**Association of preoperative clinical frailty and clinical outcomes in elderly patients with stable coronary artery disease after percutaneous coronary intervention**

# Heart and Vessels

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**Online Table 1.** Univariate and multivariate logistic regression analysis for the frail (CFS ≥ 5)

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | OR (95%CI) | *p*-value | OR (95%CI) | *p*-value |
| Advanced age (≥ 75 years) | 3.56 (1.67-7.58) | 0.001 | 7.87 (2.60-23.86) | <0.001 |
| Male sex | 0.74 (0.35-1.57) | 0.43 | | |
| BMI < 18.5 kg/m² | 1.91 (0.70-5.18) | 0.20 | | |
| History of PCI | 0.80 (0.37-1.70) | 0.56 | | |
| History of OMI | 1.30 (0.64-2.66) | 0.47 | | |
| History of stroke | 3.21 (1.47-7.01) | 0.003 | 5.63 (1.82-17.41) | 0.003 |
| History of heart failure | 2.85 (1.29-6.30) | 0.01 | 0.72 (0.23-2.26) | 0.57 |
| Hypertension | 0.54 (0.24-1.18) | 0.12 | | |
| Dyslipidemia | 0.67 (0.32-1.41) | 0.29 | | |
| Diabetes Mellitus | 1.29 (0.64-2.58) | 0.47 | | |
| Current-smoker | 1.18 (0.50-2.79) | 0.70 | | |
| COPD | 1.94 (0.76-4.94) | 0.17 | | |
| PAD | 3.20 (1.49.-6.86) | 0.003 | 2.18 (0.74-6.40) | 0.15 |
| eGFR< 60mL/min/1.73m² | 1.80 (0.88-3.68) | 0.11 | | |
| Hb < 11.0 g/dL | 3.08 (1.42-6.71) | 0.005 | 1.18 (0.38-3.62) | 0.78 |
| LVEF < 40% | 5.16 (2.07-12.90) | < 0.001 | 5.49 (1.51-19.86) | 0.01 |
| LMCA or multivessel | 1.28 (0.64- 2.57) | 0.49 | | |
| Serum albumin < 3.5 g/dL | 8.61 (3.69-20.10) | <0.001 | 11.06 (3.55-34.49) | <0.001 |

CFS; clinical frailty scale, OR; odds ratio, CI; confidence interval, BMI; body mass index, PCI;

percutaneous coronary intervention, OMI; old myocardial infarction, COPD; chronic obstructive

pulmonary disease, PAD; peripheral artery disease, eGFR; estimated glomerular filtration rate,

Hb; hemoglobin, LVEF; left ventricular ejection fraction, LMCA; left main coronary artery.

**Online Table 2a.** Clinical outcomes between the frail and non-frail group aged 65–74 years old.

| | All (N=130) | Frail group (N=11) | Non-frail group (N=119) | p-value |
|---|---|---|---|---|
| | No. patients with events (cumulative 2-year incidence; %) | | | |
| **MACE** | 18 (12.2%) | 5 (48.9%) | 13 (9.0%) | <0.001 |
| **All-cause death** | 9 (6.0%) | 4 (42.3%) | 5 (3.0%) | <0.001 |
| Cardiovascular death | 5 (4.4%) | 4 (42.3%) | 1 (1.2%) | <0.001 |
| Non-cardiovascular death | 4 (1.6%) | 0 (0.0%) | 4 (1.8%) | 0.63 |
| **Non-fatal MI** | 1 (0.9%) | 0 (0.0%) | 1 (1.0%) | 0.81 |
| **Non-fatal stroke** | 2 (0.8%) | 0 (0.0%) | 2 (0.9%) | 0.73 |
| **Heart failure requiring hospitalization** | 6 (4.7%) | 1 (9.1%) | 5 (4.3%) | 0.41 |
| **Major bleeding (BARC type 3 or 5)** | 2 (1.6%) | 0 (0.0%) | 2 (1.7%) | 0.68 |
| Gastrointestinal bleeding | 1 (0.8%) | 0 (0.0%) | 1 (0.9%) | 0.78 |
| Access site bleeding | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1.00 |
| Intracranial bleeding | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1.00 |
| Others | 1 (0.8%) | 0 (0.0%) | 1 (0.8%) | 0.76 |
| **Ischemic event (MI and ischemic stroke)** | 3 (1.7%) | 0 (0.0%) | 3 (1.8%) | 0.68 |

The number of patients with events counted during the entire follow-up. A cumulative 2-year incidence was estimated by the Kaplan-Meier method. MACE; major adverse cardiovascular event, MI; myocardial infarction, BARC; Bleeding Academic Research Consortium.

