Research Article

Role of Imaging and Correlation of Risk Factors in Detecting Pancreatic Carcinoma

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Abstract: The aim of the study is the correlation between risk factors and the pancreas carcinoma, and the imaging findings at patients with pancreatic carcinoma and analysis of advantages and disadvantages of MSCT and MRI**.** There are 97 patients included in this retrospective study that were diagnosed with the abovementioned disease in UCCK (University Clinical Center of Kosova). The imaging studies were done using ECHO Phillips, 6 and 64 MSCT Siemens and 1.5 T MR Symphony Siemens. To analyze the correlation of risk factors is used anamnesis.Out of a total of the 97 patients diagnosed with pancreas cancer, 76 cases resulted in head and neck 79.4 % (n=76), 20 cases resulted in body and tail cancers (21%), 1 cases resulted metastazis in pancreas by carcinoma in colon. Risk factors present in our study have koreluar with Diabetes Mellitus Type II 14:43%, 8.2% gastric ulcer, smoking 34.0%, 21.6% consuming alcohol. MSCT is the golden diagnostic standard regarding imaging of the pancreatic carcinoma, evaluation of its dependent vascular structures and staging of the disease. The MRI imaging modalities are able to clearly differentiate these lesions as well as biliary system, coeliac plexus and small intraductal carcinomas. Correlation risk factor of pancreatic carcinoma is closely related to according to numerous studies, in those who had more impact with risk factors, they are two times more likely in the appearance of pancreatic carcinoma.

Keywords: Pancreatic cancer, MSCT, MRI, Morbidity, Mortality, Risk factor.

INTRODUCTION

Pancreatic cancer (PC) is the 10th most common malignancy and the 4th largest cancer killer in adults [1]. Pancreatic cancer is the fourth leading cause of cancer deaths, being responsible for 7% of all cancer-related deaths in both men and women.

The accurate characterization of pancreatic neoplasm is very important for patient's management. CT and MRI have been become the most important modalitites for evaluating pancreatic lesons. Precise diagnosis of pancreatic neoplasm is not always straight forward because they freqyently show atypical imaging features and many other diseases may mimic pancreatic adenocarcinoma [2, 3].

PC is the fourth leading cause of cancer-related death in Kosovo. Pancreatic neoplasm have always been associated with a poor prognosis due to the late presentation, and hence, advanced stage of the disease at moment of the established diagnosis. Although this trend is gradually on the decline with the awareness of the existence of these disease, better radiologic imaging modalities for diagnosis in our country, diagnosis of this disease is still made in late stages and prognosis of disease is poor [4].

PC remains one of the deadliest cancers worldwide, and has a poor, five-year survival rate of 5%. Although complete surgical resection is the only curative therapy for pancreatic cancer, less than 20% of newly-diagnosed patients undergo surgical resection

with a curative intent. Due to the lack of early symptoms and the tendency of pancreatic adenocarcinoma to invade adjacent structures or to metastasize at an early stage, many patients with pancreatic cancer already have advanced disease at the time of their diagnosis and, therefore, there is a high mortality rate [5].

The estimated lifetime risk of developing pancreatic cancer is about 1 in 71 (1.41%) [6]. the disease is rare before age 45 but incidence rises rapidly after that and peaks in the seventh decade of life. The major risk factors include smoking [7], hereditary predisposition to pancreatic cancer itself or to multiple cancers [8] and to a lesser degree, chronic pancreatitis [9]. Pancreatic cancer does not exhibit early symptoms and initial symptoms are often nonspecific. Classical presentation of pancreatic cancer is present in only 13-18% of the patients and is often accompanied by pruritus, acholic stools dark urine, and weight loss [10]. Abdominal pain is present in 80-85% of patients with locally advanced or advanced disease.

Acute pancreatitis and new onset diabetes mellitus can often be the initial presentations of PC [11, 12].

