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Anatomy-specific pancreatic stump management to reduce the risk of pancreatic fistula after pancreatic head resection

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Abstract

Background: The anatomical status of the pancreatic remnant following a pancreatic head resection varies greatly among patients. The aim of this study was to improve management of the pancreatic remnant for reducing pancreatic fistula after pancreatic head resection.

Methods: Ninety-five consecutive patients who underwent an end-to-side, duct-to-mucosa pancreaticojejunostomy after pancreatic head resection were included in the study. To approximate the pancreatic stump to the jejunum, the transfixing and interrupted suture techniques were used in 51 and 44 patients, respectively. We modified the interrupted suture technique according to the anatomical status of the pancreatic remnant, i.e., the shape of the pancreatic stump and the location of the pancreatic duct.

Results: There was no operative mortality in this study. Overall, 14 patients (15%) developed a clinically relevant pancreatic fistula. Certain anatomical features, including a small pancreatic duct, a soft, nonfibrotic pancreatic gland, and a pancreatic duct adjacent to the posterior cut edge, were significantly associated with pancreatic fistula. The fistula rate in the interrupted suture group was 7%, lower than that (22%) in the transfixing suture group (p=0.036), and was not influenced by pancreatic anatomy. Multivariate analysis identified a nonfibrotic pancreas (versus fibrotic pancreas; odds ratio [OR] 12.58, 95% CI 1.2-23.9, p=0.001), a soft pancreas (versus hard pancreas; OR 4.67, CI 1.2-51.1, p=0.006), and the transfixing suture technique (versus interrupted suture technique; OR 9.91, CI 1.7-57.5, p=0.003) as significant predictors of clinically relevant pancreatic fistula.

Conclusions: Pancreatic anastomosis modified according to the pancreatic anatomy is effective in reducing the risk of pancreatic fistula formation with end-to-side, duct-to-mucosa pancreaticojejunostomy following pancreatic head resection.

Introduction

Significant advances in surgical techniques and critical care management have substantially reduced the mortality of pancreatic surgery. However, morbidity remains considerably high even in high-volume centers, approaching 40% to 50%, and pancreatic fistula still accounts for the majority of surgical complications following pancreatic head resection.[1-4]

Various risk factors for pancreatic fistula after pancreatic head resection have been identified, including advanced age,[5] duration of jaundice,[6] creatinine clearance,[6] ampullary disease,[3,4,7,8] prolonged operations,[5,7] and intraoperative blood loss.[5-7] The most generally accepted determinants of postoperative pancreatic fistula are the size of the pancreatic duct[3,8-10] and the consistency of the pancreatic remnant.[2,5,7,9,10] Despite the more than 80 different methods of pancreaticoenteric anastomosis that have been proposed for the prevention of pancreatic fistula, management of the pancreatic remnant after pancreatic head resection still remains a challenge because of the lack of a gold standard for all patients.[11]

The anatomical features of the stump of the pancreatic remnant following a pancreatic head resection vary greatly among patients, making it difficult to perform a safe pancreaticoenteric anastomosis in the same manner for all patients. In this study, we examined in detail the anatomical status of the pancreatic stump, including the actual thickness and width of the gland and the location of the main pancreatic duct, as well as the pancreatic duct size and gland consistency, in patients undergoing a pancreatic head resection. Then we evaluated the risk factors, including the remnant pancreatic anatomy, for postoperative pancreatic fistula. Moreover, we investigated the efficacy of modifying the pancreatic anastomosis technique according to the anatomical conditions of each pancreatic remnant to reduce the risk of pancreatic fistula development.

Patients and Methods

A total of 95 consecutive patients who underwent an end-to-side, duct-to-mucosa pancreaticojejunostomy after pancreatic head resection, between January 2002 and August 2008, were included in the study (**Table 1**). There were 51 men and 44 women with a mean age of 69 (range 38-86) years. Pancreatic head resection was achieved by a pylorus-preserving pancreaticoduodenectomy (PPPD; n=66), standard pancreaticoduodenectomy (PD; n=15), pancreatic head resection with segmental duodenectomy (PHRSD; n=9) or duodenum-preserving total pancreas head resection (DPPHR; n=5). The pathological conditions included intraductal papillary mucinous neoplasms of the pancreas (n=29), pancreatic ductal adenocarcinomas (n=27), bile duct carcinomas (n=21), ampullary carcinomas (n=7), chronic pancreatitis (n=4), pancreatic endocrine tumors (n=2), solid pseudopapillary tumors of the pancreas (n=2), gallbladder carcinomas (n=2), and gastric carcinoma (n=1).

Surgical Procedures of Pancreaticojejunostomy

Pancreaticojejunostomy was achieved by a double-layer method in all patients, consisting of a duct-to-mucosa anastomosis for the inner layer and an approximation between the pancreatic stump and the jejunum for the outer layer. To construct duct-to-mucosa anastomosis, a small incision with the same diameter as the pancreatic duct was made on the antimesenteric side of the jejunal limb, and anastomosis was performed between the pancreatic duct and the entire jejunal wall, with 6 to 10 interrupted sutures using a 5-0 or 6-0 polydioxanone stitch (PDSII; Ethicon, inc, Somerville, NJ). For approximating the pancreatic stump to the jejunum, the transfixing suture technique described by Kakita *et al*.[12] as "one-layer suturing" was used in 51 patients, with 6 to 8 sutures using a 4-0 polypropylene stitch (Prolene; Ethicon, Inc, Somerville, NJ), while the interrupted suture technique was employed in the remaining 44 patients, with 12 to 16 sutures using a 4-0 Prolene stitch.

In the transfixing suture technique, the sutures for the outer layer were inserted from the anterior surface of the pancreatic remnant and introduced straight through the pancreatic parenchyma to the posterior surface (**Figure 1**). The sutures then lifted the seromuscular layer of the jejunum widely enough to cover the pancreatic stump.[12] In the interrupted suture technique, the manner of outer-layer suturing was modified according to the anatomical status of the pancreatic remnant, i.e., the shape of the pancreatic stump and the location of the pancreatic duct (**Figure 2**), to achieve a tension-free approximation and also leave no dead space between the pancreatic stump and the jejunal wall. In patients with a round or an oval-shaped pancreatic stump (n=13), the sutures were arranged circumferentially around the pancreatic duct in a radial fashion (**Figure 3a**), such that the stitches were inserted from the pancreatic cut surface close to the inner suture line and introduced to the posterior surface for the posterior outer row of sutures, beginning at the posterior corner. For the placement of the anterior outer row of sutures, the stitches were inserted from the anterior pancreatic capsule and introduced close to the inner suture line. The sutures then picked up the seromuscular layer of the jejunum with the same radial arrangement (**Figure 3b**). In patients with a flat-shaped pancreatic stump (n=31), the sutures were placed perpendicularly to the major axis of the pancreatic stump with a parallel arrangement of sutures for both the anterior and posterior rows (**Figure 4**). If the pancreatic duct was located close to the posterior cut edge of the pancreatic stump within a distance of 4 mm (n=24), the first and second stitches for the posterior outer row of sutures were inserted close to the cephalic and caudal corner of the inner suture line, regardless of the shape of the pancreatic stump, and then penetrated to the posterior surface just below the pancreatic duct (**Figure 5**).

The pancreaticojejunostomy was performed by 5 different surgeons, 2 with more than 15 years and 3 with less than 15 years of surgical practice. An external pancreatic duct stent was placed in 61 patients. No sealants were employed in any patients. Two drains were routinely placed close to the ventral side of pancreatic anastomosis for peritoneal drainage in each patient.

