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 = 500,040*1* | **Heart failure with reduced ejection fraction** N = 412,335*1* | **p-value***2* |
| --- | --- | --- | --- |
| Age, y | 73 (13) | 70 (14) | <0.001 |
| Sex |  |  | <0.001 |
| Female | 316,165 (63%) | 180,465 (44%) |  |
| Male | 183,855 (37%) | 231,860 (56%) |  |
| Race |  |  | <0.001 |
| White | 340,015 (69%) | 249,740 (62%) |  |
| Asian or Pacific Islander | 9,730 (2.0%) | 8,060 (2.0%) |  |
| Black | 90,820 (19%) | 98,275 (24%) |  |
| Hispanic | 36,030 (7.4%) | 34,635 (8.6%) |  |
| Native American | 2,905 (0.6%) | 2,775 (0.7%) |  |
| Other | 10,315 (2.1%) | 10,120 (2.5%) |  |
| Elixhauser comorbidity index | 7.97 (1.97) | 7.93 (2.03) | <0.001 |
| Residential income |  |  | <0.001 |
| $1 - $51,999 | 154,595 (31%) | 141,855 (35%) |  |
| $52,000 - $65,999 | 132,230 (27%) | 107,925 (27%) |  |
| $66,000 - $87,999 | 116,365 (24%) | 89,575 (22%) |  |
| $88,000 or more | 90,095 (18%) | 64,990 (16%) |  |
| Hospital bed size |  |  | <0.001 |
| Large | 244,880 (49%) | 218,925 (53%) |  |
| Medium | 144,725 (29%) | 111,865 (27%) |  |
| Small | 110,435 (22%) | 81,545 (20%) |  |
| Hospital location/teaching status |  |  | <0.001 |
| Rural | 45,190 (9.0%) | 31,910 (7.7%) |  |
| Urban, non-teaching | 88,730 (18%) | 67,280 (16%) |  |
| Urban, teaching | 366,120 (73%) | 313,145 (76%) |  |
| Expected primary payer |  |  | <0.001 |
| Private | 56,670 (11%) | 59,485 (14%) |  |
| Medicaid | 41,590 (8.3%) | 53,060 (13%) |  |
| Medicare | 394,410 (79%) | 291,455 (71%) |  |
| Other | 7,000 (1.4%) | 7,915 (1.9%) |  |
| Hospital region |  |  | <0.001 |
| Midwest | 143,115 (29%) | 110,775 (27%) |  |
| Northeast | 97,800 (20%) | 69,985 (17%) |  |
| South | 182,320 (36%) | 159,240 (39%) |  |
| West | 76,805 (15%) | 72,335 (18%) |  |
| Hypertension | 460,555 (92%) | 370,895 (90%) | <0.001 |
| Hyperlipidemia | 287,495 (57%) | 233,485 (57%) | <0.001 |
| Peripheral vascular disease | 64,540 (13%) | 99,435 (24%) | <0.001 |
| Chronic obstructive pulmonary disease | 225,895 (45%) | 154,690 (38%) | <0.001 |
| Coronary artery disease | 211,005 (42%) | 233,360 (57%) | <0.001 |
| Dementia | 51,595 (10%) | 34,315 (8.3%) | <0.001 |
| Fluid and electrolyte imbalance | 248,555 (50%) | 206,545 (50%) | 0.11 |
| Valvular heart disease | 135,015 (27%) | 120,545 (29%) | <0.001 |
| Atrial fibrillation | 190,110 (38%) | 155,520 (38%) | 0.2 |
| BMI |  |  | <0.001 |
| Class I obesity (BMI 30.0-34.9kg/m²) | 24,750 (15%) | 18,945 (18%) |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 25,370 (16%) | 16,480 (16%) |  |
| Class III obesity (BMI ≥40.0kg/m²) | 76,400 (47%) | 35,780 (34%) |  |
| Normal weight (BMI 20.0-24.9kg/m²) | 9,745 (6.0%) | 9,595 (9.1%) |  |
| Overweight (BMI 25.0-29.9kg/m²) | 11,150 (6.9%) | 9,770 (9.2%) |  |
| Underweight (BMI ≤19.9kg/m²) | 14,105 (8.7%) | 15,100 (14%) |  |
| Presence of pacemaker | 42,770 (8.6%) | 79,730 (19%) | <0.001 |
| previous MI | 54,260 (11%) | 81,165 (20%) | <0.001 |
| Pior cardiac surgery | 67,020 (13%) | 74,840 (18%) | <0.001 |
| Depression | 91,320 (18%) | 62,600 (15%) | <0.001 |
| Cancer | 30,500 (6.1%) | 24,545 (6.0%) | 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 = 500,040*1* | **Heart failure with reduced ejection fraction** N = 412,335*1* | **p-value***2* |
| --- | --- | --- | --- |
| Died during hospitalization | 15,235 (3.0%) | 16,220 (3.9%) | <0.001 |
| Length of stay (days) | 7.0 (7.2) | 7.6 (8.7) | <0.001 |
| Inflation-adjusted total charge ($) | 76,088 (99,221) | 94,365 (158,543) | <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 | 1.47 | 1.32, 1.63 | <0.001 |
| Age, y | 1.03 | 1.02, 1.03 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 1.23 | 1.10, 1.36 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.99 | 0.66, 1.48 | >0.9 |
| Black | 0.91 | 0.79, 1.05 | 0.2 |
| Hispanic | 0.90 | 0.73, 1.11 | 0.3 |
| Native American | 0.69 | 0.28, 1.70 | 0.4 |
| Other | 1.17 | 0.84, 1.62 | 0.4 |
