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Anna Rostropowicz-Honka, Zenon Brzoza
Department of Internal Diseases, Allergology, Endocrinology and Gastroenterology, Institute of Medical Sciences, University of Opole, Opole, Poland

Type 2 Diabetes as a Factor Modifying the Course and Prognosis of Acute Pancreatitis

ABSTRACT

Objective: Acute pancreatitis (AP) and type 2 diabetes (T2D) are diseases with steadily increasing incidence. On the one hand, the presence of diabetes increases the risk of AP development; on the other hand, there is a question whether the presence of T2D adversely affects the course and prognosis of AP. In this study we attempted to demonstrate the adverse effect of T2D on the course and prognosis of AP.

Materials and methods: The retrospective study analyzed the data of 333 patients with the diagnosis of AP in the Internal Medicine Department of the University Hospital in Opole between 2015 and 2019. The patients were divided into two groups: with T2D and without T2D. The comparative analysis included data from physical examination, selected laboratory parameters, presence of concomitant diseases, abdominal computed tomography (CT) image and others. The Mann-Whitney U test was used to compare differences between the two groups of patients. All hypotheses were verified at a significance level of 5%. The normality of the distribution of parameters (variables) was tested with the nonparametric Kolmogorov-Smirnov test.

Results: It has been proven that patients with AP and T2D have a more pronounced inflammatory reaction, are more likely to have cardiovascular diseases, have worse renal function and are significantly more likely to have an image of necrotic AP on CT. The duration of hospitalization of these patients is prolonged by 3 days.

Conclusions: T2D significantly worsens the course of AP and should be considered as an adverse prognostic factor. (Clin Diabetol 2022; 11; 6: 387–392)

Keywords: type 2 diabetes, acute pancreatitis, prognosis

Introduction

Acute pancreatitis (AP) is one of the most serious emergency conditions in gastroenterology and still, despite many years of studies, observations and existence of various prognostic scales, its course and prognosis cannot be fully predicted. Changing lifestyle, diet, obesity, and alcohol consumption cause the increase in the incidence of AP worldwide. Epidemiological studies are unambiguous: in the majority of countries, the several-fold increase in the incidence of and hospitalizations due to AP has been observed. Such observations were made, among others, in the USA, Spain, Scotland, Japan and Taiwan. This trend is observed not only in Europe and North America but also in Asia [1–4]. Globally, it is estimated that there has been a ten-fold increase in the incidence over the past 40 years. The expenditures incurred by the health care system of many countries for the treatment of AP and its complications have also increased significantly [5, 6]. The most common AP causes are gallstones, alcohol, hypertriglyceridemia, biopsy, pancreas surgery and endoscopic procedure complications, pancreas and papilla of Vater neoplasms, anatomic deviations, some drugs and toxins [7].

Address for correspondence:
Dr n. med. Anna Rostropowicz-Honka
Klinika Chorób Wewnętrznych, Alergologii, Endokrynologii i Gastroenterologii, Uniwersytecki Szpital Kliniczny
Al. W. Witosa 26, 45-401 Opole
phone: +48 (77) 452 06 04
e-mail: anna.rostropowicz-honka@uni.opole.pl
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At the same time, a systematic increase in the incidence of T2D has been observed for many years. Currently, more than 422 million people worldwide suffer from diabetes, including almost 3 million in Poland [8, 9]. There are quite a lot of observational studies suggesting an increased risk of AP development T2D patients, as well as indicating the risk of severe AP in these patients [5, 10, 11]. In general, the causes of AP in people with T2D are similar to those in the whole population. Patients with T2D are mainly overweight or obese, often with lipid metabolism disorders, especially hypertriglyceridemia, i.e., those with significant risk factors for gallstones. Numerous studies have documented a higher prevalence of gallstones in patients with T2D. Gallstones, as mentioned above, is among the main etiologic factors of AP [12].

One the one hand, the presence of T2D increases the risk of AP; on the other hand, there is a question whether the presence of diabetes adversely affects the course and prognosis of this disease.

