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Worldwide Variations in Demographics, Management, and Outcomes of Acute Pancreatitis

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Supplementary Material

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Conflicts of interest

The authors disclose no conflicts.

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Abstract

BACKGROUND & AIMS: Few studies have compared regional differences in acute pancreatitis. We analyzed data from an international registry of patients with acute pancreatitis to evaluate geographic variations in patient characteristics, management, and outcomes.

METHODS: We collected data from the APPRENTICE registry of patients with acute pancreatitis, which obtains information from patients in Europe (6 centers), India (3 centers), Latin America (5 centers), and North America (8 centers) using standardized questionnaires. Our final analysis included 1612 patients with acute pancreatitis (median age, 49 years; 53% male, 62% white) enrolled from August 2015 through January 2018.

RESULTS: Biliary (45%) and alcoholic acute pancreatitis (21%) were the most common etiologies. Based on the revised Atlanta classification, 65% of patients developed mild disease, 23% moderate, and 12% severe. The mean age of patients in Europe (58 years) was older than mean age for all 4 regions (46 years) and a higher proportion of patients in Europe had comorbid conditions (73% vs 50% overall). The predominant etiology of acute pancreatitis in Latin America was biliary (78%), whereas alcohol-associated pancreatitis accounted for the highest proportion of acute pancreatitis cases in India (45%). Pain was managed with opioid analgesics in 93% of patients in North America versus 27% of patients in the other 3 regions. Cholecystectomies were performed at the time of hospital admission for most patients in Latin America (60% vs 15% overall). A higher proportion of European patients with severe acute pancreatitis died during the original hospital stay (44%) compared with the other 3 regions (15%).

CONCLUSIONS: We found significant variation in demographics, etiologies, management practices, and outcomes of acute pancreatitis worldwide. ClinicalTrials.gov number: NCT03075618.

Keywords

Pancreas; Inflammation; Drug; Treatment

Acute pancreatitis (AP) is a global leading cause of gastrointestinal-related hospital admissions.[1] The incidence of AP has been reported to be increasing in the United States and Europe.[2,3] Approximately 20% of people affected develop severe disease resulting in high morbidity and mortality.[4] Over the last decade, multiple advances have occurred in management of AP, such as the development of the revised Atlanta classification of disease severity (RAC), introduction of early goal-directed intravenous fluid resuscitation, and implementation of a minimally invasive step-up approach in subjects with symptomatic necrotic pancreatic collections.[5–7] Possibly as a consequence of these developments, case fatality of AP may have decreased; however, estimates tend to vary among different countries.[8,9]

Large, multicenter studies in AP from national registries have been recently published. However, these have been confined to national bounds, with most being in North America and Europe.[10–13] Results from these studies have revealed heterogeneity in patient characteristics, such as demographics, etiology, and risk factors of severe disease. For instance, a large Spanish study from 2018 revealed an AP mortality rate of 4.2% compared with 1% from recent reports in the United States.[13,14] Inconsistent severity definitions and methodology hinder the combination and comparison of data from different regions.

Furthermore, it is unclear whether recent advances in management of AP have gained traction throughout different areas of the world.

Lack of prospective, multinational data in AP prompted investigators around the world to create a multicenter collaboration referred as Acute Pancreatitis Patient Registry to Examine Novel Therapies in Clinical Experience (APPRENTICE).[15] This study's aim was to evaluate the geographic differences in patient characteristics, management, and outcomes of AP across 4 different geographic areas using APPRENTICE data.

Methods

Study Population

APPRENTICE is a prospective, multicenter, international consortium studying clinical characteristics of AP patients across the world.[15] The University of Pittsburgh served as the coordinating center. Ethical committee approvals were obtained from local institutional review boards at all participating centers. University of Pittsburgh's institutional review board approved this study and acted as an umbrella institutional review board for incoming centers (PRO15040389). The study was registered in clinicaltrials.gov (NCT03075618). Details on design and methodology of APPRENTICE have been previously published.[15] Adults (≥18 years old) admitted with the diagnosis of AP, willing to participate in the study, and enrolled within 2 weeks of presentation were eligible for inclusion. Patients with a history of organ transplantation, trauma-induced AP, chronic pancreatitis, and pancreatic cancer were excluded. Enrollment occurred between October 2015 and January 2018. Site investigators were responsible for identifying eligible hospital admitted patients through different screening mechanisms. In total, data from 22 sites, which reached a set minimum number of enrollment (≥15 patients/center), were included for statistical analysis (Table 1, Figure 1).

