Original Articles

Role of Endoscopic Ultrasound in the Diagnosis of Pancreas Divisum

Surinder Singh Rana*, Deepak Kumar Bhasin, Vishal Sharma, Chalapathi Rao, Kartar Singh

Department of Gastroenterology, Post Graduate Institute of Medical Education and Research (PGIMER), Sector 12, Chandigarh 160012, India

ABSTRACT

Objective: The published data on the accuracy of the detection of pancreas divisum by endoscopic ultrasound (EUS) is limited. In this study, we evaluate the accuracy of detection of pancreas divisum by radial EUS in patients with chronic pancreatitis.

Methods: We retrospectively evaluated patients with chronic pancreatitis who underwent EUS followed by endoscopic retrograde cholangiopancreatography (ERCP) in the last four years to identify patients with complete pancreas divisum.

Results: One hundred and forty six patients with chronic pancreatitis underwent EUS examination and 20 patients (13.6%) had pancreas divisum. The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy of absence of stack sign on EUS for the diagnosis of pancreas divisum were 50%, 97%, 73%, 93% and 91%, respectively and for the inability to trace pancreatic duct from the head to the body were 100%, 96%, 80%, 100% and 96%, respectively.

Conclusion: EUS can diagnose pancreas divisum in a majority of patients. Pancreas divisum can be reliably excluded if pancreatic duct could be tracked backwards from the head to the body around the genu.

Keywords: chronic pancreatitis; pancreas divisum; endosonography; computed tomography

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INTRODUCTION

Pancreas divisum is the commonest congenital anomaly of the pancreas.[1,2] Because of a failure of the ventral and dorsal pancreatic anlagens to fuse, the dorsal duct becomes the main channel of drainage of pancreatic secretion from body and the tail regions of the pancreas.[1] Whether pancreas divisum is a possible etiologic factor in causation of acute or chronic pancreatitis is a matter of immense debate.[2,3] The most likely hypothesis for it causing pancreatic diseases is that in some individuals the minor papilla orifice is small and stenotic and this leads on to high intra-pancreatic dorsal ductal pressure during active secretion that results in inadequate drainage and ductal distension. The need to diagnose pancreas divisum usually arises in the evaluation of patients with idiopathic acute pancreatitis or recurrent acute pancreatitis. Traditionally, endoscopic retrograde cholangiopancreatography (ERCP) has been the procedure of choice for diagnosis. However, the invasive nature and possible serious consequences including pancreatitis make it a less preferable choice in the present era where radiologic procedures like magnetic resonance cholangiopancreatography (MRCP) and multi-detector computed tomography (CT) are available. MRCP, non-invasively, evaluates the pancreaticobiliary ductal system and has been shown to have a good sensitivity and specificity for the diagnosis of pancreas divisum.[4] Secretin enhancement has been shown to improve the sensitivity and specificity of MRCP in diagnosing pancreas divisum.[5] Recently, endoscopic ultrasound (EUS) has become available as another option to evaluate for pancreaticobiliary diseases. EUS allows detailed evaluation of the pancreaticobiliary ductal system without injecting contrast in to these ducts. Moreover, it also provides detailed imaging of the pancreatic parenchyma. Therefore, pancreatic ductal abnormalities like pancreas divisum can also be detected by minimally invasive techniques like EUS and thus obviate the risks associated with ERCP. However, the published data on the accuracy of detection of pancreas divisum by EUS is limited.[6,7] In the current study, we retrospectively evaluated the accuracy of detection of pancreas divisum by radial EUS in patients with chronic pancreatitis.

PATIENTS AND METHODS

A retrospective analysis of the collected data base of the patients with chronic pancreatitis who underwent EUS

*To whom correspondence should be addressed.
E-mail: drsurinderrana@gmail.com
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Table 1. Performance of various EUS findings for diagnosis of pancreas divisum

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Absent stack sign (16 patients with inadequate pancreatic duct visualization excluded)	50%	97%	73%	93%	91%
Absent stack sign (16 patients with inadequate pancreatic duct visualization considered as negative exam for pancreas divisum)	40%	98%	73%	91%	89%
Inability to trace the pancreatic duct from the head to the body (16 patients with inadequate pancreatic duct visualization excluded)	100%	96%	80%	100%	96%
Inability to trace the pancreatic duct from the head to the body (16 patients with inadequate pancreatic duct visualization considered as negative exam for pancreas divisum)	80%	97%	80%	97%	95%

EUS: endoscopic ultrasound.

followed by ERCP in the last four years to identify patients with complete pancreas divisum was done. These patients were referred for EUS for accepted indications and EUS was not done solely for the purpose of this study. All patients had undergone CT scan of the abdomen and some patients had also undergone MRCP before EUS examination. An informed consent was obtained from all the patients. EUS was performed by experienced endosonologists (Rana SS and Bhasin DK) and they were blinded to the MRCP findings.

