**Effectiveness of Prophylactic Intraperitoneal Mesh Implantation for Prevention of Incisional Hernia in Patients Undergoing Open Abdominal Surgery: A Randomized Clinical Trial**

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**IMPORTANCE** Incisional hernia is a frequent complication after open abdominal surgery. Prophylactic mesh implantation in the onlay or sublay position requires dissection of the abdominal wall, potentially leading to wound-associated complications.

**OBJECTIVE** To compare the incidence of incisional hernia among patients after prophylactic intraperitoneal mesh implantation with that among patients after standard abdominal closure.

**DESIGN, SETTING, AND PARTICIPANTS** An open-label randomized clinical trial was performed in 169 patients undergoing elective open abdominal surgery from January 1, 2011, to February 29, 2014. Follow-up examinations were performed 1 year and 3 years after surgery. The study was conducted at Bern University Hospital, Bern, Switzerland, a referral center that offers the whole spectrum of abdominal surgical interventions. Patients with 2 or more of the following risk factors were included: overweight or obesity, diagnosis of neoplastic disease, male sex, or history of previous laparotomy. Patients were randomly assigned to prophylactic intraperitoneal mesh implantation or standard abdominal closure. Data were analyzed in August 2017.

**INTERVENTIONS** Intraperitoneal implantation of a polypropylene-polyvinylidene fluoride mesh with circumferential fixation.

**MAIN OUTCOMES AND MEASURES** The primary end point was the incidence of incisional hernia 3 years after surgery. Secondary end points included mesh-related complications.

**RESULTS** After the exclusion of 19 patients, 150 patients (81 in the control group and 69 in the mesh group; mean [SD] age, 64.2 [11.1] years; 102 [68.0%] male) were studied. The cumulative incidence of incisional hernia was significantly lower in the mesh group compared with the control group (5 of 69 [7.2%] vs 15 of 81 [18.5%], log-rank test \( P = .03 \)). Abdominal pain was observed in significantly more patients in the mesh group compared with the control group at 6 weeks (34 of 52 [65%] vs 26 of 59 [44%], \( P = .04 \)) but not at 12 and 36 months postoperatively. No difference in surgical site infections was observed, but time to complete wound healing of surgical site infection was significantly longer in patients with mesh implantation (median [interquartile range], 8 [6-24] weeks compared with 5 [1-9] weeks; \( P = .03 \)). Trunk extension was significantly decreased after mesh implantation compared with the control group (mean [SD], 1.73 [0.97] cm vs 2.40 [1.23] cm; \( P = .009 \)).

**CONCLUSIONS AND RELEVANCE** In patients at elevated risk for incisional hernia, prophylactic intraperitoneal mesh implantation reduces the incidence of hernia formation but with increased early postoperative pain and prolonged wound healing of surgical site infection.

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Under current guidelines, a running, slowly absorbable suture is recommended for the closure of the abdominal wall after laparotomy. However, this technique is associated with a considerable incidence of incisonal hernia. Despite a wide variability of reported incidence, relevant studies \(^2-^5\) indicate a frequency between 10% and 30% on long-term follow-up. Novel techniques, including the use of small bites, may reduce the incidence of incisional hernia after midline laparotomies. \(^6^,^7\) However, despite technical modifications, the rate of incisional hernia remains clinically significant, with an incidence of up to 13% \(^6^,^7\); therefore, it is important to reduce incisional hernia in patients undergoing open abdominal surgery.

The benefit of prophylactic mesh implantation in reducing the incidence of incisional hernia after laparotomy has been reported in previous studies. \(^8^,^9^,^10^\) Onlay or sublay mesh position was investigated in most studies, \(^10^,^11^-^13\) which requires additional dissection of the abdominal wall, is time consuming and can therefore be a hindrance in routine prophylactic mesh implantation. Furthermore, an elevated rate of seroma formation was reported after onlay and sublay mesh implantation, potentially because of the increased wound surface area. \(^8^,^14\) Intraperitoneal placement of modern dual-layered meshes could potentially overcome these limitations by reducing the time required for mesh implantation and minimizing dissection of the abdominal wall. \(^15^,^16\) Therefore, the efficacy of prophylactic intraperitoneal mesh implantation for the prevention of incisional hernia after laparotomy was tested in a randomized clinical trial.

