Acute Pancreatitis

Subjects: Gastroenterology & Hepatology

Contributor: Yanna Cao

The incidence of acute and chronic pancreatitis is increasing in the United States. Rates of acute pancreatitis (AP) are similar in both sexes, but chronic pancreatitis (CP) is more common in males. When stratified by etiology, women have higher rates of gallstone AP, while men have higher rates of alcohol- and tobacco-related AP and CP, hypercalcemic AP, hypertriglyceridemic AP, malignancy-related AP, and type 1 autoimmune pancreatitis (AIP).

acute pancreatitis chronic pancreatitis sex-associated differences

1. Introduction

Acute pancreatitis (AP) is a painful and sudden inflammatory condition of the pancreas and is the most common gastrointestinal diagnosis requiring hospitalization [1]. The incidence of AP is increasing in the United States, with a 25.2% increase in AP-related hospital admissions from 2001 to 2014 [1][2][3]. Though originally thought to be two distinct diseases, it has been shown that recurrent episodes of AP can lead to the development of chronic pancreatitis (CP), a condition characterized by progressive inflammation and fibrosis. It is now suggested that the two conditions exist on a spectrum, emphasizing the importance of understanding their etiologies and pathogeneses [4][5].

2. Sex Differences in Pancreatitis

AP is the most common disease to affect the pancreas and the most common diagnosis upon hospital admission for gastroenterological disease [5]. Numerous etiologies of AP and CP have been described, as shown in Table 1, while the impacts of sex are still actively being investigated [5][6]. In 2016, there were nearly 520,000 AP and CP hospitalizations in the United States, with 48% being female [7][8]. Although the incidence of AP is similar among males and females, male sex is associated with higher mortality [9]. Additionally, men are more likely to develop recurrent acute pancreatitis (RAP), which can lead to the development of CP by healing areas of necrosis with fibrotic tissue. Thus, men also develop CP at higher rates compared to women (12 cases per 100,000 versus 6 cases per 100,000, respectively) [4][5][10][11]. The most common etiologies of AP are gallstone pancreatitis and alcohol-induced pancreatitis, while the single most common etiology of CP is alcohol-induced [6]. However, the incidence of etiology differs when stratified by sex, as shown in Table 1. Therefore, we discuss the most common etiologies of AP and CP adjusted by sex in the following sections.

Table 1. Common Etiologies Respective to Acute or Chronic Pancreatitis (AP/CP) by Sex.

Etiology	%AP (%Male)	Country [Reference]	CP (%Male)	Country [Reference]
	24.7 (39.3)	USA [2]	3.0 (72.7)	Japan [10]
	25.8 (51.5)	Japan [12]		
	40.0 (37.0)	Australia [13]		
	55.8 (53.7)	China [14]		
Gallstone	36.9 (39.6)	UK [15]		
	31.8 (42.2)	Germany [16]		
	23.5 (39.6)	Ireland [17]		
	49.9 (39.2)	Norway [18]		
	26.8 (40.3)	Sweden [19]		
Average	35.0 (42.5)		3.0 (72.7)	
Alcohol	25.2 (72.8)	USA [2]	44.5 (70.0)	USA [20]
	32.6 (87.9)	Japan [12]	69.7 (92.3)	Japan [10]
	22.0 (79.0)	Australia [13]	71.6 (81.7)	Germany [21]

	10.0 (97.2)	China [14]		
	22.0 (77.7)	UK [15]		
	34.5 (87.8)	Germany [16]		
	23.2 (75.3)	Ireland [17]		
	9.7 (83.6)	Norway [18]		
	4.8 (80.5)	Sweden [19]		
Average	20.4 (82.4)		61.9 (81.3)	
Hypertriglyceridemia	4.9 (65.6)	USA [2]	6.1 (51.5)	USA [20]
	2.3 (69.7)	Japan [12]	0.9 (50.0)	Japan [10]
	10.4 (72.9)	China [14]		
	2.3 (61.1)	UK [22]		
Average	5.0 (67.3)		3.5 (50.8)	
Hypercalcemia	NA * (78.0)	France [23]	0.6 (66.7)	USA [20]
			0.6 (71.4)	Japan [10]
Average	NA * (78.0)		0.6 (69.1)	

