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PICTORIAL REVIEW

Post-cholecystectomy syndrome: spectrum of biliary findings at magnetic resonance cholangiopancreatography

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ABSTRACT. Post-cholecystectomy syndrome (PCS) is defined as a complex of heterogeneous symptoms, consisting of upper abdominal pain and dyspepsia, which recur and/or persist after cholecystectomy. Nevertheless, this term is inaccurate, as it encompasses biliary and non-biliary disorders, possibly unrelated to cholecystectomy. Biliary manifestations of PCS may occur early in the post-operative period, usually because of incomplete surgery (retained calculi in the cystic duct remnant or in the common bile duct) or operative complications, such as bile duct injury and/or bile leakage. A later onset is commonly caused by inflammatory scarring strictures involving the sphincter of Oddi or the common bile duct, recurrent calculi or biliary dyskinesia. The traditional imaging approach for PCS has involved ultrasound and/or CT followed by direct cholangiography, whereas manometry of the sphincter of Oddi and biliary scintigraphy have been reserved for cases of biliary dyskinesia. Because of its capability to provide non-invasive high-quality visualisation of the biliary tract, magnetic resonance cholangiopancreatography (MRCP) has been advocated as a reliable imaging tool for assessing patients with suspected PCS and for guiding management decisions. This paper illustrates the rationale for using MRCP, together with the main MRCP biliary findings and diagnostic pitfalls.

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Post-cholecystectomy syndrome (PCS) consists of a group of abdominal symptoms that recur and/or persist after cholecystectomy [1, 2]. It is defined as early if occurring in the post-operative period and late if it manifests after months or years.

Although this term is used widely, it is not completely accurate, as it includes a large number of disorders, both biliary (Table 1) and extra-biliary (Table 2) in origin, that may be unrelated to cholecystectomy [1, 2]. It has been reported that ~50% of these patients suffer from organic pancreaticobiliary and/or gastrointestinal disorders, whereas the remaining patients are affected by psychosomatic or extra-intestinal diseases. Moreover, in 5% of patients who undergo laparoscopic cholecystectomy, the reason for chronic abdominal pain remains unknown [1]. Probably because of the uncertainty in nosographic definition, the reported prevalence of PCS ranges from very low [2] to 47% [1]. Symptoms include biliary or non-biliary-like abdominal pain, dyspepsia, vomiting, gastrointestinal disorders and jaundice, with or without fever and cholangitis [1, 2]. Severe symptoms are more likely to represent a complication of cholecystectomy if they occur early or to express a definite treatable cause when compared with non-specific, dyspeptic or mild symptoms. A non-biliary aetiology of PCS should be suspected if no calculi or gallbladder abnormalities are found at cholecystectomy and symptoms are similar to those suffered pre-operatively [1]. Treatment for PCS is tailored to the specific cause and includes medication, sphincterotomy, biliary stenting, percutaneous drainage of bilomas and surgical revision for severe strictures [1–4].

The traditional imaging approach to PCS includes ultrasonography and/or CT, followed by direct cholangiography, as the gold standard [2]. Biliary scintigraphy has been advocated as a reliable non-invasive tool to evaluate sphincter of Oddi activity. Nevertheless, it has limited diagnostic accuracy compared with sphincter of Oddi manometry (SOM), which represents the gold standard for assessing functional forms of PCS [5]. Magnetic resonance cholangiopancreatography (MRCP) is a non-invasive and reliable alternative to direct cholangiography for the evaluation of the biliary tract. This has led to an increasing demand for MRCP to be used in patients with suspected PCS, despite the fact that its role in patient management has been assessed only briefly [1, 2]. The main advantages of using MRCP are its non-invasiveness and its capability to provide a roadmap for interventional treatments [1–4]. Heavily T_2 weighted images with a high bile duct-to-background contrast may be obtained either with a set of single breath-hold, single-shot turbo spin-echo projective thick slabs or by using a respiratory-triggered three-dimensional (3D) turbo spin-echo sequence for a detailed representation of the biliary tree, together with multiplanar reformations and volumetric reconstructions [2–4]. Alternatives to the standard MRCP techniques

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Table 1. Main biliary causes of post-cholecystectomy syndrome (PCS) related to cholecystectomy. (Biliary malignancies are the most frequent causes of PCS unrelated to cholecystectomy [1])

Early PCS
Retained stones in the cystic duct stump and/or common bile duct
Bile duct injury/ligature during surgery
Bile leakage
Late PCS
Recurrent stones in the common bile duct
Bile duct strictures
Cystic duct remnant harbouring stones and/or inflammation
Gallbladder remnant harbouring stones and/or inflammation
Papillary stenosis
Biliary dyskinesia

include the use of fat-saturated 3D spoiled gradient-echo sequences in conjunction with intravenous contrast agents excreted (to a varying degree) via the biliary system, such as mangafodipir trisodium, gadobenate dimeglumine or gadoxetic acid. Advantages over fluid-based techniques include biliary function assessment, background suppression of ascites and bowel fluid, and identification of biliary leaks following cholecystectomy, with a reported sensitivity and specificity of 86% and 83%, respectively (Figure 1) [6].

Lithiasis

Calculi in the common bile duct (CBD) or cystic duct remnant are the most common cause of PCS. Calculi are traditionally classified as ''retained'' or ''recurrent'', if found before or after two years following surgery, respectively. The former are likely to have been present at the time of intervention; the latter are usually ''secondary calculi'', which form as a result of biliary stasis (often caused by co-associated strictures, papillary stenosis or biliary dyskinesia) [1].

MRCP has a sensitivity of 95–100% and a specificity of 88–89% for detecting CBD calculi [1]. They appear as smoothly marginated filling defects within the CBD or cystic duct remnant, usually in the dependent position, surrounded by a thin rim of hyperintense bile (Figure 2). If a multislice technique is used, the analysis of maximum intensity projection reconstructions should be associated with a careful scrolling of source thin-slice images in order to avoid overlooking calculi, especially the smallest ones (Figure 3) [7]. When calculi are impacted in the intramural portion of the CBD, with minimal surrounding fluid, they may be not detectable on MRCP [8]. Repeated single-slice acquisitions of the biliary tree are useful to differentiate impacted calculus from the ''pseudo-calculus'' effect resulting from a prominent or spasmodic papillary sphincter (Figure 4). Dynamic scanning is also helpful in avoiding false-negative cases, as calculi are better appreciated on images obtained during sphincter relaxation [8].

