Clinicopathological features of nonalcoholic fatty liver disease in Korean young men

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<ABSTRACT>

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Background: Nonalcoholic fatty liver disease (NAFLD) is a chronic liver disease occurring without a significant alcohol consumption. Its prevalence is increasing in Korean society as a dietary pattern and life-style become more westernized and an obese population increases. Especially nonalcoholic steatohepatitis (NASH), which has a potential to progress to liver cirrhosis or even hepatocellular carcinoma, holds considerable clinical significance. In this study, we examined clinicopathological features of NASH in Korean young men using a guideline presented by NASH Clinical Research Network and classifying according to the criteria suggested by Schwimmer et al. to understand the natures and clinical progression of NAFLD.

Methods: 64 Korean young men under age 30 years (22.2 ± 2.75),

diagnosed as NAFLD by a liver biopsy, were enrolled. Retrospectively, we reviewed age, BMI, AST/ALT, total cholesterol, triglyceride, fasting plasma glucose and other clinical manifestations. Histologic findings were focused on the degrees of steatosis, lobular inflammation, periportal inflammation, hepatocellular ballooning and hepatic fibrosis. NASH was diagnosed by NAFLD activity score (NAS), proposed by Kleiner DE et al. In NASH patients, histopathological findings were classified into the three types; adult type, pediatric type and overlap type according to Schwimmer's classification.

Results: 51 cases (79.9%) were obese and had elevated AST/ALT levels (mean 76.83 ± 44.6, 171.50 ± 114.89). Pathological features of liver biopsy revealed NASH in most cases (59 cases, 92.2%) including 29 cases (45.3%) of borderline NASH and 30 cases (46.9%) of definite NASH. In this group, NAS and AST/ALT levels had a positive linear correlation and the definite NASH group showed significantly high AST/ALT levels compared to borderline NASH group. NASH group was further subclassified into three types according to Schwimmer's criteria and there were 17 cases (28.8%) of adult type, 4 cases (6.8%) of pediatric type and 38 cases (64.4%) of overlap type. NAS (mean ± SD) was 3.75 ± 0.05 in pediatric, 4.29 ± 1.16 in adult type and 4.87 ± 1.21 in overlap type, and overlap type showed higher NAS than the

pediatric type (p<0.01). Concerning on fibrosis, 36 cases (94.7%) of overlap type showed stage 2 and 3, and 4 cases (100%) of pediatric type and 15 cases (88.2%) of adult type showed stage 1. The fibrosis stage is significantly higher in the overlap type than the other types (p<0.01). Other pathological features including steatosis and lobular inflammation showed no significant difference among three types and clinical features also showed no significant difference.

Conclusion: Majority of Korean young men with nonalcoholic fatty liver disease (NAFLD) turned out to have borderline or definite NASH based on the pathological features of liver biopsy. More than half of NASH cases showed overlap type of pediatric and adult NASH, which showed higher degree of NAS and fibrosis stage compared to pediatric type. These findings suggest that overlap type of NASH in Korean young men might be disease progression starting from pediatric period.

Key words : Nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, liver biopsy, Korean young men

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I. INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a clinicopathological diagnosis characterized histologically by macrovesicular fat accumulation in hepatocytes in nonalcoholic patients with other causes of liver disease excluded.[1] It ranges from simple steatosis to steatosis accompanied by inflammation, fibrosis and other evidence of cellular injury, so called nonalcoholic steatohepatitis (NASH). NAFLD is known to be related to the obesity and metabolic syndrome (hyperinsulinemia, hypertriglyceridemia, peripheral insulin resistance, type II DM) and can progress to liver cirrhosis and even hepatocellular carcinoma.[2,3,4] In recent, as the obese population increases, the prevalence of NAFLD increases[5] and there is an rising concern about this category of disease.

Whereas laboratory tests (aspartate aminotransferase, alanine aminotransferase or gamma-glutamyl transferase) and liver imaging (ultrasound or magnetic resonance imaging or spectroscopy) may suggest NAFLD, histological evaluation is the most accurate method for diagnosing and assessing the degree of steatosis, the necroinflammatory changes and fibrosis.[2,6,7] Schwimmer et al. divided NASH into three types according to the histological characteristics.[1,10] Type 1 NASH, more common in adults, has been shown to have steatosis with ballooning degeneration and/or perisinusoidal fibrosis in the absence of portal features. Whereas type 2 NASH is observed mostly in children and is defined as the presence of portal inflammation and/or fibrosis in the absence of ballooning degeneration and perisinusoidal fibrosis.

For evaluating NASH, Brunt et al. proposed semiquantitative system, which was developed to parallel the concepts and terminology used in chronic hepatitis, commonly referred to as "grading" and "staging".[8] However this system was based on the ideas that histological diagnosis of NASH rests on a constellation of features rather than any individual features. And the system was developed only for NASH, not for the entire spectrum of NAFLD. In 2005, Clinical Research Network for NASH proposed a new system, NAFLD activity score (NAS).[2,11] This system comprised of 3 histological features and evaluated each features semiquantitatively; steatosis (0-3), lobular

inflammation (0-3) and hepatocellular ballooning (0-2). According to the summation of each scores, this system defines definite NASH as the one ≥5, borderline NASH as the one between 3 to 4, and not-NASH as the one ≤2.

