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Computed tomography assessments of pancreatic steatosis in association with anthropometric measurements: A retrospective cohort study

Pankreatik steatozun antropometrik ölçümler ile ilişkisinin bilgisayarlı tomografi değerlendirmesi: Retrospektif kohort çalışma

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Abstract

Aim: Pancreatic steatosis is the fat accumulation in the pancreatic parenchyma. It is suggested that pancreatic fat infiltration may play an important role in the prognosis of diseases such as diabetes, malignancy and pancreatitis, leading to some inflammatory processes and fibrosis, and may even play an etiological role in the progress of pancreas-related diseases. However, a limited number of studies on pancreatic steatosis are available in the literature.

The aim of this study was to investigate the relation of pancreatic steatosis with age, sex, hepatic steatosis, subcutaneous fat tissue and visceral fat tissue thickness.

Methods: Hundred patients without a history of previously known pancreas disease or diabetes mellitus were included in the study. All patients had gone under abdominal tomography scan for a suspected kidney stone. Pancreas density, visceral and subcutaneous fat tissue thickness were reviewed retrospectively. The presence of coexisting hepatosteatosis was investigated.

Results: Pancreatic steatosis was detected in 54% of 100 cases examined. There were no significant difference between the pancreatic steatosis and normal pancreas groups in terms of gender and subcutaneous fat tissue thickness (p=0.115 and p=0.511, respectively). Pancreatic steatosis increased significantly with increasing age and visceral fat tissue thickness (p=0.001 and p = 0.001, respectively). The incidence of hepatic steatosis was 42% in patients with pancreatic steatosis.

Conclusion: According to our results, pancreatic steatosis increases with age and increased visceral fat tissue thickness. Thus, elderly patients with increased visceral fat tissue must be investigated for pancreatic steatosis.

Key-words: pancreas, steatosis, visceral, subcutaneous, fat tissue

Öz

Amaç: Pankreatik yağlanma, pankreas parankiminde yağ birikimidir. Bazı inflamatuar süreçlere ve fibrozise yol açarak diyabet, malignite, pankreatit gibi hastalıkların prognozunda etkili olabileceği ve hatta pankreasla ilgili hastalıkların gelişiminde etiyolojik rol oynayabileceği öne sürülmektedir. Pankreatik yağ birikiminin yaşla, cinsiyetle ve obeziteyle artış gösterdiği düşünülmektedir. Ancak literatürde pankreas yağlanması ile ilgili sınırlı sayıda çalışma mevcuttur.

Bu çalışmada pankreas yağlanmasının; yaş, cinsiyet, subkutan yağ doku kalınlığı, visseral yağ doku kalınlığı ve hepatosteatoz ile ilişkisini araştırmak amaçlandı.

Yöntemler: Araştırmaya; bilinen pankreas hastalığı ve diabetes mellitus öyküsü bulunmayan, üriner sistem taşı araştırılması amacıyla tomografi incelemesi yapılan 100 olgu dahil edildi. Retrospektif olarak yeniden değerlendirilen tomografi görüntüleri üzerinden pankreas parankim dansitesi, visseral ve subkutan yağ doku kalınlıkları ölçüldü. Eşlik eden hepatosteatoz varlığı araştırıldı.

Bulgular: Çalışmaya dahil edilen 100 olgunun %54'ünde pankreatik yağlanma saptandı. Pankreatik yağlanma olan ve olmayan olgular karşılaştırıldığında; cinsiyet ve subkutan yağ doku kalınlığı açısından fark yoktu (sırası ile p=0,115 ve p=0,511). Pankreas yağlanması yaş ve visseral yağ doku kalınlığı arttıkça istatistiksel olarak anlamlı şekilde artmıştı (sırası ile p=0,001ve p = 0,001). Pankreatik yağlanması olan olgularda karaciğer yağlanması insidansı %42 olarak bulundu.

Sonuç: Bulgularımıza göre; yaş ve visseral yağ doku kalınlığı arttıkça pankreas yağlanması da artış göstermiştir. Bu nedenle visseral yağ doku kalınlığı artmış, ileri yaştaki olgular pankreas yağlanması açısından da araştırılmalıdır.