**Online Table 2b.** Clinical outcomes between the frail and non-frail group aged ≥ 75 years old

| | All (N=109) | Frail group (N=27) | Non-frail group (N=82) | *p*-value |
|---|---|---|---|---|
| | **No. patients with events (cumulative 2-year incidence; %)** | | | |
| **MACE** | 28 (20.3%) | 16 (48.2%) | 12 (11.1%) | <0.001 |
| **All-cause death** | 19 (16.0%) | 12 (38.0%) | 7 (8.7%) | <0.001 |
| Cardiovascular death | 4 (4.0%) | 1 (3.7%) | 3 (4.0%) | 0.88 |
| Non-cardiovascular death | 15 (12.4%) | 11 (35.6%) | 4 (5.0%) | <0.001 |
| **Non-fatal MI** | 3 (2.0%) | 1 (4.8%) | 2 (1.3%) | 0.60 |
| **Non-fatal stroke** | 2 (2.1%) | 1 (4.8%) | 1 (1.4%) | 0.30 |
| **Heart failure requiring hospitalization** | 6 (3.0%) | 3 (9.3%) | 3 (1.3%) | 0.07 |
| **Major bleeding (BARC type 3 or 5)** | 8 (7.6%) | 5 (20.5%) | 3 (3.7%) | 0.005 |
| Gastrointestinal bleeding | 3 (2.9%) | 2 (8.4%) | 1 (1.2%) | 0.06 |
| Access site bleeding | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1.00 |
| Intracranial bleeding | 2 (2.1%) | 1 (5.3%) | 1 (1.3%) | 0.27 |
| Others | 3 (2.8%) | 2 (8.4%) | 1 (1.2%) | 0.07 |
| **Ischemic event (MI and ischemic stroke)** | 4 (3.1%) | 1 (4.8%) | 3 (2.6%) | 0.83 |

The number of patients with events counted during the entire follow-up. A cumulative 2-year incidence was

