Embolic Effects of Transcatheter Mesenteric Arterial Embolization with Microspheres on the Small Bowel in a Dog Model

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ABSTRACT

Purpose: To determine the arterial distribution and ischemic effects of various particle sizes after transcatheter embolization of the small bowel in a dog model.

Materials and Methods: In 10 dogs, selective microsphere embolization was performed in six branches of the superior mesenteric artery. Microspheres were allocated into three size ranges (100–300 μm, 300–500 μm, and 500–700 μm) and four volume concentrations (0.625%, 1.25%, 2.5%, and 5%). For each size and volume concentration, embolization was performed of five branches at the origin of the last arcade. The distribution of microspheres and the range of ischemic changes of mucosa were evaluated histologically. Angiograms were categorized into two groups: group A, only the vasa recta nonopacified; group B, the last arcade or more proximal branches nonopacified.

Results: Microspheres sized 100–300 μm penetrated into intramural arteries and 500–700 μm microspheres mainly blocked arteries in the mesentery. There was a significant difference among three sizes in terms of the locations within the vasculature ($P < .0001$). The larger volume and the smaller size resulted in more ischemia. The range of ischemic changes among three sizes and among four volume concentrations was significantly different ($P = .004$ and $P < .0001$, respectively). The range of ischemic changes with 500–700 μm microspheres in group B was significantly greater than in group A (0% in group A vs 83% in group B, $P = .001$).

Conclusions: In a dog model, embolization of the small bowel limited to the vasa recta with the use if 500–700 μm microspheres reduced the range of ischemic changes.

ABBREVIATIONS

ANOVA = analysis of variance, LGI = lower gastrointestinal, NBCA = *N*-butyl cyanoacrylate

Lower gastrointestinal (LGI) arterial bleeding is defined as hemorrhage below the ligament of Treitz and includes jejunal, ileal, colonic, and rectal bleeding (1,2). LGI bleeding is often difficult to manage by endoscopic therapy, and therapeutic options in the event of endoscopic failure include surgery and transcatheter therapy (3). Microcoils have been the embolic agent of choice for LGI bleeding because they are highly visible under fluoroscopy (1,3–5). However, in clinical practice with current low-profile microcatheter technology, there are situations where the microcatheter cannot be advanced into the bleeding site of the vessel. In these cases, alternative embolic agents have to be considered, including particle and liquid agents.

Microspheres are calibrated spherical particles with diameters in the micrometer range (6–8). Because of their uniform, spherical shape and soft, smooth surface, they show a more distal distribution than nonspherical particles, and the occlusion level of the arteries can be predicted according to the particle size (9–11). Because

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the vascular resistance of a bleeding vessel is lower than that of a normal vessel, microspheres can move preferentially to the bleeding site with the blood flow (12), and the use of a small volume of microspheres with proper particle size might be enough to stop bleeding. Transcatheter arterial embolization with microspheres for LGI bleeding was reported in a retrospective clinical study (13). However, the distribution of microspheres to the normal intestine around the bleeding site is inescapable, and ischemic change can resulted. It is important to know what level of artery within the mesentery and intestine is occluded and the extent of ischemic damage caused by transcatheter arterial embolization with varying particle sizes. The purpose of this study was to determine the arterial distribution and ischemic effects of varying particle sizes after transcatheter arterial embolization of the small bowel in a dog model.

MATERIALS AND METHODS

Study Design

This study was approved by the animal care committee of our institution. Subjects for this experiment included 10 healthy male beagle dogs (weight, 10–15 kg). Selective embolization of six isolated target branches of the superior mesenteric artery was performed in each dog; 60 branches in all received embolization.

Embolic Materials

In this study, calibrated tris-acryl gelatin microspheres (Embospheres; Merit Medical Systems, South Jordan, Utah) of three size ranges (100–300 μm, 300–500 μm, and 500–700 μm) were investigated. Microspheres were prepared in 1-mL suspensions with volume concentrations of 0.625%, 1.25%, 2.5%, and 5%. All suspensions were obtained with the same iodine concentration (150 mgI/mL).

Preparation of Experimental Animals

Anesthesia was induced via subcutaneous injection of 50 μg/kg of atropine sulfate (Mitsubishi Tanabe Pharma Corporation, Osaka, Japan) and 6–8 mg/kg/h of propofol (Mylan, Inc, Tokyo, Japan) and was maintained with inhalation isoflurane (Intervet, Tokyo, Japan). The dogs were positioned supine, and their legs were tethered. The upper abdominal and right inguinal area was sterilized, and laparotomy was performed. All procedures were performed aseptically.

Selective Embolization

A 4-F short introducer sheath (Medikit Co, Ltd, Tokyo, Japan) was inserted into the right femoral artery by means of the Seldinger technique. The superior mesenteric artery was selected with a 4-F Cobra catheter (Cook Medical, Tokyo, Japan). A 1.9-F microcatheter (Carnelian PIXIE; Tokai Medical Products, Kasugai, Japan) was advanced into the origin of the last arcade of small intestines including ileum and jejunum using a 0.016-inch guide wire (Meister; Asahi Intecc, Aichi Co, Ltd, Japan). The injection of microspheres was performed slowly (< 0.5 mL/min) with fluoroscopic control using a 1.0-mL syringe. After injection of a predetermined size or quantity of microspheres, the microcatheter was purged with a volume of 3 mL of saline. For each size and volume concentration of microspheres, selective embolization of five separate arcades in the different dogs was performed. The microcatheter position was identified under direct vision, and the mesentery in the segment that received embolization was marked with string. As a rule, embolization of the neighboring two arcades was avoided.

Angiographic Evaluation

Digital subtraction angiograms were obtained before and 5 minutes after embolization for each segment by manual injection of contrast medium. To search whether the angiographic endpoint is useful for prediction of ischemic change of the small bowel, segments were divided into two groups on the basis of angiographic findings after embolization as follows: in group A, only the vasa recta nonopacified; in group B, the last arcade or more proximal branches nonopacified. The relationship between the range of ischemic changes and angiographic findings was analyzed.

Sacrifice and Histologic Evaluation

The dogs were killed with an intravenous injection of pentobarbital sodium 48 hours after transcatheter arterial embolization for investigation of ischemic changes in the small bowel. Necropsy was performed on each dog, and the small bowel was removed. The resected segments of the small bowel were fixed in a 10% neutral formaldehyde buffer for histologic evaluation. From each segment, two adjacent sections were taken from areas perceived to be the most discolored or abnormal. If there were no such changes, two sections were taken from the center of the segment that received embolization. The sections were stained with hematoxylin-eosin to identify microspheres in the vasculature and to investigate for damage to the small bowel. Histologic evaluation was performed by an experienced pathologist using microscopic examination. To evaluate the distribution of microspheres, locations were categorized into the mesenteric arteries apart from intestine, extramural arteries along the intestinal wall, and intramural arteries (**Fig 1**). The number of microspheres in each location was counted. To evaluate ischemic mucosal damage, the proportions of cross-sectional area with ischemic changes to the entire circumferential area were evaluated histologically with a percentage scale. Ischemic changes