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NAFLD Diagnosed with Abdominal Ultrasound is a Marker of Severity in Acute Pancreatitis

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Abstract

Objective: Obesity, particularly metabolic obesity, is associated with an increased incidence and enhanced severity of acute pancreatitis (AP). Non Alcoholic Fatty Liver Disease (NAFLD) is a marker of metabolic obesity, which can be easily diagnosed, with the help of initial abdominal ultrasound (AUS) routinely performed in all patients with AP upon admission to assess a biliary etiology. The aim of this study is to identify the clinical utility of detecting NAFLD by AUS in determining the severity of patients with AP

Methods: Five hundred and seventy four patients with non-alcoholic AP were divided into two groups on the basis of presence or absence of NAFLD detected by AUS at the time of admission. The diagnosis of NAFLD was based solely on imaging findings. Well-established single markers of prognosis as well as scoring systems were studied in both groups. The data was analyzed using the student's t-test, chi-square test and multivariate regression analysis.

Results: Patients with NAFLD had a more severe disease as compared to patients without NAFLD as measured by single markers of prognosis like serum albumin, mean length of stay, ICU admission and mortality as well as scoring systems like BISAP score and Modified Atlanta Classification system (P value < 0.05) BMI, by itself, was not associated with any difference in outcomes in patients with and without NAFLD as assessed by multivariate regression analysis. Age, sex and individual components of metabolic syndrome also had no influence on the prognostic markers

Conclusion: Presence of NAFLD as diagnosed by early AUS can be used as an additional single marker of prognosis in AP. The diagnosis of NAFLD is objective and almost always available at the time of initial presentation of AP.

Keywords: Metabolic obesity

Introduction

Many recent studies have identified obesity as a marker of poor prognosis in acute pancreatitis (AP). Results from meta-analysis show that obesity (defined as BMI>30) was associated with significantly higher incidence of systemic and local complication and higher rate of mortality from AP [1-3]. Several independent studies have also confirmed this observation [4-6]. Visceral obesity, which is a component of metabolic syndrome, has been recognized to have a stronger correlation with poor outcomes in patients with AP [1-7]. NAFLD is an objective marker of visceral obesity. Other objective markers of visceral obesity that have been studied in the past as prognostic markers for AP include waist circumference and visceral adipose tissue assessment on CT abdomen. Both these markers have several limitations. Although inexpensive, waist circumference currently is not routinely recorded and when done, is subject to measurement bias. CT of the abdomen is not recommended in most patients on admission. Furthermore, it is costly and involves exposure to radiation.

The aim of this study is to assess the prognostic role of Non Alcoholic Fatty Liver Disease (NAFLD), an objective and readily available marker of metabolic obesity, in patients with AP. Abdominal Ultrasound (AUS), performed on admission in all patients with AP in order to evaluate a biliary etiology, in addition helps to diagnose NAFLD.

Materials and Methods

In this retrospective electronic medical record (EMR) based study, pooled data from two institutions (Monmouth Medical Center and St Peter's University Hospital in Central New Jersey) on 574 non-alcoholic adult hospital admissions that satisfied the American College of Gastroenterology diagnostic criteria for AP was analyzed [8]. Approval from the Institutional Review Board was obtained prior to initiating the study from both institutions. As per the American Association for the Study of Liver Diseases (AASLD) criteria, significant alcohol consumption was defined as >21 drinks per week for men and >14 drinks per week for women over a minimum 2 year period [9]. On admission, abdominal imaging in the form of either Ultrasound or CT scan of the abdomen or both was available in all. The diagnosis of NAFLD or its exclusion was based solely on radiologists' interpretation of the abdominal imaging study.

On the basis of presence or absence of NAFLD, the patients were divided into two groups - group 1: patients with NAFLD and group 2: patients without NAFLD. Severity of AP was analyzed using the Bed Side Index of Severity (BISAP) score and Modified Atlanta Classification (MAC) [10,11]. Frequency of ICU admission, mean length of stay (LOS) and mortality rates in both the groups were also evaluated. Strict patient confidentiality was ensured throughout. Only the study participants from respective institutions had access to patient information.

The results were analyzed using the student's t-test and CHI square test. Using multivariate regression analysis, influence of BMI, age, sex, hypertension and DM on prognosis in the two groups was assessed. P value less than 0.05 was considered significant.

Results

The results are tabulated in Tables 1 and 2.

