**Fig. S1** Workflow of the study
Fig. S2 Platelet counts in Portico and Evolut recipients (prospective study) Values were taken at hospitalization (T0), 2-4 h after implantation (T1) and after 1, 2, and 3 days from implantation (T2, T3, T4). Graphs in a and b show the platelet count from 20 Portico patients (a, N=20 biological replicates) and 24 patients implanted with Evolut (b, N=24 biological replicates); each dot corresponds to a single observation/patient (N=1 technical replicates) taken at each indicated time (values were normalized to 100 [T0]). In each graph, Dunnett's multiple comparisons test was used to assess changes (*) vs T0 of platelet counts after TAVI. (c) Curves of platelet counts in patients implanted with Portico and Evolut. Plotted values are means of values represented in (a, Portico, N=20 biological replicates) and (b, Evolut N=24 biological replicates). Comparison between values was done at each T0-T4 time, using Student T test.
**Fig. S3** Flow cytometry assessment of platelet damage and CD36⁺ monocytes in a patient implanted with Portico In the upper histograms, CD61<sup>dim</sup>/CD42b<sup>dim</sup> (gated platelets) are consistent with injured platelets that increase after TAVI. Similarly, annexin V⁺ platelets (intermediate histograms) and CD36⁺ monocytes (lower histograms) progressively increase after TAVI.
No significant variations in IFN-γ, IL-2, IL-4, TNF-α, GM-CSF levels in patient sera before and after TAVI Cytokine levels in sera of patients implanted with Portico, Evolut and wPortico. Plotted values, for each curve, are means of biological replicates (Portico, N=7 biological replicates; Evolut, N=7 biological replicates; wPortico, N=6 biological replicates). Biological replicates, in turn, were means of technical duplicates from a single serum sample. Values are expressed as fold increase compared to the baseline (T0). In each graph, Dunnett’s multiple comparisons test was performed to compare T1-T3 values vs T0. No significance was calculated.
**Fig. S5** Comparison of IL-6 levels in TAVI recipients. IL-6 levels, measured at T0-T3, are represented as box plots of biological replicates from 7 #P, 7 #E, and 6 #wP. Each biological replicate, in turn, was the mean of technical duplicates from a single serum sample. Values are expressed as fold increase compared to the baseline (T0). Student T test served for comparison between groups.
**Table S1. Baseline and procedural features of patients treated between February 2017 and September 2019 divided according to the implanted device.**

|                                     | Overall (n=174) | #E (n=98) | #P (n=76) | P value |
|-------------------------------------|----------------|-----------|-----------|---------|
| **Baseline characteristics**        |                |           |           |         |
| Age, years                          | 81.6±5.5       | 81.6±5.9  | 81.7±4.9  | 0.905   |
| Female sex                          | 106 (60.9%)    | 57 (58.2%)| 49 (64.5%)| 0.397   |
| Arterial hypertension               | 135 (77.6%)    | 75 (76.5%)| 60 (78.9%)| 0.705   |
| Diabetes mellitus                   | 39 (22.4%)     | 21 (21.4%)| 18 (23.7%)| 0.723   |
| Atrial fibrillation                 | 30 (19.2%)     | 14 (17.5%)| 16 (21.1%)| 0.685   |
| eGFR, mL/min                        | 64.3±20.0      | 66.4±20.7 | 61.5±18.8 | 0.110   |
| Prior aortic valvuloplasty          | 8 (4.6%)       | 5 (5.1%)  | 3 (3.9%)  | 1.000   |