Data Collection

Study questionnaires were carefully designed by recognized experts in the field (Supplementary Table 1). A well-established, secure, Web-based, electronic data collection software (Research Electronic Data Capture) was used.[16] A test period of 3 months was initially undertaken with the goal to assess applicability and quality of the questionnaires. Multiple online sessions with study personnel (site investigators, coordinators) were conducted before and during the enrollment phase to ensure the uniformity of data collection, answer questions, and address technical issues. Deidentified data were collected prospectively at different hospitalization time points: admission, Day 1, Day 2, Day 3, Day 7, and discharge. Data quality was routinely monitored by a dedicated statistician at the coordinating site. Definition of different collected variables is outlined in Supplementary Table 2.

The primary clinical outcomes of interest included RAC severity, length of stay (LOS), and in-hospital mortality. Additional outcomes included AP etiology, fluid volume in the first 24 hours of admission, fluid type, analgesic use, feeding methods, and endoscopic retrograde

cholangiopancreatography (ERCP) or cholecystectomy rates in cases of biliary pancreatitis. All authors had access to the study data and reviewed and approved the final manuscript.

Statistical Analysis

Statistical analysis was performed by expert biostatisticians (X.G., G.T.) at the coordinating center. Continuous variables were summarized by median and interquartile range (IQR). Categorical variables were presented with proportions of study subjects. Preliminary comparisons of outcome variables among various geographic areas were performed using the Fisher exact test for categorical values, and the nonparametric Kruskal-Wallis test was used for continuous variables (Tables 2–5). These were used as global tests that compared patient characteristic and clinical outcomes of interest through all 4 regions. Significance was defined as a $P \leq .05$; no adjustment for multiple testing was made in these exploratory analyses.

Subsequently, we focused on the primary clinical outcomes and multivariate regression models were applied to assess whether LOS, severity, and mortality differ among the 4 geographic areas, adjusting for other patient characteristics. The geographic regions were coded by 3 dummy variables, with North America as the reference region. For multivariable analysis, a linear regression was used to evaluate LOS differences among geographic areas, and logistic regression was used to assess differences in severity (severe AP vs others) and mortality (severe patients) among different regions. Such differences in outcomes between a region (Europe, India, or Latin America) and North America were presented as odds ratios in the case of severity and mortality, or as associated model coefficients in the case of LOS (Supplementary Tables 3–5).

Multivariable models were run including the following covariates: age, gender, body mass index, Charlson Comorbidity Index, etiology, transfer status, cholecystectomy during the same admission, narcotic use, and severity (only for LOS). The covariates of age, body mass index, Charlson Comorbidity Index, and etiology were constantly kept in the model for more accurate prediction, whereas the remaining covariates dropped when not significant. The likelihood ratio test was used to compare the nested model with region and the adjusted variables as covariates and the submodel with only the adjusted variables as covariates. All analyses were performed in R version 3.5.1 (R Foundation, Vienna, Austria).

Study Participants

In total, 1680 AP patients were enrolled between August 2015 and January 2018; 68 were omitted from the analysis yielding a final number of 1612 subjects. Exclusion of these subjects was related to removal of sites with <15 subjects enrolled from the analysis (13 patients), as part of the predetermined study criteria, or because of missing RAC data (55 patients) (Table 1, Figure 1).

Results

Baseline Characteristics and Etiology

Out of the 1612 patients, median age was 49 (IQR, 34–64), and 47% were females. Biliary (45%) and alcoholic (21%) were the most common pancreatitis etiologies (Table 2). Based on RAC, 65% were classified as developing mild disease, 23% as moderately severe, and 12% as severe disease. Median LOS was 8 days (IQR, 5–13) (Table 4). Overall, 45 patients died (2.8%) during their hospitalization (Table 5).

Age, gender, ethnicity, and race distributions differed significantly by geographic areas. Patients from Indian sites were mostly males (75%), younger in age (39 years; IQR, 30–50), with alcohol being the predominant etiology (45% vs 14% in remaining geographic areas; $P < .001$). Latin American patients were mostly young (median age, 43; IQR, 29–59), females (67%), with most of AP linked to biliary etiology (78% vs 37%; $P < .001$). In contrast, European and North American subjects had a relatively equal gender distribution, with an overall older age (58 [IQR, 45–74] and 52 [IQR, 37–65], respectively; $P < .001$). Post-ERCP pancreatitis was significantly more common in North American sites (19% vs 2.8% in remaining geographic areas; $P < .001$) (Table 2). These differences were mostly driven by 2 North American sites with 50 out of 90 and 22 out of 62 enrolled patients classified as post-ERCP pancreatitis, respectively.

