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**Recurrent acute biliary pancreatitis — A frequent and preventable condition potentially associated with morbidity and mortality**

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Recurrent acute biliary pancreatitis (RABP) is a common condition associated with an increase in hospital admissions, morbidity, mortality, and healthcare costs. This editorial will attempt to discuss the issue's current status as well as actions for its prevention.

Recurrent biliary pancreatitis is a common occurrence in our setting and represents a life-threatening risk for patients as well as a considerable resource burden on our health care system, despite being preventable when clinical practice guidelines are followed.

Following complete recovery from an initial AP event, the rate of readmissions for this condition is 10-32 % (1,2). While the term "recurrent acute pancreatitis" (RAP) has been used in the medical literature since the middle of the last century, given the ambiguity associated with its definition, etiology and management, an expert group was set up in 2018 to provide a consistent, consensus, useful definition for clinicians in daily practice and, especially, to allow comparison among studies. Thus, RAP was defined as more than one AP episode, with episodes at least 3 months apart and no evidence of underlying chronic pancreatitis or data suggesting the initial event did not

resolve completely (e.g., presence of pseudocysts or walled-off necrosis) (3). Therefore, episodes of abdominal pain and/or elevated pancreatic enzymes within 3 months after an AP event are considered a complication of the index AP rather than a new episode.

RAP not only contributes to increasing care costs but also determines morbidity and mortality, has a negative social and emotional impact on patients (4), and worst of all may trigger the development of chronic pancreatitis and exocrine pancreatic insufficiency (5). Therefore, efforts should be maximized to appropriately treat a first AP episode in order to avoid recurrence.

What are the causes of RAP? Any etiology of AP may be a cause of RAP: lithiasis and biliary sludge, congenital abnormalities such as pancreas *divisum* or annular pancreas, causes of pancreatic duct obstruction such as hypertonic Oddi's sphincter, genetic disorders, autoimmune disorders, occult pancreatic malignancies, and so-called idiopathic AP, where no predisposing factor is found. Of all these, biliary lithiasis, which represents the commonest cause of AP (40-70 % of events) (6,7), also is the most common etiologic factor of RAP (32-62 %), as shown by studies reported in the literature (8-11).

The next question we pose is, which is the cause of this high rate of RAP? The answer lies, no doubt, in low adherence to recommendations made by clinical guidelines (12). While the exact timing of cholecystectomy after a first admission for biliary AP has been subject to controversy, all scientific societies presently support early laparoscopic cholecystectomy for mild biliary AP, during the same admission if possible or within 4 weeks of discharge at most (13-16). In this regard a Dutch pancreas team carried out a multicenter study in 266 patients with mild biliary AP. It showed that cholecystectomy during the same hospital stay not only prevents readmissions for biliary RAP but also reduces cholelithiasis-related morbidity and mortality without rendering the technique more challenging or increasing reversion to open surgery rates (17). Some authors even suggested that cholecystectomy be performed within 24 hours of admission for predictably mild biliary AP in patients younger than 75 years with a low surgical risk (ASA < III), which would translate into reduced hospital stay and reduced need for endoscopic retrograde cholangio-pancreatography (ERCP) subsequently (18).

Furthermore, the management of severe biliary AP, which is luckily less common, is more complex and cholecystectomy must be delayed until local complications are solved (13-16). Similarly, in patients not fit for cholecystectomy whether because of older age, morbidity, or surgery rejection, endoscopic sphincterotomy represents a good alternative to prevent further attacks of biliary AP (19,20).

In this issue of *The Spanish Journal of Gastroenterology*, Parra-Membrives et al. (21) clearly show that patients not undergoing cholecystectomy after a first episode of biliary AP are at risk of developing subsequent biliary complications; specifically, 23 of their 104 patients without cholecystectomy (22 %) developed at least one additional episode of AP.

Our experience corroborates the data reported by these authors. In our 6-year study (data pending publication), 200 of 367 patients admitted for biliary AP underwent cholecystectomy, and only 3.4 % of these had a new AP episode versus 32.9 % of those who had not undergone the procedure.