According to the Atlanta Classification modified in 2012, the course of AP may be as follows: mild, self-limiting, with no major sequelae, usually resolving in about one week: moderately severe form with transient local or systemic organ complications resolving within 48 hours, and severe with pancreatic parenchymal necrosis and severe multi-organ complications [13]. The all-cause mortality in this disease is about 5% and dramatically increases in the severe form — up to 50%, and in critically ill patients with multi-organ failure and infected pancreatic parenchymal necrosis — even 100% [13, 14]. Due to high mortality rate and limited therapeutic possibilities in AP, it is important to identify risk factors, especially potentially modifiable ones, to predict early the course of this disease.

Over the years, various multifactorial prognostic scales have been developed to monitor the disease and estimate the risk of severe AP. These scales take into account different variables, such as: age, some elements of the physical examination, as well as selected laboratory test results. Of course, individual prognostic factors also play an important role: CRP, procalcitonin and their dynamics of change.

Among the most commonly used prognostic scales, only the Ranson and Glasgow scales consider hyperglycemia accompanying AP as a prognostically unfavorable factor. The Ranson scale scores glycemia above 200 mg/dL as an unfavorable factor, whereas the Glasgow scale — glycemia above 180 mg/dL [15, 16]. Hyperglycemia in the course of AP may result from pre-existing and treated diabetes, may be a symptom of diabetes not yet recognized, and may also be an expression of acute inflammatory response and pancreatic islet damage [17].

As previously mentioned, there are observational studies as well as meta-analyses available, suggesting a worse course of AP in patients with T2D. From the epidemiological point of view, the problem of predicting the severity of the course of AP, patient monitoring, and making appropriate diagnostic and therapeutic decisions will certainly grow, considering the epidemiological data. The aim of the study was to evaluate the influence of T2D on the different aspects of the clinical course of AP.

Materials and methods

Study population and sample size

The retrospective study analyzed the data of 333 patients hospitalized between 2015 and 2019 in the Department of Internal Diseases University Hospital in Opole, with the diagnosis of AP. Among these patients, there were 68 patients with T2D treated with insulin and/or oral hypoglycemic agents. Patients were characterized in terms of age, gender and etiology of AP. Patient records were checked for the following comorbidities: cardiovascular disease, chronic renal failure (CRF) and obstructive lung diseases (asthma or chronic obstructive pulmonary disease).

Diagnostic parameters

The analysis was performed on selected laboratory results of all patients admitted with the diagnosis of AP, taking into account selected parameters of peripheral blood count, severity of inflammatory response, renal function: hemoglobin (Hb), hematocrit (Ht), leukocytosis (L), C-reactive protein (CRP), procalcitonin (PCT), creatinine, glomerular filtration rate (eGFR). Above mentioned parameters in both studied groups of patients (with and without T2D) were compared. The examination performed at admission, after 48 hours and before discharge/death of the patient were subjected to comparative evaluation. The abdominal computed tomography (CT) image, duration of hospitalization, number of patients ordered to Intensive Care Unit treatment, as well as mortality in both groups were also compared.

Statistical analysis

The U Mann-Whitney test was used to compare statistical significance of differences. All hypotheses were verified at a significance level of 5%. The normality of the distribution of parameters (variables) was tested with the Kolmogorov-Smirnov test. Statistica computer program was used for statistical calculations (StatSoft INC, USA).

Table. 1 Characteristics of Patients According to Age and Gender

Gender	Age < 39 (%)	Age 40–64 (%)	Age > 65 (%)	Total (%)
M	60 (18)	70 (21)	62 (19)	192 (58)
F	22 (7)	49 (14)	70 (21)	141 (42)
Total	82 (25)	119 (35)	132 (40)	333 (100)

F — female; M — male

Table. 2 Prevalence of Type 2 Diabetes in Patients with Acute Pancreatitis

Gender	Patients without diabetes (%)	Patients with diabetes (%)	Total (%)
M	152 (46)	40 (12)	192 (58)
F	113 (34)	28 (8)	141 (42)
Total	265 (79.6)	68 (20.4)	333 (100)

