In Vivo Study of Polyurethane-Coated Gianturco-Rosch Biliary Z-Stents

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Abstract

Purpose: Prototypes of Gianturco-Rosch Z-stents coated with polycarbonate urethane (PCU) were placed in the biliary tree of pigs, in order to test their biomechanical behavior, stability, and biocompatibility.

Methods: The stents were surgically implanted in the common bile duct of three pairs of pigs, which were killed after 1, 3, and 6 months respectively. Explanted livers from pigs of the same race, age, and size were used to provide comparative data. The bile ducts were radiologically and histopathologically examined; the stents were processed and examined by scanning electron microscopy.

Results: No complications occurred and the animals showed a normal weight gain. The main bile duct appeared radiologically and macroscopically dilated, but the stents proved to be in place. Histologically, the bile duct epithelium was destroyed, but neither hyperplastic nor inflammatory fibrotic reactions of the wall were evident. Both the metallic structure and the polymeric coating of the stents were intact. A layer of organic material with a maximum thickness of approximately 3 μm was evident on the inner surface of the stents.

Conclusion: The present in vivo study demonstrates the biocompatibility, efficacy, and stability of PCU-coated Gianturco-Rosch stents in the biliary environment.

Key words: Bile drainage—Biliary prostheses—Metallic stents

Interventional procedures for the recanalization of segments of the digestive tract and bile ducts have recently found wide clinical application. The ideal prosthesis must be completely biocompatible and stable within the biologic environment and must have a diameter similar to that of the stented segment, though being small enough to be easily inserted. Self-expanding metallic stents best meet these requirements [1] but they have two main limitations: their mesh structure is not suitable for stenting segments with fistulas and they are subject to ingrowth of tumor or reactive tissue from the stented wall [2, 3]. In order to overcome these limitations, different synthetic plastic coatings have been proposed, some of which have already been clinically tested with good results in vascular grafts [4], while others tested in esophageal [5] and biliary [6–8] obstructions have shown some drawbacks.

In 1993 the authors perfected a technique (Italian patent no. 1276342, USA patent no. 5779729, European patent no. 0627226) for coating self-expanding Gianturco-Rosch biliary Z-stents with polycarbonate urethane (PCU) [8]. This technique gives the stent wall a smooth inner surface, leaving the coated metallic structure of the prosthesis in relief on the outer surface. The coated stents were submitted to different tests which demonstrated that their mechanical and physical characteristics are suitable for the recanalization of stenotic biliary tracts.
This paper reports the results of an in vivo experimental study conducted at the Istituto Nazionale Tumori of Milan with prototypes of these prostheses.

Materials and Methods

Gianturco-Rosch prostheses coated with PCU (Corethane 50A, Corvita, Miami, FL, USA) as previously reported [9] were implanted in the main bile duct of six Landrace pigs. The aim was to verify their biomechanical behavior, structural stability, and biocompatibility in the biliary environment. Moreover we wished to verify any possible displacement of the device from the common bile duct.

In accordance with the ethical rule of using the lowest number of animals possible, the study involved the use of three pairs of animals to be killed at 1, 3, and 6 months respectively from implantation of the stent. In the event of contradictory or inconclusive findings among this group of pigs the protocol provided for another three animals to be stented. The institutional guidelines for the care and use of laboratory animals were followed throughout the study.

Each animal weighed 35 kg. After premedication with xylazine hydrochloride 10 mg/kg and atropine sulphate 0.04 mg/kg, the animal was transferred to the operating table and general anesthesia was induced with a mixture of oxygen, nitrous oxide, and halothane, initially through a mask and then through an endotracheal tube. Electrolyte solutions (Ringer’s lactate) and antibiotics (piperacillin, 1 g) were given intravenously. Laparotomy and duodenotomy were performed using standard sterile technique. The common bile duct was cannulated through the ampulla of Vater with an 11 Fr (3.7 mm) peel-away sheath containing the coated stent. Under direct visual control and by means of a pusher, the stent was inserted into the extrahepatic bile duct, below the confluence with the cystic duct. The stents had an expanded diameter of 8 mm and a body length of 15 mm. The 8 mm diameter was chosen so that the stents would fit closely inside the common bile duct, which had a normal caliber of 4–5 mm before treatment. Five double and one single body stents were used. The shortest stent was implanted in an animal with a low cystic confluence, to avoid occlusion of the cystic duct. The biliary wall was not taped around the stents, both to verify their topographic stability and to avoid any tissue damage that could be confused with that caused by the stent itself.