Trauma	0.1 (62.5)	Japan [12]	2.0 (63.6)	USA [20]
	3.5 (20.0)	Norway [18]	0.3 (66.7)	Japan [10]
Average	1.8 (41.3)		1.2 (65.2)	
Autoimmune	NA *	NA *	2.4 (46.2)	USA [20]
			NA * (75)	Japan [24]
Average			2.4 (60.6)	
Malignancy	3.6 (66.7)	China [25]	0.4 (0)	USA [20]
Average	3.6 (66.7)		0.4 (0)	

* NA = Not available.

2.1. Gallstone Pancreatitis

Gallstone pancreatitis is the most common etiology of AP and accounts for 24.7% of cases in the United States and 35.0% of cases worldwide [2][12][13][14][15][16][17][18][19][26]. The prevalence of gallstone pancreatitis increases with age, with the highest rates in both sexes seen in ages 75+, consistent with the epidemiology of gallstones in the general population [6]. Furthermore, the incidence of gallstone pancreatitis has been increasing. It is hypothesized to be secondary to increasing rates of obesity, a primary risk factor for the development of gallstones [6]. Krishna et al. found that compared to 2002–2005, in 2009–2012 there was a more than 3-fold increase in metabolic syndrome and morbid obesity, which was associated with a 13.2% increase in AP hospital admissions [1].

Reported rates of gallstone pancreatitis are significantly higher among women, representing up to 30.2% of cases compared to 19.3% of cases in men for all-cause AP [2][12][26][27]. Although it is a more common etiology in women, specifically among gallstone pancreatitis, more adverse outcomes are associated with male sex. After risk-adjustment, odds of complications related to gallstone pancreatitis and death are higher in men [28].

2.2. Alcohol-Induced

Alcohol-induced AP is the second most common cause of AP, representing 25.2% of cases in the US and 20.4% of cases worldwide [2][12][13][14][15][16][17][18][19][26][29]. Although a single episode of alcohol consumption can induce alcohol-related AP, chronic consumption is a major risk factor for the development of pancreatitis, with as much as a 4-fold increase in prevalence among subjects with a history of alcoholism [30]. Alcohol-related pancreatitis is also the most common etiology of CP, responsible for up to 49.0% of cases [6][31].

Alcohol-induced AP is more common in men, with males representing 72.8% of cases in the United States [2][29][32]. Men are also more likely to have alcohol-related CP, while non-alcoholic etiologies account for up to approximately 70.0% of CP cases in women [4][6][10][20][21][33]. Age of onset varies by sex in alcohol-related CP, with women having a peak incidence from age 35–44 and men from age 45–54 [34].

Notably, the sex differences for alcohol-induced AP and CP are diminished when similar levels of alcohol consumption are compared, thus suggesting the difference is likely due to higher rates of alcohol consumption in men [6][31][35]. However, recent studies suggest that genetic factors may also play a role. For example, variants in the X-linked gene, CLDN2, may modulate the risk for alcohol-induced pancreatitis and therefore partially explain the higher rates of alcohol-induced pancreatitis among men [36][37].

2.3. Metabolic

2.3.1. Hypertriglyceridemia

Hypertriglyceridemia (HTG) is a well-established cause of AP, accounting for up to 10.4% of cases worldwide [14][38]. HTG-induced AP typically develops in patients with an underlying genetic abnormality, such as in familial combined hyperlipidemia or familial HTG, usually in the presence of a secondary factor such as alcohol use or uncontrolled diabetes. Importantly, HTG-induced AP is associated with a severe clinical course, and patients commonly have recurrent attacks leading to frequent hospitalizations and an increased risk of CP [39].

