Eur Radiol (2011) 21:1956–1961
DOI 10.1007/s00330-011-2131-5

INTERVENTIONAL

Biodegradable polydioxanone stents: a new option for therapy-resistant anastomotic strictures of the colon

Václav Janík · Ladislav Horák · Jan Hnaníček · Jiří Málek · Hans-Ulrich Laasch

Received: 23 August 2010 / Revised: 7 March 2011 / Accepted: 10 March 2011 / Published online: 30 April 2011

Abstract
Objectives To assess the outcome of self-expandable, biodegradable stent insertion for anastomotic strictures following treatment for rectosigmoid carcinoma.
Methods Three male patients (median age 66) developed benign strictures after radiotherapy and resection of a recto-sigmoid carcinoma. These were resistant to balloon dilatation and prevented stoma reversal. Biodegradable stent insertion was performed as an experimental treatment on a named-patient basis with approval of the institutional review board. Patients had monthly follow-up with endoscopy and contrast medium enemas to monitor performance and degradation of the stents.
Results All stents were placed successfully without complications after pre-dilatation to 20 mm under fluoroscopic guidance. Stent degradation occurred in all patients 4–5 months following implantation, and long-term anastomotic patency was demonstrated in all. This allowed reversal of the colostomy and physiological defecation in two patients. Reversal was not undertaken in one due to subsequent development of liver metastases. No stent migration or occlusion occurred.
Conclusions Biodegradable stents can maintain an adequate lumen across anastomotic strictures resistant to balloon dilatation. They seem to allow stricture re-modelling resulting in maintained dilatation after degradation. This potentially allows reversal of a colostomy, which might otherwise be prevented by stricture recurrence.

Keywords Abnormalities · Radiation-induced · Absorbable implants · Anastomosis · Surgical · Balloon dilatation · Colo-rectal neoplasms

V. Janík
Department of Radiodiagnostics, 3rd Medical Faculty, Charles University, Prague, Czech Republic

L. Horák
Department of General Surgery, 3rd Medical Faculty, Charles University, Prague, Czech Republic

J. Hnaníček
2nd Department of Internal Medicine, 3rd Medical Faculty, Charles University, Prague, Czech Republic

J. Málek
Department of Anaesthesiology and Resuscitation, 3rd Medical Faculty, Charles University, Prague, Czech Republic

H.-U. Laasch (✉)
Department of Radiology, The Christie NHS Foundation Trust, Manchester M20 4BX, UK
e-mail: HUL@christie.nhs.uk

Introduction

Post-treatment strictures following resection of rectosigmoid carcinoma are rare, occurring in 1.5–4% of patients [1, 2]. They may be caused by inflammation following small anastomotic leaks or concomitant radiotherapy and usually prevent reversal of a defunctioning colostomy. Surgical treatment of these strictures by further laparotomy is technically difficult due to the post-surgical fibrosis, but a variety of transanal approaches have been described [3–6]. Accepted alternatives include thermal ablation such as laser and argon plasma coagulation, balloon dilatation or insertion of self-expanding metal stents (SEMS). Thermal

methods are only successful in short strictures less than 1 cm [7]. Balloon dilatation has a high recurrence rate and a significant risk of perforation [8]. Permanent insertion of SEMS is associated with a high rate of complications [9–11] including new stricture formation and perforation. In addition uncovered stents frequently occlude through mucosal hyperplasia, whereas covered stents have a high rate of spontaneous displacement.

The long-term success rate of the above techniques is very variable, and they often do not allow colostomy reversal.

Self-expanding biodegradable (BD) stents, originally developed for the treatment of benign oesophageal strictures, offer a new treatment option for benign strictures of the large bowel [12]. Biodegradable stents are manufactured from synthetic polymers—polyesters like polylactides, polyglycolides and polydioxanone [13, 14]. Many of these are well-established materials for suture materials and surgical prostheses. The degradation rate of biodegradable stents depends on the fibre diameter, structure of the stent mesh, the material used, temperature, pH and type of tissue in which the stent is implanted [15]. The polymers are often degraded by hydrolysis which attacks firstly the amorphous and crystalline structure of individual stent filaments [16]. Degradation products are metabolised by a series of enzymatic reactions of the Krebs cycle [12]. Degradation half-time of biodegradable fibres/bio-absorbable sutures varies within different environments in the human body [17] although degradation of polydioxanone stents in vivo seems more consistent, taking 3–4 months [18–20]. Potential complications are similar to those of metal stent insertion, and include perforation, stent migration, occlusion by mucosal hyperplasia, haemorrhage and faecal impaction.

