TISSUE ATTACHMENT STRENGTH AND ADHESION FORMATION OF INTRAABDOMINAL FIXED MESHES WITH CYANOACRYLAT GLUES

R. Ladurner¹, I. Drosse², S. Seitz¹, W. Plitz³, G. Barbaryka⁴, M. Siebeck¹, D. Bürklein¹, C. Kirchhoff¹, S. Buhman⁵, W. Mutschler¹, M. Schieker^{1,2}, T. Mussack¹

¹Department of Surgery Innenstadt, Ludwig-Maximilians-University (LMU) Munich,
 ²Experimental Surgery and Regenerative Medicine, Department of Surgery Innenstadt, University of Munich (LMU)
 ³Department of Orthopaedics Großhadern, University of Munich (LMU)
 ⁴Department of Pathology Innenstadt, University of Munich (LMU)
 ⁵Department of Radiology, University of Munich (LMU), Germany

Abstract

Objektiv: The aim of this study was to evaluate the technique of prosthetic mesh fixation in laparoscopic intraperitoneal incisional and ventral hernia repair using cyanoacrylat glue (Glubran® GEM, Viareggio, Italy) in comparison with fixation methods using spiral tacks (Protack 5mm, Tyco) or transabdominal Prolene® 4/0 sutures respectively.

Method: Through a midline laparotomy 3 pieces (3 x 3cm) of mesh (n = 60) where fixed onto the intact peritoneum on either side of a midline laparotomy in 10 New Zealand White rabbits. Two types of meshes where compared: ePTFE meshes (Gore-Tex Dual Mesh W.L. Gore & Associates, Inc. Medical Products Division, Flagstaff, Arizona, USA) and polypropylene/polyvinylfluorid meshes (Dyna Mesh® - IPOM P.J. Dahlhausen & Co. GmbH, Germany). All animals were killed after 12 weeks. Upon scoring of the adhesions the prosthetic materials were excised en bloc with the anterior abdominal wall for tensile strength analysis and histologic evaluation.

Results: In contrast to ePTFE meshes fixed with cyanoacrylat glue, PP meshes fixed with transabdominal sutures as well as with spiral tacks showed the highest percentage and tenacity of adhesions (p < 0.033). Independent of the method of fixation, ePTFE meshes revealed a significantly higher shrinkage than PP prosthesis (41% vs 17% related to original mesh surface; p < 0.033). The strength of the mesh incorporation was significantly higher in PP meshes (p < 0.033). Fixation of PP meshes with cyanoacrylat glue showed an equivalent tensile strength as ePTFE meshes fixed with spiral tacks (6.6 \pm 2.7 N vs 6.6 \pm 3.1N)

Conclusion: In this rabbit model, intraabdominal fixation of PP composite meshes with cyanoacrylat glue was equivalent to ePTFE mesh fixation with spiral tacks concerning tensile strength analysis. Adhesions between mesh and abdominal wall were found more frequently after PP fixation. In contrast, mesh shrinkage was more evident after ePTFE mesh implantation.

Key words: laparoscopic incisional hernia repair, fixation devices, cyanoacrylat glue, tensile strength, intraabdominal adhesions

INTRODUCTION

While an open surgical technique represented the gold standard of incisional hernia repair for a long time, the introduction of laparoscopic surgery in 1990 by Leblanc opened up new vistas in hernia surgery [1]. Shorter hospitalization, a lower rate of infected wounds, less pain and a lower recurrence rate were the potential advantages of the new technique. The introduction of mesh techniques has further lowered the cases of recurrence [2, 3]. The incidence of chronic pain is still unclear as only few studies have focussed on long term recurrence, pain or quality of life [4]. The source of chronic pain is still unclear. Nerve irritation caused by the inflammatory reaction against the mesh or scar tissue formation as well as nerve entrapment by regularly used fixation devices (spiral tacks, transfascial sutures) are the suspected causes. The aim of this study was to evaluate the technique of prosthetic mesh fixation in laparoscopic intraperitoneal incisional and ventral hernia repair using cyanoacrylat glue (Glubran® GEM, Viareggio, Italy) in comparison with fixation methods using spiral tacks (Protack 5mm, Tyco) or transabdominal Prolene 4/0 sutures respectively.