Parameter	Non NAFLD group **(n=381)**	NAFLD group **(n=193)**	p value
Age	53.45 ± 20.73	50.50 ± 1.30	0.0938^
Sex (Males)	124(32.5%)	74(38.3%)	0.168*
BMI	28.07 ± 5.95	30.22 ± 6.79	0.0001^
Hypertension	139(36.5%)	99(51.3%)	0.001*
Hyperlipidemia	92(24.1%)	74(38.3%)	0.000*
Diabetes	89(23.4%)	61(31.6%)	0.034*
Outcomes			
Mean BISAP score	0.544 ± 0.75	0.813 ± 0.97	0.0003^
Modified Atlanta			
(moderate to severe)	30(7.9%)	84(43.5%)	0.000*
Mean Albumin	4.02 ± 0.45	3.90 ± 0.55	0.008^
Mean Hematocrit	40.05 ± 3.81	40.25 ± 5.51	0.611^
Mean LOS	5.34 ± 6.64	7.14 ± 7.77	0.004^
ICU admission	17(4.5%)	31(16.1%)	0.000*
Mortality	1(0.3%)	5(2.6%)	0.010*

Table 1: Outcomes of patients with and without NAFLD.*Chi square test, ^Student's t-test.

	BISAP score	Albumin	Hematocrit	LOS	ICU	Mortality
Non-NAFLD						
Age	p<0.001	p>0.001	p>0.001	p>0.001	p=0.009	p<0.001
Sex	p>0.001	p>0.001	p<0.001	p>0.001	p>0.001	p>0.001
BMI >30	p>0.001	p>0.001	p=0.033	p>0.001	p>0.001	p>0.001
HTN	p<0.001	p>0.001	p>0.001	p>0.001	p=0.007	p>0.001
HLP	p<0.001	p>0.001	p>0.001	p>0.001	p=0.014	p>0.001
DM	p<0.001	p=0.044	p>0.001	p>0.001	p=0.048	no deaths
NAFLD						
Age	p>0.001	p>0.001	p<0.001	p>0.001	p>0.001	no deaths
Sex	p>0.001	p>0.001	p>0.001	p>0.001	p>0.001	no deaths
BMI >30	p>0.001	p>0.001	p>0.001	p>0.001	p>0.001	no deaths
HTN	p>0.001	p>0.001	p=0.002	p>0.001	p>0.001	no deaths
HLP	p>0.001	p>0.001	p=0.016	p>0.001	p>0.001	no deaths
DM	p>0.001	p>0.001	p>0.001	p>0.001	p>0.001	no deaths

Table 2: Multiple regression analysis showing influence of age, sex, BMI, Hypertension and Diabetes independently on outcomes in patients with and without NAFLD. ns: not significant.

Demographics

As seen in Table 1, the baseline characteristics of patients in both groups were similar. The mean age of patients in Non-NAFLD group was 53.4 years and the mean age in NAFLD group was 50.50 years. The difference between the ages was not statistically significant (p value=0.0938). The proportion of male patients in the non NAFLD group was 32.5% and in the NAFDL group was 38.3%. The difference again was not statistically significant.

Comorbidities

Patients with NAFLD, as expected, had a higher mean BMI and higher prevalence of hypertension, hyperlipidemia and diabetes. As can be seen in Table 1, the mean BMI in non-NAFLD group as 28.07 and the mean BMI in the NAFLD group was 30.22, the difference between the two groups being statistically significant (p=0.0001). Similarly, the prevalence of hypertension in the non-NAFLD and the NAFLD group was 36.5% and 51.3% respectively, the difference being statistically significant (p=0.001). The prevalence of Hyperlipidemia in the non-NAFDL group was 24.1% and in the NAFLD group was 38.3%, the difference being significant with p value of <0.0001. The prevalence of Diabetes in the non-NAFLD and NAFLD group was 23.4% and 31.6% with the difference being significant at p=0.034.

Outcomes and prognosis

Table 1 shows the data on the severity of AP in the two groups. Patients with NAFLD had a more severe disease compared to patients without NAFLD as measured by several well-validated single prognostic markers and two scoring systems. The difference was statistically (p value less than 0.05) significant for all except serum hematocrit levels between the two groups.

Single prognosis markers

The mean BISAP score in the non-NAFLD group was 0.544 and in the NAFLD group was 0.813. This difference was significant at p=0.0003. In the non-NAFLD group, the percentage of cases with Modified Atlanta severity of moderate or severe was 7.9% where as it was 43.5% in the NAFLD group. This difference was again significant statistically with p value of <0.0001. The mean albumin level in the non-NAFLD group was 4.02 and in the NAFLD group was 3.90, the difference again was significant at p=0.008.

