Inguinal hernia repair using a synthetic long-term resorbable mesh: results from a 3-year prospective safety and performance study

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Abstract

Purpose Conventional meshes for hernia repair and abdominal wall reinforcement are usually made from polypropylene, polyester or other synthetic plastic materials known to promote foreign body reactions and a state of chronic inflammation that may lead to long-term complications. A novel approach is to use long-term resorbable implants like TIGR® Matrix Surgical Mesh. Preclinical studies have shown that this mesh maintains mechanical integrity beyond the point in time where newly formed tissue is capable of carrying the abdominal loads.

Methods This was a first-in-man, prospective, pilot study performed during 2009, at two sites in Sweden. Forty patients with primary inguinal hernias were enrolled for Lichtenstein repair using TIGR® Matrix Surgical Mesh. The primary endpoint was safety as assessed by monitoring the incidence of adverse events and serious adverse events (SAEs) both related and unrelated to the mesh. The secondary endpoint was pain or discomfort. Visual Analogue Scale (VAS) 0–10 and Inguinal Pain Questionnaire were used for scoring pain and discomfort. Included patients have been followed for 36 months using ultrasound in combination with clinical examination.

Results All patients followed a normal early postoperative course. After 12 months no SAEs were reported. None of the patients with an isolated lateral inguinal hernia (LIH) had developed a recurrence but 4 (44 %) with medial and 4 (33 %) with combined hernias had recurred at 36-month follow-up. After 3-year follow-up none of the patients with LIH reported pain in the VAS-form and none of those patients could feel the sensation of a mesh in their groin. In the total study population 5 (16 %) patients experienced chronic pain in the form of mild sporadic pain and 3 (9.7 %) patients could feel the sensation of a mesh in their groin.

Conclusion The use of a synthetic long-term resorbable mesh (TIGR® Matrix Surgical Mesh) in Lichtenstein repair was found to be safe, without recurrences, and promising regarding pain/discomfort at 3-year follow-up in patients with LIH. However, patients with medial and combined inguinal hernias had high recurrence rates.

Keywords Hernia · Absorbable implant · Surgical mesh · Recurrence · Indirect inguinal hernia · Chronic pain

Introduction

Inguinal hernia repair using prosthetic reinforcing meshes has led to reduced recurrence rates since the standardization of surgical techniques in the early 1990s. With the increased success in terms of low recurrence rates, the focus has shifted towards other complications following surgery, mainly chronic postoperative pain and discomfort. Pain complications are reported in varying degrees ranging from 0 to above 40 % [1]. It can be hypothesized that the mesh itself contributes to the postoperative pain since its presence gives rise to a chronic inflammatory reaction and a foreign body response. Adverse events (AEs) involving mesh products have been described in the clinical literature [2].
It has been suggested that meshes with reduced amount of material could be beneficial in terms of pain and discomfort [3], and some aspects of pain perception have been shown to be reduced when so-called light-weight meshes are being used [4–6]. With the long-term objective of reducing pain and discomfort further, a next step would be to investigate whether a completely resorbable mesh can improve results.

In order for this approach to be considered, it is of course imperative that the already low recurrence rates remain, and that no additional patient risks are introduced. A new synthetic resorbable mesh with slow degradation rate has recently been developed and in preclinical trials with 3-year follow-up it has shown satisfactory results for treatment of full-thickness abdominal wall defects in sheep, [7] with restoration of full-thickness connective tissue and no defect recurrences. The purpose of this study is to take the next step and establish first-in-man safety data for the use of the synthetic long-term resorbable mesh for inguinal hernia repair using the Lichtenstein technique.

Methods

Approval to start the study was given by the Swedish Medical Products Agency and the regional ethics committee in February 2009. Between April and December 2009, 40 male patients aged 18 years or older with primary unilateral inguinal hernias were enrolled at two different sites in Sweden. Patients were excluded if they had strangulated or irreducible hernias or if they were unwilling or unable to give informed consent to participate in the study. Since pain was one of the outcome measurements of the study, patients were excluded if they had preexisting pain conditions unrelated to the hernia.