MATERIALS AND METHODS

10 New Zealand white rabbits, weighing 2500-3000 g were used in this study. Prior to the intervention animals were acclimatized to the vivarium for two weeks. They were kept under standard laboratory conditions (temperature 20 °C, relative humidity 50-60%, 12 light/12 h dark, feed and water ad libidum). In each animal 6 pieces of 3 x 3cm meshes (3 meshes of ePTFE and 3 meshes of polypropylene/ polyvinylfluorid (PP) on either side of the midline incision) were intraabdominally attached to the peritoneum. This study was conducted with the approval of the government of Oberbayern.

Surgical Procedure

Anaesthesia was performed with an intramuscular injection of medetomidin, fentanyl and midazolam. A

ventral midline incision of 10cm from the xiphoid process to the pubic symphysis was made. Three ePTFE (expanded Polytretrafluorethylene) meshes (3 x 3cm) were implanted on the left side of the midline incision, three polypropylene (PP) meshes (3 x 3cm) were placed on the right side. All meshes were spaced at 2 cm and fixated with a distance of 2 cm to the incision. One of each mesh types was fixed using either four spiral tacks on the corners of the implants (Protack 5mm, Tyco), four transabdominal Prolene® 4/0 sutures or cyanoacrylat glue (Glubran® GEM, Viareggio, Italy) applied evenly to the surface of the respective mesh. Following implantation the peritoneum and the midline fascia were closed in a running suture pattern using Vicryl[®] 2/0. Subcutaneous tissue was closed with a subcuticular Vicryl® 4/0 suture. After the operation the rabbits were returned to their individual cages. Postoperatively animals received an analgesic (Tramudin®), if necessary. All animals were killed 12 weeks after mesh implantation by a pentobarbital overdose (300mg/kg, i.v.).

SCORING OF ADHESIONS

Adhesion formation between the meshes and viscera and the large omentum respectively was evaluated. Density of the adhesions was evaluate macroscopically via a midline laparotomy using a scoring scale as suggested by Garrard 1999 (Table 1) [5, 6].

The percentage of adhesions covering the mesh surface was also recorded. Each mesh was subdivided into ten fields and for each of these fields the surface percentage covered by adhesions was determined separately.

MESH SHRINKAGE AND TENSILE STRENGTH

The entire abdominal wall was excised with the meshes. To evaluate shrinkage, the surface area of each mesh was measured compared with the original size (9 cm²). From each abdominal wall/mesh sample a specimen measuring 0.5 x 3 cm was cut for histology. The rest of each sample underwent fixation strength testing using a tensiometer (Zwick 0Z01). For this purpose the contact between the mesh and the abdominal wall was loosened on one side to clamp taut the free borders in the test machine. The mesh was then removed from the abdominal wall with a continuous displacement rate of 100 mm/min. Displacement force was recorded simultaneously. The maximum tensile strength was measured (Newton).

HISTOLOGY

The abdominal wall/ mesh samples were fixed in 4% formaldehyde, embedded in paraffin and sectioned at 7-10 µm. All tissue sections were stained with hematoxylin and eosin, Goldner's trichrome, as well as Ladewig staining (fibrin stains). Additionally, immunhistochemical analysis was carried out on selected samples of the different implant types using antibodies against human panzytoceratine which proved positive also for rabbit tissue. The aim of the light microscopical assessment was to give a thorough description of the tissue response to the different implant materials. The amount and quality of an inflammatory response and the extent of scar tissue formation were of particular interest. For the evaluation, special attention was paid to the interface between the abdominal wall and the meshes. To determine and compare the inflammatory response to the different materials and fixation devices used, all nucleated cells including fibrocytes, macrophages, lymphocytes, endothelial cells and monocytes were counted per high-powered field (HPF) in HE staining. The occurence of foreign body giant cells was noted separately. Trichrome staining was used to determine the dimensions of fibrous tissue around the implants. The Ladewig staining was used to assess whether or not fibrinous exsudate could still be seen in the newly formed tissue around the implants (10x magnification) (Fig. 1).

STATISTICAL ANALYSIS

Differences between the intervention groups (Gore Stapler, Gore Suture, Gore Glubran, Dyna Stapler, Dyna Suture, Dyna Glubran) were tested for significance using ANOVA post hoc with Bonferroni-Dunn correction. The comparisons were performed using STATVIEW 4.5 software (Abacus Concepts, Berkeley, CA). In view of the multiple tests between groups, significance levels were set as P < 0.0033, to indicate a global significance level of P < 0.05-

RESULTS

No intraoperative complications occured. All rabbits had an uneventful recovery and remained free from infection, disturbance of the wound healing or bowel obstruction. All prosthesis were completely reperitonealized at explantation and we noticed no mesh migration. We compared the density of the adhesions (Table 2) and the percentage of the adhesions covering the mesh surface (Table 3). The density and the percentage of the adhesions were significantly less in

Table 1. Adhesion scale from Garrard et al. and Joels et al. [5, 6].

