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Original Article

# New polyglycolic acid fabric for the prevention of postoperative pancreatic fistulas

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**KEYWORDS**
distal pancreatectomy;
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scaffold

**Summary** *Background:* The incidence of postoperative pancreatic fistula (POPF) after distal pancreatectomy is approximately 30%. The most serious complications of pancreatic resection, such as mortality and prolonged hospitalization, are unresolved despite the proposal of various surgical procedures. We developed a new polyglycolic acid (PGA) fabric composed of fine diameter fibers to prevent POPF, and macroscopically and microscopically evaluated the effects of applying it to the pancreatic remnant.
*Methods:* The ventral pancreatic surface was cauterized to create the experimental model of POPF in 33 female Wistar/ST rats. The injured sites were wrapped with nonwoven PGA fabrics of different fiber diameters and porosities in the treated rats; one group of rats remained untreated. Survival, incidence of generalized peritonitis, and microscopic findings around the pancreas were investigated.
*Results:* The PGA fabrics acted as a scaffold for tissue repair and resulted in superior survival. Generalized peritonitis was milder in the PGA treated groups. With the new PGA fabric, abundant fibroblast infiltration and a uniformly-developed, self-organized barrier wall prevented both pancreatic leak and spread of inflammation.

Conflicts of interest: No author has any financial or personal relationship with people or organizations that could potentially and inappropriately influence our work and conclusions.

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*Conclusion:* Application of the newly developed PGA fabric to the pancreatic remnant prevented POPF, and the essential factor for preventing pancreatic leak was the early formation of a self-organized barrier.


## 1. Introduction

The most serious complications of pancreatic resection are postoperative pancreatic fistula (POPF), leak, and/or abscess.[1–3] The incidence of POPF is approximately 5% following pancreaticoduodenostomy and approximately 30% following distal pancreatectomy.[4,5]

With a pancreatic leak, pancreatic juice leaks out of the pancreatic ductal system via an abnormal connection into the peri-pancreatic space or the peritoneal cavity. The leaked pancreatic juice contains digestive enzymes such as pepsin and lipase that digest the abdominal organs and vessels, potentially resulting in generalized peritonitis, paralytic ileus, bleeding from the digested vessels, intraabdominal abscess, and/or multiorgan failure. Patients experience morbidity from abdominal pain, ileus, fever, possible abscess, sepsis, and hemorrhage, and subsequent prolonged hospitalization.

Localizing the pancreatic leak and suppressing pancreatic juice production are the key factors for preventing POPF. Surgical techniques used to manage the pancreatic remnant to reduce the rate of POPF after distal pancreatectomy include suture closure, the use of various stapling devices, a combination of staple closure and reinforcement with different materials, pancreatic enteric anastomosis, and the use of fibrin sealants; however, a superior technique has not been identified.[6–10] Furthermore, despite the availability of these surgical techniques, the morbidity associated with distal pancreatectomy remains high.[11] Several pharmacological and technical interventions have also been suggested to decrease the rate of POPF but the results have been controversial.[12–15]

Polyglycolic acid (PGA) is not enzymatically degraded, but is instead degraded by hydrolysis after 3–4 weeks. Nonwoven PGA fabric functions as a scaffold for tissue regeneration or repair. We developed a new scaffold composed of a nonwoven PGA fabric made of fine-diameter fibers. The present study aimed to evaluate this newly developed PGA fabric and a commercially available PGA fabric (NEOVEIL; Gunze Co., Kyoto, Japan) to determine their efficacy in localizing the inflammation, preventing POPF, and reducing the morbidity in a rat model of surgically injured pancreas.

## 2. Materials and methods

The animal experiments were approved by the Doshisha University Animal Experimentation Committee. All surgical and anesthetic procedures were performed in accordance with the animal care guidelines of Doshisha University and European Commission Directive 86/609/EEC for animal experiments.

Thirty-seven female, 8–10 week-old Wistar/ST rats weighing 200–220 g were used. Before the experimental period, the rats were housed in the laboratory for 1 week. During the experimental period, all rats were housed separately and maintained under standard specific pathogen-free conditions: light-dark cycle of 12:12 hours, mean temperature of 23°C, and mean humidity of 50%. Standard laboratory rodent chow and water were available *ad libitum*. On the experimental day, the health condition of the rats was checked, including evidence of diarrhea, mucous discharge from the eyes or anus, or emaciation and the condition of their body hair (hair loss or filthy hair).

The rats were divided into four groups at random: three treated groups (injured pancreatic remnant was wrapped with a sheet of each material) and one nontreated group. Survival and findings of the abdominal cavity were evaluated. Following the surgical procedure, the rats were housed under the same standard conditions for 5 days.

### 2.1. Preparation of materials

Two types of nonwoven PGA fabric sheets, with differing fiber diameters and porosity, and a copolymer [lactic acid/caprolactone; p(LA/CL)] sheet were prepared.

The first PGA fabric had a mean fiber diameter of 20 μm (PGA-L) (NEOVEIL) and was produced using the needle punch method.[15] The second PGA fabric had a mean fiber diameter of 0.9 μm (PGA-S) and was produced using the melt blowing method.[14] Briefly, the PGA polymer was extruded through dies with small nozzles, attenuated with heat and a high-velocity airstream, and spun into fibers. The fibers were then randomly deposited onto a collector to form a nonwoven fabric. The two types of nonwoven PGA fabric were cut into square sheets measuring 20 mm × 20 mm in size and weighing 50.0 mg. The square sheets were sterilized by soaking them in 99.5% ethanol for 60 seconds followed by two rinse cycles in saline just prior to surgery.

The 0.1-mm thick p(LA/CL) sheet was produced by melt pressing at 15 MPa and 110°C for 5 minutes followed by quenching in ice water. To remove the water, the sheet was dried under a vacuum at room temperature for 1 day.

### 2.2. Surgical procedure for pancreatic injury

All procedures were performed under sterile conditions by specific surgeons responsible for the assigned procedure. The rats were administered isoflurane (Escain; Mairan Seiyaku, Inc., Osaka, Japan) via inhalation for anesthesia. They were also administered 6.48 mg of sodium pentobarbital (Somnopentyl; Kyoritsu Seiyaku, Inc., Tokyo, Japan) via an intraperitoneal injection.

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