Mesh characteristics

The mesh used for the study was TIGR® Matrix Surgical Mesh (Novus Scientific Pte Ltd., Singapore), a macroporous multifilament knitted construction of two different resorbable fibers: a fast and a slow-degrading synthetic copolymer. The first fiber resorbs within the initial 4 months following implantation and the mesh becomes softer and more flexible. The second fiber is completely resorbed after 3 years due to degradation by hydrolysis [7].

The initial burst strength of the mesh implant as measured according to American Society for Testing and Materials D3787 is above 300 N. This strength is comparable to existing commercially available products that range between 170 and 750 N. More than 50 % of the initial mechanical strength of the mesh, above theoretical and measured values of the highest forces acting on the abdominal wall [8, 9], is maintained during the first 26 weeks, after that the mechanical strength of the mesh is gradually lost [7].

Surgery and follow-up methods

Included patients underwent open mesh repair using the Lichtenstein technique [10]; this means reduction of the lateral sac with a rapidly absorbable suture in lateral inguinal hernias (LIH), reduction and/or inversion of the medial sac with rapidly absorbable sutures on the fascia transversalis if considered necessary in medial inguinal hernias (MIH). The mesh was fixed to the tissue with continuous polypropylene sutures to the inguinal ligament and one single suture to the aponeurotic tissue over the pubic bone and the internal oblique aponeurosis. All surgical procedures were performed by three experienced staff surgeons at Sahlgrenska University Hospital and Hallowed’s Hospital in Sweden. Operative details recorded included hernia type and size, incision length, whether the nerves were identified and preserved or divided, and any deviations from the Lichtenstein technique. Preoperative data and operation details correspond with what is found in the general population as published in the Swedish Hernia Register [11].

Adverse events, such as wound infection, hematoma, seroma, pain, among others and serious adverse event (SAEs), according to the FDA definition [12], were documented during surgery and throughout the follow-up. The monitoring included visits to the clinic at 14 days, 6, 12 and 36 months postoperatively, as well as telephone interviews by a research nurse at 1, 3 and 24 months. At the 36-month follow-up an ultrasound was performed by a radiologist experienced in hernia diagnostics, in order to identify clinically undiagnosed recurrences. All patients will continue to be monitored beyond the 3-year follow-up with respect to recurrences and other complications, through the Swedish Hernia Register.

Postoperative pain was measured using two validated methods frequently used in hernia repair research studies: an ungraded Visual Analogue Scale (VAS) ranging 0 (no pain)–10 (worst possible pain) and the Inguinal Pain Questionnaire (IPQ) [13–15].

The VAS was filled out before surgery and during the follow-up period to elucidate the pain experienced during rest, coughing, rising from lying to sitting, climbing one step in a flight of stairs and taking a 30 m indoor walk.

A symptom questionnaire and an analgesics diary were used to assess other factors related to the patients’ quality of life following surgery.

The IPQ-form was only filled in at the 36-month follow-up as a way to improve the evaluation of the pain and its effect on patients’ daily activities at this endpoint.
The date when the patients returned to paid work (if applicable) after surgery was also recorded.

In patients who were re-operated because of recurrence, a fine-needle biopsy was taken from the fascia transversalis and from the aponeurosis of the obliquus internus muscle. These patients were subsequently excluded from the follow-up program because a nonabsorbable mesh was implanted and the new surgery would interfere with the results in terms of pain from the long-term resorbable mesh.

Statistics

All statistical analyses were performed using the SAS® System (SAS Institute Inc., Cary, NC, USA). Continuous data were summarized using descriptive statistics.

Results

Forty patients gave informed consent to participate in the study. One patient was deemed unsuitable for surgery by the investigator, and one patient was excluded 6 months after surgery due to another disease that interfered with follow-up. Three additional patients failed to come to the 36-month follow-up control.

Thirty-eight patients completed the 12-month follow-up. Thirty-five patients completed the 3-year follow-up, of which four patients, re-operated for recurrence, were excluded from filling in pain forms and undergoing ultrasound examination. Two patients with recurrences but not re-operated at this time were included in the VAS and IPQ report (Fig. 1).

