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ORIGINAL RESEARCH

Single-Stitch Telescopic Bilioenterostomy in an Animal Model

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ABSTRACT

Background/Aims: An end-to-side biliodigestive anastomosis is the most common procedure performed in hepato-pancreato-biliary surgery, and this procedure may become technically demanding. A telescopic ureterovesical anastomosis is frequently used in transplant surgery. The aim of this study was to investigate the feasibility of constructing a telescopic biliodigestive anastomosis. *Methodology:* The technique-standardization ($n = 8$) and main study ($n = 3$) groups were formed from 11 pigs. A single-stitch telescopic anastomosis with a self-disposable internal stent was performed in the main study group. The animals were sacrificed at the end of the 4-week follow-up period, and cholangiograms and tissue samples were obtained. Repeated biological, hematological, and biochemical data were recorded. *Results:* No bilomas or functional biliary strictures were identified in any of the main study group animals. Light microscopy revealed intestinal metaplasia of the biliary epithelium in the portion of the bile duct telescoped inside the intestinal lumen. *Conclusions:* Telescopic bilioenterostomy with a single pull-through stitch and a self-disposable stent is quick and reproducible in animal models, and it appears to be free of complications. Further experiments with longer follow-up periods are required to confirm that this anastomotic technique does not lead to episodes of delayed cholangitis or development of adenocarcinoma.

Keywords: liver; biliary tree; hepaticojejunostomy; hepaticoduodenostomy; biliodigestive anastomosis; technique

INTRODUCTION

An end-to-side biliodigestive anastomosis is the most common procedure performed in hepato-pancreato-biliary surgery. It is used to re-establish continuity after bile duct (BD) resections [1], in bypassing or reconstructing the BD [2] and in liver transplantation [3, 4]. This procedure may become technically demanding when the BD caliber is small [5] or when it is constructed via laparoscopy [6].

Simplifying end-to-side biliodigestive anastomosis has been the focus of previous laboratory and clinical studies from as early as 1892 [7]. The aim of these previous studies was to limit suture use. Some have used stents with direct external connections, which may increase patient discomfort and the risk of complications [8, 9]. Other studies have used biodegradable stents placed with special applicators, which may increase the complexity and cost of the procedure [10–12].

For many years, a single-stitch telescopic ureterovesical anastomosis (the Taguchi technique) has been used in renal transplantation, with or without a disposable stent [13–15].

The aim of the present study was to investigate the construction feasibility, effectiveness, and safety of the single-stitch telescopic biliodigestive anastomosis with or without a disposable internal stent in an animal model.

METHODOLOGY

A total of 11 Landrace female pigs with a median weight of 27 kg (range 25 – 30 kg) were used. The

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Ethics Committee and Veterinary Authority of East Attica approved the study protocol in accordance with the 86/609 guidelines and act PD 160/May 1991 (21 April, 2010, reference number 389). The animals were fasted for one day before all of the procedures. Premedication was administered 10 min prior to intubation and consisted of intramuscular 0.5 mg/kg midazolam (Dormicum, Roche, Grenzach, Germany), 15 mg/kg ketamine hydrochloride (Narketan, Vetoquinol, Ittigen, Switzerland) and 0.045 mg/kg atropine (Atropine, Demo, Athens, Greece). Anesthesia was induced with intravenous 3 mg/kg propofol (Propofol, Fresenius Kabi, Graz, Austria), 0.012 mg/kg fentanyl citrate (Fentanyl, Janssen Cilag, Beerse, Belgium) and 0.5 mg/kg cisatracurium besylate (Nimbex, GlaxoWellcome, Greenford, UK). Anesthesia was maintained by a cuffed endotracheal tube (0.4 FiO_2, 20 breaths/min) with 1,1,1,3,3,3-hexafluoro-2-(fluoromethoxy)propane (Sevoflurane, Baxter, Deerfield, IL, USA) and intravenous 8 mg/kg/h propofol (Propofol, Fresenius Kabi, Graz, Austria), 5 mg/kg/h fentanyl citrate (Fentanyl, Janssen Cilag, Beerse, Belgium) and 25 mg/kg/h cisatracurium besylate (Nimbex, GlaxoWellcome, Greenford, UK). Before awakening, the animals received intramuscular 0.1 mg/kg neostigmine (Neostigmine, Cooper, Athens, Greece) and 0.4 mg/kg metoclopramide (Primperan, Sanofi Aventis, Frankfurt, Germany). Asepsis was established by washing the skin with a 7.5% povidone iodine solution (Betadine Surgical Scrub, Lavipharm, Athens, Greece). The skin was then washed twice with a 10% povidone iodine solution (Betadine, Vianex, Athens, Greece). The animals received five days of intramuscular 20 mg/kg/12 h cefaclor (Ceclor, Lilly, Kinsale, Ireland) for antimicrobial prophylaxis. Pain was managed by 4 mg/kg/24 h carprofen (Rimadyl, Vericore, Dundee, UK) administered intramuscularly for the first three postoperative days (or longer if needed).

