Pancreatic steatosis: a new diagnosis and therapeutic challenge in Gastroenterology

Jayanta PAUL¹ and Ambalathu Veettil Hussain SHIHAZ²

INTRODUCTION

Pancreatic steatosis (PS) is the most common benign pathologic condition of the pancreas in adult¹ and commonly related to obesity and associated insulin resistance². PS (used for all forms of pancreatic fat accumulation) has several synonyms such as: pancreatic lipomatosis, non-alcoholic fatty pancreatic disease, lipomatous pseudohypertrophy, fatty replacement, fatty pancreas and fatty infiltration. Pancreatic steatosis describes a disease ranging from infiltration of fat in the pancreas to pancreatic inflammation, and development of pancreatic fibrosis. There are multiple etiologies of this condition, such as metabolic syndrome, alcohol intake, viral infections, toxins, congenital syndromes, etc. Pancreatic steatosis is usually diagnosed by trans-abdominal ultrasound, computed tomography scan and magnetic resonance imaging. Fatty infiltration in pancreas may lead to pancreatitis, diabetes mellitus and may be a predisposing cause of pancreatic cancer. Now a day, pancreatic steatosis is a common incidental finding during abdominal ultrasonography for other reasons and is a new challenge in Gastroenterology. But there is no guideline for pancreatic steatosis till now. In this review article, we are trying to give an overall idea (etiologies, diagnosis, management, clinical significances) on pancreatic steatosis.

Definition of pancreatic steatosis

Pancreatic steatosis (PS) is defined by fat accumulation in pancreas and when there is presence of obesity or metabolic syndrome; it is called “non-alcoholic fatty pancreas disease” (NAFPD) and usually associated with NAFLD (non-alcoholic fatty liver disease)⁴. In 1933, Ogilvie first described pancreatic steatosis in literature⁴.

Aetiologies of pancreatic steatosis

There are several causes of pancreatic steatosis (FIGURE 1). Similar to NAFLD, advanced age, obesity, metabolic syndrome and insulin resistance are the common risk factors of pancreatic steatosis. Pancreatic fat content is significantly associated with greater body mass index (BMI) and advanced age⁴⁰. Prevalence is extremely low in women with age less than 50 years, but increases

| Metabolic causes | Drugs and Toxin | Infection | Others | Local causes |
|------------------|----------------|----------|--------|--------------|
| Diabetes         | Steroids       | Hepatitis B | Haemochromatosis | Chronic pancreatitis |
| Severe malnutrition | Antiretroviral | AIDS | Cystic fibrosis | Hereditary pancreatitis |
| Obesity          | Rosiglitazone  | Reovirus | Old age | Pancreatic ductal obstruction |
| Dyslipidemia     | Gemcitabine    | Cirrhosis |        |              |
| Insulin resistance | Alcohol      |          |        |              |
| Metabolic syndrome | Octreotide   |          |        |              |

FIGURE 1. Aetiologies of pancreatic steatosis.
progressively after 50 years of age\(^6\). Some medications are also responsible for pancreatic steatosis such as steroid hormones\(^{10}\), antiretroviral therapy\(^{10}\), rosiglitazone\(^{10}\), gemcitabine chemotherapy\(^{10}\) and octreotide\(^{10}\). The presence of one or more component of metabolic syndrome, such as diabetes, BMI ≥30, hypertension or hyperlipidemia is associated with 37% increased prevalence of pancreatic steatosis\(^{12}\). Chronic alcohol abuse increases pancreatic cholesteryl ester accumulation and induces pancreatic steatosis\(^{13}\) and usually is seen when person consuming more than 30 gram/day of ethanol\(^{14}\). Several infections such as acquired immunodeficiency syndrome (AIDS)\(^{15}\), chronic hepatitis B\(^{16}\) and reovirus infection\(^{17}\) can produce fatty pancreas. Haemochromatosis\(^{18}\) and malnutrition state such as kwashiorkor\(^{19}\) can also be responsible NAFPD.

**Diagnosis of pancreatic steatosis**

Pancreatic steatosis (PS) is most commonly diagnosed by using different imaging techniques\(^{1,3-7}\). FIGURE 1. When using any imaging technique to identify pancreatic steatosis, we should know that there is up to 6.2% fatty infiltration of the pancreas in normal individuals. But specificity and sensitivity of different imaging modalities has not been clearly mentioned in several articles on PS.