Rates of HTG-induced AP are higher in men than in women, with men representing 67.3% of cases [2][12][14][22][26][40]. The increased rates in men are likely due to higher rates of secondary factors, such as concurrent alcohol use and metabolic comorbidities [14]. Of note, pregnancy, hormone replacement therapy, and the use of oral contraceptive pills are risk factors for HTG-induced AP, as estrogens increase triglyceride levels by simulating very low density lipoprotein production in the liver [39][41]. In one study of pregnant women with AP, HTG was the etiology in 30.0% of cases [38].

2.3.2. Hypercalcemia

Hypercalcemia is a well-known risk factor for pancreatitis when total ionized calcium levels are ≥12.0 mg/dL or 3 mmol/L (typical upper limit of normal = 10.2 mg/dL). Over 90.0% of cases of hypercalcemia are due to primary hyperparathyroidism (PHPT) or hypercalcemia of malignancy, though less than 7.0% of patients with PHPT develop AP [42].

Interestingly, women are affected by PHPT two to three times as often as men; however, rates of AP secondary to PHPT are significantly higher among men (6.9%) compared to women (2.2%) [23][43]. This may be due to compounding risk factors, such as increased rates of alcohol intake or metabolic conditions in men, as previously described. Further investigation is needed to see if there is a sex-related link to AP secondary to PHPT.

2.4. Trauma

Post-traumatic pancreatitis is rare in the United States, representing between 0.1 and 3.5% of cases worldwide [10][12][18][20]. Two common types of trauma leading to pancreatitis are blunt abdominal trauma and post-endoscopic retrograde cholangiography. Overall, post-traumatic pancreatitis is more common among men than women, with men representing 63.6% of cases in the United States [10][20]. However, the disease mechanisms regarding the relationship between trauma and chronic pancreatitis are not clear.

2.4.1. Abdominal Trauma

Pancreatitis or pancreatic injury following abdominal trauma (both penetrating and blunt) is rare in adults [44][45][46]. The most common mechanism is blunt abdominal trauma, involving rapid force against the pancreas, resulting in possible rupture secondary to compression against the spinal vertebrae [44][47]. Siboni et al. completed a retrospective review of the National Trauma Data Bank and found that pancreatic injury had an overall incidence of 3.0%, with most injuries being low-grade [45]. Isolated pancreatic injury occurred in <1% of all abdominal injuries or 20.9% of all pancreatic injuries. Of the isolated blunt pancreatic injuries, 63.0% occurred in males [45]. Most cases are managed non-operatively [47]. In a separate retrospective review of the National Trauma Data Bank, Kuza et al. reviewed all trauma patients age >14 and found the incidence of pancreatic trauma to be 0.3%. Nearly 75.0% of these patients were male [44].

Given the rare nature of this injury, there are limited data available given to specifically identify gender differences in pancreatic injury or pancreatitis following abdominal trauma. Since there is an overall higher incidence of trauma in males, it would not be unreasonable to assume that there is a higher incidence of pancreatitis or pancreatic injury following abdominal injury in males. However, further investigation is needed to review clinical outcomes of these patients adjusted by sex.

2.4.2. Post-Endoscopic Retrograde Cholangiopancreatography (ERCP) Pancreatitis

Pancreatitis is the most common complication of post-ERCP. The incidence of post-ERCP pancreatitis varies among studies due to patient factors, procedures, and methodology; however, most studies demonstrate an incidence between 3.0 and 5.0% [48][49].

It is commonly thought that young women are at higher risk of post-ERCP pancreatitis, though this association is controversial. Several studies have found female sex to be an independent risk factor for the development of post-ERCP pancreatitis [18][50][51]. In 2015, a meta-analysis of 28 studies demonstrated an odds ratio (OR) of 1.46 for females [52]. Still, others have found no association [53][54][55]. It has been suggested that other risk factors may

increase the risk of post-ERCP pancreatitis synergistically. For instance, Sphincter of Oddi dysfunction, an independent risk factor for the development of post-ERCP pancreatitis, is more common in women overall, which could make the actual association between women and post-ERCP pancreatitis difficult to distinguish [56]. Furthermore, Freeman et al. found the highest risk of post-ERCP pancreatitis (42%) in female patients with normal serum bilirubin, Sphincter of Oddi dysfunction, and difficult biliary cannulation [50].