estimated by the Kaplan-Meier method. MACE; major adverse cardiovascular event, MI; myocardial infarction,
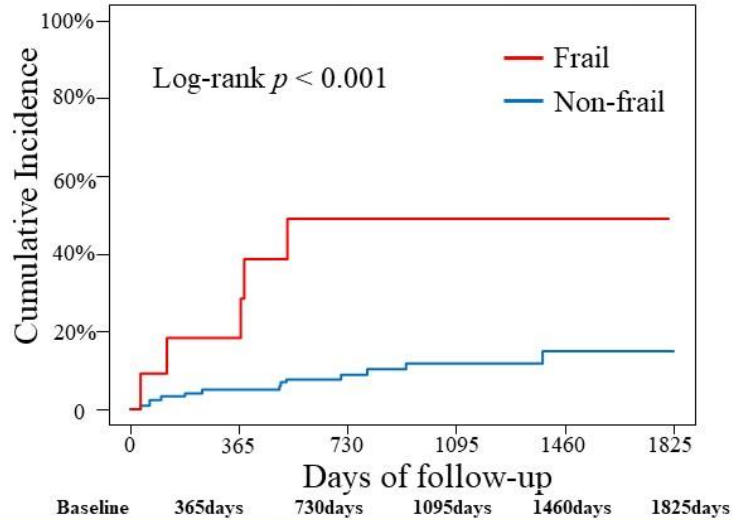
BARC; Bleeding Academic Research Consortium.
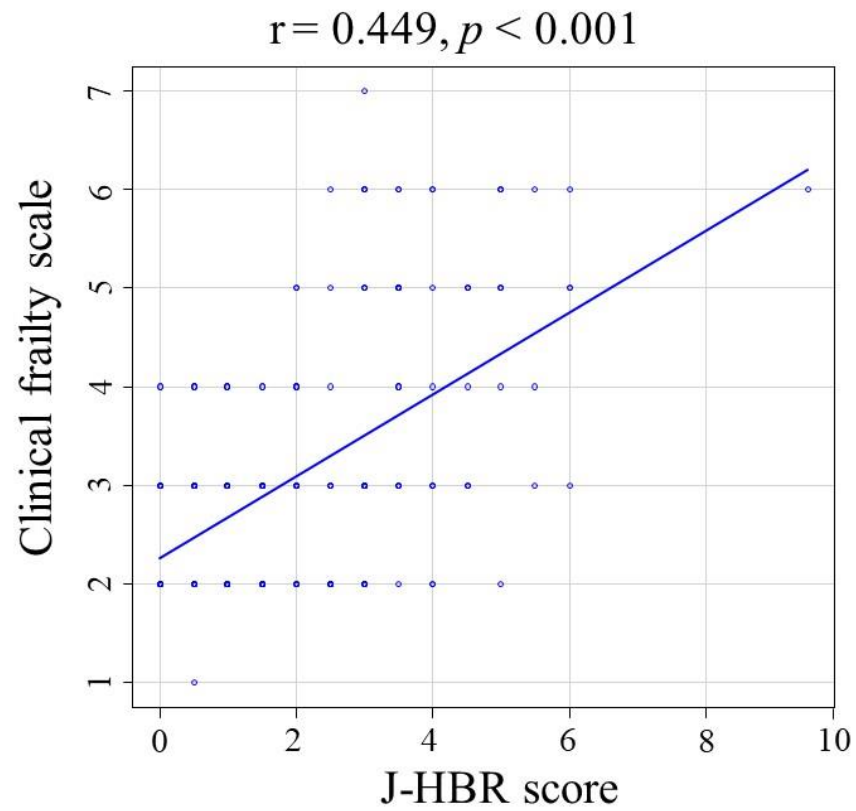
**Online Figure 1.** Correlation analysis between the Japanese version of high bleeding risk (J-HBR) score and the clinical frailty scale (CFS).
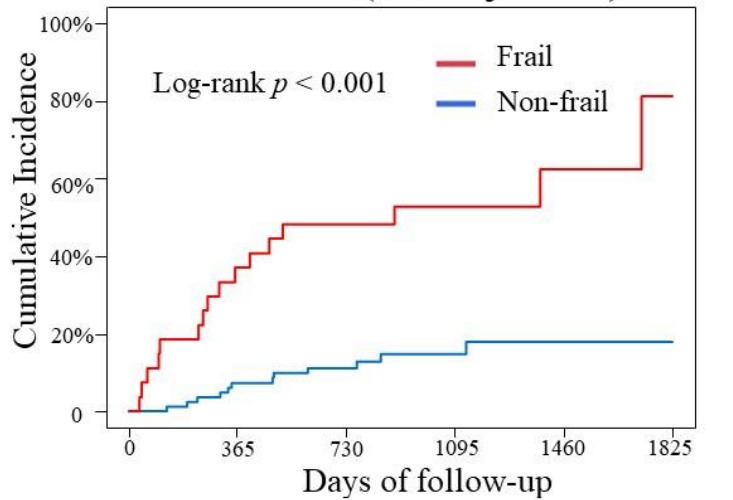
a