| Severe chronic kidney disease*      | 32 (18.4%)     | 21 (21.4%)| 11 (14.5%)| 0.240   |
| Chronic obstructive pulmonary disease| 48 (27.6%)    | 29 (29.6%)| 19 (25.0%)| 0.501   |
| Left ventricular ejection fraction, %| 51.3±8.3     | 50.9±8.4  | 51.9±8.1  | 0.439   |
| Mean aortic gradient, mmHg          | 52.4±18.0      | 52.7±19.8 | 52.0±15.5 | 0.805   |
| Peak velocity, cm/m²                | 4.6±0.6        | 4.6±0.7   | 4.6±0.6   | 0.848   |
| **Baseline therapy**                |                |           |           |         |
| Aspirin                             | 82 (60.7%)     | 31 (54.4%)| 51 (65.4%)| 0.215   |
| Clopidogrel                         | 40 (29.6%)     | 16 (28.1%)| 24 (30.8%)| 0.849   |
| Warfarin                            | 3 (2.2%)       | 1 (1.8%)  | 2 (2.6%)  | 1.000   |
| Novel oral anticoagulant            | 23 (17.0%)     | 12 (21.1%)| 11 (14.1%)| 0.356   |
| Dual antiplatelet therapy           | 32 (23.7%)     | 13 (22.8%)| 19 (24.4%)| 1.000   |
| Single antiplatelet agent plus anticoagulant | 5 (3.7%) | 2 (3.5%) | 3 (3.9%) | 1.000   |
| Triple antithrombotic therapy       | 0              | 0         | 0         | 1.000   |
| **Procedural features**             |                |           |           |         |
| Femoral access                      | 168 (96.6%)    | 95 (96.9%)| 73 (96.1%)| 0.751   |
| Closure device use                  | 169 (97.1%)    | 97 (99.0%)| 72 (94.7%)| 0.097   |
| Postdilation                        | 93 (53.4%)     | 57 (58.2%)| 36 (47.4%)| 0.157   |
| Postprocedural paravalvular regurgitation** | 0.137 |           |           |         |
| None                                | 79/141 (56.0%) | 44/80 (55.0%) | 35/61 (57.4%) | 0.778   |
| Mild                                | 57/141 (40.4%) | 31/80 (38.8%) | 26/61 (42.6%) | 0.642   |
| Moderate                            | 5/141 (3.5%)   | 5/80 (6.3%) | 0/61 (0.0%) | 0.069   |
| **Discharge features**              |                |           |           |         |
| Aspirin                             | 138 (85.7%)    | 66 (80.5%)| 72 (91.1%)| 0.071   |
| Treatment                                      | Portico (%) | Evolut (%) | Portico-Evolut | p-value |
|------------------------------------------------|--------------|------------|----------------|---------|
| Clopidogrel                                    | 118 (73.3%)  | 62 (75.6%) | 56 (70.9%)     | 0.594   |
| Warfarin                                       | 13 (8.1%)    | 4 (4.9%)   | 9 (11.4%)      | 0.155   |
| Novel oral anticoagulant                       | 28 (17.4%)   | 15 (18.3%) | 13 (16.5%)     | 0.837   |
| Dual antiplatelet therapy                      | 106 (65.8%)  | 53 (64.6%) | 53 (67.1%)     | 0.868   |
| Single antiplatelet agent plus anticoagulant   | 32 (19.9%)   | 13 (15.9%) | 19 (24.1%)     | 0.237   |
| Triple antithrombotic therapy                  | 2 (1.1%)     | 1 (1.0%)   | 1 (1.3%)       | 1.000   |
| Paravalvular regurgitation§                    |              |            |                | 0.591   |
| None                                           | 103/157 (65.6%) | 51/81 (63.0%) | 52/76 (68.4%) | 0.472   |
| Mild                                           | 49/157 (31.2%) | 28/81 (34.6%) | 21/76 (27.6%) | 0.349   |
| Moderate                                       | 2/157 (3.2%) | 2/81 (2.5%) | 3/76 (3.9%)    | 0.674   |

Values are expressed as mean±SD or n (%).

--#P= Portico recipients; #E= Evolut recipients.
eGFR= Estimated glomerular filtration rate.
