

Healthcare Utilization in Non-Alcoholic Steatohepatitis (NASH) Patients with Elevated NAFLD Activity Score (NAS): Impact of Fibrosis Levels

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Background

Metabolic dysfunction-associated steatotic liver disease (MASLD, formerly NAFLD) is marked by liver fat accumulation and is the most prevalent liver disorder worldwide. It can progress to more severe conditions such as metabolic dysfunction-associated steatohepatitis (MASH, formerly NASH), which involves not only fat but also liver inflammation and damage, significantly increasing the risk of cirrhosis and liver failure.¹ The differentiation between MASLD and MASH is critical, as MASH carries greater risks for morbidity and mortality.¹

Diagnosing MASLD and MASH typically includes assessing cardiometabolic factors, blood tests, imaging studies, and liver biopsies. A liver biopsy remains the reference standard for diagnosing MASH, crucial for evaluating steatosis, inflammation, and fibrosis, though its use is limited due to its invasive nature.² The NAFLD Activity Score (NAS) is commonly used to grade the histological severity of the disease based on steatosis, lobular inflammation, and ballooning degeneration.³

Patients with MASH have a higher risk of advancing to more severe liver diseases compared to those with MASLD, highlighting the need for early diagnosis and management to mitigate progression.¹ The increased risk of liver-related complications in MASH patients also leads to greater healthcare resource utilization, a key focus of our research.¹

Objective

To compare healthcare utilization among two groups: those with MASH, an elevated NAS score and significant liver fibrosis (SLF; Fibrosis ≥ 2) compared to those with MASH, a low NAS, and no liver fibrosis (NLF; defined as Fibrosis = 0)

Methods

A retrospective cohort study was conducted over five years within a large integrated delivery network, focusing on patients with biopsy confirmed MASH with an elevated NAS score (NAS ≥ 3).

This study compared two groups:

- Patients with MASH and NLF (n=121)
- Patients with MASH and SLF (n=111)

Healthcare utilization metrics included:

- Number of unique medications
- Emergency department (ED) visits
- Outpatient (OP) visits
- Radiology studies
- Average length of stay (LOS)
- Number of hospital admissions

All metrics are reported as totals over a five-year period.

To analyze the differences in healthcare utilization between the two groups, we employed a t-test, considering an alpha level of 0.05 as indicative of statistical significance. The analysis period spanned five years, with all patients having a minimum follow-up duration of 181 days (~6 months).

Results

Over the five-year study period, we analyzed two cohorts of patients with MASH, differentiated by their fibrosis levels: those with significant liver fibrosis (SLF) and those with no or mild liver fibrosis (NLF). The demographics are listed in Table 1. The SLF cohort comprised 111 patients, with an average age of 50.8 years (SD: 14.7), including 58 females (52.3%) and 53 males (47.7%). Predominantly, the SLF cohort was White (98 patients, 88.3%), with smaller representations in other racial categories: 5 in Other (4.5%), 3 in Unknown/Chose Not to Disclose (2.7%), 2 in Native American and Pacific Islander (1.8%), and 3 in Asian (2.7%). The NLF cohort included 121 patients, with an average age of 48.1 years (SD: 12.9), consisting of 61 females (50.4%) and 60 males (49.6%). This cohort had a similar racial distribution with 109 White patients (90.1%), 2 in Other (1.7%), 4 in Unknown/Chose Not to Disclose (3.3%), 2 in Native American and Pacific Islander (1.7%), 3 in Asian (2.5%), and 1 Black or African American (0.8%).

Figure 1. Comparison of No Liver Fibrosis (NLF) and Significant Liver Fibrosis (SLF) Groups Across Various Metrics

