Gut

*Leading article*

# Pancreas divisum: opinio divisa

"Pancreas divisum" describes the congenital anomaly in which the dorsal and ventral pancreatic glands drain separately into the duodenum. It occurs due to failure of fusion of the dorsal and ventral ducts during the seventh week of gestation and is characterised not only by the anatomical configuration but also by the physiology of duct drainage—that is, predominant drainage through the dorsal duct of Santorini.[1] The pancreas gland arises during the fifth week of gestation from three outgrowths of the primitive duodenum.[2 3] The dorsal pancreatic bud grows at first posteriorly in the midline and later comes to lie in the concavity of the duodenum. Two ventral buds develop slightly caudal to the dorsal bud and the left bud later atrophies but rarely persists to become an annular pancreas. The right ventral bud develops in association with the primitive bile duct. Later the ventral pancreas rotates posteriorly until it comes to lie on the left of the duodenum, caudal to the dorsal pancreas. The duct systems then usually fuse together, the dorsal duct forming the main duct of the body and tail while the ventral duct (Wirsung's duct) becomes the main conduit for pancreatic secretion coursing through the head and opening into the major papilla in the duodenum. The dorsal duct usually also continues to drain along its original course in the duct of Santorini through the minor or accessory papilla which opens in the duodenum proximal to the major papilla.

The discovery of pancreas divisum is usually attributed to Joseph Hyrtl (anatomist, 1810–1894), although it had been described previously in the seventeenth century. Three variants have been described[1 4]: type 1 or classical divisum in which there is total failure of fusion; type 2 in which dorsal drainage is dominant in the absence of Wirsung's duct; and type 3 or incomplete divisum where a small communicating branch is present. Large autopsy series have given estimates of 5–10% of the population for pancreas divisum with 0.13–0.9% having the incomplete variety.[5 6]

The entity is usually diagnosed at endoscopic retrograde pancreatography (ERP) when a short but normal "tree-like" ventral segment of pancreatic duct is identified after contrast is introduced through the major papilla, and a patent dorsal system draining the body and tail of the pancreas is delineated by injecting contrast through the minor papilla.[7 8] The appearance of the short ventral segment is quite typical but can be mimicked by other conditions such as previous pancreatic trauma, partial pancreatectomy, pseudocyst, and pancreatic carcinoma. This underlines the importance of confirmation by minor papilla cannulation although it has been suggested that the characteristic acinar pattern (Christmas tree appearance) around the ventral duct would not be mimicked by the appearance of a blocked duct. While ERP should be considered the gold standard for diagnosis, endoscopic ultrasound (EUS) and magnetic resonance imaging (MRI) may have a role with the advantages of being non-interventional. At EUS, the "stack sign" of bile duct, pancreatic duct, and portal vein all running in parallel adjacent to the second part of duodenum was present in 83% of patients with normal duct anatomy defined at ERP compared with 33% of patients with pancreas divisum.[9] MR pancreatography is becoming more accurate in the preliminary and non-invasive diagnosis of pancreatic disease[10] but its accuracy in diagnosing pancreas divisum remains uncertain at present.

The clinical significance of pancreas divisum has been the subject of debate for many years[11–15] with opinions varying from that of an innocent congenital anomaly to a significant risk factor for the development of pancreatic pathology. Evidence to support pancreas divisum as a risk factor for the development of pancreatic disease has come from the observation that there is an increased incidence of the anomaly in subjects with idiopathic pancreatitis of 12–26%.[16] More importantly, evidence from postmortem series and pancreatograms has shown that pathology is isolated to the dorsal part of the gland in subjects with pancreas divisum. It is proposed that in some subjects the disproportion between the small calibre of the minor papilla and the large amount of secretions from the dorsal part of the gland leads to a relative outflow obstruction from the dorsal pancreas leading to pain or pancreatitis. Thus pancreas divisum is thought to give rise to a spectrum of disease ranging from minor symptoms or chronic abdominal pain to acute relapsing or chronic pancreatitis. Compared with patients with pancreatitis and normal duct anatomy,[17] subjects with pancreas divisum tend to be younger, more often female, less likely to drink alcohol, and more often have a clinical pattern of recurrent acute attacks of pancreatitis. Attacks of pancreatitis in this setting tend to be less severe, although necrotic pseudocysts have been reported. The proposition that pancreas divisum can cause dorsal pancreatitis may be counterbalanced by a reduced incidence of gall stone pancreatitis in these individuals although this has not been specifically addressed in any study.

Despite the uncertainties as to whether pancreas divisum is a pathological entity, the finding of histological changes isolated to the dorsal pancreas has led pancreatic surgeons and latterly, pancreatic endoscopists, to decompress the dorsal gland. These treatment modalities have evolved as the development of ERCP in the 1970s made it possible to

**Abbreviations used in this paper**: ERP, endoscopic retrograde pancreatography; EUS, endoscopic ultrasound; MRI, magnetic resonance imaging.