Detailed Data Recording

Preoperative data obtained included the age, gender, history of jaundice, serum levels of albumin, total bilirubin and hemoglobin, lymphocyte counts, creatinine clearance, oral glucose tolerance test (OGTT), hemoglobin A1c (HbA1c) levels, *N*-benzoyl-L-tyrosyl-*p*-aminobenzoic acid (BT-PABA) test, profiles of the time-signal intensity curve (TIC) of the pancreas on dynamic contrast-enhanced magnetic resonance imaging (MRI), and primary disease pathology. Pancreatic TICs were obtained prior to surgery using a 1.5-T superconducting MRI system with a region of interest placed at the proposed transection line for the pancreas and were classified into 3 types: type I, characterized by a rapid rise to a peak followed by a rapid decline, indicating a normal pancreas without fibrosis; and types II and III with a slow rise to a peak followed by a slow decline or plateau, indicating a fibrotic pancreas.[13]

The intraoperative variables included texture of the pancreatic gland, diameter of the pancreatic duct (≤3mm, >3mm), thickness and width of the pancreas measured at the pancreatic stump, location of the pancreatic duct, type of pancreatic resection (PPPD, PD, PHRSD, or DPPHR), lymphadenectomy (non, regional, or extended), the outer-layer suturing technique for a pancreaticojejunostomy (transfixing suture or interrupted suture), use of a pancreatic stent, operative time, intraoperative blood loss, blood transfusion (with or without) and surgeon experience (<15yrs, ≥15yrs). The texture of the pancreas at the pancreatic stump was classified by the operating surgeon as soft (normal, friable), intermediate, or hard (fibrotic, sclerotic). The location of the pancreatic duct was evaluated at the pancreatic cut end by measuring the distance between the pancreatic duct and the cut edge of the pancreas in 4 directions, i.e., toward the anterior, posterior, superior, and inferior cut edges (**Figure 6**).

Study End Point

The end point of the primary study was postoperative pancreatic fistula. Based on the International Study Group for Pancreatic Fistula (ISGPF) clinical criteria,[14] pancreatic fistula was defined as the output via an operatively placed drain of any measurable volume of drain fluid on or after postoperative day 5, associated with an elevated amylase content greater than 3 times the upper limit of the normal serum amylase value (>390 IU/L). The severity of pancreatic fistula was classified into 3 grades as follows: grade A fistulas are transient, asymptomatic fistulas with only elevated drain amylase levels, for which treatments or deviation in clinical management are not required; grade B fistulas are clinically apparent, symptomatic fistulas that require diagnostic evaluation and therapeutic management; and grade C fistulas are severe, clinically significant fistulas that require major deviations in clinical management and aggressive therapeutic interventions.

Statistical Analyses

In strict accordance with the ISGPF classification scheme, the patients were divided into 2 groups, as patients who lacked clinical evidence of fistula (no fistula or grade A fistula) and patients with a clinically relevant pancreatic fistula (grade B or C). The aforementioned 13 preoperative and 13 intraoperative parameters were registered as presumed risk factors for pancreatic fistula. The groups were initially compared using standard univariate statistical tests (chi-square test, two-tailed Fisher's exact test, and Mann-Whitney's *U*-test, where appropriate) to identify the variables associated with pancreatic fistula. Statistically significant variables were then entered into a multivariable logistic regression analysis to assess any independent influences on postoperative pancreatic fistula. Values of $p<0.05$ were considered to be statistically significant. All confidence intervals (CI) were at the 95% level.

Results

Morbidity and Mortality

There was no operative mortality in this study. Pancreatic fistula of any extent occurred in 20 of the 95 patients (21%). There were 6 grade A fistulas, 12 grade B fistulas, and 2 grade C fistulas, presenting with a clinically relevant fistula rate of 15%. Two patients with a grade C fistula required surgical re-exploration for definitive management of the problem. Other major postoperative complications included pulmonary complications (16%), delayed gastric emptying (7%), wound infection (6%), ascending cholangitis (4%), intraabdominal abscess (3%), and biliary leakage (3%).

Risk Factors

A comparison of perioperative risk factors for the 2 study groups is shown in **Table 2**. Among the 13 preoperative parameters, the BT-PABA test result ($p=0.032$) and pancreatic TIC profile from dynamic MRI ($p<0.001$) were significant predictors of a clinically relevant fistula in univariate analyses. Patients with normal exocrine pancreatic function were likely to develop pancreatic fistula. Of the 66 patients with type I pancreatic TIC, 14 patients (21%) demonstrated a clinically relevant pancreatic fistula, whereas none of the 29 patients with type II or III pancreatic TIC displayed pancreatic fistula. No significant differences in patient age, gender, history of jaundice, or laboratory values including the concentrations of serum albumin, total bilirubin and hemoglobin, lymphocyte counts, and creatinine clearance were noted between the 2 patient groups. The results of OGTT and HbA1c levels had no impact on the occurrence of pancreatic fistula. Although a high rate of fistula was recognized in patients with bile duct carcinoma (19%), in comparison to patients with pancreatic ductal adenocarcinoma (7%) or chronic pancreatitis (0%), no significant differences in pathology were observed between the 2 patient groups.

Among the 13 intraoperative parameters, the texture of the pancreas ($p=0.035$), pancreatic duct size ($p=0.023$), location of the pancreatic duct (the distance between the pancreatic duct and the posterior cut edge of the pancreas; $P=0.041$), and the surgical procedure of pancreaticojejunostomy ($p=0.037$) were shown to be significant predictors of clinically relevant pancreatic fistula in univariate analyses. Patients with a soft pancreas or a small pancreatic duct (≤3mm) were at extremely high risk for developing pancreatic fistula. Interestingly, patients with a pancreatic duct located close to the posterior edge of the pancreatic stump were likely to develop pancreatic fistula, regardless of the thickness and width of the pancreas, and 9 of the 37 patients (24%) with such contiguity of the pancreatic duct to the posterior cut edge (≤3mm) developed pancreatic fistula. On the other hand, 11 of the 51 patients (22%) who received the transfixing suture technique for the outer layer of pancreaticojejunostomy demonstrated a clinically relevant pancreatic fistula (9 grade B fistulas and 2 grade C fistulas). Meanwhile, the fistula rate related to the interrupted suture technique was 7% (3 grade B fistulas and no grade C fistula). The type of pancreatic resection, the extent of lymphadenectomy, the operative time, intraoperative blood loss, the incidence of blood transfusion, and surgeon experience were similar for the 2 patient groups.

A multivariable logistic regression analysis of 6 factors univariately associated with pancreatic fistula, i.e., BT-PABA test, pancreatic TIC, texture of the pancreas, pancreatic duct size, location of the pancreatic duct, and anastomosis technique for pancreaticojejunostomy, identified pancreatic TIC (type I versus types II and III; odds ratio [OR] 12.58, 95% CI 1.2-23.9, p=0.001), pancreatic gland consistency (soft versus hard; OR 4.67, CI 1.2-51.1, p=0.006), and pancreaticojejunal anastomosis technique (transfixing suture versus interrupted suture; OR 9.91, CI 1.7-57.5, p=0.003) as significant independent predictors of clinically relevant pancreatic fistula (**Table 3**).

A comparison of risk factors for pancreatic fistula between the transfixing suture group and the interrupted suture group is shown in **Table 4**. In the transfixing suture group, univariate analyses identified the occurrence of pancreatic fistula to be significantly influenced by the BT-PABA test result (p=0.033), pancreatic TIC (p=0.001), pancreatic texture (p=0.001), pancreatic duct size (p<0.001), and location of the pancreatic duct (p=0.001). In the interrupted suture group, there were no significant risk factors predisposing a patient to postoperative pancreatic fistula.

Discussion

Pancreaticoenteric anastomosis still represents the "Achilles' heel" of pancreatic surgery.[15] In particular, pancreatic fistula is a leading cause of surgical complications after pancreatic head resection and is often linked with prolonged hospital stay, increased costs, and mortality.[16-18] The incidence of pancreatic fistula after pancreatic head resection ranges in the literature between 0% and 30%;[1-4,18-21] however, the fistula rate strictly depends on the definition used.[22] In 2005, the ISGPF developed a universal definition of pancreatic fistula, with a grading system able to stratify complicated patients into 3 groups as grades A, B and C, based on the clinical implications and costs of their postoperative course.[14] Grade A fistula presents with an elevated drain amylase level only and lacks any clinical consequences, i.e., a "biochemical" fistula. Contrarily, grades B and C fistulas have an intermediate or a dramatic impact on patients, requiring therapeutic interventions. In this study, we thus evaluated the risks for pancreatic fistula after pancreatic head resection in 2 different study groups, patients who lacked clinical evidence of fistula (no fistula or grade A fistula) and patients with a clinically relevant pancreatic fistula (grade B or C fistula) in strict accordance with the ISGPF classification scheme.