Anahtar kelimeler: pankreas, yağlanma, visseral, subkutan, yağ doku

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Introduction

Pancreatic steatosis (PS) is a clinical condition that occurs as a result of accumulation of free fat acids and triglycerides in the pancreatic parenchyma [1]. Although it typically affects the entire pancreas homogeneously, it is possible to observe focal and irregular uptake in the parenchyma [2]. Focal steatosis is a clinically insignificant condition, but it is important because of its ability to imitate the mass lesion [3]. Pancreatic fat infiltration was first discovered in 1993 by Ogilvie through the study of cadavers. In this study, Ogilvie showed that more pancreatic fat accumulates in overweight cadavers (17% to 9%) compared to underweight ones [4].

Infiltration of any organ with fat can lead to some inflammatory processes [5]. Non-alcohol-induced hepatic steatosis can develop pathological processes leading to steatosis, fibrosis and cirrhosis. Similarly, it has been suggested that PS may develop diabetes and malignancy due to inflammatory processes initiated by fat accumulation followed by fibrosis [6, 7]. In addition, it has been proved that steatosis in pancreas aggravates the pancreatitis due to lipotoxicity [8]. It has been thought that PS may be effective in prognosis and play an etiological role in pancreas-related diseases. However, there are limited numbers of studies available on PS, which is an important entity in the literature.

In this study, we aimed to detect the cases with PS among the cases examined with unenhanced abdominal computed tomography (CT) on suspicion of urinary stones and to investigate the relation of PS with age, sex, hepatic steatosis, subcutaneous fat tissue and visceral fat tissue thickness in these cases.

Material and Methods

After obtaining the necessary authorization from the ethics committee, the abdominal CTs taken at our hospital between January 2017 and March 2017 without contrast material were retrospectively reevaluated. The study was performed according to the Declaration of Helsinki. Written consent could not be taken due to the retrospective design of the study. All CT scans were standardized on the same device with 128-section CT (Optima CT660, General Electric Healthcare Systems, Milwaukee, USA).

A total of a hundred patients who went under noncontrast abdominal tomography scan for a suspected urinary system stone were consecutively included in the study after the application of exclusion criteria. In all cases, a tomography examination was performed in order to investigate the urinary stones, but no stone was detected. Diabetes mellitus and history of pancreatitis were the exclusion criteria.

All CT imaging was evaluated by two blinded radiologists.

Fatty infiltration of the pancreas, liver and spleen was assessed by attenuation, which was measured in Hounsfield units (HU). The raw data set was reconstructed at a thickness of 1.5 mm.

The degree of pancreatic parenchymal attenuation was measured in 4 regions of interests (ROIs) at different locations in the head, neck, body and tail of the pancreas on unenhanced CT images (Figure 1). Each ROI was a round area of 0.5 cm^2, modified according to the thickness of the pancreatic parenchyma. We considered the mean value of 4 ROIs to indicate the extent of pancreatic attenuation [9]. Pancreatic lesions and vascular structures were excluded from the measurement. We were also careful not to include the peripheral margin of the pancreas to avoid the influence of the partial volume effect. We also measured splenic attenuation on unenhanced CT images by averaging the measurements in HU from one 1cm^2 ROI. From the aforementioned pancreatic and splenic attenuation measurements, P-S, where P indicates the pancreatic attenuation and S indicates the splenic attenuation, was calculated. The differences between the mean values of them were determined. If this difference was -5 or lower, it was classified into the fatty pancreas group and the rest were classified into the non-fatty pancreas group [10].

The liver steatosis was assessed by CT scan. For each patient, the average CT attenuation values in 4 sectors (one in the left lobe, two in the right lobe, and one in the caudate lobe) of the liver and in one region of the spleen were monitored (Figure 2). Each ROI was a circular area with a diameter of 1 cm^2. Liver steatosis was assessed by averaging the four ROI measurements and we calculated the liver-to-spleen attenuation ratio on CT and the difference between hepatic and splenic attenuation on CT. Hepatic steatosis was defined as a liver-to-spleen attenuation ratio less than 0.9 or a hepatic attenuation value at least 10 HU lower than the splenic attenuation value [11, 12].