The first eight animals formed the technique-standardization group. The remaining three animals formed the main study group. A midline laparotomy was performed in all of the animals. The BD was doubly ligated, divided at the level of the duodenum and dissected free to the cystic duct confluence. The length of the mobilized BD was at least 4 cm. A 5-cm biliary stent (BS) was fashioned by trimming an 8 Fr (2.7 mm) feeding tube (Nelaton catheter, Medication Link, Hong Kong, China) with beveling at both ends. We then used needle-point electrocautery to construct a duodenotomy at the third portion of the duodenum. Four types of anastomosis were tested on the animals in the technique-standardization group (2 animals per type of anastomosis) (Figure 1). The first type of anastomosis (Figure 1a) was a modification of a purse-string hepaticojejunostomy, which was performed in accordance with Laukkarinen's method [10]. The BS was introduced 3 cm into the BD. A 4/0 polypropylene (Surgipro II, Covidien, Mansfield, MA, USA)

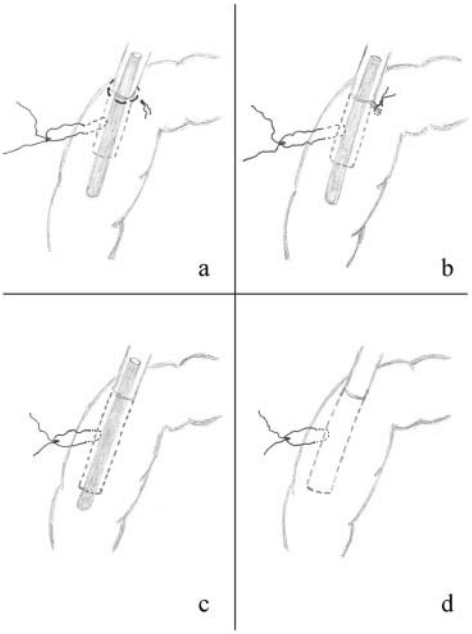

FIGURE 1 The different types of telescopic biliodigestive anastomosis tested on the technique-standardization group.

purse-string suture was placed at the duodenotomy site. A 5/0 polydioxanone (PDS II, Ethicon, Somerville, NJ, USA) pull-through suture was used at the BD wall to introduce and secure the BD/BS complex for at least 1 cm within the duodenal lumen. The anastomosis was

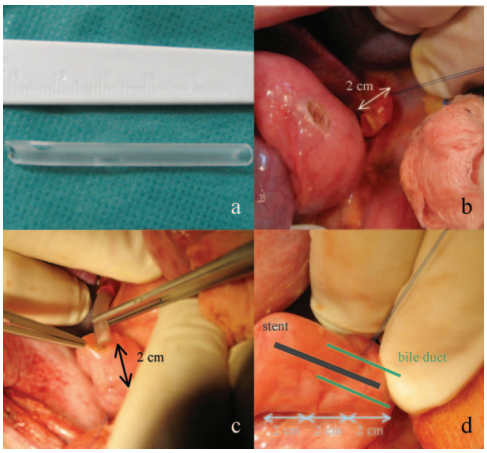

FIGURE 2 The biliodigestive anastomosis technique. (a) A bibeveled 5-cm biliary stent was fashioned by trimming an 8 Fr feeding tube. (b) A double-needle 5/0 PDS suture was placed 2 cm from the cut-end of the bile duct. A duodenotomy with a mucosal opening <1 mm was performed. (c) The stent was introduced 3 cm into the bile duct. The 5/0 PDS suture was placed through the mucosal opening 2 cm from the edge of the duodenotomy. (d) The BS/BD complex was gently placed through the duodenotomy by pulling the suture. Thus, all 4 cms of the dissected bile duct were introduced into the duodenum. The anastomosis was completed by tying the suture.

