Supplemental Methods

SIRS criteria

The SIRS criteria were defined according to existing guidelines **(1)**, as assessed during the first 48 hours post TAVI by monitoring at the intermediate care unit: 1) temperature <36 or >38°C; 2) heart rate (HR) >90 beats per minute; 3) respiratory rate >20 per minute (or pCO2 < 32 mmHg); 4) white blood cell (WBC) count <4 or >12 x 10^9/L. To avoid the influence of a potentially misleading, isolated vital sign, we considered HR and respiratory rate positive only if two or more recordings exceeded the predefined threshold. While the conventional definition of SIRS implies the occurrence of two or more criteria, we employed stricter SIRS definition (with at least three criteria being met, and hence indicative of a more marked systemic inflammatory response), as described previously **(2)**.

Enumeration of major leukocyte subsets

Absolute counts of granulocytes, monocytes ($CD14^+$), total lymphocytes, $CD3^+$ lymphocytes and their major subsets, $CD4^+$ and $CD8^+$ T cells, were determined in 120 patients using a four-color BD TruCount flow cytometric assay (BD Biosciences). An extended, 6-color variant (with inclusion of anti-human CD16 and CD66b antibodies) of the TruCount Assay, allowing discrimination of monocyte (classical, intermediate, non-classical) and granulocyte (neutrophils, eosinophils) subsets was measured in 101 (out of 129) consecutive patients as described before **(3)**. Please see the **Supplemental Tables 1 and 2** for further antibody and compensation setting details.

Enumeration of specific T-cell subpopulations

Briefly, 100-µl aliquots of whole blood were stained with a cocktail of the following (anti-human) conjugated monoclonal antibodies: CD45-BV510, CD3-BV421, CD4-FITC, CD8-PerCp-Cy5.5, CD194(CCR4)-PE-Cy7, CD196(CCR6)-AlexaFluor647, CD183(CXCR3)-APC-Cy7 (all BioLegend), and CCR10-PE (BD Biosciences) for 'CD4 Panel 1'; and CD45-BV510, CD3-BV421, CD4-PE, CD25-AlexaFluor488, and CD127-AlexaFluor647 for 'CD4 Panel 2'. The samples were then lysed using Pharm Lyse (BD Biosciences) according to the manufacturer's instructions, followed by wash steps. Analysis was performed using a BD FACSCanto II machine with FACSDiva software (BD Biosciences). T cell gating and subclassification was performed based on the established models **(4)**, by dividing $CD4^+$ T cells into Th1 ($CCR4^-CCR6^-CCR10^-CXCR3^+$), Th2 ($CCR4^+CCR6^-CCR10^-CXCR3^-$), Th9 ($CCR4^-CCR6^+$), Th17 ($CCR4^+CCR6^+CCR10^-CXCR3^-$), Th22 ($CCR4^+CCR6^+CCR10^+CXCR3^-$), Th17/Th1 ($CCR4^-CCR6^+CCR10^-CXCR3^+$), and Tregs ($CD4^+CD25^+CD127^-$). Cell count for each subset was calculated as the count of the parent population (derived from TruCount assay) multiplied by the percentage of the parent cells within the subset gate. Please see the **Supplemental Tables 3 and 4** for further antibody and compensation setting details.

Serum cytokine measurements

Cytokine concentrations were measured from baseline serum samples (collected before TAVI) available in 80 patients using a flow-bead-based multiplex assay (LEGENDplex™ Human Essential Immune Response Panel, Cat. No. 740930, BioLegend), which allows for simultaneous quantification of 13 key targets essential for immune response, including IL-4, IL-2, CXCL10 (IP-10), IL-1β, TNF-α, CCL2 (MCP-1), IL-17A, IL-6, IL-10, IFN-γ, IL-12p70, CXCL8 (IL-8), and free active TGF-β1. The assay was performed according to manufacturer's

instructions. Shortly, the capture beads were mixed and incubated with diluted serum of patients in 96-V-bottom-plate and incubated for 2 hours at room temperature on a plate shaker. Subsequently, a biotinylated detection antibody cocktail was added and incubated followed by a secondary staining with Streptavidin-phycoerythrin (SA-PE). After a last washing step, bead samples were resuspended in appropriate volume of wash buffer and analysed on a BD LSRFortessa™ X-20 cell analyzer and with LEGENDplex v8.0 software (BioLegend).

Echocardiography and left ventricular remodeling parameter

Transthoracic echocardiography was performed according to the American Society of Echocardiography and the European Association of Echocardiography recommendations **(5)**. Echocardiographic follow-up data were acquired post TAVI from 90 patients (median follow-up: 134 days). Remodeling parameters, such as the end-diastolic septum wall thickness (SWTd), posterior LV wall thickness (PWTd), and the diameter of the left ventricle (LVIDd) were quantified using 2D echo recordings.

LVMi was calculated as LV mass = $0.8\,(1.04\,[\mathrm{LVID}+\mathrm{PWTd}+\mathrm{SWTd}]^3 - [\mathrm{LVID}]^3)+0.6\,\mathrm{g}$

and subsequently indexed to body surface area.

RWT was calculated by dividing the sum of SWTd and PWTd by the LVIDd.

Gradient boosted trees algorithm in the prediction of mortality after TAVI

The classifier was trained to predict one year survival vs non-survival using a reduced set of variables, which were chosen based on the results of the univariate Cox regression model. Variables which were proven to have high or low hazard ratios as well as p-values <0.05 were entered into the model. In order to compensate for the significant class imbalance, a synthetic

minority class oversampling technique (SMOTE) was used. All calculations were performed using Python 3.6 and scikit-learn software package **(6)**. We observed significant variability in the classifier's performance depending on the split of the data into training and test sets. In order to obtain reliable results, we performed random splits 50 times and then averaged the results.

References

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6. Pedregosa F, Varoquaux G, Gramfort A et al. Scikit-learn: Machine learning in Python. Journal of machine learning research. 2011;12:2825-2830.