Type of adhesions	Score
No adhesions	1
Filmy adhesions, easily broken manually	2
Dense adhesions, requiring blunt dissection to separate viscera from mesh	3
Very dense adhesions, viscera matted to mesh surface, requiring sharp dissection to separate viscera from mesh	4

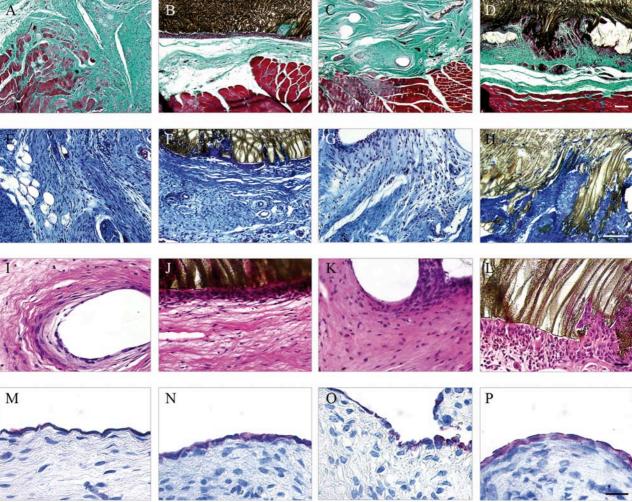


Fig. 1.
Pictures A-D Goldner's trichrome, 5x magnification, bar: 100μm Pictures E-H Ladewig, 10x magnification, bar: 100μm Pictures I-L HE, 20x magnification, bar: 50μm Pictures M-P Pancytokeratin, 40x magnification, bar: 20μm

 $\begin{array}{l} A,E,I,M:\ Gore-Tex^{\circledR}\ mesh\ (staples/sutures)\\ D,H,L,P:\ Gore-Tex^{\circledR}\ mesh\ (Glubran^{\circledR})\\ B,F,J,N:\ DynaMesh-Ipom^{\circledR}\ (staples/sutures)\\ C,G,K,O:\ DynaMesh-Ipom^{\circledR}\ (Glubran^{\circledR}) \end{array}$

Stainings in Goldner's trichrome allow easy assessment of the extent of fibrous tissue at the interface between the implants and the abdominal wall; Ladewig staining specifically marks fibrin which was not seen twelve weeks postoperatively; in HE note particularly the arrangement of nucleated cells around the implant; mesothelialization of all implants was proven by panzytoceratin staining.

the ePTFE group compared to the PP meshes. ePTFE meshes fixed with cyanoacrylat glue showed the lowest, PP meshes fixed with transfabdominal sutures and tacks the highest percentage of adhesions. Independent of the fixation modality ePTFE meshes showed in general statistically significant more pronounced shrinkage than PP prosthesis (Table 4). The strength of the mesh incorporation was significantly higher in PP meshes. Fixation with transabdominal sutures was significantly stronger (p < 0.033) in both ePTFE and PP meshes in comparison to spiral tacks and Glubran[®]. The strongest fixation device in both implant types proved to be the transabdominal sutures. Tensile strength of ePTFE meshes fixed by spiral tacks was equal to PP meshes fixed with Glubran[®].

The relative macroporosity of PP meshes allowed for slightly more ingrowth of fibrous tissue and accordingly scar formation directly around and in close proximity to the fibres of the implant itself, compared to the ePTFE meshes. Comparing the groups, the inflammatory reaction to the latter was slightly higher when using the amount of nucleated cells per HPF as an indicator. While in the PP meshes the total amount of cells was slightly lower and these were equally distributed throughout the newly formed tissue, an overall higher number of cells could be seen with the ePTFE meshes. Beyond that, the distribution of cells differed, in that a conspicuously high amount of mononuclear granulocytes were found in a palisade-like order directly on the surface of the implant mater-

Table 2. Adhesion tenacity from Garrard et al. and Joels et al. [5, 6].

