**Online Supplementary Materials**

**Supplementary Figure I. Cumulative Density Function for Readmissions within 30 Days in Takotsubo syndrome**

**Supplementary Table I. Independent Predictors of Inhospital Mortality After Index Hospitalization With Takotsubo Syndrome**

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**Supplementary Figure I. Cumulative Density Function for Readmissions within 30 Days in Takotsubo syndrome**

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**Supplementary Table I. Independent Predictors of Inhospital Mortality After Index Hospitalization With Takotsubo Syndrome**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **Unadjusted OR** | **Lower CI** | **Higher CI** | **P value** | **Adjusted OR** | **Lower CI** | **Higher CI** | **P value** |
| Malignancy | 1.96 | 1.56 | 2.46 | <0.001 | 1.68 | 1.29 | 2.17 | <0.001 |
| Age≥70 yrs | 1.81 | 1.49 | 2.19 | <0.001 | 1.85 | 1.49 | 2.30 | <0.001 |
| Smoking | 0.71 | 0.58 | 0.88 | <0.001 | 0.72 | 0.57 | 0.91 | 0.006 |
| Fluid and electrolyte | 3.80 | 3.17 | 4.56 | <0.001 | 2.06 | 1.67 | 2.55 | <0.01 |
| Pulmonary Circ Disease | 3.81 | 2.65 | 5.48 | <0.001 | 1.86 | 1.18 | 2.93 | 0.008 |
| Chronic Pulmonary disease | 1.41 | 1.15 | 1.74 | <0.001 | 1.31 | 1.04 | 1.65 | 0.022 |
| Cardiogenic shock | 11.26 | 9.18 | 13.82 | <0.001 | 5.80 | 4.53 | 7.43 | <0.001 |
| Cardiac arrest | 16.88 | 13.10 | 21.74 | <0.001 | 8.63 | 6.34 | 11.76 | <0.001 |
| Arrhythmia | 2.66 | 2.19 | 3.24 | <0.001 | 1.62 | 1.31 | 2.01 | <0.001 |

Abbreviations: OR, odds ratio; CI, confidence interval.

**Supplementary Table II. Independent Predictors of 30-Day Total Mortality After Index Hospitalization With Takotsubo Syndrome\***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **Unadjusted OR** | **Lower CI** | **Higher CI** | **P value** | **Adjusted OR** | **Lower CI** | **Higher CI** | **P value** |
| Malignancy | 1.93 | 1.55 | 2.42 | <0.001 | 1.62 | 1.25 | 2.10 | <0.001 |
| Age≥70 yrs | 1.87 | 1.55 | 2.26 | <0.001 | 1.88 | 1.51 | 2.34 | <0.001 |
| Smoking | 0.75 | 0.63 | 0.93 | <0.001 | 0.77 | 0.62 | 0.96 | 0.019 |
| Fluid and electrolyte | 3.74 | 3.14 | 4.45 | <0.001 | 2.15 | 1.76 | 2.63 | <0.001 |
| Pulmonary Circ Disease | 3.85 | 2.68 | 5.55 | <0.001 | 1.90 | 1.22 | 2.96 | <0.001 |
| Chronic pulmonary disease | 1.58 | 1.31 | 1.90 | <0.001 | 1.45 | 1.18 | 1.79 | <0.001 |
| Cardiogenic shock | 9.39 | 7.66 | 11.51 | <0.001 | 4.82 | 3.78 | 6.16 | <0.001 |
| Cardiac arrest | 14.18 | 11.08 | 18.16 | <0.001 | 7.60 | 5.64 | 10.26 | <0.001 |
| Arrhythmia | 2.47 | 2.05 | 2.97 | <0.001 | 1.52 | 1.24 | 1.85 | <0.001 |
| Family Hx of CAD | 0.36 | 0.21 | 0.63 | <0.001 | 0.58 | 0.34 | 0.98 | 0.042 |

Abbreviations: OR, odds ratio; CI, confidence interval; CAD, coronary artery disease.

\*Thirty-day total mortality included inhospital mortality and 30-day readmission mortality together.