Nevertheless, despite the above data and recommendations by clinical practice guidelines (12), early cholecystectomy remains uncommon (during the same admission or within 2-4 weeks of discharge at most). This lack of adherence to clinical practice guidelines is unfortunately widespread, as shown in the literature. In our country, according to Bejarano et al. (22), despite a high rate of cholecystectomies after mild biliary AP (70.6 %), waiting time (median, 97 months) is far longer than recommended. The authors warn of the negative consequences longer waiting lists had for their patients, where 51 of 55 admissions for recurrent biliary AP corresponded to non-cholecystectomized individuals. In the Italian study by Stigliano et al. (11), which assessed the recurrence rate of biliary AP, 38.4 % of patients had undergone no cholecystectomy or ERCP, and only 16.8 % of those cholecystectomized had received the procedure within a reasonable time frame of 30 days. The situation is similar in the USA, where Berger et al. (23) described that only 56 % of their patients had early cholecystectomy performed. This fact improved their RABP rate (5 % vs 20 %), and when the reasons why no surgery had been carried out were investigated, surprisingly, up to 22 % of their patients had not even been referred to a surgeon. On the other hand, in the national American study by Bial et al. (24), same-admission

cholecystectomy rates in the USA have worsened over time: 48.7 % in 2004 and 46.9 % in 2009, decreasing further down to 45 % in 2014, with no parallel increase in sphincterotomies. These authors blame delayed cholecystectomy on attempts at shortening hospital stays to deceitfully reduce admission-associated costs even at the risk of future readmissions, which would ultimately raise health care expenses.

In summary, in answering the question whether there is a way of decreasing readmissions for AP, we may safely say there is one in the significant subset of patients readmitted for RABP, namely early cholecystectomy. However, we are all aware of the long waiting lists for surgery hospitals have, and the shortage of health care resources at present. It is therefore crucial that fluent communications with surgeons be established so that following mild AP these patients may be prioritized for cholecystectomy during the same admission or within 30 days of discharge at most. ERCP with sphincterotomy would be a valid alternative for patients unfit for cholecystectomy. By complying with the recommendations offered by clinical guidelines on the management of biliary AP not only shall we reduce health care expenses but also AP-associated morbidity and mortality. While AP is certainly not a malignancy, it does determine significant quality-of-life issues and a potential risk for functional deterioration and progression to chronic pancreatic disease.

## REFERENCES

1. Yadav D, O'Connell M, Papachristou GI. Natural history following the first attack of acute pancreatitis. *Am J Gastroenterol* 2012;107:1096-103. DOI: 10.1038/ajg.2012.126
2. Jagannath S, Garg PK. Recurrent Acute Pancreatitis: Current Concepts in the Diagnosis and Management. *Curr Treat Options Gastro* 2018;16:449-65. DOI: 10.1007/s11938-018-0196-9.
3. Guda NM, Muddana V, Whitcomb DC, et al. Recurrent Acute Pancreatitis International State-of-the-Science Conference with Recommendations. *Pancreas* 2018;47(6):653-66. DOI: 10.1097/MPA.0000000000001053