This study aimed to assess whether BD stents can be safely used to achieve long-term patency in therapy resistant anastomotic strictures of the colon allowing stoma reversal. At present BD stents are not licensed for the colon and need to be used on a named-patient/off-label basis with agreement of the institutional review boards.

Materials and methods

Between February and December 2008 biodegradable stents were placed in 3 male patients. Long-course radiotherapy with 45 Gy had been administered 5 weeks before surgery in all; no adjuvant chemotherapy had been given. Conventional surgery had been performed by a board-certified specialist colo-rectal surgeon of 37 years' experience. The patients developed therapy-resistant anastomotic strictures that prevented reversal of the defunctioning colostomies.

Patient 1

A 64-year-old patient developed an anastomotic leak after low anterior resection of a T3N0M0 rectal carcinoma. This was managed by a defunctioning transverse colostomy six days after the original surgery. The leak had healed 5 months later but a 45mm long anastomotic stricture with a diameter of 4 mm had developed, preventing stoma reversal. A total of six separate balloon dilatations only resulted in stricture recurrence, and an 8 cm long Ella-BD stent was placed.

Patient 2

A 66-year-old patient with a T3N0M0 rectal carcinoma had an initially uncomplicated low anterior resection, but over several months developed a 3 mm wide, 30 mm long stricture of the anastomosis associated with a persisting sinus. A defunctioning stoma was created 7 months after the original surgery. After five separate dilatations a lumen of approximately 20 mm was achieved. A 6 cm Ella-BD stent was inserted to prevent stricture recurrence.

Patient 3

A 66-year-old man developed anastomotic insufficiency resulting in a small pelvic abscess following resection of a T3N1M0 rectal carcinoma. A transverse colostomy was created on day 8. A year later the abscess had resolved, but a 2 mm wide, 30 mm long anastomotic stricture had developed. After 3 attempts at balloon dilatation an 8 cm BD stent was inserted.

Patients were selected for biodegradable stent insertion on the basis of assumed cure but continued need for repeated dilatation. It was hoped to achieve long-term patency allowing stoma reversal.

Before biodegradable stent insertion, tumour recurrence was excluded, the function of the anal sphincter complex verified and the patients re-staged with CT. All patients had multiple previous balloon dilatations that did not result in long-term patency.

Indications for BD stent implantation and follow-up were discussed during multidisciplinary team meetings. All patients were informed about the limitations and risks of the procedures and gave written consent. All procedures were approved by the ethics committees of the Teaching Hospital Královské Vinohrady and the 3rd Medical Faculty of the Charles University, Prague.

The procedures were performed under sedo-analgesia using a combination of clonidine, midazolam and ketamine. Stents were placed under fluoroscopic control with patients lying supine or on their left side. After the stricture was outlined by injection of a water-soluble contrast agent

(Scanlux 300, Sanochemia Pharmazeutika AG, Vienna, Austria) a 0.035" stiff guidewire (Amplatz, COOK, Bloomington, IN, USA) was placed into the descending colon and the stricture further assessed by gentle hand inflation of a 30 mm dilatation balloon (Largeglide, Teutonia Technology AG, Karlsruhe, Germany). Where a minimum lumen of 20 mm was not present, dilatation was performed to that diameter.

The stents used were Ella-BD oesophageal stents (ELLA-CS, Hradec Kralove, Czech Republic), with a trunk diameter of 25 mm, flaring to 31 mm at both stent ends (Fig. 1). The stents are uncovered and woven from a polydioxanone monofilament analogous to conventional enteral stents. Smaller diameters and lengths between 60 and 135 mm have now become available. The long-term elasticity is not as good as with metal stents and in order to avoid loss of radial force they are supplied unconstrained in a separate container. The stents are loaded manually prior to placement into a standard 28Fr. delivery system for metal oesophageal stents (Ella-HV) of the same manufacturer. The delivery system has a usable length of 75 cm, which allows placement up to the distal descending colon. The stents are radiolucent and not visualised on conventional fluoroscopy. Three radiopaque markers are attached at each stent end with a further marker in the middle of the stent. Release is by withdrawal of the constraining sheath.