Bile duct injury and biliary leaks

The rate of bile duct injuries is slightly higher using laparoscopic surgery than open surgery (0.5% and 0.15%, respectively) [3]. In general, a laparoscopic approach allows less complete traction of the gallbladder and cystic duct than open surgery. This can lead to incomplete isolation of anatomical structures and/or traction injury. The main causes of ductal injury are erroneous cutting of bile ducts, inadvertently placed clips or ligatures, periductal bile leakage resulting in fibrosis and thermal injury owing to electrocautery [3]. Common sites of biliary leaks include injured ducts, the cystic duct stump and the gallbladder stump. Fluid collections in the gallbladder bed occur in up to 14% of patients following cholecystectomy and tend to resolve spontaneously; collections persisting for more than a week or fluid outside the gallbladder bed raise the suspicion of a biliary leak and/or injury [1].

Bile duct injury manifests as a leak, stricture or transection [9]. Strictures and transection appear as a focal narrowing or abrupt interruption of the bile duct, respectively, with or without biliary dilatation upstream (Figure 5). The distinction between biliary stricture and transection is often impossible. Nevertheless, a complete lack of visualisation on source and projection images is highly suspicious for duct disruption [9]. Injuries derived from laparoscopic cholecystectomy are usually more extensive than those following an open surgical approach; they may involve major intrahepatic bile ducts and are more frequent in patients with anatomic variants [3, 10]. Evolution of duct injury is towards duct stricture formation and fibrosis/atrophy of the obstructed liver segment [10].

A hilar and/or subhepatic fluid collection close to the CBD or strictured ducts, or in the right side of the abdomen, is suspicious of a biliary origin, particularly if a thin hyperintense connection to the biliary tree is demonstrated (Figure 6). Nevertheless, biloma is often indistinguishable from post-operative collections or

Table 2. Main extrabiliary causes of post-cholecystectomy syndrome (modified from [1])

Gastrointestinal causes	Extra-intestinal causes
Acute/chronic pancreatitis (and complications)	Psychiatric and/or neurological disorders
Pancreatic tumours	Coronary artery disease
Pancreas divisum	Intercostal neuritis
Hepatitis	Wound neuroma
Oesophageal diseases	Unexplained pain syndromes
Peptic ulcer disease	
Mesenteric ischaemia	
Diverticulitis	
Organic or motor intestinal disorders	

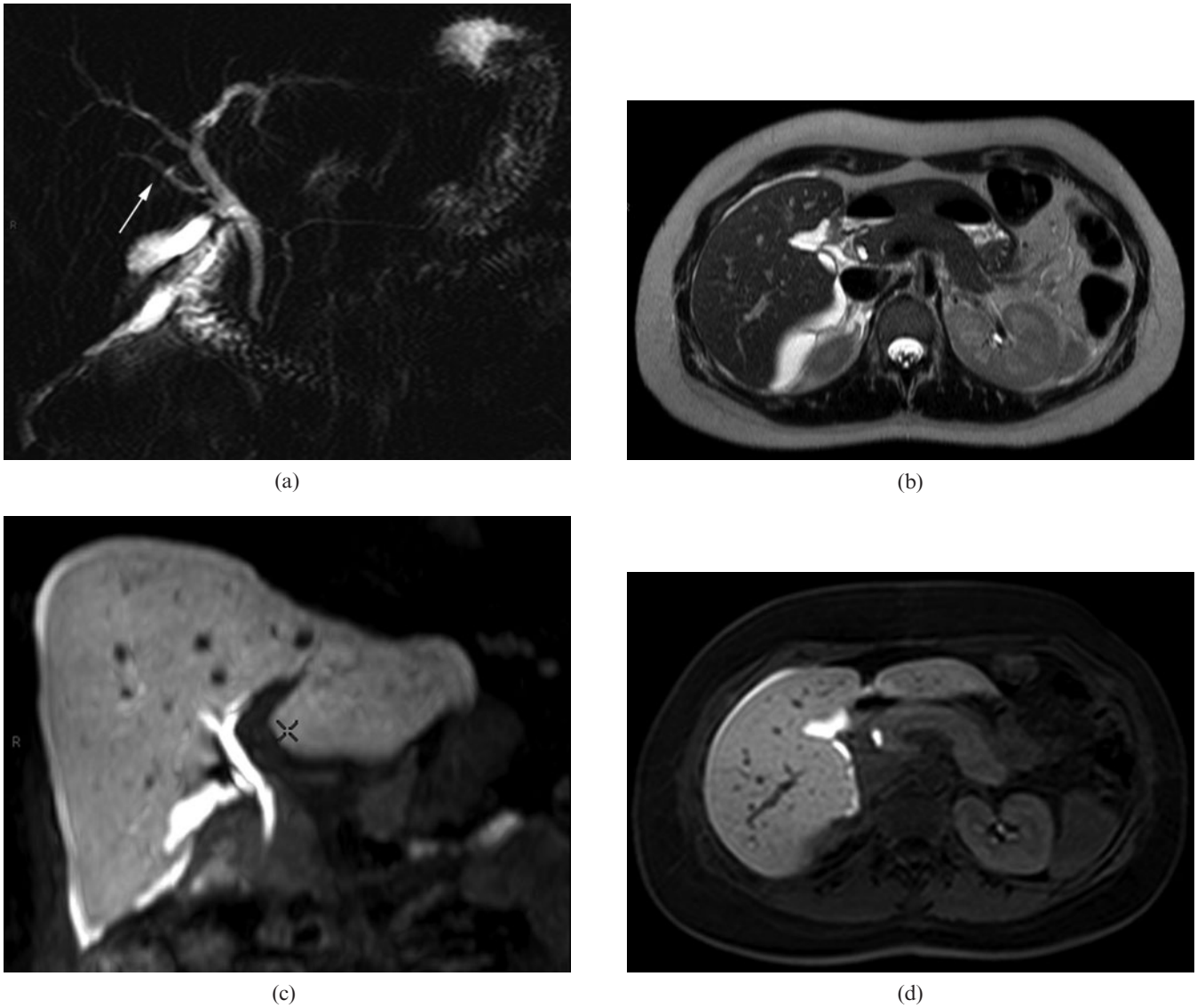


Figure 1. A 31-year-old female patient presenting with right upper abdominal pain 1 week after laparoscopic cholecystectomy. (a) T_2 weighted projective magnetic resonance cholangiopancreatography image shows an elongated hyperintense fluid collection proximal to the cystic duct stump, along with a small amount of subhepatic free fluid, which is well delineated in the axial T_2 weighted single-shot fast spin-echo image. (b) An aberrant right intrahepatic bile duct is visible (arrow in (a)). (c) Coronal and (d) axially reformatted T_1 weighted fat saturated three-dimensional gradient echo images obtained 20 min after intravenous injection of gadoxetic acid document the passage of contrast agent from the cystic duct stump into the fluid collection and the subhepatic space, demonstrating the presence of a bile leak. (Courtesy of Celso Matos, MD, Brussels, Belgium.)

haemorrhage, unless direct cholangiography is performed to demonstrate contrast leak [3].

