EDITORIAL

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Current Clinical Assessment of Prognosis of Chronic Pancreatitis

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Chronic pancreatitis is defined as a fibro-inflammatory syndrome of the pancreas, where recurrent episodes of inflammation result in fibrotic pancreatic parenchyma and limitation or even loss of its functions [1, 2]. The diagnosis of chronic pancreatitis is based on the evaluation of morphological changes using imaging methods, mainly computed tomography (CT) and magnetic resonance imaging (MRI), the findings of which are often associated with changes in pancreatic function [3]. Chronic pancreatitis is not a rare disease, with a prevalence of 15–50/100,000 inhabitants and an incidence of about 5/100,000 inhabitants/year [4-6].

Chronic pancreatitis is a disease characterized by different clinical manifestations and a long-term evolution of changes from the initial, asymptomatic stage to the terminal stage, characterized by the presence of significant complications. From this point of view, markers have an important role in determining the prognosis of the disease.

In most people, the diagnosis of chronic pancreatitis is based on the assessment of morphological changes provided by a range of imaging methods. A range of systems and schemes exist which evaluate morphological markers and their severity according to findings on ultrasound, MRI, computed tomography (CT), invasive endoscopic retrograde cholangio-pancreatography (ERCP), or endoscopic ultrasonography (Rosemont system) [7, 8]. However, changes in pancreatic morphology, symptoms of chronic pancreatitis and pancreatic function do not correlate completely with each other and thus no reliable comment can be made on the severity and prognosis of the disease [9, 10]. For example, the study by Kempeneers et al. [10] described a high variability and heterogeneity of pain in people with chronic pancreatitis.

Classification and prognostic stratification of chronic pancreatitis is a long-term process. The classification produced in the Marseille International Symposium in 1984 was invaluable in defining the disease and identifying subtypes of pancreatitis and clinical manifestation [11]. Another classification system – the Cambridge classification of 1983 - evaluated endoscopic retrograde pancreatography signs. This system does not include the parameters of exocrine/endocrine pancreatic function and extra-pancreatic complications [12]. The Cambridge classification described a clinical grading system of chronic pancreatitis for the first time. The Cambridge criteria remain the standard for grading chronic pancreatitis. The Zurich classification published in 1997 and 1998 evaluated patients with an alcoholic form of chronic pancreatitis [13, 14]. However, this system did not provide prognostic or disease -stage related information. The study of Bagul and Siriwardena, published in 2006, describes the development of a three-stage clinical classification system for chronic pancreatitis – the Manchester Classification clinical grading system for chronic pancreatitis [15]. A three stage system separates patients with chronic pancreatitis – mild stage, moderate stage and end-stage. Five essential criteria were used for the imaging of the mild and moderate stage: endoscopic retrograde pancreatogram (ERP)/ magnetic resonance pancreatogram (MRP)/ CT evidence of chronic pancreatitis, abdominal pain, analgesia, exocrine-endocrine pancreatic function and peri-pancreatic complication. The criteria for end-stage were ERP/MRP/CT evidence of chronic pancreatitis, one or more extra-pancreatic complications: biliary stricture or segmental portal hypertension or duodenal stenosis, plus, one or more of the following diabetes or steatorrhea. This was the first study which demonstrated prognostic information according to the categorization of the severity of chronic pancreatitis [15]. The term "end-stage" chronic pancreatitis is also important in the evaluation of prognosis, complications and the optimal therapy of chronic pancreatitis. Other systems, including Heildeberg

or Kerala, help to describe the progression of the disease by grading the severity on the basis of clinical symptoms [16, 17].

The character or accuracy of the chosen method of evaluation is of fundamental importance in terms of the assessment of the severity and prognosis of chronic pancreatitis [18]. At present, the M-ANNHEIM criteria are recommended for the assessment of the severity and the Chronic Pancreatitis Prognosis Score (COPPS) system for the determination of prognosis at one-year follow-up intervals [19].

The M-ANNHEIM classification was first described in 2007 and identifies risk factors for chronic pancreatitis: A (alcohol), N (nicotine), N (nutritional factors), H (heredity), E (efferent pancreatic duct factors), I (immune factors), M (metabolic factors) [7]. The M-ANNHEIM classification is used in the prediction of the clinical course of chronic pancreatitis, including the need for possible surgical treatment. M-ANNHEIM clinical staging and the severity index are considered appropriate approaches for determining the stage and severity of chronic pancreatitis.

