Study protocol

Prophylactic mesh implantation for the prevention of incisional hernia

Department for Visceral Surgery and Medicine
University Hospital Bern
Inselspital Bern
CH-3010 Bern
Switzerland

1. Summary

Introduction:
Incisional hernia is one of the most common complication in general abdominal surgery. An overall incidence of 20% has been found in retrospective studies, ranging in up to 50% of patients with selected risk factors such as obesity.

In the general surgical patient the current standard is the closure of the abdominal wall using a running, slowly absorbable suture. With this well established clinical practice the incidence remains high and incisional hernia repair must be performed frequently in order to treat patients' symptoms and to prevent progression of the hernia and possible complications. Consequently, in high risk patients prophylactic mesh implantation is performed routinely in our institution.

Aim
To compare prophylactic mesh implantation to conventional abdominal closure in a high-risk population.

Endpoints
Primary endpoint: incidence of incisional hernia
Secondary endpoints:
- direct in-hospital costs
- intraoperative complications
- postoperative complications

Study design
Prospective two-armed randomized controlled trial

Duration
Recruitment of n=150 patients: 2 years
Follow up: 3 years per patient

Inclusion criteria
- Occurrence of at least two of the following factors:
  - Male gender
  - Malignant tumor present
  - Body mass index above 25 kg/m2
  - Previous laparotomy
- Elective Operation
- Patient > 18 years
- Written informed consent

Exclusion criteria
- Previous intra-abdominal mesh placement
- Emergency procedures
- Previous incisional hernia
- Inflammatory bowel disease (Crohn's Disease, Ulcerative colitis)

Risk analysis:
Complications associated with mesh implantation such as lesions to intraabdominal organs or intestinal fistula are extremely rare. Additionally discomfort and decreased mobility for trunk rotation after implantation of large mesh have been rarely reported.

Potential of the study:
Incisional hernia after laparotomy is a frequent clinical problem, which is associated with significant morbidity and cost. This study may reveal that prophylactic mesh implantation reduces hernia recurrence in a highly selected group of patients. This effect is potentially associated with no additional costs.

2. Signatures

PD Dr. Guido Beldi

Oberarzt

3. Background and Aim

Incisional hernia is one of the most common complication in general abdominal surgery. An overall incidence of 20% has been found in retrospective studies, ranging up to 50% in patients with selected risk factors such as obesity [1, 2]. Incisional hernias are associated with a high morbidity such as intestinal incarceration, chronic discomfort and pain of the patient [3].

The gold standard for the closure of the abdominal wall is a running slowly absorbable suture [4, 5]. Despite this well established clinical practice a high incidence of incisional hernia is observed with up to 26% [6] in selected patients and repair must be performed frequently in order to treat patients symptoms and to prevent progression of the hernia [3]. Prophylactic mesh implantation has been shown to be safe in patients undergoing bariatric surgery [7, 8]. However, the prefascial site of mesh placement in this study was associated with additional surgical site infections.

Modern dual layered meshes were introduced more than 10 years ago [9]. These meshes were successfully used for laparoscopic repair of incisional hernia and are associated with significant reduction of surgical site infection compared to conventional incisional hernia repair [10-12].

Since 2005 we implanted intra-abdominal dual-layered meshes in order to prevent incisional hernia in high-risk patients. A total of 52 high-risk patients received a mesh. No additional morbidity such as small bowel obstruction, intestinal fistula or lesions of intra-abdominal organs was observed. After a median clinical follow-up of 18 months we observed postoperative incisional hernia in 2 (4%) of these patients which is significantly lower to the other series [1, 2]. We perform this technique routinely in this subset of patients in our department.

With these encouraging results prophylactic mesh implantation is now performed in all patients with a specific risk profile as detailed below. This approach however, may be more expensive at the initial operation compared to standard abdominal closure without mesh implantation. However, given the relevant costs for reoperations that are between 6 to 20 times higher than the implantation of a prophylactic mesh it seems probable that prophylactic mesh implantation is cost-effective. In particular the costs for incisional hernia repair in our institution range from 11,481 ± 4,806 CHF for laparoscopic repair to 14,680 ± 12,032 CHF for open repair [11]. Cost-effectiveness will be assessed as a secondary outcome parameter.

With this study we want to prospectively compare the outcomes and costs between implantation of a prophylactic mesh and suture only. The main endpoints of the study are incidence of incisional hernia and cost.