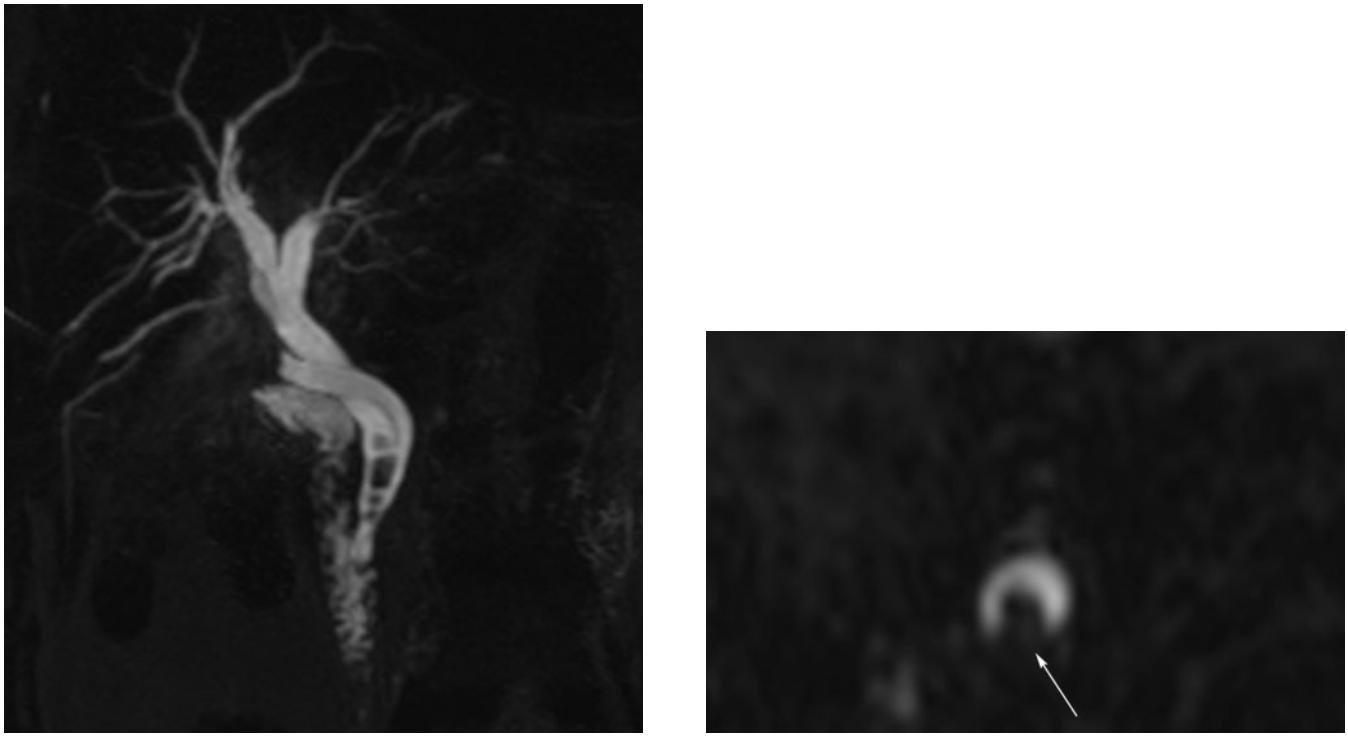
Strictures

Strictures occur in up to 0.6% of cases after cholecystectomy. If not involving previously injured anatomical variants, strictures usually occur because the CBD is injured during clamping or ligation of the cystic duct close to its insertion [10]. Strictures are the most common late complication of biliary surgery, developing a few months to years after cholecystectomy.

On MRCP, they appear as a narrowing of the luminal signal and are usually short with smooth regular margins (Figure 7). The typical locations of strictures are in the CBD, near the insertion of the cystic duct, or at the hepatic confluence [10]. Defining the site and extent of a stricture (according to the Bismuth classification shown in Figure 8) is of crucial importance, particularly when bilio-digestive reconstruction is planned. MRCP tends to overestimate the length (and the extent) of the stricture, especially when the duct immediately distal to the stricture is collapsed (but not strictured). This can lead to misinterpretation of the position of the distal end of the stenosis [4]. The use of the multislice technique, with a careful analysis of source images, helps to reduce the risk of overestimating the stricture length [4].

Biliary dyskinesia and papillary stenosis

The term ''biliary dyskinesia'' has traditionally been used to refer to primarily motor forms of sphincter of



(a) (b)

Figure 2. A 60-year-old female patient presenting with colic pain in the abdominal right upper quadrant 3 weeks after laparoscopic cholecystectomy. (a) Maximum intensity projection reconstruction of the biliary tree shows multiple calculi in the distal portion of the common bile duct as small filling defects, surrounded by a thin rim of bile signal. Mild biliary dilation is present upstream. The redundant cystic stump inserts at the medial aspect of the common bile duct. (b) The dependent position of the filling defect (arrow) is of help in differentiating it from pneumobilia in patients with previous sphincterotomy or biliodigestive anastomosis.

Oddi dysfunction (SOD) (Table 3). It occurs more frequently years after cholecystectomy, and is diagnosed in 9–11% of patients with abdominal pain [11]. Papillary stenosis has been described as an organic variant of SOD related to a fibrotic narrowing of the sphincter in response to inflammatory processes from pancreatitis or gallstone migration through the papilla [11]. The causes of abdominal pain in these patients are thought to be impeded flow, resulting in ductal hypertension, distension and inflammation. SOM remains the gold standard with which to diagnose SOD and to stratify therapy. Nevertheless, abnormal SOM findings are not frequent in SOD Types II and III (Table 3) and do not differ reliably between primary motor and stenotic forms [11]. The role of MRCP in diagnosing SOD is still undefined, as correlation with endoscopic retrograde cholangiopancreatography or biliary manometry has been poorly investigated, and differentiation between stenotic or spasmotic papilla is difficult. State-of-the-art MRCP techniques may serve as a first-line non-invasive tool with which to demonstrate biliary abnormalities in patients with possible SOD [11].

