

Supplementary data

Supplementary Table 1. Detailed patient characteristics.

| | Without ¹ LVOT calcification (n=358) | With ² LVOT calcification (n=358) | <i>p</i> -value |
|---|--|---|-----------------|
| MSCT baseline parameters regarding location of calcification in LVOT | | | |
| Calcium volume LVOT total, mm ³ | 0 (0.0, 0.6) | 49.1 (21.8, 97.1) | <0.001 |
| Calcium volume LCC, mm ³ | 0 (0.0, 0.0) | 14.7 (1.6, 48.9) | <0.001 |
| Calcium volume NCC, mm ³ | 0 (0.0, 0.0) | 10.6 (0, 41.3) | <0.001 |
| Calcium volume RCC, mm ³ | 0 (0.0, 0.0) | 0 (0, 7.9) | <0.001 |
| Maximum calcium volume under LCC | - | 177 (49.4) | - |
| Maximum calcium volume under NCC | - | 40 (11.1) | - |
| Maximum calcium volume under RCC | - | 141 (39.4) | - |
| Okuno mild ³ | - | 10 (11.6) | - |
| Okuno moderate ⁴ | - | 54 (62.8) | - |
| Okuno severe ⁵ | - | 22 (25.6) | - |
| Outcome and mortality | | | |
| Stroke timepoint, d | 2.9±2.6 | 2.7±4.3 | 0.91 |
| Stroke <48 hrs | 5 (55.6) | 14 (66.7) | 0.87 |
| Stroke >48 hrs | 4 (44.4) | 7 (33.3) | 0.87 |
| 30-day mortality | 10 (2.8) | 22 (6.1) | 0.05 |
| 1-year mortality | 33 (9.2) | 60 (16.8) | 0.004 |
| Mortality during whole follow-up | 58 (16.2) | 83 (23.2) | 0.02 |
| Follow-up period, yrs | 1.03 (0.94, 1.13) | 1.02 (0.91, 1.10) | - |
| <p>¹ Without ≤10 mm³ LVOT calcium volume. ² With >10 mm³ LVOT calcium volume. ³ Okuno et al [11], mild: 1 nodule of calcification extending <5 mm in any dimension and covering <10% of the perimeter of the LVOT; ⁴ Okuno moderate: 2 nodules of calcification or 1 extending >5 mm in any direction or covering >10% of the perimeter of the LVOT; ⁵ Okuno severe: multiple nodules of calcification of single focus extending >10 mm in length or covering >20% of the perimeter of the LVOT.</p> <p>Values are mean±SD, n (%) unless otherwise indicated or median (interquartile range). LCC: left coronary cusp; MSCT: multislice computed tomography; NCC: non-coronary cusp; RCC: right coronary cusp</p> | | | |

Supplementary Table 2. Categorisation of LVOT calcification: subgroup analyses of patients with LVOT calcium volume >10 mm³.

| All-cause mortality and stroke | | | |
|--|---|------------------------------------|-----------------|
| | Patients alive and no stroke (n=320) | Patients dead or stroke (n=38) | <i>p</i> -value |
| Quantitative calcium scoring by MSCT | | | |
| Calcium volume LVOT total, mm³ | 47.9 (21.4, 96.6) | 54.2 (33.4, 109.4) | 0.30 |
| Calcium volume LCC, mm³ | 14.0 (1.6, 47.6) | 24.5 (3.0, 60.8) | 0.39 |
| Calcium volume NCC, mm³ | 9.7 (0, 39.6) | 23.3 (0, 48.5) | 0.33 |
| Calcium volume RCC, mm³ | 0 (0, 8.3) | 0 (0, 2.5) | 0.33 |
| | Patients alive and no stroke (n= 75) | Patients dead or stroke (n= 11) | <i>p</i> -value |
| Classification by Okuno et al¹ | | | |
| Mild² | 9 (12.0) | 1 (9.1) | 1.00 |
| Moderate³ | 46 (61.3) | 8 (72.7) | 0.69 |
| Severe⁴ | 20 (26.7) | 2 (18.2) | 0.82 |
| Macroscopic aspects | | | |
| Coverage of perimeter of LVOT (%) | 9.0 (6.5, 17.7) | 12.1 (10.1, 16.1) | 0.23 |
| Number of nodules | 1 (1.0, 2.0) | 2.0 (1.0, 2.0) | 0.21 |
| Nodule length, mm | 6.3 (3.8, 9.9) | 3.1 (2.4, 8.8) | 0.11 |
| Intraluminal protrusion of nodule, mm | 2.5 (1.9, 3.3) | 2.5 (1.8, 3.1) | 0.72 |
| VARC-3 early safety⁵ | | | |
| | Endpoint reached (n=245) | Endpoint not reached (n=110) | <i>p</i> -value |
| Quantitative calcium scoring by MSCT | | | |
| Calcium volume LVOT total, mm³ | 47.0 (20.9, 97.0) | 54.0 (23.9, 97.9) | 0.58 |
| Calcium volume LCC, mm³ | 15.0 (1.9, 47.5) | 13.0 (1.0, 52.8) | 0.71 |
| Calcium volume NCC, mm³ | 9.0 (0.0, 34.4) | 16.1 (0, 49.1) | 0.27 |
| Calcium volume RCC, mm³ | 0 (0.0, 10.0) | 0 (0, 2.4) | 0.08 |
| | Endpoint reached (n=60) | Endpoint not reached (n=24) | <i>p</i> -value |
| Classification by Okuno et al¹ | | | |