Pancreatic fistula of any extent occurred in 20 of the 95 pancreatic-head-resection patients (21%) in this study, and 14 (15%) of the fistula cases were clinically relevant. The BT-PABA test result, pancreatic TIC profile, pancreatic texture, pancreatic duct size, location of the pancreatic duct, and surgical procedure of pancreaticojejunostomy were shown to be significantly associated with clinically relevant pancreatic fistula. Multivariate analysis identified that the pancreatic TIC, gland consistency, and pancreaticojejunal anastomosis technique were significant independent predictors of pancreatic fistula. All these risk factors, except for the anastomosis technique, were pancreatic anatomy-related factors; both the BT-PABA test results and pancreatic TIC profiles obtained from dynamic contrast-enhanced MRI well reflect the pancreatic anatomy, especially the degree of pancreatic fibrosis.[13] Patients undergoing pancreatic head resection have been categorized grossly into 2 groups based on the anatomical status of the pancreatic remnant: patients with a soft, fragile pancreas or small pancreatic duct, who are considered at high risk for pancreatic fistula; and patients with a fibrotic, firm pancreas or dilated pancreatic duct, who are at low risk.[2,3,5,7-10,23-25] Our results mirrored these reported data.

A unique result of our analysis was that the location of the pancreatic duct had a significant impact on a patient’s predisposition to developing pancreatic fistula after pancreatic head resection. Within the body and tail of the pancreas, the pancreatic duct lies slightly cephalad to a line drawn midway between the superior and inferior edges of the pancreas, and the duct is also more posterior than anterior.[26] In our study group the average thickness of the pancreatic stump and that of the pancreatic parenchyma beneath the pancreatic duct were 16.5 mm and 4.1 mm, respectively. Patients who had a pancreatic duct located close to the posterior cut edge within a distance of 3 mm were highly associated with pancreatic fistula, although neither the thickness/width of the pancreatic stump nor the distance between the pancreatic duct and the anterior, superior, or inferior cut edge of the pancreas had any impact on the development of pancreatic fistula. During double-layer pancreaticojejunal anastomosis, a duct-to-mucosa anastomosis can be safely applied even to a pancreatic duct adjacent to the posterior cut edge. However, such an anatomical situation of the pancreatic duct would make more difficult a safe approximation between the pancreatic stump and the jejunal wall, especially in its posterior corner, and would likely result in pancreatic fistula.

Possible pancreatic stump management for reducing the risk of pancreatic fistula and subsequent septic complications after pancreatic head resection may involve the use of ultrasonically activated shears[27] or an ultrasonic dissector[28,29] during pancreas transection, optimizing the blood supply to the pancreas,[30] duct-to-mucosa pancreaticoenteric anastomosis,[31-34] dunking pancreatojejunostomy,[19,25,35] pancreaticogastrostomy,[16,25,33,36,37] use of a pancreatic duct stent,[38] omental wrapping of skeletonized major vessels,[39,40] or intraoperative octreotide administration via the gastroduodenal artery.[41] In this study, we modified the outer-layer interrupted suture technique according to the anatomical status of each pancreatic remnant. As a consequence, a lower fistula rate of 7% was achieved in this group, compared to the transfixing suture group with a fistula rate of 22%. In addition, the fistula rate for the interrupted suture technique was the same, whether it was performed on a soft or firm pancreas, a small or large pancreatic duct, or even to a pancreatic duct adjacent to the posterior cut edge. By contrast, the fistula rate was significantly influenced by the pancreatic anatomy in the transfixing suture group. Sugiyama et al.[28] examined 4 patients with a soft pancreas and a small main pancreatic duct and indentified from 5 to 7 microscopic pancreatic ducts on the cut surface of the resected pancreas following a pancreaticoduodenectomy. We believe that the existence of small pancreatic ducts that are exposed on the transected pancreatic surface can lead to pancreatic juice leakage and, ultimately, major anastomotic leakage after a pancreaticoduodenectomy, and the uniform transfixing suture technique, rather than the interrupted suture technique which is tailored to the pancreatic anatomy, may therefore have the limitations in preventing leaks from small side branches on the pancreatic cut surface, or may even produce leaks from the suture injury to the main pancreatic duct itself. Although a standardized single approach to pancreatic anastomosis may help to reduce operative morbidity after pancreatic head resection,[42] it is reasonable to modify the pancreatic anastomosis depending on the diverse intraoperative pancreatic scenarios because the anatomical features of the pancreatic stump vary greatly among patients. In performing a double-layer pancreaticojejunostomy, we generally recommend a radial arrangement of the outer-layer interrupted sutures around the pancreatic duct for a round or an oval-shaped pancreatic stump, while a parallel arrangement of the sutures perpendicularly to the major axis of the pancreatic stump for a flat-shaped pancreatic stump. To achieve a close, safe approximation between the pancreatic stump and the jejunal wall in patients with a pancreatic duct adjacent to the posterior cut edge of the pancreatic stump, the first and second stitches for the posterior outer row of sutures should be placed close to the cephalic and caudal corner of the pancreatic duct, and then penetrated to the posterior surface just below the pancreatic duct.

In conclusion, the presence of a small pancreatic duct, a soft pancreatic gland without fibrosis, a high output of pancreatic juice, and a pancreatic duct adjacent to the posterior cut edge increases the risk of developing a clinically relevant pancreatic fistula following a pancreatic head resection. Modification of the anastomosis technique for the approximation of the pancreatic stump to the jejunum according to the anatomical status of the pancreatic remnant is effective in reducing the fistula rate when performing an end-to-side, duct-to-mucosa pancreaticojejunostomy.

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Figure Legends

Figure 1. The transfixing suture technique for pancreaticojejunostomy. The sutures for the outer layer are inserted from the anterior surface of the pancreatic remnant, introduced straight through the pancreatic parenchyma to the posterior surface, and then lifted the seromuscular layer of the jejunum.

Figure 2. Anatomical variation of the pancreatic stump: (a) A round-shaped pancreatic stump, (b) An oval-shaped pancreatic stump, (c) A flat-shaped pancreatic stump, (d) A pancreatic duct adjacent to the posterior cut edge.

Figure 3. The interrupted suture technique for pancreaticojejunostomy in patients with a round or an oval-shaped pancreatic stump. (a) The outer row of sutures is arranged circumferentially around the pancreatic duct in a radial fashion. (b) Anterior outer row of sutures between the pancreatic stump and the jejunal seromuscular layer in a patient with an oval-shaped pancreatic stump.

Figure 4. The interrupted suture technique for pancreaticojejunostomy in patients with a flat-shaped pancreatic stump. (a) The outer row of sutures is placed perpendicularly to the major axis of the pancreatic stump in a parallel fashion. (b) Posterior outer row of sutures between the pancreatic stump and the jejunal seromuscular layer in a patient with a flat-shaped pancreatic stump.

Figure 5. The interrupted suture technique for pancreaticojejunostomy in patients with a pancreatic duct close to the posterior cut edge of the pancreatic stump (a). The first and second stitches for the posterior outer row of interrupted sutures in a patient with a pancreatic duct adjacent to the posterior cut edge (b). The stitches are inserted from the pancreatic cut surface close to the cephalic and caudal corner of the proposed inner suture line, and then penetrate to the posterior surface of the pancreas just below the pancreatic duct. A sonde is placed in the main pancreatic duct.