On MRCP, narrowing of the papilla ranges from a mild, progressive and smoothly marginated stricture to a lack of visualisation of the sphincteric segment (Figure 9), with no clear cause of extrinsic compression. The stricture may extend to the distal aspect of the CBD or main pancreatic duct, and can be associated with a variable degree of biliary and/or pancreatic proximal ductal dilatation. A dynamic evaluation with repeated single thick slices is mandatory to verify whether stenosis is temporary and due to physiological contraction. According to Van Hoe et al [8, 12], a spasmodic sphincter shows no morphological variations and appears either as a prolonged lack of visualisation of the sphincter (Figure 10) or as a thin rim of signal entrapped in a asymmetrically narrowed sphincter (Figure 11).

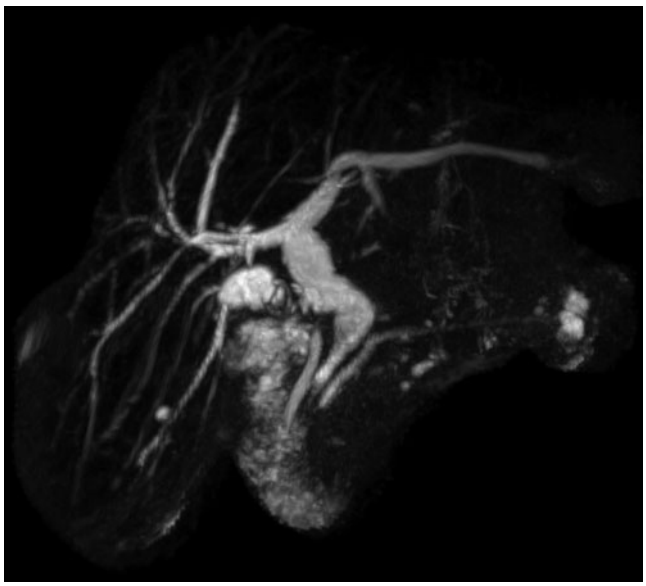
Other biliary findings

The presence of a gallbladder remnant after subtotal cholecystectomy (performed inadvertently or as a surgical option) is very rare. The remnant becomes symptomatic if harbouring gallstones or chronic inflammation. MRCP depicts the remnant filled with bile at the extremity of the cystic duct [1]. Further rare causes of PCS include biliary ascariasis (frequent in tropical and subtropical countries), choledochocele and neuromas and/or granuloma of the cystic duct stump [1].

Conclusions

MRCP techniques are reliable for identifying biliary causes of PCS. Accurate assessment of the site and type of biliary abnormality provides a road-map for interventional procedures, and is crucial for tailoring patients' therapy.

The main limitation of MRCP in evaluating PCS is the evaluation of SOD. As main pancreatic duct dilatation is



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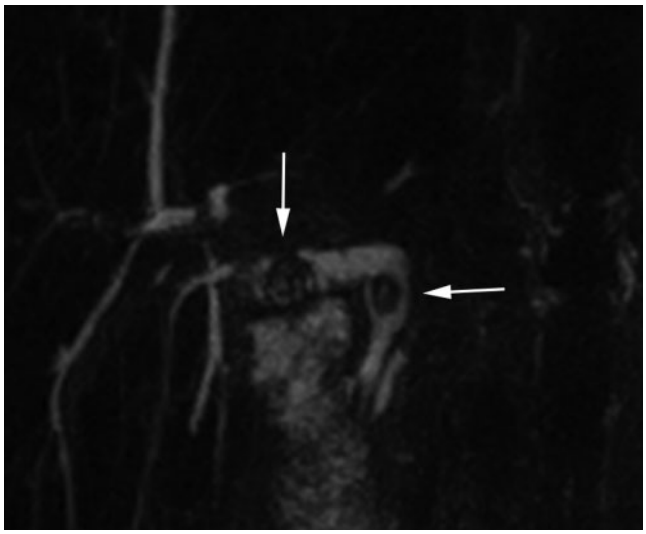

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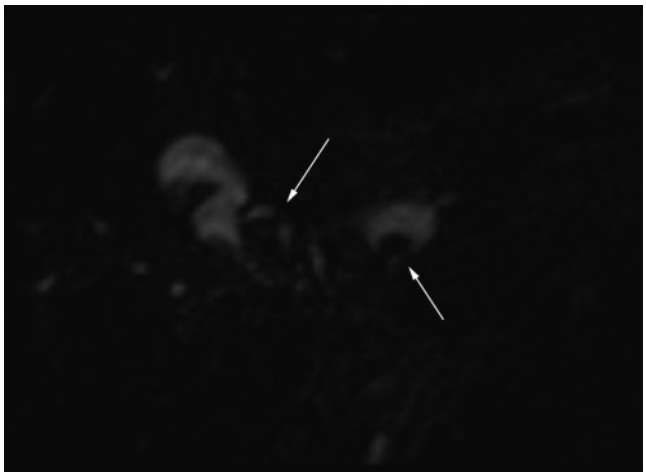


(c)

Figure 3. A 72-year-old female several years after cholecystectomy, who was referred for magnetic resonance cholangiopancreatography because of dyspeptic syndrome and vague upper abdominal pain. (a) Coronal maximum intensity projection (MIP) reconstruction from thin T_2 weighted source images depicts dilation of the upper two-thirds of the common bile duct, intrahepatic biliary tree and cystic duct remnant. A careful scrolling of the (b) coronal and (c) axial thick MIP images better shows the presence of two smoothly marginated filling defects in the cystic duct remnant and in the common bile duct below its insertion, respectively (arrows). The patient's symptoms were relieved after calculi extraction.