The stents were positioned centred on the middle of the strictures ensuring that the radiopaque markers on both ends exceeded the margins of the stricture by at least 2 cm to allow for stent shortening on deployment. If the stent did not expand sufficiently after release, dilatation was performed to a minimum diameter of 20 mm. The day after the implantation both sigmoidoscopy and a water-soluble contrast medium enema was performed to evaluate the position and patency of the stent. If satisfactory, the patient was discharged. Endoscopy as well as contrast enema was repeated at one-month intervals to monitor stent position, patency and degradation and exclude tumour recurrence with repeated biopsies. Particular attention was paid to stent performance, notably maintained stent expansion, stent migration, stent occlusion and possible bowel perforation.

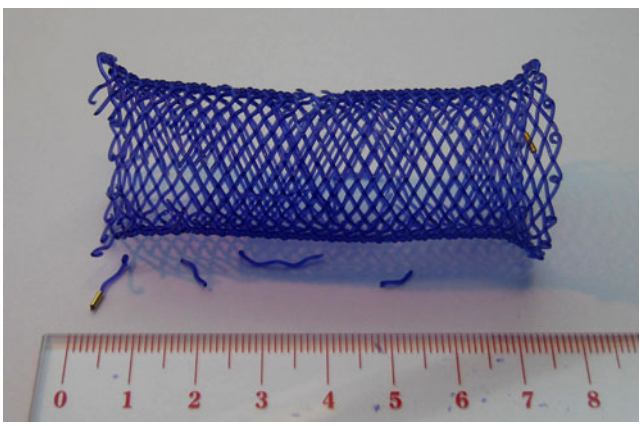

Fig. 1 Ella-BD oesophageal stent showing signs of degradation after 18 months' exposure to room air

Results

Insertion of the radio-lucent stents was easily performed under fluoroscopic guidance—no complications occurred. Endoscopy showed the degradation process to result in a change in stent colour from the original blue to off-white. In addition a mild hyperplastic mucosal reaction was observed around the stent mesh, but this did not compromise the lumen (Fig. 2) and regressed spontaneously after stent degradation in all patients.

Monthly follow-up with endoscopy and contrast medium enema showed complete stent degradation after 4 months in all patients (Fig. 3, 4 and 5). Stoma reversal was performed 5 weeks later in patient one, 6 months later in patient 2. Both are asymptomatic, with normal bowel movements 8 and 4 months after stoma reversal. Despite a good radiological technical result with essentially complete expansion of the stent and stricture, stoma reversal was not performed in patient 3 because unresectable hepatic metastases had developed after stent insertion, and the patient was referred for palliative chemotherapy.

No complications occurred, specifically neither stricture recurrence nor perforation were observed. All stents showed maintained dilatation; none collapsed, displaced or occluded from mucosal hypertrophy. The potential for faecal impaction could not be assessed as patients had a defunctioning colostomy and stoma reversal was only performed after stent degradation.

Discussion

Biodegradable stents represent a new therapeutic option for benign strictures of the gastrointestinal tract. First experience with poly-L-lactate biodegradable stents for treatment of benign oesophageal strictures was reported in 1997 [13]. First enteral placement was performed in patients with Crohn's disease using polydioxanone stents in 2009 [12].

Compared with balloon dilatation the expansion process is slower and more protracted, potentially resulting in reduced trauma and re-fibrosis of the stricture. More importantly the maintained dilatation preserves the lumen over 3–5 months [12–16], potentially allowing remodelling of the stricture around the stent and increasing long-term patency, as seen in our patients.