Figure 6. Distance measurement between the pancreatic duct and the cut edge of the pancreatic remnant in the direction of the (a) anterior, (b) posterior, (c) superior, and (d) inferior cut edges.

Table 1. Indication for pancreatic head resection

	No. of patients	Surgery			
		PPPD	PD	PHRSD	DPPHR
Intraductal papillary mucinous neoplasm of the pancreas	29	15	3	7	4
Pancreatic ductal adenocarcinoma	27	19	8	0	0
Bile duct carcinoma	21	20	1	0	0
Ampullary carcinoma	7	5	1	1	0
Chronic pancreatitis	4	4	0	0	0
Endocrine tumor of the pancreas	2	0	0	1	1
Solid pseudopapillary tumor of the pancreas	2	2	0	0	0
Gallbladder carcinoma	2	1	1	0	0
Gastric carcinoma	1	0	1	0	0

PPPD: pylorus-preserving pancreaticoduodenectomy

PD: pancreaticoduodenectomy

PHRSD: pancreatic head resection with segmental duodenectomy

DPPHD: duodenum-preserving total pancreas head resection

Table 2. Univariate analysis of perioperative risk factors for clinically relevant pancreatic fistula following pancreatic head resection

Variables	Overall (n = 95)	Clinically relevant fistula (n = 14)	No fistula[a] (n = 81)	*P* value
Age (years) (mean ± SD)	68.9±9.7	66.3±9.8	69.4±9.5	0.219
Gender				0.142
Male	51	10 (20)	41 (80)	
Female	44	4 (9)	40 (91)	
History of jaundice				0.723
Yes	31	4 (13)	27 (87)	
No	64	10 (16)	54 (84)	
Laboratory values				
Lymphocyte (1000/mm^3)	2.0±0.7	1.9±0.4	2.0±0.5	0.236
Hemoglobin (g/dl)	12.5±07	12.8±0.6	12.3±0.4	0.581
Albumin (g/dl)	3.8±0.8	3.7±0.7	3.8±0.6	0.769
Total bilirubin (mg/dl)	1.5±1.9	1.6±1.7	1.5±1.4	0.734
Creatinine clearance (ml/min)	68±20	66±18	69±16	0.292
Oral glucose tolerance test				0.334
Normal	43	8 (19)	35 (81)	
Impaired, Diabetic	52	6 (12)	46 (88)	
Hemoglobin A1c (%)	5.8±1.2	6.0±1.5	5.6±0.9	0.412
BT-PABA test (%)	60.7±14.0	67.5±12.9	59.5±13.8	0.032
TIC of the pancreas				< 0.001
Type I	66	14 (21)	52 (79)	
Type II, III	29	0 (0)	29 (100)	
Pathology				0.291
IPMN	29	4 (14)	25 (86)	
Pancreatic ductal adenocarcinoma	27	2 (7)	25 (93)	
Bile duct carcinoma	21	4 (19)	17 (81)	
Ampullary carcinoma	7	1 (14)	6 (86)	
Chronic pancreatitis	4	0 (0)	4 (100)	
Others	7	3 (43)	4 (57)	
Texture of the pancreas				0.035
Soft	52	11 (21)	41 (79)	
Intermediate	22	2 (9)	20 (91)	
Hard	21	1 (5)	20 (95)	
Pancreatic duct size (mm)				0.023
≤3	57	12 (21)	45 (79)	
>3	38	2 (5)	36 (95)	
Thickness of the pancreas (mm)	16.5±3.7	16.6±3.8	16.3±3.4	0.878
Width of the pancreas (mm)	28.1±5.6	28.3±6.3	27.9±5.5	0.866
Location of the pancreatic duct: distance between the pancreatic duct and the cut edge of the pancreatic remnant (mm)				
(a) to the anterior edge	9.1±2.6	10.3±3.1	8.7±2.4	0.121
(b) to the posterior edge	4.1±1.7	3.3±1.9	4.3±1.7	0.041
(c) to the superior edge	11.3±3.5	11.4±2.7	11.1±3.5	0.838
(d) to the inferior edge	13.7±9.5	14.1±4.8	13.6±4.9	0.791
(e) to the posterior edge				0.037
≤3mm	37	9 (24)	28 (76)	
>3mm	58	5 (9)	53 (91)	
Type of pancreatic resection				0.571
PPPD	66	10 (15)	56 (85)	
PD	15	3 (20)	12 (80)	
PHRSD	9	1 (11)	8 (89)	
DPPHR	5	0 (0)	5 (100)	
Lymphadenectomy				0.961
Non	6	1 (17)	5 (83)	
Regional	30	4 (13)	26 (87)	
Extended	59	9 (15)	50 (85)	
Pancreaticojejunal anastomosis				0.036
Transfixing suture	51	11 (22)	40 (78)	
Interrupted suture	44	3 (7)	41 (93)	
Use of a pancreatic stent				0.209
Yes	61	11 (18)	50 (82)	
No	34	3 (9)	31 (91)	
Operative time (hours)	8.3±1.0	8.4±1.5	8.3±0.9	0.835
Blood loss (ml)	872±287	864±323	876±223	0.661
Blood transfusion				0.989
With	27	4 (15)	23 (85)	
Without	68	10 (15)	58 (85)	
Surgeon experience				0.913
<15yrs	26	4 (15)	22 (85)	
≥15yrs	69	10 (14)	59 (86)	

[a]: No fistula indicates patients who lacked clinical evidence of fistula - no fistula or Grade A fistula
Values in parentheses are percentages of row totals.
BT-PABA: *N*-benzoyl-L-tyrosyl-*p*-aminobenzoic acid
TIC: time-signal intensity curve
IPMN: Intraductal papillary mucinous neoplasm of the pancreas
PPPD: pylorus-preserving pancreaticoduodenectomy
PD: pancreaticoduodenectomy
PHRSD :pancreatic head resection with segmental duodenectomy
DPPHR: duodenum-preserving total pancreatic head resection

Table 3. Multivariate analysis of perioperative risk factors for clinically relevant pancreatic fistula following pancreatic head resection

Variables	Odds ratio for clinically relevant fistula	95% CI	*p*-value
BT-PABA test (%)	1.04	0.9-1.1	0.204
TIC of the pancreas			
Type II, III	1	-	
Type I	12.58	1.2-23.9	0.001
Texture of the pancreas			
Hard	1	-	
Intermediate	1.26	0.7-6.3	0.982
Soft	4.67	1.2-51.1	0.006
Pancreatic duct size			
>3mm	1	-	
≤3mm	4.05	0.4-40.3	0.186
Distance between the pancreatic duct and the posterior cut edge of the pancreas			
>3mm	1	-	
≤3mm	1.31	0.2-7.0	0.748
Pancreaticojejunal anastomosis			
Interrupted suture	1	-	
Transfixing suture	9.91	1.7-57.5	0.003

BT-PABA: N-benzoyl-L-tyrosyl-p-aminobenzoic acid

TIC: time-signal intensity curve

95% CI: 95% confidence intervals

Table 4. Univariate analysis of perioperative risk factors for clinically relevant pancreatic fistula following pancreatic head resection in comparison between the transfixing suture group and the interrupted suture group

Variables	Transfixing suture			Interrupted suture		
	Clinically relevant fistula (n = 11)	No fistula[a] (n = 40)	*P* value	Clinically relevant fistula (n = 3)	No fistula[a] (n = 41)	*P* value
BT-PABA test (%)	68.9±14.1	58.5±15.6	0.033	62.7±7.5	60.4±11.9	0.742
TIC of the pancreas			0.001			0.963
Type I	11 (31)	24 (69)		3 (10)	28 (90)	
Type II, III	0 (0)	16 (100)		0 (0)	13(100)	
Texture of the pancreas			0.001			0.628
Soft	9 (41)	13 (59)		2 (7)	28 (93)	
Intermediate	1 (6)	16 (94)		1 (20)	4 (80)	
Hard	1 (8)	11 (92)		0 (0)	9(100)	
Pancreatic duct size			< 0.001			0.309
≤3mm	11 (37)	19 (63)		1 (4)	26 (96)	
>3mm	0 (0)	21(100)		2 (12)	15 (88)	
Distance between the pancreatic duct and the posterior cut edge of the pancreas			0.001			0.079
≤3mm	9 (45)	11 (55)		0 (0)	17(100)	
>3mm	2 (6)	29 (94)		3 (12)	23 (88)	

[a]: No fistula indicates patients who lacked clinical evidence of fistula - no fistula or Grade A fistula

Values in parentheses are percentages of row totals.