In up to 75% of the cases, the tumor is located within pancreatic head mostly sparing the uncinate process. Tumors in the pancreatic head often present early with biliary obstruction. However, tumors in the body and tail can remain asymptomatic till late in disease stage. Imaging techniques currently used for diagnosis and preoperative staging of pancreatic cancer include abdominal ultrasound (US), contrast-enhanced computed tomography(CT), magnetic resonance imaging (MRI), MR cholangiopancreatography (MRCP) and invasive imaging modalities like endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS).

With the continuing substantial improvements in CT technology, the capacity of MDCT for the detection, diagnosis, and local staging of pancreatic cancer has increased. MDCT is very effective for detecting and staging adenocarcinoma, with a sensitivity of up to 90% for detection and an accuracy of 80% -90% for staging [13, 14].

The aim of paper
The aim of the study is the correlation between risk factors and the pancreas carcinoma,and the imaging findings at patients with pancreatic carcinoma and analysis of advantages and disadvantages of MSCT and MRI.

MATERIALS AND METHODS
This retrospective research study includes 97 patients first time diagnosed with pancreatic cancer, examined in the period form 2011-2014 in the Clinic of Radiology at University Clinical Center of Kosova.

Only patients that were first time diagnosed with pancreatic neoplasm were included and evaluated in this research.Abdominal Ultrasound, MSCT 64 slice Sensation and MSCT 6 slice Emotion were used for CT examination of patients. MRI images are obtained with MRI 1.5T Symphony.

The anamnestic data were obtained from the patients followed by analytic studies that included factors as: age, gender, associated diseases, genetic factors, lab analysis and vital indicators including morbidity and mortality.

This retrospective research study includes 97 patients recently diagnosed with pancreatic cancer, 2011-2014 at the UCCK. The main important factors included in this study are: age, sex and risk factors that altogether have considerable influence in incidence of pancreatic cancer.

RESULTS
In our study we were taken 97 patients diagnosed for the first time in the Radiology Clinic - University Clinical Centre in Pristina, 2011- 2014, and have proved these results as follows: age group has been affected with 61 to 70 years old with 40 cases or (41.2%) in both sexes with no significant change but less presented to age over 80 years old of both sexes with 2 cases or (2.1%) (Table 1).

Table 1: Pancreatic carcinoma cases by age group and gender

Age- group	Gender		Total N (%)
	F	M	
<40	1	3	4 (4.1)
41-50	1	3	4 (4.1)
51-60	7	14	21 (21.6)
61-70	17	23	40 (41.2)
71-80	5	21	26 (26.8)
>80	1	1	2 (2.1)
Total N (%)	32 (33.0)	65 (67.0)	97 (100.0)

Localization based on the highest number shown on the head or neck with 76 cases (78.4%) and body - or tail with 20 cases (20.6%) and 1 case of pancreatic metastasis (1.0%) and according to the statement head clinical neck localization occurs quickly because the earliest symptoms even when informed is not the size that is not much different resektabile and longevity of those patients. Location tail body is sitting compared with developed countries because many pacinetë die undiagnosed or very late stages that have short lifes pan 2 months.

Of all the cases diagnosed during the period 2011-2014 or 76 cases (78.4%) are presented further in the head-neck and 20 cases or (20.6%) in the body-tail and 1 case or (1.0%) metastasis in the pancreas (Table 2).

A total of 85 cases have resulted in tumor size> 2 cm, and 11 cases with <2cm (Table 3).

Table 2: Cases of carcinoma of the pancreas by localization

Diagnosing and localization			
Localization	Carcinoma of pancreas in body and tail	Carcinoma of pancreas in head and neck	Metastasis in pancreas
Rastet N (%)	20 (20.6)	76 (78.4)	1(1.0)

In finding previously noted distant metastasis 43.3% (Table 4) With local infiltration are found under localization: 15.4% in the stomach, in the duodenum and papilla Water 26.8%, in lien 2%, mesenterium 44.3%% and 85.5% in regional limfonodes.