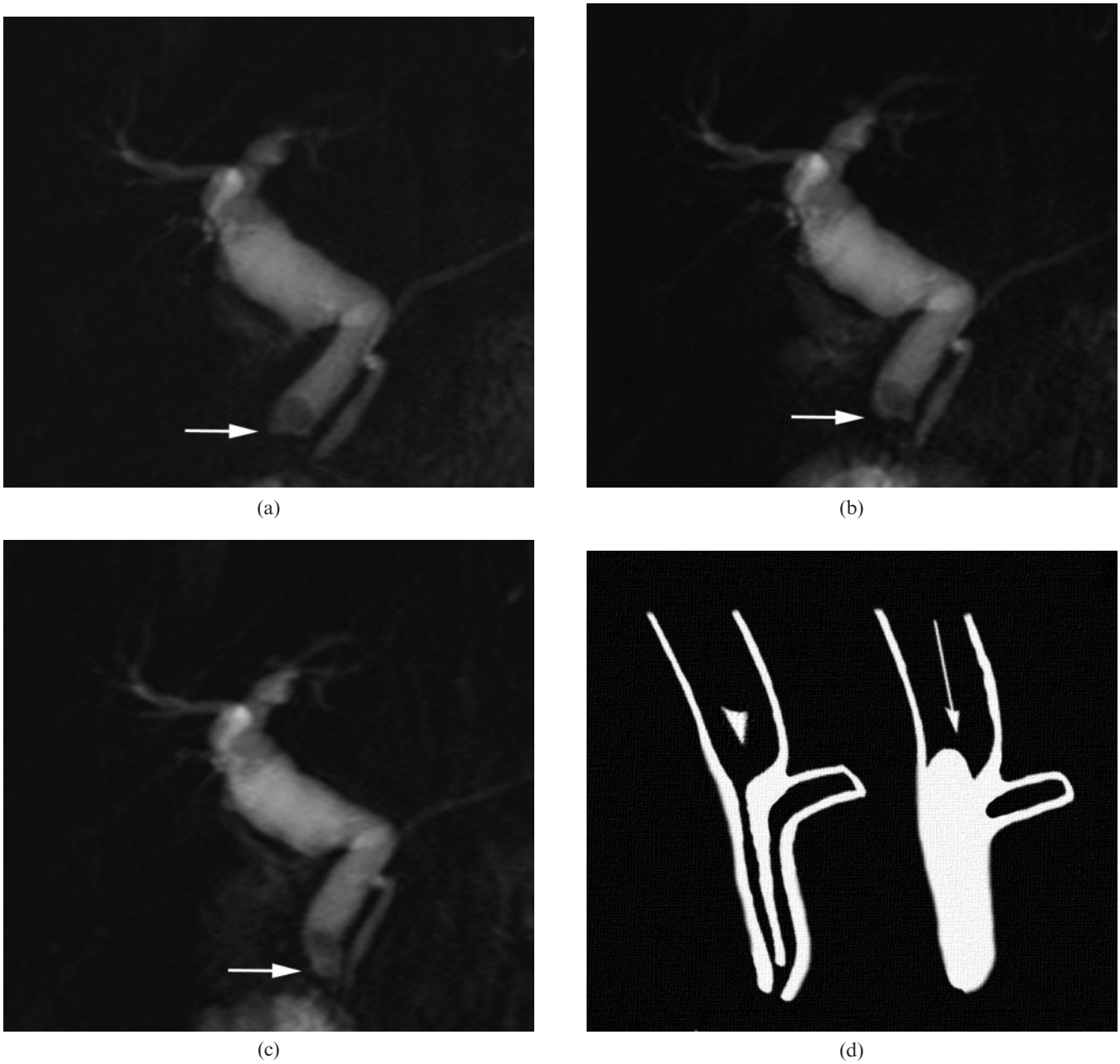
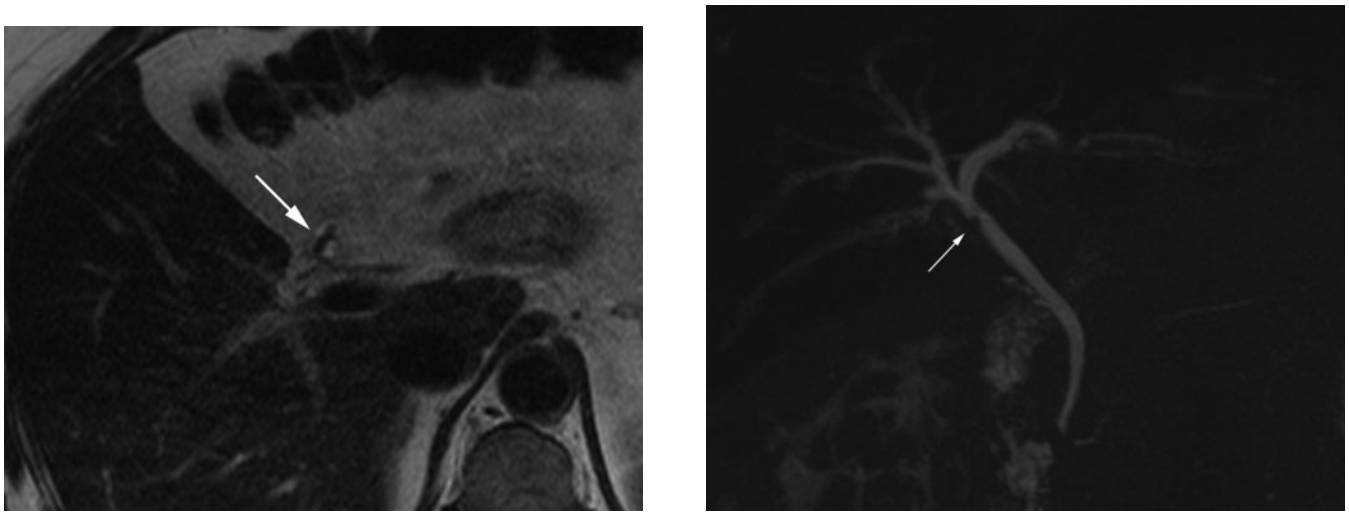


Figure 4. A 57-year-old female patient presenting with biliary-like pain years after cholecystectomy. (a) The heavily T_2 weighted thick slab depicts a calculus in the distal common bile duct and biliary dilatation upstream. The papillary region looks abruptly narrowed, with a concave appearance of the distal border of the suprasphincteric part of the common bile duct (arrow). (b and c) A set of complementary repeated thick slabs demonstrates that the appearance is transitory (arrows). (d) As illustrated, this is caused by a forceful contraction of the superior sphincteric region (arrowhead) with its retrograde ''invagination'' (arrow) [7].



(a) (b)

Figure 5. A 52-year-old male patient who underwent laparoscopic cholecystectomy 5 years previously. Because of several episodes of cholangitis since the time of surgery caused by a known clip inadvertently positioned at the common bile duct just below the hepatic confluence, the patient underwent repeated balloon dilatation procedures. (a) On an axial T_2 weighted turbo spin-echo image, the clip appears as an intensely low-signal structure that partially overlaps the anterior aspect of the common bile duct (arrow). (b) On coronal maximum intensity projection reconstruction from volumetric thin source images, the injury manifests as a wall-sided focal filling defect, causing a moderate luminal stricture (arrow) with slight biliary dilation upstream.