BT-PABA: *N*-benzoyl-L-tyrosyl-*p*-aminobenzoic acid

TIC: time-signal intensity curve

Figure 1

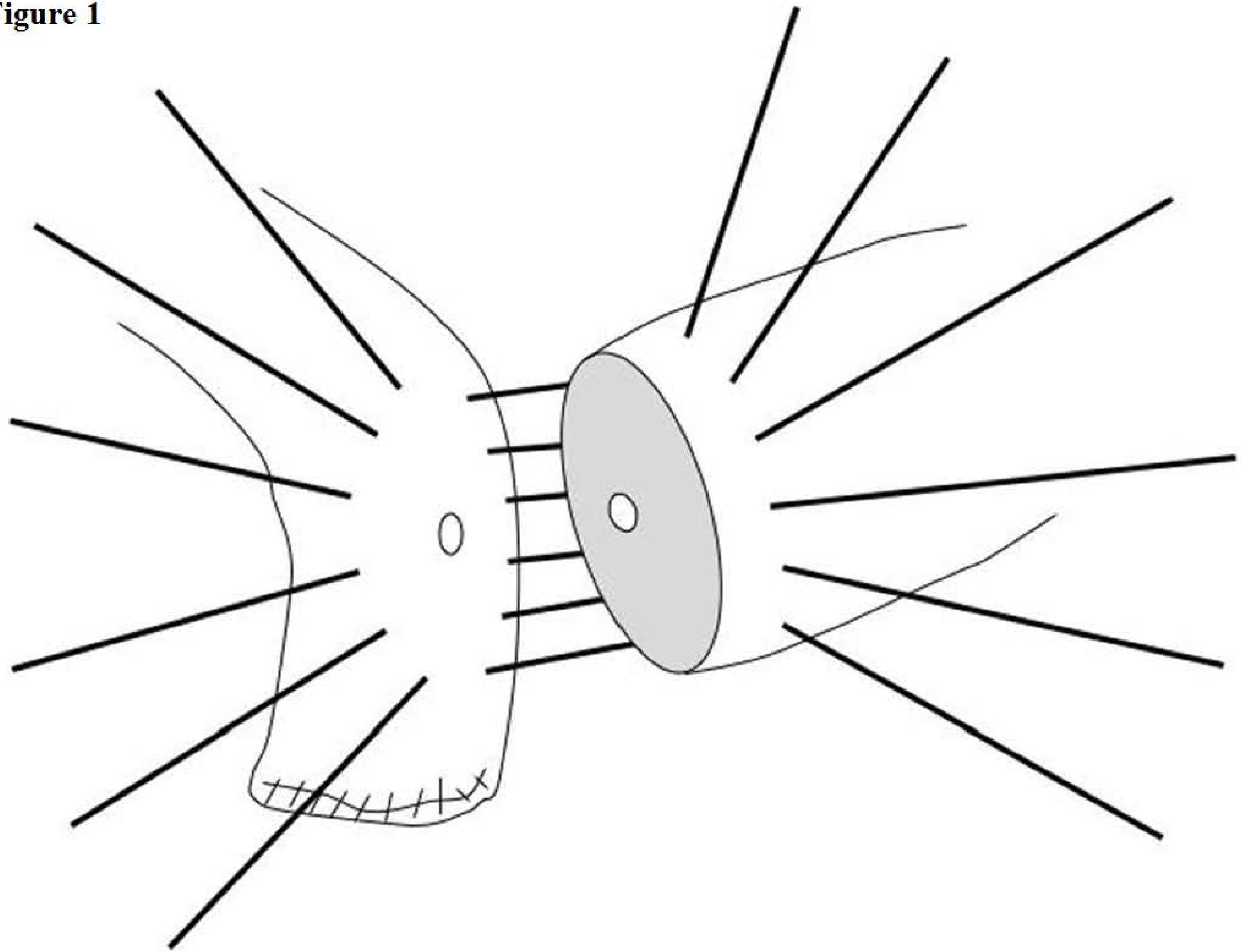