CHRONIC PANCREATITIS PROGNOSIS SCORE (COPPS)

This score predicts a short to medium term prognosis for the development of chronic pancreatitis [8]. The primary markers of the COPPS score include the number of hospitalizations for chronic pancreatitis, the length of hospitalization in days, and the severity of disease, which we refer to as markers of disease severity. These disease severity data are correlated with four parameters, namely body mass index (BMI), C-reactive protein (CRP), glycosylated hemoglobin (HbA1c) and platelet count. Using a numerical scale of 0–10, the intensity of pancreatic pain over the prior seven days is assessed [9, 10]. These five parameters allow the severity of chronic pancreatitis to be divided into three categories, labelled A, B and C, which is very similar to the Child-Pugh-Turcot score in hepatology. For people with COPPS A, COPPS B and COPPS C, the score is in the range of 5–6 points, 4–9 points and 10–15 points, respectively (Table I). Patients in the COPPS B and COPPS C categories require more frequent treatment during the 12-month follow-up period [1]. A study by Beyer et al. [8] and a prospective Indian study by Maheshwari et al. [20] confirmed the correlation between a high COPPS score and both the number and duration of hospitalizations. This prognosis is determined by the expected duration of hospitalization and rehospitalizations during the 12-month follow-up [8]. In Maheshwari's study, evaluating 177 patients with chronic pancreatitis, 11% of subjects were categorized as COPPS A, 60% as COPPS B, and 29% were categorized as COPPS C. There was no difference between the categories according to gender, age, type of employment, but also no difference in the presence of pancreatic calcifications. However, the duration of loss of work capacity, including the Karnowski index, was significant in relation to the positivity of the COPPS B and C categories. The alcoholic form of chronic pancreatitis was found more frequently in persons in categories B and C. Younger individuals were predominant in the study, the mean age was 39 years old, and 65% of the subjects enrolled were men. The Indian study confirmed that COPPS is an effective marker of the short-term (up to 1 year) prediction of the prognosis of chronic pancreatitis. In particular, the existence of a very strong correlation between COPPS value and the number or duration of hospitalizations, including the frequency of rehospitalizations, should be emphasized.

Table I. Chronic pancreatitis prognostic score (COPPS)

Parameter	Points		
	1	2	3
Pain intensity scale (0-10)	0-2	3-6	7-10
HbA1c (%)	> 6.0	5.5-6.0	< 5.5
CRP (mg/L)	< 3.1	3.1-20.0	> 20.0
BMI (kg/m^2)	25	18-25	< 18
COPPS A 5-6 points, COPPS B 7-9 points, COPPS C 10-15 points			

BMI: body mass index; CRP: C reactive protein; HbA1c: glycosylated hemoglobin.

TRINITY SCORE

In 2023, Laura Keaskin et al. [21] published a retrospective cohort study and analyzed data from 154 patients with newly diagnosed chronic pancreatitis. The patients were divided into two categories – with less than one hospital admission in the 6 years following diagnosis of chronic pancreatitis and the group of patients with more than one hospital admission. The following factors were evaluated: age, gender, smoking history, history of alcohol excess, history of alcohol abuse, exocrine and endocrine function, etiology of chronic pancreatitis (alcoholic, biliary, idiopathic others), BMI, pain – WHO analgesic ladder (Table II). The most common etiology for chronic pancreatitis was alcohol (> 60%). Smoking and alcohol consumption accelerated the disease progression [22]. A recent systematic

Table II. Trinity score - a clinical scoring system for patients with chronic pancreatitis

Etiology		BMI		Pain medications	
Idiopathic/other	0 points	Normal weight	0 points	No regular therapy	0 points
Alcoholic	1 point	Underweight	3 points	NSAIDs	5 points
Biliary	2 points	Overweight	2 points	Weak opioid	3 points
		Obese	1 point	Strong opioid	5 points
If male gender, add 1 point					
0-3 points		0–3 points		0-6 points	

Summary: 0-3 points represents a 0-25 % risk of more than 1 pancreatitis-related admission in the six years following diagnosis, 4-7 points: a risk between 25-50%, 8-10 points: a risk between 50-75%, 10-12 points: a risk between 75-80 %. NSAID: nonsteroidal anti-inflammatory drug.

review stated that weight loss affects 22% of patients with chronic pancreatitis at the time of diagnosis. The review also noted that 28% of patients had diabetes mellitus at the time of diagnosis, 30% of patients had endocrine dysfunction and about 40% had exocrine pancreatic dysfunction.

