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A novel animal model of gastrointestinal obstruction for the development of stent

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ABSTRACT

Background: The need for newer gastrointestinal (GI) stents has been continuously raised. Newly developed stents are generally tested for physical properties *in vitro* and directly introduced to clinical practice because there is no reliable animal model of GI obstruction. The aim of this study was to establish an animal model both that can represent obstruction of the GI tract and be used to develop new stents.

Material and methods: Surgical obstruction of the descending colon by wrapping with a nonabsorbable synthetic mesh and rubber bands was made in 17 healthy mongrel dogs. Four days later, a covered self-expanding metallic stent was placed for the obstructed segment in each dog under fluoroscopic guidance. Patency and migration of the inserted stents were evaluated clinically on a daily basis and fluoroscopically on a weekly basis. After sacrifice of the dogs, the degree and extent of residual colonic obstruction were assessed fluoroscopically. The specimen of the colonic obstructed segment was examined microscopically.

Results: In all 17 mongrel dogs, segmental obstruction in the descending colon was successfully created and confirmed with fluoroscopic examination using a contrast medium. The percentage of luminal narrowing ranged from 99%–100%. Stent placement was technically successful in all 17 dogs. During the follow-up period, stent migration occurred in 12 dogs and indwelling time of a stent ranged from 0–95 d (mean 29.2 ± 38.8 d). On postmortem pathologic examination, it was found that fibrosis had newly formed outside the colonic longitudinal muscle layer in all dogs.

Conclusions: Our canine colonic obstruction model is the first animal model that can be feasible for developing a new design of stent and provide *in vivo* data on complications, particularly stent migration.

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1. Introduction

Malignant gastrointestinal (GI) tract obstruction is one of the common complications in patients with primary or metastatic malignancy of the abdomen and pelvis. Stent placement is established as an effective and safe palliative treatment or as an alternative to surgery [1–6]. Stent can be placed in corrosive stricture or benign anastomotic stenosis after surgery of esophagus, stomach, and colon as well [7–9].

Various kinds of metallic stents have been developed and they have both advantages and disadvantages [3,10–12]. Common complications include migration of stent, reocclusion, and perforation of GI tract, and the reported rates reached up to 30% [13–16]. Therefore, the need for newer stents has been continuously raised. In general, newly developed stents have been tested for physical properties *in vitro* and then directly introduced to clinical practice [17,18].

The aim of this study was to establish an animal model of GI obstruction that is suitable for evaluating performances and characteristics of a GI stent *in vivo*.

2. Methods

2.1. Animal model

Surgical obstruction of the descending colon was made in 17 healthy mongrel dogs weighing from 19–28.5 kg. The dogs were acclimated for 7 d before experiments. They were individually housed and maintained at an environmental temperature of 22°±°2°C and on a 12/12-h light–dark cycle. They were fed a canine diet (Purina Korea Co, Seoul, Korea) with water and *ad libitum*. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared and published by our institute.

After general anesthesia with mixture of tiletamine hydrochloride and zolazepam 1.5 mg/kg (Virbac, Carros, France), xylazine 2 mg/kg (Byer, Chempark Leverkusen, Germany), and gas anesthetic agents (2% isoflurane), the animals were positioned supine and draped in a sterile fashion. A segment of the descending colon was exposed after a lower midline incision. The colonic segment was wrapped with a nonabsorbable synthetic mesh (PROLENE Mesh, ETHICON, Inc, Somerville, NJ) with the length of the mesh ranging from 6.7–8.4 cm that depended on a diameter of the descending colon of each dog. After the mesh was wrapped around the colon, it was punched to make four holes of 0.5 cm in diameter with intervals of 1 cm at each end. We also made four corresponding holes in the mesentery with blunt dissection according to locations of the holes in a mesh. We passed four flat rubber bands (5 cm × 0.5 cm × 0.1 cm) through these holes in a mesh and the mesentery. The rubber band was tightened to induce the colonic lumen collapsed. We fixed rubber bands with contact adhesives instead of making a knot with suture material. Surgical suture material was used to put together the mesh and rubber band and to fix them to the colonic wall (Fig. 1). The abdomen was closed surgically after applying adhesion barrier (Sepra film; Genzyme Biosurgery, Cambridge, MA) to the operation site to reduce bowel adhesion. All animals tolerated the operation well. Cefovecin sodium was administered once after surgery and lactulose syrup daily.

This study was approved by the Institutional Animal Care and Use Committee, and all the procedures were conducted in accordance with the 'Guide for Care and Use of Laboratory Animals' published by the National Institutes of Health and the Ethical guidance of the International Association for the Study of Pain.

2.2. Lesion confirmation and stent placement

On the fourth day after laparotomy, under general anesthesia, fluoroscopic examination with contrast media was performed to confirm obstruction of the colon *via* anal route with a 5 Fr catheter. Self-expanding covered metallic stents (Bonastent, Standard Sci-Tech Inc, Seoul, Korea and Hanarostent, MI Tech Co Ltd, Seoul, Korea) were placed in the obstructed segments of the colon with fluoroscopy. The size of the self-expanding metallic stents was 18 mm in diameter and 10 cm in length for all dogs.

2.3. Follow-up

Stent patency and migration were evaluated clinically by assessing the dogs and fecal material on a daily basis and fluoroscopically on a weekly basis. Dogs were sacrificed at the time of stent migration or at the end of 12 wk, which was the

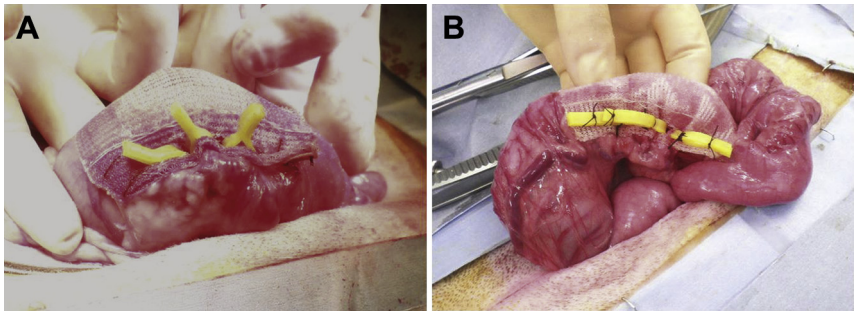

Fig. 1 – After wrapping the colon with a surgical mesh, rubber bands were passed through holes in the mesh and mesentery. Rubber bands were tightened and fixed with glue (A) and subsequently with surgical ties (B).