## MACE (65–74 years)

Log-rank $p < 0.001$

— Frail
— Non-frail

| | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events | | 2 | 5 | 5 | 5 | |
| No patients at risk | 11 | 8 | 3 | 2 | 2 | |
| Cumulative incidence | | 18.2% | 48.9% | 48.9% | 48.9% | |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events | | 6 | 10 | 12 | 13 | 13 |
| No patients at risk | 119 | 113 | 76 | 45 | 21 | 4 |
| Cumulative incidence | | 5.0% | 9.0% | 11.8% | 14.9% | 14.9% |

b

## MACE ( ≥75years)

Log-rank $p < 0.001$

— Frail
— Non-frail

| | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events | | 10 | 13 | 14 | 15 | 16 |
| No patients at risk | 27 | 17 | 12 | 6 | 3 | 1 |
| Cumulative incidence | | 37.0% | 48.2% | 52.9% | 62.3% | 81.1% |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events | | 6 | 9 | 11 | 12 | 12 |
| No patients at risk | 82 | 76 | 54 | 31 | 11 | 1 |
| Cumulative incidence | | 7.3% | 11.1% | 14.6% | 17.7% | 17.7% |

## c

### Survival (65–74 years)



Log-rank *p* < 0.001

— Frail
— Non-frail
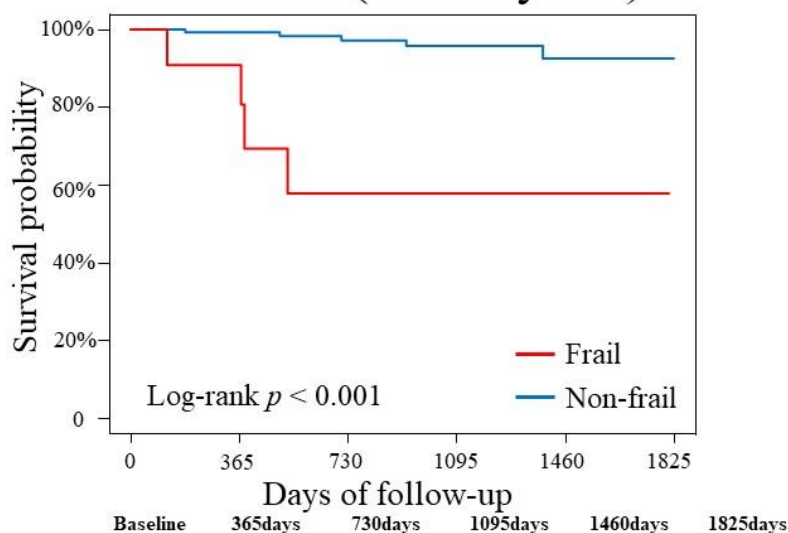
|  | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events |  | 1 | 4 | 4 | 4 |  |
| No patients at risk | 11 | 9 | 3 | 2 | 2 |  |
| Survival probability |  | 90.9% | 57.7% | 57.7% | 57.7% |  |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events |  | 1 | 3 | 4 | 5 | 5 |
| No patients at risk | 119 | 118 | 80 | 48 | 21 | 4 |
| Survival probability |  | 99.2% | 97.0% | 95.6% | 92.2% | 92.2% |

## d

### Survival (≥75 years)



Log-rank *p* < 0.001
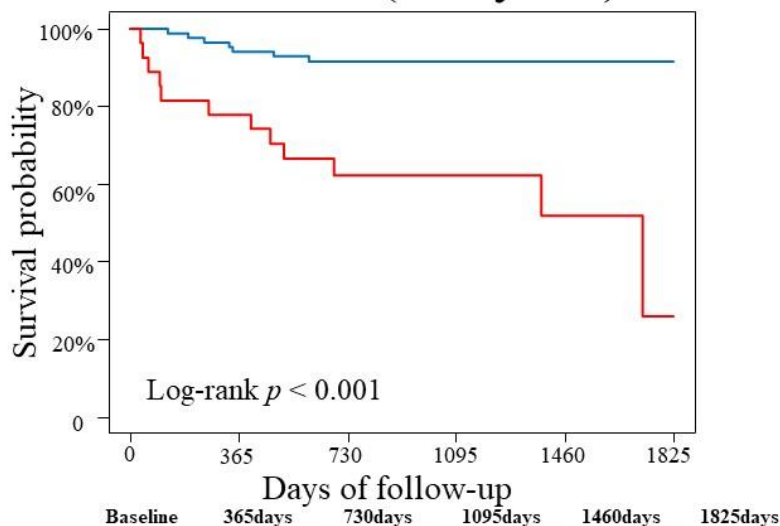
|  | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events |  | 6 | 10 | 10 | 11 | 12 |
| No patients at risk | 27 | 21 | 14 | 8 | 4 | 1 |
| Survival probability |  | 77.8% | 62.0% | 62.0% | 51.7% | 25.9% |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events |  | 5 | 7 | 7 | 7 | 7 |
| No patients at risk | 82 | 77 | 54 | 32 | 11 | 1 |
| Survival probability |  | 93.9% | 91.3% | 91.3% | 91.3% | 91.3% |