Table 3: Size of pancreatic carcinoma in diagnosis

Size	
<2cm	> 2cm
11 %(n=11)	89 % (n=86)

Table 4: Distant metastases of pancreatic carcinoma

Pancreatic carcinoma in body and tail with meta in hepar	19.6 %(n=19)
Pancreatic carcinoma in head and neck with meta in hepar	10.3%(n=10)
Other	70.1%(n=68)

Images of PC achieved in our Institution (MRI and MSCT)

Fig. 1a: NCE MSCT scan pf pancreas: Axial plane. Expansive process of tail and body of pancreas solid mass with cystic-necrotic component

Fig. 2a: CE MSCT scan pf pancreas: Axial plane. Expansive process of tail and body of pancreas solid mass with cystic-necrotic component
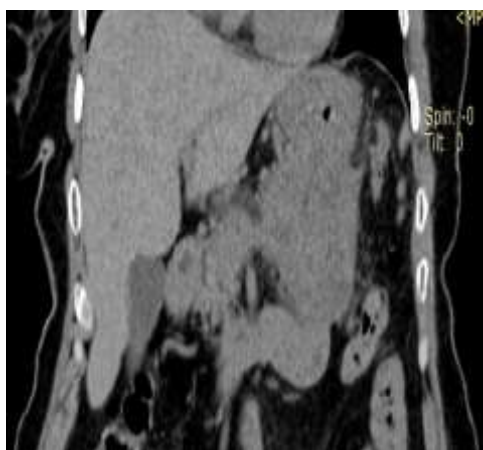

Fig. 1b: NCE MSCT scan pf pancreas: Coronal plane. Expansive process of tail and body of pancreas solid mass with cystic-necrotic component
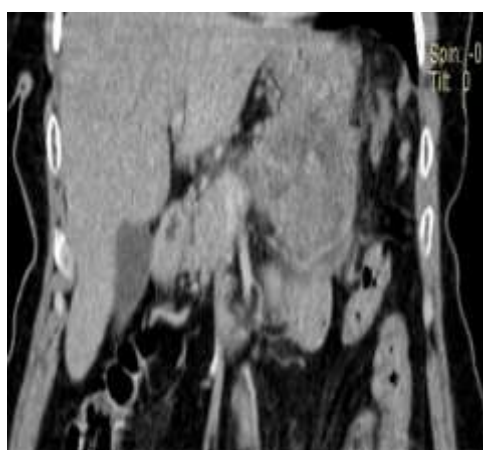

Fig. 2b: CE MSCT scan pf pancreas: Coronal plane. Expansive process of tail and body of pancreas solid mass with cystic-necrotic component
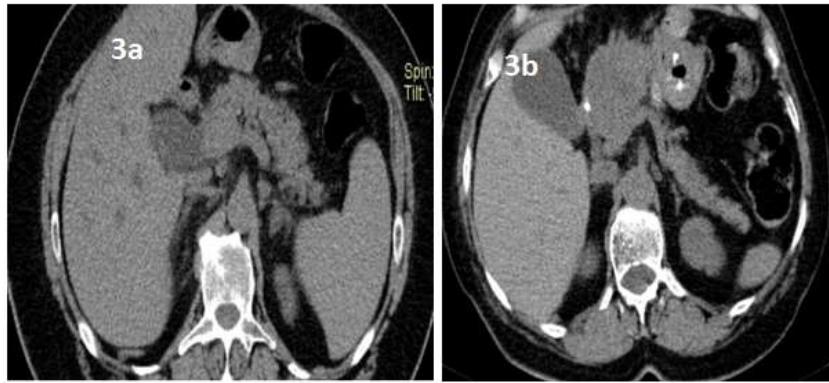
Fig. 3a, 3b: CE MSCT of upper abdomen: Axial plane: Pancreas haed and neck neoplasm with local infiltration of adjacent blood vessel and infiltration in duoden and dilatation biliari tree ductus.

