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%) |  |
| Hospital bed size |  |  | <0.001 |
| Large | 254,220 (49%) | 225,295 (53%) |  |
| Medium | 150,660 (29%) | 115,580 (27%) |  |
| Small | 116,005 (22%) | 84,530 (20%) |  |
| Hospital location/teaching status |  |  | <0.001 |
| Rural | 47,500 (9.1%) | 33,265 (7.8%) |  |
| Urban, non-teaching | 92,605 (18%) | 69,685 (16%) |  |
| Urban, teaching | 380,780 (73%) | 322,455 (76%) |  |
| 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 | 479,320 (92%) | 382,430 (90%) | <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 | 255,665 (49%) | 210,930 (50%) | 0.034 |
| Valvular heart disease | 140,640 (27%) | 124,005 (29%) | <0.001 |
| Atrial fibrillation | 198,540 (38%) | 160,570 (38%) | 0.11 |
| BMI |  |  | <0.001 |
| Class I obesity (BMI 30.0-34.9kg/m²) | 25,660 (15%) | 19,450 (18%) |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 26,335 (16%) | 16,930 (16%) |  |
| Class III obesity (BMI ≥40.0kg/m²) | 78,885 (47%) | 36,505 (34%) |  |
| Normal weight (BMI 20.0-24.9kg/m²) | 10,070 (6.0%) | 9,900 (9.1%) |  |
| Overweight (BMI 25.0-29.9kg/m²) | 11,610 (6.9%) | 9,965 (9.2%) |  |
| Underweight (BMI ≤19.9kg/m²) | 14,625 (8.7%) | 15,550 (14%) |  |
| 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 |
| Depression | 94,465 (18%) | 64,350 (15%) | <0.001 |
| Cancer | 31,470 (6.0%) | 25,145 (5.9%) | 0.2 |
| *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 | 1.48 | 1.34, 1.65 | <0.001 |
| Age, y | 1.03 | 1.02, 1.03 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 1.23 | 1.10, 1.37 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.97 | 0.65, 1.45 | 0.9 |
| Black | 0.92 | 0.80, 1.06 | 0.3 |
| Hispanic | 0.89 | 0.72, 1.11 | 0.3 |
| Native American | 0.80 | 0.35, 1.81 | 0.6 |
| Other | 1.15 | 0.83, 1.60 | 0.4 |
| Elixhauser comorbidity index | 1.31 | 1.26, 1.35 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | 0.91 | 0.80, 1.04 | 0.2 |
| $66,000 - $87,999 | 0.89 | 0.78, 1.03 | 0.12 |
| $88,000 or more | 0.92 | 0.78, 1.08 | 0.3 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.84 | 0.67, 1.05 | 0.13 |
| Medicare | 0.86 | 0.73, 1.01 | 0.074 |
| Other | 1.40 | 0.98, 1.99 | 0.068 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.09 | 0.92, 1.28 | 0.3 |
| South | 0.98 | 0.86, 1.11 | 0.7 |
| West | 0.88 | 0.74, 1.04 | 0.14 |
| Hospital bed size |  |  |  |
| Large | — | — |  |
| Medium | 0.96 | 0.85, 1.09 | 0.6 |
| Small | 0.88 | 0.77, 1.01 | 0.075 |
| Hospital location/teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 0.90 | 0.73, 1.11 | 0.3 |
| Urban, teaching | 0.91 | 0.75, 1.09 | 0.3 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 0.52 | 0.44, 0.61 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.73 | 0.66, 0.81 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 0.79 | 0.68, 0.91 | 0.002 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 0.84 | 0.75, 0.95 | 0.005 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | 0.71 | 0.64, 0.80 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 0.77 | 0.68, 0.88 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 1.10 | 0.93, 1.30 | 0.3 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 1.09 | 0.91, 1.32 | 0.4 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.08 | 1.83, 2.36 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 0.95 | 0.85, 1.06 | 0.4 |
| BMI |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 0.86 | 0.69, 1.06 | 0.14 |
| Class III obesity (BMI ≥40.0kg/m²) | 1.31 | 1.11, 1.54 | 0.002 |
| Normal weight (BMI 20.0-24.9kg/m²) | 1.63 | 1.32, 2.02 | <0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | 1.28 | 1.03, 1.59 | 0.026 |
| Underweight (BMI ≤19.9kg/m²) | 2.13 | 1.78, 2.56 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | 0.80 | 0.68, 0.96 | 0.014 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | 1.04 | 0.88, 1.23 | 0.7 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | 0.69 | 0.60, 0.79 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | 0.93 | 0.78, 1.10 | 0.4 |
| 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 | 0.61 | 0.46, 0.75 | <0.001 |
| Age, y | -0.01 | -0.02, -0.01 | 0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 0.41 | 0.26, 0.56 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.49 | -0.33, 1.3 | 0.2 |
| Black | -0.04 | -0.23, 0.16 | 0.7 |
| Hispanic | -0.10 | -0.38, 0.18 | 0.5 |
| Native American | -0.03 | -0.78, 0.72 | >0.9 |
| Other | 0.31 | -0.32, 0.93 | 0.3 |
| Elixhauser comorbidity index | 0.60 | 0.55, 0.66 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -0.18 | -0.36, 0.00 | 0.045 |
| $66,000 - $87,999 | -0.07 | -0.28, 0.13 | 0.5 |
| $88,000 or more | 0.17 | -0.09, 0.42 | 0.2 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.09 | -0.22, 0.40 | 0.6 |
| Medicare | -0.22 | -0.45, 0.01 | 0.061 |