2.5. Autoimmune

Autoimmune pancreatitis (AIP) is a rare form of CP that accounts for fewer than 2.4% of cases in the United States and is classified into two subtypes [6]. Type 1 AIP, or lymphoplasmacytic sclerosing pancreatitis, is characterized by IgG4 positive plasma cells and lymphocytes [57][58]. Type 2 AIP, or idiopathic duct-centric pancreatitis, is IgG4 negative.

In contrast to most autoimmune diseases that preferentially affect young women, the overall male to female ratio of AIP is 2.94:1 [24]. The most affected age group also differs between males and females (70–79 versus 60–69 years of age) [24]. Furthermore, changes to sex preferences are observed when adjusted for subtypes of AIP. For instance, no sex differences have been observed in Type 2 AIP [58]. In contrast, men older than 60 years of age are more likely to have Type 1 AIP [58]. Type 1 AIP is generally thought to be related to IgG4-related systemic diseases with extrapancreatic manifestations, such as primary sclerosing cholangitis, an autoimmune destruction of the bile ducts, also more commonly seen in males [57].

References

1. Krishna, S.G.; Kamboj, A.K.; Hart, P.A.; Hinton, A.; Conwell, D.L. The Changing Epidemiology of Acute Pancreatitis Hospitalizations: A Decade of Trends and the Impact of Chronic Pancreatitis. Pancreas 2017, 46, 482–488.
2. Gapp, J.; Hall, A.G.; Walters, R.W.; Jahann, D.; Kassim, T.; Reddymasu, S. Trends and Outcomes of Hospitalizations Related to Acute Pancreatitis: Epidemiology from 2001 to 2014 in the United States. Pancreas 2019, 48, 548–554.
3. Akshintala, V.S.; Hutfless, S.M.; Yadav, D.; Khashab, M.A.; Lennon, A.M.; Makary, M.A.; Hirose, K.; Andersen, D.K.; Kalloo, A.N.; Singh, V.K. A Population-Based Study of Severity in Patients with Acute on Chronic Pancreatitis. Pancreas 2013, 42, 1245–1250, doi:10.1097/mpa.0b013e3182a85af3.
4. Machicado, J.D.; Yadav, D. Epidemiology of Recurrent Acute and Chronic Pancreatitis: Similarities and Differences. Dis. Sci. 2017, 62, 1683–1691, doi:10.1007/s10620-017-4510-5.
5. Sankaran, S.J.; Xiao, A.Y.; Wu, L.M.; Windsor, J.A.; Forsmark, C.E.; Petrov, M.S. Frequency of Progression from Acute to Chronic Pancreatitis and Risk Factors: A Meta-analysis.

Gastroenterology 2015, 149, 1490–1500.e1, doi:10.1053/j.gastro.2015.07.066.