Management

Data on patient management are presented in Table 3. The amount of intravenous fluids administered over the first 24 hours was similar among India, Latin America, and North America (range, 3–3.2 L); however, it was significantly lower in Europe (2.5 L; $P < .001$). Lactated Ringer solution and normal saline were the 2 main types of intravenous fluids administered in all regions except Latin America. Lactated Ringer solution was the dominant type of fluid in India (92%) in contrast to Latin America, where it was rarely used (7%; $P < .001$). The major types of fluids given in Latin America were normal saline (61%) and Hartman (32%), a balanced solution similar to lactated Ringer solution, which is not widely available in this region.

The use of analgesics was markedly variable across the world. In Europe, nonsteroidal anti-inflammatory medications comprised the mainstay of pain management (68%). Indian sites, however, used tramadol in 91% of their patients, whereas Latin American centers frequently used opioids (59%), nonsteroidal anti-inflammatory medications (48%), and tramadol (34%). In contrast, opioid analgesics constituted the cornerstone of analgesia in North America at 93% of subjects in contrast to 27% in the remaining regions ($P < .001$). Furthermore, 64% of subjects in North America were discharged on opioid analgesics compared with 2.7% in other geographic areas ($P < .001$).

European centers had the highest ratio of enteral to parenteral nutrition at 10:1 (32% vs 3% in subjects with moderate or severe disease), whereas total parenteral nutrition was most commonly administered in India in 27% of patients compared with 20% receiving enteral nutrition (ratio <1:1). The frequency of ERCP among subjects with biliary AP was significantly higher in North America (45% vs 14% for the remaining sites; P

< .001). With respect to same admission cholecystectomy, considerable variations were noted among patients with mild acute biliary pancreatitis; it was performed in 60% of such patients in Latin America, whereas in only 15% in India ($P < .001$). Moreover, early pancreatic interventions among patients with moderate or severe disease were more frequently performed in India (23% vs 7% in the remaining regions; $P < .001$).

Clinical Outcomes

When comparing the LOS among mild AP, patients in North America were found to stay in the hospital the shortest time (4 days) compared with other regions (7 days; $P < .001$). Severe AP developed in 23% of Indian patients compared with 9% in the rest of world ($P < .001$) (Table 4). Intensive care unit admissions were highest in Indian centers at 37.9% (Table 5). In-hospital mortality was found to be the highest in Europe (5.7%), followed by India (3.3%), Latin America (2.3%), and North America (0.6%; $P < .001$) (Table 5). Among European sites included, in-hospital mortality in different countries was distributed as such: Greece, 0%; Spain, 5%; Lithuania, 6.4%; and Romania, 8.6%.

Multivariate Analysis of Outcomes

Based on multivariable regression analyses that adjusted for potential confounders, such as age, gender, body mass index, Charlson score, etiology, transfer status, and other factors, the odds of severe AP were 11.2 times higher in Europe (95% confidence interval [CI], 5.8–21.6), 7 times higher in India (95% CI, 3.8–12.8), and 5.6 times higher in Latin America (95% CI, 2.8–11.1), compared with North America ($P < .001$) (Supplementary Table 3). LOS was 4.3 days longer (95% CI, 3.5–5.4) in Europe, 1.1 days longer (95% CI, −0.1 to 2.3) in India, and 6.4 days longer (95% CI, 5.2–7.7) in Latin America when compared with North America ($P < .001$) (Supplementary Table 4). The odds ratios for same-admission mortality among patients with severe AP was 10.4 (95% CI, 2.7–40.5) in Europe, 4.2 (95% CI, 0.9–18.8) in India, and 8.3 (95% CI, 1.7–41.3) in Latin America when compared with North America ($P < .001$) (Supplementary Table 5).