**Ultrasonography in diagnosis of pancreatic steatosis**

Ultrasonography (USG) is widely available to detect PS but obesity and bowel gas may cause invisibility of pancreas. To diagnose pancreatic steatosis, pancreas echogenicity is traditionally compared with kidney echogenicity. Hyperechogenic pancreas can be seen in both pancreatic fibrosis and in fatty pancreas. Pancreatic steatosis can be classified into four grades by identifying patterns of pancreas echogenicity in abdominal USG (FIGURE 2); grade 0: when pancreas and renal echogenicity are similar; grade 1: when pancreas echogenicity is increased and is slightly higher than in the kidney; grade 2: when substantial increase in pancreas echogenicity than renal echogenicity but the retroperitoneal fat echogenicity is more than pancreatic echogenicity; and grade 3: the pancreas echogenicity is ≥ retroperitoneal fat echogenicity\(^{19,20}\).

**Computed tomography (CT) in diagnosis of pancreatic steatosis**

Focal pancreatic steatosis can be presented as a hypo attenuating mass lesion on CT scan\(^{21}\). Non contrast computed tomography (CT) can be used to diagnose PS. Disadvantages of CT scan are exposure to radiation, high cost and can miss focal fatty replacement of pancreas. Fatty pancreas can be classified by CT scan into five grades depending on site of pancreatic involvement (FIGURE 2); Grade 0– normal appearance without fatty replacement, Grade 1– fatty infiltration involving less than 25% of given pancreatic region, Grade 2– fatty replacement that involved 25%–50% of a given pancreatic region, Grade3– fatty replacement involving 50%–75% of a given pancreatic regions; and Grade 4 corresponded to fatty infiltration which involves more than 75% of a given pancreatic region\(^{12}\). Fat concentration in pancreas is positively correlated with attenuation indexes in CT scan; this finding suggests that unenhanced CT is useful non-invasive assessment of pancreatic fat\(^{23}\).

**Endoscopic ultrasonography in diagnosis of pancreatic steatosis**

Endoscopic ultrasound (EUS) is superior to CT scan and magnetic resonance imaging (MRI). The disadvantages are invasive procedure, risk of complications and needs of sedation. EUS is still the most sensitive investigation for pancreas screening but till now pancreatic biopsy is the best method to measure pancreatic fat concentration\(^{24}\). However, it is unethical to use EUS as a screening tool\(^{25}\). EUS grading system adapted from radiology incorporating the echo-texture of the pancreas relative to the spleen as well as the ability to visualize the main pancreatic duct and “salt and pepper” dots in the parenchyma has been suggested to assess fatty pancreas\(^{12}\).

**Magnetic resonance imaging for diagnosis of PS**

Magnetic resonance imaging (MRI) can estimate fat concentration in pancreas with high accuracy. MRI may be the test of choice for detection of intrapancreatic fat but available data is little to correlate pancreatic steatosis on MRI or EUS with histology. During MRI, commonly three methods are used to measure the fat in the pancreas. Advanced chemical shift-based gradient echo magnetic resonance imaging technique that measures the proton-density-fat-fraction (PDFF) has been shown to accurately quantify liver fat fraction when compared with the magnetic resonance spectroscopy (MRS) technique\(^{26}\) and reliably measures pancreatic fat content when compared with other MRI imaging techniques\(^{27}\).

**Pathological classification**

Pathologically pancreatic steatosis is classified into homogenous pancreatic lipomatosis and non homogenous pancreatic lipomatosis. Again non homogenous lipomatosis is classified into four types; type 1a: head is usually replaced by fat, type 1b: head, neck and body are replaced by fat, type 2a: head and uncinate process replaced by fat, type 2b: most of the pancreas except the peribiliary region is replaced by fat\(^{28}\). However, histological examination is not recommended for only diagnosis of pancreatic steatosis.