6. Yadav, D.; Lowenfels, A.B. The Epidemiology of Pancreatitis and Pancreatic Cancer. Gastroenterology 2013, 144, 1252–1261, doi:10.1053/j.gastro.2013.01.068.
7. Albeiruti, R.; Chaudhary, F. S0057 Gender Differences in Outcomes in Patients with Pancreatitis: A Contemporary Analysis. J. Gastroenterol. 2020, 115, S28.
8. Kroner, P.T.; Kesler, A.M.; Abader, P.; Afsh, M.; Ciofoaia, V.; Lukens, F. Sa1318—Differences in Outcomes and Etiologies of Acute Pancreatitis Based on Gender. J. Gastroenterol. 2020, 115, S315.
9. Sharma, S.; Aburayyan, K.; Aziz, M.; Acharya, A.; Vohra, I.; Khan, A.; Haghbin, H.; Nehme, C.; Ghazaleh, S.; Weissman, S. Gender Differences in Outcomes of Acute Pancreatitis in Hospitalized Patients: Results from Nationwide Analysis. J. Gastroenterol. 2020, 115, S38–S39.
10. Hirota, M.; Shimosegawa, T.; Masamune, A.; Kikuta, K.; Kume, K.; Hamada, S.; Kihara, Y.; Satoh, A.; Kimura, K.; Tsuji, I.; et al. The sixth nationwide epidemiological survey of chronic pancreatitis in Japan. Pancreatology 2012, 12, 79–84, doi:10.1016/j.pan.2012.02.005.
11. Petrov, M.S.; Yadav, D. Global epidemiology and holistic prevention of pancreatitis. Rev. Gastroenterol. Hepatol. 2019, 16, 175–184, doi:10.1038/s41575-018-0087-5.
12. Masamune, A.; Kikuta, K.; Hamada, S.; Tsuji, I.; Takeyama, Y.; Shimosegawa, T.; Okazaki, K.; Matsumoto, R.; Kume, K.; Miura, S.; et al. Clinical practice of acute pancreatitis in Japan: An analysis of nationwide epidemiological survey in 2016. Pancreatology 2020, 20, 629–636, doi:10.1016/j.pan.2020.04.013.
13. Nesvaderani, M.; Eslick, G.D.; Vagg, D.; Faraj, S.; Cox, M.R. Epidemiology, aetiology and outcomes of acute pancreatitis: A retrospective cohort study. J. Surg. 2015, 23, 68–74, doi:10.1016/j.ijsu.2015.07.701.
14. Zheng, Y.; Zhou, Z.; Li, H.; Li, J.; Li, A.; Ma, B.; Zhang, T.; Liao, Q.; Ye, Y.; Zhang, Z.; et al. A Multicenter Study on Etiology of Acute Pancreatitis in Beijing During 5 Years. Pancreas 2014, 44, 409–414, doi:10.1097/mpa.0000000000000273.
15. Roberts, S.E.; Akbari, A.; Thorne, K.; Atkinson, M.; Evans, P.A. The incidence of acute pancreatitis: Impact of social deprivation, alcohol consumption, seasonal and demographic factors. Pharmacol. Ther. 2013, 38, 539–548, doi:10.1111/apt.12408.
16. Lankisch, P.G.; Karimi, M.; Bruns, A.; Maisonneuve, P.; Lowenfels, A. Temporal Trends in Incidence and Severity of Acute Pancreatitis in Lüneburg County, Germany: A Population-Based Study. Pancreatology 2009, 9, 420–426, doi:10.1159/000209217.
17. O'Farrell, A.; Allwright, S.; Toomey, D.; Bedford, D.; Conlon, K. Hospital admission for acute pancreatitis in the Irish population, 1997 2004: Could the increase be due to an increase in

alcohol-related pancreatitis? Public Health 2007, 29, 398–404, doi:10.1093/pubmed/fdm069.