Figure 1: Extent of pancreatic parenchymal attenuation was measured in 4 regions of interest (black circles) at different locations in the head, neck, body and tail of the pancreas on unenhanced computed tomography images

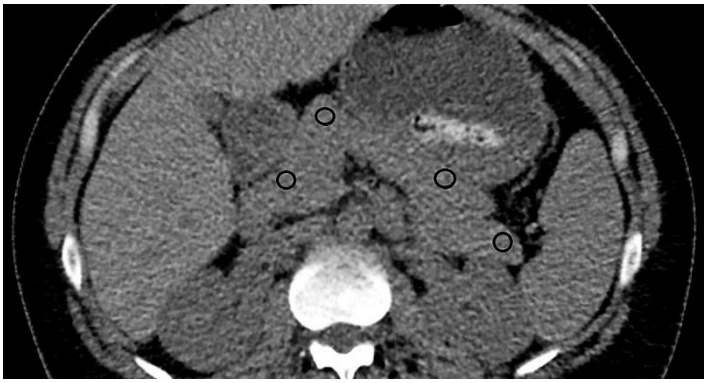
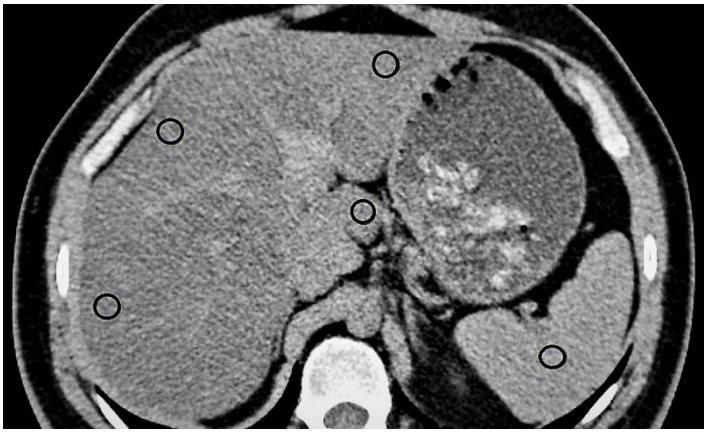
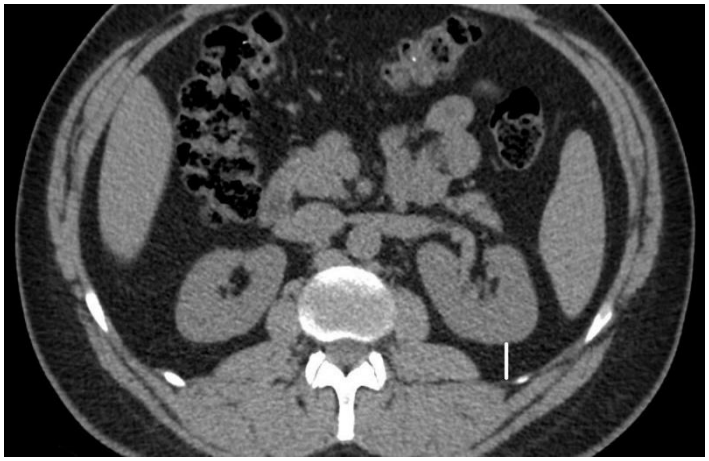


Figure 2: The degree of liver attenuation was measured in 4 regions of interest (black circles) in different sectors in the liver. The degree of spleen attenuation was measured in 1 region of interest in the spleen.



Abdominal subcutaneous fat tissue was measured bilaterally at the point 5 cm lateral to the umbilicus [13]. As an indicator of visceral obesity, the perirenal fat pad was measured in millimeter as the vertical distance between the left posterior renal capsule and the junction of the abdominal wall and paraspinal musculature (Figure 3) at the level of the left renal vein [14].

Figure 3:. The perirenal fat pad was measured in mm as the vertical distance between the left posterior renal capsule and the junction of the abdominal wall and paraspinal musculature (white line) at the level of the left renal vein



The cases were divided into two groups according to CT findings: Group 1 as those with PS and Group 2 as those without PS. The two groups were compared in terms of visceral and subcutaneous fat tissue thickness, age and gender.