4. Hypothesis and Endpoints

Hypothesis:
Prophylactic implantation of an intra-peritoneal mesh in a high risk population reduces the incidence of incisional hernia.

This hypothesis is based on studies, showing the safety of intra-abdominal mesh implantation [13]. The study will focus on a high-risk population, who is most likely to benefit from the procedure.

Endpoints:
Primary endpoint:
- incidence of incisional hernia

Secondary endpoints:
- direct in-hospital costs, including rehospitalizations
  - only hernia related hospitalizations are included
- Intra-operative complications:
  - lesions to intra-abdominal organs
  - bleeding
- postoperative complications:
  - surgical site infection
  - intestinal fistula
  - small bowel obstruction
  - postoperative pain
  - mobility of the trunk

5. Study design

Prospective, two armed, controlled, randomized study

6. Study population

Inclusion criteria:
The overall incidence of incisional hernia has been assessed only in retrospective series. In large series an incidence of 19 – 26 per cent [6] has been found in general surgical patients. Prospective assessment of incidence of incisional hernia exists only for specific cohorts of patients such as patients undergoing orthotopic liver transplantation or bariatric surgery.

Multivariate analysis of retrospective data have shown that the following preoperatively known factors are independent risk factors for incisional hernia: male gender, body mass index larger than 25kg/m2, malignancy, previous abdominal incision [1, 6, 14].

In order to analyze a population with a high risk for incisional hernia formation, we will include patients with at least two of the above-mentioned risk factors.

Sample size calculation:
With the selection of high risk patients for incisional hernia we expect an incidence of incisional hernia of 25% 3 years post operation [6]. With implanted mesh we expect to lower the incidence of incisional hernia to 5% as observed in our cohort. For the sample size calculation we estimate the level of significance at 5% and a power of 80%. It is estimated that the accrual of patients is constant and that we lose 20% at follow-up. Correction for alpha spending (O'Brian-Flemming) was attributed. Therefore, we need a total of 150 patients to be included into the study.

Duration:
Accrual rate: 75 pat / year. Time of patient accrual: Patient recruitment 2 years.
Follow up: 3 years per patient.
Study duration: 5 years

Interim analysis will be performed after inclusion of 50% of patients.

- Stop criteria assessed from available 12 month follow-up data:
  - Significantly increased complication rate in the treatment group.
  - Significant difference in hernia recurrence between the two groups.
  - Difference in hernia recurrence of less than 5%.

Inclusion criteria

- Occurrence of at least two of the following factors:
  - Male gender
  - Malignant tumor present
  - Body mass index above 25 kg/m2
  - Previous laparotomy
- Elective Operation
- Patient > 18 years
- Written informed consent

Exclusion criteria

- Previous intra-abdominal mesh placement
- Emergency procedures
- Previous incisional hernia
- Inflammatory bowel disease (Crohn's Disease, Ulcerative colitis)

Method of randomization

- Randomization.com
- Permutated blocks of 30 patients
- Sealed numbered envelopes

7. Intervention

Control group
The main operation will be performed as planned. For the closure of the abdominal wall, a standard technique will be applied using a running suture of PDS 1 loop. The distance of the sutures to the fascial border is 1cm and the distance between two stitches is not more than 1cm. The total length of suture is at least 4 times the total length of the abdominal incision.

Treatment group
The main operation will be performed as planned. Prior to the closure of the abdominal wall a mesh will be implanted in a standardized fashion: A Dynamesh IPOM mesh will be used for the present study. The mesh has a width of 15cm and is tailored to overlap lateral and cranial boarders at least 5cm. The mesh will be placed intra-abdominally and fixed using intra-abdominal stitches using Prolene 2/0 in all four corners. After the initial fixation of the mesh in all quadrants, the boarders of the mesh will be adapted using Prolene 2/0 running sutures. The fixation aims to prevent any intestinal structures to herniate onto the mesh. Afterwards, the abdominal wall is closed as described in the control group.

8. Investigations

Preoperative investigations:

- Standardized interview with the assessment of abdominal pain using the visual analog scale (0-10). Clinical exam investigating the impairment of mobility of the trunk (Inclination, reclination, rotation) all measured in degrees.