All our patients received a polydioxanone BD stent, originally designed for oesophageal strictures, where its

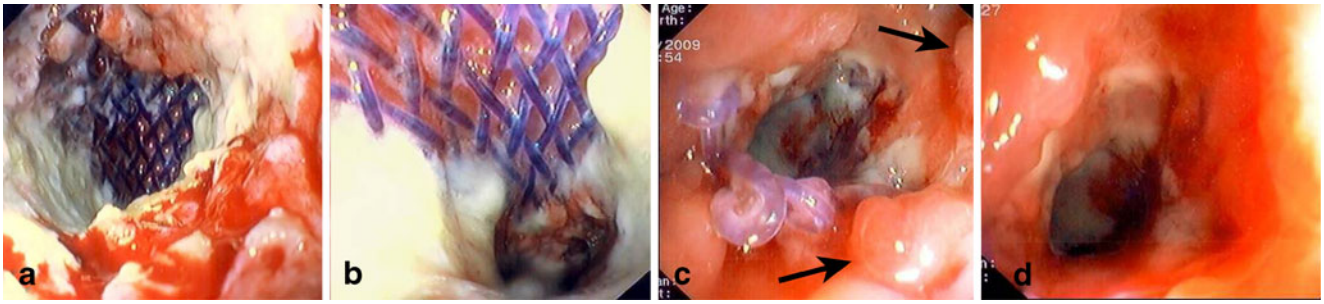

Fig. 2 Endoscopic appearance. **a** The stent has a deep blue colour immediately after implantation. **b** After 1 month the stent fibres are expanded and of a lighter blue. **c** 4 months after implantation the stent material has a translucent appearance and partial fragmentation can be seen. Mild nodular mucosal hyperplasia is present around the stent end (arrows). **d** 5 months after the implantation the stent has disappeared, the anastomosis remains patent

properties have been confirmed in benign as well as malignant disease [19]. The largest stent version was used with a trunk diameter of 25 mm, flaring to 31 mm, which is larger than most metal colonic stents. No persistent pain and no migration were observed suggesting appropriate sizing. The BD stents are radiolucent, demarcated on fluoroscopy only by gold markers. As with woven metal stents, significant stent shortening occurs from both ends on deployment, as the constrained length in the delivery system is almost twice the nominal length (a table of stent shortening is enclosed in the manufacturer's "Instructions for Use"). Operators need to be aware of these characteristics as they are disconcerting if not anticipated.

Ella-BD stents are slightly weaker and have a lower long-term elasticity than Nitinol stents and are supplied separate from the delivery system. The strictures in our patients occurred in bowel submitted to radiotherapy and had been resistant to repeated balloon dilatation. Because of this pre-dilatation was performed to 20 mm to ensure adequate stent expansion, however, more experience in this context is require to establish whether this is necessary; radial force seems to be sufficient to ensure stent expansion in non-surgical strictures of the oesophagus without pre-dilatation.

Potential complications of biodegradable stent insertion include perforation, stent migration, faecal impaction and further stenosis from mucosal hyperplasia.

Perforation is usually a complication of balloon dilatation and this should be performed with care and to a lesser diameter than that of the stent trunk. In the oesophagus further expansion of strictures by the radial force of the stent alone has been observed and pre-dilatation may only be required if the delivery system cannot be passed.

Migration of uncovered stents is less frequent than that of covered stents, but this is increased if pre-dilatation obliterates the stricture fixing the stent. Stents may be displaced by hard faeces and patients who do not have a diverting stoma should be given regular stool softening laxatives as well as taking plenty of fluid orally. Patients with a stoma are at lower risk of experiencing stent migration, but the passage of stools may well contribute to long-term patency. However in our first two patients the