Statistical analysis was performed with SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD). The student t test was used to compare fatty pancreas and non-fatty pancreas group. Independent samples t test was used to compare the age, subcutaneous and visceral fat thickness and gender data between two groups, whereas the qualitative and the coexistence of PS and hepatosteatosis data of two groups were compared using the Chi square test. Statistical significance was set at $p<0.05$.

Results

Meanage of the patients was 47±11.2 years with a range from 20 to 90 years 52 (52%) of the cases were male and 48 (48%) were female.

PS was detected in 54 cases (54%) of the cases examined (Group 1). There were 46 cases (46%) in Group 2. The mean age of the patients in Group 1 (52±8.7 years) was significantly higher than the patients in Group 2 (41±6.3 years) (p=0.001). In group 1, there were 32 male (59%) and 22 (41%) female patients. The groups were similar with regard to gender distribution (p=0.115). The demographic data and anthropometric measurements are given in Table 1.

There was no significant difference between the the groups in terms of subcutaneous fat tissue thickness (p=0.511). However, visceral fat tissue thickness was found to be significantly increased in Group 1 compared to Group 2(p=0.001).

The rate of coexistence of hepatic steatosis and PS was 42% (n=23). There were 33 cases (33%) of hepatic steatosis in the whole patient group. In the group 1 of 54 patients with PS, 23 (46%) patients had co-existing hepatic steatosis. In the group 2 of 46 patients without PS a total of 10 (22%) patients had hepatic steatosis (p=0.027).

Table 1. The demographic data and measurements of the two groups

	Group 1 (n=54)	Group 2 (n=46)	p
Age (year)	52±8.7	41±6.3	0.001
Male/female (n/n)	32/22	20/26	0.115
Average subcutaneous fat tissue thickness (mm)	26.2±2	25±4	0.511
Average visceral fat tissue thickness (mm)	13.6±3	6.2±1	0.001
Hepatic steatosis	23	10	0.027

Discussion

It has been suggested that obesity and associated insulin resistance may play a role in pancreatic adipocyte infiltration and that PS may develop in obesity cases as a consequence. Similar to non-alcohol-induced hepatic steatosis resulting from peripheral lipolysis, the term of “non-alcohol-induced PS” has been suggested [15]. PS is a process that begins with fat accumulation in pancreas and leads to inflammation. Similar to fibrosis that can occur in case of hepatosteatosis, to cirrhosis that may develop due to it and to possible formation of hepatocellular cancer, PS is also thought to play a role in the formation of fibrosis and adenocarcinoma [16]. Pancreatic cancer ranks near the top in mortality rates due to cancer [17]. It has been observed that a high body mass index (BMI) increases the relative risk of pancreatic cancer formation and the structure of fat distribution in central obesity is an independent risk factor for pancreatic cancer [18, 19].

CT is an important tool in measuring the amount of solid organs and intraabdominal fat tissue [20]. A high amount of fat accumulation in the visceral adipose tissue is known as visceral obesity. This body structure has been associated with metabolic syndrome, cardiovascular diseases and cancers such as prostate, breast and colon [21].

The ethiogenesis of PS is unknown and may be associated with the direct toxic effect of fat replacement in acinar and islet cells [22]. There is no specific biomarker for detecting PS [23]. At the present time, the gold standard for quantitative assessment of intraabdominal fat tissue is CT and magnetic resonance imaging [24].

Obesity is the main risk factor and etiological reason for PS [25]. Lipotoxicity is a cause of dysfunction of the pancreas beta cells [26]. There are views about the onset of exocrine pancreas deficiency after fat deposition in pancreas acinar cells [27]. There are studies which correlate insulin resistance to PS [28].

CT is one of the most popular and useful methods for measuring visceral lipidosis [29]. There are studies claiming that the fat accumulation in pancreas may differ between individuals with the same BMI [30, 31]. Another study in the literature found that PS is significantly associated with systolic hypertension, hyperglycemia, dyslipidemia and obesity comparing the two groups with normal and fatty pancreas [32]. Similar to our study, as a result of his autopsy studies, Ogilvie found that the visceral lipidosis and PS are significantly associated [4].