*defined as eGFR<30 mL/min.; **data available for 141 patients; §data available for 157 patients.
| Baseline characteristics | Overall (n=64) | #E (n=24) | #P (n=20) | #wP (n=20) | P value |
|--------------------------|---------------|-----------|-----------|-------------|---------|
| Age, years               | 80.9±5.3      | 80.3±5.3  | 82.0±5.6  | 80.5±6.4    | 0.561   |
| Female sex               | 41 (64.1%)    | 15 (62.5%)| 14 (70.0%)| 12 (60.0%)  | 0.789   |
| Arterial hypertension    | 51 (79.7%)    | 19 (79.2%)| 17 (85.0%)| 15 (75.0%)  | 0.732   |
| Diabetes mellitus        | 17 (26.%)     | 6 (25.0%) | 5 (25.0%) | 6 (30.0%)   | 0.916   |
| Atrial fibrillation      | 17 (27.4%)    | 7 (31.8%) | 7 (35.0%) | 3 (15.0%)   | 0.354   |
| eGFR, mL/min             | 68.3±22.2     | 70.4±21.2 | 63.1±21.4 | 71.1±24.5   | 0.456   |
| Prior aortic valvuloplasty | 2 (3.1%)   | 0 (0.0%)  | 2 (10.0%) | 0 (0.0%)    | 0.103   |
| Severe chronic kidney disease* | 6 (9.4%)  | 2 (8.3%)  | 3 (15.0%) | 1 (5.0%)    | 0.542   |
| Chronic obstructive pulmonary disease | 18 (28.1%) | 6 (25.0%) | 4 (20.0%) | 8 (40.0%)   | 0.339   |
| Left ventricular ejection fraction, % | 51.5±6.8 | 51.2±7.6 | 51.8±7.1 | 51.8±5.8    | 0.948   |
| Mean aortic gradient, mmHg | 52.4±17.3   | 47.2±11.4 | 51.6±15.2 | 59.5±22.7   | 0.060   |
| Peak velocity, cm/m²      | 4.6±0.7       | 4.4±0.6   | 4.5±0.4   | 5.0±0.9     | 0.283   |
| Baseline therapy          |               |           |           |             |         |
| Aspirin                   | 40 (67.8%)    | 15 (68.2%)| 13 (65.0%)| 12 (70.6%)  | 1.000   |
| Clopidogrel               | 21 (35.6%)    | 8 (36.4%) | 5 (25.0%) | 8 (47.1%)   | 0.360   |
| Warfarin                  | 2 (3.4%)      | 2 (9.1%)  | 0         | 0           | 0.326   |
| Novel oral anticoagulant  | 15 (25.4%)    | 5 (22.7%) | 7 (35.0%) | 3 (17.7%)   | 0.488   |
| Dual antiplatelet therapy | 18 (30.5%)    | 8 (36.4%) | 4 (20.0%) | 6 (35.3%)   | 0.464   |
| Single antiplatelet agent plus anticoagulant | 5 (8.5%) | 2 (9.1%) | 2 (10.0%) | 1 (5.9%)    | 1.000   |
| Triple antithrombotic therapy | 2 (3.4%) | 1 (4.6%) | 1 (5.0%) | 0           | 1.000   |
| Procedural features       |               |           |           |             |         |
| Femoral access            | 63 (98.4%)    | 23 (95.8%)| 20 (100.0%)| 20 (100.0%) | 0.429   |
| Closure device use        | 60 (93.8%)    | 23 (95.8%)| 20 (100.0%)| 17 (85.0%)  | 0.127   |
| Postdilation              | 37 (57.8%)    | 13 (54.2%)| 11 (55.0%)| 13 (65.0%)  | 0.734   |
| Postprocedural paravalvular regurgitation** |           |           |           |             | 0.873   |
| None                      | 32/42 (76.2%) | 11/15 (73.3%)| 12/16 (75.0%)| 9/11 (81.8%)|         |
| Mild                      | 10/42 (23.8%) | 4/15 (26.7%)| 4/16 (25.0%)| 2/11 (18.2%)|         |
| Discharge features        |               |           |           |             |         |
| Aspirin                   | 59 (93.7%)    | 22 (91.7%)| 18 (94.7%)| 19 (95.0%)  | 1.000   |
| Treatment                              | Patients 1 | Patients 2 | Patients 3 | Patients 4 | p-value |
|----------------------------------------|------------|------------|------------|------------|---------|
| Clopidogrel                            | 45 (71.4%) | 16 (66.7%) | 15 (79.0%) | 14 (70.0%) | 0.731   |