To maximize the benefit-risk ratio, prophylactic mesh implantation would ideally be performed in patients at elevated risk for hernia development. Previous studies \(^17^-^18\) explored the outcome of prophylactic mesh implantation after specific procedures with elevated risk for incisional hernia, such as bariatric or abdominal vascular surgery. The current study explores a population undergoing general abdominal surgery, including hepatobiliary, pancreatic, and upper and lower gastrointestinal tract surgery. A population at risk was defined by patient-related risk factors that can be recognized preoperatively. Such stratification allows identification of patients at elevated risk for incisional hernia development, who potentially benefit the most from mesh implantation. Numerous preoperative recognizable risk factors for incisional hernia have been described in the literature, including overweight or obesity, low hemoglobin level, uremia, male sex, old age, smoking, previous laparotomy, and diagnosis of neoplastic disease. \(^2^-^4,^19^-^25\) To ensure practicability in daily clinical routine, only strong risk factors were included for stratification that are dichotomous, occur frequently, and are easy to identify. Thus, the following risk factors were used for patient stratification: overweight or obesity, diagnosis of neoplastic disease, male sex, and history of laparotomy. Patients with at least 2 of these risk factors were included. With this study design, we tested the hypothesis that primary mesh implantation in an intraperitoneal position reduces the risk of incisional hernia in a population at risk.

**Methods**

**Trial Design**
An open-label randomized clinical trial with 1:1 randomization in 2 parallel groups was performed at the Department of Visceral Surgery and Medicine in the University Hospital of Bern, Bern, Switzerland. The trial protocol can be found in Supplement 1. The study was conducted under the working title ProphMesh. The study, including the increase of sample size, was approved by the Ethical Committee of the Canton of Bern.

**Participants**
Patients seen at the visceral surgical outpatient department who were scheduled for open abdominal surgery from January 1, 2011, to February 29, 2014, were assessed for eligibility. Inclusion criteria were age older than 18 years, elective operation, and the presence of at least 2 of the following risk factors for incisional hernia development: body mass index above 25 (calculated as weight in kilograms divided by height in meters squared), diagnosis of neoplastic disease, male sex, and history of laparotomy. Exclusion criteria were previous intraperitoneal mesh placement, previous incisional hernia, emergency procedures, and patients with inflammatory bowel disease. All patients had to sign informed consent forms before inclusion in the study. Data were deidentified with a key according to Swiss regulations. Data were analyzed in August 2017.

**Interventions**
The scheduled operation was performed as planned. In the control group, the abdominal wall was closed according to the institutional standard operating procedure, using a slowly absorbable running suture (USP 1 PDS II loop, Ethicon, Johnson & Johnson). The distance of the stitches to the fascial border was 1 cm, and the distance between stitches was also 1 cm. In the intervention group, a mesh was implanted before closure of the abdominal wall in a standardized fashion. A double-layered polypropylene-polyvinylidene fluoride mesh (Dynamesh-IPOM, FEG Textiltechnik) was tailored to overlap lateral and cranial-caudal borders by at least 5 cm. The mesh was placed intraperitoneally and fixed to the abdominal wall using single stitches with polypropylene sutures (USP 2-0
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Outcomes
Data collection was performed at the outpatient department preoperatively and at 6 weeks, 1 year, and 3 years postoperatively. Patients were interviewed according to the respective questionnaires, and a clinical examination was performed by observers not otherwise involved in the planning or conduct of the study.

The primary outcome of the study was the incidence of an incisional hernia as defined by the European Hernia Society: an abdominal wall gap with or without bulge in the area of the postoperative scar palpable by clinical examination.26 The patients were seen for follow-up visits at the outpatient department and examined by a qualified physician with at least 2 years of surgical training. Imaging studies were performed if there was uncertainty about the diagnosis. Mean follow-up time was 16.9 months in the control group and 18.7 months in the intervention group.