In Korea, as like other countries in Asia, there is an increase in obese populations and NAFLD patients. However the data are not sufficient to understand the clinicopathological characteristics and the nature of NAFLD in Korea. Liver biopsy is necessary to evaluate and diagnose NAFLD, however the invasiveness of the procedure makes it difficult to be performed, particularly in children. In Korea, many young men (age under 30) get liver biopsies for diagnosing NAFLD when they have a health check-up for the obligatory military service. This study was aimed to histologically classify NAFLD and to compare pathological characteristics and clinical findings for understanding natural and clinical progress of NAFLD in Korea.

II. MATERIALS AND METHODS

1. Subjects and data collections

We identified subjects under age 30, who admitted for a liver biopsy to evaluate abnormal liver enzymes in the military health check-up and were diagnosed as NAFLD at Severance Hospital and Yongdong Severance Hospital from January 1992 to July 2008. We retrospectively reviewed the charts of the subjects. All biopsy specimens were examined by one liver pathology specialist according to the criteria proposed by Brunt et al in 1999.[8]

In all subjects the diagnosis of NAFLD was made following exclusion of causes of chronic hepatitis including hepatitis B, hepatitis C, autoimmune hepatitis, drug toxicity, chronic alcohol intake (≥30g/day) and having history of resection of small intestine.

2. Measurements of subjects

Charts for all subjects were reviewed for age, sex, weight, height and history of diabetes. Body mass index (BMI) was calculated as the weight (kg) divided by the height (m) squared. Obesity status was determined using the International Obesity Taskforce (IOTF) classification in 2000[12] and defined as the one having BMI ≥ 25 kg/m^2.

3. Serum chemistry

Results of liver enzyme (serum aspartate aminotransferase and alanine aminotransferase), fasting plasma glucose, total cholesterol and triglyceride were recorded at the time of biopsy obtained.

4. Pathological classification and diagnosis of NASH

Among NAFLD patients, NAFLD activity score (NAS)[2] was calculated and NASH was defined using the criteria (Table 1).

Table 1. Definition of nonalcoholic steatohepatitis and scoring by NASH activity score

Item	Definition	Score
Steatosis	<5%	0
	5-33%	1
	>33%-66%	2
	>66%	3
Lobular inflammation	No foci	0
	<2 foci per 200x field	1
	2-4 foci per 200x field	2
	>4 foci per 200x field	3
Ballooning	None	0
	Few ballooning cells	1
	Many cells/prominent ballooning	2

0-2 not-NASH, 3-4 borderline NASH, ≥5 definite NASH

Note. According to the criteria proposed by Clinical Research Network for NASH[2]

For evaluating histological characteristics of NASH patients, we categorized NASH into three types (adult type, pediatric type and overlap type) using the classification proposed by Schwimmer et al. in 2005[1] (Table 2).

Table 2. Definition of nonalcoholic steatohepatitis type

<table>
<tr><td></td><td colspan="3">Adult type</td><td colspan="3">Pediatric type</td><td>Overlap Type¶</td></tr>
<tr><td>Ballooning degeneration</td><td>+</td><td>+</td><td>-</td><td colspan="3" rowspan="2">-</td><td>+</td></tr>
<tr><td>Perisinusoidal fibrosis</td><td>-</td><td>+</td><td>+</td><td>+</td></tr>
<tr><td>Steatosis</td><td colspan="7">+</td></tr>
<tr><td>Portal inflammation</td><td colspan="3" rowspan="2">-</td><td>+</td><td>+</td><td>-</td><td>+</td></tr>
<tr><td>Portal fibrosis</td><td>-</td><td>+</td><td>+</td><td>+</td></tr>
</table>

+: feature is present.

-: feature is absent.

¶: Overlap type represents those biopsies that demonstrated steatosis along with at least one feature from adult type and pediatric type.

Note. According to the classification of Schwimmer et al.[1]

5. Statistical analysis

Means, standard deviations and percentages were reported for various dermographic and clinical features. Chi-square tests were used to compare univariate association of histological characteristics with NASH classification by Schwimmer et al. For comparison of clinical characteristics between three groups classified by NAS and Schwimmer's criteria, ANOVA test was used. Simple Pearson correlation test was used to identify relationships between the severity of NAS and the clinical features. P-value of 0.05 or less was considered to indicate statistical significance. All statistical analysis was performed using SPSS 12.0.

III. RESULTS

1. Dermographic data of all subjects

Total 64 patients and specimen were collected. Average age was 22.2 ± 2.75 years old and most of them had abnormal liver enzymes (AST; 76.83 ± 44.64, ALT; 171.50 ± 114.89). Total cholesterol and triglyceride were 189.34 ± 38.51 (101-350) and 179.52 ± 97.86 (62-583). According to the IOTF classification in 2000, 51 patients (79.7%) were obese. There were 4 diabetes patients (6.3%). By NAS criteria, 5 were not-NASH (7.8%), 29 were borderline NASH (45.3%) and 30 were definite NASH (46.9%).

2. Comparison of baseline characteristics between three groups classified by NAS

Comparing three groups classified by NAS, there was no significant difference in age, BMI, total cholesterol, triglyceride and fasting plasma glucose. The prevalence of diabetes was higher in NASH group (n=4, 6.8%) than in not-NASH group (n=0, 0%) without statistical significance. In NASH group, AST and ALT were higher than in not-NASH group (Table 3). Especially definite NASH group showed significantly higher AST and ALT levels than the other two groups (Figure 1, 2). And there was a linear correlation between AST or ALT and NAS (Figure 3, 4).