Discussion

In this large prospectively collected registry, significant differences in AP patient demographics, etiology, management approaches, severity, and clinical outcomes were seen around the world. Observed differences in etiology and demographics likely reflect a tight inter-connection between age, gender, and etiology. In Indian sites, where the most preponderant AP etiology was alcohol, most patients were young men. Previous studies have revealed a high proclivity of alcoholic pancreatitis in young Indian adults with heavy drinking patterns.[2,17–19] More specifically, a recent study from India published in 2018 reported an average age of 40 years with alcoholic pancreatitis representing 42% of all etiologies.[20] In Latin American sites, females were the predominant gender with biliary etiology being the most common. Latin America is known to have the highest rate of gallstone disease (more common among women) compared with other parts of the world.[21,22] A study in 2015 emanating from Argentina revealed similar findings, with biliary etiology accounting for 88% of all causes, and 58% of subjects being females.[12] Along the

same lines, older age among subjects from Europe is congruent with a study published in 2018 from this region.[13]

With regards to AP management, discrepancies in intravenous fluid volume and type administered over the first 24 hours are likely related to differences in accessibility to certain types of fluids, but most importantly, lack of high-quality evidence supporting which type and what amount of fluid is optimal, as highlighted in the recent American Gastroenterological Association guidelines in 2018.[23–27] Our findings further support the need for adequately powered, multicenter, randomized controlled trials comparing the efficacy of different fluid resuscitation protocols in AP patients.

The finding of disproportionally higher rate of opioid prescription during hospitalization and at the time of discharge in the North American sites is alarming. Of interest, a meta-analysis comparing nonsteroidal anti-inflammatory medications versus opioids for pain control in AP subjects revealed no difference in the efficacy between the 2 treatments.[28,29] It is not entirely clear why such divergences exist between North American centers compared with the rest of the world. Notably, no clear statements are included in the current societal guidelines addressing optimal strategies for analgesia in AP.

Based on strong evidence, current guidelines recommend limited use of urgent ERCP only among biliary AP patients with suspicion of cholangitis or biliary obstruction.[23] Our study showed that the rate of ERCPs performed in patients with biliary AP was much higher in North American sites. Impressive discrepancies have been previously reported in different counties (ie, 81% in Hungary, 52% in the United States, and 9% in Argentina).[10–12] The discrepancies observed in our study are difficult to explain; they are possibly related to referral bias, local practice patterns, and compensation structure differences.

Recent evidence supports same admission cholecystectomy among patients with biliary AP.[23,24] Our study revealed that the rate of same admission cholecystectomy varied significantly with the highest seen in Latin America and lowest in India. On further discussion with site investigators, it seems that AP patients are traditionally admitted under surgical care in Latin America, making performance of inpatient cholecystectomy logistically easier. A recent publication from Latin America confirmed these findings, where 54% of biliary AP subjects underwent same admission cholecystectomy.[12] In contrast, the low rate of same admission cholecystectomy in India could be explained by the high rate of transfers in the participating sites combined with patient preference to undergo this relatively simple operation locally at a later time.

Robust evidence highlights the use of enteral nutrition over total parenteral nutrition, and delaying pancreatic interventions in patients with moderate and severe AP, which is endorsed by current practice guidelines.[5,23,30,31] These recommendations were least adhered to in Indian centers, which is possibly accentuated by the higher rate of transfers.

It is clear from the management practices seen in our study that the adherence to current evidence-driven societal guidelines varies significantly between different geographic regions of the world. Only a minority of the previously mentioned practice patterns could be explained based on availability of resources. Thus, certain aspects of AP management, such

as the excessive administration of opioid analgesics and performance of ERCP in North American centers, overuse of total parenteral nutrition, and early pancreatic interventions in Indian sites, seem to lag behind the evidence. Additional effort is clearly needed to augment clinical implementation of certain therapeutic approaches supported by strong evidence in AP.

The finding that patients with mild AP in North American centers had a shorter LOS compared with other regions is consistent with a recent report showing that the overall LOS of AP in the United States has decreased from 6.5 days in 1997 to 4.7 in 2015.[1] This is likely related to incentive policies that have been applied over the last 2 decades in the United States resulting in shortening inpatient admissions.[32]

Our study revealed higher death rate among European sites when compared with other geographic regions. This observation could potentially be related to older age and higher rate of comorbid conditions seen in the European centers, both of which have been linked to mortality.[33] Notably, this difference persisted after adjustment for pertinent covariates in our multivariate analysis raising the question of other contributing factors. The lower mortality rate in North America seems consistent with recent reports indicating a decreased mortality over the last decade in the United States, possibly related to improved quality of intensive care unit care, and optimal timing for interventions.[14,34] Factors pertaining to baseline health and socioeconomic factors could possibly have contributed to these discrepancies in mortality.