EUS examination was done using radial scanning echoendoscope (EG-3670 URK radial echoendoscope, Pentax Inc., Tokyo, Japan) at 7.5 MHz. The diagnosis of pancreas divisum was suggested by looking for following two signs on EUS: (1) absence of stack sign and presence of crossed duct sign; and (2) inability to follow the pancreatic duct from the major papilla to the pancreatic body. First, an attempt to obtain the "stack sign" was made. To obtain the stack sign, the echoendoscope was positioned in the duodenal bulb in the long scope position and the balloon inflated after positioning the tip of the scope in the apex of the bulb. From this position, the distal common bile duct, ventral pancreatic duct and the portal vein can be seen to run in parallel with bile duct being closest to the transducer (stack sign). If stack sign could not be elucidated, an attempt was made to look for "crossed duct sign" (bulb view showing Santorini duct crossing common bile duct). Thereafter, an attempt was made to follow the pancreatic duct from the major papilla to the pancreatic body by gently withdrawing the scope and giving it a clockwise rotation. Similarly, keeping the echoendoscope in the stomach, the pancreatic duct was traced from the body of the pancreas towards the head. The diagnosis of pancreas divisum was suggested if the stack sign could not be elucidated or cross duct sign could be elucidated. The diagnosis of pancreas divisum was excluded if the pancreatic duct could be traced from the major papilla to the pancreatic body or it could be traced from the body dipping at the genu towards the major papilla. The diagnosis of pancreas divisum was confirmed on pancreatogram obtained during ERCP performed subsequently for treatment of pain.

RESULTS

One hundred and forty six patients [male: 102 (69.8%); age range: 16-62 years; mean age: 36.9 ± 11.4 years] with chronic pancreatitis underwent EUS examinations. Fifty two patients (35.6%) patients had chronic calcific pancreatitis and 72 (49.3%) patients had history of significant alcohol intake. A total of 20 cases (13.6%) of pancreas divisum were diagnosed by ERCP. On EUS, pancreatic duct could not be adequately visualized in 16 patients (poor duct visualization possibly due to its small diameter in 9 patients, acoustic shadowing because of dense calcification in 4 patients and presence of large pseudocysts in 3 patients) (Fig. 1) and 4 of these 16 patients had pancreas divisum. The pancreatic duct could be well visualized in the remaining 130 patients and 16 of these patients had pancreas divisum.

Of these 130 patients, the stack sign could not be demonstrated in 11 patients and 8 of these patients had pancreas divisum (Fig. 2, 3). The 3 patients with absent stack sign and absence of pancreas divisum had tight strictures in the head area causing dilatation of upstream pancreatic duct in body and tail. Of these 11 patients, crossed duct sign could be demonstrated in only 2 patients and both of these patients had pancreas divisum (Fig. 4). None of the patients without pancreas divisum had positive crossed duct sign. However, 8/119 (6.7%) of the patients with presence of stack sign had pancreas divisum and all these 8 patients had markedly dilated dorsal and ventral ducts. The pancreatic duct could be traced from the papilla in the pancreatic head to the pancreatic body in 110 patients and none of these patients had pancreas divisum. Also, in all these patients, the pancreatic duct could be seen dipping downwards towards

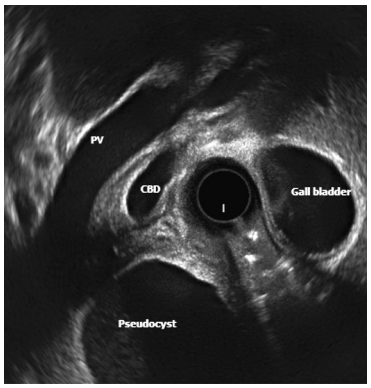

Figure 1. Radial EUS. Pancreatic duct could not be visualized because of presence of pseudocyst in the head of pancreas. CBD: common bile duct; EUS: endoscopic ultrasound; PV: portal vein.