**Supplementary Table III. Causes of Readmission in all takotsubo syndrome patients**

|  |  |  |
| --- | --- | --- |
| **Causes of Readmission** | **CCS codes** | **Frequency (%)** |
| **Cardiac causes** |  | **21.6** |
| Heart failure | 108 | 10.62 |
| Arrhythmia | 106 | 4.70 |
| Angina and Chronic Ischemic Heart Disease | 101 | 2.60 |
| Acute myocardial infarction | 100 | 2.23 |
| Non-specific chest pain | 102 | 1.93 |
| Cardiac arrest | 107 | 1.10 |
| **Other cardiac causes** |  | **9.0** |
| Other circulatory (heart) disease/Complication of hypertension | 98, 99, 104, 117 | 2.83 |
| Syncope | 245 | 0.73 |
| Myocarditis/pericarditis | 97 | 0.70 |
| Valvular heart disease | 96 | 0.45 |
| Conduction disorder | 105 | 0.40 |
| **Non-cardiac causes** |  | **69.4** |
| Infectious | 2, 4, 122, 135, 148, 159, 197, 201 | 19.76 |
| Respiratory | 103, 127, 128, 129\*, 130, 131, 133, 134 | 12.44  |
| Others | 81, 85, 199, 205, 211, 212, 231, 248, 251, 252, 259, N/S | 6.9 |
| Gastrointestinal | 120, 138, 140, 141, 145, 146, 149, 151, 152, 153, 154, 155, 230, 246, 250 | 6.39 |
| Endocrine/Metabolic | 50, 51, 55, 58 | 4.4 |
| Neuropsychiatric/Substance | 83, 95, 242, 653, 657, 659, 660, 661 | 3.42 |
| Genitourinary  | 157, 158, 163, 164 | 3.08 |
| Hematologic/oncologic | 19, 42, 45, 59, 60, 62 | 1.99 |
| Stroke/Transient ischemic attack | 109, 110, 112, 113 | 1.56  |
| Peripheral vascular disease | 114, 115, 116, 118 | 1.48  |
| Trauma | 226, 233, 234, 244 | 1  |
| Complication of medical procedure or implant/graft | 237, 238 | 8.8 |
| Rehabilitation | 254 | 1.14 |

\*Aspiration pneumonitis (CCS 129) was included in the respiratory problem.

**Supplementary Table IV. Causes of Readmission in takotsubo syndrome patients with malignancy**

|  |  |  |
| --- | --- | --- |
| **Causes of Readmission** | **CCS codes** | **Frequency (%)** |
| **Cardiac causes** |  | **18.3** |
| Heart failure | 108 | 8.1 |
| Arrhythmia | 106 | 4.9 |
| Angina and Chronic Ischemic Heart Disease | 101 | 1.8 |
| Acute myocardial infarction | 100 | 0.8 |
| Non-specific chest pain | 102 | 2.6 |
| Cardiac arrest | 107 | 0.1 |
| **Other cardiac causes** |  | **6.2** |
| Other circulatory (heart) disease/Complication of hypertension | 98, 99, 104, 117 | 4.3 |
| Syncope | 245 | 0.2 |
| Myocarditis/pericarditis | 97 | 1.6 |
| Valvular heart disease | 96 | 0.1 |
| Conduction disorder | 105 | 0 |
| **Non-cardiac causes** |  | **75.5** |
| Infectious | 2, 4, 122, 135, 148, 159, 197, 201 | 20.1 |
| Respiratory | 103, 127, 128, 129\*, 130, 131, 133, 134 | 8.4 |
| Others | 81, 85, 199, 205, 211, 212, 231, 248, 251, 252, 259, N/S | 10.9 |
| Gastrointestinal | 120, 138, 140, 141, 145, 146, 149, 151, 152, 153, 154, 155, 230, 246, 250 | 7.8 |
| Endocrine/Metabolic | 50, 51, 55, 58 | 3.1 |
| Neuropsychiatric/Substance | 83, 95, 242, 653, 657, 659, 660, 661 | 3.8 |
| Genitourinary  | 157, 158, 163, 164 | 4.6 |
| Hematologic/oncologic | 19, 42, 45, 59, 60, 62 | 6.7 |
| Stroke/Transient ischemic attack | 109, 110, 112, 113 | 2.5 |
| Peripheral vascular disease | 114, 115, 116, 118 | 1.2 |
| Trauma | 226, 233, 234, 244 | 0.9 |
| Complication of medical procedure or implant/graft | 237, 238 | 5.5 |
| Rehabilitation | 254 | 0 |

\*Aspiration pneumonitis (CCS 129) was included in the respiratory problem.