This study has several strengths. It is the first of its kind to characterize differences in demographics, etiology, clinical profile, and management patterns and clinical outcomes in AP, by giving a snapshot of subject characteristics across different geographic regions of the world. Prior studies tackling this topic were limited by national bounds and lack of standardized methods for data acquisition. Distinctive attributes, which contribute to this study's strength, include its prospective nature, the large sample size with balanced representation between the different geographic areas with inclusion of at least 300 subjects from each studied region. Another important feature is the recent time of data acquisition over the last 3 years, following the introduction of the RAC, thus accurately reflecting current practices.[7,24] Moreover, most included sites were large, reputable institutions, with a high degree of expertise relating to pancreatic diseases. Furthermore, data collection was standardized, under rigorous monitoring resulting in a high data completeness rate, and quality. Finally, at the conclusion of the data collection process, to better understand regional practice patterns, an additional step was undertaken in obtaining site investigators' input into explaining the observed results.

With regards to the study's limitations, certain parts of the world, such as Africa, the Middle East, or East Asia, were not represented. Moreover, most participating sites were academic tertiary care hospitals, which may introduce a bias potentially affecting the generalizability of our results. Especially in North America, major ERCP referral centers were included whose unusual practice mix may not reflect that of the typical large American hospital. Finally, the proportion of subjects enrolled in the study compared with all AP patients hospitalized at each site varied based on available research resources.

In conclusion, we present a bird's-eye view of the variations in clinical characteristics of AP patients across the world by using a large, prospective, international registry. There seems to be remarkable variations in frequency of AP etiologies in different regions. The therapeutic interventions specific to each region are in certain aspects strikingly divergent, and in many occasions lag behind current evidence. Outcomes, such as LOS and mortality, are largely variable. In addition to depicting key features of AP, the results from this study may serve as a reference guide for designing future clinical trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used in this paper:

AP	acute pancreatitis
CI	confidence interval
ERCP	endoscopic retrograde cholangiopancreatography
IQR	interquartile range
LOS	length of stay
RAC	revised Atlanta classification

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What You Need to Know

Background

We analyzed data from an international registry of patients with acute pancreatitis to evaluate geographic variations in patient characteristics, management, and outcomes.

Findings

We found large variations in causes, treatment, and severity of acute pancreatitis worldwide.

Implications for patient care

Standards are needed for management of acute pancreatitis.