Fig. 3c: CE MSCT of upper abdomen: Coronar plane: Pancreas haed and neck neoplasm with local infiltration of adjacent blood vessel and infiltration in duoden and dilatation biliari tree ductus
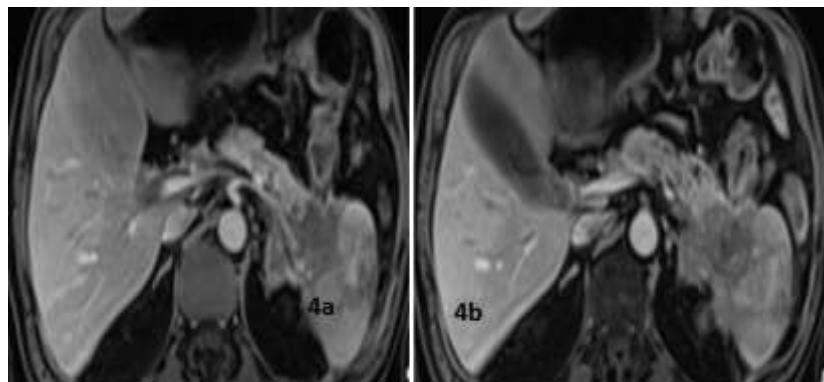

Fig. 4a, 4b: CE MRI of upper abdomen: Axial plane: Pancreas tail neoplasm with infiltration of spleen and liver metastase.
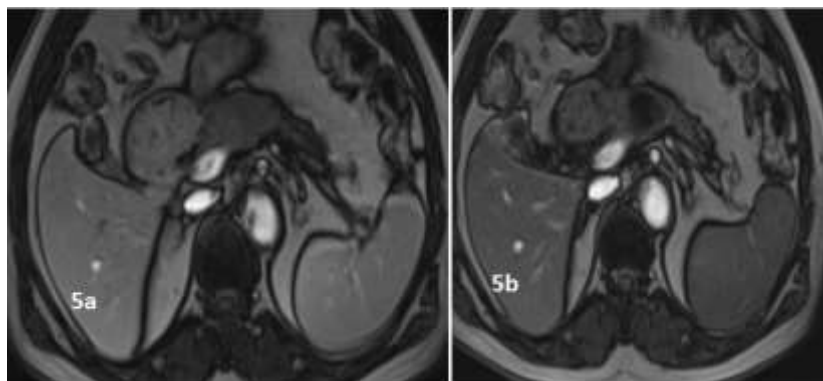
Fig. 5a, 5b: CE MRI of upper abdomen: Axial plane: Pancreas head and neck neoplasm with dilatation ductus pancreaticus and atrophy body and tail.
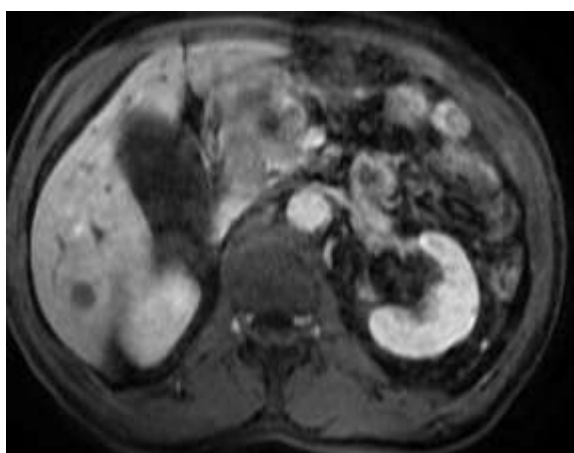

Fig. 6a: CE MRI of upper abdomen: Axial plane: Pancreas head and neck neoplasm with with local infiltration of adjacent blood vessel and infiltration in duoden, distance metastases (liver)
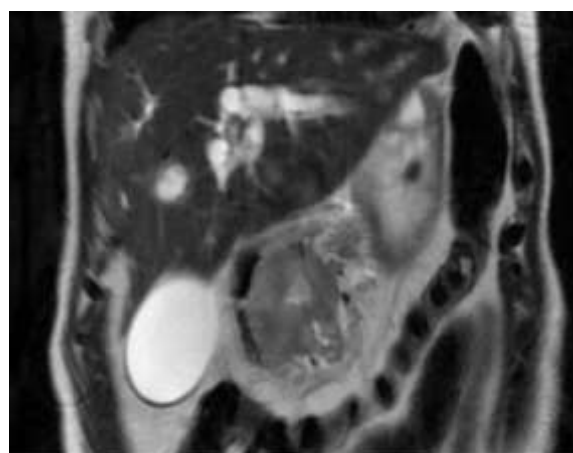

Fig. 6b: CE MRI of upper abdomen: Coronal plane: Pancreas head and neck neoplasm with with local infiltration of adjacent blood vessel and infiltration in duoden, distance metastases (liver).