Secondary outcomes were the occurrence of postoperative complications; hematoma, intestinal paralysis, and inhospital mortality were reported until 30 days postoperatively. Fistula formation, small-bowel obstruction, and surgical site infection (SSI) were reported for the whole follow-up period; these outcomes occurred similarly between the two groups (Table 1).

Statistical Analysis
Continuous variables were described using means (SDs). For categorical values, numbers (percentages) were calculated. Differences between groups were compared using the 2-tailed, unpaired t test or Mann-Whitney test for continuous variables and the Fisher exact test for categorical variables. Statistical significance was defined as 2-sided P < .05. In this intent-to-treat analysis, patients randomized to the mesh group were analyzed in the mesh group even if the mesh was explanted during follow-up. Patients in the control group were analyzed in the control group even if they underwent additional surgery with eventual prophylactic mesh implantation. Analysis was performed using SPSS statistical software, version 21 (IBM Corp) and Prism software, version 6 (GraphPad). A Kaplan-Meier curve of the occurrence of incisional hernias stratified by treatment group was plotted, and a log-rank test was used to compare the hernia incidence between the groups.

Results
Demographics
A total of 169 patients were randomized into a control group (n = 86) or a mesh group (n = 83). Nineteen patients were excluded from the study during surgery because new information that conflicted with the inclusion or exclusion criteria became evident (existing incisional hernia, finding of an implanted mesh), second-look surgery became necessary, or surgery revealed a terminal stage of disease (peritoneal carcinomatosis) with the surgeon disagreeing with mesh implantation. Therefore, 81 patients in the control group and 69 in the mesh group were studied (mean [SD] age, 64.2 [11.1] years; 102 [68.0%] male). Details are shown in Figure 1. Baseline data were similar between groups (Table 1).

Primary Outcome
The incidence of incisional hernia 3 years after surgery was significantly higher in the control group vs the mesh group (15 of 81 [18.5%] vs 5 of 69 [7.2%]). Comparison of the cumulative hazard curves revealed a statistically significant difference between the groups (log-rank test P = .03) (Figure 2). In both groups, most hernias occurred during the first year after surgery. Follow-up at 1 year resulted in incisional hernia in 13 of 51 individuals (25.5%) in the control group vs 3 of 45 individuals (6.7%) in the mesh group. At the 3-year follow-up visit, 7 of the 30 control group patients (23.3%) presented with a hernia compared with 3 of 30 mesh group patients (10.0%).

Sample Size
On the basis of existing studies, we expected 25% of control patients from our at-risk population to develop an incisional hernia during the 3 years. In patients with an implanted mesh, an incidence of approximately 5% was expected, as observed in patients undergoing similar operations in our department before the initiation of the study.29

We calculated that a total of 150 patients needed to be included in the study to demonstrate the difference, presuming a 2-sided level of significance at 5% and a power of 80%. This number also allowed for a loss to follow-up of up to 20% in the patient sample. Because of the unexpectedly high number of patients (n = 19) excluded from the study during surgery, the aimed sample size was increased from 150 to 170 to ensure that 150 patients were treated according to randomization. An amendment was written and approved by the local ethics committee on February 12, 2013.

Randomization
Randomization was performed in permuted blocks of 30 patients, using the online tool randomization.com by an external study nurse. Sealed and numbered envelopes that contained the allocated group were prepared and opened during surgery before abdominal wall closure.

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Reasons for hernia occurrence in the mesh group were mesh removal in one patient and an additional laparotomy with abdominal wall closure using resorbable suture material in another patient. For the other patients with hernia occurrence in the intervention group, the reason for failure of the implanted mesh remains unclear.

Secondary Outcomes
There was no statistically significant difference between the control and intervention groups concerning occurrence of hematoma (1.2% vs 1.4%; P > .99), intestinal paralysis (4.9% vs 4.4%; P > .99), length of hospital stay (13.5 vs 13 days; P = .46), or in-hospital mortality (3.7% vs 1.4%; P = .62) (Table 2). The incidence of small-bowel obstruction was similar between the groups during the entire observation time (Table 2). No enterocutaneous fistula was observed in either group during follow-up. The incidence of SSI was not statistically different between the control (18 of 69 [26.1%]) and mesh (11 of 61 [18.0%]) groups (P = .30). However, in patients with SSI, completion of wound healing took longer in the mesh group compared with the control group (median [interquartile range], 8 [6-24] weeks vs 6 [4-8] weeks).

Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Group (n = 81)</th>
<th>Mesh Group (n = 69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), y</td>
<td>65 (56.5-70)</td>
<td>67 (58-72)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>26.7 (4.8)</td>
<td>27.6 (4.6)</td>
</tr>
<tr>
<td>ASA classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>19 (23.5)</td>
<td>18 (26.1)</td>
</tr>
<tr>
<td>3</td>
<td>55 (67.9)</td>
<td>47 (68.1)</td>
</tr>
<tr>
<td>4</td>
<td>7 (8.6)</td>
<td>4 (5.8)</td>
</tr>
<tr>
<td>Immunosuppressants or corticosteroid therapy</td>
<td>3 (3.7)</td>
<td>4 (5.8)</td>
</tr>
</tbody>
</table>

Incisional hernia risk factors:
- BMI > 25: 50 (61.7) vs 51 (73.9)
- Diagnosis of neoplastic disease: 67 (82.7) vs 54 (78.3)
- Male: 56 (69.1) vs 46 (66.7)
- Previous laparotomy: 60 (74.1) vs 51 (73.9)

Type of surgery:
- Upper GI tract: 12 (14.8) vs 14 (20.3)
- Lower GI tract: 19 (23.5) vs 17 (24.6)
- Hepatobiliary: 18 (22.2) vs 20 (29.0)
- Pancreatic: 30 (37.0) vs 15 (21.7)
- Other: 2 (2.5) vs 3 (4.3)

Type of incision:
- Midline laparotomy: 30 (37.0) vs 31 (44.9)
- Transverse laparotomy: 51 (63.0) vs 38 (55.1)

Operation duration, mean (SD), min: 293 (109) vs 275 (102)

Mesh implantation duration, mean (SD), min: NA vs 25 (8)

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); GI, gastrointestinal; IQR, interquartile range; NA, not applicable.

* Data are presented as number (percentage) of patients unless otherwise specified.
compared with 5 [1-9] weeks; \( P = .03\). Surgical wound revisions were more frequent in the mesh group (Table 2).

Pain was similar between the groups during hospital stay (Table 3). At 6 weeks, significantly more patients in the mesh group reported postoperative pain compared with patients in the control group (34 of 52 [65.4%] vs 26 of 59 [44.1%]; effect size, 21.3%; 95% CI, 4%-41%; \( P = .04\)). Pain intensity was higher in the mesh group compared with the control group at 6 weeks (mean VAS score, 1.61 vs 0.83; VAS score difference, 0.78; 95% CI, 0.10-1.46; \( P = .02\)). At 1 and 3 years after surgery, no difference in pain perception was observed between the groups (Table 3).

Trunk extension, assessed by elongation of umbilical-xiphoid distance, was significantly reduced in the mesh group compared with the control group at 12 months (2.40 cm vs 1.73 cm; effect size, 0.675; 95% CI, 0.18-1.11; \( P = .009\)) but not at 36 months after surgery. Trunk flexion, as assessed by finger-to-floor distance, was not significantly different between the groups at all follow-up time points (eFigure in Supplement 2).

Discussion

Our findings reveal that prophylactic intraperitoneal mesh implantation significantly reduces the incidence of incisional hernia 3 years after laparotomy compared with standard abdominal closure in a high-risk population. This study confirms previous reports\(^8\)-\(^10,\)\(^29\) that found similar effects of prophylactic mesh implantation. The current study has 2 main differences to most previous reports.\(^8,\)\(^9\) First, the study population represents patients with elevated risk profile for hernia development that are patient and not procedure related. Second, a double-layered mesh was implanted in an intraperitoneal position, whereas previous studies\(^10,\)\(^12\) explored mesh implantation in onlay or sublay positions.

The incidence of incisional hernia in the control group was above average for an elective surgical population but in the same range as reported in current studies\(^9,\)\(^12\) on prophylactic mesh...
Implantation in at-risk patient collectives. This finding indicates that the simple scoring system used allows identification of a population at elevated risk for hernia development based on personal risk factors that can be recognized preoperatively.

