**Supplementary table 1. Clinical variables associated with iron deficiency in severe aortic stenosis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Univariable OR (95% CI)** | **p- value** | **Multivariable OR (95% CI)** | **p-value** |
| Age, per year | 1.02 (1.01-1.41) | 0.011 |  |  |
| Female vs male | 2.54 (1.74-3.72) | <0.001 | 1.70 (1.11-2.61) | 0.015 |
| Diabetes mellitus type I and II, yes or no | 1.75 (0.98-3.12) | 0.055 |  |  |
| ACEi/ARB, yes or no | 0.66 (0.45-0.96) | 0.028 | 0.59 (0.39-0.90) | 0.013 |
| Malignancy (previous/active) | 1.66 (0.94-2.94) | 0.079 |  |  |
| Antacids /PPI | 2.35 (1.33-4.15) | 0.003 | 2.32 (1.26-4.30) | 0.007 |
| EuroSCORE II, log | 1.43 (1.14-1.79) | 0.002 |  |  |
| 6-minute walk test, per meter | 0.997 (0.996-0.999) | 0.002 |  |  |
| Summary PCS (sf36-v2) | 0.98 (0.96-0.99) | 0.009 |  |  |
| EQ-5D VAS score | 0.99 (0.98-1.00) | 0.062 |  |  |
| BSA | 0.21 (0.09-0.50) | <0.001 |  |  |
| Aortic valve area, per 0.1 cm2 | 0.78 (0.71-0.87) | <0.001 | 0.84 (0.75-0.93) | 0.001 |
| Haemoglobin (Hgb), g/dl | 0.72 (0.63-0.82) | <0.001 | 0.78 (0.68-0.90) | <0.001 |
| NT- pro- BNP, log pmol/L | 1.22 (1.06-1.40) | 0.006 |  |  |
| CRP, log mg/L | 1.14 (0.97-1.33) | 0.11 |  |  |
| Charlson comorbidity index: |  |  |  |  |
| 1-2 versus 0 | 1.29 (0.87-1.92) | 0.20 |  |  |
| ≥3 versus 0 | 1.79 (0.99-3.25) | 0.056 |  |  |
| CCS Score: |  |  |  |  |
| 1-2 versus 0 | 0.88 (0.60-1.29) | 0.51 |  |  |
| 3-4 versus 0 | 1.95 (0.86-4.45) | 0.11 |  |  |

Values are odds ratio (OR) with 95% Confidence interval (CI). Iron deficiency was defined as ferritin level < 100 μg/L or ferritin 100-299 μg/L with a transferrin saturation <20%

Abbreviations: log, logarithmic transformation of the original variable to make it normally distributed; PCS, Physical Component Summary; EQ-5D UK, EuroQol 5-dimension United Kingdom, BSA, body surface area; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; PPI, proton-pump inhibitor; CCS, Canadian Cardiovascular Society; NT-proBNP, N-terminal pro brain natriuretic peptide; CRP, C-reactive protein

**Supplementary table 2. Short- (A) and long-term (B) mortality analyses on iron deficiency. The tables show the number of patients and events in each group.**

**A**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Iron deficiency | Total number | Number of events | Number of censored |
| Conservatively treated | 0 | 45 | 9 | 36 |
| 1 | 46 | 8 | 38 |
| Overall | 91 | 17 | 74 |
| Operated | 0 | 173 | 7 | 166 |
| 1 | 200 | 14 | 186 |
| Overall | 373 | 21 | 352 |

**B**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Iron deficiency | Total number | Number of events | Number of censored |
| Conservatively treated | 0 | 45 | 28 | 17 |
| 1 | 46 | 29 | 17 |
| Overall | 91 | 57 | 34 |
| Operated | 0 | 173 | 29 | 144 |
| 1 | 200 | 43 | 157 |
| Overall | 373 | 72 | 301 |

**Supplementary table 3. Determinants of one-year mortality among conservatively treated patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Hazard ratio** | **95% CI** | **p-value** |
| Age, years | 1.02 | 0.94-1.12 | 0.63 |
| Gender (female) | 1.17 | 0.33-4.10 | 0.81 |
| NYHA class III-IV | 1.69 | 0.45-6.29 | 0.43 |
| Coronary artery disease | 7.01 | 1.93-25.4 | **0.003** |
| Diabetes mellitus | 2.16 | 0.51-9.14 | 0.30 |
| Atrial fibrillation, all types | 0.97 | 0.30-3.12 | 0.96 |
| LVEF | 0.98 | 0.92-1.03 | 0.36 |
| Anemia | 4.58 | 1.30-16.11 | **0.018** |

The associations between baseline variables and mortality were assessed with multivariable cox regression analysis. LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

**Supplementary table 4. Determinants of one-year MACE among operated and conservatively treated patients**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Operated patients** | | | **Conservatively treated patients** | | |
| **Variable** | **Hazard ratio** | **95% CI** | **p-value** | **Hazard ratio** | **95% CI** | **p-value** |
| Age, years | 1.00 | 0.97-1.03 | 0.96 | 1.06 | 0.98-1.15 | 0.17 |
| NYHA class III-IV | 2.00 | 1.11-3.63 | **0.022** | 1.66 | 0.54-5.16 | 0.38 |
| Coronary artery disease | 1.71 | 0.95-3.09 | 0.075 | 3.81 | 1.41-10.36 | **0.009** |
| Diabetes mellitus | 2.22 | 1.10-4.48 | **0.025** | 1.21 | 0.32-4.55 | 0.78 |
| LVEF | 0.98 | 0.96-1.01 | 0.21 | 0.97 | 0.93-1.01 | 0.14 |
| Iron deficiency | 1.11 | 0.63-1.97 | 0.72 | 0.66 | 0.25-1.75 | 0.40 |

The associations between baseline variables and MACE (major adverse cardiovascular events) were assessed with multivariable cox regression analysis. CI, confidence interval; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.