Preoperative data and operation details for the 39 patients who underwent surgery are shown in Table 1. All patients followed a normal early postoperative course as confirmed by the 14-day visit to the clinic and the 1-month telephone follow-up. The mean time to return to work was 12 days (1–35).

No SAEs were recorded during this period. AEs unlikely related to the mesh were ear pain, ear infection, viral encephalitis, muscular weakness, prostate cancer and urinary retention/dysuria, one patient with each diagnosis. No seroma, wound infection or hematoma needing follow-up or treatment was found.

Recurrence

No patient with an isolated LIH had developed a hernia recurrence at the 3-year follow-up. All recurrences have been found in either the MIH group or in the combined inguinal hernia (CIH) group, four patients in each group (Table 2).
During the follow-up period in total 8 (22.8 %) patients were diagnosed with recurrences: one patient before the 12-month follow-up, three patients before the 24-month follow-up and four patients at 36-month follow-up. Of the patients with recurrences, five have been re-operated with laparoscopic technique and one with a Lichtenstein approach. Two patients have so far declined a re-operation.

The anatomical location of the recurrences as confirmed by re-operation or ultrasound has also been medial in 7 (87 %) patients and remains unclear by ultrasound in 1 (13 %) patient which had primarily a CIH and declined a re-operation. All recurrences found by physical examination were confirmed by ultrasound.

No remnants of foreign material were found using fine-needle biopsies on any of the five laparoscopically re-operated patients, one 24 months and four 36 months after the primary surgery. No fine-needle biopsy was taken on the open re-operated patient because patient’s consent had not been obtained.

### Chronic postoperative pain

The pain experienced diminished over time as compared to before surgery: no patients experienced any severe pain, defined as VAS = 5 in the VAS-form, or pain that interfered with activities in the IPQ-form, other than before surgery. At the 3-year follow-up all patients with isolated LIH reported no pain in the VAS-form and only one patient (7 %) with LIH experienced mild pain in the IPQ-form, but this pain did not affect daily activities.

Of the study population, 10 (26.3 %) patients reported mild pain (VAS ≤ 3) at 3 months, which declined to 8 (21.1 %) at 6 months, and 5 (13.5 %) after 1 year. At the 3-year follow-up, chronic pain was reported by 2 (8 %) patients in the study population without recurrence. In the total study population excluding re-operated patients but including patients with recurrence, chronic pain was reported by 4 (12.9 %) patients in the VAS-form (VAS > 0) and 5 (16 %) patients in the IPQ-form. No relation between identification of the nerves and chronic pain was found.

At 3-year follow-up no patients with isolated LIH, could feel a mesh sensation in their groin and only 3 (9.7 %) patients had such sensation in the total study population.

The comprehensive results from the VAS questionnaires are presented in Tables 3 and 4 and the results from the IPQ-form in Table 5. Other assessments related to quality of life that were part of the symptoms questionnaires are shown in Table 6.

### Discussion

Resorbable meshes

Inguinal hernia repair is one of the more commonly performed procedures in general surgery and the introduction...
of prosthetic meshes has led to a drastic improvement in recurrence rates. Pain and discomfort remain an unsolved problem, however, and it has been shown that a reduction of the amount of permanent material implanted can improve the situation [4–6]. This study has been performed using a long-term resorbable synthetic mesh, with the primary objective of showing that this approach is feasible and acceptable from a patient safety point of view. Concerns related to the use of resorbable materials have been raised on several occasions, but mostly in the context of quickly resorbing materials such as glycolide sutures and meshes or polyglycolic acid/trimethylene carbonate mesh that completely lose their mechanical integrity within weeks [17–19].

The concept of using a long-term resorbable mesh for hernia repair differs from previous experiences as it allows for normal wound healing mechanisms to act before the mesh loses its mechanical contribution, given that the mesh is accommodating enough to transfer loads to the new tissue, thereby mechanically stimulating collagen remodeling [20, 21]. Furthermore, the now widespread use of prostheses of biological origin, of which some are enzymatically degraded in a relatively short time, has shown that soft tissue defects may sometimes only need reinforcement and restoration, not permanent repair, and that native connective tissue can be strong enough to carry bodily loads once the reinforcing implant has been degraded [22, 23].