**Online Figure 2.** Kaplan–Meier analysis of the cumulative incidence of the primary outcome measure and survival probability between the two groups, the frail group (CFS ≥ 5), and the non-frail (CFS < 5). (a) The primary outcome measure between the two groups (in patients 65–74 years old). (b) The primary outcome measure between the two groups (in patients ≥ 75 years old). (c) Survival probability between the two groups (in patients 65–74 years old). (d) Survival probability between the two groups (in patients ≥ 75 years old).
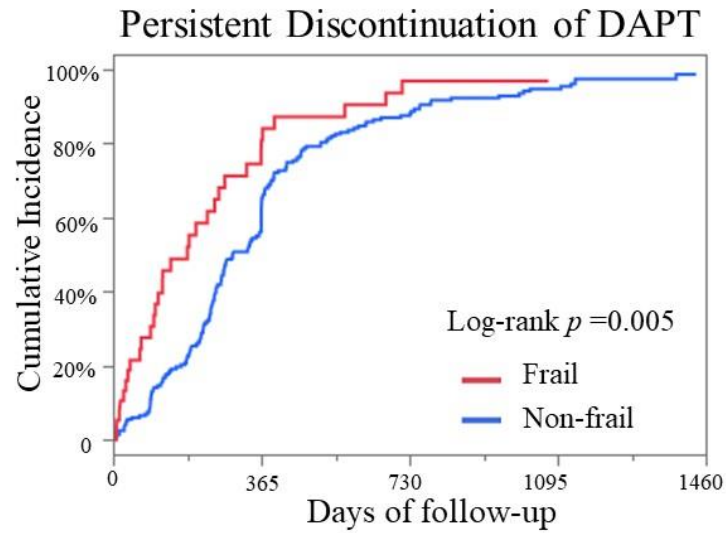
MACE; major adverse cardiovascular event, CFS; clinical frailty scale.