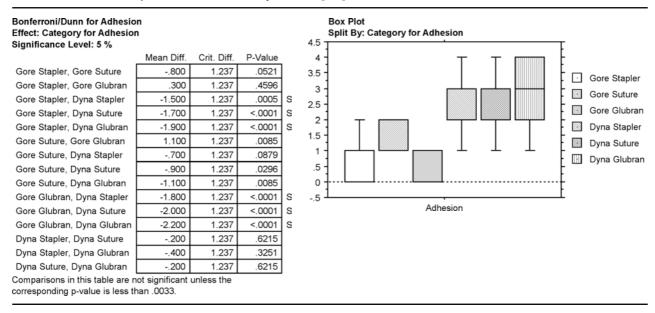
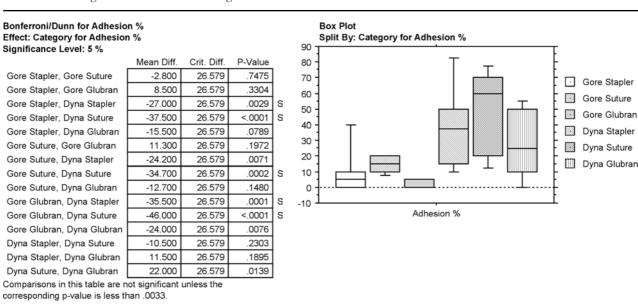


Table 3. Percentage of the adhesions covering the mesh surface.



ial. The occurence of foreign body giant cells did not seem to differ between the groups. Mesothelialization, however, could be shown for both implant materials equally, using the aforementioned panzytoceratine staining. The evaluation of the samples stained with Ladewig revealed that regardless of the implant material and fixation device used; only minor amounts of fibrinous exsudate remained after an implantation period of twelve weeks.

DISCUSSION

Incisional hernia complicate about 10% of laparotomies and the repair with conventional techniques is associated with high recurrence rates of 30-50 % [2, 7, 8]. Surgical repair using different prosthesis is becoming increasingly common. Different operative

techniques of hernioplasty are used. The laparoscopic repair of incisional hernia is a relatively new approach. Recent studies of laparoscopic hernia repair confirmed that the technique is associated with minimal postoperative morbidity and shorter hospitalization [9, 10]. The basic concept of this technique includes the dissection of all adhesions, clear identification of the fascial defect, closure of the hernia by a properly fixed mesh and a sufficient overlap of the prosthesis [11]. For reliable fixation of the implant, transabdominal sutures along the edges of the mesh and helical coils made of titanium are used in combination. Whether or not mesh fixation with spiral tacks alone is satisfactory is still up for discussion [11-13]. It is widely recommended to use either six to eight nonabsorbable monofilament sutures at the corners and along the edges of the implants or spiral tacks (Pro-

Table 4. Mesh surface at explantation (cm²). Mean \pm SD. The original size of each mesh was 9 cm².

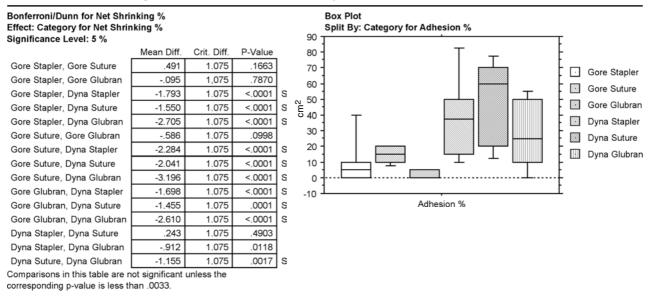
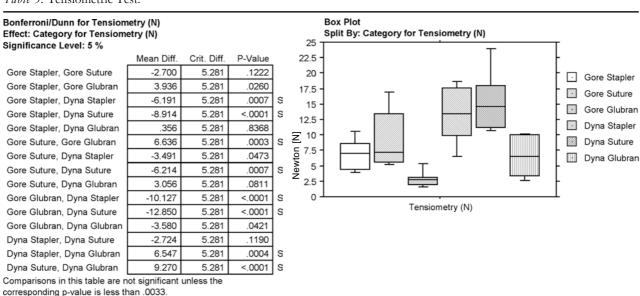


Table 5. Tensiometric Test.