| | | | |
|--|--------------------------|-----------------------------|-----------------|
| Mild² | 6 (10.0) | 3 (12.5) | 1.00 |
| Moderate³ | 36 (60.0) | 17 (70.4) | 0.50 |
| Severe⁴ | 18 (30.0) | 4 (16.7) | 0.33 |
| Macroscopic aspects | | | |
| Coverage of perimeter of LVOT, % | 10.8 (6.7, 18.7) | 10.6 (6.8, 14.3) | 0.91 |
| Number of nodules | 1 (1.0, 2.0) | 1 (1.0, 2.0) | 0.44 |
| Nodule length, mm | 6.5 (4.0, 10.1) | 5.3 (2.4, 9.1) | 0.15 |
| Intraluminal protrusion of nodule, mm | 2.5 (2.0, 3.3) | 2.8 (1.8, 3.6) | 0.55 |
| VARC-3 device success⁶ | | | |
| | Endpoint reached (n=251) | Endpoint not reached (n=92) | <i>p</i> -value |
| Quantitative calcium scoring by MSCT | | | |
| Calcium volume LVOT total, mm³ | 44.9 (20.3, 88.1) | 67.4 (31.7, 117.1) | <0.01 |
| Calcium volume LCC, mm³ | 14.5 (1.8, 47.4) | 13.0 (1.2, 59.4) | 0.77 |
| Calcium volume NCC, mm³ | 5.7 (0, 32.5) | 23.1 (1.1, 54.6) | <0.01 |
| Calcium volume RCC, mm³ | 0 (0, 4.5) | 0 (0, 10.0) | 0.13 |
| | Endpoint reached (n=61) | Endpoint not reached (n=18) | <i>p</i> -value |
| Classification by Okuno et al¹ | | | |
| Mild² | 7 (11.5) | 2 (11.1) | 1.00 |
| Moderate³ | 38 (62.3) | 11 (61.1) | 1.00 |
| Severe⁴ | 16 (26.2) | 5 (27.8) | 1.00 |
| Macroscopic aspects | | | |
| Coverage of perimeter of LVOT, % | 10.3 (6.6, 17.6) | 11.4 (7.3, 21.1) | 0.45 |
| Number of nodules | 1.0 (1.0, 2.0) | 1.0 (1.0, 2.0) | 0.68 |
| Nodule length, mm | 6.3 (3.7, 10.4) | 6.9 (2.5, 9.9) | 0.67 |
| Intraluminal protrusion of nodule, mm | 2.5 (1.9, 3.3) | 2.5 (1.9, 2.8) | 0.58 |
| ¹ Okuno et al [11]. ² mild: 1 nodule of calcification extending <5 mm in any dimension and covering <10% of the perimeter of the LVOT. ³ moderate: 2 nodules of calcification or 1 extending >5 mm in any direction or covering >10% of the perimeter of the LVOT. ⁴ severe: multiple nodules of calcification of single focus extending >10 mm in length or covering >20% of the perimeter of the LVOT. ⁵ VARC-3 early safety endpoint after 30 days (positive endpoint, see Methods). ⁶ VARC-3 device success endpoint after 30 days (positive endpoint, see Methods). Values are mean±SD, n (%) unless otherwise indicated or median (interquartile range). LCC: left coronary cusp; MSCT: multislice computed tomography; NCC: non-coronary cusp; RCC: right coronary cusp | | | |