F — female; M — male

Results

The study group consisted of 333 patients. In order to assess the dynamics of increase in the number of hospitalizations of patients with the diagnosis of AP, the hospital database available since 1997 was verified. Similarly, during the 5-year period, i.e., from 1997 to 2001, a total of 132 patients with this diagnosis were hospitalized. On the other hand, during the last 5 years (2015–2019), this number increased to 333, which gives a 2.5-fold increase in the number of patients treated for AP over the period of approximately 20 years. In the analyzed group of patients, there were 192 males and 141 females (Tab. 1). AP in our group was caused by cholelithiasis (58.6%), alcohol (32.7%), idiopathic cause (3.6%), pancreatic cancer (3.3%), endoscopic retrograde cholangiopancreatography (ERCP) (0.9%), hypertriglyceridemia (0.6%) and autoimmunity (0.3%). T2D was present in 20.4% of AP patients (Tab. 2). Comorbid cardiovascular diseases (including ischemic heart disease, history of ischemic stroke, peripheral artery disease, aortic aneurysm and heart failure) were present in 25% of AP with T2D and in 11.6% of patients without T2D, CRF (diagnosed before the episode of AP) in 4.4% and 0.4% respectively. Comorbid diseases of respiratory system were found only in patients without diabetes (1.9%). The data presented above show that in both analyzed groups of patients, the percentage of patients with T2D and cardiovascular diseases or CRF differs from the percentage of patients with the same comorbidities but without T2D. The prevalence of cardiovascular disease is 2.5 times more common than in patients without T2D.

Comparing the mean hemoglobin concentration and hematocrit value in the two groups of patients, statistically significant differences were found for the measurements at 48 hours and final; patients with T2D showed a greater tendency to anemia. On the other hand, the leukocytosis value was significantly higher in patients with T2D and AP — on admission, patients in this group had higher leukocytosis and this trend continued at subsequent follow up, with statistically significant differences. The inflammatory reaction was also monitored by the sensitive acute phase protein, CRP, which was observed to increase 48 hours after admission. The group of patients with T2D was characterized by statistically significantly higher CRP values in the second measurement. However, such relation was not observed for procalcitonin. Worse renal function, expressed by higher creatinine concentration and mildly decreased eGFR was present in patients with T2D in all three measurements and these differences were statistically significant and their value corresponded to stage II chronic renal failure (Tab. 3). However, the clinical course of the disease is different. Abdominal computed tomography (CT) was indicated to be performed in 150 patients with severe AP. There were 119 patients without diabetes and 32 patients with T2D. The groups were not statistically significantly different from each other. However, statistically significant differences in CT images were observed. Necrotic form of AP was diagnosed in 11 patients with T2D and in 20 patients without this disease. Proportionally, a higher percentage of patients with T2D had severe AP course and these differences were statistically significant. The number of patients requiring transfer to the Intensive Care Unit was small — 9 patients in total, which constituted 2.7% of all hospitalized patients. This included 2 patients with T2D and 7 patients without diabetes. The differences were not statistically significant. Among the group of 68 patients with T2D, 4 patients died, while in the group of 265 patients with AP without contaminant T2D, 8 patients died. No statistically significant differences were found in this regard either. On the other hand, the two groups of patients with AP differed in the hospitalization duration time. Patients with T2D stayed an average of 11.6 days in the hospital, while those without diabetes stayed 8.9 days; this difference was statistically significant (Tab. 3).

Discussion

AP is a serious disorder with an uncertain prognosis, frequently resulting in systemic complications.

Table. 3 Comparison of Values of Selected Laboratory Parameters in Consecutive Measurements and the Incidence of Different Parameters Characterizing Acute Pancreatitis Course in Both Analyzed Groups

Variable	Patients with diabetes	Patients without diabetes	P-value
Hb1 (g/dL)	14.1	14.3	< 0.32
Hb2	12.2	12.8	< 0.02
Hb3	11.8	12.7	< 0.01
Ht1 (%)	41.6	41.9	< 0.54
Ht2	36.8	38.4	< 0.03
Ht3	35.7	38	< 0.01
L1 (10^3/μL)	14.1	11.9	< 0.01
L2	11.5	9.8	< 0.02
L3	9.4	8.4	< 0.04
CRP1 (mg/L)	54.4	49.6	< 0.64
CRP2	185.7	134	< 0.01
CRP3	45.8	43	< 0.30
PCT1 (ng/mL)	2.4	2.1	< 0.16
PCT2	1.4	1.3	< 0.06
PCT3	0.3	0.2	< 0.37
Creatinine1 (mg/dL)	1.2	0.9	< 0.01
Creatinine2	1.1	0.8	< 0.01
Creatinine3	0.9	0.8	< 0.01
eGFR1 (mL/min/1.73m^2)	71.1	86.8	< 0.00
eGFR2	78.4	92.1	< 0.00
eGFR3	85.6	94.6	< 0.00
CT	32 (47.1%)	119 (42.9%)	0.54
Edema	21 (65.6%)	99 (83.2%)	< 0.00
Necrosis	11 (34.4%)	20 (16.8%)	< 0.00
ICU	2 (2.9%)	7 (2.6%)	0.89
Death	4 (5.9%)	8 (3%)	0.25