tack® 5mm Auto Suture) spaced at 1cm along the borders of the meshes. Fatty tissue around the falciforme ligament and between the plicae mediales must be dissected in order to allow sufficient fixation of the spiral tacks. Using spiral tacks for fixation, elements with a diameter of 4 mm are screwed into the abdominal wall at a depth of 3.8mm. Staples of a conventional hernia stapler have a depth of penetration of 2 mm. In experimental studies on 20 human cadavers the shear force resistance of a mesh fixed by a spiral tacks was up to four times higher than that of a mesh fixed with conventional staples [12]. Despite certain drawbacks (see below) spiral tacks are so far the best tool for mesh fixation in laparoscopic hernia repair not least because the coil-like screwing movement of the spiral tacks allows intraoperatively, if necessary, easy removal of the devices without dam-

aging either tissue or mesh. Mesh fixation with transabdominal sutures and spiral tacks are important measures to prevent mesh migration and hernia recurrence [9, 11]. None the less both fixation methods have to be challenged since they can be the source of persistent postoperative pain. It is widely agreed that the most likely cause of such pain results either from an entrapment of intercostals nerves coursing between different layers of the abdominal wall musculature or local muscle ischemia [14]. Beyond that the use of spiral tacks is in some cases associated with postoperative complications such as adhesion formation between the intestines and the abdominal wall or - in rare cases – even perforations of the small intestine [14-16].

The optimal solution for the fixation of intraperitoneal placed meshes has not been found yet. Cyanoacrylates have been introduced in surgical procedures and are mainly used as embolic agents by interventional radiologists and endoscopists. Also in pediatric laparoscopic surgery these materials are made use of [17-19]. Glubran® (GEM, Viareggio, Italy) is a synthetic N-butyl-cyanoacrylate glue. The product polymerizes quickly (1-2 sec to 1min) only when in contact with blood and tissues therewith avoiding undesired polymerization in the needle during injection. The glue is eliminated by hydrolytic degradation after 30-40 days to 6 month. Up to now Glubran® has not been evaluated for mesh fixation in laparoscopic incisional hernia repair. The aim of this study was to evaluate with two different mesh materials (ePTFE, PP) whether it is possible to achieve satisfactory fixation of those implants with glue. No difference was noted in mesh motion between glue, tacks and transfascial suture group. In this study we analyzed mesh tissue fixation strength by tensiometric measurements. The results of the analysis showed that tensile strength of PP meshes fixed by glue is nearly identical to the fixation of ePTFE meshes using spiral tacks. As a matter of course at 12 weeks both the tensile strength of the fixation device and the tissue integration of the mesh in the abdominal is measured. The poor results of the fixation strength testing for the ePTFE meshes fixed with glue might be a result of the interference of the cyanoacraylat glue with the incorporation of the material. Complete incorporation of the mesh is an important requirement for a durable and long-lasting hernia repair. Fibrocytic and collagen tissue ingrowth of the host tissue is proportional to the degree of the material's porosity. It is well known that polypropylene meshes are better incorporated in the abdominal wall than ePTFE meshes [20]. The degree of the integration of prosthesis used in abdominal wall hernia repair depends on the structure of the biomaterial. ePTFE (Dual Mesh®) has a pore size of less than 3_m on the visceral side which prevents adhesions as well as host tissue in growth. The opposite side is more coarsely textured with pore sizes of 22µm allowing sufficient host tissue infiltration. Despite the rough surface of the newer generation of ePFTE meshes with an increased collagen deposition around the biomaterial, the lattice-like structure of polypropylene meshes still promotes uniform and unbroken infiltration of the host more effectively resulting in a more thorough incorporation of the meshes in the resulting scar.

Concerning the effect of different fixation techniques on the tissue response it can be said that within the groups of one implant material only minor deviations concerning the criteria mentioned above were to be seen. However, there was a slight tendency of the tissue glue to evoke a more pronounced cellular reaction.

CONCLUSION

Firm mesh fixation is crucial for successful laparoscopic intraperitoneal abdominal wall hernia repair. In this rabbit model, intraabdominal fixation of PP composite meshes with cyanoacraylat glue was equivalent to ePTFE mesh fixation with spiral tacks concerning tensile strength analysis. Adhesions between mesh and

abdominal wall were found more frequently after PP fixation. In contrast, mesh shrinkage was more evident after ePTFE mesh implantation. Concerning the effect of different fixation techniques on the tissue response it can be said that within the groups of one implant material only minor deviations concerning the criteria mentioned above, were to be seen.

For future applications it might become possible to use synthetic glues for the fixation of meshes in hernia repair either in combination with – or even without – spiral tacks or transabdominal sutures. This might help to overcome some of the problems associated with conventional surgical techniques such as chronic pain therewith optimizing patient satisfaction.