| Other | 0.13 | -0.45, 0.71 | 0.7 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.1 | 0.78, 1.4 | <0.001 |
| South | 0.49 | 0.28, 0.70 | <0.001 |
| West | -0.43 | -0.71, -0.15 | 0.003 |
| Hospital bed size |  |  |  |
| Large | — | — |  |
| Medium | -0.92 | -1.1, -0.72 | <0.001 |
| Small | -1.3 | -1.6, -1.1 | <0.001 |
| Hospital location/teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 1.2 | 0.87, 1.4 | <0.001 |
| Urban, teaching | 1.9 | 1.6, 2.1 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -1.1 | -1.4, -0.80 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -0.71 | -0.85, -0.56 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | -0.13 | -0.35, 0.09 | 0.2 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | -0.11 | -0.25, 0.04 | 0.2 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -0.78 | -0.93, -0.63 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | -0.34 | -0.51, -0.17 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 0.36 | 0.09, 0.62 | 0.008 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 0.37 | 0.06, 0.68 | 0.021 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.1 | 1.9, 2.2 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 0.03 | -0.12, 0.18 | 0.7 |
| BMI |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | -0.25 | -0.45, -0.04 | 0.019 |
| Class III obesity (BMI ≥40.0kg/m²) | 0.59 | 0.39, 0.80 | <0.001 |
| Normal weight (BMI 20.0-24.9kg/m²) | 1.1 | 0.83, 1.4 | <0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | 0.75 | 0.45, 1.1 | <0.001 |
| Underweight (BMI ≤19.9kg/m²) | 1.4 | 1.1, 1.7 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -0.81 | -1.0, -0.60 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -0.44 | -0.63, -0.26 | <0.001 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | -0.22 | -0.41, -0.02 | 0.030 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -0.68 | -0.85, -0.51 | <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 | 13,511 | 10,983, 16,040 | <0.001 |
| Age, y | -588 | -716, -460 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 5,914 | 3,749, 8,079 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 22,346 | 6,595, 38,096 | 0.005 |
| Black | -3,355 | -6,303, -407 | 0.026 |
| Hispanic | 15,082 | 9,719, 20,445 | <0.001 |
| Native American | -14,094 | -22,843, -5,345 | 0.002 |
| Other | 22,929 | 6,059, 39,800 | 0.008 |
| Elixhauser comorbidity index | 8,007 | 6,902, 9,113 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -1,315 | -4,001, 1,370 | 0.3 |
| $66,000 - $87,999 | -689 | -3,878, 2,500 | 0.7 |
| $88,000 or more | 6,835 | 2,311, 11,359 | 0.003 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | -8,671 | -13,964, -3,378 | 0.001 |
| Medicare | -4,724 | -8,911, -538 | 0.027 |
| Other | 2,078 | -8,491, 12,646 | 0.7 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 23,286 | 17,074, 29,498 | <0.001 |
| South | 14,333 | 10,816, 17,851 | <0.001 |
| West | 39,533 | 33,045, 46,020 | <0.001 |
| Hospital bed size |  |  |  |
| Large | — | — |  |
| Medium | -13,315 | -17,295, -9,335 | <0.001 |
| Small | -21,077 | -24,929, -17,224 | <0.001 |
| Hospital location/teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 25,954 | 22,078, 29,829 | <0.001 |
| Urban, teaching | 35,931 | 32,617, 39,246 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -19,722 | -24,525, -14,919 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -2,419 | -4,568, -271 | 0.027 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | -1,353 | -4,821, 2,115 | 0.4 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 8,212 | 5,909, 10,515 | <0.001 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -9,778 | -12,089, -7,468 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 3,604 | 581, 6,628 | 0.019 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | -4,850 | -8,073, -1,628 | 0.003 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 3,400 | -801, 7,601 | 0.11 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 22,367 | 20,144, 24,590 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 95 | -2,314, 2,503 | >0.9 |
| BMI |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | -5,003 | -8,351, -1,655 | 0.003 |
| Class III obesity (BMI ≥40.0kg/m²) | -535 | -3,655, 2,584 | 0.7 |
| Normal weight (BMI 20.0-24.9kg/m²) | 8,121 | 3,330, 12,912 | <0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | 8,168 | 3,356, 12,981 | <0.001 |
| Underweight (BMI ≤19.9kg/m²) | 11,351 | 6,550, 16,152 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -12,987 | -16,800, -9,173 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -10,737 | -13,529, -7,946 | <0.001 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | -10,718 | -13,266, -8,170 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -16,510 | -19,371, -13,650 | <0.001 |
| Abbreviation: CI = Confidence Interval | | | |