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**:
  + 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** | **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 | 73 (13) | 70 (14) | <0.001 |
| Sex |  |  | <0.001 |
| Female | 330,210 (63%) | 186,740 (44%) |  |
| Male | 190,655 (37%) | 238,655 (56%) |  |
| Race |  |  | <0.001 |
| White | 354,990 (70%) | 258,350 (62%) |  |
| Asian or Pacific Islander | 10,010 (2.0%) | 8,290 (2.0%) |  |
| Black | 94,210 (18%) | 100,970 (24%) |  |
| Hispanic | 37,305 (7.3%) | 35,570 (8.5%) |  |
| Native American | 3,025 (0.6%) | 2,855 (0.7%) |  |
| Other | 10,755 (2.1%) | 10,390 (2.5%) |  |
| Elixhauser comorbidity index | 7.94 (1.98) | 7.91 (2.03) | 0.001 |
| Residential income |  |  | <0.001 |
| $1 - $51,999 | 160,825 (31%) | 146,185 (35%) |  |
| $52,000 - $65,999 | 137,745 (27%) | 111,610 (27%) |  |
| $66,000 - $87,999 | 121,180 (24%) | 92,425 (22%) |  |
| $88,000 or more | 94,155 (18%) | 67,050 (16%) |  |
| Expected primary payer |  |  | <0.001 |
| Private | 58,710 (11%) | 61,025 (14%) |  |
| Medicaid | 42,755 (8.2%) | 54,060 (13%) |  |
| Medicare | 411,755 (79%) | 301,790 (71%) |  |
| Other | 7,275 (1.4%) | 8,100 (1.9%) |  |
| Hospital region |  |  | <0.001 |
| Midwest | 148,350 (28%) | 113,875 (27%) |  |
| Northeast | 102,585 (20%) | 72,805 (17%) |  |
| South | 190,475 (37%) | 164,665 (39%) |  |
| West | 79,475 (15%) | 74,060 (17%) |  |
| Hypertension | 42,155 (8.1%) | 29,455 (6.9%) | <0.001 |
| Hyperlipidemia | 299,290 (57%) | 240,825 (57%) | <0.001 |
| Peripheral vascular disease | 67,155 (13%) | 102,640 (24%) | <0.001 |
| Chronic obstructive pulmonary disease | 234,725 (45%) | 159,285 (37%) | <0.001 |
| Coronary artery disease | 220,005 (42%) | 240,850 (57%) | <0.001 |
| Dementia | 53,610 (10%) | 35,555 (8.4%) | <0.001 |
| Fluid and electrolyte imbalance | 253,820 (49%) | 209,790 (49%) | 0.013 |
| Valvular heart disease | 70,515 (14%) | 61,135 (14%) | <0.001 |
| Atrial fibrillation | 198,540 (38%) | 160,570 (38%) | 0.11 |
| Obesity | 156,735 (30%) | 92,240 (22%) | <0.001 |
| Presence of pacemaker | 44,780 (8.6%) | 82,540 (19%) | <0.001 |
| previous MI | 56,800 (11%) | 83,995 (20%) | <0.001 |
| Pior cardiac surgery | 70,565 (14%) | 77,805 (18%) | <0.001 |
| Malnutrition | 49,315 (9.5%) | 47,560 (11%) | <0.001 |
| Cancer | 31,260 (6.0%) | 25,995 (6.1%) | 0.3 |
| *1*Mean (SD); n (%) | | | |
| *2*Design-based KruskalWallis test; Pearson's X^2: Rao & Scott adjustment | | | |

## Outcomes Table:

| **Characteristic** | **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 | 15,395 (3.0%) | 16,390 (3.9%) | <0.001 |
| Length of stay (days) | 6.9 (7.1) | 7.5 (8.6) | <0.001 |
| Inflation-adjusted total charge ($) | 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 |  |  |  |
| Heart failure with preserved ejection fraction | — | — |  |
| Heart failure with reduced ejection fraction | 1.42 | 1.35, 1.50 | <0.001 |
| Age, y | 1.03 | 1.02, 1.03 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 1.12 | 1.06, 1.18 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 1.01 | 0.85, 1.20 | >0.9 |
| Black | 0.89 | 0.83, 0.97 | 0.004 |
| Hispanic | 0.98 | 0.89, 1.08 | 0.7 |
| Native American | 0.81 | 0.55, 1.20 | 0.3 |
| Other | 0.95 | 0.80, 1.14 | 0.6 |
| Elixhauser comorbidity index | 1.23 | 1.21, 1.25 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | 0.92 | 0.86, 0.99 | 0.022 |
| $66,000 - $87,999 | 0.89 | 0.82, 0.96 | 0.002 |
| $88,000 or more | 0.89 | 0.82, 0.97 | 0.006 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.78 | 0.69, 0.89 | <0.001 |
| Medicare | 0.80 | 0.73, 0.88 | <0.001 |
| Other | 1.29 | 1.06, 1.57 | 0.009 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.12 | 1.02, 1.22 | 0.013 |
| South | 0.97 | 0.91, 1.05 | 0.5 |
| West | 0.96 | 0.88, 1.05 | 0.4 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 0.68 | 0.60, 0.77 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.71 | 0.67, 0.75 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 0.90 | 0.84, 0.97 | 0.006 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 0.91 | 0.86, 0.97 | 0.002 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | 0.83 | 0.78, 0.88 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 0.88 | 0.81, 0.95 | 0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 1.07 | 0.99, 1.16 | 0.090 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 1.29 | 1.18, 1.41 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.13 | 2.00, 2.27 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 1.02 | 0.96, 1.08 | 0.6 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | 0.67 | 0.63, 0.72 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | 0.70 | 0.64, 0.76 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | 0.95 | 0.88, 1.03 | 0.2 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 1.59 | 1.49, 1.70 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | 0.82 | 0.75, 0.89 | <0.001 |
| Abbreviations: CI = Confidence Interval, OR = Odds Ratio | | | |