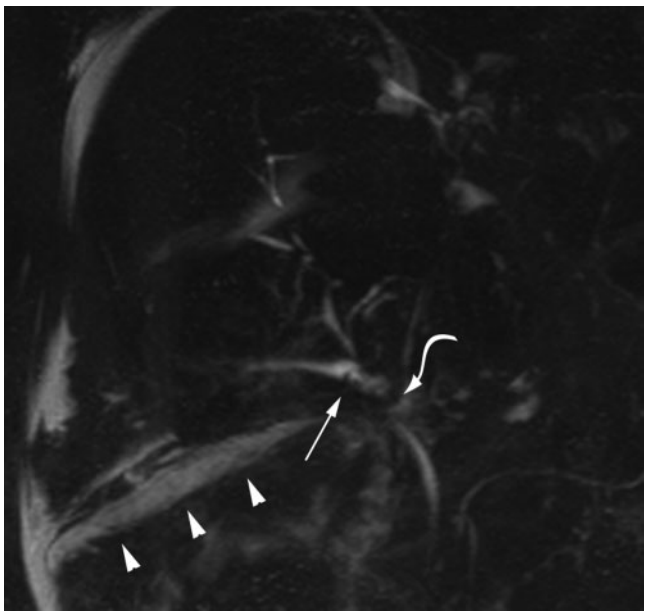


Figure 6. A 78-year-old male patient presenting with abdominal pain, fever and altered liver function tests in the post-operative period after laparoscopic cholecystectomy. Thick coronal maximum intensity projection reconstruction from T_2 weighted thin source images shows a thin rim of hyperintense fluid signal contiguous with the cystic duct stump (arrow). Free fluid is present in the perihepatic space, especially in the subhepatic site (arrowheads). Moreover, a focal stricture of the common bile duct is appreciable just below the insertion of the cystic duct remnant, suggesting a co-existing injury (curved arrow).

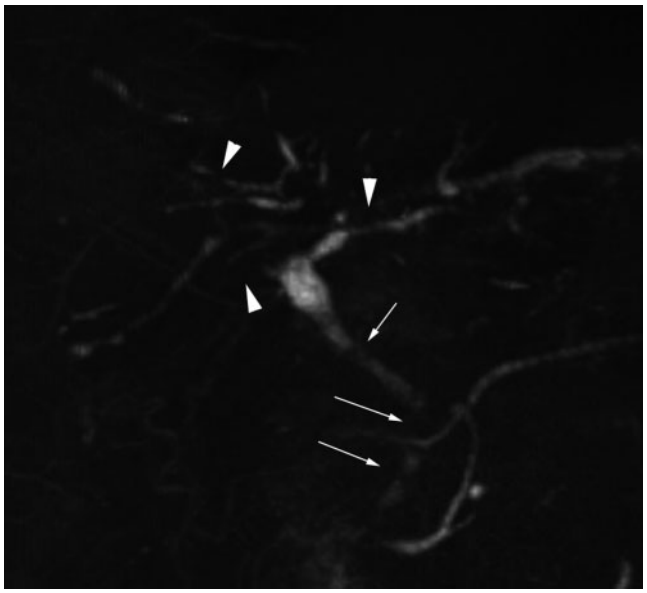


Figure 7. A 70-year-old male patient with a history of recurrent lithiasis and cholangitis after open cholecystectomy. Several previous endoscopic cholangiopancreatograms had been performed. Coronal maximum intensity projection reconstruction from a volumetric turbo spin-echo heavily T_2 weighted sequence shows multiple moderate-to-severe strictures of variable length along the course of the common bile duct (arrows) and intrahepatic bile ducts (arrowheads). No calculi were visible at the time of examination. Strictures were a consequence of either previous common bile duct operative injury or scarring from repeated calculi migration and cholangitis.

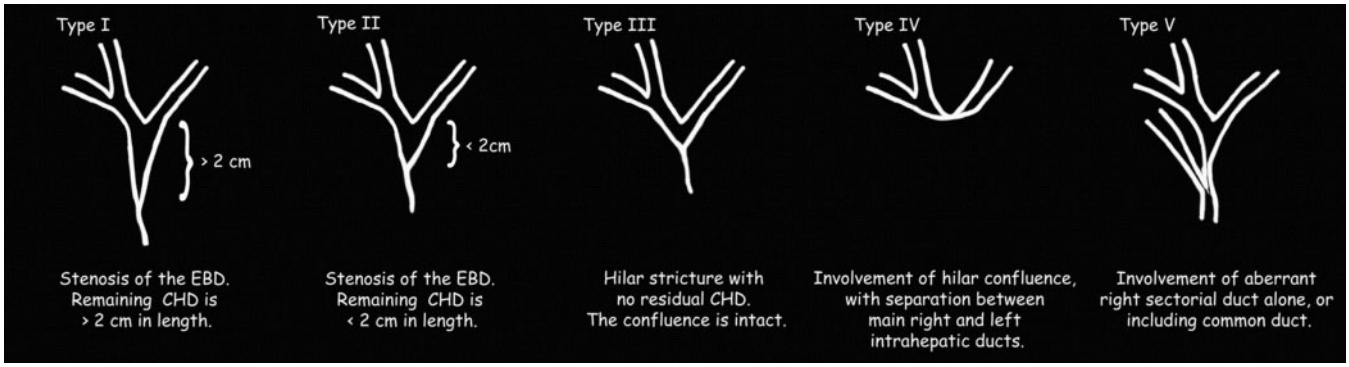
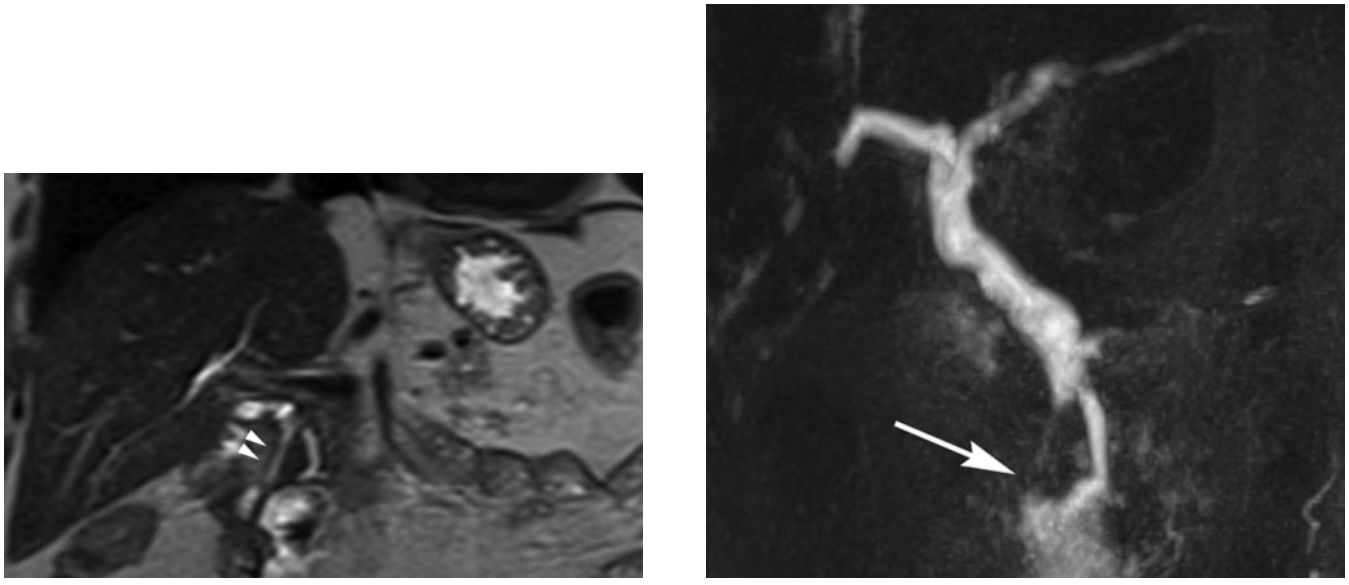