Recurrences in patients with LIH

Recurrence rates will unavoidably be in focus when degradable materials are discussed in the context of abdominal wall surgery, especially in the light of the evidence of hernias being caused by an altered collagen metabolism or alteration of tissue remodeling [18, 24].

Our results show large differences between recurrences of lateral and MIH, in our case no recurrences in LIH but a high recurrence rate in MIH, when using a long-term degradable mesh, as assessed at 3-year follow-up.

We performed a classical Lichtenstein technique meaning that we used a nonabsorbable polypropylene suture to fix the mesh, but none of those stitches was positioned so that they closed the hernia defect. The reduction of the lateral sac was made with a rapidly absorbable suture. Previous publications have shown that this suture may be enough to prevent hernia recurrences in children but not in adults [25, 26].

Taking these facts into account, it is more probable that the absence of recurrence in patients with LIH depend on the implant utilized in our study.

A recently published pilot study showed a high recurrence rate 3 years after the primary operation in both LIH and MIH using a short-term absorbable mesh made of polyglycolic acid/trimethylene carbonate [19]. The differences in the rate of recurrences in LIH between that study

### Table 3 Pre- and post-operative pain as according to the VAS (graded 0–10)

|                          | Before surgery (n = 39) | 12 months (n = 38) | 36 months (n = 31) |
|--------------------------|------------------------|--------------------|--------------------|
| At rest                  | 1.0 (2.5)              | 0.1 (0.1)          | 0.1 (0.1)          |
| On coughing              | 1.5 (4.0)              | 0.1 (0.1)          | 0.1 (0.8)          |
| When rising from lying to sitting | 2.2 (5.5)        | 0.2 (0.2)          | 0.1 (0.2)          |
| When climbing one step in a flight of stairs | 1.3 (2.9)     | 0.1 (0.1)          | 0.1 (0.1)          |
| When taking a 30 m indoor walk | 1.6 (3.3)     | 0.1 (0.1)          | 0.1 (0.6)          |
| Overall (calculated as mean of the 5 scores above) | 1.5 (0.2)      | 0.1(0.0)           | 0.1 (0.0)          |

Values are mean (std)

### Table 4 Number of patients without and with pain as measured using VAS at the 3-year follow-up (n = 31)

|                          | VAS = 0 | VAS 0–3 | VAS 3–5 | VAS >5 |
|--------------------------|---------|---------|---------|--------|
| At rest                  | 31      | 0       | 0       | 0      |
| On coughing              | 31      | 0       | 0       | 0      |
| When rising from lying to sitting | 31      | 0       | 0       | 0      |
| When climbing one step in a flight of stairs | 27      | 3       | 1       | 0      |
| When taking a 30 m indoor walk | 31      | 0       | 0       | 0      |
| Total no. of patients with any pain at anytime | 27      | 3       | 1       | 0      |

### Table 5 Summary of results of IPQ-form at the 3-year follow-up (n = 31)

| Pain estimation                                      | Before operation | Right now | Worst pain past week |
|------------------------------------------------------|------------------|-----------|----------------------|
| No pain                                              | 5 (16.1)         | 27 (87.0) | 26 (83.8)            |
| Can easily be ignored                                | 5 (16.1)         | 3 (9.6)  | 4 (12.9)             |
| Cannot be ignored, no interference with daily activities | 7 (22.5)        | 1 (3.2)  | 1 (3.2)              |
| Interference with concentration on chores and daily activities | 8 (25.8)      | 0 (0.0)  | 0 (0.0)              |
| Interference with most activities                    | 5 (16.1)         | 0 (0.0)  | 0 (0.0)              |
| Need bed rest because of pain                        | 0 (0.0)          | 0 (0.0)  | 0 (0.0)              |
| Need prompt medical advice because of pain           | 1 (3.2)          | 0 (0.0)  | 0 (0.0)              |

Values are number of patients with percentages in parenthesis
and the present study could be explained by the differences in the time of resorption for the different meshes. The polyglycolic acid/trimethylene carbonate mesh loses more than 50 % of the initial mechanical strength after 6 weeks [19] in contrast to TIGR® Matrix Surgical Mesh which starts losing mechanical strength after about 6 months [7]. Tissue remodeling with newly formed collagen filaments and developing enough strength to replace the implant can take time, and that may be the reason why the quickly resorbable mesh failed.