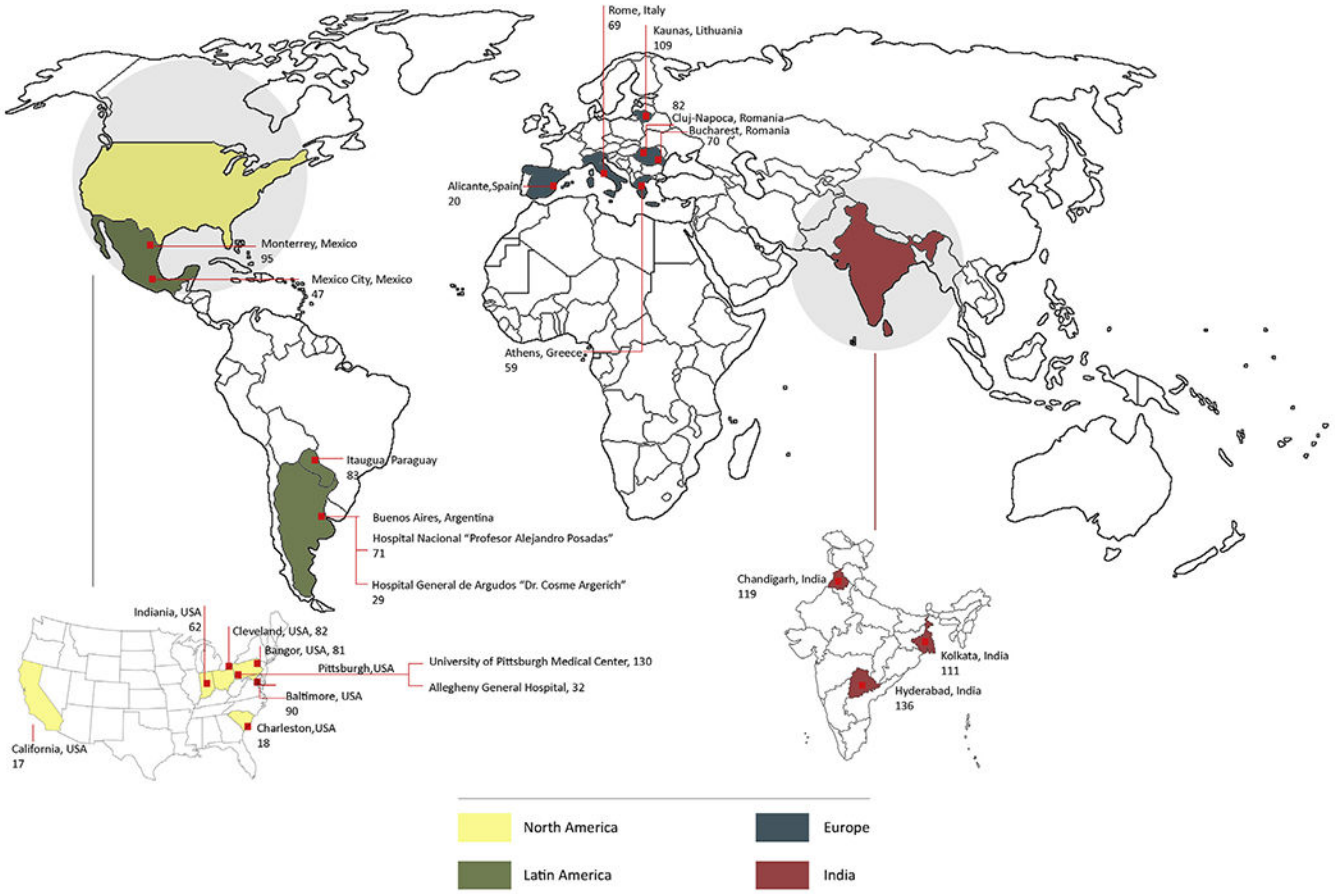

Figure 1.
Location of centers and enrollment per center.

Table 1.

Characteristics of Participating Centers

Center	Geographic area	Total enrolled	Estimated number of beds	Estimated number of AP admissions/year	Estimated rate of transfers, %
LUHS, Kaunas, Lithuania	Europe	109	>1000	100–200	50–75
University of Medicine, Cluj-Napoca, Romania	Europe	82	101–200	50–100	25–50
University of Medicine, Bucharest, Romania	Europe	70	>1000	100–200	<25
Sapienza University, Rome, Italy	Europe	69	301–500	50–100	<25
Attikon University, Athens, Greece	Europe	59	501–750	50–100	<25
Investigación, Alicante, Spain	Europe	20	751–1000	100–200	<25
AIG, Hyderabad, India	India	136	201–300	200–300	>75
Postgraduate Institute, Chandigarh, India	India	119	>1000	300–500	50–75
Apollo Gleneagles, Kolkata, India	India	111	501–750	50–100	<25
UAN, Monterrey, Mexico	Latin America	95	301–500	100–200	<25
Hospital Nacional, Itaugua, Paraguay	Latin America	83	301–500	100–200	<25
Nacional “Posadas,” Buenos Aires, Argentina	Latin America	71	301–500	100–200	<25
Universidad Autónoma, Mexico City, Mexico	Latin America	47	201–300	50–100	25–50
Hospital de Argudos, Buenos Aires, Argentina	Latin America	29	301–500	50–100	25–50
UPMC, Pittsburgh, PA	North America	130	751–1000	100–200	50–75
Johns Hopkins, Baltimore, MD	North America	90	>1000	100–200	25–50
Cleveland Clinic, Cleveland, OH	North America	82	>1000	>500	25–50
EMMC, Bangor, ME	North America	81	301–500	100–200	25–50
Indiana University, Indianapolis, IN	North America	62	201–300	200–300	50–75
AGH, Pittsburgh, PA	North America	32	501–750	300–500	25–50
MUSC, Charleston, SC	North America	18	751–1000	200–300	50–75
Kaiser, Los Angeles, CA	North America	17	301–500	100–200	<25

AGH, Allegheny General Hospital; AIG, Asian Institute of Gastroenterology; AP, acute pancreatitis; EMMC, Eastern Maine Medical Center; LUHS, Lithuanian University of Health Sciences; MUSC, Medical University of South Carolina; UAN, Universidad Autónoma de Nueva; UPMC, University of Pittsburgh Medical Center.

Table 2.