| Warfarin                               | 5 (7.9%)   | 4 (16.7%)  | 1 (5.3%)   | 0           | 0.146   |
| Novel oral anticoagulant               | 16 (25.4%) | 6 (25.0%)  | 6 (31.6%)  | 4 (20.0%)  | 0.668   |
| Dual antiplatelet therapy              | 42 (66.7%) | 14 (58.3%) | 14 (73.7%) | 14 (70.0%) | 0.595   |
| Single antiplatelet agent plus anticoagulant | 21 (33.3%) | 10 (41.7%) | 7 (36.8%)  | 4 (20.0%)  | 0.316   |
| Triple antithrombotic therapy          | 4 (6.3%)   | 1 (4.2%)   | 3 (15.0%)  | 0           | 0.190   |
| Paravalvular regurgitation             |            |            |            |            | 0.802   |
| None                                   | 38/63 (60.3%) | 16/24 (66.7%) | 11/19 (57.9%) | 11/20 (55.0%) | 0.709   |
| Mild                                   | 23/63 (36.5%) | 8/24 (33.3%) | 7/19 (36.8%) | 8/20 (40.0%) | 0.900   |
| Moderate                               | 2/63 (3.2%) | 0/24 (0.0%) | 1/19 (5.3%) | 1/20 (5.0%) | 0.273   |

Values are expressed as mean±SD or n (%).

nP= Portico recipients; #P= Portico with extra-rinsing recipients; #E= Evolut recipients.
eGFR= Estimated glomerular filtration rate; **data available for 42 patients; §data available for 63 patients.
**Table S3. Comparative overview of selected transcatheter aortic valve systems.**

|                  | EVOLUT PRO Medtronic | EVOLUT PRO+ Medtronic | EVOLUT R Medtronic | PORTICO Abbott Structural Heart |
|------------------|----------------------|-----------------------|--------------------|---------------------------------|
| **Delivery**     | Self-expanding        | Self-expanding        | Self-expanding     | Self-expanding                  |
| **Design**       | Supra-annular valve  | Supra-annular valve  | Supra-annular valve| Intra-annular valve             |
| **Frame**        | Nitinol               | Nitinol               | Nitinol            | Nitinol                         |
| **Leaflets**     | Porcine pericardium  | Porcine pericardium  | Porcine pericardium| Bovine pericardium              |
| **Sheath size**  | 16 Fr (16 Fr for 34 mm prosthesis) | 14 Fr (16 Fr for 34 mm prosthesis) | 14 Fr (16 Fr for 34 mm prosthesis) | 18/19 Fr (14/15 Fr with FlexNav system) |
| **Prosthesis size** | 23-26-29 mm           | 23-26-29-34 mm        | 23-26-29-34 mm     | 23-25-27-29 mm                  |
| **Annular diameter** | From 18 to 26 mm     | From 18 to 30 mm      | From 18 to 30 mm   | From 19 to 27 mm                |
| **Storage solution** | Glutaraldehyde       | Glutaraldehyde       | Glutaraldehyde     | Formaldehyde                    |
| **Recapturable** | Yes                  | Yes                   | Yes                | Yes                             |
| **Repositionable** | Yes                  | Yes                   | Yes                | Yes                             |
| **Retrievable**  | Yes                  | Yes                   | Yes                | Yes                             |
| **Comments**     | Compared with Evolut R, an outer pericardial skirt was added to reduce paravalvular leak | Evolut Pro+ is compatible with smaller sheaths and offers a 34-mm valve with outer pericardial sheath | Large cell geometry and intra-annular leaflet position preserve coronary access, provides early valve function and hemodynamic stability throughout the procedure. |