

Progression of Pancreatic Morphologic Changes and Endocrine Dysfunction After Acute Pancreatitis: Preliminary Results of the Longitudinal Goulash-Plus Cohort Study

Approximately 96% to 98% of patients survive acute pancreatitis (AP),¹ yet many are exposed to significant long-term risks that are often overlooked. AP may be followed by recurrent acute pancreatitis (RAP) episodes and early chronic pancreatitis (ECP), which can eventually progress to chronic pancreatitis (CP).^{2,3} Progression of endocrine dysfunction, defined as the combined proportion of newly diagnosed prediabetes and diabetes mellitus (DM), may also reach 35% in the first year after the first AP episode and 59% in the fifth year.⁴ However, the timing of the progression and underlying mechanisms are not fully understood.

The aim of the Goulash-Plus clinical study⁵ is thus to monitor and investigate the clinical progression of AP in the recurrence and development of CP and the development of endocrine insufficiency (diabetes, prediabetes) after AP.

Goulash-Plus is an observational, prospective, multicenter follow-up study enrolling AP patients from 4 centers (ISRCTN registration number: 63396106, ethical permission number: 5753-2/2018/EKU). Patients were grouped into AP, RAP (2 AP episodes without CP diagnosis), ECP (≥ 3 AP episodes or specific signs on imaging without CP diagnosis), and CP groups based on the morphology status of the pancreas. Endocrine status was used to form normal, prediabetes, and diabetes groups. Patients' morphologic and endocrine status was determined at inclusion (baseline characteristics) and during the yearly follow-up visits. The basic characteristics of the population and groups are shown in [Supplementary Figures 1A and 2A](#).

The 4-year follow-up data for the first 360 patients were analyzed for this ongoing study. Of the population under examination, 43.1% ($n = 155$) were women and 56.9% ($n = 205$) were men. The mean age was 54.5 ± 14.6 years.

On the basis of the morphologic categorization, 269 patients (74.7%) were classified into the AP group at baseline, 43 (11.9%) into the RAP group, 25 (6.9%) into the ECP group, and 23 (6.4%) into the CP group. By the end of the fourth year of follow-up, the proportion of patients with a RAP, ECP, or CP morphologic status more than doubled to 55.1% (95% confidence interval [CI], 47.48%–62.49%) from 25.3% (95% CI, 21.09%–30.04%) at baseline ([Figure 1A](#)). Among the 269 patients with a single AP at baseline, progression to RAP, ECP, or CP affected 35.1% by the fourth year ([Figure 1B](#)). Among the 157 with a single AP and normal endocrine status at baseline, 28.6% (95% CI, 22.11%–36.11%) experienced morphologic progression by the fourth year ([Figure 1C](#)). The percentage of new patients with recurrent AP episodes was the highest (7.3%) at the first-year follow-up ([Figure 1D](#) and [Supplementary Figure 1B](#)), whereas the results for patients with

progression of pancreatic morphologic changes were 21.2% in the first 2 years and 11.5% in the second 2 years ([Figure 1E](#) and [Supplementary Figure 1C](#)). The yearly change was statistically significant in the first ($P < .001$), second ($P < .001$), and fourth years ($P = .0007$) ([Supplementary Figure 1D](#)).

