Outcomes in HFrEF vs HFpEF in Patients with Iron Deficiency Anemia

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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 Iron deficiency anemia.
* **HF Categories**:
  + Without heart failure
  + Heart failure with reduced ejection fraction
  + Heart failure with preserved ejection fraction
* **ICD Codes**:
  + HFrEF = I50.2 and I50.4
  + HFpEF = I50.3
* **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)

## Baseline Table:

| **Characteristic** | **Without heart failure** N = 2,743,705*1* | **Heart failure with preserved ejection fraction** N = 520,885*1* | **Heart failure with reduced ejection fraction** N = 425,405*1* | **p-value***2* |
| --- | --- | --- | --- | --- |
| Age, y | 58 (20) | 73 (13) | 70 (14) | <0.001 |
| Sex |  |  |  | <0.001 |
| Female | 1,777,560 (65%) | 330,210 (63%) | 186,740 (44%) |  |
| Male | 965,955 (35%) | 190,655 (37%) | 238,655 (56%) |  |
| Race |  |  |  | <0.001 |
| White | 1,556,620 (58%) | 354,990 (70%) | 258,350 (62%) |  |
| Asian or Pacific Islander | 82,230 (3.1%) | 10,010 (2.0%) | 8,290 (2.0%) |  |
| Black | 600,870 (22%) | 94,210 (18%) | 100,970 (24%) |  |
| Hispanic | 332,010 (12%) | 37,305 (7.3%) | 35,570 (8.5%) |  |
| Native American | 23,455 (0.9%) | 3,025 (0.6%) | 2,855 (0.7%) |  |
| Other | 83,625 (3.1%) | 10,755 (2.1%) | 10,390 (2.5%) |  |
| Elixhauser comorbidity index | 4.86 (2.21) | 7.94 (1.98) | 7.91 (2.03) | <0.001 |
| Residential income |  |  |  | <0.001 |
| $1 - $51,999 | 888,875 (33%) | 160,825 (31%) | 146,185 (35%) |  |
| $52,000 - $65,999 | 707,520 (26%) | 137,745 (27%) | 111,610 (27%) |  |
| $66,000 - $87,999 | 613,780 (23%) | 121,180 (24%) | 92,425 (22%) |  |
| $88,000 or more | 481,475 (18%) | 94,155 (18%) | 67,050 (16%) |  |
| Expected primary payer |  |  |  | <0.001 |
| Private | 782,475 (29%) | 58,710 (11%) | 61,025 (14%) |  |
| Medicaid | 586,665 (21%) | 42,755 (8.2%) | 54,060 (13%) |  |
| Medicare | 1,305,760 (48%) | 411,755 (79%) | 301,790 (71%) |  |
| Other | 65,435 (2.4%) | 7,275 (1.4%) | 8,100 (1.9%) |  |
| Hospital region |  |  |  | <0.001 |
| Midwest | 621,480 (23%) | 148,350 (28%) | 113,875 (27%) |  |
| Northeast | 496,995 (18%) | 102,585 (20%) | 72,805 (17%) |  |
| South | 1,093,735 (40%) | 190,475 (37%) | 164,665 (39%) |  |
| West | 531,495 (19%) | 79,475 (15%) | 74,060 (17%) |  |
| Hypertension | 1,547,895 (56%) | 42,155 (8.1%) | 29,455 (6.9%) | <0.001 |
| Hyperlipidemia | 891,295 (32%) | 299,290 (57%) | 240,825 (57%) | <0.001 |
| Peripheral vascular disease | 177,945 (6.5%) | 67,155 (13%) | 102,640 (24%) | <0.001 |
| Chronic obstructive pulmonary disease | 600,035 (22%) | 234,725 (45%) | 159,285 (37%) | <0.001 |
| Coronary artery disease | 394,015 (14%) | 220,005 (42%) | 240,850 (57%) | <0.001 |
| Dementia | 194,255 (7.1%) | 53,610 (10%) | 35,555 (8.4%) | <0.001 |
| Fluid and electrolyte imbalance | 1,106,395 (40%) | 253,820 (49%) | 209,790 (49%) | <0.001 |
| Valvular heart disease | 80,765 (2.9%) | 70,515 (14%) | 61,135 (14%) | <0.001 |
| Atrial fibrillation | 276,410 (10%) | 198,540 (38%) | 160,570 (38%) | <0.001 |
| Obesity | 497,640 (18%) | 156,735 (30%) | 92,240 (22%) | <0.001 |
| Presence of pacemaker | 54,265 (2.0%) | 44,780 (8.6%) | 82,540 (19%) | <0.001 |
| previous MI | 109,195 (4.0%) | 56,800 (11%) | 83,995 (20%) | <0.001 |
| Pior cardiac surgery | 99,390 (3.6%) | 70,565 (14%) | 77,805 (18%) | <0.001 |
| Malnutrition | 323,035 (12%) | 49,315 (9.5%) | 47,560 (11%) | <0.001 |
| Cancer | 287,150 (10%) | 31,260 (6.0%) | 25,995 (6.1%) | <0.001 |
| *1*Mean (SD); n (%) | | | | |
| *2*Design-based KruskalWallis test; Pearson's X^2: Rao & Scott adjustment | | | | |