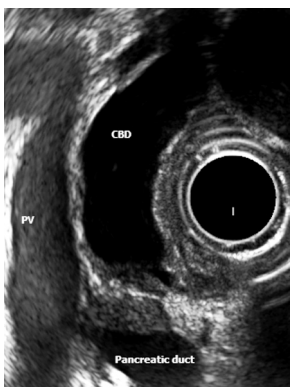

Figure 2. Radial EUS in patient with chronic pancreatitis with no pancreas divisum and benign biliary stricture: Stack sign present with dilated CBD and pancreatic duct along with PV seen. CBD: common bile duct; EUS: endoscopic ultrasound; PV: portal vein.

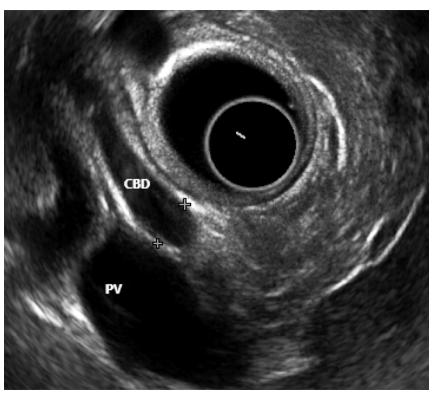

Figure 3. Radial EUS. Stack sign absent with only CBD and PV seen. Pancreatic duct not seen in the stack suggesting a possibility of pancreas divisum. CBD: common bile duct; EUS: endoscopic ultrasound; PV: portal vein.

the major papilla when viewed from the stomach (Fig. 5). The pancreatic duct could not be traced from the head to the body region of pancreas in 20 patients and 16 of these patients had pancreas divisum. These four patients without pancreas divisum had stricture in the genu of pancreas causing loss of continuity of the pancreatic duct on EUS and this was detected by ERCP performed subsequently. In 12 patients, the pancreatic duct could be seen going straight towards the minor papilla when viewed from the stomach and all these patients had pancreas divisum (Fig. 6).

The overall sensitivity, specificity, positive predictive value,

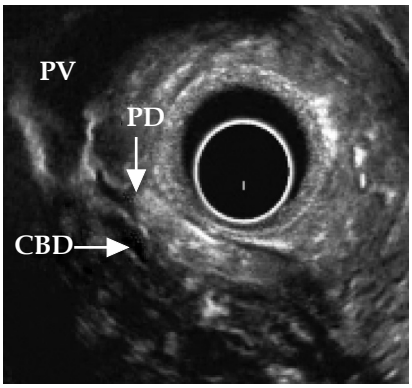

Figure 4. Radial EUS image from the duodenum showing the PD crossing the CBD towards the minor papilla suggesting pancreas divisum (crossed duct sign). CBD: common bile duct; EUS: endoscopic ultrasound; PD: pancreatic duct; PV: portal vein.

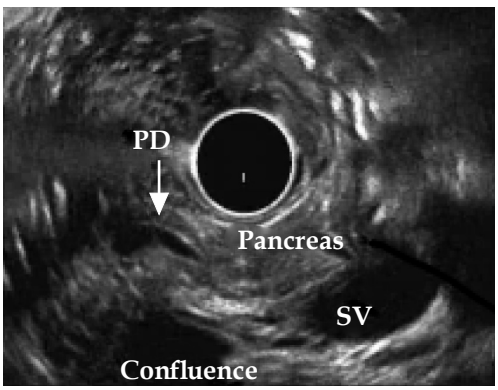

Figure 5. Radial EUS showing PD dipping downwards at genu towards the head in patient without pancreas divisum. EUS: endoscopic ultrasound; PD: pancreatic duct; SV: splenic vein.