Table 3. Comparison of baseline characteristics between three groups classified by NASH activity score

	Not-NASH(n=5)	Borderline NASH(n=29)	Definite NASH(n=30)	*p*-value
Age(years)	22.4 ± 3.05	21.93 ± 2.14	22.33 ± 3.26	0.84
AST(IU/L)	64.40 ± 30.24	56.97 ± 29.23	98.10 ± 49.88	< 0.01
ALT(IU/L)	121.80 ± 56.73	120.28 ± 75.17	229.27 ± 127.57	< 0.01
Chol(mg/dL)	189.40 ± 39.73	188.86 ± 42.57	189.82 ± 35.35	0.996
TG(mg/dL)	136.00 ± 42.98	216.53 ± 118.19	160.82 ± 81.78	0.120
FPG(mg/dL)	94.40 ± 6.57	98.79 ± 26.48	106.15 ± 31.57	0.522
BMI(kg/m^2)	29.98 ± 4.46	29.67 ± 4.04	29.49 ± 4.80	0.971
Numbers of obese patients(%)¶	4 (80%)	26 (89.6%)	21 (70%)	0.281

BMI= Body mass index ; Chol= Total cholesterol ; TG= Triglyceride ;

FPG= Fasting plasma glucose; NAS=NASH activity score

¶: By IOTF classification in 2000[12], obese patient is defined as the one having BMI ≥ 25 kg/m^2