Postoperative investigations:

- Regular clinical investigation at discharge by the treating surgeon
- All patients receive a follow-up phone call 30 days after the operation to assess incidence of surgical site infections and other complications.
- Follow up controls for the study will be performed after 6 weeks, 12 months and 36 months.
- Incisional hernia will be diagnosed by clinical examinations and in doubt by computed tomography. Postoperative clinical investigations are free of charge for the patient. Additional investigations that may be required for the regular treatment of the patient such as computed tomography will be billed to the health insurance.
- Postoperative abdominal pain is assessed for seven days during the hospitalization using visual analog scale (0-10).
- At follow up patients undergo a standardized interview with the assessment of abdominal pain using the visual analog scale (0-10).
- At follow up a clinical exam is performed investigating the impairment of morbidity of the trunk (Inclination, reclination, rotation) all measured in degrees.

Direct in-hospital costs:
For the determination of costs only in-hospital costs will be included in the analysis. Only hospitalizations that directly relate to complications or reoperations of the incisional hernia will be included in the study. Data of costs are provided by the controlling department of the Department of Visceral Surgery and Medicine of the University Hospital of Bern (Inselspital).

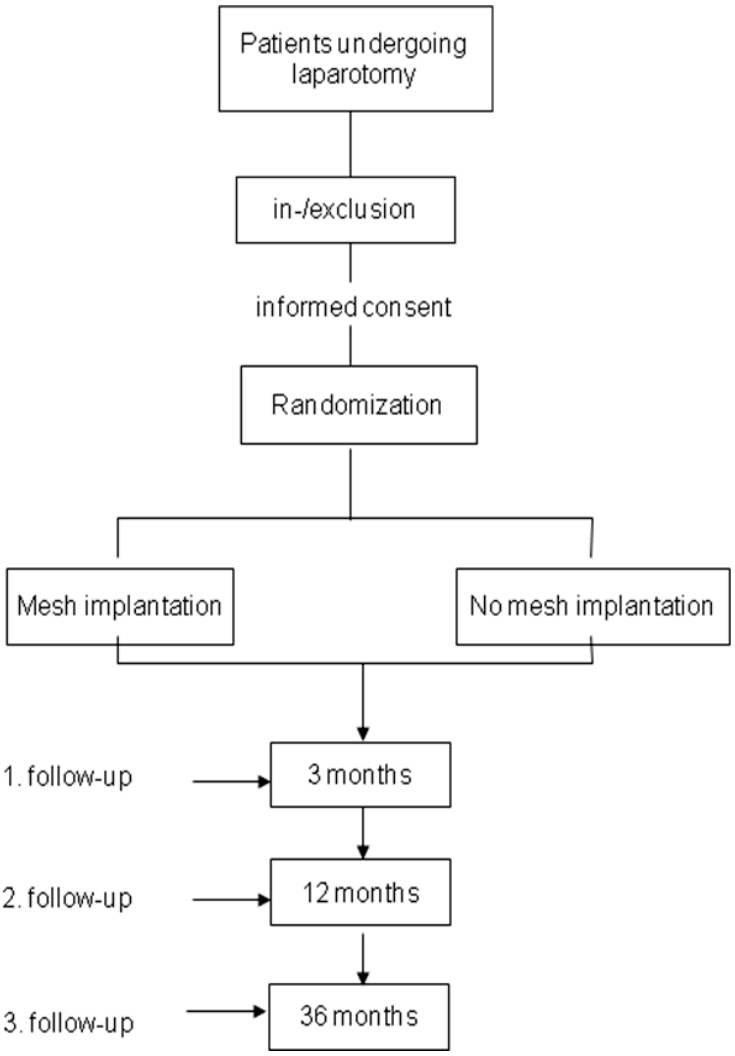
9. References

1. Hoer, J., et al., *[Factors influencing the development of incisional hernia. A retrospective study of 2,983 laparotomy patients over a period of 10 years]*. Chirurg, 2002. **73**(5): p. 474-80.
2. Yahchouchy-Chouillard, E., et al., *Incisional hernias. I. Related risk factors.* Dig Surg, 2003. **20**(1): p. 3-9.
3. Cassar, K. and A. Munro, *Surgical treatment of incisional hernia.* Br J Surg, 2002. **89**(5): p. 534-45.
4. van 't Riet, M., et al., *Meta-analysis of techniques for closure of midline abdominal incisions.* Br J Surg, 2002. **89**(11): p. 1350-6.
5. O'Dwyer, P.J. and C.A. Courtney, *Factors involved in abdominal wall closure and subsequent incisional hernia.* Surgeon, 2003. **1**(1): p. 17-22.
6. Sorensen, L.T., et al., *Smoking is a risk factor for incisional hernia.* Arch Surg, 2005. **140**(2): p. 119-23.
7. El-Khadrawy, O.H., et al., *Prophylactic prosthetic reinforcement of midline abdominal incisions in high-risk patients.* Hernia, 2009. **13**(3): p. 267-74.
8. Strzelczyk, J.M., et al., *Randomized clinical trial of postoperative hernia prophylaxis in open bariatric surgery.* Br J Surg, 2006. **93**(11): p. 1347-50.