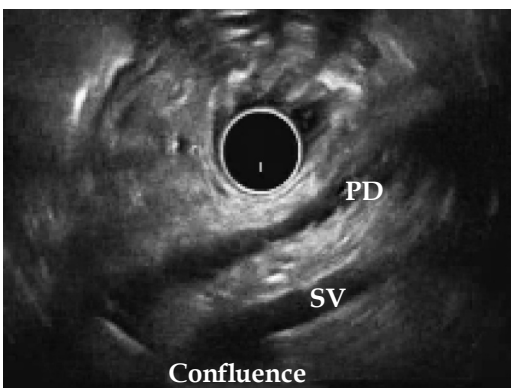

Figure 6. Radial EUS showing PD not dipping downwards at genu but going straight towards the minor papilla in patient with pancreas divisum. EUS: endoscopic ultrasound; PD: pancreatic duct; SV: splenic vein.

negative predictive value and accuracy for absence of stack sign on EUS for the diagnosis of pancreas divisum were 50%, 97%, 73%, 93% and 91%, respectively. If all the 16

patients with inadequate pancreatic duct visualization were regarded as negative EUS examinations, the overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy for absence of stack sign on EUS for the diagnosis of pancreas divisum were 40%, 98%, 73%, 91% and 89%, respectively. The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy for the inability to trace the pancreatic duct from the head to the body on EUS for the diagnosis of pancreas divisum were 100%, 96%, 80%, 100% and 96%, respectively. If all the 16 patients with inadequate pancreatic duct visualization were regarded as negative EUS examinations, the overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy for the inability to trace the pancreatic duct from the head to the body on EUS for the diagnosis of pancreas divisum were 80%, 97%, 80%, 97% and 95%, respectively.

DISCUSSION

The diagnosis of pancreas divisum is traditionally based on ERCP findings of a difficult cannulation of major papilla and pancreatogram obtained via major papilla revealing a short duct of Wirsung. And the pancreatogram obtained by cannulating the minor duct, however, reveals the dorsal duct running across the length of pancreas. As EUS also allows detailed evaluation of the pancreaticobiliary ductal system without injecting contrast in to these ducts, it can help in detecting various pancreatic ductal anomalies. Several EUS criteria for diagnosis of pancreas divisum, both for radial and linear endosonography have been proposed, but very few studies have evaluated the accuracy of these criteria.

Bhutani *et al*.[6] evaluated 6 patients with pancreas divisum and attempted to obtain a stack sign in them. These results were compared with the EUS results of 30 patients without pancreas divisum. They were able to obtain a stack sign in 2/6 (33%) patients with pancreas divisum and this was significantly lower than the frequency of obtaining stack sign in patients without pancreas divisum (83.3%; $P = 0.04$). The stack sign was falsely positive in 2 patients with pancreas divisum. The overall accuracy was 80% with positive predictive value of 44%. However, this study was confounded by the fact that the endosonologist was aware of the diagnosis. In our study, the EUS was done prior to the ERCP and the operator was not aware of the presence or absence of pancreas divisum. Also, 8 of the patients in our study with presence of stack sign had pancreas divisum and all the 8 patients had markedly dilated dorsal and ventral ducts. The overall accuracy in our study was 91% with a positive predictive value of 73%.

Linear endosonography has also been evaluated for diagnosing pancreas divisum. Lai *et al*.[8] using linear echoendoscope, excluded the diagnosis of pancreas divisum if the pancreatic duct followed continuously from the major papilla into the pancreatic body or crossed the endosonographic border between the ventral and dorsal pancreatic anlagen. The lack of either of these findings was considered suggestive of pancreas divisum. The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy of EUS using these criteria for diagnosing pancreas divisum were found to be 95%, 97%, 86%, 99% and 97%, respectively. In our study, the pancreatic duct could be traced from the papilla in the pancreatic head to the pancreatic body in 110 patients and none of these patients had pancreas divisum. The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy for the inability to trace the pancreatic duct from the head to the body on EUS for the diagnosis of pancreas divisum were 100%, 96%, 80%, 100% and 96%, respectively.

Our results suggest that EUS is a promising, minimally invasive investigation method for diagnosis of pancreas divisum with an accuracy of 97% and moderate positive predictive value of 80%. Also, pancreas divisum can be accurately excluded if the main pancreatic duct could be tracked backwards from the head to the body around the genu. Non-visualization of the pancreatic duct is one of the most important factors that limited the positive predictive value of EUS for diagnosing pancreas divisum. Secretin stimulated EUS can potentially help in better visualization of the pancreatic duct and thus can help in improving our ability to diagnose pancreas divisum.[9]

In conclusion, EUS can reliably exclude pancreas divisum if the main pancreatic duct could be tracked backwards from the head to the body around the genu. Absence of stack sign, inability to trace the pancreatic duct from the major papilla in the head to the body and ability to trace the pancreatic duct going straight in the body of pancreas towards minor papilla are EUS features that can help in diagnosis of pancreas divisum.

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