Table 5: Correlation of risk factors and the incidence of carcinoma of the pancreas

Correlation of risk factors and the incidence of carcinoma of the pancreas													Other N (%)
Age group	>40		41-50		51-60		61-70		71-80		>80		
Gender	F	M	F	M	F	M	F	M	F	M	F	M	
Diabetis Mellitus	0	0	1	0	2	2	5	2	0	2	0	0	14 (14.43)
Ulcera peptica	0	0	0	0	1	1	3	2	0	1	0	0	8 (8.2)
Smoking	1	1	1	0	7	5	3	12	0	3	0	0	33 (34.0)
Alcohol	0	1	0	1	0	6	0	11	0	2	0	0	21 (21.6)
Other	0	1	0	2	0	0	5	0	5	11	1	1	21 (21.6)
Total N (%)	1 (1.03)	3 (3.09)	1 (1.03)	3 (3.09)	7 (7.22)	14 (14.4)	17 (17.5)	23 (23.7)	5 (5.15)	21 (21.6)	1 (1.03)	1 (1.03)	97 (100.0)

Correlation with risk factors present in our study have koreluar with Diabetes Mellitus type II 14:43%, 8.2% gastric ulcer, smoking 34.0%, 21.6% alcohol consuming (tab.5)

Patients who still live from the moment of diagnosis were 6 cases or (6.2%) of them still live. According morbidity rate of patients diagnosed with pancreatic carcinoma per 100,000 inhabitants by the total number of inhabitants 1820,631 are presented in this form:

Table 6: The morbidity rate of patients with pancreatic carcinoma

Years	Diseased	Morbidity (1:100000)
2011	13	0.7
2012	26	1.4
2013	27	1.5
2014	31	1.7

No. the inhabitants 1820631

Of the total number of diagnosed with carcinoma of the pancreas (still alive) highest rate was recorded in 2013 with 27 cases and the morbidity rate (1.5: 100,000). The lowest number was recorded in 2011 with 13 cases and morbidity rate (0.7: 100,000). The average morbidity rate for the period 2011-2014 is (5.3: 100,000), (Table 6).

Table 7: The mortality rate of patients diagnosed with pancreatic carcinoma

Years	The dead	Moratality (1:100000)
2011	0	0
2012	26	1.4
2013	14	0.8
2014	51	2.8
Total	91	5

No. the inhabitants 1820631

Of the total number of cases of deaths from pancreatic carcinoma (91), the greatest number of deaths was recorded in 2014 with 51 cases, while the lowest number was recorded in 2013 me14 cases. In 2011 not call any dead. The average number of deaths per year is 22.7.Nga total number of cases of deaths from pancreatic carcinoma (91), the highest rate of mortality was recorded in 2014 (2.8: 100,000 inhabitants), while the lowest rate was recorded in 2013 by (0.8: 100,000). Moratilitetit rate average for the period 2011-2014 was 5.0: 100,000 bhanorë (Table 7).

DISCUSSION AND CONCLUSION

Incidence of PC in Kosovo is increasing, but according to world-wide data it is reaching the incidence of developed countries. This is explained by utilization of advanced imaging modalities in routine examination of patients with complains suspected for pancreatic disease [15].