When evaluated age-wise, the patient group with PS was older. In an autopsy study including 394 cases, a significant correlation was found between PS and age. In this study, which was divided into 4 levels according to the severity of steatosis, it was found that severe PS was reduced in people who had a long-term disease and this finding was interpreted as PS may be partially reversible [33]. There are studies showing increased accumulation of pancreatic fat, especially in patients over 60 years of age. However, this has not been proven by prospective studies [34, 35]. The rate of coexistence of hepatic steatosis and PS can be as near as 67% according to some studies in the literature [10, 15]. In another ultrasonographic study, 68% of patients with PS had fatty liver, but 97% of patients with fatty liver had fatty pancreas [3]. In a study by Patel et al, they found a positive correlation between the level of steatosis in liver and the pancreas in a group of patients who were diagnosed with nonalcoholic fatty liver disease by liver biopsy [36].The incidence of hepatic steatosis was 42% in patients with PS in our study. This situation can be interpreted as that the PS can be observed before hepatic steatosis as a precursor of metabolic syndrome. Although it has been stated in the literature that it is

often associated with hepatic steatosis, our study and some other studies observed that this association rate may not be as high. As a different clinical entity than hepatic steatosis, PS may be a precursor of hepatic steatosis. However, there is a need for new large-scale studies in this subject.

Since the height and weight information of the subjects participated in our study could not be reached, no comparison was made in terms of BMI. In addition, cases were evaluated based only on CT findings and biochemical parameters such as lipid and glucose were not included in the study. These were the limitations of our study.

In conclusion, according to our study, PS increases as the age and visceral fat tissue thickness increase. Visceral fat thickness has been found to be larger in patients who have fat accumulation in pancreas. Thus, it may be said that the visceral fat accumulation, may also cause fat accumulation in pancreas.

