Clinical Outcomes of NAFLD/NASH in HF-CKD-T2DM

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## Preamble:

* **Data Source**: Cross-sectional analysis of the National Inpatient Sample (NIS) from 2018 to 2020.
* **Patient Selection**: Included all inpatient admissions with HF-CKD-T2DM.
* **HF-CKD-T2DM + NAFLD/NASH Categories**:
  + HF-CKD-T2DM with NAFLD/NASH
  + HF-CKD-T2DM without NAFLD/NASH
* **ICD Codes**:
  + NASH = K75.81
  + NAFLD = K76.0
* **Primary Outcomes**:
  + In-hospital all-cause mortality
  + Total hospital length of stay (days)
  + Total charge, inflation adjusted to 2020 ($)
* **Software:** All analyses were performed using R Version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria)

## NAFLD/NASH Outcomes:

### Baseline Table:

| **Characteristic** | **Without NAFLD/NASH** N = 4,345,720*1* | **With NAFLD/NASH** N = 40,215*1* | **p-value***2* |
| --- | --- | --- | --- |
| Age, y | 71 (12) | 67 (12) | <0.001 |
| Sex |  |  | 0.14 |
| Female | 1,993,470 (46%) | 18,800 (47%) |  |
| Male | 2,352,085 (54%) | 21,415 (53%) |  |
| Race |  |  | <0.001 |
| White | 2,590,115 (61%) | 25,625 (65%) |  |
| Asian or Pacific Islander | 126,245 (3.0%) | 1,200 (3.0%) |  |
| Black | 948,775 (22%) | 6,650 (17%) |  |
| Hispanic | 458,450 (11%) | 4,800 (12%) |  |
| Native American | 32,145 (0.8%) | 280 (0.7%) |  |
| Other | 104,710 (2.5%) | 1,010 (2.6%) |  |
| Elixhauser comorbidity index | 7.63 (1.84) | 9.06 (1.85) | <0.001 |
| Residential income |  |  | 0.10 |
| $1 - $51,999 | 1,477,640 (34%) | 13,075 (33%) |  |
| $52,000 - $65,999 | 1,166,165 (27%) | 11,085 (28%) |  |
| $66,000 - $87,999 | 963,150 (22%) | 9,075 (23%) |  |
| $88,000 or more | 676,700 (16%) | 6,260 (16%) |  |
| Expected primary payer |  |  | <0.001 |
| Private | 486,400 (11%) | 6,385 (16%) |  |
| Medicaid | 360,490 (8.3%) | 4,355 (11%) |  |
| Medicare | 3,412,780 (79%) | 28,660 (71%) |  |
| Other | 82,230 (1.9%) | 780 (1.9%) |  |
| Hospital region |  |  | <0.001 |
| Midwest | 1,081,650 (25%) | 11,015 (27%) |  |
| Northeast | 745,455 (17%) | 5,380 (13%) |  |
| South | 1,766,575 (41%) | 15,675 (39%) |  |
| West | 752,040 (17%) | 8,145 (20%) |  |
| Hospital bedsize |  |  | <0.001 |
| Large | 2,151,370 (50%) | 20,995 (52%) |  |
| Medium | 1,274,695 (29%) | 11,445 (28%) |  |
| Small | 919,655 (21%) | 7,775 (19%) |  |
| Hospital location and teaching status |  |  | <0.001 |
| Rural | 377,915 (8.7%) | 2,880 (7.2%) |  |
| Urban, non-teaching | 822,370 (19%) | 7,625 (19%) |  |
| Urban, teaching | 3,145,435 (72%) | 29,710 (74%) |  |
| Hypertension | 406,380 (9.4%) | 3,040 (7.6%) | <0.001 |
| Hyperlipidemia | 2,735,430 (63%) | 27,285 (68%) | <0.001 |
| Coronary artery disease | 2,371,545 (55%) | 21,320 (53%) | 0.006 |
| Hyperlipidemia | 440,530 (10%) | 4,195 (10%) | 0.4 |
| Hyperlipidemia | 1,470,715 (34%) | 13,130 (33%) | 0.029 |
| Hyperlipidemia |  |  | <0.001 |
| Class I obesity (BMI 30.0-34.9kg/m²) | 227,685 (18%) | 2,595 (15%) |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 238,025 (19%) | 3,445 (20%) |  |
| Class III obesity (BMI ≥40.0kg/m²) | 616,385 (48%) | 9,785 (57%) |  |
| Normal weight (BMI 20.0-24.9kg/m²) | 51,435 (4.0%) | 265 (1.6%) |  |
| Overweight (BMI 25.0-29.9kg/m²) | 86,355 (6.8%) | 770 (4.5%) |  |
| Underweight (BMI ≤19.9kg/m²) | 56,875 (4.5%) | 230 (1.3%) |  |
| Presence of pacemaker | 609,385 (14%) | 4,570 (11%) | <0.001 |
| previous MI | 714,590 (16%) | 6,520 (16%) | 0.6 |
| Hypothyroidism | 813,210 (19%) | 8,305 (21%) | <0.001 |
| Malnutrition | 318,880 (7.3%) | 2,460 (6.1%) | <0.001 |
| Fluid and electrolyte imbalance | 2,161,345 (50%) | 21,585 (54%) | <0.001 |
| Cancer | 168,705 (3.9%) | 1,385 (3.4%) | 0.044 |
| *1*Mean (SD); n (%) | | | |
| *2*Design-based KruskalWallis test; Pearson's X^2: Rao & Scott adjustment | | | |