Figure 1. Comparison of AST in three groups classified by NASH activity score

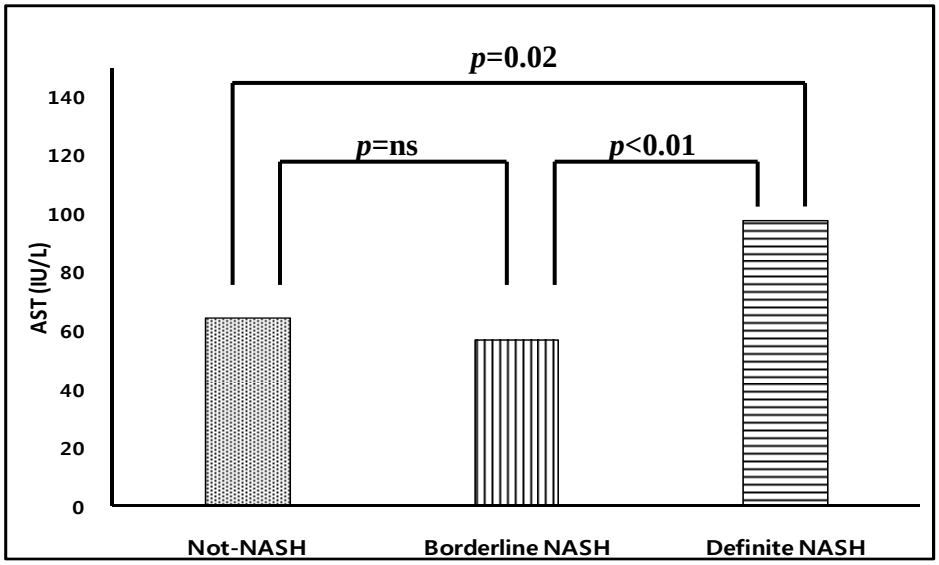


Figure 2. Comparison of ALT in three groups classified by NASH activity score

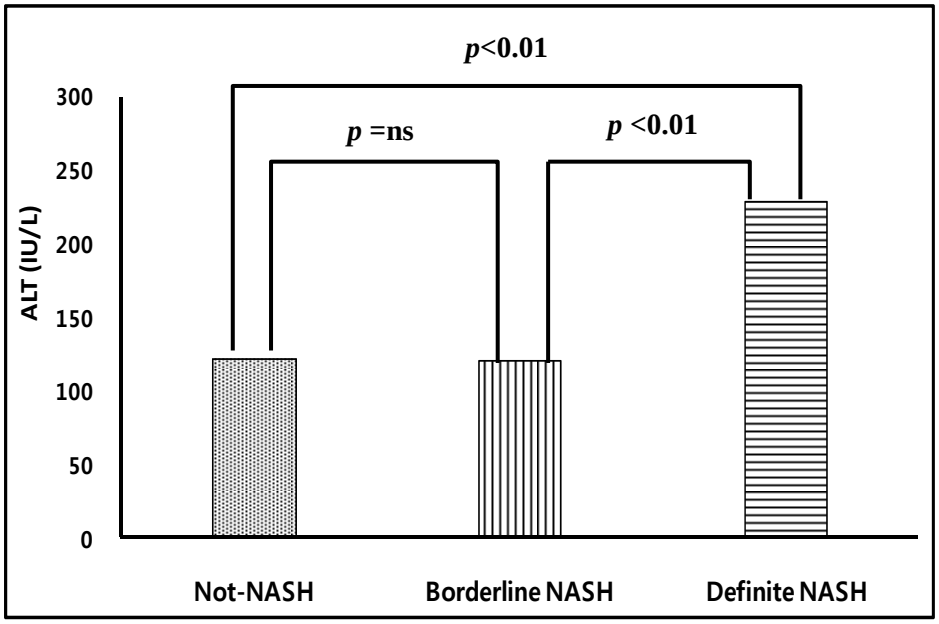


Figure 3. Correlation between AST and NASH activity score in three groups

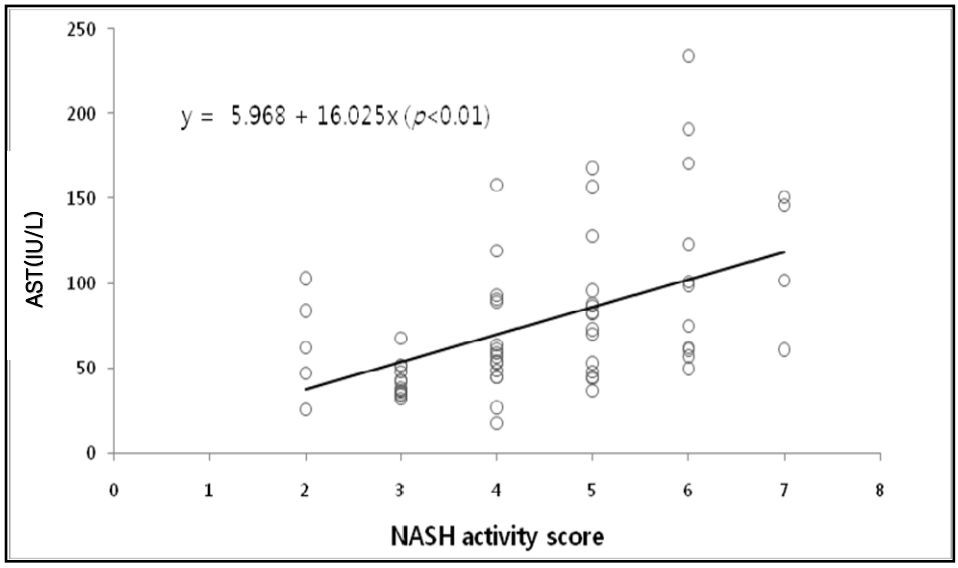
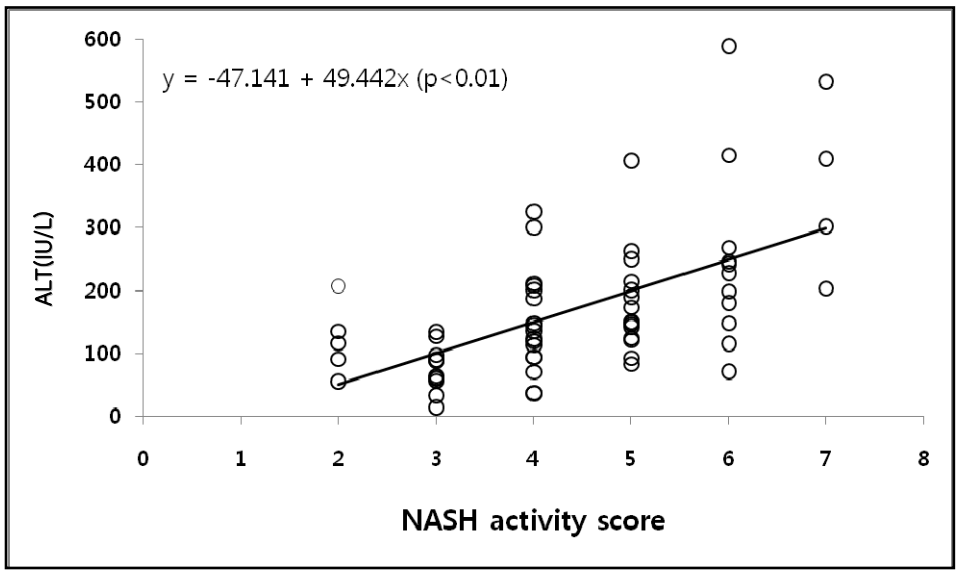