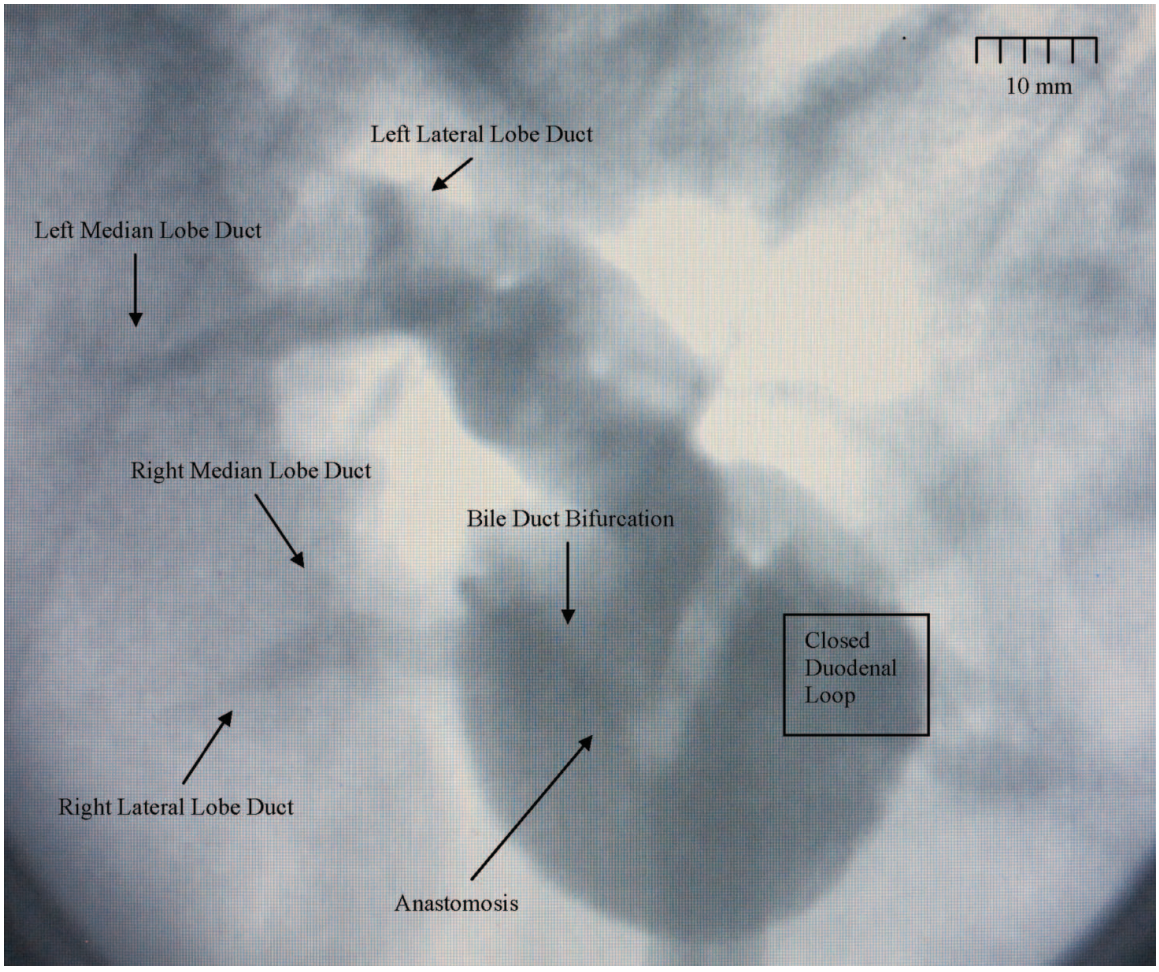

FIGURE 3 The closed duodenal loop intraoperative cholangiogram at the end of the 4-week follow-up period. This picture depicts animal #1. The cholangiogram was performed at 20 cm H_20 pressure. Notice that the gallbladder was not observed at this pressure level.

completed by tightening and tying the purse-string suture. In the second type of anastomosis (Figure 1b), the purse-string suture was replaced with a 4/0 Prolene suture that approximated the remaining duodenotomy gap after inserting the BD / BS complex. For the third type of anastomosis (Figure 1c), the 4/0 Prolene suture was eliminated. In addition, the BD / BS complex was introduced at least 2 cm into the duodenal lumen instead of only 1 cm. In the fourth type of anastomosis (Figure 1d), the BS and 4/0 Prolene suture were both eliminated. In this procedure, the BD was introduced at least 2 cm into the duodenal lumen. The experimentation in the technique-standardization group ended at this point, and all eight animals were euthanized by 20 ml of intravenous pentobarbital sodium/benzyl alcohol (Dolethal, Vetoquinol, Buckingham, UK) and exsanguination.

The third anastomosis procedure (Figure 2) was performed on all three animals of the main study group (Figure 2), and the procedure was completed with a layered abdominal wall closure. The animal and operative data were recorded. In addition, repeated blood (white cell count and hemoglobin) and serum (glucose, urea, creatinine, alanine aminotransferase, total and direct bilirubin, γ-glutamyltransferase, alkaline phosphatase and amylase) tests were performed on postoperative days 1, 7, 14, and 28.

At the end of the 4-week follow-up period, the three animals in the main study group underwent a laparotomy. Closed duodenal loop intraoperative cholangiographies were performed at 20-cm H_20 pressure, and the livers were sampled for histology. The animals were then euthanized by 20 ml of intravenous pentobarbital sodium/benzyl alcohol (Dolethal, Vetoquinol, Buckingham, UK) and exsanguination. Finally, the biliodigestive anastomoses were sampled for histology.

