DOI: 10.1002/ueg2.12229

EDITORIAL

UNITED EUROPEAN GASTROENTEROLOGY ueg journal WILEY

"Car body appearance and engine": The morphology-function correlation in chronic pancreatitis

Chronic pancreatitis (CP) is a complex disease characterized by a continuous or recurrent inflammation of the pancreas[1] that results in progressive and irreversible morphologic alterations causing pain and impairment of pancreatic function. Typical findings are focal necrosis, fibrosis, enlarged and irregular pancreatic duct, intraductal stones and calcifications.[2,3] As such alterations more often occur in late CP, different classifications divide the disease in early and advanced stages based on structural findings (Cambridge,[4] Rosemont[5]) and also etiology, symptoms and functionality (Manchester,[6] M-ANNHEIM[7] and others). The advantage of the Cambridge classification is the comparability of stage classification independent of the used imaging modality as Cambridge 0–4 was defined for endoscopic ultrasound, computed tomography or magnetic resonance imaging as well. However, none of the classifications published so far was prospectively evaluated to predict prognosis, course and complications of patients with CP.[8] In addition, several cohort studies failed to correlate in particular early morphological alterations and pancreatic insufficiency but found positive correlation in advanced stages of CP.[9]

In the current issue of UEG-Journal, Nordaas and colleagues[10] analyzed the association between structural alterations of patients with CP and complications, mainly endocrine and exocrine insufficiency. This was a cross-sectional analysis including more than 700 patients from the multicentric Scandinavian-Baltic-Pancreatic-Club database with CP classified by the M-ANNHEIM-criteria. In- and exclusion criteria as well as outcomes were clearly defined. In general, the authors found that a continuous organ involvement meaning structural abnormalities in the entire pancreas was associated with both pancreatic exocrine and endocrine insufficiency. Moreover, severe calcifications, main pancreatic duct obstruction and pancreatic atrophy were linked to exocrine insufficiency. These findings are clearly comprehensible as exocrine insufficiency usually occurs if less than 10% of the pancreas remain functionally active and the entire pancreas reveals structural abnormalities.[11] Notably, the authors also found a negative association between pancreatic pseudocysts and diabetes. Diabetes was not associated with pancreatic atrophy although the authors described such a link in their own prior publications.[12] In another previous report from the same consortium, the "inflammatory cluster", that include pseudocysts, was associated with alcoholic etiology.[13] In the latest study, analysis was corrected for current alcohol consumption, but association with etiology is not evaluated in depth. These discrepancies may also depend on the limitations of a cross-sectional design in a database-related study where not all necessarily information are available for each patient. Moreover, there is a risk of a selection bias as distinct subgroups may be over- or underreported. Indeed, patients with more symptoms and an "inflammatory" pattern are more likely to undergo imaging studies.

What could we learn from this large study of the Scandinavian-Baltic-Pancreatic-Club? Out of more than 700 patients with strictly classified CP, abnormalities involving the whole pancreas are associated with both exocrine and endocrine insufficiency. However, association is not causation and a long-term observational study of such a large CP-cohort will ever hard to become reality. This study also demonstrated that CP is still a complex disease with variable complaints and complications. Structural alterations are important to diagnose the disease but remain less helpful to identify patients who will develop complications or a severe course in a timely manner and are therefore candidates for intensive surveillance. Several questions are unanswered and need future investigation: What is the importance of the so-called painless chronic pancreatitis that usually occurs in elderly people[14,15] and often is underreported in such database studies? Moreover, different classifications of CP have to be evaluated in prospective studies to determine accuracy and predictive value for the development of exocrine and endocrine insufficiency. Finally, a "simple" association with a structural finding in cross-sectional imaging or endoscopic ultrasound may not be sufficient to help identifying patients at risk for complications. It is likely that in the near future, the use of artificial intelligence applications able to include serial monitoring of multiple radiomics, clinical, biochemical and environmental factors in an automated, unbiased tool, will fill the gaps between imaging and clinical course in CP.