Figure 4. Correlation between ALT and NASH activity score in three groups

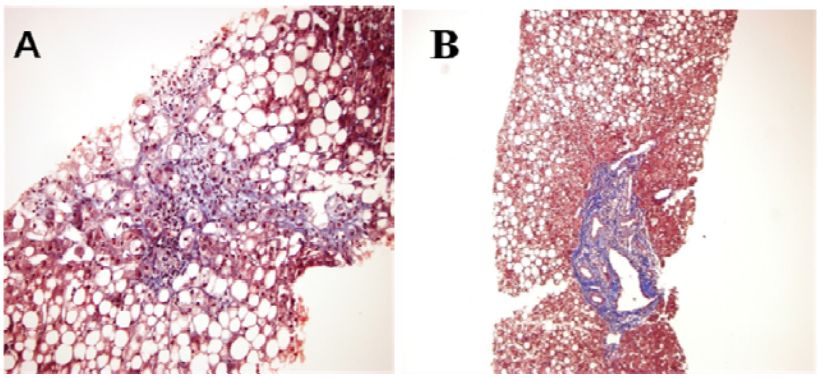


3. Pathological and clinical characteristics of NASH classified by Schwimmer's classification

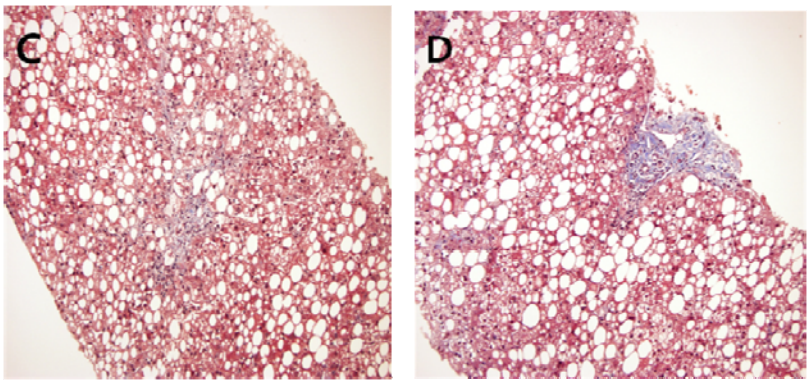
There were 59 NASH patients who had NAS score over 3. By Schwimmer's classification, there were 17 adult type NASH (28.8%), 4 pediatric type NASH (6.8%) and 38 overlap type NASH (64.4%) (Figure 5). In pathological characteristics, there was no difference in steatosis (p=0.576) and lobular inflammation (p=0.477) between three groups (Table 4). About fibrosis, there were inter-group differences between three groups. In overlap type, stage 2 fibrosis was prominent than in the other two groups (Figure 6).

There was no statistical inter-group difference in clinical characteristics between three types of NASH (Table 5). However in comparison between pediatric type NASH group and overlap type NASH group, age and NAS of pediatric type group were lower than those of overlap type group in statistical significance (age; p=0.029, NAS; p=0.009). None of pediatric type NASH patient belonged to the definite NASH and over a half of overlap type NASH patient (57.9%) was in the definite NASH (Figure 7).

Figure 5. Histological characteristics of nonalcoholic steatohepatitis classified by Schwimmer's classification



(A) Adult type NASH showing prominent ballooning degeneration with Mallory bodies, moderate steatosis, perisinusoidal fibrosis in zone 3 (TRC x200)
(B) Pediatric type NASH showing moderate steatosis, portal inflammation and fibrosis (TRC x100)



(C), (D) Overlap type NASH showing zone 3 injury of adult type (C) and portal inflammation and fibrosis of pediatric type (D) (TRC x200)

Table 4. Pathological characteristics of NASH classified by Schwimmer's classification

		Adult type (n=17)	Pediatric type (n=4)	Overlap type (n=38)	***p***-value
Steatosis	0	0 (0%)	0 (0%)	0 (0%)	0.576
	1	3 (17.6%)	0 (0%)	9 (23.7%)	
	2	11 (64.7%)	2 (50%)	21 (55.3%)	
	3	3 (17.6%)	2 (50%)	8 (21.1%)	
Fibrosis	0	2 (11.8%)	0 (0%)	0 (0%)	<0.01
	1A	12(70.6%)	0 (0%)	0 (0%)	
	1B	3 (17.6%)	0 (0%)	0 (0%)	
	1C	0 (0%)	4 (100%)	2 (5.3%)	
	2	0 (0%)	0 (0%)	36 (94.7%)	
	3	0 (0%)	0 (0%)	0 (0%)	
	4	0 (0%)	0 (0%)	0 (0%)	
Lobular inflammation	0	1 (5.9%)	0 (0%)	0 (0%)	0.477
	1	9 (52.9%)	3 (75%)	19 (50%)	
	2	7 (41.2%)	1 (25%)	19 (50%)	
	3	0 (0%)	0 (0%)	0 (0%)	
Portal inflammation	0	17 (100%)	1 (25%)	9 (23.7%)	<0.01
	1	0 (0%)	3 (75%)	29 (76.3%)	
Ballooning degeneration	0	5 (29.4%)	4 (100%)	2 (5.3%)	<0.01
	1	8 (47.1%)	0 (0%)	19 (50%)	
	2	4 (23.5%)	0 (0%)	17 (44.7%)	

Figure 6. Comparison of pathological characteristics of nonalcoholic steatohepatitis classified by Schwimmer's classification