**Clinical significances**

Development of diabetes mellitus: Wang et al. (2014) in their study found that the patients with fatty pancreas has an higher risk of development of diabetes than patients without fatty pancreas\(^{29}\).

| Grading of Pancreatic steatosis | USG Findings | CT findings |
|---------------------------------|--------------|-------------|
| Grade 0                         | When pancreas and renal echogenicity are similar | Normal appearance without fatty replacement |
| Grade 1                         | When pancreas echogenicity was slightly higher than in the kidney | Fatty infiltration involving less than 25% of given pancreatic region |
| Grade 2                         | When substantial increase in pancreas echogenicity than renal echogenicity but lower than the retroperitoneal fat echogenicity | Fatty replacement that involved 25%–50% of a given pancreatic region |
| Grade 3                         | The pancreas echogenicity is similar to or higher than the retroperitoneal fat | Fatty replacement involving 50%–70% of a given pancreatic regions |
| Grade 4                         | Fatty infiltration which involves more than 75% of a given pancreatic region |

FIGURE 2. Pancreatic steatosis grading by trans abdominal ultrasonography (UGS) and abdominal computed tomography (CT).
Correlation between non-alcoholic fatty liver and non-alcoholic fatty pancreas

Pancreatic steatosis is common in patients with NAFLD, and pancreatic fat content positively correlates with liver steatosis grading determined by histology\(^{(46,47)}\). Patients with histology-determined liver fibrosis have significantly less pancreatic fat infiltration than those without evidence of liver fibrosis\(^{(48)}\). Fatty infiltration in pancreas causes β-cell dysfunction, which may also lead to hepatic steatosis\(^{(49)}\) and pancreatic fat also may play a role in the development of non alcoholic steatohepatitis (NAS)\(^{(47)}\).

Differential diagnosis

Pancreatic steatosis of the dorsal caudal pancreas must be distinguished from dorsal pancreatic agenesis. Lipomatous pseudohypertrophy of the pancreas has probably been considered as a differential diagnosis of pancreatic steatosis\(^{(50,51)}\).

Management of pancreatic steatosis (FIGURE 3)

There is no specific treatment for fatty pancreas. Until now and newly diagnosed patients with type 2 diabetes mellitus (DM2) have significantly greater pancreatic fat content\(^{(40)}\). Pancreatic islets cell fat infiltration leads to a reduced insulin secretion and increases development of DM2\(^{(31)}\). Presence of >25% pancreatic fatty infiltration is associated with significantly increased risk of development of type 2 diabetes mellitus and generalized atherosclerosis\(^{(32)}\).

Postoperative pancreatic fistula: developing a pancreatic fistula is significantly increased after pancreatic surgery in patients with pancreatic steatosis\(^{(33,34)}\), and have a ten times higher risk of incidence of fistula formation in pancreas than those with fibrotic pancreas\(^{(35)}\).

Carotid atherosclerosis: pancreatic steatosis is an independent risk factor for the development of carotid atherosclerosis in non-obese subjects with type 2 diabetes mellitus. So, it could be a marker of higher risk of cardiovascular disease, especially in non-obese individuals\(^{(40)}\).

Pancreatitis: risk factors of pancreatic steatosis such as obesity and components of metabolic syndrome are known risk factors for acute pancreatitis. When acute pancreatitis due to any aetiology affects fatty pancreas, it is usually severe in intensity\(^{(37)}\) and also is a significant risk factor for developing subclinical chronic pancreatitis\(^{(48)}\). Pancreatic carcinoma: fatty pancreas is independently associated with an increased risk of development of pancreatic carcinoma\(^{(3,39)}\). PS promotes dissemination and lethality of pancreatic carcinoma by alteration of tumour microenvironment, enhanced tumour spread\(^{(40)}\). Patients with increased pancreatic fat have a poor outcome than those who develop cancer in a pancreas without steatosis. Chronic inflammation with excessive fat accumulation might be the cause of cell injury and development of pancreatic carcinoma\(^{(41)}\). But another study found that there is no association between fatty pancreas and chronic pancreatitis or carcinoma of pancreas\(^{(12)}\). Non-alcoholic fatty liver disease (NAFLD) is positively correlated with pancreatic cancer in these patients and NAFLD patients with pancreatic cancer have poorer outcome than patients without NAFLD\(^{(42)}\). Pathophysiology of development of pancreatic cancer in NAFPD is similar to how NAFLD causes liver cancer\(^{(4)}\).