4. Machicado JD, Gougol A, Stello K, et al. Acute pancreatitis has a long-term deleterious effect on physical health related quality of life. *Clin Gastroenterol Hepatol* 2017;15:1435-43. DOI: 10.1016/j.cgh.2017.05.037
5. Sankaran SJ, Xiao AY, Wu LM, et al. Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis. *Gastroenterology* 2015;149:1490-500. DOI: 10.1053/j.gastro.2015.07.066
6. Hammad AY, Ditillo M, Castanon L. Pancreatitis. *Surg Clin N Am* 2018;98:895-913. DOI: 10.1016/j.suc.2018.06.001
7. Tenner S, Baillie J, DeWitt J, et al. American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013;108(9):1400-15. DOI: 10.1038/ajg.2013.218
8. Zhang W, Shan HC, Gu Y. Recurrent acute pancreatitis and its relative factors. *World J Gastroenterol* 2005;11:3002-4. DOI: 10.3748/wjg.v11.i19.3002
9. Mallick B, Shrama DJ, Siddappa P, et al. Differences between the outcome of recurrent acute pancreatitis and acute pancreatitis. *JGH Open* 2018;2:134-8. DOI: 10.1002/jgh3.12060
10. Gao YJ, Li YQ, Wang Q, et al. Analysis of the clinical features of recurrent acute pancreatitis in China. *J Gastroenterol* 2006;41(7):681-5. DOI: 10.1007/s00535-006-1820-3
11. Stigliano S, Belisario F, Piciucchi M, et al. Recurrent biliary acute pancreatitis is frequent in a real-world setting *Dig Liver Dis* 2018;50(3):277-82. DOI: 10.1016/j.dld.2017.12.011
12. Kamal A, Akhuemonkhan E, Akshintala VS, et al. Effectiveness of guideline-recommended cholecystectomy to prevent recurrent pancreatitis. *Am J Gastroenterol* 2017;112:503-10. DOI: 10.1038/ajg.2016.583
13. Crockett SD, Wani S, Gardner TB, et al. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology* 2018;154:1096-101. DOI: 10.1053/j.gastro.2018.01.032
14. Uhl W, Warshaw A, Imrie C, et al. International Association of Pancreatology: IAP Guidelines for the Surgical Management of Acute Pancreatitis.

- Pancreatology 2002;2:565-73. DOI: 10.1159/000071269
15. Kimura Y, Takada T, Kawarada Y, et al. Guidelines for the management of acute pancreatitis: treatment of gallstone-induced acute pancreatitis. *J Hepatobiliary Pancreat Surg* 2006;13:56-60. DOI: 10.1007/s00534-005-1052-6
  16. United Kingdom guidelines for the management of acute pancreatitis. British Society of Gastroenterology. *Gut* 1998;42(Suppl 2):S1-13. DOI: 10.1136/gut.42.2008.s1
  17. da Costa DW, Bouwense SA, Schepers NJ, et al. Same admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. *Lancet* 2015;386:1261-8. DOI: 10.1016/S0140-6736(15)00274-3
  18. Mueck KM, Wei S, Pedroza C, et al. Gallstone Pancreatitis Admission Versus Normal Cholecystectomy—a Randomized Trial (Gallstone PANC Trial). *Annals Surg* 2019;270(3):519-27. DOI: 10.1097/SLA.0000000000003424
  19. Tenner S, Baillie J, DeWitt J, et al. American College of Gastroenterology Guideline: Management of Acute Pancreatitis. *Am J Gastroenterol* 2013;108:1400-15. DOI: 10.1038/ajg.2013.218
  20. García de la Fíla-Molina I, García-García de Paredes A, Martínez-Ortega A, et al. Biliary sphincterotomy reduces the risk of acute gallstone pancreatitis recurrence in non-candidates for cholecystectomy. *Dig and Liver Dis* 2019;51:1567-73. DOI: 10.1016/j.dld.2019.05.007
  21. Parra-Membrives P, García-Vico A, Martínez-Baena D, et al. Long-term outcome of patients with biliary pancreatitis not undergoing cholecystectomy. A retrospective study. *Rev Esp Enferm Dig* 2021;114(2):xx-xx. DOI: 10.17235/reed.2021.7891/2021
  22. Bejarano-González N, Romaguera-Monzonis A, García-Borobia FJ, et al. Cómo afecta el retraso de la colecistectomía tras la pancreatitis aguda litiásica en la aparición de recidivas. Consecuencias de la falta de recursos. *Rev Esp Enferm Dig* 2016;108(3):117-22.
  23. Berger S, Taborda-Vidarte CA, Woolard S, et al. Same-Admission Cholecystectomy Compared with Delayed Cholecystectomy in Acute Gallstone

Pancreatitis: Outcomes and Predictors in a Safety Net Hospital Cohort. South Med J 2020;113(2):87-92. DOI: 10.14423/SMJ.0000000000001067

24. Bilal M, Kline KT, Trieu JA, et al. Trends in same-admission cholecystectomy and endoscopic retrograde cholangiopancreatography for acute gallstone pancreatitis: A nationwide analysis across a decade. Pancreatology 2019;19:524-30. DOI: 10.1016/j.pan.2019.04.008