| Elixhauser comorbidity index | 1.30 | 1.26, 1.35 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | 0.91 | 0.79, 1.04 | 0.2 |
| $66,000 - $87,999 | 0.88 | 0.77, 1.02 | 0.090 |
| $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 | 0.85 | 0.72, 1.01 | 0.066 |
| Other | 1.36 | 0.95, 1.95 | 0.091 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.07 | 0.91, 1.26 | 0.4 |
| South | 0.97 | 0.85, 1.11 | 0.6 |
| West | 0.87 | 0.73, 1.04 | 0.13 |
| Hospital bed size |  |  |  |
| Large | — | — |  |
| Medium | 0.97 | 0.85, 1.09 | 0.6 |
| Small | 0.87 | 0.76, 1.00 | 0.053 |
| Hospital location/teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 0.88 | 0.71, 1.09 | 0.3 |
| Urban, teaching | 0.89 | 0.74, 1.08 | 0.2 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | 0.52 | 0.44, 0.61 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | 0.73 | 0.66, 0.82 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | 0.80 | 0.69, 0.93 | 0.003 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 0.84 | 0.75, 0.95 | 0.005 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | 0.71 | 0.64, 0.79 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 0.78 | 0.69, 0.88 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 1.09 | 0.92, 1.29 | 0.3 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 1.09 | 0.90, 1.32 | 0.4 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.05 | 1.80, 2.34 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 0.95 | 0.85, 1.07 | 0.4 |
| BMI |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | 0.85 | 0.69, 1.05 | 0.14 |
| Class III obesity (BMI ≥40.0kg/m²) | 1.30 | 1.10, 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) | 1.27 | 1.02, 1.58 | 0.033 |
| Underweight (BMI ≤19.9kg/m²) | 2.13 | 1.77, 2.56 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | 0.78 | 0.66, 0.93 | 0.007 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | 1.04 | 0.88, 1.23 | 0.6 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | 0.68 | 0.59, 0.79 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | 0.95 | 0.80, 1.12 | 0.5 |
| 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 | 0.62 | 0.47, 0.77 | <0.001 |
| Age, y | -0.01 | -0.02, 0.00 | 0.002 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 0.41 | 0.26, 0.56 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 0.56 | -0.28, 1.4 | 0.2 |
| Black | -0.05 | -0.24, 0.15 | 0.6 |
| Hispanic | -0.11 | -0.39, 0.18 | 0.5 |
| Native American | 0.04 | -0.73, 0.81 | >0.9 |
| Other | 0.31 | -0.33, 0.95 | 0.3 |
| Elixhauser comorbidity index | 0.61 | 0.55, 0.66 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -0.18 | -0.36, 0.00 | 0.047 |
| $66,000 - $87,999 | -0.07 | -0.27, 0.14 | 0.5 |
| $88,000 or more | 0.17 | -0.10, 0.43 | 0.2 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | 0.08 | -0.24, 0.39 | 0.6 |
| Medicare | -0.21 | -0.45, 0.02 | 0.074 |
| Other | 0.10 | -0.49, 0.68 | 0.7 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 1.1 | 0.82, 1.4 | <0.001 |
| South | 0.50 | 0.29, 0.72 | <0.001 |
| West | -0.44 | -0.73, -0.16 | 0.002 |
| Hospital bed size |  |  |  |
| Large | — | — |  |
| Medium | -0.93 | -1.1, -0.73 | <0.001 |
| Small | -1.3 | -1.6, -1.1 | <0.001 |
| Hospital location/teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 1.2 | 0.88, 1.5 | <0.001 |
| Urban, teaching | 1.9 | 1.6, 2.1 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -1.1 | -1.4, -0.85 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -0.71 | -0.86, -0.57 | <0.001 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | -0.12 | -0.34, 0.11 | 0.3 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | -0.12 | -0.27, 0.03 | 0.10 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -0.80 | -0.96, -0.65 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | -0.34 | -0.52, -0.16 | <0.001 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | 0.34 | 0.06, 0.61 | 0.015 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 0.36 | 0.04, 0.68 | 0.027 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 2.0 | 1.9, 2.2 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | 0.01 | -0.14, 0.17 | 0.9 |
