synthetic Mesh (n = 125)	**Biological Mesh (n = 128)**	***P*-value**
Operation time (min)	85 (63–106.5)	90 (69–110)	0.52
Length of stay in hospital (d)	5 (3–6)	5 (3–7)	0.13
Primary endpoint: at least 1 major complication	13 (10.4%)	32 (25.0%)	0.01

Data are n (%) or median (IQR).



	Months after surgery						
Patients at risk	**0**	**6**	**12**	**18**	**4**	**30**	**36**
Open synthetic	61	58	57	57	57	57	57
Open biological	66	57	55	53	53	52	50
Lap. synthetic	64	60	58	57	57	57	56
Lap. biological	62	54	51	46	46	46	46

FIGURE 2. Kaplan-Meier analysis for primary endpoint. The *x*-axis shows the time in months until the occurrence of a major complication.

TABLE 5. Other Postoperative Morbidity

	Open Synthetic (n = 61)	Open Biological (n = 66)	Lap Synthetic (n = 64)	Lap Biological (n = 62)
Local morbidity				
Wound dehiscence	1	1	0	0
Wound sinus	0	2	0	1
Wound infection	3	5	2	3
Hematoma/bleeding	1	3	1	4
Seroma	5	19	7	7
Intraabdominal abscess	1	1	0	0
Peritonitis (all before discharge)	1	0	1	0
Paralytic ileus	0	2	4	6
Mechanical obstruction	0	0	2	3
Bulging	9	18	10	14
Trocar herniation	0	1	1	1
Serious adverse events (by definition)				
Definitely/probably related to mesh	1	3	2	5
Definitely/probably related to procedure	4	8	7	7

Data are n.

respectively. None of the comparisons between the groups reached statistical significance.

DISCUSSION

In this European RCT with patients who underwent elective VHR of noncontaminated sites, we did not demonstrate superiority of the laparoscopic approach in terms of major complications. More importantly, the biological mesh showed significant inferiority compared to synthetic material for hernia recurrence.

Although we were not able to include the anticipated number of patients this study is, to our knowledge, the largest RCT comparing laparoscopic vs. open VHR. There was no difference in the long-term recurrence rate between both approaches. At the time of study conception, the closure of the fascial defect in laparoscopic repair was not routinely applied. Today, this technique is more popular especially in larger hernias, to decrease the risk for seroma and to reduce (pseudo)recurrences.[12] We already highlighted that early reoperations were mainly done for wound related problems, and this did not seem to be related to the open approach per se, but more to the open placement of the biological mesh. Late reoperation rates were low and did not differ between both groups. Mesh infection does not seem to be a major clinical problem regardless of the anatomical localization of the mesh. This is remarkable because the synthetic meshes used were polypropylene without large pores or even with microporous structure (ePTFE mesh). These materials are thought to be more prone to infection than the new generation of large pore meshes.[13] Nonetheless, both techniques provided a durable repair at 3 years.

Our data are in line with 2 others recently published large RCTs comparing an identical open and laparoscopic approach in incisional hernias.[14–16] With the cumulative number of patients reporting with wound problems being half in the laparoscopic versus

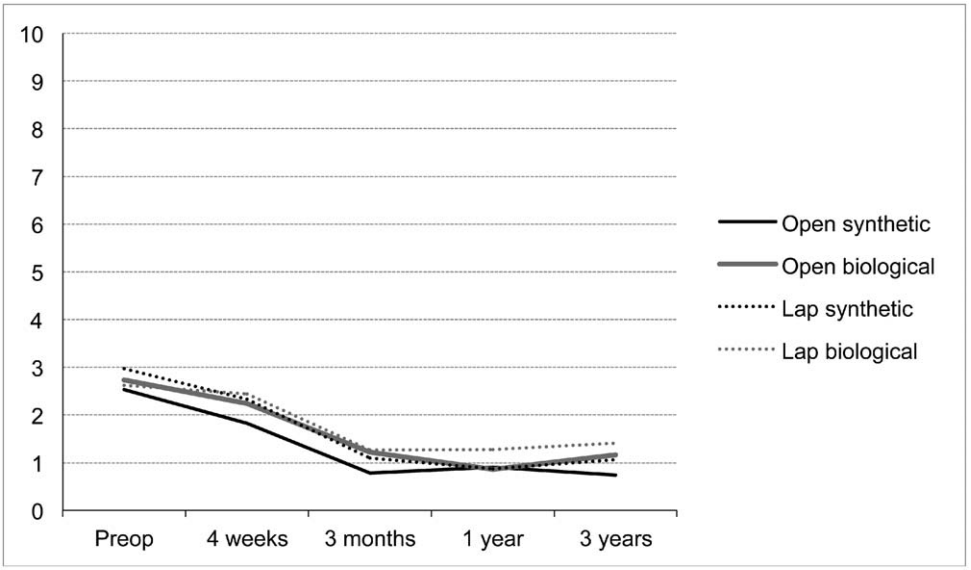
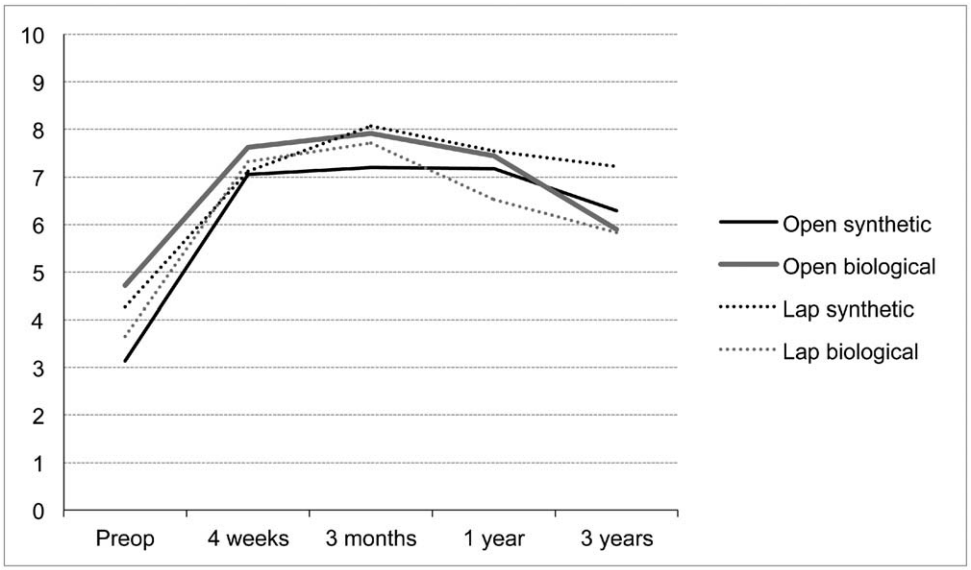