# Causes of all-cause
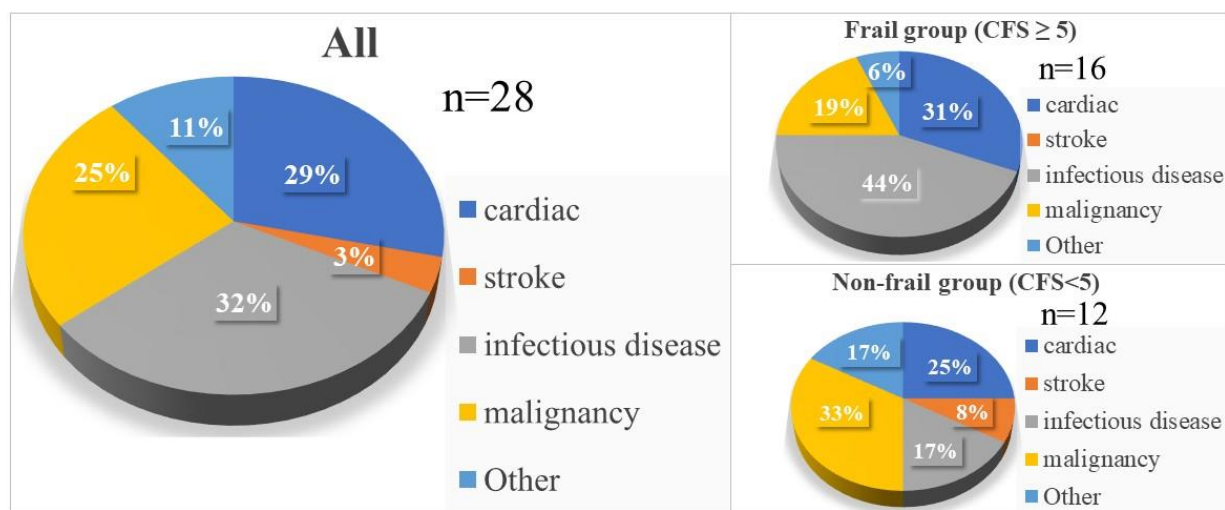


**Online Figure 3.** Cause of all-cause death between the two groups, the frail group (CFS ≥ 5) and

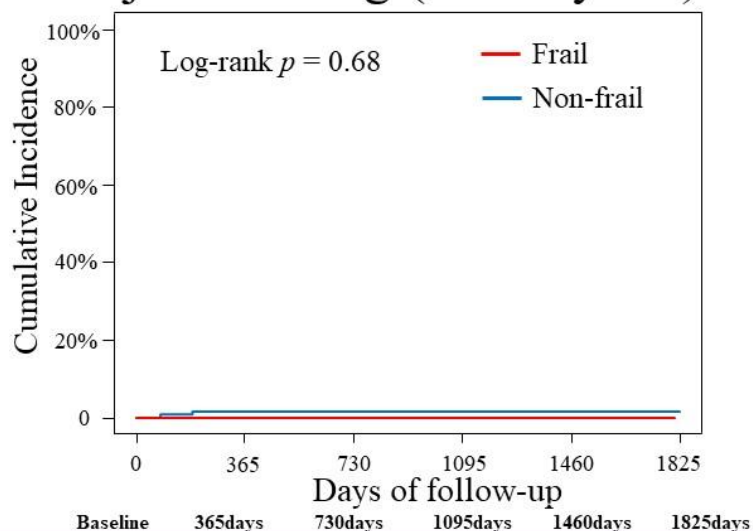the non-frail group (CFS < 5).

CFS; clinical frailty scale.

## Persistent Discontinuation of DAPT



| | Baseline | 365days | 730days | 1095days | 1460days |
|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | |
| No patients with discontinuation | | 26 | 32 | | |
| No patients at risk | 38 | 8 | 1 | | |
| Cumulative incidence | | 77.6% | 96.8% | | |
| **Non-frail (CFS < 5)** | | | | | |
| No patients with discontinuation | | 109 | 167 | 179 | |
| No patients at risk | 201 | 82 | 22 | 8 | |
| Cumulative incidence | | 56.1% | 87.6% | 94.8% | |

**Online Figure 4.** Kaplan–Meier analysis for the persistent discontinuation of DAPT between the

two groups, the frail group (CFS ≥ 5) and the non-frail group (CFS < 5).

DAPT; Dual Antiplatelet therapy, CFS; clinical frailty scale.
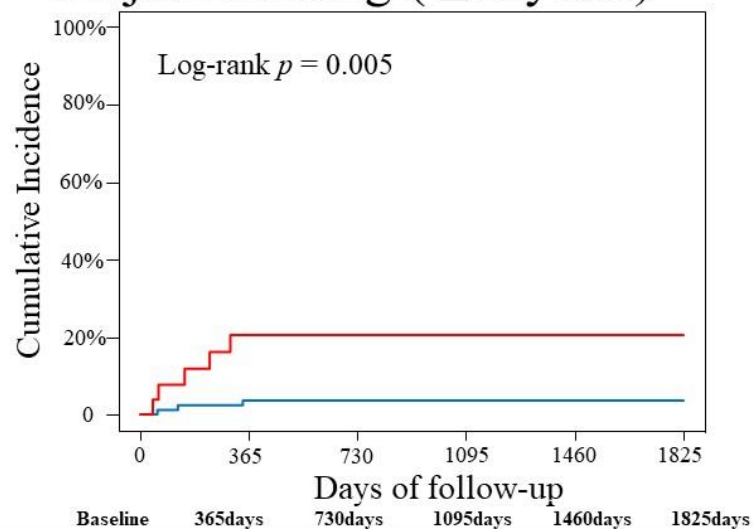
# a                    Major Bleeding (65–74 years)



| | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events | | 0 | 0 | 0 | 0 | |
| No patients at risk | 11 | 9 | 3 | 2 | 2 | |
| Cumulative incidence | | 0.0% | 0.0% | 0.0% | 0.0% | |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events | | 2 | 2 | 2 | 2 | 2 |
| No patients at risk | 119 | 116 | 78 | 48 | 21 | 4 |
| Cumulative incidence | | 1.7% | 1.7% | 1.7% | 1.7% | 1.7% |