| BMI |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | -0.25 | -0.46, -0.03 | 0.023 |
| Class III obesity (BMI ≥40.0kg/m²) | 0.60 | 0.40, 0.81 | <0.001 |
| Normal weight (BMI 20.0-24.9kg/m²) | 1.2 | 0.85, 1.5 | <0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | 0.76 | 0.45, 1.1 | <0.001 |
| Underweight (BMI ≤19.9kg/m²) | 1.4 | 1.1, 1.7 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -0.84 | -1.1, -0.62 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -0.44 | -0.62, -0.25 | <0.001 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | -0.23 | -0.44, -0.03 | 0.023 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -0.67 | -0.85, -0.50 | <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 | 13,750 | 11,168, 16,332 | <0.001 |
| Age, y | -590 | -721, -459 | <0.001 |
| Sex |  |  |  |
| Female | — | — |  |
| Male | 6,029 | 3,808, 8,250 | <0.001 |
| Race |  |  |  |
| White | — | — |  |
| Asian or Pacific Islander | 23,569 | 7,291, 39,847 | 0.005 |
| Black | -3,864 | -6,855, -873 | 0.011 |
| Hispanic | 15,227 | 9,762, 20,691 | <0.001 |
| Native American | -13,994 | -23,057, -4,930 | 0.002 |
| Other | 23,412 | 6,135, 40,688 | 0.008 |
| Elixhauser comorbidity index | 8,064 | 6,932, 9,195 | <0.001 |
| Residential income |  |  |  |
| $1 - $51,999 | — | — |  |
| $52,000 - $65,999 | -1,380 | -4,131, 1,371 | 0.3 |
| $66,000 - $87,999 | -842 | -4,104, 2,419 | 0.6 |
| $88,000 or more | 6,582 | 1,976, 11,188 | 0.005 |
| Expected primary payer |  |  |  |
| Private | — | — |  |
| Medicaid | -9,073 | -14,471, -3,675 | <0.001 |
| Medicare | -4,851 | -9,140, -562 | 0.027 |
| Other | 1,729 | -9,009, 12,468 | 0.8 |
| Hospital region |  |  |  |
| Midwest | — | — |  |
| Northeast | 23,908 | 17,510, 30,305 | <0.001 |
| South | 14,541 | 10,951, 18,131 | <0.001 |
| West | 39,902 | 33,292, 46,512 | <0.001 |
| Hospital bed size |  |  |  |
| Large | — | — |  |
| Medium | -13,601 | -17,664, -9,537 | <0.001 |
| Small | -21,409 | -25,331, -17,487 | <0.001 |
| Hospital location/teaching status |  |  |  |
| Rural | — | — |  |
| Urban, non-teaching | 26,467 | 22,521, 30,413 | <0.001 |
| Urban, teaching | 36,641 | 33,263, 40,018 | <0.001 |
| Hypertension |  |  |  |
| No | — | — |  |
| Yes | -20,381 | -25,338, -15,425 | <0.001 |
| Hyperlipidemia |  |  |  |
| No | — | — |  |
| Yes | -2,303 | -4,505, -102 | 0.040 |
| Peripheral vascular disease |  |  |  |
| No | — | — |  |
| Yes | -1,184 | -4,733, 2,366 | 0.5 |
| Coronary artery disease |  |  |  |
| No | — | — |  |
| Yes | 8,328 | 5,968, 10,689 | <0.001 |
| Chronic obstructive pulmonary disease |  |  |  |
| No | — | — |  |
| Yes | -10,068 | -12,434, -7,702 | <0.001 |
| Valvular heart disease |  |  |  |
| No | — | — |  |
| Yes | 3,974 | 885, 7,064 | 0.012 |
| Dementia |  |  |  |
| No | — | — |  |
| Yes | -5,237 | -8,550, -1,924 | 0.002 |
| Cancer |  |  |  |
| No | — | — |  |
| Yes | 3,318 | -972, 7,608 | 0.13 |
| Fluid and electrolyte imbalance |  |  |  |
| No | — | — |  |
| Yes | 22,083 | 19,805, 24,362 | <0.001 |
| Atrial fibrillation |  |  |  |
| No | — | — |  |
| Yes | -36 | -2,504, 2,433 | >0.9 |
| BMI |  |  |  |
| Class I obesity (BMI 30.0-34.9kg/m²) | — | — |  |
| Class II obesity (BMI 35.0-39.9kg/m²) | -4,917 | -8,363, -1,471 | 0.005 |
| Class III obesity (BMI ≥40.0kg/m²) | -533 | -3,740, 2,674 | 0.7 |
| Normal weight (BMI 20.0-24.9kg/m²) | 8,246 | 3,313, 13,178 | 0.001 |
| Overweight (BMI 25.0-29.9kg/m²) | 8,454 | 3,505, 13,402 | <0.001 |
| Underweight (BMI ≤19.9kg/m²) | 11,386 | 6,447, 16,325 | <0.001 |
| Presence of pacemaker |  |  |  |
| No | — | — |  |
| Yes | -13,286 | -17,205, -9,368 | <0.001 |
| previous MI |  |  |  |
| No | — | — |  |
| Yes | -10,786 | -13,654, -7,919 | <0.001 |
| Depression |  |  |  |
| No | — | — |  |
| Yes | -10,961 | -13,572, -8,350 | <0.001 |
| Pior cardiac surgery |  |  |  |
| No | — | — |  |
| Yes | -16,717 | -19,664, -13,771 | <0.001 |
| Abbreviation: CI = Confidence Interval | | | |