## Outcomes Table:

| **Characteristic** | **Without heart failure** N = 2,743,705*1* | **Heart failure with preserved ejection fraction** N = 520,885*1* | **Heart failure with reduced ejection fraction** N = 425,405*1* | **p-value***2* |
| --- | --- | --- | --- | --- |
| Died during hospitalization | 46,190 (1.7%) | 15,395 (3.0%) | 16,390 (3.9%) | <0.001 |
| Length of stay (days) | 5.8 (7.6) | 6.9 (7.1) | 7.5 (8.6) | <0.001 |
| Inflation-adjusted total charge ($) | 66,606 (100,022) | 74,877 (98,061) | 92,846 (156,520) | <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** |
| --- | --- | --- | --- |
| Heart failure categories |  |  |  |
| Without heart failure | — | — |  |
| Heart failure with preserved ejection fraction | 0.54 | 0.51, 0.58 | <0.001 |
| Heart failure with reduced ejection fraction | 0.76 | 0.71, 0.81 | <0.001 |
| Age, y | 1.03 | 1.03, 1.04 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 1.21 | 1.17, 1.26 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 1.27 | 1.16, 1.40 | <0.001 |
| Black | 1.03 | 0.98, 1.08 | 0.3 |
| Hispanic | 1.10 | 1.04, 1.17 | 0.002 |
| Native American | 0.77 | 0.60, 0.99 | 0.039 |
| Other | 1.19 | 1.08, 1.32 | <0.001 |
| Elixhauser comorbidity index | 1.33 | 1.32, 1.35 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | 0.92 | 0.88, 0.96 | <0.001 |
| $66,000 - $87,999 | 0.86 | 0.82, 0.90 | <0.001 |
| $88,000 or more | 0.83 | 0.79, 0.88 | <0.001 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.88 | 0.83, 0.94 | <0.001 |
| Medicare | 0.75 | 0.71, 0.79 | <0.001 |
| Other | 1.45 | 1.29, 1.62 | <0.001 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.18 | 1.11, 1.26 | <0.001 |
| South | 0.93 | 0.89, 0.98 | 0.010 |
| West | 0.98 | 0.92, 1.04 | 0.5 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 0.56 | 0.53, 0.58 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.70 | 0.67, 0.73 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 0.90 | 0.85, 0.95 | <0.001 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 0.95 | 0.91, 1.0 | 0.029 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | 0.81 | 0.78, 0.84 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 0.80 | 0.75, 0.86 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 1.12 | 1.07, 1.18 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 1.41 | 1.34, 1.48 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.27 | 2.17, 2.37 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 1.11 | 1.06, 1.16 | <0.001 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | 0.68 | 0.64, 0.71 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | 0.66 | 0.61, 0.71 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | 0.97 | 0.91, 1.04 | 0.4 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 1.40 | 1.34, 1.46 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | 0.80 | 0.75, 0.86 | <0.001 |
| Abbreviations: CI = Confidence Interval, OR = Odds Ratio | | | |