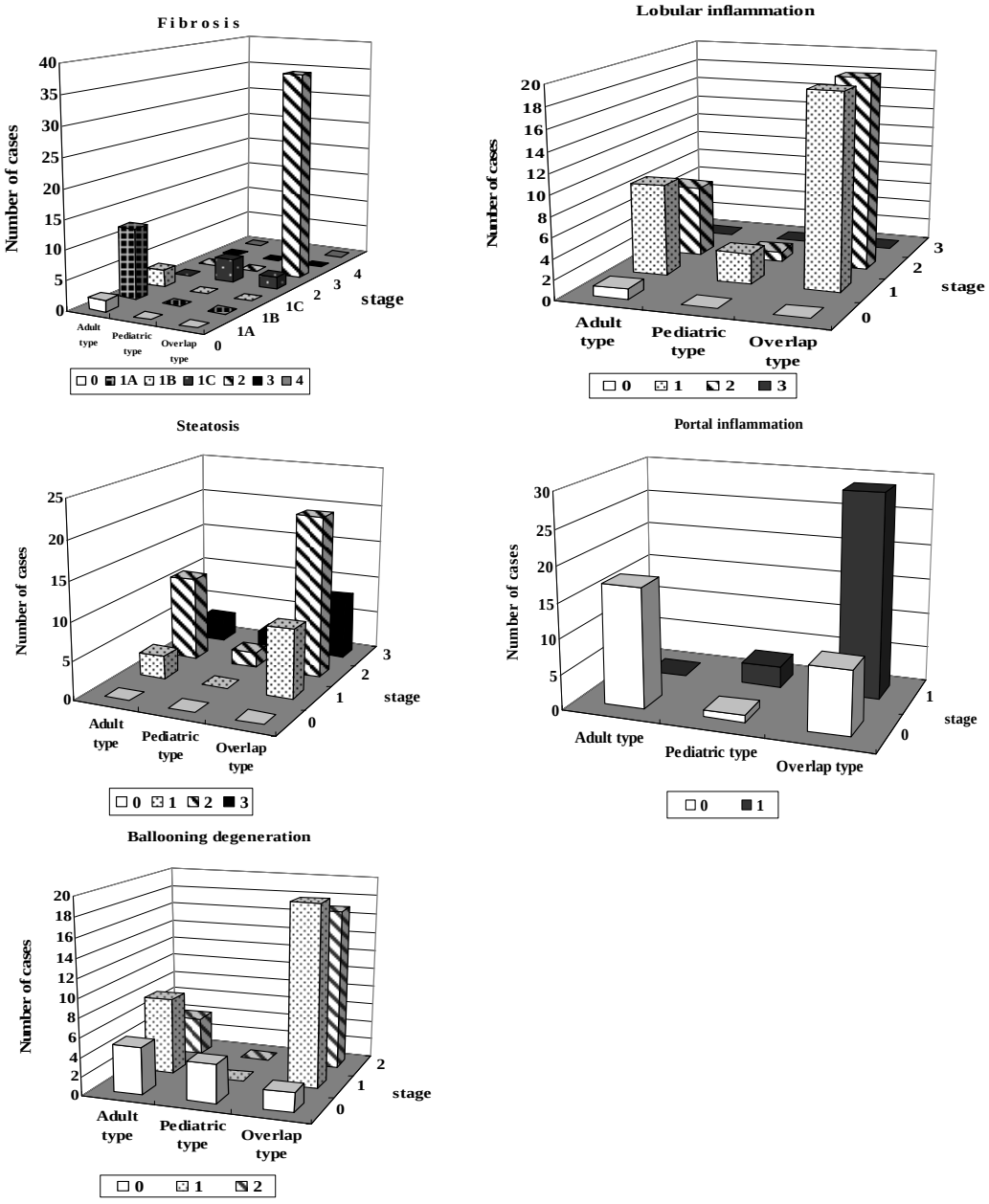
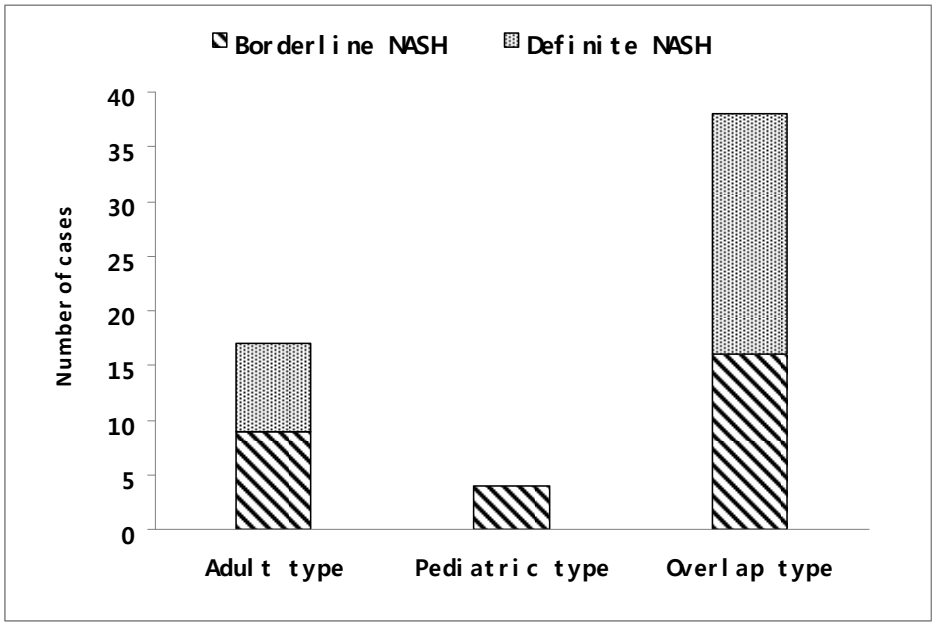


Table 5. Clinical characteristics of nonalcoholic steatohepatitis classified by Schwimmer's classification

	Adult type (n=17)	Pediatric type(n=4)	Overlap type(n=38)	***p***-value
Age(years)	21.82 ± 2.90	20.75 ± 0.96	22.4 ± 2.80	0.447
BMI(kg/m^2)	28.92 ± 3.68	32.23 ± 1.52	29.61 ± 4.85	0.405
AST(IU/L)	78.82 ± 49.11	70.00 ± 13.19	78.29 ± 46.98	0.939
ALT(IU/L)	161.76 ± 103.07	153.25 ± 70.28	184.29 ± 128.65	0.753
Chol(mg/dL)	185.31 ± 35.54	222.50 ± 30.84	187.44 ± 40.03	0.206
TG(mg/dL)	173.55 ± 76.08	188.75 ± 58.96	189.79 ± 118.57	0.910
FPG(mg/dL)	96.33 ± 12.00	125.75 ± 59.16	102.33 ± 29.45	0.200
NAS	4.29 ± 1.16	3.75 ± 0.50	4.87 ± 1.21	0.082