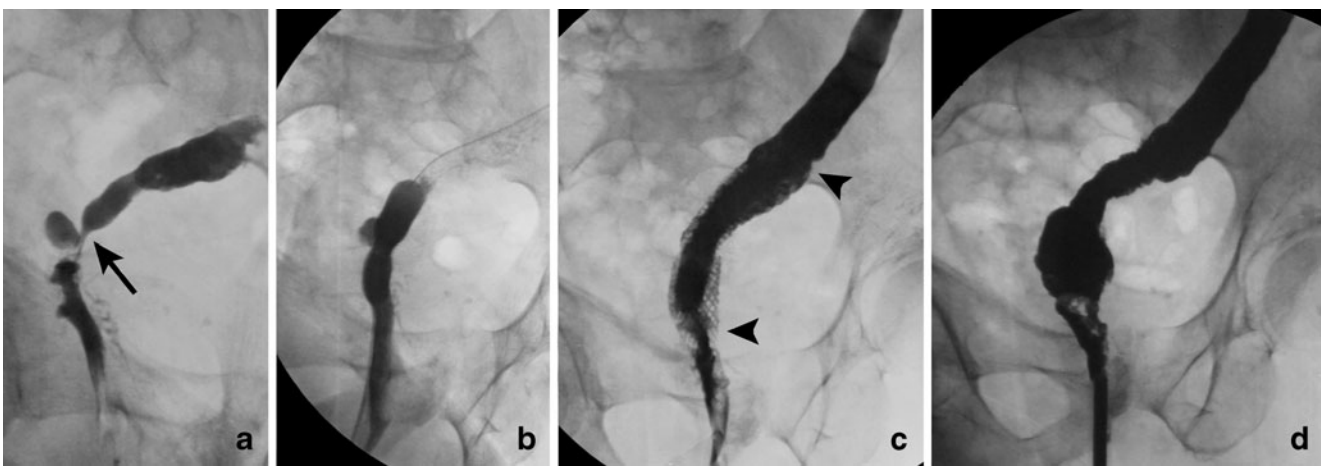

Fig. 3 Patient 1. **a** Contrast medium enema demonstrates a tight stricture of the rectal anastomosis (arrow). **b** Balloon dilatation, note the waist on the balloon identifying the stricture. **c** Appearances immediately after stent insertion, the stent (arrowheads) is radiolucent, but "stained" by contrast medium. **d** Fluoroscopic image before stoma reversal: The stent has disappeared and the anastomosis is patent

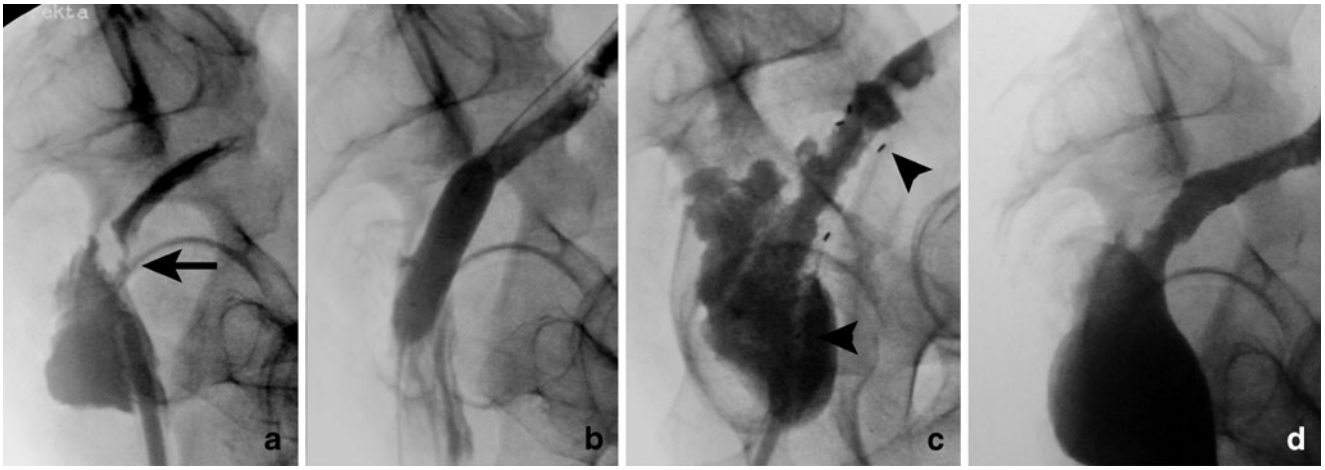

Fig. 4 Patient 2. **a** Tight anastomotic stricture (arrow). **b** Balloon dilatation before stent insertion. **c** Deployed stent with radiopaque markers (arrowheads) showing full immediate expansion. **d** Patent anastomosis after 5 months; the stent has dissolved

stoma was only reversed after stricture recurrence had been excluded by long-term follow-up. In the third patient it was prohibited by the development of metastases after stent insertion, not by failure of stricture dilatation.