Endocrine status of the patients at baseline was normal for 212 (59.1%). In contrast, 98 (27.3%) were prediabetic at baseline, and 49 (13.6%) were diabetic, increasing to 76.4% (95% CI, 68.9%–82.52%) combined by the fourth year ([Figure 1F](#)). The proportion of diabetic patients nearly doubled by the first year follow-up and tripled by the fourth year, from 13.6% (95% CI, 10.44%–17.53%) to 25.8% (95% CI, 21.33%–30.84%) and to 39.2% (95% CI, 31.70%–47.24%), respectively. Among patients with a single AP at baseline, the percentage of prediabetes and diabetes combined grew from 41.5% (95% CI, 35.76%–47.48%) at baseline to 74.2% (95% CI, 64.89%–81.74%) in the fourth year ([Figure 1G](#)). In the population with a single AP episode and normal endocrine status ($n = 157$), 54.4% (95% CI, 42.2%–66.09%) had prediabetes or DM at the fourth-year follow-up ([Figure 1H](#)). During the 4-year follow-up, the progression of the endocrine status (the proportion of new prediabetes and new diabetes combined) was the highest in the first 2 years (30.4%, 21.2%, 8.2%, and 12.4%, respectively), as shown in [Figure 1I](#) and [Supplementary Figure 2B](#). The yearly change was statistically significant in the first ($P < .001$) and second ($P < .001$) years ([Supplementary Figure 2C](#)).

Within the population with a single AP episode at baseline, we found that 35.1% experienced morphologic status progression by the fourth year after AP and that endocrine dysfunction occurred in 74.3%. Further, progression was the most dynamic in the first 2 years. The results of the current investigation are thus consistent with our earlier recommendations of (1) defining ECP as having ≥ 3 AP episodes, and (2) considering ECP patients as a high-risk population for CP development; however, further validation is warranted in the final analysis of the Goulash-Plus study.

A single AP episode is known to double the risk of developing DM.⁶ In addition, the 74.3% prevalence of prediabetes and diabetes combined in the fourth year after a

Abbreviations used in this paper: AP, acute pancreatitis; CI, confidence interval; CP, chronic pancreatitis; DM, diabetes mellitus; ECP, early chronic pancreatitis; RAP, recurrent acute pancreatitis.

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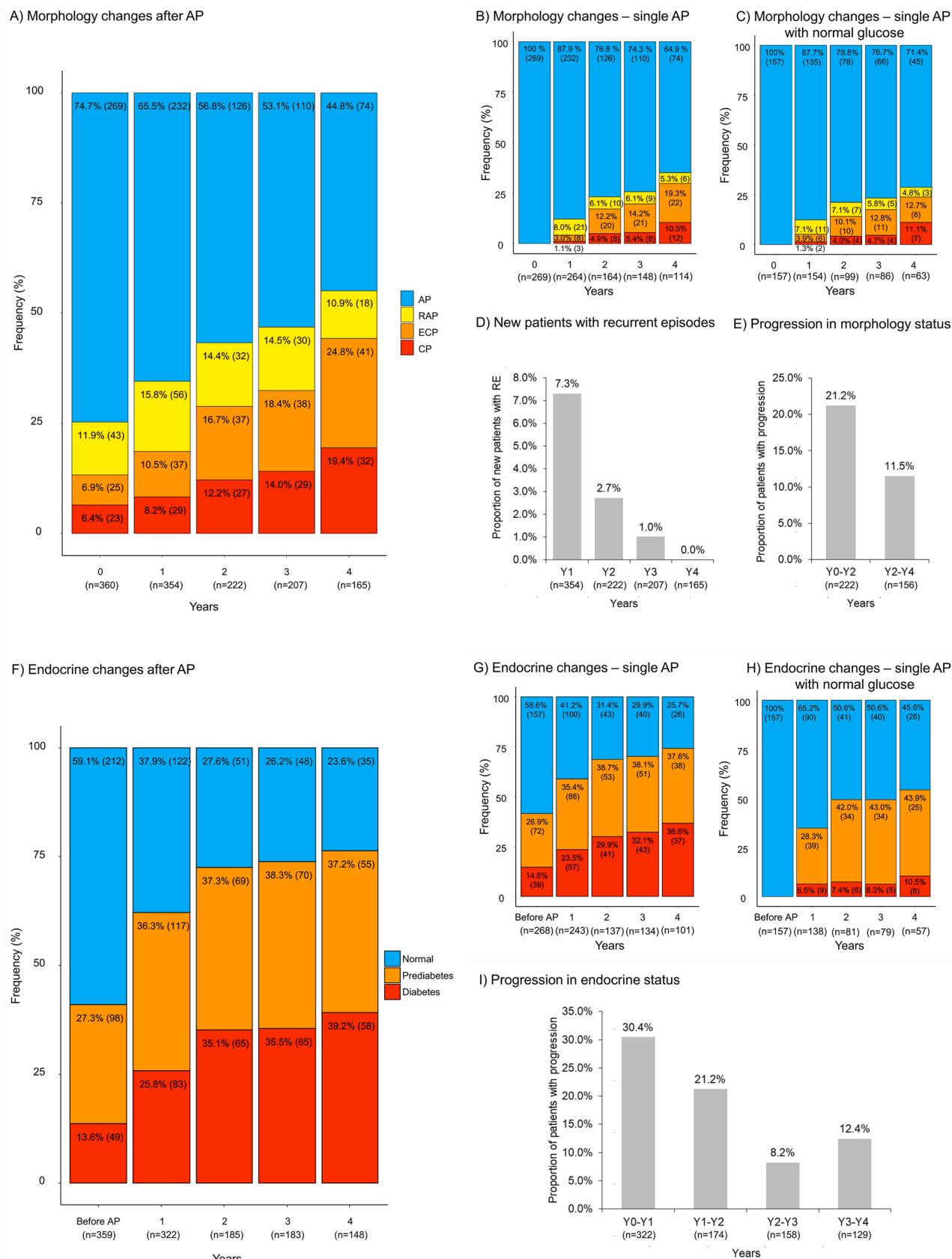