The role of long-term resorbable meshes in LIH repair cannot be elucidated from this study because of the limited number of patients and the study was not designed for subgroup analysis, but so far we have not found any recurrences in patients operated upon for LIH in this study.

Recurrences in patients with MIH

The present study has found that the anatomical location for the hernia recurrence was almost exclusively in the fascia transversalis (87 %), also recurrence as an MIH. The national rate of recurrence in the Swedish Hernia Register is 4.6 % for MIH and 2.4 % for LIH [11]. It suggests that the surprisingly high rates of recurrences in the fascia transversalis found in this study did not come only from aleatoric factors.

A possible explanation for the higher recurrence rate after MIH operations when using a long-term resorbable mesh could be that the pathophysiology differs much more between MIH and LIH than what was previously thought. In other words, patients with MIH possibly have a more marked alteration of their tissue remodeling, thereby being unable to form a scar tissue strong enough to replace the mesh during the course of its resorption.

Other studies have shown the same pattern: Rodrigues et al. [27] showed lower collagen content per milligram of fascia transversalis in MIH patients than in LIH patients. Bellon et al. [28] demonstrated increased levels of factors that help degradation of collagen as matrix metalloproteinase 2 (MMP-2) and transforming growth factor B1 expression in fascia transversalis of MIH patients compared with patients with LIH or control patients. Abci et al. [29] found lower expression of the inhibitor of MMP-2: tissue inhibitor of metalloproteinase-2 in fascia transversalis in patients with MIH compared with those with LIH or control patients and Kayaoglu et al. [30] showed lower levels of copper, a cofactor of an enzyme in collagen tissue metabolism, in plasma and in the hernia sac of MIH patients in comparison to LIH patients. A recently published article by Vestergaard et al. [31] found that cumulative exposure to daily heavy lifting activities was associated with the risk of LIHs but not with MIH.

These findings, including the results of our study, support the notion that different pathophysiological mechanisms are involved in MIH and LIH, which must be taken into account when selecting the most appropriate technique and implant for inguinal hernia surgery. This study strengthens the idea that resorbable meshes are not enough to prevent recurrences in patients with MIH.

Pain

The performance parameters investigated in this study show promising results in terms of pain and foreign body sensation. Both these parameters were constantly declining during the course of the follow-up period, reaching low levels after 1 year.

In the clinical literature, there is a remarkable spread in the data concerning the risk of pain and discomfort after inguinal hernia surgery (20–45 %) as well as follow-up methods [1, 32]. The ambiguous preexisting data, combined with the subjectivity of pain measurements, leaves any comparison between different studies of low scientific value at this point. Even when taking into account that patients with preexisting pain conditions unrelated to the hernia were excluded, the results of this study on chronic pain (0 % in the VAS-form, 7 % in the IPQ-form) and mesh sensation (0 %) in patients with LIH at the 3-year follow-up are so good that it opens the door for larger, randomized studies to confirm these findings.