9. LeBlanc, K.A. and W.V. Booth, *Laparoscopic repair of incisional abdominal hernias using expanded polytetrafluoroethylene: preliminary findings.* Surg Laparosc Endosc, 1993. **3**(1): p. 39-41.
10. Olmi, S., et al., *Laparoscopic versus open incisional hernia repair: an open randomized controlled study.* Surg Endosc, 2007. **21**(4): p. 555-9.
11. Beldi, G., et al., *Laparoscopic ventral hernia repair is safe and cost effective.* Surg Endosc, 2006. **20**(1): p. 92-5.
12. Forbes, S.S., et al., *Meta-analysis of randomized controlled trials comparing open and laparoscopic ventral and incisional hernia repair with mesh.* Br J Surg, 2009. **96**(8): p. 851-8.
13. Kingsnorth, A. and K. LeBlanc, *Hernias: inguinal and incisional.* Lancet, 2003. **362**(9395): p. 1561-71.
14. Hoer, J., et al., *[Prevention of incisional hernia]*. Chirurg, 2002. **73**(9): p. 881-7.

10. Appendices

1. Flowchart
2. Patientenfragebogen präoperativ
3. Datenerhebung Hospitalisation
4. Datenerhebung Operation
5. Datenerhebung Nachkontrollen

Flowchart


Patients undergoing laparotomy
in-/exclusion
informed consent
Randomization
Mesh implantation
No mesh implantation
1. follow-up
3 months
2. follow-up
12 months
3. follow-up
36 months

Datenerhebung **präoperativ**

Name, Vorname		**Geb. Datum**	

Random. Nr.		**Op. Datum**	

Ein- und Ausschlusskriterien

Alter > 18 Jahre	Ja ☐	Nein ☐
Mann	Ja ☐	Nein ☐
BMI > 25kg/m2	Ja ☐	Nein ☐
Maligner Tumor	Ja ☐	Nein ☐
Frühere Laparotomie	Ja ☐	Nein ☐
Informed consent	Ja ☐	Nein ☐
Elektive Operation	Ja ☐	Nein ☐

Bereits Netz implantiert	Ja ☐	Nein ☐
Bekannte Narbenhernie	Ja ☐	Nein ☐
Chronisch entzündliche Darmerkrankung	Ja ☐	Nein ☐

Eintritt (Datum)	Austritt (Datum)	

Diagnose: _____

Voroperation:

Datum	Indikation	Operation	Inzision (median, quer)	Länge (cm)

Nebendiagnosen:

1.
2.
3.

Medikamente:

1.
2.
3.

Körperliche Betätigung
leicht ☐ schwer ☐

Nikotin
nein ☐ ja ☐ Pack years:

Klinische Untersuchung

Gewicht bei Eintritt kg	
Grösse bei Eintritt cm	
BMI kg/m2	
ASA (1-4)	
Inklination: Abstand Fingerspitzen zu Boden	
Reklination	
Rotation	

Abstand Xyphoid-Umbilicus im aufrechten Stand _____cm

Abstand Xyphoid-Umbilicus in maximaler Reklination _____cm

Abdominales Spannungsgefühl durch das Netz bei Rotation des Oberkörpers nach links oder rechts Ja ☐ Nein ☐

Abstand Spina iliaca ant. sup. rechts-links im Stand _____cm

Datenerhebung **Hospitalisation**

Name, Vorname		**Geb. Datum**	

Random. Nr.		**Op. Datum**	

Schmerzerfassung (VAS) postop Tag 1 – 7

	8.00 Uhr	12.00 Uhr	16.00 Uhr	20.00 Uhr
Tag 1				
Tag 2				
Tag 3				
Tag 4				
Tag 5				
Tag 6				
Tag 7				

Schmerzmittelerfassung postop Tag 1 – 7 (Ja/Nein)