Figure 1. Morphology and endocrine changes after AP. (A) Morphologic changes in the total AP population. (B) Morphologic changes among patients with a single AP episode. (C) Morphologic changes among patients with a single AP episode and normal glucose status. (D) New patients with recurrent (RE) AP events in the total AP population. (E) Progression of pancreatic morphologic changes. (F) Endocrine changes in the total AP population. (G) Endocrine changes among patients with a single AP episode. (H) Endocrine changes among patients with a single AP episode and normal glucose status. (I) Progression in the endocrine status in the total AP population.

single AP episode was higher in our study than in earlier ones.^{4,7} Moreover, in our current investigation most of the morphologic and endocrine progression occurred within the first 2 years after AP. Therefore, imaging-based follow-up to detect morphologic progression and annual oral glucose tolerance testing to identify endocrine status progression might be recommended in the first 2 years after AP.

It is essential, however, to identify patients at higher risk of progression. Although several risk factors for DM development after AP were identified in earlier studies,^{4,7–9} future investigations should focus on identifying early clinical, laboratory, and imaging biomarkers and easily available prediction tools, such as the Early Achievable Severity (EASY) Index,¹⁰ which can predict the risk of CP or diabetes within the first 2 years after AP to improve long-term outcomes and optimize monitoring. Such efforts could facilitate the development of personalized follow-up protocols, helping to minimize unnecessary testing in low-risk patients while directing attention and resources toward those at greater risk.

Given the high incidence of pancreatic abnormalities observed, national and international guidelines may propose a targeted 2-year follow-up strategy after AP to assess both morphologic and endocrine complications.

ALEXANDRA MIKÓ

Institute for Translational Medicine
Medical School
University of Pécs
Pécs, Hungary, and
Department of Medical Genetics
Medical School
University of Pécs
Pécs, Hungary

NELLI FARKAS

Institute for Translational Medicine
Medical School
University of Pécs
Pécs, Hungary, and
Institute of Bioanalysis
Medical School
University of Pécs
Pécs, Hungary

ÁRON VINCZE

Division of Gastroenterology
First Department of Medicine
Medical School
University of Pécs
Pécs, Hungary

FERENC IZBÉKI

Department of Medicine, Gastroenterology and Hepatology
Szent György Teaching Hospital of County Fejér
Székesfehérvár, Hungary