Considering the finding that the mesh was 100 % resorbed at the 3-year follow-up, it is also interesting to further investigate the origin of the pain that a proportion of the patients still can feel in certain situations. Another intriguing finding is the mesh sensation that remains in a small subset of the patients after the mesh itself has been resorbed completely. We leave it to future trials to investigate the potential of the long-term resorbable mesh

| Table 6 | Factors related to patient quality of life following surgery at 6, 12 and 36 months |
|---------|---------------------------------|---------------------------------|---------------------------------|
|         | 6 months (n = 38) | 12 months (n = 38) | 36 months (n = 31) |
| Normal sensation in the groin | Ye 24 (63.2) No 14 (36.8) | Ye 31 (81.6) No 7 (18.4) | Ye 25 (80.6) No 6 (19.4) |
| Can feel a mesh in the groin | Ye 7 (18.4) No 30 (81.6) | Ye 4 (10.5) No 34 (89.5) | Ye 3 (9.7) No 28 (90.3) |

Values in parenthesis are percentages calculated from the number of subjects with available data at respective visit.
concept in terms of reduction of chronic postoperative pain after LIH repair, as it was not the primary objective for this study.

Conclusion

The use of a synthetic long-term resorbable mesh (TIGR® Matrix Surgical Mesh) in Lichtenstein repair was found to be safe, without recurrence, and promising regarding pain/discomfort at the 3-year follow-up in patients with LIH. However, patients with MIH and CIH had high recurrence rates.

The definitive role of long-term degradable implants to reduce the risk of chronic postoperative pain after inguinal hernia repair for lateral hernias must be investigated in larger randomized studies.

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References

1. Nienhuijs S, Staal E, Strobbbe L, Rosman C, Groenewoud H, Bleichrodt R (2007) Chronic pain after mesh repair of inguinal hernia: a systematic review. Am J Surg 194:394–400
2. Amid PK (2004) Radiologic images of meshoma: a new phenomenon causing chronic pain after prosthetic repair of abdominal wall hernias. Arch Surg 139(2):1297–1298
3. Bringman S, Conze J, Cucurullo D, Deprest J, Junge K, Klosteraffen B, Parra-Davila E, Ramshaw B, Schumpelick V (2010) Hernia repair: the search for ideal meshes. Hernia 14:81–87
4. O’Dwyer PJ, Kingsnorth AN, Molloy RG, Small PK, Lammers B, Horeyseck G (2005) Randomized clinical trial assessing impact of a lightweight or heavyweight mesh on chronic pain after inguinal hernia repair. Br J Surg 92(2):166–170
5. Post S, Weiss B, Willer M, Neufang T, Lorenz D (2004) Randomized clinical trial of lightweight composite mesh for Lichtenstein inguinal hernia repair. Br J Surg 91(1):44–48
6. Bringman S, Wollert S, Osterberg J, Smedberg S, Granlund H, Heikkinen TJ (2006) Three-year results of a randomized clinical trial of lightweight or standard polypropylene mesh in Lichtenstein repair of primary inguinal hernia. Br J Surg 93(9):1056–1059
7. Hjort H, Mathisen T, Alves A, Clermont G, Bouttrand JP (2012) Three-year results from a preclinical implantation study of a long-term resorbable surgical mesh with time-dependent mechanical characteristics. Hernia 16:191–197
8. Klinge U, Klosterhalfen B, Conze J, Limberg W, Obolenksi B, Ottinger AP, Schumpelick V (1998) Modified mesh for hernia repair that is adapted to the physiology of the abdominal wall. Eur J Surg 164(12):951–960
9. Cobb WS, Burns JM, Kercher KW, Matthews BD, Norton JH, Heniford BT (2005) Normal intraabdominal pressure in healthy adults. J Surg Res 129(2):231–235
10. Amid PK, Shulman AG, Lichtenstein IL (1996) Open “tension-free” repair of inguinal hernias: the Lichtenstein technique. Eur J Surg 162(6):447–453
11. Swedish Hernia Register (2013), http://www.svensktbrackregister.se. Accessed 22 Apr 2014