According to our studies, the M/F ratio is 2:1 (67/30) that is different from similar studies done in Europian countries (M/F ratio is 1.6:1) [16]. The results obtained in Balkan countries are approximately same as Europens (M/F is 1.5:1) [17], while resulted statistics in UK are inversed (M/F is 1:1.3) [18]. Has to be mentioned that the number of patients included in our last, abovementioned study was 97 - out of overall number of 289 patients examined in previous more comprehensive statistical group (the ratio in this group was M/F is 1.7: 1). As to age/group, all statistics show that the most attached fraction is 61-70 year age group [19].

As results, there is increased number of different diseases in Kosovo, still counting the cardio-vascular disturbances as a main cause of death followed by neoplastic malignant diseases. The pancreatic cancer itself is the fourth etiologic factor of death caused by gastro-intestinal diseases in both gender groups - 61 -70 male age group and 61-70 female age group (2:1. ratio).

The early diagnosis of pancreatic carnder correlates (as in other studies) with Tu localization – the tumors of the head were easily diagnosed (in contrary to body and tail Tu that were diagnosed in advanced stages).

The percentage of cases with nearby and distant metastases (30%) - especially in liver, are similar to the results obtained in other countries

According to world statistics, 75% of resulting in head and neck which correlates well with our study because of symptomatology earlier, while in the body and tail 15-20% 5-10% which compared to our study no difference sinifikant up 10% [20].

These statistics result lower than the proportion of cases in developed countries. This numeral are a reflection of the lack of a national strategy to fight cancer of the pancreas in Kosovo, lack of basic health insurance public and later symptomatology and non-specific symptoms of this type of cancer. All these circumstances are considered to be factors that limit the complete examination of a certain number of patients ranging from clinical examination and up to the imaging, surgical and conservative treatment of histological examination finalized. Based on these arguments, the figures do not say that patients in this geographical area have fewer predispositions for cancer localization.

Using advanced technological methods makes it easier diagnosis: MSCT is golden method for diagnosis, and management instruments stadifikimin patients diagnosed with carcinoma of the pancreas. RM helps in verification of cystic tumor, peripancreatic tissue and milimetric distal metastases.

MRCP enabled intraductal tumor diagnosis and differentiation of focal chronic pancreatitis more as problem diagnosis yet.The exposure to the other risk factors (alcohol, diabetes mellitus tip II, high calories diet etc) during last period is increased among the Kosovo's population (according to recent epidemiologic studies).

The gathering of anamnestic data related to the particular fields of the disease was difficult process at considerable number of the patients due to their low level of health education

The number of nicotine addicted individuals in Kosovo is much higher than in other countries (especially comparing with western European countries). But this fact did not implicate the higher incidence of the newly discovered pancreatic cancers in Kosovo and this known risk factor could not be treated as the main cause of the disease in our study [21, 22].The genetic factor – as very important one regarding the incidence of the pancreatic cancer was not studied in proper way in Kosovo due to the lack of the modern laboratories and Public Health Institutions that gather and processes information in this particular field of medicine.

Another, (rare in these days in Europe) potentially serious risk factor, is the impact of higher level of radioactive uranium that was part of the bombs that were used during the NATO bombing attacks in Kosovo during 1999-2000. There is still not any serious and comprehensive medical study regarding this issue due to different military and institutional limitations.

Having in consideration the cancer's very high mortality, an important part of the strategy that aims to minimize its burden is to understand the importance of causes of the disease, and if possible to reduce exposure to known risk factors. High priority should be given to the efforts that control smoking and alcohol use.

Smoking is the strongest environmental risk factor known to cause pancreatic cancer. Carcinogens derived from tobacco smoke probably reach the pancreas via the bloodstream after being absorbed from the lungs or from the upper aero-digestive tract. In addition, there is a possibility that ingested tobacco products reach the pancreas directly after reflux into the pancreatic ductal system from the duodenum. If this mode of exposure is correct, it could partly explain the large number of pancreatic cancers that occur in the head of the pancreas.

Nearly all published reports show that exposure to tobacco products increases the risk of pancreatic cancer, usually with about a 2-fold increased risk, compared to non-smokers [23, 24].