Figure 2

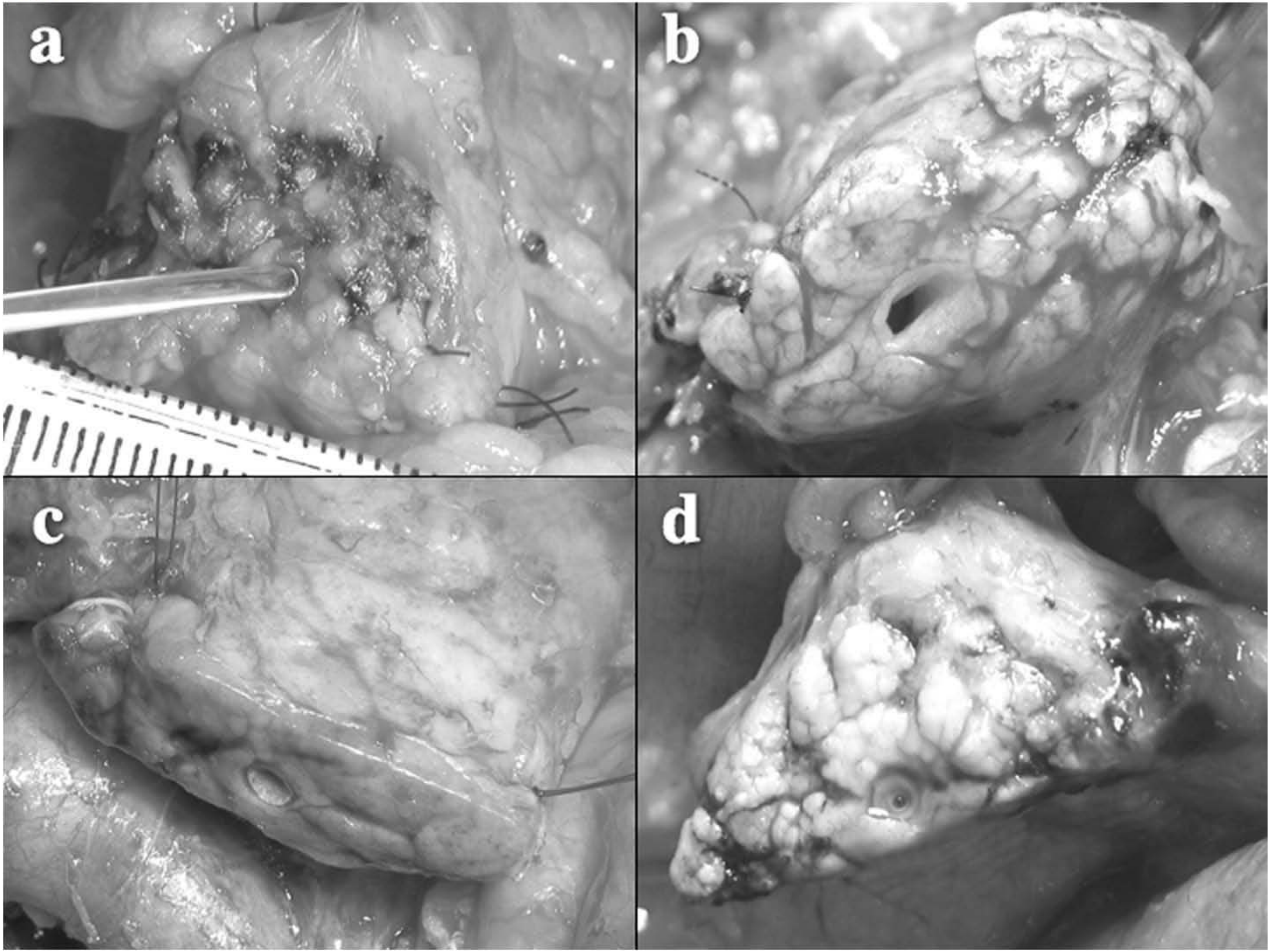

Figure 3a

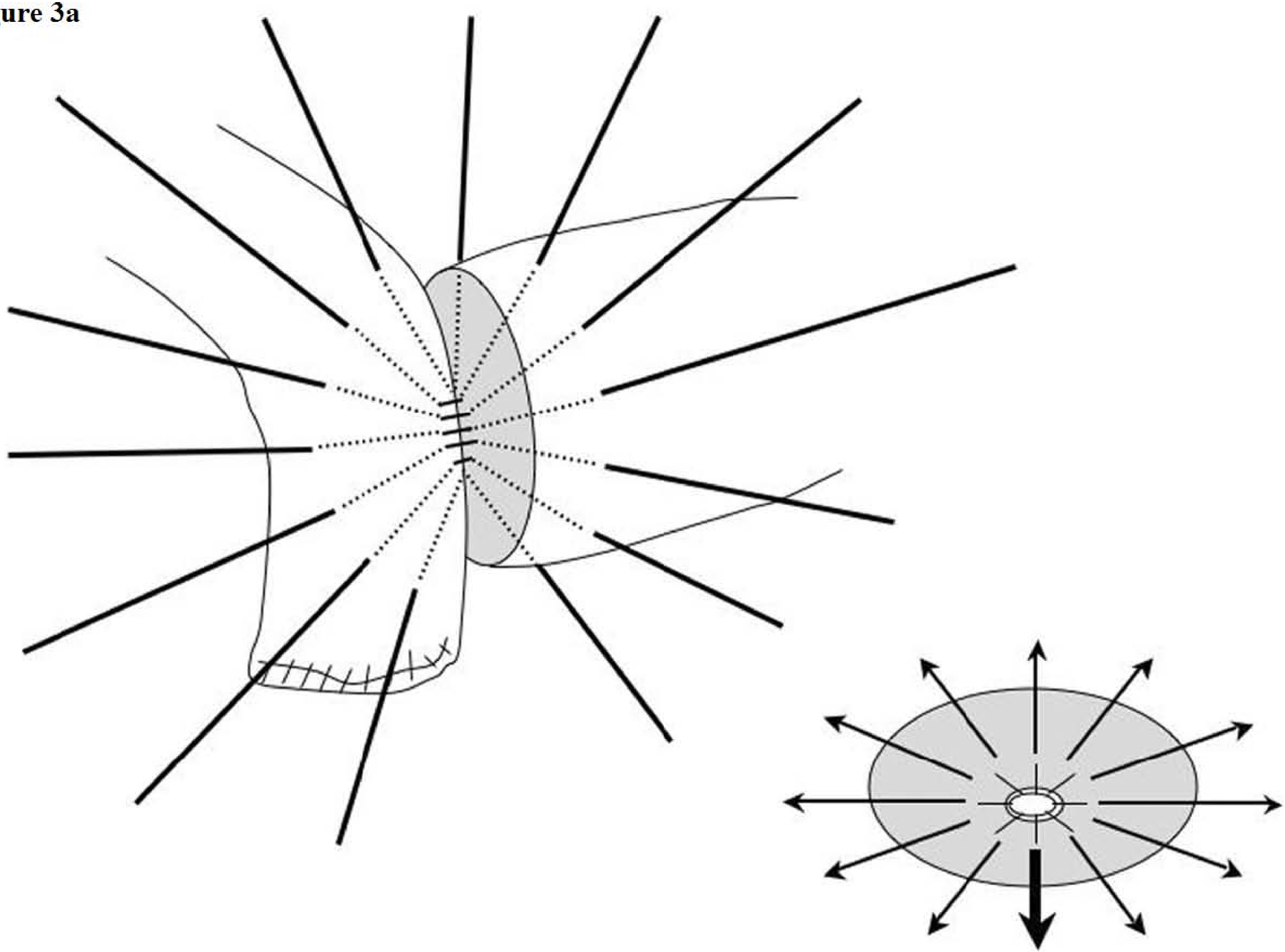

Figure 3b