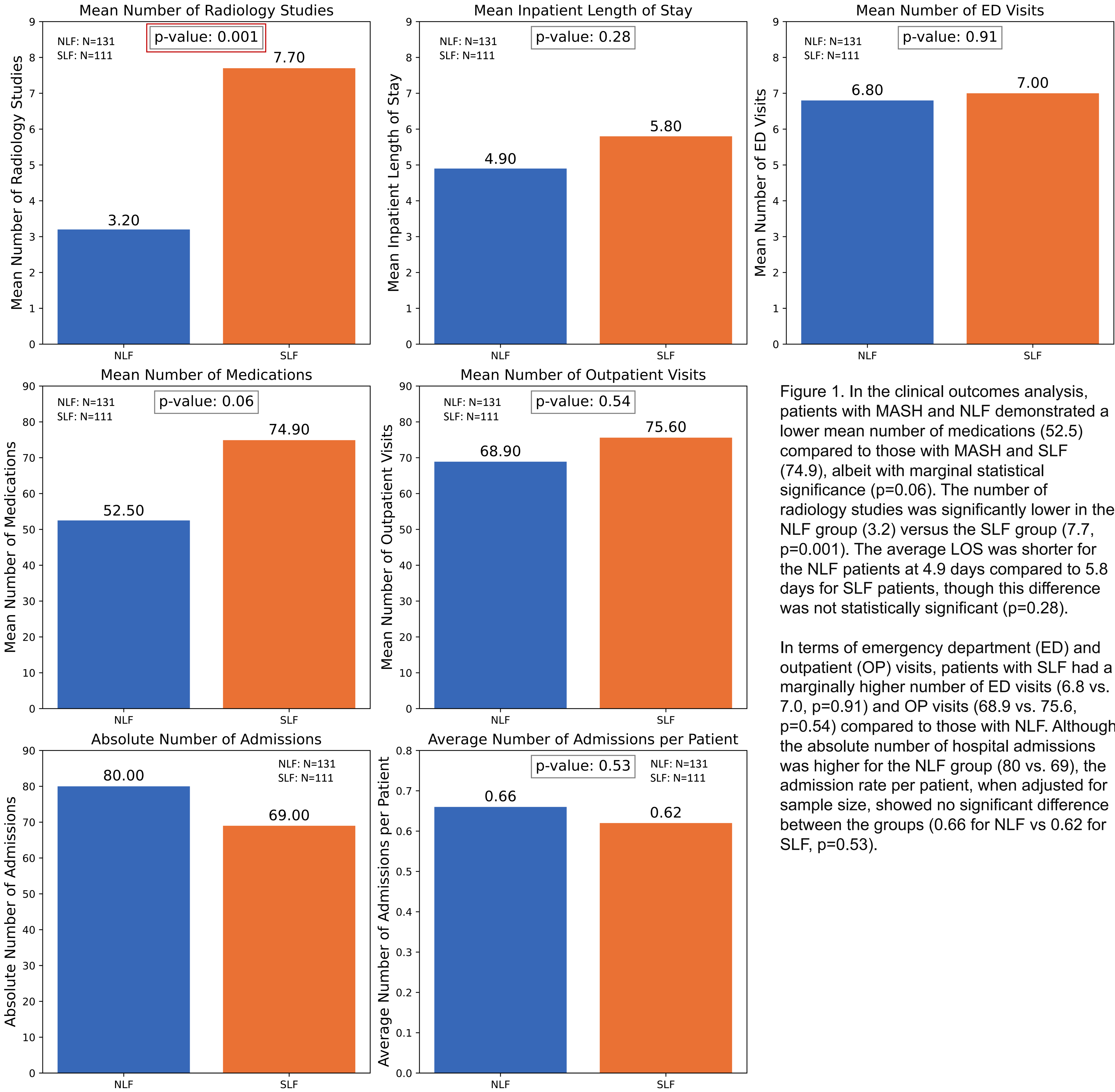


Figure 1. In the clinical outcomes analysis, patients with MASH and NLF demonstrated a lower mean number of medications (52.5) compared to those with MASH and SLF (74.9), albeit with marginal statistical significance (p=0.06). The number of radiology studies was significantly lower in the NLF group (3.2) versus the SLF group (7.7, p=0.001). The average LOS was shorter for the NLF patients at 4.9 days compared to 5.8 days for SLF patients, though this difference was not statistically significant (p=0.28).

In terms of emergency department (ED) and outpatient (OP) visits, patients with SLF had a marginally higher number of ED visits (6.8 vs. 7.0, p=0.91) and OP visits (68.9 vs. 75.6, p=0.54) compared to those with NLF. Although the absolute number of hospital admissions was higher for the NLF group (80 vs. 69), the admission rate per patient, when adjusted for sample size, showed no significant difference between the groups (0.66 for NLF vs 0.62 for SLF, p=0.53).