Carcinoma of the pancreas is considered to be the fourth agent of death caused by gastro-intestinal disease in both gender groups 61 -70 age group (ratio M: F rezultu 2: 1 ratio compared to other countries M: F 1.3: 1) [25, 26]. In this study the trend of mortality of patients diagnosed with UCCK during 2011-2014 and the results show an increasing trend for both sexes and age groups for in Kosovo during the 2011-2014 period showed total rate to 5.0 per 100,000 summary residents presenting in detail the years: in 2011 the mortality rate resulting 0.0: 100,000, in 2012 the mortality rate 1.4: 100,000, in mortality resulted 2013- 0.8: 100,000 and in the year the mortality rate in 2014 resulted in 2.8 per 100,000 inhabitants

Similar studies were done in different countries and the highest mortality rate in men was reported in Hungarian – 11.56 per 100.000, followed by Armenia 10.81, Albania 10.7, Croatia 9.47, Russia 8.83, Finland 7.14, per 100.000 and Czech Republic 7.13.

The lowest mortality rates were found in Cyprus and Turkey, both in men (3.69 – 3.72 per 100.000) respectively women (2.43 and 2.49 per 100.000) [27].

Compared with the other European countries and USA with higher incidence frequency, the mortality rate registered in Kosovo during 2011-2014 was 2.7-3.8 in 100.000 residents.

Since diagnostic and treatment improvements in the last decades have not substantially influenced the survival rate of pancreatic cancer, the rise of mortality rate in Kosovo follows the higher incidence rate due to improvement of diagnostic methods. International differences in mortality rates and temporal trends suggest that etiology of pancreatic cancer is influenced by environmental factors, especially smoking, but also by nutritional and dietary factors, obesity, alcohol use, diabetes mellitus, and peptic ulcerations [28].

REFERENCES
1. Pancreatic Cancer imaging: Which Method by E.Santo - 2004 http://springpublishing .org/ index. php/APCI/article/view/4
2. Common and unusual CT and MRI manifestations of pancreatic adenocarcinoma: a pictorial review Min-Jie Yang, Su Li, Yong-Guang Liu, Na Jiao, and Jing-Shan Gong Quant Imaging Med Surg, 2013; 3(2): 113–120.
3. Pancreatic imaging mimics: part 1, imaging mimics of pancreatic adenocarcinoma.Coakley F[VI], Hanley-Knutson K, Mongan J, Barajas R, Bucknor M, Qayyum A. AJR Am J Roentgenol. 2012; 199(2): 301-308.
4. Pancreatic imaging mimics: part 2, pancreatic neuroendocrine tumors and their mimics Raman S[PI], Hruban RH, Cameron JL, Wolfgang CL, and

Fishman EK.AJR Am J Roentgenol, 2012**;** 199(2): 309-**3**18.

5. Mimics of pancreatic ductal adenocarcinomaMahmoud M. Al-Haëary, a Ravi K. Kaza,a Shadi F. Azar,a,b Julie A. Ruma,a,b and Isaac R. Francisa Cancer Imaging. 2013; 13(3): 342–349.

6. American Cancer Society What are the key statistics about pancreatic cancer? 2011 Jun 21. In: Pancreatic Cancer [Internet]. American Cancer Society, Inc. c2011. Available from: http://www. cancer. org/ cancer/pancreaticcancer/detailedguide/pancreatic-cancer-key-statistics

7. Lynch SM, Vrieling A, Lubin JH, Kraft P, Mendelsohn JB, Hartge P, Stolzenberg-Solomon RZ; Cigarette smoking and pancreatic cancer: a pooled analysis from the pancreatic cancer cohort consortium. American journal of epidemiology, 2009; 170(4): 403-413.

8. Tersmette AC, Petersen GM, Offerhaus GJA, Falatko FC, Brune KA, Goggins M, Hruban RH; Increased risk of incident pancreatic cancer among first-degree relatives of patients with familial pancreatic cancer. Clinical Cancer Research, 2011; 7(3): 738-744.

9. Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, Andersen JR, Domellof L; Pancreatitis and the risk of pancreatic cancer. New England Journal of Medicine, 1993; 328(20): 1433-1437.