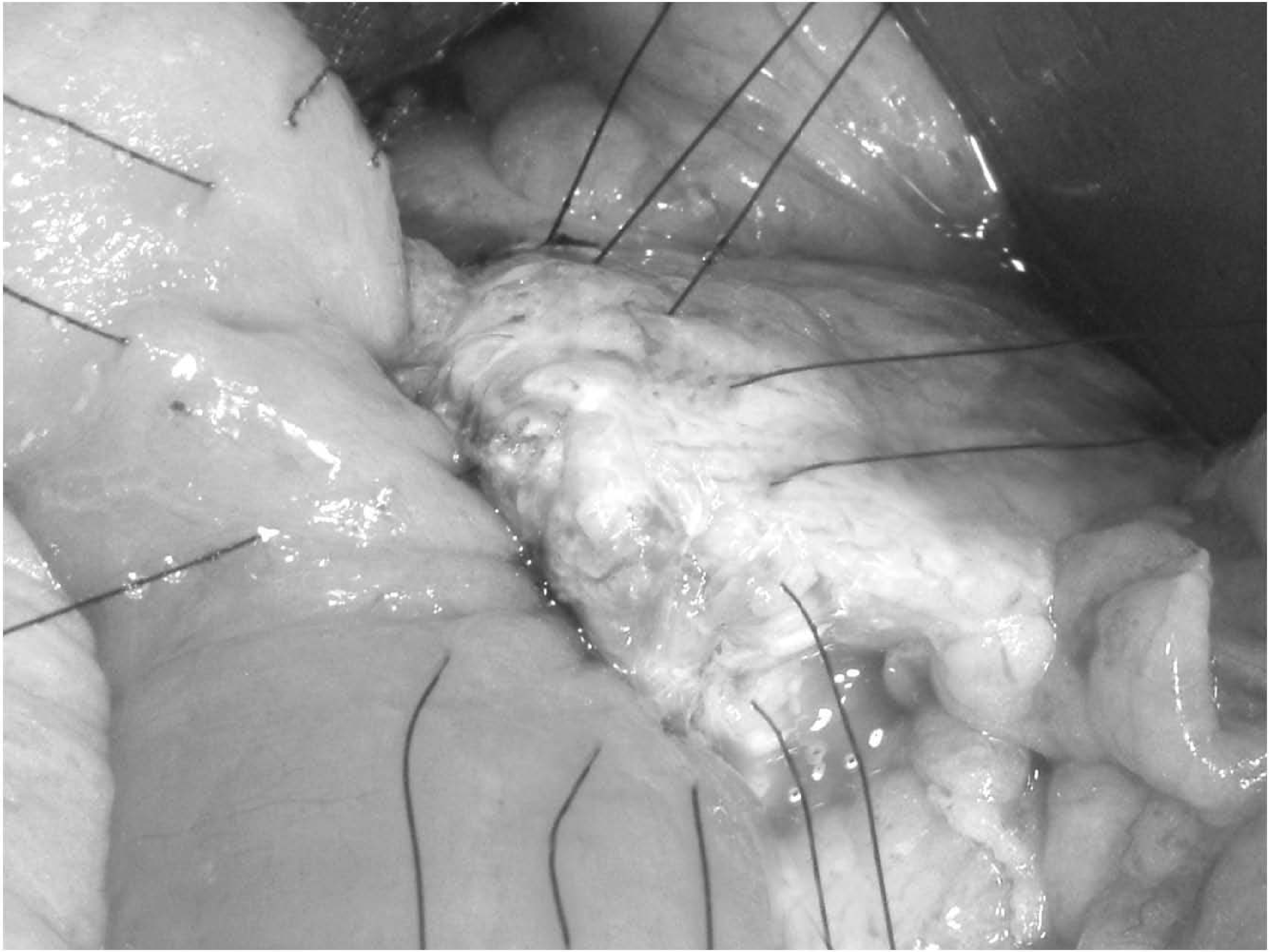

Figure 4a

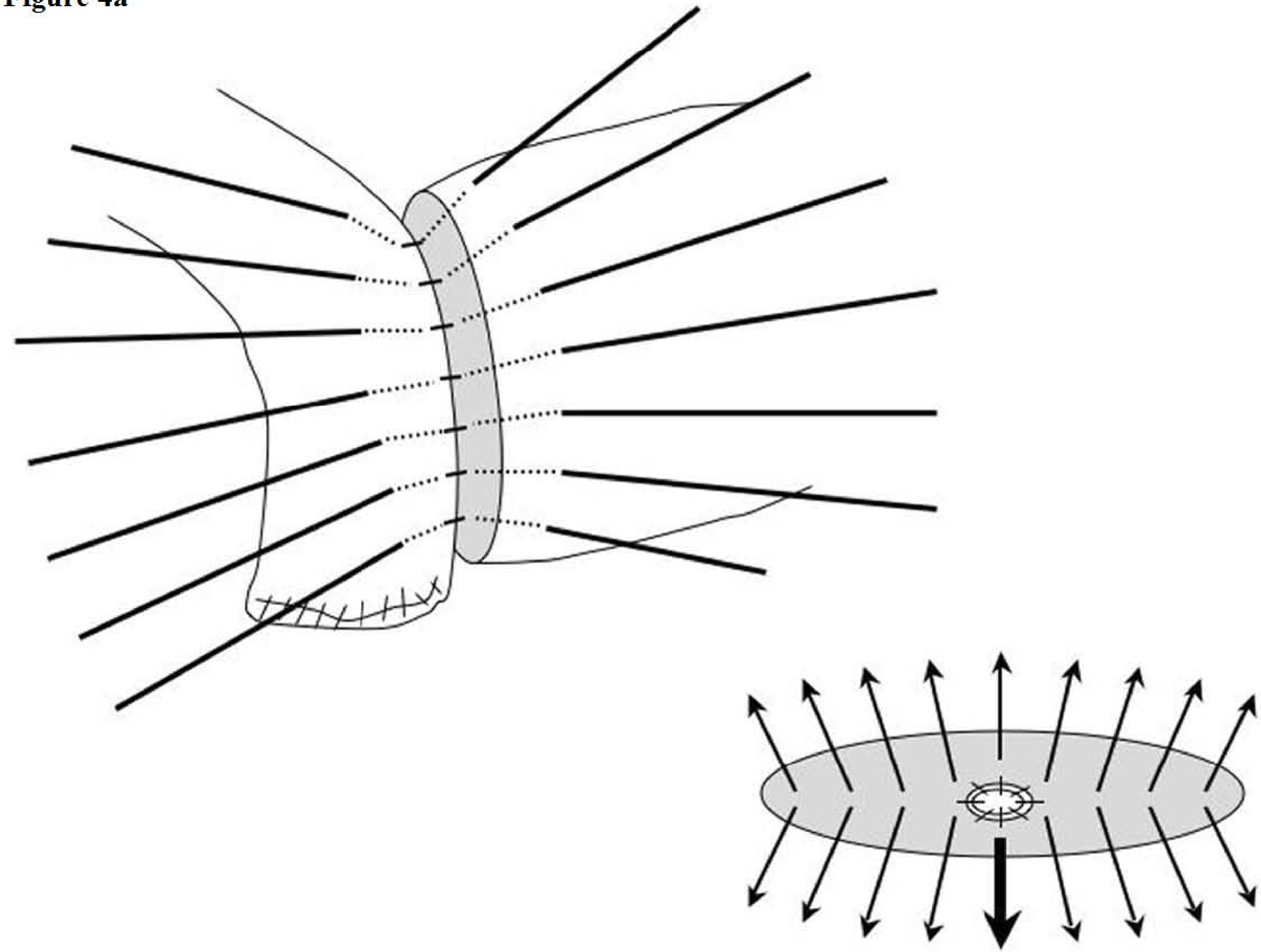

Figure 4b

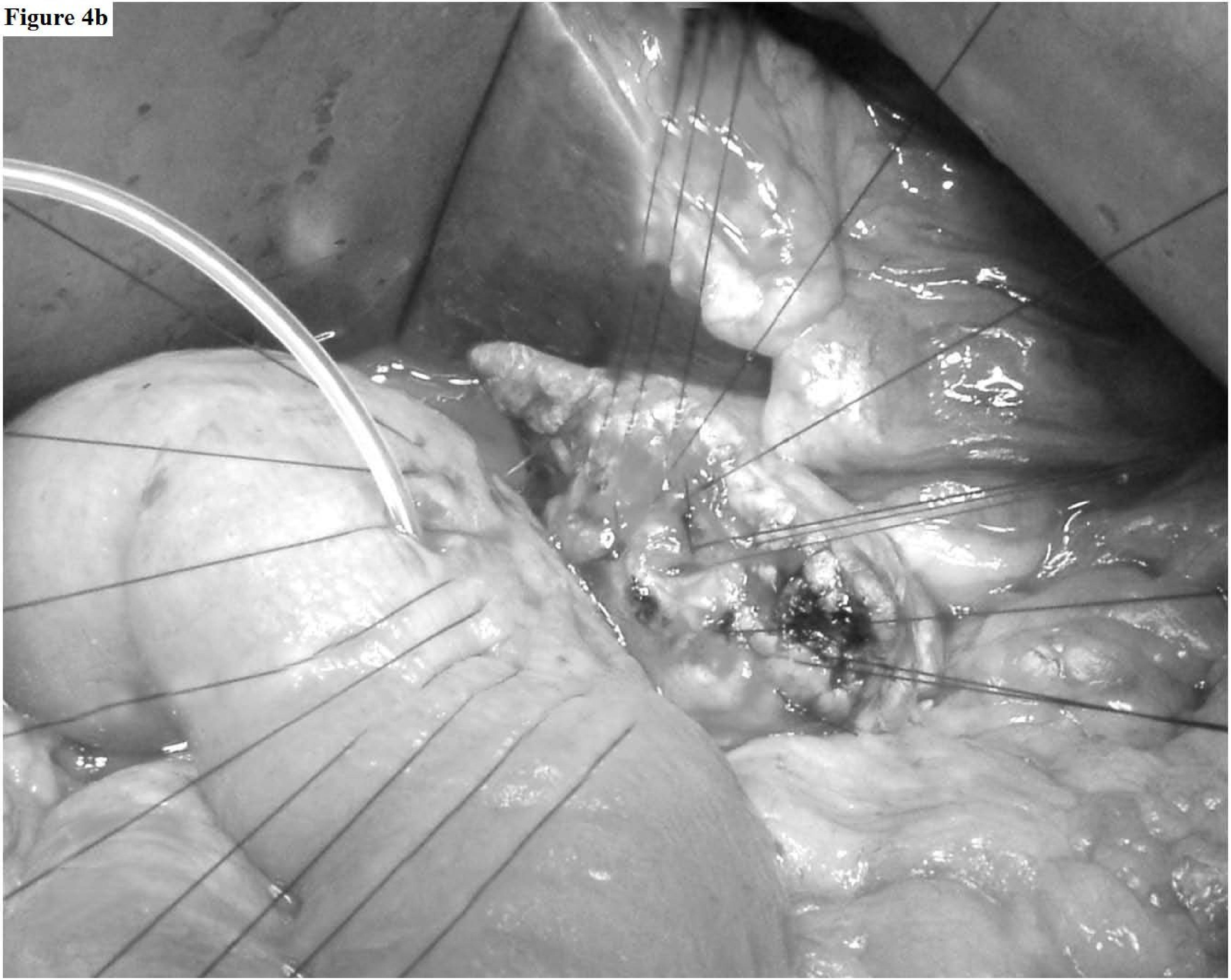