BMI= Body mass index ; Chol= Total cholesterol ; TG= Triglyceride ;
FPG= Fasting plasma glucose ; NAS= NAFLD activity score

Figure 7. Composition of the definite nonalcoholic steatohepatitis and borderline nonalcoholic steastohepatitis in three types classified by Schwimmer′s classification



IV. DISCUSSION

The aim of this study is to know clinicopathological characteristics and natural history of NAFLD in Korean young men by using a semiquantitative diagnostic method and classifying them into three groups (adult type, pediatric type and overlap type). Recently in Korea, as the obese population increases, the prevalence of metabolic syndrome increases concurrently. Metabolic syndrome, especially insulin resistance and visceral obesity, is known to be closely related to the incidence of NAFLD.[13,14,15]. In recent studies, NAFLD itself is strongly related with chronic fatal complications in nonhypertensive and nondiabetic adults[16] and even in children.[17] Visceral obesity is thought to cause fatty accumulation in hepatocytes and this leads hepatic insulin resistance,[18,19] and these changes in turn cause NAFLD or NASH by means of inflammation, oxidative stress and immunologic alterations.[13,20,21,22] Not only in adults but in children and adolescents, obesity is one of the most related factor causing hepatic fatty changes. Some studies found that in obese children, 12-25% of them had elevated serum ALT and 42-77% have abnormal liver ultrasound findings.[10,23,24,25,26,27] In severe obese adolescents (mean BMI 59kg/m^2), about 83% of the subjects had biopsy-proven steatosis.[28] But NAFLD and NASH are difficult to diagnose because a liver biopsy is the only method to diagnose the disease. Serum chemistry (*e.g.*, alanine aminotransferase) and radiologic

modalities (*e.g.*, ultrasonography, computed tomography, magnetic resonance imaging and magnetic resonance spectroscopy) cannot distinguish a simple steatosis from NASH[1,6,30,31] and can only be used as the screening test, not for the diagnosis.[10] Moreover these methods have no definite quantitative criteria of assessing the degree of the diseases. NAS (NAFLD activity score), designed for diagnosing NASH semiquantitatively by scoring pathologic characteristics, can be used for measuring the activity of NAFLD. In this study, definite NASH group had higher AST and ALT levels than the others. And statistically NAS had a linear correlation with AST and ALT (Figure 3, 4). Therefore, not presenting fibrosis status, NAS can be a good parameter of the acute status of NAFLD combining with clinical contexts.

In 2005, Schwimmer et al[1] reported histopathological characteristics of pediatric NAFLD. Until then, histologic features were studied mostly in adults and macrovesicular steatosis, perisinusoidal or pericellular fibrosis, foci of lobular inflammation, lipid granulomas, Mallory hyaline and megamitochondria were found in adult type NAFLD.[8] The diagnosis of NASH in adults are made by the combination of macrovesicular steatosis with ballooning changes of hepatocytes and/or perisinusoidal fibrosis in an appropriate clinical context.[29] However the presence of steatosis along with portal inflammation and/or fibrosis in the absence of ballooning degeneration and perisinusoidal fibrosis is a common

feature of the pediatric NASH in Schwimmer's study.[1] According to the previous study, NASH can be classified by the histological characteristics. Type 1 NASH has the adult type histologic feature. Type 2 NASH shows the pediatric type histologic features. Overlap type NASH has the characteristics of type 1 and type 2. In Schwimmer's study of 100 children, subjects with simple steatosis were 16 (16%), type 1 NASH were 17 (17%), type 2 NASH were 51 (51%) and overlap type were 16 (16%). In our study, only 4 cases (6.2%) were pediatric NASH and over a half (59%) were overlap type NASH. This difference may be due to the difference of age. In our study, age of subjects was postpuberty, which might contribute to the difference in the distribution of NASH type. It can be speculated that as growing older, pediatric type NASH may progress to overlap type NASH by adding adult type NASH trait.

Our study shows that in the pediatric type NASH group, though not statistically significant, not only AST or ALT, but NAS is lower than in the overlap type NASH group (Table 5). As NAS is the one of activity marker of NAFLD, pediatric type alone is thought to be a milder form than the overlap type. Hence clinicians should start more aggressive and earlier exercise and dietary therapy when clinically NASH is suspected in any young men.

Several criticisms of this study are that because of difficulty in diagnosing NAFLD, only small numbers of subjects were involved and subjects were all

men. Especially in children and adolescents, type 1 NASH was predominant in girls and type 2 NASH in boys.[1] This sexual difference may be associated the difference of the hormonal levels and this difference must be more prominent after the puberty. So comparison between two sexes after the adolescence is worth for understanding the hormonal impacts on NAFLD. Secondly, as it is a cross-sectional study, there was no clinical data representing the severity of the insulin resistance and oxidative stress. As mentioned above, NAFLD and NASH are rendered as the consequences of the hepatic insulin resistance and the hepatocyte fatty accumulation. In the West of Scotland Coronary Prevention Study,[32,33] increased ALT (≥29 U/L) and CRP (≥3 mg/L) was one of the predicted values for the incident type 2 diabetes mellitus and hepatic fatty accumulation. In the other study of middle-aged Japanese men,[34] gamma-glutamyl transferase was found to be a predictor for developing metabolic syndrome. To understand interactive effects and possible mechanisms between NAFLD and metabolic syndrome, further study of other clinical data and histophathological characteristics will be needed.