Mucosal hyperplasia resulting in re-obstruction after oesophageal BD stenting has been described [20, 21], both cases responded well to a single balloon dilatation and resolved completely after stent dissolution. Both reports are fairly critical of BD stents on the basis of the mucosal reaction; however the treatment resulted in long-term patency of strictures that had failed to respond to conventional therapy. In our cases endoscopic follow-up showed only a mild hyperplastic reaction, which resolved after stent degradation, suggesting this to be a reversible result of chronic irritation.

Biodegradable stents are more expensive that metal stents and fluoroscopic insertion is approximately twice as expensive as balloon dilatation. However with a short term patency of 4 months until stent degradation and the increased likelihood of long-term success it makes economic sense to consider BD stent insertion if strictures recur within 4–6 months after dilatation. In addition there are the reduced risk of perforation and the improved quality of life for the patient. Compared to metal stents BD stents do not require a removal procedure within 4–6 weeks with the associated cost and potential for complications. In addition there is a longer dwell time of the BD stent giving a longer initial symptom-free interval as well as the increased potential for stricture remodelling and long-term success.

The limitations of this study are the small number of patients and the relatively short follow-up period of less than one year. However the positive results justify exploring this treatment strategy on a larger scale.

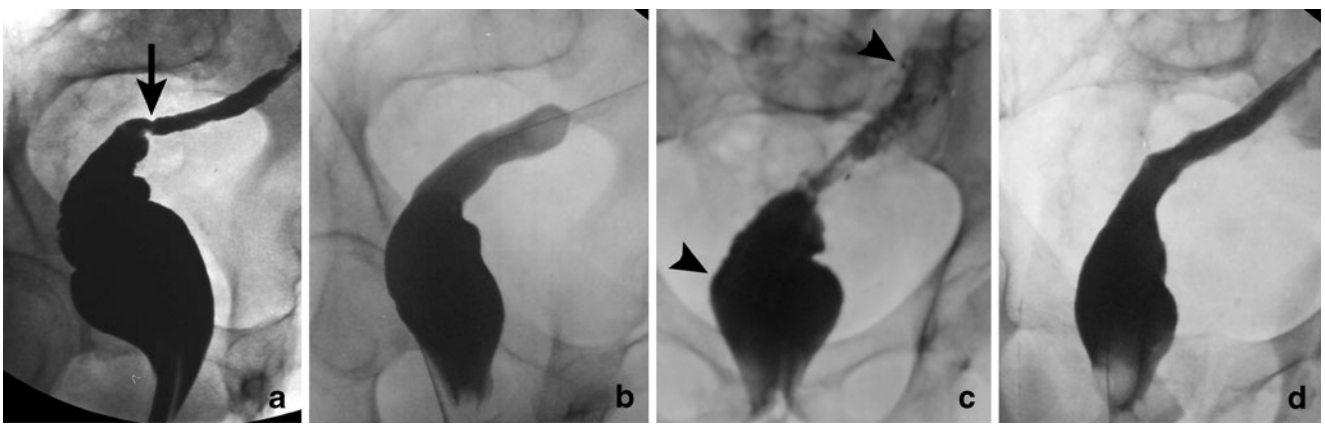

Fig. 5 Patient 3. **a** A short, annular stricture is present in the upper rectum (arrow); note the small calibre of the defunctioned proximal colon. **b** Balloon dilatation before stent insertion. **c** Partly disintegrated BD stent (arrowheads) 3 months after implantation. **d** Fully degraded stent and patent anastomosis 5 months after stent placement

Conclusion

Initial experience suggests that biodegradable stents indeed present a new treatment option for anastomotic strictures following colonic surgery. Long-term patency may be better than after balloon dilatation, allowing stoma reversal and restoration of physiological defecation.

Acknowledgement H.-U. Laasch has acted as a technical consultant for Ella-CS.