Table 1. Patient Demographics		
	SLF	NLF
Cohort		
Sample Size	111	121
Median Follow-up (years)	4.2	4.6
Age (years)		
Mean (Standard Deviation)	50.8 (14.7)	48.1 (12.9)
Gender		
Female	58 (52.3%)	61 (50.4%)
Male	53 (47.7%)	60 (49.6%)
Race		
White	98 (88.3%)	109 (90.1%)
Other	5 (4.5%)	2 (1.7%)
Unknown / Chose Not to Disclose	3 (2.7%)	4 (3.3%)
Native American and Pacific Islander	2 (1.8%)	2 (1.7%)
Asian	3 (2.7%)	3 (2.5%)
Black or African American	0 (0.0%)	1 (0.8%)
Comorbidities		
Type 2 DM	19 (17.1%)	23 (19.0%)
HTN	22 (19.8%)	32 (26.4%)
Hypercholesterolemia	14 (12.6%)	18 (14.9%)
MI History	11 (9.9%)	10 (8.3%)
Morbid Obesity (BMI > 30)	26 (23.4%)	35 (28.9%)

Table 1. Demographics for the SLF and NLF patient cohorts. Both groups are similar in composition, with a slight majority of females in each. The average age is around 50, with SLF patients being slightly older on average. The majority in both cohorts are White, with other racial groups represented in small percentages. Differences between the cohorts are minimal, indicating comparable demographic profiles.

The analysis of MASH patients reveals that those with significant liver fibrosis (SLF) require more medications and radiology studies compared to those without (NLF), indicating higher healthcare resource utilization. This highlights the significant impact of liver fibrosis severity on patient care and resource allocation.

Discussion

This retrospective cohort study evaluated healthcare utilization patterns in MASH patients, comparing those with significant liver fibrosis (SLF) to those without liver fibrosis (NLF):

Healthcare Utilization Differences:

- Patients with NLF used fewer medications and underwent fewer radiology studies than those with SLF, suggesting a simpler disease course or lower disease burden.
- A p-value (p=0.06) in medication usage indicates a trend worth exploring in larger or varied settings.
- A significant difference in radiology study usage (p=0.001) highlights increased diagnostic needs in SLF, reflecting potentially more severe disease.

Hospital Stay and Visits:

- Length of stay (LOS) data showed a trend towards shorter hospitalizations for NLF patients, possibly indicating less severe disease.
- Minor differences in ED and OP visits did not show a definitive pattern, suggesting external factors may influence these metrics.

Study Limitations and Weaknesses:

- Limited global generalizability due to the geographical and racial homogeneity of the study sample—predominantly white patients from a single US region.
- Findings may not fully represent global or racially diverse MASH populations.

Implications for Future Research:

- The similarity in adjusted hospital admissions across both groups suggests that factors other than liver fibrosis severity might influence hospitalization rates.
- Future studies should investigate these variables to better understand hospitalization drivers in MASH as well as the role of fibrosis in driving increases in outpatient and radiology utilization.

Conclusions

In summary, this study highlights distinct patterns of healthcare utilization between MASH patients with and without significant liver fibrosis, underscoring the importance of fibrosis level in patient management and healthcare planning. While patients with SLF tend to utilize more radiology studies, possibly reflecting more severe disease, the overall healthcare utilization across other metrics is relatively comparable between the groups. These insights contribute to a deeper understanding of the healthcare needs of MASH patients, guiding more tailored and effective clinical strategies to manage this increasingly prevalent liver condition. Further research is needed to validate these findings and explore their implications in broader and more diverse patient populations.

References

- Chan WK, Chuah KH, Rajaram RB, Lim LL, Ratnasingam J, Vethakkan SR. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): A State-of-the-Art Review. *J Obes Metab Syndr*. 2023;32(3):197-213. doi:10.7570/jomes23052
- Zoncapé M, Liguori A, Tsochatzis EA. Non-invasive testing and risk-stratification in patients with MASLD. *Eur J Intern Med*. 2024; ISSN 0953-6205. doi:10.1016/j.ejim.2024.01.013
- Brunst EM, Kleiner DE, Wilson LA, Belt P, Neuschwander-Tetri BA; NASH Clinical Research Network (CRN). Nonalcoholic fatty liver disease (NAFLD) activity score and the histopathologic diagnosis in NAFLD: distinct clinicopathologic meanings. *Hepatology*. 2011;53(3):810-820

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