### Outcomes Table:

| **Characteristic** | **Without NAFLD/NASH** N = 4,345,720*1* | **With NAFLD/NASH** N = 40,215*1* | **p-value***2* |
| --- | --- | --- | --- |
| Died during hospitalization | 224,955 (5.2%) | 1,610 (4.0%) | <0.001 |
| Length of stay (days) | 6.8 (7.4) | 7.0 (7.7) | <0.001 |
| Inflation-adjusted total charge ($) | 83,318 (128,270) | 87,446 (128,901) | <0.001 |
| *1*n (%); Mean (SD) | | | |
| *2*Pearson's X^2: Rao & Scott adjustment; Design-based KruskalWallis test | | | |

### Multivariable Logistic Regression:

#### All-Cause Mortality:

| **Characteristic** | **OR** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| NASH\_NAFLD\_Categories |  |  |  |
| Without NAFLD/NASH | — | — |  |
| With NAFLD/NASH | 0.69 | 0.56, 0.84 | <0.001 |
| Age, y | 1.02 | 1.02, 1.03 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 1.11 | 1.06, 1.16 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 1.05 | 0.92, 1.20 | 0.5 |
| Black | 0.88 | 0.83, 0.94 | <0.001 |
| Hispanic | 1.11 | 1.03, 1.20 | 0.008 |
| Native American | 1.32 | 1.04, 1.66 | 0.021 |
| Other | 1.08 | 0.94, 1.25 | 0.3 |
| Elixhauser comorbidity index | 1.23 | 1.22, 1.25 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | 0.93 | 0.88, 0.98 | 0.005 |
| $66,000 - $87,999 | 0.92 | 0.87, 0.98 | 0.006 |
| $88,000 or more | 0.94 | 0.88, 1.01 | 0.085 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.82 | 0.74, 0.91 | <0.001 |
| Medicare | 0.89 | 0.83, 0.95 | <0.001 |
| Other | 1.30 | 1.12, 1.51 | <0.001 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.17 | 1.09, 1.26 | <0.001 |
| South | 1.00 | 0.94, 1.06 | 0.9 |
| West | 1.02 | 0.95, 1.10 | 0.6 |
| Hospital bedsize |  |  |  |
| Large | — | — |  |
| Medium | 0.92 | 0.87, 0.97 | 0.002 |
| Small | 0.84 | 0.79, 0.90 | <0.001 |
| Hospital location and teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 1.19 | 1.07, 1.31 | <0.001 |
| Urban, teaching | 1.27 | 1.16, 1.39 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 0.64 | 0.58, 0.70 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.62 | 0.59, 0.64 | <0.001 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 0.89 | 0.85, 0.93 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.81 | 0.76, 0.88 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 1.01 | 0.97, 1.06 | 0.6 |
| Hyperlipidemia |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 1.02 | 0.95, 1.11 | 0.5 |
| Class III obesity (BMI ≥40.0kg/m²) | 1.38 | 1.29, 1.47 | <0.001 |
| Normal weight (BMI 20.0-24.9kg/m²) | 1.19 | 1.07, 1.33 | 0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | 1.11 | 1.02, 1.22 | 0.021 |
| Underweight (BMI ≤19.9kg/m²) | 1.71 | 1.55, 1.89 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | 0.75 | 0.70, 0.80 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | 0.89 | 0.83, 0.95 | <0.001 |
| Hypothyroidism |  |  |  |
| No | — | — |  |
| Yes | 0.71 | 0.67, 0.75 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 1.76 | 1.64, 1.88 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.22 | 2.11, 2.33 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 1.09 | 0.99, 1.19 | 0.070 |
| Abbreviations: CI = Confidence Interval, OR = Odds Ratio | | | |