The formalin-fixed, paraffin-embedded anastomoses, and liver specimens were stained with hematoxylin and eosin. A histological analysis was performed using light microscopy at X25 and X400 magnification. For the biliodigestive anastomosis specimens, the levels of mucosal atrophy, mucosal inflammation, mucosal metaplasia, submucosal vascularization, submucosal fibrosis, scar formation, and

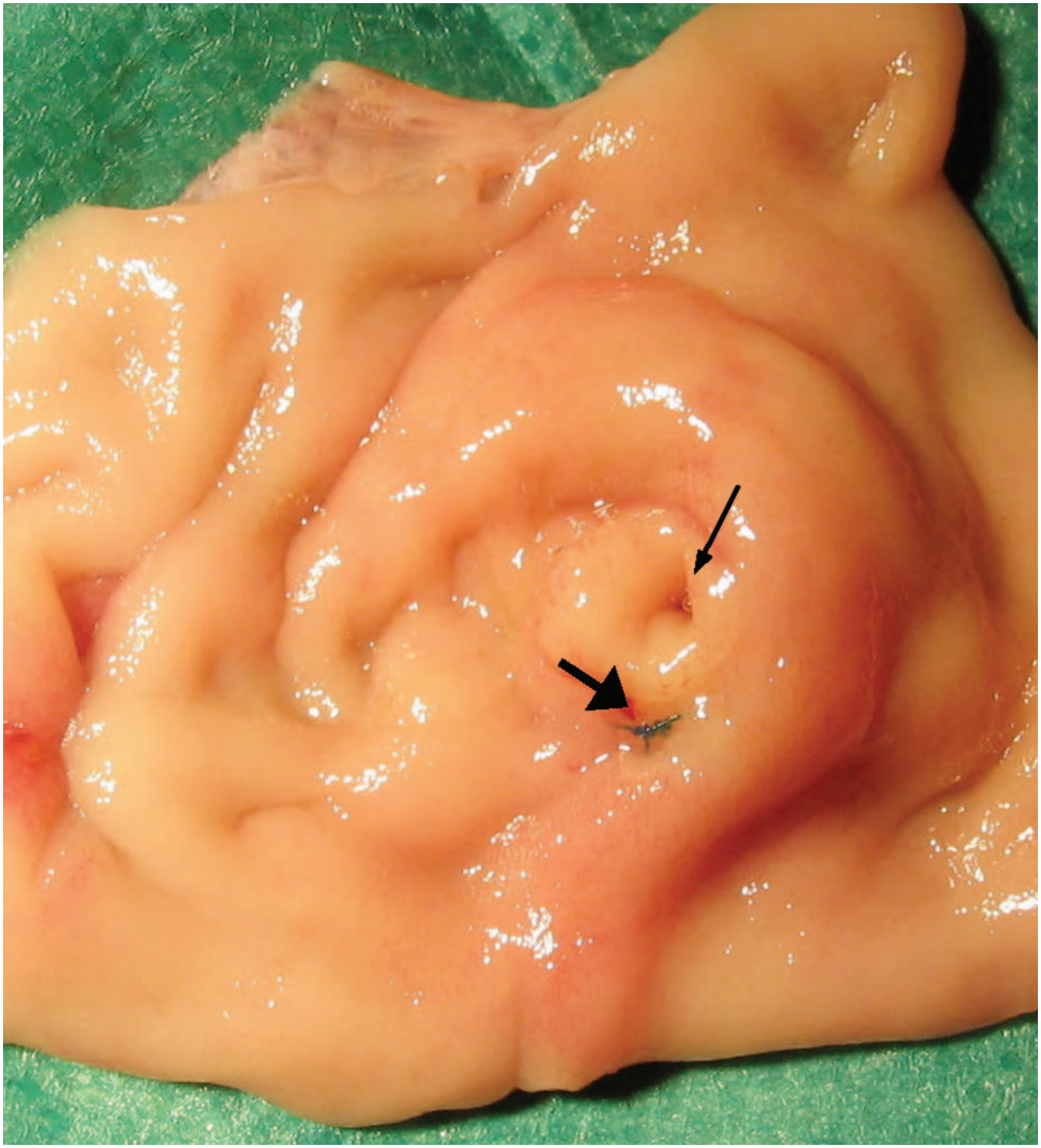

FIGURE 4 The macroscopic appearance of the biliodigestive anastomosis at the end of the 4-week follow-up period. Thin arrow: orifice of the anastomosis. Thick arrow: single pull-through 5/0 PDS stitch. This specimen is from animal #2. Notice that the knot was inverted inside the intestinal lumen, even though it was initially placed on the outside. This inversion was not seen in any of the other animals in the group.

foreign body granuloma formation were evaluated on a scale ranging from 0 to 3. For the liver specimens, the levels of periportal or bridging necrosis, portal inflammation, and cholestasis were evaluated on a scale ranging from 0 to 3.