Figure 8. Bismuth classification of bile duct strictures after duct injury, according to their location and relationship to the hepatic duct bifurcation [9]. EBD, extrahepatic bile duct; CHD, common hepatic duct.

Table 3. The Milwaukee classification of sphincter of Oddi dysfunction [10]

Type	Clinical criteria	Prevalence of abnormal SOM (%)	Treatment of choice
I	Typical biliary-like pain Liver function tests elevated by two-fold Dilated CBD (diameter ⩾12 mm) on ERCP Delayed drainage of contrast medium in duodenum on ERCP (>45 min)	65–86	Sphincterotomy
II	Typical biliary-like pain One or more (but not all) additional criteria	50	Sphincterotomy in patients. with altered SOM
III	Typical biliary-like pain only	28	Medication

SOM, sphincter of Oddi manometry; CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography.



(a) (b)

Figure 9. An 80-year-old female patient presenting with a history of recurrent biliary-like intense pain after previous open cholecystectomy for calculi. (a) Coronal T_2 weighted single-shot fast spin-echo image at the level of the distal intrapancreatic common bile duct depicts a smoothly marginated homogeneous stricture of the distal common bile duct (arrowheads). (b) On coronal maximum intensity projection reconstruction, the stricture involves the papillary region (arrow), with relative sparing of the main pancreatic duct. There is associated biliary tract dilation upstream. No masses were found at extended contrast-enhanced MRI of the upper abdomen. This appearance, probably representing scarring from calculi migration, was confirmed at follow-up; sphincterotomy and stent placement provided symptom relief.