Pancreatic exocrine insufficiency: pancreatic steatosis can lead to exocrine pancreatic insufficiency (EPI) by (1) fat droplet accumulation in pancreatic acinar cells and consequent lipotoxicity, (2) destruction of acinar cells by both inflammation and fatty replacement, (3) by negative paracrine effect of adipocytes. Exocrine function in NAFPD patients has never been extensively investigated. In few case reports, patients with weight loss and massive steatorrhea were found to have severe pancreatic steatosis diagnosed by abdominal computed tomograms (CT scan) in whom the administration of pancreatic extracts improved symptoms\(^{(43,44)}\). Cardiovascular risk: risk factors of fatty pancreas are also risk factors of cardiovascular accident. The presence of NAFPD on ultrasonography is associated with increased aortic intima media thickness and epicardial adipose tissue\(^{(45)}\). Therefore, it could be a marker of a higher risk of cardiovascular disease. Pancreatic enzymes level in PS: few study\(^{(46)}\) showed that serum amylase value is significantly lower in patients with fatty pancreas compared to normal pancreas individuals but another study indicates that there is no association between fatty pancreas and serum amylase or lipase concentrations\(^{(32)}\). Benign pancreatic hyperenzymemia (BPH) or Gullo’s syndrome is a diagnosis of exclusion and diagnosed by persistently elevated pancreatic enzymes without any clinical or pathological evidence of pancreatic disease. There is no relationship between NAFPD and Gullo’s syndrome.

| Metabolic causes | Drugs and Toxin | Infection | Others | Local causes |
|-----------------|----------------|-----------|--------|-------------|
| Diabetes        | Steroids       | Hepatitis B | Haemochromatosis | Chronic pancreatitis |
| Severe malnutrition | Antiretroviral | AIDS     | Cystic fibrosis | Hereditary pancreatitis |
| Obesity         | Rosiglitazone  | Reovirus  | Old age     | Pancreatic ductal obstruction |
| Dyslipidemia    | Gemcitabine    |           |         |             |
| Insulin resistance | Alchol         | Octreotide |         |             |
| Metabolic syndrome |             |           |         |             |

Presence of one or more of the above risk factors

Identification of fatty pancreas by following imaging modalities

Ultrasoundography
Computed tomography (CT)
Endoscopic ultrasonography
Magnetic resonance imaging (MRI)

Differential diagnosis of pancreatic steatosis

Dorsal pancreatic agenesis
Lipomatous pseudohypertrophy of the pancreas

Clinical significances

Development of diabetes
Post operative pancreatic fistula formation
Increased risk of carotid atherosclerosis
Increased risk of cardiovascular risk

Increased risk of pancreatic carcinoma
Insufficiency
Low serum pancreatic enzymes level

Management of pancreatic steatosis

There is no specific treatment for fatty pancreas. Until now there are no approved drugs for NAFPD treatment. It treatment depends upon the underlying cause and if it is correctable, it may reduce pancreatic fat infiltration.

Conclusion

Early interventions of predisposing factors of pancreatic steatosis such as management of each components of metabolic syndrome can improve quality of life and prevent complications.

FIGURE 3. Flow chart of a practical approach of pancreatic steatosis (aetiology, diagnosis, clinical significance and management).
there are no approved drugs for NAFPD treatment. Treatment of PS depends on the underlying cause and if it is correctable, it may reduce pancreatic fat infiltration. If patient is having metabolic syndrome then tight diabetes control, diet restriction, physical exercise and weight reduction may improve condition. Pancreatic steatosis can be treated with a healthy diet, exercise, less meat consumption, and smoking cessation (12).

CONCLUSION

In majority cases, pancreatic steatosis is an incidental finding during trans-abdominal ultrasonography. It is commonly associated with metabolic syndrome, alcohol abuse and patients with non alcoholic fatty liver disease. NAFPD is usually diagnosed by radiological investigations such as abdominal USG, abdominal CT scan or abdominal MRI. Fatty pancreas has an increased risk of development of diabetes, pancreatic fistula after pancreatic surgery, development of carotid atherosclerosis in non-obese individuals, risk of development of pancreatic carcinoma, developing subclinical chronic pancreatitis and exocrine pancreatic insufficiency. Therefore early diagnosis and interventions for predisposing factors of pancreatic steatosis such as each component of metabolic syndrome can improve quality of life and prevent complications. But Until now there are no approved specific drugs for NAFPD treatment.