The Trinity clinical score seems useful in the prediction of the risk of pancreatitis-related hospitalization in newly diagnosed patients with chronic pancreatitis [23]. The gender, pain medication, being underweight, overweight or having obese BMI and alcoholic or biliary etiology were associated with an increased risk of pancreatitis-related hospital admission.

While several disease scoring systems have been reported for acute pancreatitis, e.g. the Glasgow scoring system [24] or the Ranson criteria [25], which were part of the Best Clinical Practice for acute pancreatitis at the time, similar to the Mayo score, which is part of therapeutic assessments, the situation is different for determining the prognosis of chronic pancreatitis. However, the publication by Beyer et al. [8] from 2017 was undoubtedly a breakthrough. This study was the first to report a prognostic assessment of chronic pancreatitis according to the COPPS.

A recent study from USA published in this year, provided data from 279 patients (median age 53 years, 51% females) with chronic pancreatitis [26]. COPPS score was calculated with baseline data and stratified by severity (low, moderate and high). The mean COPPS was 8.4. The severity distribution was 13.3% low, 66% moderate and 20.8% high. 37.6% of patients had one or more hospitalization for any reason, 32.2 % of subjects had one or more pancreas-related hospitalization. The prevalence of continued drinking at follow-up was higher in the low and moderate groups. All primary outcomes were significantly different between severity groups: hospitalization for any reason (number, p=0.004), and pancreas related hospitalization (p=0.02).

DISCUSSION

The main difference between COPPS and Trinity system is timing for prognostic evaluation. Trinity score system predicts the probability of a more-pancreatitis-related hospitalisation in the 6 years following a diagnosis of chronic pancreatitis. COPPS assesses disease progression and prognosis at a one-year follow-up interval. The individual parameters included in COPPS are BMI, CRP, platelet acount, glycosylated hemoglobin and pancreatic pain intensity. Trinity scoring system evaluates gender, pain medication, body weight, and etiology of chronic pancreatitis.

Nevertheless, the study published in 2020 by Rahman et al. [27], based on 235 full-text reviews and 49 other publications, concluded that the scoring systems available in practice do not fully reflect current medical advances and procedures, nor are they frequently used in clinical practice.

The COPPS system has been shown to be affected by the geographic region where it is used [20]. Advances and improvements in the effectiveness of chronic pancreatitis management have corresponded with advances in our understanding of the etiology, pancreatic function and symptoms, such as pancreatic pain, exocrine and endocrine pancreatic function, as well as increasingly accurate imaging modalities and diagnostic findings. With an efficient scoring system, we will be able to classify and characterize all forms of complications of chronic pancreatitis. In addition, we will be able to more accurately score the severity of chronic pancreatitis, both in routine clinical assessments and as part of studies, including interventional studies, and thus make more accurate and timely statements about the optimal treatment modality and the expected prognosis of the course of the disease [28]. However, whether COPPS can predict e.g. therapeutic response in chronic pancreatitis cannot be reliably expressed at present. Similarly, the role of metabolomics as prognostic markers of the disease cannot yet be unequivocally evaluated positively, although some findings are promising. From the above, it is evident that further prospective and multicenter studies are needed [8].

Prognostication is important in chronic pancreatitis; it can predict which patients with chronic pancreatitis will develop more severe discomfort and disability. An important fact is that the accurate diagnosis of an early form of chronic pancreatitis is essential for prognostic systems of chronic pancreatitis [29].

CONCLUSIONS

The COPPS prognostic scoring system is currently considered to have adequate accuracy in determining the prognosis of chronic pancreatitis. However, further prospective studies on this topic are required.

Conflicts of interest: None to declare.

Authors' contribution: B.K. conceived the study. P.D. and D.S. drafted the manuscript. M.P. and M.B. collected the literature resources. P.D., J.D. and M.U. revised the manuscript for important intellectual contents.

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