The quantitative data are shown as the median with range and the mean with standard deviation. A one-sample Student's *T* test was used to test for statistically significant differences between the calculated mean and previously reported normal values.

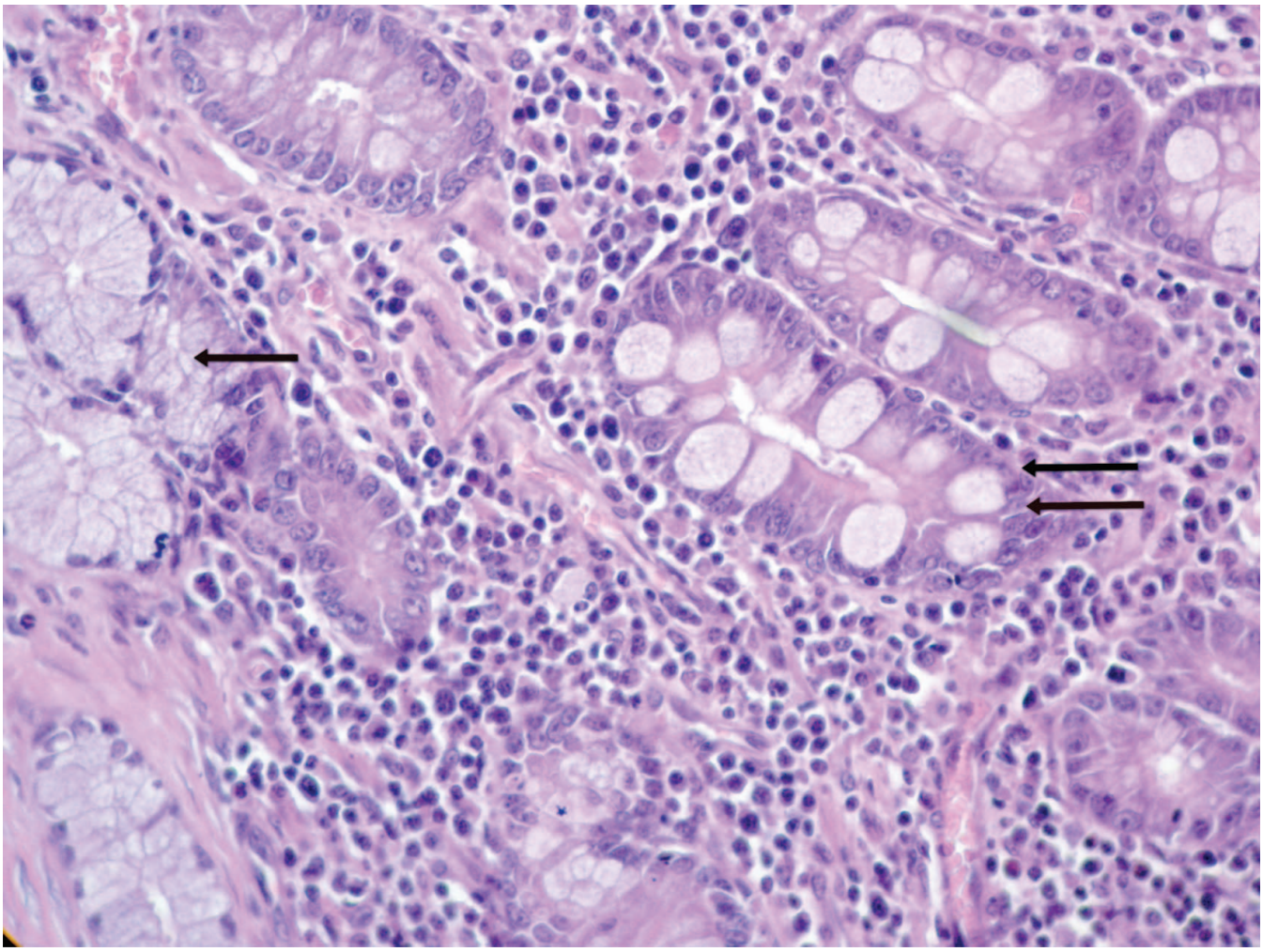

FIGURE 5 Intestinal metaplasia of the single-stitch telescopic biliodigestive anastomosis. This specimen is from animal #1. On the left (double arrows), intestinal metaplasia of ductal glands with goblet cells was observed, while on the right (single arrow), pseudopyloric metaplasia of the ductal epithelium was also observed (H&E, X400).