CRP — C-reactive protein; CT — computed tomography; eGFR — glomerular filtration rate; Hb — hemoglobin; Ht — hematocrit; ICU — admission to intensive care unit; L — leukocytes; PCT — procalcitonin

It is important to identify risk factors, potentially negatively modifying AP course. T2D is supposed to be one of them. The above presented results are in partial agreement with literature data. T2D as a chronic metabolic disease may negatively affect the course and prognosis of AP. The main role is played by chronic hyperglycemia and visceral adipose tissue as a site of synthesis of numerous proinflammatory cytokines. Increased levels of, among others, TNF-α, amylin and interleukin 6 (Il-6) were observed in patients with AP and diabetes [18]. The aforementioned proinflammatory cytokines affect the exocrine cells of the pancreas stimulating their excessive secretion, disturb the blood flow through the pancreatic capillaries, and contribute to increased insulin resistance. The role of Il-6 in the development of acute pancreatic necrosis is very important. This proinflammatory cytokine is responsible not only for generating pancreatic necrosis, but also for lung tissue damage and the development of acute respiratory failure in these patients. This may explain the more frequent occurrence of this severe complication in patients with AP and T2D [19]. Excessive activity of proinflammatory cytokines within the adipose tissue surrounding the pancreas in obese patients is more likely responsible for the development of pancreatic necrosis in the course of AP [4, 20].

Chronic hyperglycemia is the main factor responsible for the so-called oxidative stress that results in the generation of free oxygen radicals damaging various tissues and organs. This phenomenon concerns also the pancreas and may participate in the pathogenesis of AP [18, 21]. The aforementioned pathomechanisms, known and described in patients with T2D, contribute to the initiation, maintenance and severity of AP, as well as systemic reactions, such as respiratory failure, or multi-organ failure, which are severe complications of AP. They are also responsible for necrosis of this organ.

Another unfavorable prognostic factor in patients with AP and T2D is more frequent coexistence of cardiovascular, neurological and chronic renal failure. In the study, a higher prevalence of cardiovascular diseases in patients with T2D was documented, which correlates with other scientific sources [4]. Higher concentration of creatinine is a recognized parameter, occurring in prognostic scales. Impaired glomerular filtration rate particularly affects patients with T2D and is one of the most frequently observed chronic microvascular complications. The analyzed material also demonstrated impaired renal function in this group of patients, corresponding to G2 stage, and the results were statistically significantly different. A worse course and prognosis of AP in patients with T2D and chronic renal failure was also documented [11, 22, 23].

CRP values may increase in the first hours after the onset of symptoms. CRP value in our patients varied significantly; patients with T2D had higher levels 48 hours after admission. The study by Pallisera et al. [24] documented that CRP ≥ 120 mg/L is a sensitive prognostic parameter of severe AP, but its increase manifests later, after 24 to 48 hours. The results of our study group were consistent with those discussed above. Similar findings were reported by other authors, and the CRP concentration ≥ 150 mg/L after 72 hours correlates with 80% sensitivity and specificity with the development of necrosis [13, 25]. Significantly higher CRP concentration in patients with AP and T2D were also observed by Zhao et al. [26] in their study: 135 ± ± 22 versus 80 ± 29 mg/dL in patients without diabetes.