**Supplementary Table V. Causes of Readmission in takotsubo syndrome patients without malignancy**

|  |  |  |
| --- | --- | --- |
| **Causes of Readmission** | **CCS codes** | **Frequency (%)** |
| **Cardiac causes** |  | **22.3** |
| Heart failure | 108 | 11.14 |
| Arrhythmia | 106 | 3.29 |
| Angina and Chronic Ischemic Heart Disease | 101 | 2.42 |
| Acute myocardial infarction | 100 | 1.67 |
| Non-specific chest pain | 102 | 3.5 |
| Cardiac arrest | 107 | 0.28 |
| **Other cardiac causes** |  | **9.5** |
| Other circulatory (heart) disease/Complication of hypertension | 98, 99, 104, 117 | 6.46 |
| Syncope | 245 | 0.87 |
| Myocarditis/pericarditis | 97 | 1.55 |
| Valvular heart disease | 96 | 0.35 |
| Conduction disorder | 105 | 0.27 |
| **Non-cardiac causes** |  | **68.1** |
| Infectious | 2, 4, 122, 135, 148, 159, 197, 201 | 12.04 |
| Respiratory | 103, 127, 128, 129\*, 130, 131, 133, 134 | 12.41  |
| Others | 81, 85, 199, 205, 211, 212, 231, 248, 251, 252, 259, N/S | 8.8 |
| Gastrointestinal | 120, 138, 140, 141, 145, 146, 149, 151, 152, 153, 154, 155, 230, 246, 250 | 9.45 |
| Endocrine/Metabolic | 50, 51, 55, 58 | 3.7 |
| Neuropsychiatric/Substance | 83, 95, 242, 653, 657, 659, 660, 661 | 4.75 |
| Genitourinary  | 157, 158, 163, 164 | 3.62 |
| Hematologic/oncologic | 19, 42, 45, 59, 60, 62 | 0.99 |
| Stroke/Transient ischemic attack | 109, 110, 112, 113 | 3.96  |
| Peripheral vascular disease | 114, 115, 116, 118 | 2.33  |
| Trauma | 226, 233, 234, 244 | 1.2 |
| Complication of medical procedure or implant/graft | 237, 238 | 4.85 |
| Rehabilitation | 254 | 0.11 |

\*Aspiration pneumonitis (CCS 129) was included in the respiratory problem.

**Supplementary Table VI. Costs and Charges over 30-days after Index Hospitalization for Takotsubo syndrome with or without Malignancy**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcomes** | **Overall** | **TTS with malignancy** | **TTS without malignancy** | **P Value†** |
| **Number of patients, n (%)** | 61583 (100) | 7542 (12.2) | 54041 (87.8) |  |
| **Charge (index hospitalization), $** | 39498 (25935-68521)\* | 46876 (28416-87536 | 38593 (25481-66425) | <0.001 |
| **Cumulative charges (index hospitalization + 30-day readmission), $** | 41830 (26501-75167) | 50936 (29819-97989) | 40735 (26160-72619) | <0.001 |
| **Cost (index hospitalization), $** | 11427 (7999-17933) | 13344 (8909-24171) | 11194 (7900-17933) | <0.001 |
| **Cumulative costs (index hospitalization + 30-day readmission), $** | 11998 (8181-20564) | 14686 (9294-27337) | 11704 (8065-19630) | <0.001 |

Abbreviations: TTS, Takotsubo syndrome.

\*All values are shown as a median (interquartile range).

†Mann-Whitney-Wilcoxon test was used in all comparisons.