Although the sample size was small ($n = 3$), the nonparametric Kruskal–Wallis test was used to test for statistically significant differences between groups of quantitative data. Differences of $P \leq .05$ were considered statistically significant. The statistical analyses were performed with SPSS 16.0 for Mac (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the four types of biliodigestive anastomosis performed in the technique-standardization group ($n = 8$, Figure 1), only the last procedure showed immediate postconstruction bile leakage (in both animals). The other three procedures were bile-proof in all six of the animals. The third type of biliodigestive anastomosis was tested on the main study group because it was the simplest to conduct.

In the main study group ($n = 3$), the mean operative time was 42.00 ± 3.00 min (median 40 min, range 39 – 45 min). The mean anastomotic time was 5.33 ± 1.52 min (median 5 min, range 4 – 7 min). All of the animals gained weight during the 4-week follow-up. The mean body weight before the second procedure was 39.67 ± 0.57 kg (median 40 kg, range 39 – 40 kg).

At the time of the laparotomy, none of the three animals had evident bilomas or other intra-abdominal collections. The biliary stent could no longer be palpated inside any of the three anastomoses. A cholangiogram revealed a BD diameter of <6 mm and a nondilated intrahepatic biliary tree in all of the animals (Figure 3). The macroscopic appearances of all three anastomoses were characterized by smooth BD blending in the duodenal wall with a > 2-mm orifice (Figure 4).

In the histological analysis of the biliodigestive anastomoses, the most prominent finding was the detection of focal intestinal metaplasia of the ductal epithelium in all three cases. Moreover, the first anastomosis also displayed pseudopyloric metaplasia (Figure 5). Other findings included slight-to-moderate inflammation and mild submucosal vascularization,