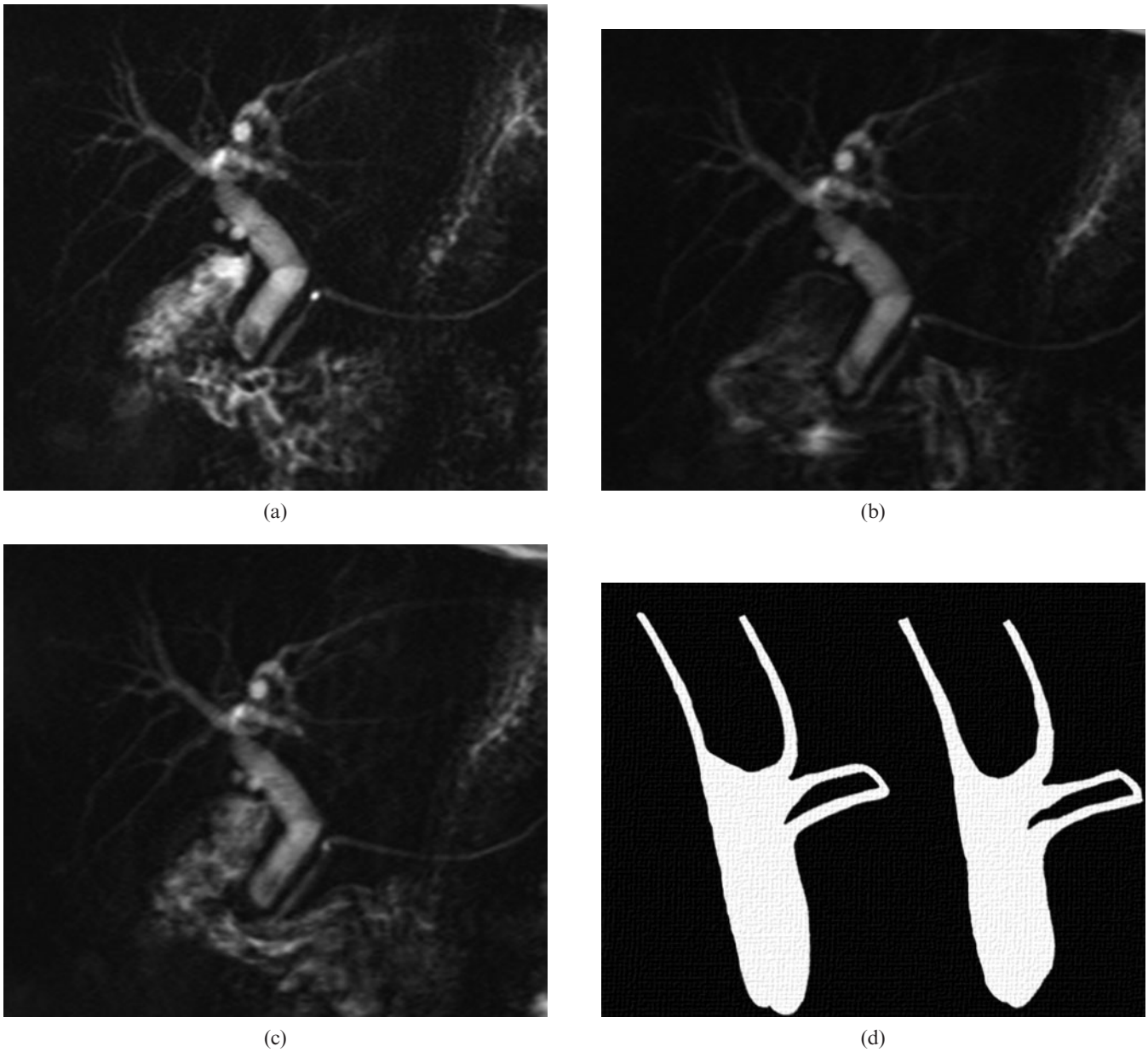


Figure 10. A case of epigastric pain and elevation of serum bilirubin in a 71-year-old female patient 15 years after cholecystectomy. Magnetic resonance cholangiopancreatography found a calculus in the distal common bile duct. A complementary dynamic examination with repeated single-slice heavily T_2 weighted single-shot fast spin-echo sequences (a–c) shows no variation in the morphology of the papillary region. (d) As suggested by the scheme, elevation in the basal pressure and/or fibrosis results in a minimal or absent variation of the sphincter during contraction (left) and relaxation (right).

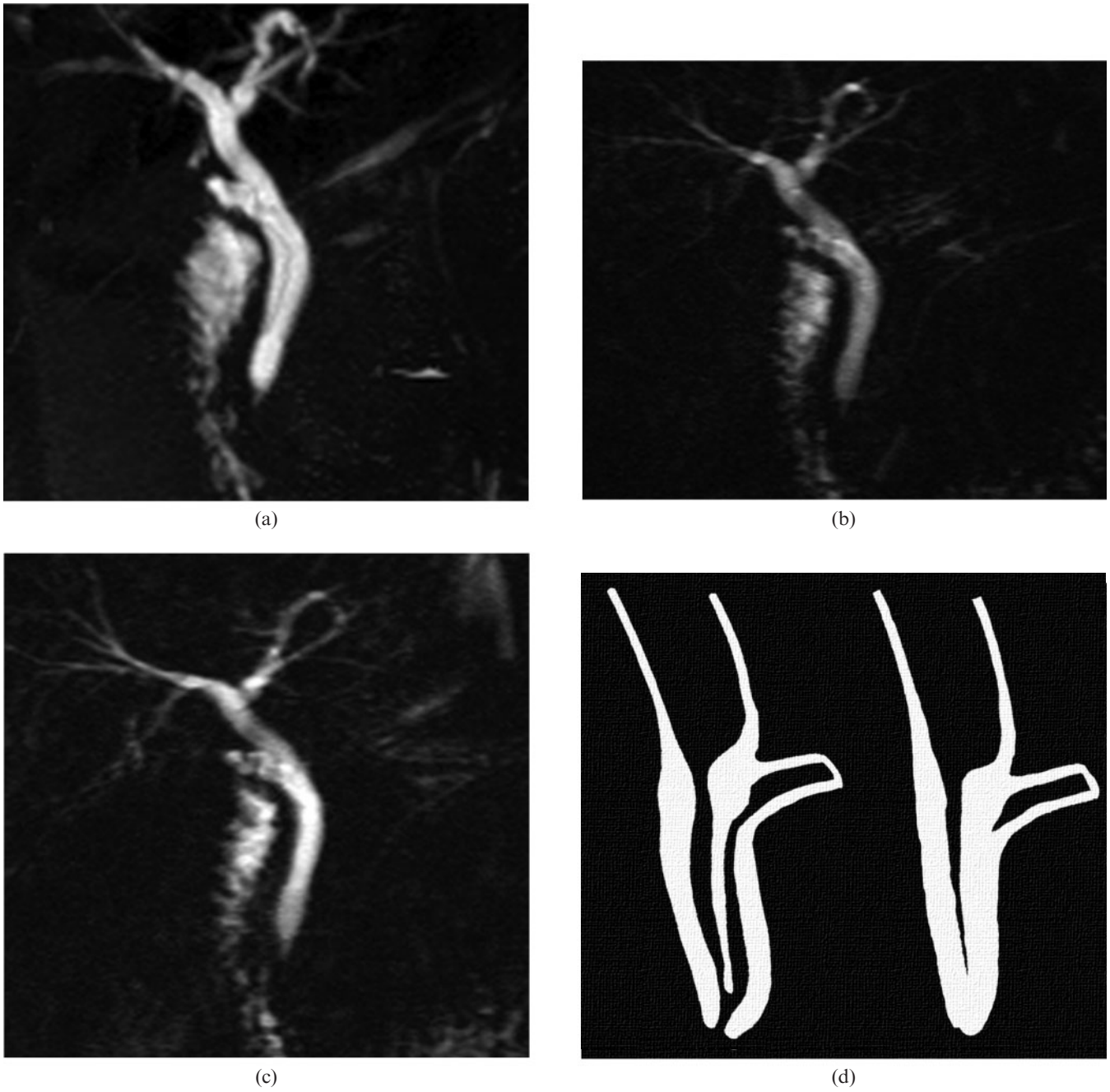


Figure 11. A case of recurrent biliary-like pain in a 39-year-old male patient who underwent laparoscopic cholecystectomy 5 years previously. A retained calculus was found a few days after surgery, which was extracted by sphincterotomy. Preliminary magnetic resonance cholangiopancreatography with a multislice technique (a) depicted a short tapered stricture of the sphincteric region, which is shown to maintain the same morphology during the dynamic study with repeated coronal single-slice heavily T_2 weighted single-shot fast spin-echo sequences (b–c). (d) As illustrated in the scheme, spasm and/or fibrosis of the papilla causes irregular contraction of the sphincter, causing a small amount of bile to remain in the lumen.

commonly found in patients with SOD and flow obstruction, secretin-enhanced MRCP has been advocated as a potential non-invasive diagnostic tool able to improve MRCP diagnostic performance [13]. Secretin is a polypeptide hormone that induces stimulation of pancreatic secretion of bicarbonate-rich fluid and a transient increase in the tone of the sphincter of Oddi. To date, the evaluation of main pancreatic duct dilation (degree and timing pre and post stimulation) and duodenal filling before and after stimulation in patients with suspected SOD has been limited, and data regarding its ability to predict SOD are controversial [13]. A general consideration could be that secretin-enhanced MRCP represents an initial non-invasive tool for evaluating patients with PCS to exclude organic underlying disorders such as chronic pancreatitis.

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