

Metabolic signature might be an option to identify patients with early CP

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Metabolites are biomarkers measured in blood, urine, stool and tissue samples, determined by several factors, most importantly by the gut microbiota and changes in the metabolism from underlying diseases. Theoretically, specific diseases lead to changes in both factors that result in specific metabolomic profiles characterising these disorders. In recent years, metabolomic profiling for the diagnosis and the prognostic assessment of GI diseases has been an emerging and new tool; there are examples of metabolomics in diagnosing and assessing chronic GI disorders such as cancers, IBD and cirrhosis.¹⁻⁶

The recent studies on metabolomics have assessed its potential roles in gastroenterology patients' care, but it is not yet part of the daily routine.

In *Gut*, Adam *et al* report a very important study, which aimed to assess metabolomics' diagnostic potential in chronic pancreatitis (CP).⁷ Patients with unequivocally diagnosed CP had been identified by a set of criteria, including radiological changes and severely abnormal pancreatic function tests.⁸⁻¹⁰ Their metabolomic profiles were compared against three control groups, the first in the identification and then two control groups in the external validation studies. In the three steps of the study, there were three independent CP groups. The authors identified eight metabolites with which the tool can identify CP with an area under the curve (AUC) 0.85 (95% CI: 0.801 to 0.91) from an EDTA blood sample and an AUC 0.87 (95% CI: 0.81 to 0.95) from serum. These results prove that their metabolomic profiling tool has good diagnostic accuracy. We shall ask the question: In which area of daily clinical practice could this new tool be used most effectively? Is it the established CP or early CP?

We all know that CP is characterised by the irreversible loss of exocrine and endocrine function of the pancreas from chronic inflammation.¹¹ It is often accompanied by morphological changes of the pancreas detectable by various radiological methods.

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Notably, the diagnosis of established CP is rarely challenging. Therefore, assessing the cost/benefit ratio and the limited access to the methodology, it is very unlikely that this specific metabolomic profile will be routinely used to diagnose CP. However, the most exciting clinical question is how to identify patients who will develop CP when there are no detectable radiologic features, significant clinical symptoms or overt exocrine insufficiency. Patients with early CP could benefit from interventions, and the full-blown CP could be prevented or significantly delayed. Therefore, we propose that the metabolomic profiles of patients with early CP and a high risk for developing advanced CP are analysed. The question arises, which patient population would benefit the most from the metabolomic test?

Our study group just published an analysis of a small cohort in which patients with three or more acute pancreatitis episodes have a high probability of developing CP.¹² Therefore, based on Adam *et al*'s study, we decided to retest our observation in a large international cohort of patients with acute pancreatitis (AP). Between 2012 and 2019, from 13 countries and 30 medical centres, 2461 patients were enrolled into the Acute Pancreatitis Registry initiated by the Hungarian Pancreatic Study Group. The AP diagnosis was defined according to the International Association of Pancreatology (IAP)/American Pancreatic Association (APA) guidelines.¹³ The analysed cohort was representative of the complete AP cohort. The proportion of mild, moderately severe and severe cases was 71.0%, 23.7% and 5.3%. Our data analysis showed that the proportion of patients developing CP is exponentially and directly associated with the number of AP episodes (1.6%, 5.8% and 21% with 1, 2 and 3 AP episodes, respectively, [table 1](#)).

Therefore, we believe that patients with three or more AP episodes with no morphological changes would be the best candidates in a longitudinal clinical trial to test the hypothesis of whether this newly developed metabolomic profile would be a good diagnostic tool to identify patients with early CP.

Contributors PH conceptualised the study. BE and AS extracted and analysed the data. PH, AS and BE

Table 1 The proportion of patients in percentages developing CP

Number of acute pancreatitis episodes (n)	CP (n)	no-CP (n)	Number of patients (n)	Percentage (%) of the patients developing CP
1	28	1706	1734	1.6
2	18	295	313	5.8
3	22	83	105	21
4	21	47	68	30.9
5	15	22	37	40.5
6	14	12	26	53.8
7	10	9	19	52.6
8+	15	11	26	57.7
Total cases	143	2185	2328	6.1

CP, chronic pancreatitis; no-CP, patients without chronic pancreatitis.

interpreted the data. BE wrote the manuscript. BE, AS and PH reviewed and contributed to the manuscript before finalisation and submission.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study was approved by the National Public Health Centre (Nemzeti Népegészségügyi Központ), under the ID: 17787-8/2020/EÜIG. All participants in this study provided written informed consent.

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