12. FDA. http://www.fda.gov/safety/medwatch/howtoreport/ucm053087.htm. Accessed 22 Apr 2014
13. Corney CA, Duffy K, Serpell MG, O’Dwyer PJ (2002) Outcome of patients with severe chronic pain following repair of groin hernia. Br J Surg 89:1310–1314
14. Loos MJ, Houterman S, Sheltina MR, Roumen RM (2008) Evaluating postherniorrhaphy groin pain: visual analogue or verbal rating scale? Hernia 12:147–151
15. Fränneby U, Gunnarsson U, Andersson M, Heuman R, Nordin P, Nygren O et al (2008) Validation of en Inguinal Pain Questionnaire for assessment of chronic pain after groin hernia repair. Br J Surg 95:488–493
16. Turk DC, Okifuji A (2001) Pain terms and taxonomies. In: Loeser Jr., A. et al. (eds) Pain: mechanisms and clinical implications. Lippincott Williams and Wilkins, Philadelphia, pp 18–25
17. Chu CC (1982) The effect of pH on the in vitro degradation of polyglycolic lactide) copolymer absorbable sutures. J Biomed Mater Res 16(2):117–124
18. Franz MG (2006) The biology of hernias and the abdominal wall. Hernia 10(6):462–471
19. Symeonidis D, Efthimiou M, Koukoulis G, Athanasiou E, Manaloidis I, Tsivaras G (2013) Open inguinal hernia repair with the use of polyglycolic acid/trimethylene carbonate absorbable mesh: a critical update of the long-term results. Hernia 17:85–87
20. Altman GH, Horan RL, Martin I, Farhadi J, Stark PR et al (2009) Cell differentiation by mechanical stress. Faseb J 16:270–272
21. Nagel T, Kelly DJ (2010) Mechanoregulation of mesenchymal stem cell differentiation and collagen organization during skeletal tissue repair. Biomech Model Mechanobiol 9(3):359–372
22. Clarke KM, Lantz GC, Salisbury SK, Badyak SF, Hiles MC, Voytik SL (1996) Intestine submucosa and polypropylene mesh for abdominal wall repair in dogs. J Surg Res 60(1):107–114
23. El-Gazzaz G, Erem H, Aytac E, Salcedo L, Stocchi L, Kiran R (2012) Risk of infection and hernia recurrence for patients undergoing ventral hernia repair with non-absorbable or biological mesh during open bowel procedures. Tech Coloproctol. doi:10.1007/s10151-012-0928-0
24. Klinge U, Zheng H, Si Z, Schumpelick V, Bhardwaj RS, Muys L, Klosterhalfen B (1999) Expression of the extracellular matrix proteins collagen I, collagen III and fibronectin and matrix metalloproteinase-1 and -13 in the skin of patients with inguinal hernia. Eur Surg Res 31(6):48–490
25. Mhert JH, Brown M, Kroult W, Woodward B (1963) Indirect recurrences of inguinal hernias. Am J Surg 106(6):958–965
26. Nyhus LM, Klein MS, Rogers FB (1991) Review. Curr Probl Surg 28(6):401–450
27. Rodrigues A, Rodrigues C, Pereira A, Yoo J (2002) Quantitative analysis of collagen and elastic fibers in the transversalis fascia in direct and indirect inguinal hernia. Rev Hosp Clin Fac Med S Paulo 57(6):265–270

Hernia (2014) 18:723–730 729
28. Pascual G, Corrales C, Gomez-Gil V, Buján J, Bellón M (2007) TGF-B1 overexpression in the transversalis fascia of patients with direct inguinal hernia. Eur J Clin Invest 37(6):516–521
29. Abci I, Bigi S, Altan A (2005) Role of TIMP-2 in fascia transversalis on development of inguinal hernias. J Invest Surg 18:123–128
30. Kayaoglu H, Hazinedaroglu S, Erkek A, Kocaturk P, Kavas G, Aribal D (2005) Comparison of the plasma and hernia sac tissue copper levels in direct and indirect inguinal hernia patients. Biol Trace Elem Res 108(1–3):53–59
31. Vestergaard M, Frost P, Bay-Nielsen M, Wulff S (2013) Impact of occupational mechanical exposures on risk of lateral and medial inguinal hernia requiring surgical repair. Occup Environ Med 69:802–809
32. Nienhuijs SW, van Oort I, Keemers-Gels ME, Strobbe LJ, Rosman C (2005) Randomized clinical trial comparing the Prolene® Hernia System, mesh plug repair and Lichtenstein method for open inguinal hernia repair. Br J Surg 92:33–38