References

1. Sciume C, Geraci G, Pisello F, Arnone E, Romeo M, Modica G (2008) Mechanical versus manual anastomoses in colorectal surgery. Personal experience G Chir 29:505–510
2. Lustosa SA, Matos D, Atallah AN, Castro AA (2001) Stapled versus handsewn methods for colorectal anastomosis surgery. Cochrane Database Syst Rev:CD003144
3. Ovnat A, Peiser J, Avinoah E, Charuzi I (1989) A new approach to rectal anastomotic stricture. Dis Colon Rectum 32:351–353
4. Hagiwara A, Sakakura C, Shirasu M, Torii T, Hirata Y, Yamagishi H (1999) Sigmoidofiberscopic incision plus balloon dilatation for anastomotic cicatricial stricture after anterior resection of the rectum. World J Surg 23:717–720
5. Chew SS, King DW (2002) Use of endoscopic titanium stapler in rectal anastomotic stricture. Dis Colon Rectum 45:283–285
6. Mukai M, Kishima K, Iizuka S et al (2009) Endoscopic hook knife cutting before balloon dilatation of a severe anastomotic stricture after rectal cancer resection. Endoscopy 41(Suppl 2):E193–E194
7. Sebastian S, Johnston S, Geoghegan T, Torreggiani W, Buckley M (2004) Pooled analysis of the efficacy and safety of self-expanding metal stenting in malignant colorectal obstruction. Am J Gastroenterol 99:2051–2057
8. Fregonese D, Di Falco G, Di Toma F (1990) Balloon dilatation of anastomotic intestinal stenoses: long-term results. Endoscopy 22:249–253
9. Geiger TM, Miedema BW, Tsereteli Z, Sporn E, Thaler K (2008) Stent placement for benign colonic stenosis: case report, review of the literature, and animal pilot data. Int J Colorectal Dis 23:1007–1012
10. Small AJ, Young-Fadok TM, Baron TH (2008) Expandable metal stent placement for benign colorectal obstruction: outcomes for 23 cases. Surg Endosc 22:454–462
11. Bonin EA, Baron TH (2010) Update on the indications and use of colonic stents. Curr Gastroenterol Rep 12:374–382
12. Rejchrt S, Kopacova M, Bartova J, Vacek Z, Bures J (2009) Intestinal biodegradable stents. Initial experience in the Czech Republic. Folia Gastroenterol Hepatol 7:2–5
13. Fry SW, Fleischer DE (1997) Management of a refractory benign esophageal stricture with a new biodegradable stent. Gastrointest Endosc 45:179–182
14. Saito Y, Tanaka T, Andoh A et al (2007) Usefulness of biodegradable stents constructed of poly-l-lactic acid monofilaments in patients with benign esophageal stenosis. World J Gastroenterol 13:3977–3980
15. Laukkarinen J, Nordback I, Mikkonen J, Karkkainen P, Sand J (2007) A novel biodegradable biliary stent in the endoscopic treatment of cystic-duct leakage after cholecystectomy. Gastrointest Endosc 65:1063–1068
16. Laukkarinen J, Lamsa T, Nordback I, Mikkonen J, Sand J (2008) A novel biodegradable pancreatic stent for human pancreatic applications: a preclinical safety study in a large animal model. Gastrointest Endosc 67:1106–1112
17. Freudenberg S, Rewerk S, Kaess M, Weiss C, Dorn-Beinecke A, Post S (2004) Biodegradation of absorbable sutures in body fluids and pH buffers. Eur Surg Res 36:376–385
18. Petrtyl J, Bruha R, Horak L, Zadorova Z, Dosedel J, Laasch HU (2010) Management of benign intrahepatic bile duct strictures: initial experience with polydioxanone biodegradable stents. Endoscopy 42(Suppl 2):E89–E90
19. Stivaros SM, Williams LR, Senger C, Wilbraham L, Laasch HU (2010) Woven polydioxanone biodegradable stents: a new treatment option for benign and malignant oesophageal strictures. Eur Radiol 20:1069–1072
20. Orive-Calzada A, Alvarez-Rubio M, Romero-Izquierdo S et al (2009) Severe epithelial hyperplasia as a complication of a novel biodegradable stent. Endoscopy 41(Suppl 2):E137–E138
21. Hair CS, Devonshire DA (2010) Severe hyperplastic tissue stenosis of a novel biodegradable esophageal stent and subsequent successful management with high-pressure balloon dilation. Endoscopy 42(Suppl 2):E132–E133