Fatty Liver (Simple Steatosis): The earliest stage where excess fat accumulates in liver cells without causing significant inflammation or damage. Often asymptomatic and reversible with lifestyle changes. Generally benign하며 Non-alcoholic 측면에서 NAFL가 같은 듯인 듯. NAFLD Activity Score에도 보이듯이 5% 이상, 1+ 이면 Steatosis 여부에 체크하기. Fatty Liver 단계부터 이후들을 다 NAFLD라고도 말하는 듯 (사진보면 [3])

Non-Alcoholic Steatohepatitis (NASH) with different degrees of fibrosis: In some individuals, simple fatty liver progresses to NASH, which involves liver inflammation and cellular damage along with fat accumulation. NASH can lead to more serious liver injury and fibrosis. Chronic inflammation in NASH can lead to the formation of scar tissue (fibrosis) in the liver. Fibrosis can vary in severity, ranging from mild to severe, depending on the extent and distribution of scar tissue -> 사진 [3]이 잘 이해가 안 되는게 NASH는 Inflammation, Ballooning, Steatosis 다 1점 이상이어야함 from AASLD Guidance [1] 어쨌든 NAS 5 이상 === NASH 이다. (Hence the term Bx-proven NASH). Can progress to cirrhosis, liver failure, and liver cancer.

Cirrhosis: Advanced fibrosis eventually progresses to cirrhosis, where normal liver tissue is replaced by extensive scar tissue, leading to severe loss of liver function. Cirrhosis is often irreversible and can result in liver failure. (이것이 곧 Fibrosis Stage 4)

Hepatocellular Carcinoma (HCC): In some cases, cirrhosis increases the risk of developing HCC, a primary liver cancer. HCC is a severe, life-threatening condition often associated with a poor prognosis.

**NAFLD Activity Score** (=NAS from NASH-CRN System), Fibrosis stage까지 포함한 것은 SAF Score [2, 3] (SAF Score랑 NAFLD Fibrosis Score (NFS)를 햇갈리지 말자)

이 표는 이 논문 Appendix 에서 얻음[4]

| **Histologic Feature** | **Score** | **Definition** |
| --- | --- | --- |
| Steatosis | 0 | <5% |
| 1 | 5–33% |
| 2 | 34–66% |
| 3 | >66% |
| + | | |
| Hepatocyte ballooning | 0 | None |
| 1 | Few |
| 2 | Many |
| + | | |
| Lobular Inflammation | 0 | None |
| 1 | 1-2 foci per 20 X field (=less than 2) |
| 2 | 2-4 foci per 20 X field |
| 3 | >4 foci per 20 X field |
| **= NAFLD activity score (NAS); range 0**–**8** | | |
| Fibrosis Stage | 0 | No fibrosis  1: Zone 3 Perisinusoidal Fibrosis |
| 1a | Zone 3 mild perisinusoidal fibrosis |
| 1b | Zone 3 moderate perisinusoidal fibrosis |
| 1c | Portal or portal fibrosis only \* (다른데[5]에서는 Portal/periportal fibrsosis라고 함. 교수님이 주신 Paper에서도) |
| 2 | Zone 3 + portal/periportal fibrosis \* (다른데[5]에서는 Perisinusoidal and  portal/periportal fibrosis 라고 함. 교수님이 주신 Paper에서도) |
| 3 | Bridging fibrosis |
| 4 | Cirrhosis |

[6]: NAS 5 이상과 Histological data, Clinical data의 관계에 대한 탐구

The diagnosis of nonalcoholic steatohepatitis (NASH) is defined by the presence and pattern of specific histological abnormalities on liver biopsy (three lesions (장애) that comprise grade: Steatosis, inflammation, ballooning -> NAFLD score 의 탄생 배경 말하는 듯). A separate system of scoring the features of nonalcoholic fatty liver disease (NAFLD) called the NAFLD Activity Score (NAS) was developed as a tool to measure changes in NAFLD during therapeutic trials. However, some studies have used threshold values of the NAS, specifically NAS ≥5, as a surrogate for the histologic diagnosis of NASH. Higher values of the NAS were associated with higher levels of alanine aminotransferase and aspartate aminotransferase, whereas the diagnosis of SH was associated with features of the metabolic syndrome -> NAS에 대한 문제점 (Correlation이 다소 떨어지기는 한다)

Active and potentially reversible injury -> “grade”

Potentially less reversible and characterized by collagen deposition that may evolve toward more permanent remodeling -> “stage” (뭔가 grade는 NAS Score, Stage는 Fibrosis 단계 의미하는 듯)

The study further highlights that not all biopsies with NAS ≥ 5 have findings that meet diagnostic criteria of definite SH, and that some cases of NAS ≤ 4 do, indicating that the a threshold value of a NAS > 5 cannot be used reliably to establish the presence or absence of NASH. -> 우리가 4를 Probable NASH 로 포함했다는 것에 대한 근거로 사용할 수 있을 듯.

추가로

**Liver Related Events (LREs) Definition** [7-9]

(교수님 말씀 필기): LRE: Liver Related Events -> Cirrhosis Complications, Ascites, Variceal bleeding, HEP (Hepatic Encephalopathy), HRS (Hepatorenal Syndrome), HCC (Hepatocellular Carcinoma), LT (Liver Transplant) 등

**BMI, VFI, SFI, SMI Excel File 기준**

BMI: Fibroscan baseline Weight, Height 사용하여 계산. Underweight (<18.5), normal range (<23), overweight (<25), obese (<30), severe obesity [10]

우선 교수님께서 Multi Slice는 표시 안 하셨으니 Single Slice 기준으로 해보자! 참고문헌도 Single Slice [11]는 있는데 Multi Slice는 없음

VFI: AVF / (Height in m) 제곱 (AVF: Abdominal Visceral Fat = VFA mask volume multi slice cm^3) -> single slice 기준의 VFI도 있음 (분모는 동일)

SFI: SF / (Height in m) 제곱 (SFI = SCI: Subcutaneous Fat Index, SF = SCA: Subcutaneous Fat mask volume multi slice cm^3) -> single slice 기준의 SFI도 있음

c.f. TFI: VFI + SFI 도 있음, AVF/SF Volume Ratio (=VSR)

SMI: Muscle / (Height in m) 제곱 (SMI: Skeletal Muscle Index -> mask area single slice cm^2)

추가로 Liver/Spleen HU (Mean HU Whole Volume의 비율), Spleen (Mask Volume – Whole Volume cm^3), Muscle HU (Mean HU Single Slice) 도 노란색으로 표시해주셨는데 여쭤보기

HU (Hounsfield Unit) [12]: a measurement used in CT imaging to quantify the density (voxel values) of tissues. 높을수록 White (Dense)

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