KEYWORDS

chronic pancreatitis, complications, morphology, pancreas, pancreatic function

CONFLICT OF INTEREST

The authors have nothing to disclose.

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REFERENCES

1. Mayerle J, Sendler M, Hegyi E, Beyer G, Lerch MM, Sahin-Toth M. Genetics, cell biology, and pathophysiology of pancreatitis. Gastroenterology. 2019;156(0016–5085(Linking)):1951–68.
2. Olesen SS, Mortensen LH, Zinck E, Becker U, Drewes AM, Nøjgaard C, et al. Time trends in incidence and prevalence of chronic pancreatitis: a 25-year population-based nationwide study. United Eur Gastroenterol J. 2021;9(1):82–90.
3. de Rijk FE, Kempeneers MA, Bruno MJ, Besselink MG, van Goor H, Boermeester MA, et al. Suboptimal care for chronic pancreatitis patients revealed by moderate to low adherence to the United European Gastroenterology evidence-based guidelines (HaPanEU): a Netherlands nationwide analysis. United Eur Gastroenterol J. 2020;8(7):764–74.
4. Wiersema MJ, Hawes RH, Lehman GA, Kochman ML, Sherman S, Kopecky KK. Prospective evaluation of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in patients with chronic abdominal pain of suspected pancreatic origin. Endoscopy. 1993;25(9):555–64.
5. Catalano MF, Sahai A, Levy M, Romagnuolo J, Wiersema M, Brugge W, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. Gastrointest Endosc. 2009;69(7):1251–61.
6. Bagul A, Siriwardena AK. Evaluation of the Manchester classification system for chronic pancreatitis. JOP J Pancreas. 2006;7(4):390–6.
7. Schneider A, Löhr JM, Singer MV. The M-ANNHEIM classification of chronic pancreatitis: introduction of a unifying classification system based on a review of previous classifications of the disease. J Gastroenterol. 2007;42(2):101–19.
8. Mayerle J, Jansen PL, Lorenz P, Beyer G, Hoffmeister A, Lerch MM. S3-Leitlinie Pankreatitis – Editorial der Deutschen Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS) (September 2021 – AWMF Registernummer 021-003) – Neue Leitlinie zur akuten und chronischen Pankreatitis (New guideline for acute and chronic pancreatitis). Z Gastroenterol. 2022;60(3):297–8.
9. Bozkurt T, Braun U, Leferink S, Gilly G, Lux G. Comparison of pancreatic morphology and exocrine functional impairment in patients with chronic pancreatitis. Gut. 1994;35(8):1132–6.
10. Nordaas I, Tjora E, Dimcevski G, Haldorsen IS, Olesen SS, Drewes A, et al. Structural imaging findings are related to clinical complications in chronic pancreatitis. United Eur Gastroenterol J. 2022. https://doi.org/10.1002/ueg2.12228
11. DiMagno EP, Go VL, Summerskill WH. Relations between pancreatic enzyme outputs and malabsorption in severe pancreatic insufficiency. N Engl J Med. 1973;288(16):813–15.
12. Olesen SS, Hagn-Meincke R, Drewes AM, Steinkohl E, Frøkjaer JB. Pancreatic atrophy and exocrine insufficiency associate with the presence of diabetes in chronic pancreatitis patients, but additional mediators are operative. Scand J Gastroenterol. 2021;56(3):321–8.
13. Olesen SS, Nøjgaard C, Poulsen JL, Haas SL, Vujasinovic M, Löhr M, et al. Chronic pancreatitis is characterized by distinct complication clusters that associate with etiological risk factors. Off J Am Coll Gastroenterol ACG. 2019;114(4):656–64.
14. Hollenbach M, Barresi L. Shedding light on painless chronic pancreatitis. Dig Liver Dis. 2020;52(11):1331–2.
15. Amodio A, De Marchi G, de Pretis N, Crinò SF, D'Onofrio M, Gabbrielli A, et al. Painless chronic pancreatitis. Dig Liver Dis. 2020;52(11):1333–7.