### Multivariable Linear Regression:

#### Length of Stay:

| **Characteristic** | **Beta** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| Heart failure categories |  |  |  |
| Without heart failure | — | — |  |
| Heart failure with preserved ejection fraction | -0.12 | -0.20, -0.04 | 0.005 |
| Heart failure with reduced ejection fraction | 0.41 | 0.31, 0.50 | <0.001 |
| Age, y | -0.01 | -0.01, -0.01 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 0.72 | 0.68, 0.76 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.20 | 0.05, 0.35 | 0.008 |
| Black | 0.26 | 0.19, 0.32 | <0.001 |
| Hispanic | -0.03 | -0.12, 0.05 | 0.5 |
| Native American | -0.03 | -0.29, 0.24 | 0.8 |
| Other | 0.44 | 0.29, 0.59 | <0.001 |
| Elixhauser comorbidity index | 0.54 | 0.53, 0.56 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -0.08 | -0.14, -0.03 | 0.003 |
| $66,000 - $87,999 | -0.06 | -0.12, 0.00 | 0.066 |
| $88,000 or more | -0.01 | -0.09, 0.07 | 0.8 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.52 | 0.45, 0.59 | <0.001 |
| Medicare | 0.07 | 0.01, 0.13 | 0.026 |
| Other | 0.42 | 0.28, 0.57 | <0.001 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 0.79 | 0.67, 0.90 | <0.001 |
| South | 0.27 | 0.18, 0.36 | <0.001 |
| West | -0.08 | -0.19, 0.04 | 0.2 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -0.26 | -0.31, -0.21 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -0.35 | -0.39, -0.30 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | -0.01 | -0.08, 0.06 | 0.8 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | -0.08 | -0.13, -0.02 | 0.003 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -0.57 | -0.62, -0.53 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | -0.30 | -0.38, -0.22 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 0.73 | 0.65, 0.82 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 0.05 | -0.02, 0.12 | 0.2 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 1.4 | 1.3, 1.4 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 0.07 | 0.01, 0.12 | 0.014 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | -0.08 | -0.14, -0.03 | 0.002 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -1.0 | -1.1, -0.92 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -0.48 | -0.55, -0.41 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 3.1 | 3.0, 3.2 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -0.70 | -0.76, -0.63 | <0.001 |
| Abbreviation: CI = Confidence Interval | | | |

#### Inflation Adjusted Total Charge:

| **Characteristic** | **Beta** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| Heart failure categories |  |  |  |
| Without heart failure | — | — |  |
| Heart failure with preserved ejection fraction | -5,792 | -7,343, -4,241 | <0.001 |
| Heart failure with reduced ejection fraction | 9,682 | 7,369, 11,995 | <0.001 |
| Age, y | -172 | -202, -142 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 8,898 | 8,280, 9,517 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 10,685 | 7,906, 13,464 | <0.001 |
| Black | 2,992 | 1,800, 4,184 | <0.001 |
| Hispanic | 11,624 | 9,650, 13,599 | <0.001 |
| Native American | -15,147 | -18,155, -12,138 | <0.001 |
| Other | 16,330 | 13,095, 19,565 | <0.001 |
| Elixhauser comorbidity index | 6,430 | 5,999, 6,861 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -50 | -1,125, 1,024 | >0.9 |
| $66,000 - $87,999 | 1,544 | 246, 2,842 | 0.020 |
| $88,000 or more | 6,400 | 4,528, 8,271 | <0.001 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | -3,968 | -5,022, -2,915 | <0.001 |
| Medicare | -4,140 | -5,075, -3,204 | <0.001 |
| Other | 1,724 | -818, 4,265 | 0.2 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 17,787 | 14,764, 20,810 | <0.001 |
| South | 11,199 | 9,274, 13,124 | <0.001 |
| West | 33,846 | 30,205, 37,487 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -631 | -1,484, 222 | 0.15 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -831 | -1,541, -121 | 0.022 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 4,017 | 2,784, 5,250 | <0.001 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 7,915 | 7,010, 8,821 | <0.001 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -7,325 | -8,157, -6,493 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 10,145 | 8,586, 11,704 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | -6,007 | -7,000, -5,014 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 4,476 | 3,371, 5,580 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 16,042 | 15,191, 16,893 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 2,985 | 2,113, 3,857 | <0.001 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | 1,855 | 980, 2,729 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -16,482 | -17,871, -15,092 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -10,317 | -11,423, -9,211 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 31,373 | 29,388, 33,358 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -14,321 | -15,406, -13,236 | <0.001 |
| Abbreviation: CI = Confidence Interval | | | |