Following this procedure the pairs of animals were kept under observation for 1, 3, and 6 months. Then they were killed under general anesthesia and the liver, duodenum, and pancreas were removed en bloc. Before removing the stent, cholangiography was performed through the ampulla of Vater. The anatomic specimen was macroscopically studied at our Department of Pathology, where the stent was removed and the specimen fixed with 10% formalin for 24 hr; the histologic preparations were stained with hematoxylin–eosin.

The anatomic and radiologic patterns of bile ducts of livers explanted from four pairs of Landrace pigs were used for comparison. Since it was impossible, because of logistic difficulties, to perform intraoperative cholangiography, livers from the first pair of animals, of the same age and size as the stented pigs at the time of operation, gave us the basal caliber of the main bile duct, which was 4–5 mm before and 6–7 mm immediately after implantation of a stent. Livers from the other three pairs of animals, matched for age and size with the stented pigs at the time of autopsy, gave us the reference caliber of the main bile duct without the stent, for each period of observation.

Samples of each removed stent were analyzed at the Laboratory of Scanning Electron Microscopy (SEM) of the Silk Experimental Station, where they were submitted to two different chemical treatments: one to study the organic deposit on their surface [10], the other to check the condition of the polymeric coating [11]. In the first treatment the samples were fixed with 2.5% glutaraldehyde solution in 0.1 cacodylate buffer (pH 7.2), dehydrated through a graded series of ethanol (up to 100%) and critical point-dried using carbon dioxide. The purpose of this treatment was to instantly block all molecular and macromolecular components of the organic deposits and thus prevent autolysis and putrefaction. Coagulation and stabilization of the structural and soluble proteins were necessary to prevent the occurrence of artifacts during the subsequent phases of dehydration and exposure to the electronic beam. This “freezing” of organic deposits allows a correct assessment at SEM of the layers of proteins, bacteria, and host cells that had adhered while the stent was in place. The second treatment, enzymatic digestion, was performed by leaving the sample in 2.5% trypsin, in a phosphate buffer at 37°C for 3 days and then in sodium dodecyl sulphate (SDS) at 50°C for 7 days. After repeated rinses in distilled water the specimen was left to dry. The aim of this treatment was to eliminate organic deposits from the device surface, thus permitting observation and assessment of the morphology of the polymeric coating.

All specimens were mounted on albumin stubs, sputter-coated with gold and examined with a Leica-Cambridge Stereoscan 440 microscope at 3–7 kV acceleration voltage.

Results

Insertion of the stent into the biliary tree was accomplished easily in all pigs and the bile flowed normally into the duodenum through the papilla once the introducer was removed. The postoperative period and follow-up were uneventful. All animals showed a normal weight gain. At re-laparotomy no evidence of inflammatory reaction was observed in the hepatoduodenal ligament; the liver and pancreas appeared normal. The stent proved to be in place at inspection. The main bile duct showed a mean caliber ranging from 8 to 16 mm, depending largely on the duration of stenting, while the bile duct caliber of the largest animal (100 kg at 9 months of age) in the control group was less than 5 mm (Fig. 1). At histologic examination the bile duct wall showed absence of epithelium for lengths that were variable but always exceeded the stent length, without any hyperplastic epithelial reaction. The submucosa was normal after 1 month, with no inflammation or granulomatous reaction, but after 3 and 6 months signs of fibrosis were present (Fig. 2).

The stents were macroscopically intact, in both their metallic structure and polymeric coating, with completely open lumens. All stents maintained their original diameter. The SEM investigation of samples showed a deposit of amorphous organic material on the polymeric film, probably of protein origin, and precipitates of biliary salts (Figs. 3, 4). The deposit grew progressively thicker the longer the stent was in place. At the end of the first month small bacterial