The incidence of incisional hernia was significantly lower in the mesh group, showing that intraperitoneal mesh implantation is effective for prevention of hernia development. Among the 5 hernias that developed in the mesh group, 2 occurred because of technical aspects during secondary surgery, including mesh removal and mesh adaptation using resorbable suture material.

In our study, the calculated number needed to treat is 8.9; accordingly, 9 patients have to undergo prophylactic mesh implantation to prevent 1 incisional hernia. This number is in line with the current literature that shows a number needed to treat between 5 and 10 for prophylactic mesh implantation in patients undergoing surgical procedures with an increased risk of hernia formation. Because not every incisional hernia needs surgical repair, the number needed to treat to prevent 1 hernia repair is likely to be higher. We believe that risk assessment for incisional hernia should be performed to keep the number needed to treat low and to reduce unnecessary mesh implantations.

The recently published results of the Small Bites Versus Large Bites for Closure of Abdominal Midline Incisions (STITCH) trial revealed a decrease of incisional hernias after 1 year of follow-up with a small-bite technique. Because not every incisional hernia needs surgical repair, the number needed to treat to prevent 1 hernia repair is likely to be higher. We believe that risk assessment for incisional hernia should be performed to keep the number needed to treat low and to reduce unnecessary mesh implantations.

Implantation of a mesh in an intraperitoneal position was not associated with an increase in the incidence of SSI. However, patients who developed SSI experienced delayed wound healing (Table 2). Such delayed wound healing is most likely the consequence of secondary infection of the prosthesis. The median healing time in the mesh group was 2 months; 5 of 12 patients had a chronic wound, defined as a healing time of more than 3 months. The fact that more than half of patients with mesh infection healed without mesh removal may be because the mesh was based on polypropylene and not on polyester that is more prone to chronic infection. Small-bowel obstruction, which potentially may occur after mesh implantation, was not significantly different between the 2 groups at long-term follow-up. No fistula was detected in either group, which is in line with the literature.

Chronic postoperative pain is a potential challenge in hernia surgery and after prophylactic mesh placement. Prevalence and intensity of pain 6 weeks postoperatively were significantly higher in the mesh group compared with the control group. This elevated pain might be caused by tension through mesh fixation sutures in the abdominal wall or by inflammatory reaction to the implanted mesh. However, there was no difference in pain at long-term follow-up.

A preventive measure should be simple and fast in its application, which is where we see the advantage of the intraperitoneal onlay mesh technique. The mesh can be implanted without creating an additional wound surface area because no further dissection of the abdominal wall is needed. In the present study, clinically relevant long-term mesh-associated complications, such as erosion and formation of adhesions, were not observed.

Limitations

Limitations of the study include the high rate of unavailability for follow-up, the exclusion of patients during surgery, and lack of quality-of-life assessment. Because this study investigated a high-risk population with a significant fraction of patients with malignant disease, mortality was observed in some patients before reaching the end point. In the power calculation, a loss to follow-up of 20% was initially calculated. Therefore, the actual loss of patients was underestimated, mainly because of mortality and withdrawal from study participation. However, there was no difference in loss to follow-up between the 2 groups. Mesh implantation needed to be documented in the operation report to inform medical personnel responsible for aftercare and to ensure patient safety. Therefore, masking of the patient and the assessor during follow-up visits was not possible. To minimize bias, the assessor was a person not involved in the study and patient care. The elevated exclusion of patients randomized to receive mesh implantation may represent a reluctance of surgeons to implant a mesh prophylactically, especially in patients excluded because of a terminal stage of disease. This approach represents another limitation of this study. However, post hoc analysis revealed no major different baseline characteristics in patients intraoperatively excluded. Such reluctance to implant a mesh highlights the need for a better definition of patients who benefit from mesh implantation.

Conclusions

Prophylactic intraperitoneal mesh implantation in patients at risk for incisional hernia is feasible and effective to prevent hernia formation. Adverse effects of mesh implantation include delayed wound healing of SSI, early postoperative pain, and reduced trunk extension.
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Original Investigation

Research

REFERENCES