FIGURE 3. Change over time for abdominal wall pain. The *x*-axis shows the postoperative follow-up in months; the *y*-axis shows mean VAS 0–10 (0 is best). VAS indicates visual analog scale.



The x-axis shows the postoperative follow-up in months; the y-axis shows mean VAS 0-10 (10 is best).

FIGURE 4. Change over time for patient satisfaction. The *x*-axis shows the postoperative follow-up in months; the *y*-axis shows mean VAS 0–10 (10 is best). VAS indicates visual analog scale.

the open approach (n = 6 vs n = 12) we confirm the findings of Rogmark et al.[15] Intraoperative complications and operative time were significantly higher in the laparoscopic arm of the Dutch study,[14] whereas this was not the case in the Swedish and in our study.[15] Our finding that the laparoscopic approach leads to a reduction of the LOS by 1 day does not seem in line with the 2 other studies. However, the timing of discharge is influenced by many different medical and social aspects.

Based on reports of major long-term complications of permanent synthetic mesh intraperitoneally,[5,6] there is a growing trend to place the mesh extraperitoneally while using the minimally invasive approach.[17,18] Still, our data emphasize that the ''standard'' laparoscopic intraperitoneal onlay mesh mesh technique without defect closure in small/medium-sized hernias remains a valid option especially for patients with multiple risk factors for wound complications.[19] Data from high quality large prospective registries including long-term follow-up are needed to confirm the external validity of this and other RCTs.[20,21]

Despite their high cost and the low evidence of their efficacy, biological meshes have been widely adopted by surgeons.[9] This is to our knowledge the first RCT comparing the use of biological versus synthetic mesh in elective VHR. We excluded patients with contaminated hernia sites to minimize the number of potential variables affecting outcome in complex hernias.

The most relevant finding of our study was the unexpected overall 3-fold higher recurrence rate with biological mesh after 3 years. This difference was mainly seen in the laparoscopic arm. Recent data suggest that bridging a defect with a biological mesh without defect closure will lead to increased (pseudo)recurrences.[9] Therefore, the surgical technique used in this trial in the laparoscopic arms might be partially responsible for the discouraging results using biological mesh. Consequently, this might explain to a certain extent the better results obtained by others with this type of mesh in laparoscopic repair including fascial closure.[22] However, we believe this is not the only issue, since our hernia recurrence rate in the open biological mesh arm (with defect closure), was also increased compared to synthetic mesh.

Thus, although the retromuscular position has been suggested to be ideal for a biological mesh placement,[23,24] the remodeling process with this mesh is inadequate even after fascial closure. This explains the more frequent bulging after biological mesh repair and why almost all recurrent hernias were seen within the first year postoperatively. Although some patients with a recurrent hernia have been reoperated, wound complications were the main indication for reoperation. Also for reoperation rate, the incidence was higher for the biological mesh groups (more than 3-fold difference in the open arms), but this did not reach significance. The fact that more seromas and other wound complications were seen in the open biological mesh group might point towards an inadvertent foreign body reaction after implantation of small intestinal submucosa scaffolds.[25] Whether this process is an important factor in the unfavorable remodeling process remains speculation. Lastly, we also hypothesized that the biological mesh would improve patient reported outcomes such as abdominal wall pain and overall satisfaction, compared with the ''heavy-weight'' materials used in the synthetic mesh arms. However, this did not seem to be clinically relevant, although this result might be confounded partially by the negative experience of biological mesh patients developing a recurrence or needing a reoperation.

Since this large RCT was performed in 17 different European (non-)academic centers, we believe our data provide thorough evidence and a realistic reflection of the ''effectiveness'' of this intervention. It also emphasizes the mere importance of publication of negative results.

This study has also limitations. The trial was prematurely discontinued with only 40% of the planned patients recruited. Furthermore, 4 years after patient inclusion, the incompleteness of the study data was an important issue highlighted by the IDMC. The Investigators and the SC invested largely into this during the following years and this was one of the reasons to explain the delay of our final analysis. Lastly, Surgisis Gold is one of the first generation of biological meshes. Since the initiation of this study other biological meshes are available. Generalizing the findings of LAPSIS to these other meshes may not be appropriate.

In conclusion, the use of a Surgisis Gold biological mesh has no place in the surgical treatment of clean noncomplex ventral hernias. The laparoscopic and the open approach are valid options in small and medium-sized ventral hernias.

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