18. Omdal, T.; Dale, J.; Lie, S.A.; Iversen, K.B.; Flaatten, H.; Ovrebo, K. Time trends in incidence, etiology, and case fatality rate of the first attack of acute pancreatitis. J. Gastroenterol. 2011, 46, 1389–1398, doi:10.3109/00365521.2011.605464.
19. Sandzén, B.; Rosenmüller, M.; Haapamäki, M.M.; Nilsson, E.; Stenlund, H.; Öman, M. First attack of acute pancreatitis in Sweden 1988–2003: Incidence, aetiological classification, procedures and mortality—A register study. BMC Gastroenterol. 2009, 9, 18, doi:10.1186/1471-230X-9-18.
20. Coté, G.A.; Yadav, D.; Slivka, A.; Hawes, R.H.; Anderson, M.A.; Burton, F.R.; Brand, R.E.; Banks, P.A.; Lewis, M.D.; DiSario, J.A.; et al. Alcohol and Smoking as Risk Factors in an Epidemiology Study of Patients with Chronic Pancreatitis. Gastroenterol. Hepatol. 2011, 9, 266–273, doi:10.1016/j.cgh.2010.10.015.
21. Lankisch, P.; Assmus, C.; Maisonneuve, P.; Lowenfels, A. Epidemiology of pancreatic diseases in Lüneburg county. Pancreatology 2002, 2, 469–477, doi:10.1159/000064713.
22. Charlesworth, A.; Steger, A.; Crook, M.A. Acute pancreatitis associated with severe hypertriglyceridaemia; A retrospective cohort study. J. Surg. 2015, 23, 23–27, doi:10.1016/j.ijsu.2015.08.080.
23. Carnaille, B.; Oudar, C.; Pattou, F.; Combemale, F.; Rocha, J.; Proye, C. Pancreatitis and Primary Hyperparathyroidism: Forty Cases. ANZ J. Surg. 1998, 68, 117–119, doi:10.1111/j.1445-2197.1998.tb04719.x.
24. Masamune, A.; Kikuta, K.; Hamada, S.; Tsuji, I.; Takeyama, Y.; Shimosegawa, T.; Okazaki, K. Nationwide epidemiological survey of autoimmune pancreatitis in Japan in 2016. Gastroenterol. 2019, 55, 462–470, doi:10.1007/s00535-019-01658-7.
25. Cao, X.; Wang, X.; Xu, X.; Lu, Y.; Zhao, B.; Zhang, X.; Chen, Q. Pancreatoduodenectomy for Periampullary Tumors Presenting with Acute Pancreatitis. Res. Pr. 2020, 2020, 7246895, doi:10.1155/2020/7246895.
26. Yadav, D.; O'Connell, M.; Papachristou, G.I. Natural history following the first attack of acute pancreatitis. J. Gastroenterol. 2012, 107, 1096–1103.
27. Lankisch, P.G.; Assmus, C.; Lehnick, D.; Maisonneuve, P.; Lowenfels, A.B. Acute Pancreatitis: Does Gender Matter? Dis. Sci. 2001, 46, 2470–2474, doi:10.1023/a:1012332121574.
28. Shen, H.-N.; Wang, W.-C.; Lu, C.-L.; Li, C. Effects of Gender on Severity, Management and Outcome in Acute Biliary Pancreatitis. PLoS ONE 2013, 8, e57504, doi:10.1371/journal.pone.0057504.
29. Yang, A.L.; Vadhavkar, S.; Singh, G.; Omary, M.B. Epidemiology of Alcohol-Related Liver and Pancreatic Disease in the United States. Intern. Med. 2008, 168, 649–656,

doi:10.1001/archinte.168.6.649.