Comparison of AP Patient Demographics in Different Geographic Regions

Variable	Europe (n = 409)	India (n = 366)	Latin America (n = 325)	North America (n = 512)	Total (n = 1612)	*P* value
Age, median (IQR)	58 (45–74)	39 (30–50)	43 (29–59)	52 (37– 65)	49 (34–64)	< .001
Gender, male (%)	203 (49.6)	274 (74.9)	108 (33.5)	258 (50.6)	843 (52.5)	< .001
Ethnicity, Hispanic or Latino (%)	3 (0.7)	0 (0.0)	303 (97.4)	20 (4.0)	326 (20.6)	< .001
Race (not Hispanic) (%)						
Asian Indian	2 (0.5)	361(99.2)	0 (0.0)	6 (1.2)	36 (29.3)	< .001
Black or African American	0 (0.0)	0 (0.0)	0 (0.0)	82 (16.9)	82 (6.5)	
White	397 (99.3)	0 (0.0)	8 (100.0)	386 (79.4)	791 (62.9)	
Others	1 (0.3)	3 (0.8)	0 (0.0)	12 (2.5)	16 (1.3)	
CCI >1 (%)	298 (72.9)	132 (36.1)	153 (47.1)	314 (61.3)	897 (55.6)	< .001
Obesity, BMI ≥30 (%)	111 (28.5)	27 (7.4)	86 (27.0)	220 (43.3)	444 (28.0)	< .001
Etiology (%)						
Biliary	206 (50.4)	102 (27.9)	249 (78.1)	170 (33.3)	727 (45.3)	< .001
Alcohol	78 (19.1)	163 (44.5)	6 (1.9)	89 (17.5)	336 (20.9)	
Idiopathic	74 (18.1)	77 (21.0)	22 (6.9)	92 (18.0)	265 (16.5)	
Hypertriglyceridemia	19 (4.6)	7 (1.9)	19 (6.0)	30 (5.9)	75 (4.7)	
Post-ERCP	13 (3.2)	8 (2.2)	15 (4.7)	97 (19.0)	133 (8.3)	
Other	19 (4.6)	9 (2.5)	8 (2.5)	32 (6.3)	68 (4.2)	
Current smoking	103 (26.1)	95 (26.0)	38 (11.9)	129 (25.3)	365 (23.0)	< .001
Current alcohol use	194 (49.1)	166 (45.4)	57 (17.9)	189 (37.1)	606 (38.1)	< .001
Recurrent AP	95 (23.2)	75 (20.5)	42 (13.2)	185 (36.3)	397 (24.8)	< .001
Transfers (%)	81 (19.8)	260 (71.0)	35 (11.0)	171 (33.5)	547 (34.1)	< .001

NOTE. *P* values were calculated based on Fisher exact for categorical variables and Kruskal-Wallis global tests for continuous variables. Overall data completion rate was more than 95% for each of the variables.

AP, acute pancreatitis; BMI, body mass index; CCI, Charlson Comorbidity Index; ERCP, endoscopic retrograde cholangiopancreatography; IQR, interquartile range.

Table 3.

Comparison of AP Management Practices in Different Regions

Variable	Europe (n = 409)	India (n = 366)	Latin America (n = 325)	North America (n = 512)	Total (n = 1612)	*P* value
Intravenous fluids						
Amount, median (IQR)[a]	2.5 (2.0–3.6)	3.2 (2.0–4.5)	3.0 (2.5–3.8)	3.0 (2.0–4.2)	3.0 (2.0–4.0)	< .001
Type of fluid, LR (%)	315 (77.0)	337 (92.3)	24 (7.4)	253 (49.4)	930 (57.7)	< .001
Inpatient pain management (%)						
NSAIDs	277 (67.7)	1 (0.3)	155 (47.7)	91 (17.8)	524 (32.5)	< .001
Tramadol	184 (45.0)	334 (91.3)	111 (34.2)	40 (7.8)	669 (41.5)	< .001
Opioids	41 (11.9)	90 (24.9)	167 (59.0)	454 (92.5)	752 (50.8)	< .001
Opioids at discharge (%)	1 (0.3)	2 (0.6)	17 (6.2)	314 (64.3)	334 (23.3)	< .001
Nutritional support (%)						
Enteral nutrition[b]	34 (31.8)	43 (19.9)	15 (15.3)	46 (34.8)	138 (25.0)	< .001
TPN[b]	3 (2.8)	59 (27.3)	4 (4.1)	9 (6.8)	75 (13.6)	< .001
ERCP[c]	29 (14.4)	17 (16.8)	34 (14.1)	76 (44.7)	156 (21.9)	< .001
Cholecystectomy[d]	52 (31.7)	6 (15.0)	101 (59.8)	52 (42.6)	211 (42.6)	< .001
Early pancreatic intervention[b]	9 (8.4)	50 (23.1)	5 (5.1)	9 (6.8)	73 (13.2)	< .001

NOTE. *P* values are based on Fisher exact for categorical variables and Kruskall-Wallis global tests for continuous one. Missing data: Narcotics use during hospitalization was missing in 65 patients in Europe, 4 in India, 23 in Latin America, and 21 subjects in North America. Overall data completion rate for narcotics during hospitalization was 91.8%. Narcotics at discharge were missing in 90 patients in Europe, 16 in India, 51 in Latin America, and 24 subjects in North America. The overall data completion rate for narcotics at discharge was 88.8%; all other variables had overall data completion rate of more than 95%.