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diagnose this entity. Endoscopic sphincterotomy of the minor papilla was described by Cotton 20 years ago.[18] Results of the initial series were often disappointing but technical refinements has led to renewed enthusiasm for the endoscopic treatment of pancreatic disease.[19–21] Endoscopic techniques have included periodic exchange of minor papillary endoprostheses or minor duct sphincterotomy. A combination of both techniques has been described where a needle-knife sphincterotomy is undertaken over, and guided by, the prior placement of a stent across the minor papilla.[22 23] Pancreatitis complicating these procedures remains a concern, and long term stenting of the pancreatic duct has been reported to result in chronic ductal changes.[24] Short term stenting can be helpful in gauging a symptomatic response in order to predict which patients might benefit from sphincterotomy. In a surgical series of 37 patients undergoing sphincteroplasty, the authors describe how the minor papilla was cannulated with a lacrimal probe following its identification by means of intravenous secretin.[25] Following initial incision into the papilla, a large gush of juice was reportedly observed in 28 of 34 patients, supporting the theory of relative obstruction. Thirteen of these patients had previously failed endoscopic attempts at cannulation of the minor papilla and in each case, operative findings demonstrated marked scarring and stricture formation.

Meaningful interpretation of a number of surgical and endoscopic studies is hampered by restricted numbers of cases, heterogeneous groupings of patients, and limited follow up periods. Direct comparison of surgical and endoscopic series is difficult although complication rates from surgery seem to be less frequent. Surgical series with more than 20 patients followed for more than two years report reduction in bouts of pancreatitis in at least 50% of patients and improvement in pain scores in even more, with morbidity less than 5% and morality less than 1%.[3 25–27] Endoscopic series have been smaller with shorter follow up periods,[22 28] and the results are less convincing with possibly a higher complication rate. It is apparent from the majority of these larger studies that a cohort of patients with pancreas divisum who present with acute pancreatitis may benefit from decompression of the minor papilla. The results appear to be especially beneficial in those patients where the changes of chronic pancreatitis in the dorsal gland are mild or absent and in those patients with clinically acute relapsing pancreatitis. Results are less satisfactory when decompression is undertaken for the pain of chronic pancreatitis in the absence of divisum and are even less convincing in subjects with pancreatic-type pain without evidence of pancreatitis or divisum. There are even fewer reports of decompression for patients with the incomplete type of divisum but a single centre series of 32 patients reported similar results to those for classical divisum.[29]

If pancreas divisum plays a causative role in pancreatitis, one might expect an increased incidence of other pancreatic pathology also. Anecdotal reports of biliary or pancreatic malignancy in patients with pancreas divisum do not amount to demonstration of increased incidence.[30 31] The recent description of the biochemical basis for hereditary pancreatitis and its mechanisms due to mutations in the cationic trypsinogen gene[32] has provoked renewed interest in the pathogenesis of pancreatitis. Although there are reports of familial pancreas divisum associated with occurrences of pancreatitis,[33 34] it is unclear if these are associated with mechanical/obstructive or mutational/biochemical mechanisms of pancreatitis. Further work on the potential for trypsinogen activation in pancreas divisum may be useful in helping to determine if this entity is truly a risk factor for pancreatitis.

Selection of patients likely to benefit from these procedures remains problematic. If structural or functional obstruction to drainage in pancreas divisum results in pathology, it would seem reasonable to be able to demonstrate this. Increased pressure measured by minor papilla manometry appears to be an inconsistent finding.[35] Prolonged dilatation of the dorsal duct following secretin stimulation (15–30 minutes in the presence of minor papilla stenosis versus three minutes in normal subjects) during sonographic or MR pancreatographic evaluation of the pancreatic duct has been proposed as a predictive test for patients likely to benefit from decompression but requires further validation studies.[36]

Pancreas divisum is a relatively common congenital anomaly but it is apparent that only 5–10% of those individuals develop pancreatic related symptoms. Therefore, a further factor such as minor papillary insufficiency or stenosis leading to relative obstruction of the dorsal pancreatic duct would appear to be a prerequisite for these complications to arise. The diagnosis should be considered in patients with idiopathic acute pancreatitis of a recurrent or relapsing nature. A complete assessment, including dorsal duct cannulation, is essential in these patients. There remains great uncertainty for the individual patient found to have pancreas divisum as to whether endoscopic or surgical sphincterotomy would be beneficial, although it is apparent that a certain group of patients with acute relapsing pancreatitis may benefit. Temporary drainage if dilatation is present may be helpful to aid a decision on more definitive management. Clearly, development of further reliable tests is important, hopefully involving relatively non-invasive techniques such as MRI or EUS. Following a thorough evaluation, evidence to date seems to favour surgical intervention but comparative endoscopic studies would be helpful.

L QUEST
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