30. Yadav, D.; Eigenbrodt, M.L.; Briggs, M.J.; Williams, D.K.; Wiseman, E.J. Pancreatitis: Prevalence and risk factors among male veterans in a detoxification program. Pancreas 2007, 34, 390–398.
31. Machicado, J.D.; Rebours, V.; Yadav, D. Epidemiology of Chronic Pancreatitis. Pancreapedia 2016, doi:10.3998/panc.2016.13.
32. Lankisch, P.G.; Lowenfels, A.B.; Maisonneuve, P. What is the Risk of Alcoholic Pancreatitis in Heavy Drinkers? Pancreas 2002, 25, 411–412, doi:10.1097/00006676-200211000-00015.
33. Romagnuolo, J.; Talluri, J.; Kennard, E.; Sandhu, B.S.; Sherman, S.; Cote, G.A.; Al-Kaade, S.; Gardner, T.B.; Gelrud, A.; Lewis, M.D.; et al. Clinical Profile, Etiology, and Treatment of Chronic Pancreatitis in North American Women: Analysis of a Large Multicenter Cohort. Pancreas 2016, 45, 934–940.
34. Yadav, D.; Timmons, L.J.; Benson, J.T.; Dierkhising, R.A.; Chari, S.T. Incidence, Prevalence, and Survival of Chronic Pancreatitis: A Population-Based Study. J. Gastroenterol. 2011, 106, 2192–2199, doi:10.1038/ajg.2011.328.
35. Frulloni, L.; Gabbrielli, A.; Pezzilli, R.; Zerbi, A.; Cavestro, G.M.; Marotta, F.; Falconi, M.; Gaia, E.; Uomo, G.; Maringhini, A.; et al. Chronic pancreatitis: Report from a multicenter Italian survey (PanCroInfAISP) on 893 patients. Liver Dis. 2009, 41, 311–317, doi:10.1016/j.dld.2008.07.316.
36. Aghdassi, A.A.; Weiss, F.U.; Mayerle, J.; Lerch, M.M.; Simon, P. Genetic susceptibility factors for alcohol-induced chronic pancreatitis. Pancreatology 2015, 15, S23–S31, doi:10.1016/j.pan.2015.05.476.
37. Whitcomb, D.C.; LaRusch, J.; Krasinskas, A.M.; Klei, L.; Smith, J.P.; Brand, R.E.; Neoptolemos, J.P.; Lerch, M.M.; Tector, M.; Sandhu, B.S.; et al. Common genetic variants in the CLDN2 and PRSS1-PRSS2 loci alter risk for alcohol-related and sporadic pancreatitis. Genet. 2012, 44, 1349–1354, doi:10.1038/ng.2466.
38. Jin, J.; Yu, Y.-H.; Zhong, M.; Zhang, G.-W. Analyzing and identifying risk factors for acute pancreatitis with different etiologies in pregnancy. Matern. Neonatal Med. 2014, 28, 267–271, doi:10.3109/14767058.2014.913132.
39. Scherer, J.; Singh, V.; Pitchumoni, C.S.; Yadav, D. Issues in hypertriglyceridemic pancreatitis: An update. Clin. Gastroenterol. 2014, 48, 195–203.
40. Goyal, H.; Smith, B.; Bayer, C.; Rutherford, C.; Shelnut, D. Differences in Severity and Outcomes Between Hypertriglyceridemia and Alcohol-Induced Pancreatitis. Am. J. Med. Sci. 2016, 8, 82–87, doi:10.4103/1947-2714.177307.
41. Aljenedil, S.; Hegele, R.A.; Genest, J.; Awan, Z. Estrogen-associated severe hypertriglyceridemia with pancreatitis. Clin. Lipidol. 2017, 11, 297–300, doi:10.1016/j.jacl.2016.12.006.

42. Whitcomb, D.C.; North American Pancreatitis Study Group. Pancreatitis: TIGAR-O Version 2 Risk/Etiology Checklist with Topic Reviews, Updates, and Use Primers. Transl. Gastroenterol. 2019, 10, e00027.

43. Yeh, M.W.; Ituarte, P.H.G.; Zhou, H.C.; Nishimoto, S.; Liu, I.-L.A.; Harari, A.; Haigh, P.I.; Adams, A.L. Incidence and Prevalence of Primary Hyperparathyroidism in a Racially Mixed Population. Clin. Endocrinol. Metab. 2013, 98, 1122–1129, doi:10.1210/jc.2012-4022.

44. Kuza, C.M.; Hirji, S.A.; Englum, B.R.; Ganapathi, A.M.; Speicher, P.J.; Scarborough, J.E. Pancreatic Injuries in Abdominal Trauma in US Adults: Analysis of the National Trauma Data Bank on Management, Outcomes, and Predictors of Mortality. J. Surg. 2020, 109, 193–204, doi:10.1177/1457496919851608.

45. Siboni, S.; Kwon, E.; Benjamin, E.; Inaba, K.; Demetriades, D. Isolated blunt pancreatic trauma: A benign injury? Trauma Acute Care Surg. 2016, 81, 855–859.

46. Søreide, K.; Weiser, T.G.; Parks, R.W. Clinical update on management of pancreatic trauma. HPB 2018, 20, 1099–1108, doi:10.1016/j.hpb.2018.05.009.