A significantly higher percentage of patients with T2D were diagnosed with necrotizing AP based on abdominal CT. In addition, the duration of their hospitalization was longer by about 3 days compared to the group of patients without T2D, which is undoubtedly caused by more severe course of the disease and more frequent occurrence of local or systemic complications. Such observations are also reported by other authors [2, 27]. A longer hospital stay is of course also of economic importance. The available literature also emphasizes the necessity of more frequent admission of patients with AP and diabetes to the Intensive Care Unit [4]. In the discussed group of patients, there were no significant differences in this respect. Mortality is an extremely important index in the analyzed context. Depending on the AP, it ranges from several to several dozen percent. Also in this respect, patients with concomitant T2D have a worse prognosis. In several studies, a higher mortality in this group of patients was observed [28]. In the discussed group of patients, no statistically significant difference was demonstrated in this respect.

Conclusions

Acute pancreatitis is still associated with the risk of serious complications, uncertain prognosis and risk of death. T2D is a factor negatively modifying the course and prognosis of this disease. It is important to quickly identify patients at risk of severe disease course, including those with diabetes, and stratify their risk. Coexistence of T2D should be taken into account in the prognostic estimation of the AP course.

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Conflict of interest

None declared.

REFERENCES

1. Fagenholz P, Castillo CD, Harris N, et al. Increasing United States Hospital Admissions for Acute Pancreatitis, 1988–2003. Annals of Epidemiology. 2007; 17(7): 491–497, doi: 10.1016/j.annepidem.2007.02.002, indexed in Pubmed: 17448682.
2. Kingsnorth A, O'Reilly D. Acute pancreatitis. BMJ. 2006; 332(7549): 1072–1076, doi: 10.1136/bmj.332.7549.1072, indexed in Pubmed: 16675814.
3. Urushihara H, Taketsuna M, Liu Y, et al. Increased risk of acute pancreatitis in patients with type 2 diabetes: an observational study using a Japanese hospital database. PLoS One. 2012; 7(12): e53224, doi: 10.1371/journal.pone.0053224, indexed in Pubmed: 23300896.
4. Shen HN, Lu CL, Li CY. Effect of diabetes on severity and hospital mortality in patients with acute pancreatitis: a national population-based study. Diabetes Care. 2012; 35(5): 1061–1066, doi: 10.2337/dc11-1925, indexed in Pubmed: 22446175.
5. Noel RA, Braun DK, Patterson RE, et al. Increased risk of acute pancreatitis and biliary disease observed in patients with type 2 diabetes: a retrospective cohort study. Diabetes Care. 2009; 32(5): 834–838, doi: 10.2337/dc08-1755, indexed in Pubmed: 19208917.
6. Lowenfels AB, Maisonneuve P, Sullivan T. The changing character of acute pancreatitis: epidemiology, etiology, and prognosis. Curr Gastroenterol Rep. 2009; 11(2): 97–103, doi: 10.1007/s11894-009-0016-4, indexed in Pubmed: 19281696.
7. Girman CJ, Kou TD, Cai B, et al. Patients with type 2 diabetes mellitus have higher risk for acute pancreatitis compared with those without diabetes. Diabetes Obes Metab. 2010; 12(9): 766–771, doi: 10.1111/j.1463-1326.2010.01231.x, indexed in Pubmed: 20649628.
8. Global Report on Diabetes. World Health Organization 2016. https://www.who.int/publications/i/item/9789241565257 (25.04.2022).
9. NFZ o zdrowiu. Cukrzyca, Centrala Narodowego Funduszu Zdrowia Departament Analiz i Strategii, Warszawa 2019. https://ezdrowie.gov.pl/portal/home/badania-i-dane/zdrowe-dane/raporty/nfz-o-zdrowiu-cukrzyca (25.04.2022).
10. Shen HN, Chang YH, Chen HF, et al. Increased risk of severe acute pancreatitis in patients with diabetes. Diabet Med. 2012; 29(11): 1419–1424, doi: 10.1111/j.1464-5491.2012.03680.x, indexed in Pubmed: 22506974.
11. Mikó A, Farkas N, Garami A, et al. Preexisting Diabetes Elevates Risk of Local and Systemic Complications in Acute Pancreatitis: Systematic Review and Meta-analysis. Pancreas. 2018; 47(8): 917–923, doi: 10.1097/MPA.0000000000001122, indexed in Pubmed: 30113426.

