

Insufficient implementation of the IAP/APA guidelines on aetiology in acute pancreatitis: Is there a need for implementation managers in pancreatology?

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Identifying the aetiology of acute pancreatitis (AP) on admission is crucially important in selecting the best and, in some cases, the most specific therapy. For example, early endoscopic retrograde cholangiopancreatography is the best intervention in biliary AP with cholangitis, lipid-lowering therapy in hypertriglyceridaemia-induced AP, pancreatic stent placement in pancreatic duct obstruction-evoked AP or steroid therapy in autoimmune pancreatitis. Unfortunately, the cause of AP remains unclear in almost a quarter of all cases, a situation which could be due to either an insufficient diagnostic work-up or other unknown aetiological factors. In addition, the importance of clear information on aetiology is underlined by the fact that the cause of about 40% of fatal AP cases is idiopathic.^{1,2} It should also be emphasised that knowing the aetiology is not only crucial for the index AP, but also essential in preventing recurrent or chronic pancreatitis.^{3,4} Therefore, it is not surprising that the current IAP/APA guidelines suggest endoscopic ultrasound (EUS) or magnetic resonance cholangiopancreatography (MRCP) after a negative work-up for biliary AP.⁵ Moreover, a genetic test is recommended after a second episode of idiopathic

pancreatitis in order to diagnose hereditary pancreatitis or to understand the genetic risks of AP.⁵

In this current issue of the *United European Gastroenterology Journal*, Hallensleben et al. investigate the diagnostic work-up and outcomes of 'presumed' idiopathic AP after the first attack of AP. Out of 191 first episodes of idiopathic AP patients, 176 underwent additional diagnosis, and the aetiological factor was identified in 64/176 (36%) patients. The underlying cause was mostly an occult biliary stone or neoplasm, which established an aetiological diagnosis, leading to a lower recurrence rate in these patients (15% vs. 43%). They concluded that additional diagnostic evaluations and stronger adherence to the current guidelines could identify the aetiology in one third of cases.⁶ The study was conducted brilliantly. However, the article did not share information on the level of diagnostic awareness (i.e. how many idiopathic cases were due to an insufficient on-admission diagnostic work-up) or adherence to the last part of recommendation A3 of the guidelines, which advises genetic testing after the second episode of idiopathic AP.

Table 1. Distribution of aetiology of AP according to our AP registry with 2400 cases.

Aetiology	First AP (N = 1791)	Second AP (N = 325)	Third or more AP (N = 284)
Idiopathic	358 (20%)	76 (24%)	70 (24%)
Biliary	835 (47%)	82 (25%)	20 (7%)
Alcohol induced	261 (15%)	84 (26%)	106 (37%)
Hypertriglyceridaemia, hyperlipidaemia induced	65 (4%)	21 (6%)	21 (7%)
Alcohol + hypertriglyceridaemia	47 (3%)	15 (5%)	6 (2%)
Combined	78 (4%)	10 (3%)	18 (6%)
Post ERCP	54 (3%)	6 (2%)	0
Other	93 (5%)	31 (10%)	43 (15%)

Values shown are n (%).

AP: acute pancreatitis; ERCP: endoscopic retrograde cholangiopancreatography.

Table 2. Imaging during hospital stay.

	First idiopathic AP (N = 358)	Second idiopathic AP (N = 76)
CT scan	126 (35%)	22 (29%)
Ultrasound	250 (70%)	55 (72%)
MRI	1 (0%)	2 (3%)
No imaging	17 (5%)	4 (5%)

Values shown are *n* (%).

CT: computed tomography; MRI: magnetic resonance imaging.

Table 3. Laboratory measurements during hospital stay.

	First idiopathic AP (N = 358)	Second idiopathic AP (N = 76)
Chol	85 (24%)	18 (24%)
TG	101 (28%)	22 (29%)
se-bi	268 (75%)	62 (82%)
GOT	242 (68%)	52 (68%)
GPT	231 (65%)	50 (66%)
ALP	291 (81%)	60 (79%)
gGT	297 (83%)	59 (78%)

Values shown are *n* (%).

Chol: cholesterol; TG: triglyceride; se-bi: serum bilirubin level; GOT: glutamic oxaloacetic transaminase; GPT: glutamic pyruvic transaminase; ALP: alkaline phosphatase; gGT: gamma-glutamyl transferase.

Therefore, in this brief, but very important study, we analysed the international, multicentre, prospective AP registry operated by the Hungarian Pancreatic Study Group to answer the remaining two questions. We investigated 2400 cases of AP uploaded from 30 centres in 13 countries between 2012 and 2019. Of these, 1791 patients had a single AP attack, 325 had two and 284 had three or more (Table 1). Investigation of the first episode of AP showed that biliary, alcoholic and hypertriglyceridaemia-induced AP represent the three most common aetiological factors responsible for the inflammation. However, 20% of cases remained idiopathic, which is quite similar to the data published by Hallensleben et al.⁶ (Table 1). Surprisingly, our results showed that 5% of the patients left the hospital after the first and second attacks of AP without any imaging at all (Table 2). As regards the laboratory parameters, 25% of patients had no diagnostic work-up for biliary AP (Table 3). Furthermore, the greatest insufficiency in aetiology screening concerned lipid-induced (triglyceride or cholesterol) pancreatitis: these measurements were lacking in 71–76% of cases (Table 3).

In the second part of our study, we investigated the additional diagnostic work-up for all idiopathic AP after index admission. There was no search for biliary, anatomic or cancer aetiology by EUS or MRCP in 91% of the cases, for autoimmune AP in 98% of

Table 4. Additional diagnostic work-up to identify the aetiology after the first and the second episode of idiopathic AP.

	First idiopathic AP (N = 358)	Second idiopathic AP (N = 76)
CT scan	24 (7%)	3 (4%)
EUS	18 (5%)	11 (14%)
MRCP	16 (4%)	9 (12%)
IgG4	6 (2%)	5 (7%)
Viral serology	20 (6%)	4 (5%)
Genetic testing	5 (1%)	9 (12%)

Values shown are *n* (%).

EUS: endoscopic ultrasound; MRCP: magnetic resonance cholangiopancreatography.

them, for genetic AP in 99% or for virus-induced AP after the first attack in 94% (Table 4). A similar but slightly better pattern was observed investigating the second AP. However, we cannot be sure whether the diagnostic work-up in these patients was not completed during or after the first attack (Table 4).

We have previously shown that the implementation of the IAP/APA guidelines is marked by major insufficiencies. Data from 9728 patients collected from 22 countries showed that Section F17 of the guidelines on the prevention of infectious complications is rarely used. In many countries, around 50% of patients receive antibiotics incorrectly.^{7,8} Section L36 of the guidelines recommends index admission cholecystectomy, which is still not applied in most hospitals.⁹

All in all, it is extremely depressing that scientists spend a great deal of money on research and guidelines, but they do not appear in everyday practice. Based on these unpleasant data, it would appear to be high time to create a new post, that of implementation manager, responsible for strict adherence to management guidelines in order to ensure cost effectiveness and high quality in patient care.

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