10. Kalser MH, Barkin J, Macintyre JM; Pancreatic cancer. Assessment of prognosis by clinical presentation. Cancer, 1985; 56(2): 397-402.

11. Chang MC, Su CH, Sun MS, Huang SC, Chiu CT, Chen MC, Lin JT; Etiology of acute pancreatitis--a multi-center study in Taiwan. Hepatogastroenterology, 2003; 50(53): 1655.

12. Calle EE, Murphy TK, Rodriguez C, Thun MJ, Heath CËJr; Diabetes mellitus and pancreatic cancer mortality in a prospective cohort of United States adults. Cancer Causes Control. 1998; 9(4): 403–410.

13. 28 doi:10.3748/wjq.v20.i24.7864://www.ncbi.nlm.nih. gov/pmc/articles/PMC4069314/

14. Tomislav Dragovich, MD, PhD Chief, Section of Hematology and Oncology, Banner MD Anderson Cancer Center, Pancreatic Cancer ,Oct 8, 2014; 280605.

15. Pancreatic Cancer imaging: Which Method by E.Santo Available from: //springpublishing. org/index. php/APCI/article/view/4`

16. Lowenfels AB, Maisonneuve P; Epidemiology and Prevention of Pancreatic Cancer.Jpn J Clin Oncol 2004; 34(5): 238-244.

17. Silverman DT, Dunn JA, Hoover RN, Schiffman M, Lillemoe KD, Schoenberg JB, et al. Cigarette smoking and pancreas cancer: a case-control study based on direct interviews. J Natl Cancer Inst, 1994; 86(20): 1510–1516.

18. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM; GLO BOCAN 2008 , Cancer Incidence and Mortality Worldwide :IARC Cancer Base No.10.Lyon : International Agency for Research on cancer:2010. Available from :http:globocan.iarc.fr.Accessed: July 4,2013.

19. Raptopoulos V, Steer ML, Sheiman RG, et al. The use of helical CT and CT angiography to predict vascular involvement from pancreatic cancer: correlation with findings at surgery. AJR Am J Roentgenol, 1997; 168(4):971-977.

20. Mahesh Kumar Neelal Andand; FRCR: Chief Editor: John Karani, MBBS, FRCR Pancreatic Adenocarcinoma, 2015.

21. Farrow DC, Devis S; Diet and the risk of pancreatic cancer in men. Am J epidemiol, 1990; 132: 423-431.

22. Norell SE, Ahlbom A, Erwald R, et al. Diet and pancraeatic cancer: a case controle study. Am J Epidemiol 1986; 124:894-902?

23. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM .GLO BOCAN 2008 , Cancer Incidence and Mortality Worldwide :IARC Cancer Base No.10.Lyon : International Agency for Research on cancer :2010.Available from :http:globocan.iarc.fr.Accessed: July 4,2013.

24. Howlader N, Noone A M, Krapcho M, Neyman N, Aminou R, Altekruse SF, et al, editors . SEER Cancer Statistics Revieë , 1975-2009(Vintage 2009 Population_ Bethesda ,MD : National Cancer Institute : Availble from : http/seer .cancer .gov /crs/1975-2009 pops 09/Accessed : July 4 , 2013

25. Pancreatic cancer mortality in Serbia from 1991-2010 a joinpoint analysis. Milena Ilic, Hristina Vlajinac, Jelena Marinkovic and Nikola Kocev Croat Med J, 2013; 54(4): 369–375.

26. American Cancer Society. Cancer facts and figures for African Americans 2009-2010. Available From http://www.acsevents.org/downloads/STT/cffaa_20 09-2010.pdf. Accessed February 5, 2010.

27. Iodice S, Gandini S, Maisonneuve P, Lowenfels AB; Tobacco and the risk of pancreatic cancer: a review and meta-analysis. Langenbeck's Archives of Surgery, 2008; 393(4): 535-545.

28. Univeristy of Southern California, Departament of Surgery. Adenocarcinoma of the pankreas.