47. Wiik-Larsen, J.; Thorsen, K.; Sandve, K.O.; Søreide, K. Incidence and characteristics of pancreatic injuries among trauma patients admitted to a Norwegian trauma centre: A population-based cohort study. J. Gastroenterol. 2020, 55, 1347–1353, doi:10.1080/00365521.2020.1829032.

48. Freeman, M.L.; Nelson, D.B.; Sherman, S.; Haber, G.B.; Herman, M.E.; Dorsher, P.J.; Moore, J.P.; Fennerty, M.B.; Ryan, M.E.; Shaw, M.J.; et al. Complications of Endoscopic Biliary Sphincterotomy. Engl. J. Med. 1996, 335, 909–919, doi:10.1056/nejm199609263351301.

49. Loperfido, S.; Angelini, G.; Benedetti, G.; Chilovi, F.; Costan, F.; De Berardinis, F.; De Bernardin, M.; Ederle, A.; Fina, P.; Fratton, A. Major early complications from diagnostic and therapeutic ERCP: A prospective multicenter study. Endosc. 1998, 48, 1–10, doi:10.1016/s0016-5107(98)70121-x.

50. Freeman, M.L.; DiSario, J.A.; Nelson, D.B.; Fennerty, M.; Lee, J.G.; Bjorkman, D.J.; Overby, C.S.; Aas, J.; Ryan, M.E.; Bochna, G.S.; et al. Risk factors for post-ERCP pancreatitis: A prospective, multicenter study. Endosc. 2001, 54, 425–434, doi:10.1067/mge.2001.117550.

51. Masci, E.; Mariani, A.; Curioni, S.; Testoni, P.A. Risk Factors for Pancreatitis Following Endoscopic Retrograde Cholangiopancreatography: A Meta-Analysis. Endoscopy 2003, 35, 830–834, doi:10.1055/s-2003-42614.

52. Ding, X.; Zhang, F.; Wang, Y. Risk factors for post-ERCP pancreatitis: A systematic review and meta-analysis. Surgeon 2015, 13, 218–229, doi:10.1016/j.surge.2014.11.005.

53. Cheng, C.-L.; Sherman, S.; Watkins, J.L.; Barnett, J.; Freeman, M.; Geenen, J.; Ryan, M.; Parker, H.; Frakes, J.T.; Fogel, E.L.; et al. Risk Factors for Post-ERCP Pancreatitis: A Prospective

Multicenter Study. J. Gastroenterol. 2006, 101, 139–147, doi:10.1111/j.1572-0241.2006.00380.x.

54. Katsinelos, P.; Lazaraki, G.; Chatzimavroudis, G.; Gkagkalis, S.; Vasiliadis, I.; Papaeuthimiou, A.; Terzoudis, S.; Pilpilidis, I.; Zavos, C.; Kountouras, J. Risk factors for therapeutic ERCP-related complications: An analysis of 2,715 cases performed by a single endoscopist. Gastroenterol. 2014, 27, 65–72.
55. Li, G.-Z.; Wang, F.; Fang, J.; Zha, H.-L.; Zhao, Q. Risk Factors for Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: Evidence from 1786 Cases. Sci. Monit. 2018, 24, 8544–8552, doi:10.12659/msm.913314.
56. Pekgöz, M. Post-endoscopic retrograde cholangiopancreatography pancreatitis: A systematic review for prevention and treatment. World J. Gastroenterol. 2019, 25, 4019–4042, doi:10.3748/wjg.v25.i29.4019.
57. Cai, O.; Tan, S.-Y. From Pathogenesis, Clinical Manifestation, and Diagnosis to Treatment: An Overview on Autoimmune Pancreatitis. Res. Pr. 2017, 2017, 1–11, doi:10.1155/2017/3246459.
58. Shimosegawa, T.; Chari, S.T.; Frulloni, L.; Kamisawa, T.; Kawa, S.; Mino-Kenudson, M.; Kim, M.H.; Klöppel, G.; Lerch, M.M.; Löhr, M.; et al. International consensus diagnostic criteria for autoimmune pancreatitis: Guidelines of the International Association of Pancreatology. Pancreas 2011, 40, 352–358.