### Multivariable Linear Regression:

#### Length of Stay:

| **Characteristic** | **Beta** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| NASH\_NAFLD\_Categories |  |  |  |
| Without NAFLD/NASH | — | — |  |
| With NAFLD/NASH | -0.57 | -0.79, -0.35 | <0.001 |
| Age, y | -0.01 | -0.01, 0.00 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 0.15 | 0.08, 0.21 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.32 | 0.05, 0.59 | 0.021 |
| Black | 0.11 | 0.01, 0.20 | 0.024 |
| Hispanic | 0.01 | -0.12, 0.14 | 0.9 |
| Native American | 0.05 | -0.31, 0.41 | 0.8 |
| Other | 0.32 | 0.09, 0.56 | 0.008 |
| Elixhauser comorbidity index | 0.40 | 0.38, 0.43 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -0.07 | -0.16, 0.01 | 0.079 |
| $66,000 - $87,999 | 0.00 | -0.09, 0.09 | >0.9 |
| $88,000 or more | 0.09 | -0.03, 0.21 | 0.12 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.14 | -0.01, 0.30 | 0.074 |
| Medicare | -0.35 | -0.45, -0.25 | <0.001 |
| Other | -0.16 | -0.39, 0.08 | 0.2 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.1 | 0.93, 1.2 | <0.001 |
| South | 0.46 | 0.35, 0.58 | <0.001 |
| West | -0.41 | -0.57, -0.25 | <0.001 |
| Hospital bedsize |  |  |  |
| Large | — | — |  |
| Medium | -0.86 | -0.97, -0.76 | <0.001 |
| Small | -1.4 | -1.5, -1.3 | <0.001 |
| Hospital location and teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 0.97 | 0.82, 1.1 | <0.001 |
| Urban, teaching | 1.8 | 1.7, 2.0 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -0.18 | -0.28, -0.08 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -0.96 | -1.0, -0.89 | <0.001 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | -0.22 | -0.28, -0.16 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -0.11 | -0.21, 0.00 | 0.042 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.11 | 0.04, 0.17 | 0.001 |
| Hyperlipidemia |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 0.08 | 0.00, 0.16 | 0.039 |
| Class III obesity (BMI ≥40.0kg/m²) | 0.95 | 0.88, 1.0 | <0.001 |
| Normal weight (BMI 20.0-24.9kg/m²) | -1.1 | -1.2, -0.85 | <0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | -0.19 | -0.32, -0.06 | 0.005 |
| Underweight (BMI ≤19.9kg/m²) | -0.33 | -0.58, -0.08 | 0.010 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -0.90 | -0.99, -0.82 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -0.54 | -0.61, -0.47 | <0.001 |
| Hypothyroidism |  |  |  |
| No | — | — |  |
| Yes | -0.55 | -0.63, -0.48 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 3.5 | 3.3, 3.7 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.0 | 1.9, 2.0 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 0.06 | -0.11, 0.24 | 0.5 |
| Abbreviation: CI = Confidence Interval | | | |

#### Inflation Adjusted Total Charge:

| **Characteristic** | **Beta** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| NASH\_NAFLD\_Categories |  |  |  |
| Without NAFLD/NASH | — | — |  |
| With NAFLD/NASH | -11,388 | -14,744, -8,033 | <0.001 |
| Age, y | -489 | -549, -429 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 6,475 | 5,453, 7,497 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 10,235 | 2,791, 17,679 | 0.007 |
| Black | -2,748 | -4,477, -1,018 | 0.002 |
| Hispanic | 16,198 | 13,155, 19,242 | <0.001 |
| Native American | -8,042 | -14,109, -1,976 | 0.009 |
| Other | 25,478 | 19,100, 31,856 | <0.001 |
| Elixhauser comorbidity index | 6,192 | 5,506, 6,879 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -116 | -1,701, 1,469 | 0.9 |
| $66,000 - $87,999 | -94 | -2,032, 1,843 | >0.9 |
| $88,000 or more | 4,252 | 1,424, 7,080 | 0.003 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | -8,136 | -10,896, -5,377 | <0.001 |
| Medicare | -6,260 | -8,323, -4,197 | <0.001 |
| Other | -1,590 | -6,587, 3,406 | 0.5 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 23,191 | 19,174, 27,208 | <0.001 |
| South | 17,545 | 15,008, 20,082 | <0.001 |
| West | 41,691 | 36,383, 47,000 | <0.001 |
| Hospital bedsize |  |  |  |
| Large | — | — |  |
| Medium | -14,091 | -17,110, -11,071 | <0.001 |
| Small | -24,036 | -27,039, -21,034 | <0.001 |
| Hospital location and teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 27,883 | 25,171, 30,596 | <0.001 |
| Urban, teaching | 40,421 | 38,022, 42,821 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 334 | -1,536, 2,205 | 0.7 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -9,891 | -11,128, -8,653 | <0.001 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 6,069 | 4,991, 7,146 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 15,271 | 13,188, 17,354 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 2,534 | 1,341, 3,727 | <0.001 |
| Hyperlipidemia |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | -252 | -1,645, 1,140 | 0.7 |
| Class III obesity (BMI ≥40.0kg/m²) | 5,947 | 4,540, 7,354 | <0.001 |
| Normal weight (BMI 20.0-24.9kg/m²) | -22,312 | -25,691, -18,934 | <0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | -5,989 | -8,220, -3,758 | <0.001 |
| Underweight (BMI ≤19.9kg/m²) | -7,630 | -12,188, -3,073 | 0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -16,041 | -17,577, -14,505 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -9,660 | -10,913, -8,408 | <0.001 |
| Hypothyroidism |  |  |  |
| No | — | — |  |
| Yes | -10,212 | -11,555, -8,869 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 43,959 | 40,228, 47,689 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 23,074 | 21,831, 24,316 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | -1,334 | -3,995, 1,327 | 0.3 |
| Abbreviation: CI = Confidence Interval | | | |