REFERENCES

- LeBlanc KA, Booth WV. Laparoscopic repair of incisional abdominal hernias using expanded polytetrafluoroethylene: preliminary findings. Surg Laparosc Endosc 1993; 3:30.41
- Cassar K, Munro A. Surgical treatment of incisional hernia. Br J Surg 2002; 89:534-545.
- Nilsson E, Haapaniemi S. Hernia registers and specialization. Surg Clin North Am 1998; 78:1141-55, ix.
- 4. Martin-Duce A, Noguerales F, Villeta R, Hernandez P, Lozano O, Keller J, Granell J. Modifications to Rives technique for midline incisional hernia repair. Hernia 2001; 5:70-72.
- Garrard CL, Clements RH, Nanney L, Davidson JM, Richards WO. Adhesion formation is reduced after laparoscopic surgery. Surg Endosc 1999; 13:10-13.
- Joels CS, Matthews BD, Kercher KW, Austin C, Norton HJ, Williams TC, Heniford BT. Evaluation of adhesion formation, mesh fixation strength, and hydroxyproline content after intraabdominal placement of polytetrafluoroethylene mesh secured using titanium spiral tacks, nitinol anchors, and polypropylene suture or polyglactin 910 suture. Surg Endosc 2005; 19:780-785.
- 7. Farthmann EH, Mappes HJ. [Tension-free suture of incisional hernia]. Chirurg 1997; 68:310-316.
- 8. George CD, Ellis H. The results of incisional hernia repair: a twelve year review. Ann R Coll Surg Engl 1986; 68:185-187.
- 9. Heniford BT, Park A, Ramshaw BJ, Voeller G. Laparoscopic ventral and incisional hernia repair in 407 patients. J Am Coll Surg 2000; 190:645-650.
- LeBlanc KA, Booth WV, Whitaker JM, Bellanger DE. Laparoscopic incisional and ventral herniorrhaphy in 100 patients. Am J Surg 2000; 180:193-197.
- LeBlanc KA. The critical technical aspects of laparoscopic repair of ventral and incisional hernias. Am Surg 2001; 67:809-812.
- Hollinsky C, Gobl S. Bursting strength evaluation after different types of mesh fixation in laparoscopic herniorrhaphy. Surg Endosc 1999; 13:958-961.
- Ben Haim M, Kuriansky J, Tal R, Zmora O, Mintz Y, Rosin D, Ayalon A, Shabtai M. Pitfalls and complications with laparoscopic intraperitoneal expanded polytetrafluoroethylene patch repair of postoperative ventral hernia. Surg Endosc 2002; 16:785-788.
- 14. Carbonell AM, Harold KL, Mahmutovic AJ, Hassan R, Matthews BD, Kercher KW, Sing RF, Heniford BT. Local injection for the treatment of suture site pain after laparoscopic ventral hernia repair. Am Surg 2003; 69: 688-691.
- Koehler RH, Begos D, Berger D, Carey S, LeBlanc K, Park A, Ramshaw B, Smoot R, Voeller G. Minimal adhesions to ePTFE mesh after laparoscopic ventral incisional

- hernia repair: reoperative findings in 65 cases. JSLS 2003; 7:335-340.
- Ladurner R, Mussack T. Small bowel perforation due to protruding spiral tackers: a rare complication in laparoscopic incisional hernia repair. Surg Endosc 2004;18: 1001.
- 17. Goh PM, Kum CK, Toh EH. Endoscopic patch closure of malignant esophagotracheal fistula using Histoacryl glue. Surg Endosc 1994; 8:1434-1435.
- 18. Feretis C, Dimopoulos C, Benakis P, Kalliakmanis B, Apostolidis N. N-butyl-2-cyanoacrylate (Histoacryl) plus sclerotherapy versus sclerotherapy alone in the treatment of bleeding esophageal varices: a randomized prospective study. Endoscopy 1995; 27:355-357.
- 19. Esposito C, Damiano R, Settimi A, De Marco M, Maglio P, Centonze A. Experience with the use of tissue adhesives in pediatric endoscopic surgery. Surg Endosc 2004; 18:290-292.

 Amid PK, Shulman AG, Lichtenstein IL, Hakakha M. Biomaterials for abdominal wall hernia surgery and principles of their applications. Langenbecks Arch Chir 1994; 379:168-171.

Received: May 29, 2007 / Accepted: March 11, 2008

Address for correspondence:
Roland Ladurner, MD
Department of Surgery Innenstadt
Ludwig-Maximilians-University (LMU)
Nussbaumstrasse 20
80336 München
Germany

Tel: +49-89-5160-2642 Fax: +49-89-5160-2578

E-mail: Roland.Ladurner@med.uni-muenchen.de