AP, acute pancreatitis; ERCP, endoscopic retrograde cholangiopancreatography; IQR, interquartile range; LR, lactated Ringer solution; NSAIDs, nonsteroidal anti-inflammatory drugs; TPN, total parenteral nutrition.

[a]Amount in liters within initial 24 hours of admission.

[b]Among revised Atlanta classification moderately severe or severe patients.

[c]Among biliary AP patients.

[d]Among RAC mild biliary AP patients.

Table 4.

Comparison of AP Severity in Various Regions of the World

Severity based on RAC (%)	Europe (n = 409)	India (n = 366)	Latin America (n = 325)	North America (n = 512)	Total (n = 1612)	*P* value[a]
Mild	296 (73.4)	148 (40.7)	213 (68.5)	374 (73.9)	1031 (65.1)	< .001
Moderately severe	59 (14.6)	134 (36.8)	75 (24.1)	94 (18.6)	362 (22.9)	
Severe	48 (11.9)	82 (22.5)	23 (7.4)	38 (7.5)	191 (12.1)	

NOTE. Data completion rate is more than 95%.

AP, acute pancreatitis; RAC, revised Atlanta classification.

[a]Fisher exact test was used as a global test to assess the association between regions and RAC severity.

Table 5.

Comparison of AP LOS, ICU Admissions, and In-hospital Mortality Among Various Regions Within Each RAC Group and Among All Study Participants

	Europe (n = 409)	India (n = 366)	Latin America (n = 325)	North America (n = 512)	Total (n = 1612)	*P* value
LOS per RAC groups						
Mild AP, median (IQR)	7 (6–10)	7 (5–9)	10 (6–16)	4 (3–6)	6 (4–10)	< .001[a]
Mod. severe, median (IQR)	11 (8.5–18)	10 (7– 15)	17 (8.–26)	8.0 (6–12.8)	11 (7–16)	< .001[a]
Severe, median (IQR)	28 (25– 41)	19 (13–25)	19 (13–25)	20 (13.5–32.5)	20 (14–31)	< .001[a]
Overall, median (IQR)	8 (6–12)	9 (6–15)	11 (7–19)	5 (3–8)	8 (5–13)	< .001[b]
ICU per RAC groups (%)						
Mild AP	2 (0.7)	18 (12.2)	0 (0.0)	9 (2.4)	29 (2.8)	< .001[c]
Mod. severe	11 (18.6)	54 (40.3)	3 (4.0)	26 (27.7)	93 (25.8)	< .001[c]
Severe AP	39 (81.2)	66 (80.5)	10 (43.5)	33 (86.8)	148 (77.5)	< .001[c]
Overall	54 (13.3)	138 (37.9)	13 (4.2)	68 (13.4)	273 (17.2)	< .001[d]
Mortality in various RAC groups (%)						
Mild AP	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Mod. severe	2 (3.4)	1 (0.8)	0 (0.0)	0 (0.0)	3 (0.8)	.12[e]
Severe AP	21 (43.8)	11 (13.4)	7 (30.4)	3 (7.9)	42 (28.2)	< .001[e]
Overall	23 (5.7)	12 (3.3)	7 (2.3)	3 (0.6)	45 (2.8)	< .001[f]

NOTE. Data completion rate is more than 95%.

AP, acute pancreatitis; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; Mod. severe, moderately severe; NA, *P* value non-calculable; RAC, revised Atlanta criteria.

[a]Kruskal-Wallis test was used to assess the association between regions and LOS within different severity groups.

[b]Kruskal-Wallis test was also applied for the association between regions and LOS among all participants.

[c]Fisher exact test was used to assess the association between regions and ICU admissions within different severity groups.

[d]Fisher exact test was also applied for the association between regions and ICU admissions among all study participants.

[e]Fisher exact test was used to assess the association between region and mortality (assessed in moderately severe and severe groups; no death seen in mild AP group).

[f] Fisher exact test was also applied for the association between hospital mortality and regions among all study participants.