Figure 5a

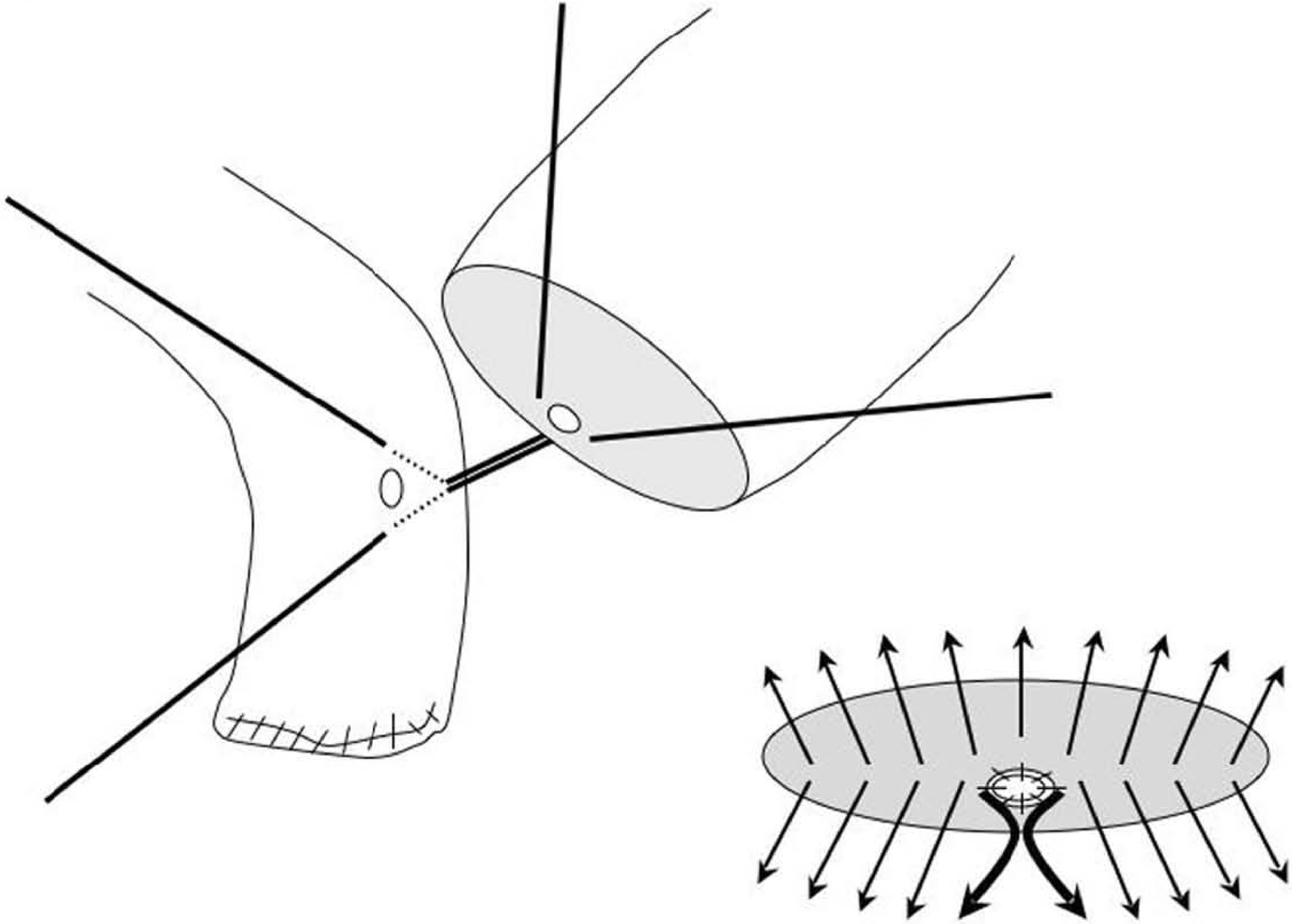

Figure 5b

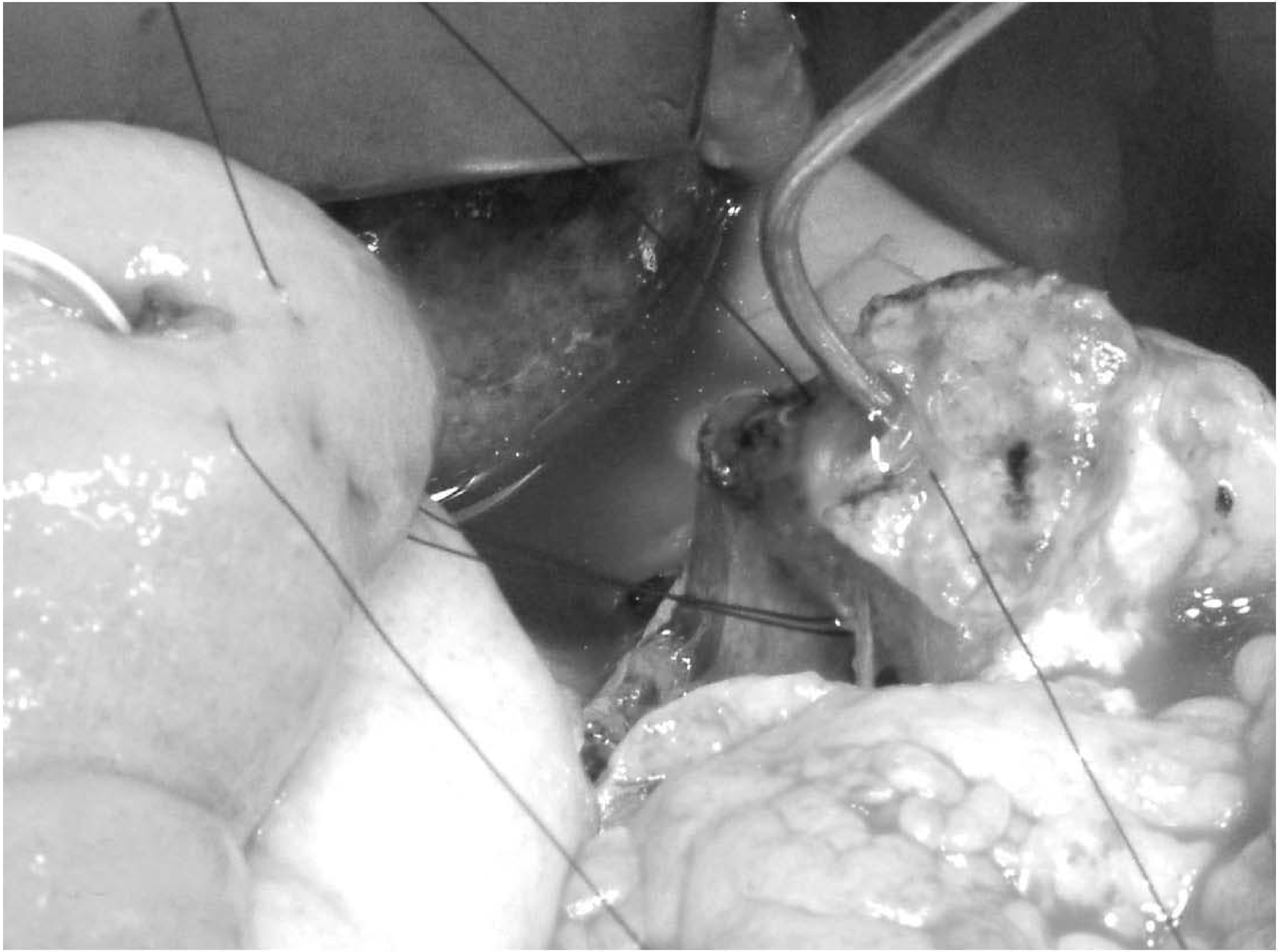

Figure 6