Clinical outcomes

The clinical outcomes also were significantly different in both the groups. The mean length of stay in the non-NAFLD group was 5.34 days where as the mean length of stay in the NAFLD group was 7.14 days with the difference being significant at p=0.04. The rate of ICU admission in the non-NAFLD group and the NAFLD group were 4.5% and 16.1% respectively, again significant statistically at p <0.0001. The mortality between the two groups was also different, with the non-NAFLD group having one case whereas the NAFLD group having 5 cases (p=0.01)

Multivariate analysis

Table 2 summarizes the results of multivariate regression analysis determining the individual effects of age, sex, BMI, hypertension, hyperlipidemia and diabetes on the BISAP score, mean albumin, hematocrit, length of stay, ICU admission and mortality. Increased BMI, by itself, was not associated with any difference in outcomes in patients with NAFLD and without NAFLD. Age, sex and individual components of metabolic syndrome did not influence the prognostic markers. P value less than 0.05 was considered significant.

Discussion

Our study shows that NAFLD is an additional marker of severity in patients with AP. As compared to patients without NAFLD, patients with NAFLD had a more severe course of AP as measured by several well-validated single prognostic markers as well as scoring systems. The diagnosis of NAFLD is available easily at the time of presentation since an initial AUS is performed in all patients with suspected AP. Although presently performed in all patients with AP, it is being performed solely to diagnose a biliary etiology for AP and seldom attention is paid to the echogenicity of liver. Based on our findings, we recommend that the AUS be used for the diagnosis of NAFLD in addition to determining a biliary etiology.

The association between obesity and AP has been looked at in a number of studies, which correlated an increased incidence and worsened severity of AP. From a meta-analysis of 11 prospective studies with a pooled population of 8702 individuals, the pooled relative risk (RR) for developing AP in individuals with a normal BMI as compared to individuals with a BMI of greater than 25 was 1.43 (95% CI 1.09-1,87, p Value <0.01). The pooled data of 3 studies involving 1029 individuals shows that the relative risk of developing AP in individuals with a waist circumference >105 cm as compared to individuals with a waist circumference <75 cm was 2.37 (95% CI 1.50-3.74) [12]. Obesity as measured by BMI has also been shown to adversely affect the prognosis in patients with AP. In a meta-analysis, obesity (defined as BMI >30) was associated with significantly higher incidence of systemic and local complication and higher rate of mortality [1-3]. Several independent studies have also confirmed this observation [4-6].

Visceral obesity determines the severity of many diseases and not obesity as measured by BMI estimation. A smaller number of recent studies have specifically assessed the role of visceral obesity in poor prognosis of AP [13-15]. Lipotoxicity is related to visceral adiposity and fatty liver than with generalized obesity. The pathogenesis of increased severity with visceral obesity is postulated to be related to pro-inflammatory cytokines. Lipotoxic visceral fat is associated with metabolic syndrome and is known to secrete pro-inflammatory cytokines like TNF-α, Interleukin-6 and Leptin [16-18]. These cytokines, in turn, promote the complications of metabolic syndrome by a pro-inflammatory state [19]. AP is a cytokine mediated disease and many, if not all, systemic complications of AP are attributed to the pro-inflammatory cytokines. Patients with severe AP are noted to have increased visceral fat, higher serum cytokines (example: Interleukin 6, Monocyte chemoattractant protein -1) and adipokines(eg – resistin and visfatin) [20] NAFLD is an objective marker of visceral obesity. The role of fatty pancreas in patients with NAFLD is not clear [21]. Metabolic fat (central, visceral obesity), as measured by waist circumference or visceral adipose tissue assessment on CT abdomen, predicts a poor outcome in patients with AP better as compared to Body Mass Index (BMI) [13-15]. Although inexpensive, waist circumference currently is not routinely recorded and when done, is subject to measurement bias [13]. CT of the abdomen is not recommended in most patients on admission. AST, ALT levels poorly correlate with NAFLD, further they are abnormal in biliary AP. AUS on the other hand, is routinely performed in all patients to rule out a biliary etiology for AP. On AUS, presence of fatty liver demonstrates a diffuse increase in echogenicity as compared to the kidneys. Although both false positives and false negatives can occur, the diagnosis of NAFLD can be established with a reasonable accuracy on AUS. The sensitivity and specificity of AUS for detecting hepatic fatty infiltration is 93% and 77% respectively as compared to histology as a gold standard [22]. Above all, AUS is inexpensive with no radiation risk.

Limitation of this study is its retrospective nature. We do not know whether NAFLD itself predisposes to AP.

In conclusion, presence of NAFLD as diagnosed by early AUS can be used as an additional single marker of prognosis in AP. The diagnosis of NAFLD is objective and almost always available at the time of initial presentation of AP.

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