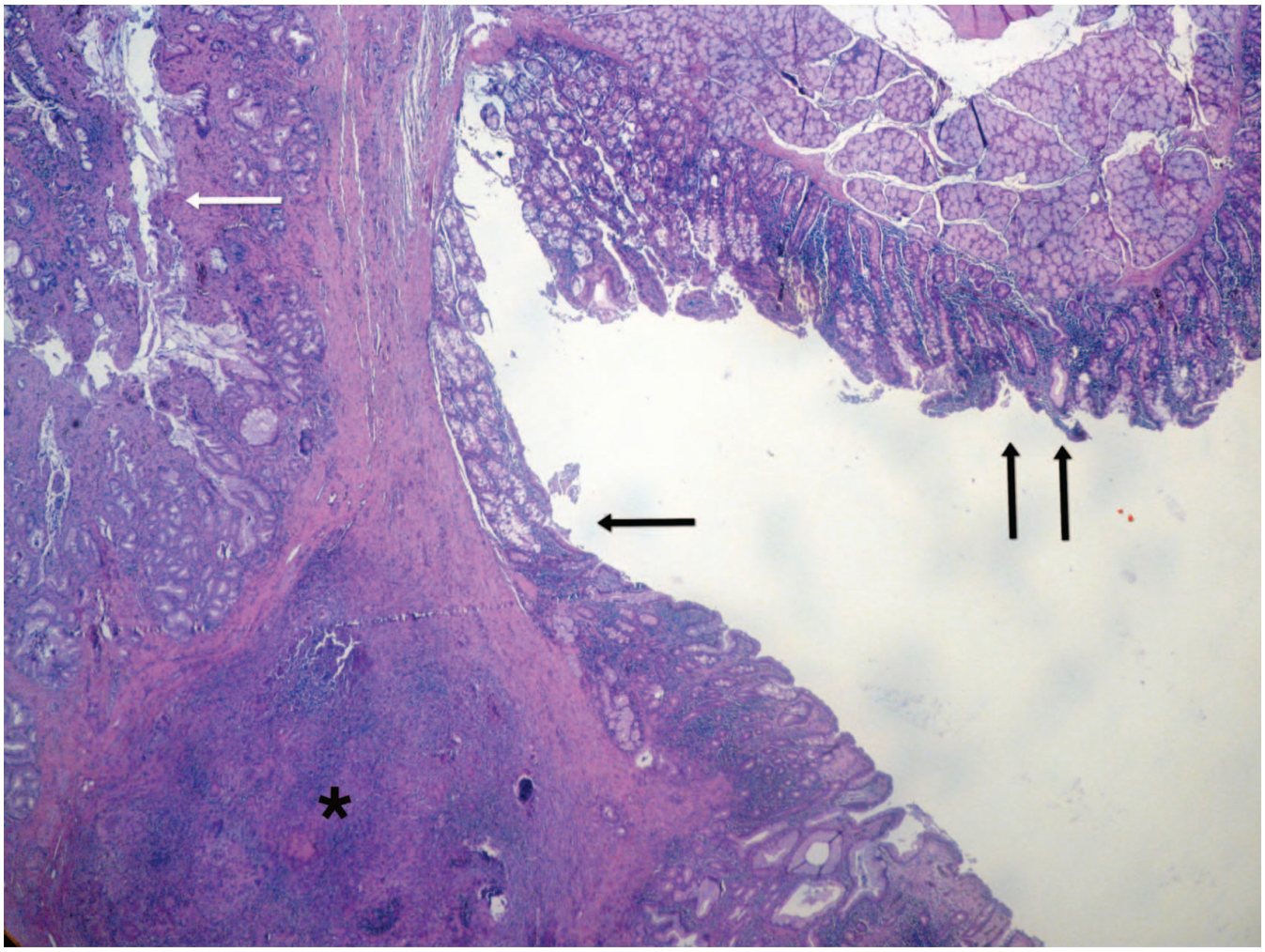

FIGURE 6 The histological analysis of the biliodigestive anastomosis. This specimen is from animal #1. The duodenal mucosa is shown on the top right section of the image (double arrows), while the bile duct lumen is shown on the top left (white arrow). The anastomosis between the bile duct and duodenum is shown in the center (single arrow), accompanied by moderate inflammation and foreign body granuloma formation (asterisk) (H&E, X25).

submucosal fibrosis, and scar formation (Figure 6). Foreign body granulomas were found in two cases. Minimal to absent mucosal atrophy was identified (Table 1). No cholestasis or other prominent abnormal findings were identified in the histological analysis of the liver specimens (data not shown).

TABLE 1 Pathology scores of biliodigestive anastomosis and liver specimens as assessed by light microscopy

Observation	Animal #1	Animal #2	Animal #3
Mucosal atrophy	1	0	0
Mucosal inflammation	2	1	2
Mucosal metaplasia	1	1	2
Submucotic vascularization	1	0	1
Submucotic fibrosis	2	0	0
Scar formation	1	0	0
Foreign body granuloma	2	1	0

During the follow-up period, all three animals had blood and serum laboratory values within the normal limits [16]. In addition, these values followed no significant trends during the follow-up period (Table 2).

DISCUSSION

In the present study, we investigated a simplified telescopic biliodigestive anastomosis technique that utilizes a single pull-through stitch and disposable internal stent. This technique results in a quick, reproducible, and technically undemanding anastomosis that may be utilized in ducts of any caliber and that were shown to be fully functional and free of complications in the pig models. Although this anastomotic technique has been previously described in the urology literature [14], using it for biliodigestive anastomoses has never, to our knowledge, been reported.

TABLE 2 Hematological and biochemical parameters of the main study group ($n = 3$) during the postoperative follow-up period of 4 weeks

Lab. Value	PostOp. Day	Mean	St. Deviation	Median	Range	*P*
WBC	1st	11333	1350	11300	10000–13000	0.723
	7th	12533	3980	13700	8100–15800	
	14th	12200	1044	12700	11000–13000	
	28th	11900	500	11900	11400–12400	
Hb	1st	10.8	1.10	10.8	9.8–12.0	0.433
	7th	10.0	0.55	9.9	9.5–10.6	
	14th	9.7	0.80	9.9	8.9–10.5	
	28th	10.4	0.26	10.3	10.2–10.7	
Glu	1st	103	7	104	96–110	0.599
	7th	98	24	88	81–126	
	14th	88	10	91	76–97	
	28 th	97	22	92	77–122	
Ur	1st	32.0	5.5	33.0	26.0–37.0	0.447
	7th	27.6	4.6	25	25–33	
	14th	26.0	0.0	26	26–26	
	28th	26.6	7.5	30	18–32	
Cr	1st	1.03	0.05	1.00	1.00–1.10	0.542
	7th	0.93	0.35	0.90	0.60–1.30	
	14th	0.80	0.26	0.90	0.05–1.00	
	28th	1.03	0.20	1.10	0.80–1.20	
ALT	1st	58	12	58	46–71	0.345
	7th	54	22	48	36–79	
	14th	41	2	40	40–45	
	28th	43	5	42	39–49	
γ-GT	1st	31	2	31	29–34	0.089
	7th	35	2	36	32–37	
	14th	36	6	34	31–44	
	28th	26	4	27	22–31	
AlkPhos	1st	169	49	182	115–212	0.152
	7th	162	46	185	109–192	
	14th	104	4	102	102–109	
	28th	114	18	117	95–131	
TBil	1th	0.08	0.04	0.10	0.03–0.11	0.553
	7th	0.22	0.25	0.11	0.04–0.51	
	14th	0.09	0.01	0.09	0.08–0.10	
	28th	0.10	0.00	0.10	0.01–0.01	
DBil	1st	0.04	0.03	0.05	0.01–0.08	0.858
	7th	0.10	0.09	0.07	0.02–0.21	
	14th	0.04	0.01	0.05	0.04–0.05	
	28th	0.05	0.02	0.07	0.03–0.07	
Amy	1st	2482	421	2630	2007–2811	0.715
	7th	2388	890	2831	1364–2971	
	14th	2221	484	2416	1670–2578	
	28th	2513	281	2506	2235–2798	