### Multivariable Linear Regression:

#### Length of Stay:

| **Characteristic** | **Beta** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| Heart failure categories |  |  |  |
| Heart failure with preserved ejection fraction | — | — |  |
| Heart failure with reduced ejection fraction | 0.49 | 0.41, 0.56 | <0.001 |
| Age, y | -0.03 | -0.04, -0.03 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 0.35 | 0.28, 0.42 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.42 | 0.03, 0.81 | 0.036 |
| Black | 0.17 | 0.06, 0.28 | 0.003 |
| Hispanic | 0.18 | -0.03, 0.39 | 0.089 |
| Native American | -0.20 | -0.65, 0.25 | 0.4 |
| Other | 0.81 | 0.49, 1.1 | <0.001 |
| Elixhauser comorbidity index | 0.49 | 0.46, 0.52 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -0.07 | -0.18, 0.03 | 0.2 |
| $66,000 - $87,999 | 0.06 | -0.05, 0.17 | 0.3 |
| $88,000 or more | 0.25 | 0.11, 0.39 | <0.001 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.27 | 0.05, 0.48 | 0.016 |
| Medicare | -0.14 | -0.28, -0.01 | 0.040 |
| Other | -0.03 | -0.32, 0.27 | 0.9 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 0.93 | 0.75, 1.1 | <0.001 |
| South | 0.36 | 0.22, 0.50 | <0.001 |
| West | -0.35 | -0.53, -0.16 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -0.22 | -0.36, -0.08 | 0.002 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -0.60 | -0.67, -0.52 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | -0.03 | -0.14, 0.08 | 0.6 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 0.06 | -0.02, 0.14 | 0.12 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -0.59 | -0.67, -0.51 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | -0.18 | -0.29, -0.08 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 0.34 | 0.22, 0.46 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 0.27 | 0.12, 0.42 | <0.001 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 1.9 | 1.8, 2.0 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 0.09 | 0.01, 0.16 | 0.023 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | -0.03 | -0.12, 0.07 | 0.6 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -0.89 | -0.99, -0.79 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -0.59 | -0.68, -0.49 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 3.2 | 3.0, 3.4 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -0.72 | -0.80, -0.64 | <0.001 |
| Abbreviation: CI = Confidence Interval | | | |

#### Inflation Adjusted Total Charge:

| **Characteristic** | **Beta** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| Heart failure categories |  |  |  |
| Heart failure with preserved ejection fraction | — | — |  |
| Heart failure with reduced ejection fraction | 13,146 | 11,596, 14,695 | <0.001 |
| Age, y | -844 | -928, -759 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 6,150 | 4,854, 7,446 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 19,203 | 12,594, 25,813 | <0.001 |
| Black | 624 | -1,435, 2,682 | 0.6 |
| Hispanic | 19,693 | 15,195, 24,191 | <0.001 |
| Native American | -15,218 | -22,737, -7,698 | <0.001 |
| Other | 32,202 | 24,158, 40,246 | <0.001 |
| Elixhauser comorbidity index | 6,385 | 5,753, 7,018 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -172 | -2,062, 1,719 | 0.9 |
| $66,000 - $87,999 | 2,749 | 694, 4,803 | 0.009 |
| $88,000 or more | 10,892 | 7,860, 13,923 | <0.001 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | -8,080 | -11,850, -4,309 | <0.001 |
| Medicare | -3,319 | -5,880, -758 | 0.011 |
| Other | -1,758 | -7,235, 3,718 | 0.5 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 21,917 | 17,497, 26,336 | <0.001 |
| South | 11,956 | 9,148, 14,764 | <0.001 |
| West | 40,510 | 34,081, 46,939 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -129 | -2,882, 2,625 | >0.9 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -3,360 | -4,729, -1,990 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 940 | -929, 2,810 | 0.3 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 10,477 | 9,051, 11,903 | <0.001 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -8,984 | -10,508, -7,460 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 13,275 | 11,227, 15,323 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | -5,591 | -7,259, -3,923 | <0.001 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 2,870 | 328, 5,413 | 0.027 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 21,886 | 20,400, 23,372 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 2,191 | 948, 3,435 | <0.001 |
| Obesity |  |  |  |
| No | — | — |  |
| Yes | -2,970 | -4,697, -1,242 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -14,512 | -16,351, -12,674 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -12,237 | -13,912, -10,562 | <0.001 |
| Malnutrition |  |  |  |
| No | — | — |  |
| Yes | 40,491 | 36,222, 44,760 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -15,682 | -17,105, -14,260 | <0.001 |
| Abbreviation: CI = Confidence Interval | | | |