	PDA	Morphine	Paracetamol	Novalgin	NSAR
Tag 1					
Tag 2					
Tag 3					
Tag 4					
Tag 5					
Tag 6					
Tag 7					

Komplikationen:

			Datum
Wundinfekt	Ja ☐	Nein ☐	
Intestinale Fistel	Ja ☐	Nein ☐	
Serom	Ja ☐	Nein ☐	
Ileus	Ja ☐	Nein ☐	
Hämatom	Ja ☐	Nein ☐	
Reoperation	Ja ☐	Nein ☐	
Andere	Ja ☐	Nein ☐	

Bemerkungen:

Datenerhebung **Operation**

Name, Vorname		**Geb. Datum**	

Random. Nr.		**Op. Datum**	

Operateur: _____

Operation: _____

Dauer Operation (Gesamtdauer in min):

Dauer Implantation Netz (min):

Intraoperative Komplikationen

Art	Behandlung
Blutung	
Darmverletzung	
Netzkomplikationen	

Bemerkungen:

Datenerhebung **Follow Up**

Name, Vorname		**Geb. Datum**	

Random. Nr.		**Op. Datum**	

	Datum
6 Wochen	
12 Monate	
36 Monate	

Untersucher:

Anamnese: _____

	Tage postoperativ
Wiederaufnahme Arbeit	
Wiederaufnahme normale Aktivität/Sport	

Hatten Sie in der letzten Woche Schmerzen?

	Wo	Wie oft (1-4)	Wie stark (VAS 0-10)	Bemerkungen
Ja				

Wie oft: 1: <1/Woche, 2: >/Woche, 3: täglich, 4: mehrmals täglich

Komplikationen / Befunde:

			Bemerkungen
Hämatom	Ja ☐	Nein ☐	
Wundinfekt	Ja ☐	Nein ☐	
Intestinale Fistel	Ja ☐	Nein ☐	
Rezidiv	Ja ☐	Nein ☐	
Ileus/Passagestörung	Ja ☐	Nein ☐	
Trokarhernie	Ja ☐	Nein ☐	
Andere	Ja ☐	Nein ☐	

Klinische Untersuchung

Inklination: Abstand Fingerspitzen zu Boden	
Reklination	
Rotation	

Abstand Xyphoid-Umbilicus im aufrechten Stand _____cm

Abstand Xyphoid-Umbilicus in maximaler Reklination _____cm

Abdominales Spannungsgefühl durch das Netz bei Rotation des Oberkörpers nach links oder rechts Ja ☐ Nein ☐

Abstand Spina iliaca ant. sup. rechts-links im Stand _____cm

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

Universitätsklinik für Viszerale Chirurgie und Medizin
Klinikdirektoren:
Prof. Dr. med. Dr. h. c. Daniel Candinas, Viszeralchirurgie
Prof. Dr. med. Andrew J.S. Macpherson, Gastroenterologie
Prof. Dr. med. Jean-François Dufour, Hepatologie

Kantonale Ethikkommission
Postfach 56
3010 Bern

Bern, 22. November 2011

Amendment 1

Studie: Prophylactic mesh implantation for the prevention of incisional hernia
KEK Nummer: 094/10

Sehr geehrte Frau Dr. Pfiffner,

Wir haben ein zusätzliches Item im follow up CRF hinzugefügt, da ein Endpunkt nicht vorhanden war.

Die Änderung im Anhang ist markiert.

Freundliche Grüsse

PD Dr. med. Guido Beldi
Leitender Arzt

-CRF Follow up

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

Universitätsklinik für Viszerale Chirurgie und Medizin
Klinikdirektoren:
Prof. Dr. med. Dr. h. c. Daniel Candinas, Viszeralchirurgie
Prof. Dr. med. Andrew J.S. Macpherson, Gastroenterologie
Prof. Dr. med. Jean-François Dufour, Hepatologie

Kantonale Ethikkommission
Fr. Dr. D. Pfiffner
Postfach 56
3010 Bern

Bern, 20.08.2013

Amendment_2

Studie: Prophylactic mesh implantation for the prevention of incisional hernia
KEK Nummer: 094/10

Sehr geehrte Frau Dr. Pfiffner

Wegen sehr hoher Drop out Rate (Todesfälle wegen Malignität) haben wir 20 zusätzliche Patienten randomisiert.

Freundliche Grüsse

Prof. Dr. med. Guido Beldi
Leitender Arzt