# b                    Major Bleeding (≥75years)



| | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events | | 5 | 5 | 5 | 5 | 5 |
| No patients at risk | 27 | 18 | 13 | 7 | 3 | 1 |
| Cumulative incidence | | 20.5% | 20.5% | 20.5% | 20.5% | 20.5% |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events | | 3 | 3 | 3 | 3 | 3 |
| No patients at risk | 82 | 77 | 54 | 32 | 11 | 1 |
| Cumulative incidence | | 3.7% | 3.7% | 3.7% | 3.7% | 3.7% |

## c  Myocardial infarction and ischemic stroke (65–74 years)



| | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events | | 0 | 0 | 0 | 0 | |
| No patients at risk | 11 | 9 | 3 | 2 | 2 | |
| Cumulative incidence | | 0.0% | 0.0% | 0.0% | 0.0% | |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events | | 1 | 2 | 3 | 3 | 3 |
| No patients at risk | 119 | 117 | 78 | 47 | 21 | 4 |
| Cumulative incidence | | 0.9% | 1.8% | 3.2% | 3.2% | 3.2% |

## d  Myocardial infarction and ischemic stroke ( ≥75years)
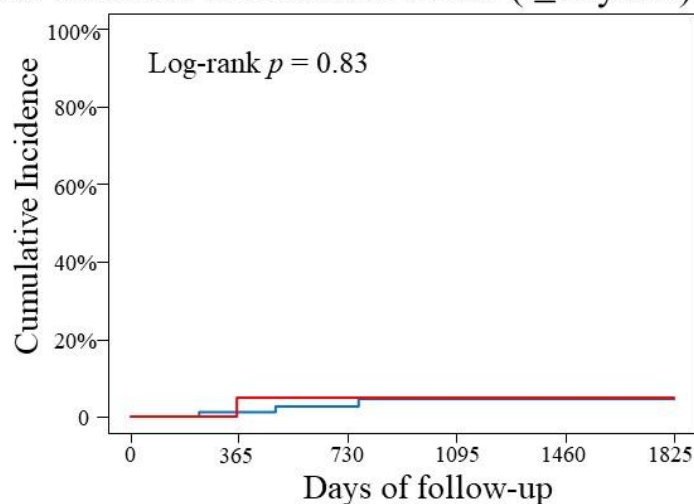


| | Baseline | 365days | 730days | 1095days | 1460days | 1825days |
|---|---|---|---|---|---|---|
| **Frail (CFS ≥ 5)** | | | | | | |
| No patients with events | | 1 | 1 | 1 | 1 | 1 |
| No patients at risk | 27 | 20 | 13 | 7 | 3 | 1 |
| Cumulative incidence | | 4.8% | 4.8% | 4.8% | 4.8% | 4.8% |
| **Non-frail (CFS < 5)** | | | | | | |
| No patients with events | | 1 | 2 | 3 | 3 | 3 |
| No patients at risk | 82 | 77 | 54 | 31 | 11 | 1 |
| Cumulative incidence | | 1.2% | 2.6% | 4.5% | 4.5% | 4.5% |

**Online Figure 5.** Kaplan–Meier analysis of the cumulative incidence of the secondary outcome

measure between the two groups, the frail group (CFS ≥ 5), and the non-frail (CFS < 5).

(a) The secondary bleeding outcome measure between the two groups (in patients 65–74 years old).

(b) The secondary bleeding outcome measure between the two groups (in patients ≥ 75 years old).

(c) The secondary ischemic outcome measure between the two groups (in patients 65–74 years old).

(d) The secondary ischemic outcome measure between the two groups (in patients ≥ 75 years old).

CFS; clinical frailty scale.