Authors’ contribution

Paul J: conceptualization, methodology, supervision, writing-original draft, writing-review & editing. Shihaz AVH: conceptualization, writing-review & editing.

Orcid

Jayanta Paul: 0000-0003-1188-1766. Ambalathu Veettil Hussain Shihaz: 0000-0001-5581-8166.

REFERENCES

1. Ozbulbul, N, Yurdakul, M, Tola, M. Does the visceral fat tissue show better correlation with the fatty replacement of the pancreas than with BMI? Eurasion J Med. 2010;42:24-7.
2. van Geenen EJ, Smits MM, Schreuder TC, van der Peet DL, Bloemena E, Mulder CJ. Nonalcoholic fatty liver disease is related to nonalcoholic fatty liver disease of pancreas. Pancreas. 2010;39:1185-90.
3. Pezzilli R, Calculi L. Pancreatic steatosis: Is it related to either obesity or diabetes mellitus? World J Diabetes. 2015;4:415-9.
4. Smits MM, van Geenen EJ. The clinical significance of pancreatic steatosis. Nat Rev Gastroenterol Hepatol. 2011;8:169-77.
5. Stamm BH. Incidence and diagnostic significance of minor pathologic changes in the adult pancreas at autopsy: a systematic study of 112 autopsies in patients without known pancreatic disease. Hum Pathol. 1984;15:677-83.
6. Rosso E, Casnadi S, Pessaux P, Casnadi S, Pessaux P, Oussoultsoglou E, Panaro F, Mahfud M, et al. The role of “fatty pancreas” and of BMI in the occurrence of pancreatic fibrosis after pancreactoduodenectomy. J Gastrointest Surg. 2009;13:1845-51.
7. Wong VW, Wong GL, Yeung DK, et al. Fatty pancreas, insulin resistance, and β-cell function: a population study using fat-water magnetic resonance imaging. Am J Gastroenterol. 2014;109:589-97.
8. Villarroya F, Domingo P, Giralt M. Drug-induced lipotoxicity: lipodystrophy associated with HIV-1 infection and antiretroviral treatment. Biochim Biophys Acta. 2010;1801:392-9.
9. Fernandes-Santos C, Evangelista Carneiro R, de Souza Mendonca L, Barbosa Aguíla M, Mandarim-de-Lacerda CA. Rosiglitazone aggravates nonalcoholic fatty pancreatic disease in C57BL/6 mice fed high-fat and high-sucrose diet. Pancreas. 2009;38:808-86.
10. Makay O, Kazimi M, Aydin U, Nart D, Yilmaz F, Zeytunlu M, et al. Fat replacement of the malignant pancreatic tissue after neoadjuvant therapy. Int J Clin Oncol. 2010;15:88-92.
11. Yu T, Liu R, Li M, Li X, Qiang O, Huang W, Tang C. Effects of octreotide on fatty infiltration of the pancreas in high-fat diet induced obesity rats. Wei Sheng Yan Jiu. 2014;43:186-92.
12. Serpe PS, Ohri A, Sanaka S, Berzin TM, Seshon S, Bennett G, et al. A prospective evaluation of fatty pancreas by using EUS. Gastrointest Endosc. 2011;73:987-93.
13. Wilson JS, Colley PW, Sosula L, Pirola RC, Chapman BA, Somer JB. Alcohol causes a fatty pancreas. A rat model of ethanol-induced pancreatic steatosis. Alcohol Clin Exp Res. 1982;6:117-21.
14. Noronha M, Salgadinho A, Ferreira De Almeida MJ, Deelting DA, Bordalo O. Alcohol and the pancreas. I. Clinical associations and histopathology of minimal pancreatic inflammation. Am J Gastroenterol. 1981;76:114-9.
15. Oliveira NM, Ferreira FA, Yonamine RV, Cheetier EZ. Antiretroviral drugs and acute pancreatitis in HIV/AIDS patients: is there any association? A literature review. Einstein (Sao Paulo). 2014;12:112-9.
16. Sasaki M, Nakanuma Y, Ando H. Lipomatous pseudohyperplasty of the pancreas in a patient with cirrhosis due to chronic hepatitis B. Pathol Int. 1998;48:566-8.
17. Walters MN, Leak PJ, Joske RA, Stanley NF, Perret DH. Murine infection with reovirus 3: pathology of infection with types 1 and 2. Br J Exp Pathol. 1965;46:200-12.
18. Diamond I, Vallbona C. Kwashiorkor in a North American white male. Pediatrics. 1980;25:248-57.
19. Lee JS, Kim SH, Jun DW, Han JH, Jang EC, Park JY, et al. Clinical implications of fatty pancreas: correlations between fatty pancreas and metabolic syndrome. World J Gastroenterol. 2009;15:1869-75.
20. Marks WM, Filly RA, Callen PW. Ultrasonic evaluation of normal pancreatic echogenicity and its relationship to fat deposition. Radiology. 1980;137:475-9.
21. Hague J, Amin Z. Focal pancreatic lesion: can a neoplasm be confidently excluded? Br J Radiol. 2006;79:677-83.
22. Soyer P, Spelle L, Pelage JP, Dufresne AC, Rondeau Y, Gouhiri M, et al. Cystic fibrosis in adolescent and adults: Fatty replacements of the pancreas CT evaluation and functional correlation. Radiology. 1999;210:611-5.
23. Kim SY, Kim H, Cho JY, Lim S, Cha K, Lee KH, et al. Quantitative assessment of pancreatic fat by using unenhanced CT: pathologic correlation and clinical implications. Radiology. 2014;271:104-12.
24. Lesmana CRA, Ho KY, Lesmana LA. Impact of endoscopic ultrasound procedures in various pancreatic disorders in Indonesia based on a case series in a private hospital. Case Rep Gastroenterol. 2015;9:206-14.

