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 study[5] 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 1*A* and 2*A*.

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 1*A*). Among the 269 patients with a single AP at baseline, progression to RAP, ECP, or CP affected 35.1% by the fourth year (Figure 1*B*). 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 1*C*). The percentage of new patients with recurrent AP episodes was the highest (7.3%) at the first-year follow-up (Figure 1*D* and Supplementary Figure 1*B*), 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 1*E* and Supplementary Figure 1*C*). The yearly change was statistically significant in the first ($P < .001$), second ($P < .001$), and fourth years ($P = .0007$) (Supplementary Figure 1*D*).

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 1*F*). 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 1*G*). 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 1*H*). 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 1*I* and Supplementary Figure 2*B*. The yearly change was statistically significant in the first ($P < .001$) and second ($P < .001$) years (Supplementary Figure 2*C*).

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

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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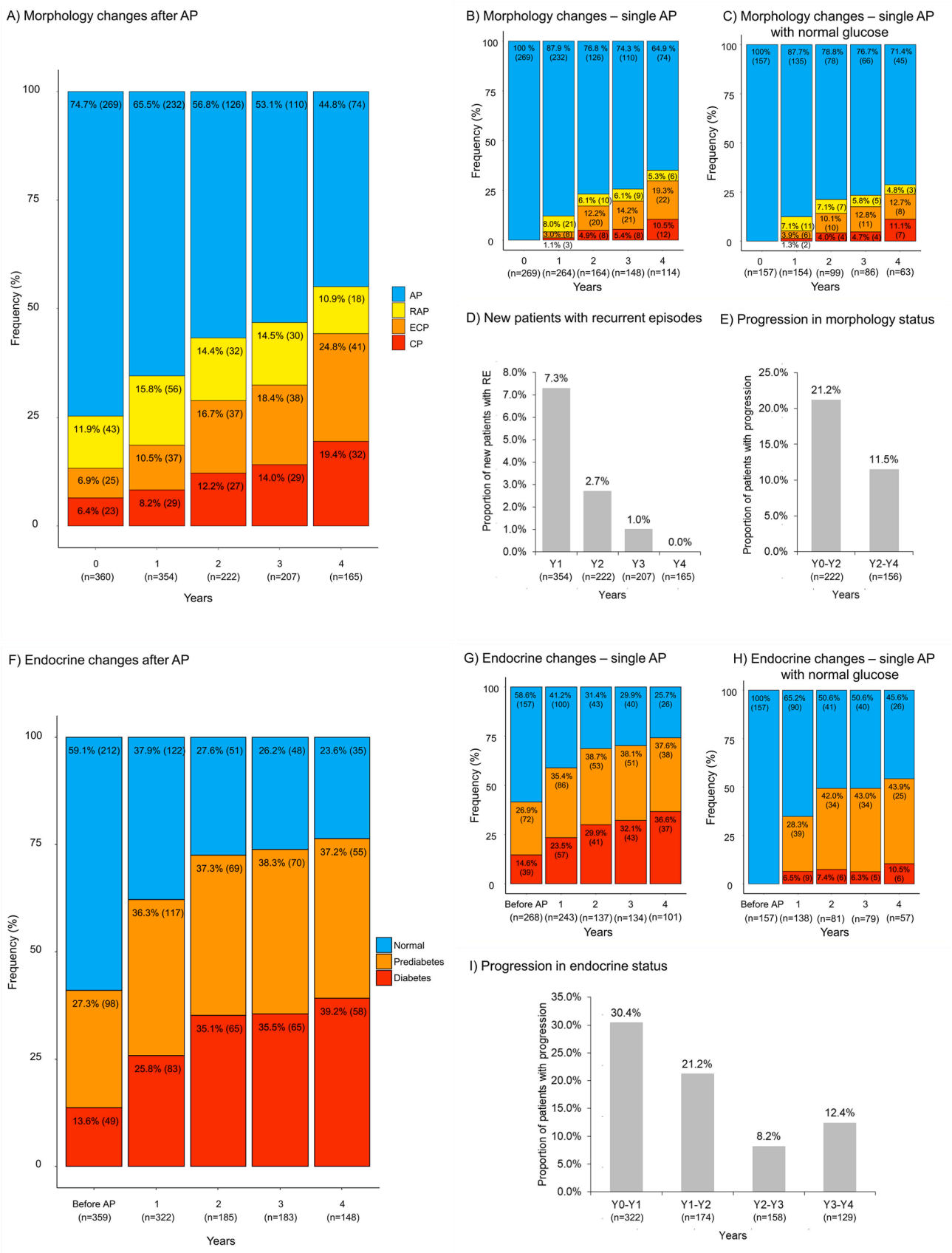

Figure 1. Morphology and endocrine changes after AP. (*A*) Morphologic changes in the total AP population. (*B*) Morphologic changes among patients with a single AP episode. (*C*) Morphologic changes among patients with a single AP episode and normal glucose status. (*D*) New patients with recurrent (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.

prediabetes and diabetes combined in the fourth year after a 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.

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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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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.