WBC, white blood cell count in cells/mL; **Hb,** hemoglobin in g/dL; **Glu,** glucose in mg/dL; **Ur,** urea in mg/dL; **Cr,** creatinine in mg/dL; **ALT,** alanine aminotransferase in IU/L; **γ-GT,** γ-glutamyltransferase in IU/L; **AlkPhos,** alkaline phosphatase in IU/L; **TBil,** total bilirubin in mg/dL; **DBil,** direct bilirubin in mg/dL; **Amy,** amylase in IU/dL

The technique-standardization group results verified an important observation made by previous authors. A stent should be used whenever an attempt to reduce the number of sutures in a biliodigestive anastomosis is made [8, 10, 12, 17]. In the absence of a regular suture line, an external or internal stent likely prevents early postoperative bile leaks, thus allowing the anastomosis to heal and eventually seal without complications. Furthermore, the stent ensures BD patency whenever a purse-string suture is used [8, 10]. In the present study, we utilized a stent fashioned from a cheap, plain plastic tube. In addition, we eliminated as much jejunal suturing as possible in a step-wise fashion. First, we replaced the jejunal purse-string suture with a simple approximating suture; when no leak was observed, we completely eliminated the jejunal suture. This change did not lead to bile leaks. A further attempt to eliminate the stent failed, indicating that its use was mandatory.

Based on the technique-standardization observations, we hypothesized that a non-anchored simple internal stent (the third anastomotic technique) would prevent both bile leaks and delayed intestinal transit. The main study group results confirmed this

hypothesis. No immediate or delayed bile leakages were identified, and no impacted BD stents were retrieved during the second laparotomies.

The intraluminal macroscopic appearance of the anastomosis yielded two important observations. First, although the BD was introduced approximately 4 cm inside the duodenal lumen, it became totally integrated with the intestinal wall by the end of the 4-week follow-up period. Simultaneously, the BD anchoring stitch was found in close proximity to the anastomotic orifice, despite being initially placed 2 cm away from the duodenotomy. Scar formation and collagen remodeling are likely responsible for these observations [18]. Second, there was a discrepancy between the BD and anastomotic diameters. Indeed, the anastomotic orifice was half the size of the BD. Despite their caliber differences, fluoroscopy revealed a normal extrahepatic and intrahepatic biliary tree. Furthermore, no abnormal laboratory values associated with biliary obstruction were recorded. Some authors have suggested that a wider anastomosis is preferable [10]. However, because no functional disturbances were detected in this study, we believe that the discrepancy between the BD and anastomotic diameters had no biological effects. In addition, this discrepancy may help to prevent sump syndrome from developing [19]. Studies with longer follow-up periods (>12 months) are required to determine the impact of a single-stitch telescopic anastomosis with a disposable stent on delayed cholangitis development.

The microscopic appearance of the anastomoses also yielded important observations. The mucosal inflammation, mild submucosal vascularization, mild submucosal fibrosis, mild scaring, and foreign body granuloma formation may be regarded as normal postoperative reactions and partially attributed to the transient presence of the plastic stent. However, the most important observation was the intestinal metaplasia of the BD mucosa. The metaplastic changes were identified primarily in the BD portion that was introduced into the intestinal lumen. It is difficult to determine if these changes were transient or chronic, especially because they were not observed in a study with a 6-month follow-up [10]. Studies with longer follow-up periods are required to determine whether a single-stitch telescopic anastomosis with a disposable stent leads to chronic intestinal metaplasia of the BD mucosa. Although intestinal (and pseudopyloric) metaplasia has frequently been described within the biliary epithelium [20], it is of paramount importance to clarify whether the technique proposed in this study is associated with chronic metaplastic changes because intestinal metaplasia of the gastric mucosa has been implicated as a precancerous lesion leading to gastric cancer [21, 22]; a similar role in adenocarcinoma formation has been postulated for intestinal metaplasia of the biliary epithelium [23, 24].

In conclusion, a telescopic bilioenterostomy with a single pull-through stitch and an internal, self-disposable stent yielded good results in pigs. It appears to be free of complications and is quick, reproducible, and easily applied to small caliber ducts. Further animal experiments with longer follow-up periods are required to confirm that this anastomotic technique does not lead to episodes of delayed cholangitis or adenocarcinoma development. Hepato-pancreato-biliary surgical oncology and liver transplantation could greatly benefit from developing a fast, reliable, and universally applicable technique for bilioenterostomy.

Declaration of Interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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