

## Supplemental Methods

### Fibrosis analysis

Image processing was conducted using Definiens Developer XD<sup>®</sup> object-oriented image analysis software. The process consisted of three steps: automated separation of tissue from glass/background, detection of whitespace within tissue and detection of SAB fibrosis (red) stain. Images were loaded into the software in Baccus native file format. Images were down-sampled to 2.5% and a Gaussian blur with a kernel size of 7x7 was applied. An automated and adaptive threshold was calculated and applied to the image, thereby segmenting the Tissue from the glass slide. The automatic threshold algorithm uses a combination of intensity histogram-based methods and a homogeneity measurement to calculate a threshold which divides the selected set of pixels into two subsets so that heterogeneity is increased to a maximum. The generated classification mask of the tissue region was then overlaid onto a 5x copy of the image. The auto-adaptive threshold was then applied in a 2 stage approach. First, a threshold was calculated for the set of pixels within the tissue region only. The resulting segmentation separated the high intensity, homogeneous whitespace regions from the tissue body. A second threshold was then calculated using the remaining set of pixels in the tissue, segmenting the SAB stain.

**Supplemental Table 1.** Characteristics of patients hospitalized for heart failure (HF) between January, 1986 and January, 2002 who subsequently did or did not have autopsy.

	<b>Autopsy</b>	<b>No Autopsy</b>	<b>p value</b>
n	441	5999	
Age at HF admission	72±15	73±13	0.21
Male	57%	56%	0.69
Creatinine at HF admission	1.5±1.0	1.6±1.0	0.52
Hemoglobin at HF admission	12.2±2.2	12.1±2.1	0.38
Hypertension	59%	54%	0.04
Coronary Disease	65%	57%	0.002
Diabetes	32%	34%	0.38
Atrial Fibrillation	30%	33%	0.15
Ejection fraction at time of HF event			0.57
Ejection fraction <50%, n (%)	170 (39%)	2128 (37%)	
Ejection fraction ≥ 50%, n (%)	158 (36%)	2454 (40%)	
Ejection fraction not measured, n (%)	113 (25%)	1417 (23%)	

**Supplemental Table 2. Characteristics of HFpEF patients according to sex**

	<b>Female</b>	<b>Male</b>	<b>P value</b>
N	62	47	
Age at heart failure event, yrs	75±14	73±13	0.34
Age at death, yrs	78±14	75±12	0.22
Hypertension (%)	73%	81%	0.31
Diabetes mellitus (%)	37%	49%	0.22
Clinical diagnosis of coronary disease	50%	76%	0.005
Ejection fraction at heart failure event, %	60±8	57±9	0.08
<b>Autopsy Findings</b>			
Weight at autopsy, kg	75±30	88±22	0.02
Height at autopsy, cm	161±8	173±9	<0.001
Body mass index at autopsy, kg/m <sup>2</sup>	29±10	29±7	0.76
Body surface area at autopsy, m <sup>2</sup>	1.80±0.36	2.04±0.27	<0.001
Heart weight at autopsy, g	499±138	601±172	0.002
Percent expected heart weight, %	182±45	174±59	0.46
Gross left ventricular hypertrophy	65%	74%	0.26
Gross right ventricular hypertrophy	44%	51%	0.44
Gross infarct (old)	31%	62%	0.001
Gross fibrosis	18%	19%	0.85
Gross infarct (new)	10%	13%	0.61
Left ventricular dilatation	37%	40%	0.72
Right ventricular dilatation	53%	43%	0.27
Atrial dilatation	55%	57%	0.79
Microscopic fibrosis	63%	49%	0.14
Microscopic hypertrophy	32%	30%	0.78
Microscopic infarct	11%	26%	0.053
Coronary disease score	10.0±3.7	12.5±3.2	<0.001
% Fibrosis (WFDM)	12.4±9.6	13.0±7.7	0.77

Abbreviations: WFDM, whole-field digital microscopy