12. Aune D, Vatten LJ. Diabetes mellitus and the risk of gallbladder disease: A systematic review and meta-analysis of prospective studies. J Diabetes Complications. 2016; 30(2): 368–373, doi: 10.1016/j.jdiacomp.2015.11.012, indexed in Pubmed: 26684168.
13. Banks PA, Bollen TL, Dervenis C, et al. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013; 62(1): 102–111, doi: 10.1136/gutjnl-2012-302779, indexed in Pubmed: 23100216.
14. Petrov MS, Shanbhag S, Chakraborty M, et al. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology. 2010; 139(3): 813–820, doi: 10.1053/j.gastro.2010.06.010, indexed in Pubmed: 20540942.
15. Ranson JH, Rifkind KM, Roses DF, et al. Prognostic signs and the role of operative management in acute pancreatitis. Surg Gynecol Obstet. 1974; 139(1): 69–81, indexed in Pubmed: 4834279.
16. Moore EM. A useful mnemonic for severity stratification in acute pancreatitis. Ann R Coll Surg Engl. 2000; 82(1): 16–17, indexed in Pubmed: 10700760.
17. Richardson A, Park W. Acute pancreatitis and diabetes mellitus: a review. The Korean Journal of Internal Medicine. 2021; 36(1): 15––24, doi: 10.3904/kjim.2020.505, indexed in Pubmed: 33147904.
18. Pendharkar S, Singh R, Petrov M. Pro-inflammatory cytokine-induced lipolysis after an episode of acute pancreatitis. Archives of Physiology and Biochemistry. 2018; 124(5): 401–409, doi: 10.1080/13813455.2017.1415359, indexed in Pubmed: 29235373.
19. Solanki NS, Barreto SG, Saccone GTP. Acute pancreatitis due to diabetes: the role of hyperglycaemia and insulin resistance. Pancreatology. 2012; 12(3): 234–239, doi: 10.1016/j.pan.2012.01.003, indexed in Pubmed: 22687379.
20. Abu Hilal M, Armstrong T. The impact of obesity on the course and outcome of acute pancreatitis. Obes Surg. 2008; 18(3): 326–328, doi: 10.1007/s11695-007-9298-5, indexed in Pubmed: 18202895.
21. Shafqet M, Sharzehi K. Diabetes and the Pancreatobiliary Diseases. Curr Treat Options Gastroenterol. 2017; 15(4): 508–519, doi: 10.1007/s11938-017-0163-x, indexed in Pubmed: 29079901.
22. Chouhan V, Monachese M, Saleh M, et al. Sa1389 - Baseline Chronic Kidney Disease is a Risk Factor for Severity and Mortality in Acute Pancreatitis: A Multicenter Study. Gastroenterology. 2018; 154(6): S-288, doi: 10.1016/s0016-5085(18)31320-9.
23. Golay V, Roychowdhary A. Acute pancreatitis in chronic kidney disease--a common but often misunderstood combination. Ren Fail. 2012; 34(10): 1338–1340, doi: 10.3109/0886022X.2012.718951, indexed in Pubmed: 23002785.
24. Pallisera A, Jorba R, Ramia J, et al. Biological markers of severity in acute pancreatitis. Open Medicine. 2014; 9(4): 550–555, doi: 10.2478/s11536-014-0503-3.
25. Hirota M, Takada T, Kawarada Y, et al. JPN Guidelines for the management of acute pancreatitis: severity assessment of acute pancreatitis. J Hepatobiliary Pancreat Surg. 2006; 13(1): 33–41, doi: 10.1007/s00534-005-1049-1, indexed in Pubmed: 16463209.
26. Zhao X, Chang Mei H, Chen L, et al. An increased level of haemoglobin A1C predicts a poorer clinical outcome in patients with acute pancreatitis. Clin Endocrinol (Oxf). 2012; 77(2): 241–245, doi: 10.1111/j.1365-2265.2011.04252.x, indexed in Pubmed: 21988175.
27. Nawaz H, O'Connell M, Papachristou GI, et al. Severity and natural history of acute pancreatitis in diabetic patients. Pancreatology. 2015; 15(3): 247–252, doi: 10.1016/j.pan.2015.03.013, indexed in Pubmed: 25937079.
28. Huh JiH, Jeon H, Park SM, et al. Diabetes Mellitus is Associated With Mortality in Acute Pancreatitis. J Clin Gastroenterol. 2018; 52(2): 178–183, doi: 10.1097/MCG.0000000000000783, indexed in Pubmed: 28009683.