V. CONCLUSION

- This study was aimed to histologically classify NAFLD and diagnose NASH in Korean young men, and to compare clinicopathological characteristics by using new guidelines.

- Approximately over 90% of Korean young men with nonalcoholic fatty liver disease (NAFLD) turned out to have NASH by applying NAS (92.2%). Especially in definite NASH group, AST, ALT level was higher than in the other groups. As NAS had a linear correlations with AST or ALT, it can be a good parameter of the acute status of NAFLD and NASH in clinical contexts.

- Histopathological characteristics of NASH patients mostly had overlapping traits of both adult and pediatric types (64.4%) in contrast to pediatric type alone (6.8%). And overlap type had higher AST and ALT levels and NAS than pediatric type though in statistical significance.

- In conclusion, it is possible to speculate that the pattern of NASH in Korean young men is in the middle of transition from pediatric to adult type and proper management of pediatric NASH should be of great importance in preventing disease progression.

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< Abstract In Korean>

우리 나라 젊은 성인 남자에서 비알코올성 지방간질환의 임상 병리학적 특징

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전 누 리

배경: 비알코올성 지방간질환 (NAFLD)은 과도한 알코올의 섭취 없이 나타나는 만성 간질환으로 최근 서구화된 식생활과 그 영향으로 인한 비만인구의 증가로 인해 우리 나라에서도 발병률이 증가하고 있다. 특히 비알코올성 지방간염 (NASH)은 간경변증이나 간암으로도 진행할 수 있어 본 질환의 중요성은 크다. 본 연구는 우리 나라의 젊은 성인 남자에서 NASH Clinical Research Network 의 진단기준에 의해 NASH로 진단한 환자들의 임상 및 병리학적 특징을 조사하였고 이를 Schwimmer등의 분류 기준에 따라 분류하여 본 질환의 임상 경과와 특성을 알아보고자 하였다.

방법: 간생검에서 비알코올성 지방간질환으로 진단받은 30세 이하(16-25세)의 젊은 성인 남자 (n=64)를 대상으로 나이, 체질량지수 (BMI), AST, ALT, 총콜레스테롤, 중성지방, 공복 혈당, 임상적 소견들과 조직병리학적 소견들을 후향적으로 조사하였다. 조직학적 특성은 지방증 정도, 소엽의 염증 정도, 문맥 주위 염증 정도, 간세포의 ballooning degeneration과 간섬유화 정도를 측정하였다. 비알코올성 지방간염 (NASH)는 Kleiner DE 등이 제안한 NAFLD activity score (NAS)를 기준으로 진단하였다. NASH 환자들은 Schwimmer등의 분류법에 따라 adult type, pediatric type과 overlap type의 세 가지로 조직학적 분류하였다.

결과: 51명 (79.9%)이 비만하였고 높은 AST, ALT 수치를 나타내었다 (76.83 ± 44.6, 171.50 ± 114.89). 간생검 상 59명 (92.2%)이 NASH소견을 보였으며 29명 (45.3%)은 borderline NASH였고 30명 (46.9%)은 definite NASH였다. NASH로 진단된 군에서 NAS는 AST 또는 ALT와 양의 선형관계를 나타내었고 definite NASH군은 borderline NASH군에 비해 유의하게 AST 및

ALT가 높았다. NASH군은 Schwimmer등의 분류에 따라 3가지 type으로 분류되었고, 17명 (28.8%)이 adult type, 4명 (6.8%)이 pediatric type 그리고 38명 (64.4%)이 overlap type이었다. NAS (평균 ± 표준편차)는 pediatric type이 3.75 ± 0.05, adult type 4.29 ± 1.16, overlap type 4.87 ± 1.21이었으며 overlap type은 pediatric type에 비해 NAS가 통계학적으로 의미있게 높았다 (p<0.01). 간섬유화의 경우 overlap type 중 36명 (94.7%)이 stage 2의 섬유화를 지녔으며, 4명의 모든 pediatric type (100%)과 adult type 15명 (88.2%)은 stage 1의 섬유화 정도를 보였다. Overlap type은 다른 type에 비해 유의하게 높은 섬유화 정도를 지녔다 (p<0.01). 지방증 정도와 소엽의 염증 정도를 포함한 다른 병리학적 특성들과 임상적 특징들은 세 군에서 유의한 차이를 보이지 않았다.

결론: 우리 나라 젊은 성인 남자에서 비알코올성 지방간염은 대부분 간생검상 borderline NASH나 definite NASH 소견을 보였다. NASH 중 절반 이상은 pediatric type와 adult type NASH의 특성을 모두 지닌 overlap type이였으며, 이 type은

pediatric type에 비해 높은 NAS와 섬유화 정도를 보였다. 이러한 소견들은 우리 나라 젊은 성인 남자에서 나타나는 overlap type NASH의 경우 소아 시기에서 발병하여 지속적으로 진행되고 있음을 제시하고 있다.

핵심되는 말 : 비알코올성 지방간질환, 비알코올성 지방간염, 간생검, 대한민국 젊은 성인 남자