References

1. Patel S, Bellon EM, Haaga J, Park CH. Fat replacement of the exocrine pancreas. Am J Roentgenol. 1980;135: 843-5.
2. Mortelé KJ, Rocha TC, Streeter JL, Taylor AJ. Multimodality imaging of pancreatic and biliary congenital anomalies. Radiographics. 2006;26:715-31.
3. de Oliveira Andrade LJ, Guimarães LR, Cadete RBF, Sá Sodré H, Santana de Melo PR, Conrado de Souza E. Pancreatic steatosis and its association with nonalcoholic fatty liver disease evaluated by ultrasonography. BJMHH. 2015;3:37-43.
4. Ogilvie RF. The islands of Langerhans in 19 cases of obesity. J Pathol Bacteriol. 1933;37:473-8.
5. Farrell GC, Larter CZ. Nonalcoholic fatty liver disease: from steatosis to cirrhosis. Hepatology. 2006;43:99–112.
6. Carter R, Mouralidarane A, Soeda J, Ray S, Pombo J, Saraswati R, et al. Non-alcoholic fatty pancreas disease pathogenesis: a role for developmental programming and altered circadian rhythms. PLoS One. 2014;21:9:89505.
7. Mathur A, Marine M, Lu D, Swartz-Basile DA, Saxena R, Zyromski NJ, et al. Nonalcoholic fatty pancreas disease. HPB. 2007;9:312–18.
8. Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ, Shiva SS, et al. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. Sci Transl Med. 2011;3:110.
9. 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.
10. 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.
11. Kawamoto S, Soyer PA, Fishman EK, Bluemke DA. Nonneoplastic liver disease: evaluation with CT and MR imaging. RadioGraphics. 1998;18:827–48.
12. Park SH, Kim PN, Kim KW, Lee SW, Yoon SE, Park SW, et al. Macrovesicular hepatic steatosis in living donors: use of CT for quantitative and qualitative assessment. Radiology. 2006;239:105–12.
13. Kim J, Lim H, Lee SI, Kim YJ. Thickness of Rectus Abdominis Muscle and Abdominal Subcutaneous Fat Tissue in Adult Women: Correlation with Age, Pregnancy, Laparotomy, and Body Mass Index. Arch Plast Surg. 2012;39:528-33.
14. 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. 2011;13:404-10.
15. 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.
16. Tariq H, Nayudu S, Akella S, Glandt M, Chilimuri S. Non-Alcoholic Fatty Pancreatic Disease: A Review of Literature. Gastroenterology Res. 2016;9:87-91.
17. Michaud DS. Epidemiology of pancreatic cancer. Minerva Chir. 2004;59:99-111.
18. Larsson SC, Orsini N, Wolk A. Body mass index and pancreatic cancer risk: a meta-analysis of prospective studies. Int J Cancer. 2007;120:1993-8.
19. Patel AV, Rodriguez C, Bernstein L, Chao A, Thun MJ, Calle EE. Obesity, recreational physical activity, and risk of pancreatic cancer in a large US cohort. Cancer Epidemiol Biomarkers Prev. 2005;14:459–66.
20. Speliotes EK, Massaro JM, Hoffmann U, Foster MC, Sahani DV, Hirschhorn JN, et al. Liver fat is reproducibly measured using computed tomography in the Framingham Heart Study. J Gastroenterol Hepatol. 2008;23:894–9.
21. Shuster A, Patlas M, Pinthus JH, Mourtzakis M. The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis. Br J Radiol. 2012;85:1-10.
22. Ou HY, Wang CY, Yang YC, Chen MF, Chang CJ. The association between nonalcoholic fatty pancreas disease and diabetes. PLoS One. 2013;8.
23. Wang D, Yu XP, Xiao WM, Jiao XP, Wu J, Teng DL, et al. Prevalence and clinical characteristics of fatty pancreas in Yangzhou, China: A cross-sectional study. Pancreatology. 2018;18:263-8.
24. Seidell JC, Bakker CJ, van der Kooy K. Imaging techniques for measuring adipose-tissue distribution -- a comparison between computed tomography and 1.5-T magnetic resonance. Am J Clin Nutr. 1990;51:953–7.
25. Dağdeviren M, Altay M, Nalbant E. Pancreatic steatosis: diagnosis and clinical significance. J Contemp Med. 2017;7:1-6.
26. van Raalte DH, van der Zij NJ, Diamant M. Pancreatic steatosis in humans: cause or marker of lipotoxicity? Curr Opin Clin Nutr Metab Care. 2010;13:478-85.
27. Cnop M, Hannaert JC, Hoorens A, Eizirik DL, Pipeleers DG. Inverse relationship between cytotoxicity of free fatty acids in pancreatic islet cells and cellular triglyceride accumulation. Diabetes. 2001;50:1771-7.
28. Wong VW, Wong GL, Yeung DK, Abrigo JM, Kong AP, Chan RS, Chim AM, 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.
29. Seidell JC, Oosterlee A, Thijssen MA, Burema J, Deurenberg P, Hautvast JG, et al. Assessment of intra-abdominal and subcutaneous abdominal fat: relation between anthropometry and computed tomography. Am J Clin Nutr. 1987;45:7–13.
30. Tushuizen ME, Bunck MC, Pouwels PJ, Bontemps S, van Waesberghe JH, Schindhelm RK, et al. Pancreatic fat content and beta-cell function in men with and without type 2 diabetes. Diabetes Care. 2007;30:2916-21.
31. Tiikkainen M, Bergholm R, Vehkavaara S, Rissanen A, Häkkinen AM, Tamminen M, et al. Effects of identical weight loss on body composition and features of insulin resistance in obese women with high and low liver fat content. Diabetes. 2003;52:701-7.
32. Wu W-C, Wang C-Y. Association between non-alcoholic fatty pancreatic disease (nafpd) and the metabolic syndrome: case–control retrospective study. Cardiovascular Diabetology. 2013;12:77.
33. Olsen TS. Lipomatosis of the pancreas in autopsy material and its relation to age and overweight. Acta Pathol Microbiol Scand A. 1978;86:367-73.
34. Noronha M, Salgadinho A, Ferreira De Almeida MJ, Dreiling DA, Bordalo O. Alcohol and the pancreas. I. Clinical associations and histopathology of minimal pancreatic inflammation. Am J Gastroenterol. 1981;76:114-9.
35. Gan L, Chitturi S, Farrell GC. Mechanisms and implications of age-related changes in the liver: nonalcoholic Fatty liver disease in the elderly. Curr Gerontol Geriatr Res. 2011;2011:831536.
36. 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 nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2013;37:630-9.