ANDREA SZENTESI

Institute for Translational Medicine
Medical School
University of Pécs
Pécs, Hungary

PÉTER HEGYI

Institute for Translational Medicine
Medical School
University of Pécs
Pécs, Hungary, and
Centre for Translational Medicine
Semmelweis University
Budapest, Hungary, and
Institute of Pancreatic Diseases
Semmelweis University
Budapest, Hungary, and
Translational Pancreatology Research Group
Interdisciplinary Centre of Excellence for Research
Development and Innovation
University of Szeged
Szeged, Hungary

HUNGARIAN PANCREATIC STUDY GROUP

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at <https://doi.org/10.1053/j.gastro.2025.09.034>.

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Correspondence

Address correspondence to: Péter Hegyi, MD, PhD, DSc, MAE, Institute of Pancreatic Diseases, Semmelweis University, Tömörcsok útca 25-29, H-1085 Budapest, Hungary. e-mail: hegyi2009@gmail.com.

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The Hungarian Pancreatic Study Group includes Noémi Gede,¹ Vivien Vass,¹ Dalma Doboszai,¹ László Gajdán,² Veronika Lillik,^{2,3} Patrícia Sarlós,⁴ Beáta Bódis,⁵ Emese Sipster,⁶ Dániel Pécsi,^{1,4} Katalin Márta,⁷ Dorottya Tarján,⁷ Bálint Erőss,⁷ Nándor Faluhelyi,⁸ Péter Jenő Hegyi,^{3,7} Marie Engh,³ Mária Papp,⁹ Péter Mátrai,¹ Zsolt Abonyi-Tóth,^{3,10} Miklós Sahin-Tóth,¹¹ Ole H Petersen,¹² Markus M. Lerch,¹³ John P. Neoptolemos,¹⁴ Kálmán Tóth,^{15,16} Erzsébet Lankó,¹⁶ Péter Kanizsai,¹⁷ Szilárd Váncsa,³ Rita Nagy,³ Benedek