25. Larghia A, Petronec MB, Galassoa D, Ardidiacono PG. Endoscopic ultrasound in the evaluation of pancreaticobiliary disorders. Dig Liver Dis. 2010;42:6-15.

26. Kang GH, Cratu I, Shieh- mortarza M, Wolfson T, Gamst AC, Hamilton G, et al. Reproductibility of MRI determined proton density fat fraction across two different MR scanner platforms. J Magn Reson Imaging. 2011;34:928-34.

27. Schwenzer NF, Machann J, Martirosian P, Stefan P, Schraml C, Fritsche A, et al. Quantification of pancreatic lipomatosis and liver steatosis by MRI: comparison of in/opposed-phase and spectral-spatial excitation techniques. Invest Radiol. 2008;43:330-7.

28. Mortele KJ, Rocha TC, Streeter JL, Taylor AJ. Multimodality imaging of pancreatic and biliary congenital anomalies. Radiographics. 2006;26:715-31.

29. Wang CY, Ou HY, Chen MF, Chang TC, Chang CJ. Enigmatic ectopic fat: prevalence of non-alcoholic fatty pancreas disease and its associated factors in a Chinese population. J Am Heart Assoc. 2014;3:e00297.

30. Chai J, Liu P, Jin E, Su T, Zhang J, Shi K, et al. MRI chemical shift imaging of the fat content of the pancreas and liver of patients with type 2 diabetes mellitus. Exp Ther Med. 2016;11:476-80.

31. Lameloise N, Muzzin P, Prentki M, Assimacopoulos-Jeannet F. Uncoupling protein 2: a possible link between fatty acid excess and impaired glucose-induced insulin secretion? Diabetes. 2001;50:803-9.

32. Stamm BH. Incidence and diagnostic significance of minor pathologic changes in the adult pancreas at autopsy: a systematic study of 112 autopsies in patients without known pancreatic disease. Hum Pathol. 1984;15:677-83.

33. Mathur A, Marine M, Lu D, Swartz-Basile DA, Saxena R, Zyromski NJ, Pitt HA. Nonalcoholic fatty pancreas disease. HPB (Oxford). 2007;9:312-8.

34. Tranchant H, Gausaux S, Rebours V, Vullierme MP, Dokmak S, Levy P, et al. Preoperative CT scan helps to predict the occurrence of severe pancreatic fistula after pancreaticoduodenectomy. Ann Surg. 2012;256:139-45.

35. Patel AC, Yagnik VD. Evaluation of risk factors for postoperative pancreatic fistula following pancreaticoduodenectomy. Formos J Surg. 2019;52:76-83.