Tinusz,^{1,18} Erős Adrienn,¹ Zsolt Szakács,^{1,18} Péter Varjú,^{1,18} Anikó Nóra Szabó,¹ Noémi Zádori,^{1,19} Lajos Szakó,^{1,17} Alexandra Bálint,¹ Brigitta Teutsch,³ Andrea Párnitzky,^{1,20} Dóra Mosztbacher,¹ Szilárd Gódi,⁴ Judit Bajor,⁴ József Czimmer,⁴ Imre Szabó,⁴ Anita Illés,⁴ Gabriella Pár,⁴ Roland Hágendorn,⁴ Zsolt Márton,¹⁸ Tamás Nagy,²¹ Attila Miseta,²¹ András Vereczkei,²² Dezső Kelemen,²² Veronika Dunás-Varga,² Adrienn Halász,² Roland Fejes,² Pál Maurovics-Horvát,²³ Pál Ákos Deák,²⁴ Ibolya Kocsis,²⁵ Barna Vásárhelyi,²⁵ László Zúbek,²⁶ Zsolt Molnár,²⁶ Fruzsina Petlickij,⁷ Klaudia Káplár,⁷ Zoltán Hajnádý,⁷ Olga Julia Zahariev,⁷ Bettina Csilla Budai,^{7,27} Luca Havelda,⁷ Tamás Hussein,⁷ Balázs Lázár,⁷ Péter Sahin,⁷ Tamás Tornaí,⁷ Mónika Lipp,⁷ Emese Fürst,⁷ Edina Tari,^{2,3} Orsolya Eperjesi,⁷ Zoltán Bánfalvi,⁷ Boglárka Barna,⁷ Orsolya Urbán,⁷ Zita Kormos,⁷ Laura Tóth,⁷ and Andrea Harnos^{3,10}; from the ¹Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary; ²Szent György Teaching Hospital of County Fejér, Székesfehérvár, Hungary; ³Centre for Translational Medicine, Semmelweis University, Budapest, Hungary; ⁴Division of Gastroenterology, First Department of Medicine, Medical School, University of Pécs, Pécs, Hungary; ⁵2nd Department of Internal Medicine and Nephrological Center, Medical School, University of Pécs, Pécs, Hungary; ⁶Department of Internal Medicine and Haematology, Semmelweis University, Budapest, Hungary; ⁷Institute of Pancreatic Diseases, Semmelweis University, Budapest, Hungary; ⁸Department of Medical Imaging, Medical School, University of Pécs, Pécs, Hungary; ⁹Department of Gastroenterology, Institute of Internal Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary; ¹⁰Department of Biostatistics, University of Veterinary Medicine, Budapest, Hungary; ¹¹Department of Surgery, University of California Los Angeles, Los Angeles, California; ¹²School of Biosciences, Cardiff University, Cardiff, United Kingdom; ¹³Department of Medicine, Ludwig Maximilian University Hospital, Munich, Germany; ¹⁴Department of General, Visceral and Transplantation Surgery, Heidelberg University Hospital, Heidelberg, Germany; ¹⁵Division of Cardiology, First Department of Medicine, Medical School, University of Pécs, Pécs, Hungary; ¹⁶Szentágotthai Research Centre, University of Pécs, Pécs, Hungary; ¹⁷Department of Emergency Medicine, Medical School, University of Pécs, Pécs, Hungary; ¹⁸First Department of Medicine, Medical School, University of Pécs, Pécs, Hungary; ¹⁹Department of Anaesthesiology and Intensive Therapy, Medical School, University of Pécs, Pécs, Hungary; ²⁰Heim Pál National Pediatric Institute, Budapest, Hungary; ²¹Department of Laboratory Medicine, Medical School, University of Pécs, Pécs, Hungary; ²²Department of Surgery, Medical School, University of Pécs, Pécs, Hungary; ²³Medical Imaging Centre, Department of Radiology, Semmelweis University, Budapest, Hungary; ²⁴Department of Interventional Radiology, Semmelweis University, Budapest, Hungary; ²⁵Institute of Laboratory Medicine, Semmelweis University, Budapest, Hungary; ²⁶Department of

Anesthesiology and Intensive Therapy, Semmelweis University, Budapest, Hungary; and ²⁷Department of Dietetics and Nutritional Sciences, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary.

Andrea Szentesi and Péter Hegyi contributed equally to this work. The authors are grateful for the contributions of all the patients who consented to participate, the members of the Hungarian Pancreatic Study Group (HPSG), and their colleagues who took part in the data collection, data cleaning, and analysis at the Institute of Pancreatic Diseases at Semmelweis University and at the Institute for Translational Medicine, University of Pécs.

CRedit Authorship Contributions

Alexandra Mikó, MD, PhD (Conceptualization: Equal; Formal analysis: Supporting; Methodology: Supporting; Project administration: Lead; Visualization: Equal; Writing – original draft: Equal)

Nelli Farkas, PhD (Formal analysis: Lead; Methodology: Equal; Visualization: Lead; Writing – review & editing: Supporting)

Aron Vincze, MD, PhD (Data curation: Equal; Validation: Equal; Writing – review & editing: Supporting)

Ferenc Izbéki, MD, PhD (Data curation: Equal; Validation: Supporting; Writing – review & editing: Supporting)

Andrea Szentesi, PhD (Conceptualization: Supporting; Formal analysis: Lead; Methodology: Lead; Project administration: Equal; Visualization: Lead; Writing – original draft: Equal)

Péter Hegyi, MD, PhD, DSc (Conceptualization: Lead; Funding acquisition: Lead; Methodology: Supporting; Supervision: Lead; Writing – original draft: Equal)

Conflicts of interest

The authors disclose no conflicts.

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Data Availability

Original raw data are available from the corresponding author upon reasonable request.