36. Kim MK, Chun HJ, Park HJ, Yeo DM, Baek KH, Song KH, et al. The association between ectopic fat in the pancreas and subclinical atherosclerosis in type 2 diabetes. Diabetes Res Clin Pract. 2014;106:590-6.

37. Van Geenen EJ, Smits MM, Schreuder TC, van der Peet DL, Bloemena E, Mulder CJ. Nonalcoholic fatty liver disease is related to nonalcoholic fatty pancreas disease. Pancreas. 2010;39:1185-90.

38. Fuji M, Ohno Y, Yamada M, Kamada Y, Miyoshi E. Impact of fatty pancreas and lifestyle on the development of subclinical chronic pancreatitis in healthy people undergoing a medical check up. Environ Health Prev Med. 2019;24:10.

39. Hori M, Takahashi M, Hiraoka N, Yamaji T, Mutoh M, Ishigamori R, et al. Association of pancreatic Fatty infiltration with pancreatic ductal adenocarcinoma. Clin Transl Gastroenterol. 2014;5:e53.

40. Mathur A, Hernandez J, Shaheen F, Shroff M, Dahal S, Morton C, et al. Preoperative computed tomography measurements of pancreatic steatosis and visceral fat: prognostic markers for dissemination and lethality of pancreatic adenocarcinoma. HPB (Oxford). 2011;13:404-10.

41. Jeannet FA. Fat storage in pancreas and in insulin-sensitive tissues in pathogenesis of type 2 diabetes. Int. J. Obes. 2004;28:53-57.

42. Chang CF, Tseng YC, Huang HH, Shih YL, Hsieh TY, Lin HH. Exploring the relationship between nonalcoholic fatty liver disease and pancreatic cancer by computed tomographic survey. Intern Emerg Med. 2018;13:191-7.

43. Lozano M, Navarro S, Perez-Ayuso R, Llach J, Ayuso C, Guevara MC, Ros E. Lipomatosis of the pancreas: an unusual cause of massive steatorrhea. Gastroenterol Clin Biol. 1998;3:580-2.

44. Aubert A, Gornet JM, Hammel P, Lévy P, O’Toole D, Raszniewski P, et al. Diffuse primary fat replacement of the pancreas: an unusual cause of steatorrhea. Gastroenterol Clin Biol. 2007;31:303-6.

45. Selim Kul S, Aységül Karadeniz A, Dursun I, Şahin S, Faruk Cırkıoğlu O, Raşp Sayın M, et al. Non-Alcoholic Fatty Pancreas Disease is Associated with Increased Epicardial Adipose Tissue and Aortic Intima-Media Thickness. Acta Cardiol Sin. 2019;35:118-25.

46. Wu WC, Wang CY. Association between non-alcoholic fatty pancreatic disease (NAFPD) and the metabolic syndrome: casecontrol retrospective study. Cardiovasc Diabetol 2013;12:77.

47. Nacif LS, Rocha-Santos V, Claro LCL, Vintimilla A, Ferreira LA, Arantes RM, et al. Liver biopsy may facilitate pancreatic graft evaluation: Positive association between liver steatosis and pancreatic graft adipose infiltration. Clinics (Sao Paulo). 2018; 73:e49.

48. Patel NS, Peterson MR, Brenner DA, Heba E, Sirlin C, Loomba R. Association between novel MRI-estimated pancreatic fat and liver histology-determined steatosis and fibrosis in non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 2013;37:630-9.

49. Hannakainen JC, Borra R, Linderborg K, Kallio H, Kiss J, Lepomäki R, et al. Liver and pancreatic fat content and metabolism in healthy monozygotic twins with discordant physical activity. J Hepatol. 2011;54:545-52.

50. Yasuda M, Niina Y, Uchida M, Fujinori N, Nakamura T, Oono T, et al. A case of lipomatous pseudohyper trophy of the pancreas diagnosed by typical imaging. JOP. 2010;11:385-8.

51. Shimada M, Shihabara K, Kitamura H, Demura Y, Hada M, Takehara A, et al. Lipomatous pseudohyper trophy of the pancreas taking the form of huge massive lesion of the pancreatic head. Case Rep Gastroenterol. 2010;4:457-6.

52. Ramkisson R, Gardner TB. Pancreatic Steatosis: An Emerging Clinical Entity. Am J Gastroenterol. 2019;114:1726-34.