

Table S1. Mean±SD sTfR levels and p-values according to impaired vs preserved submaximal exercise capacity (defined as 6MWT distance <300 meters), and according to impaired vs preserved global QoL (overall summary score of the Minnesota Living with Heart Failure Questionnaire ≥upper tertile)

	Submaximal exercise capacity		
	Preserved submaximal exercise capacity (n=111)	Impaired exercise capacity (n=91)	P-value
sTfR levels, mean (SD)	1.32 (0.61)	1.53 (0.72)	p=0.030
	Quality of Life		
	Preserved QoL (n=137)	Impaired QoL (n=69)	P-value
Overall score			
sTfR levels, mean (SD)	1.38 (0.61)	1.53 (0.77)	p=0.151
Physical dimension			
sTfR levels, mean (SD)	1.43 (0.74)	1.44 (0.42)	p=0.846
Emotional dimension			
sTfR levels, mean (SD)	1.37 (0.61)	1.55 (0.78)	p=0.058
Social dimension			
sTfR levels, mean (SD)	1.37 (0.60)	1.55 (0.79)	p=0.067

Table S2. Adjusted GAM models to explore the parametric and non-parametric associations between sTfR and submaximal exercise capacity (distance walked in the 6MWT in meters) and QoL scores.

	Log (sTfR)	
Dependent variables	Parametric p-value	Non-parametric p-value
Submaximal exercise capacity		
Distance walked in the 6 minutes walking test (meters)	<0.001	0.138
Quality of Life measured with the Minnesota Living with HF Questionnaire		
Overall summary score (Global QoL)	0.006	0.615
Physical dimension	0.002	0.398
Emotional dimension	0.061	0.596
Social dimension	0.418	0.548

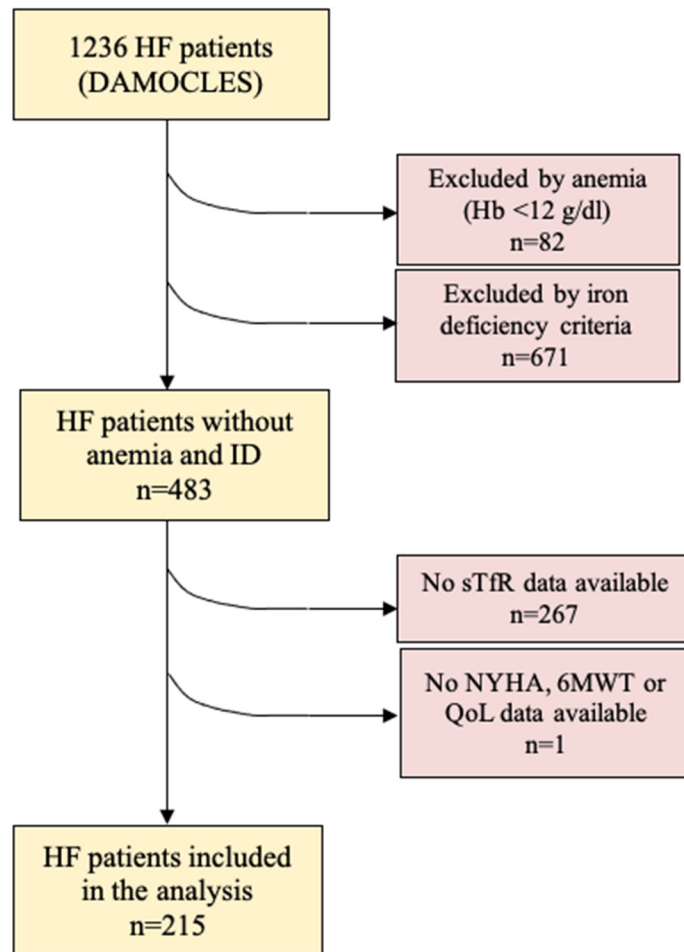
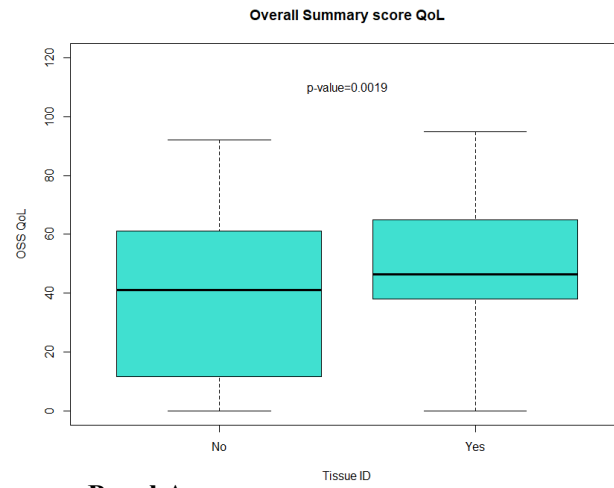
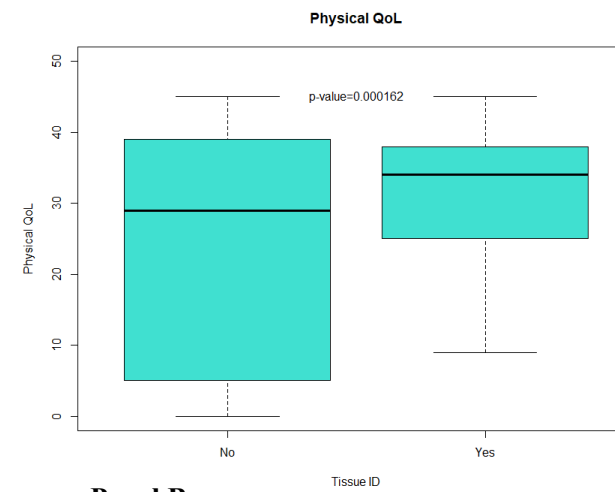


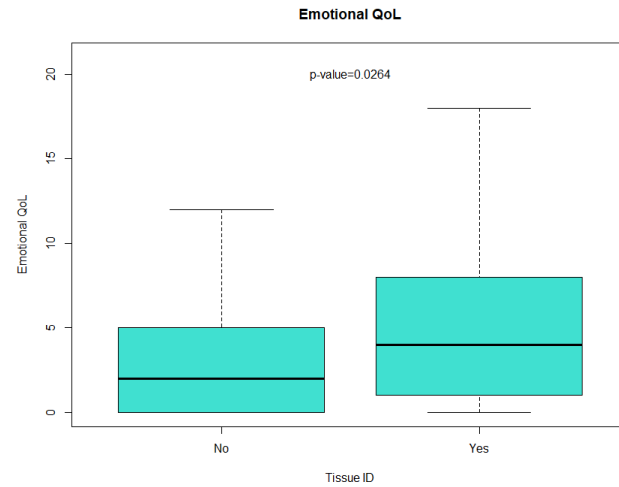
Figure S1. Patient flow diagram of the enrolment in the DAMOCLES study for present analysis.



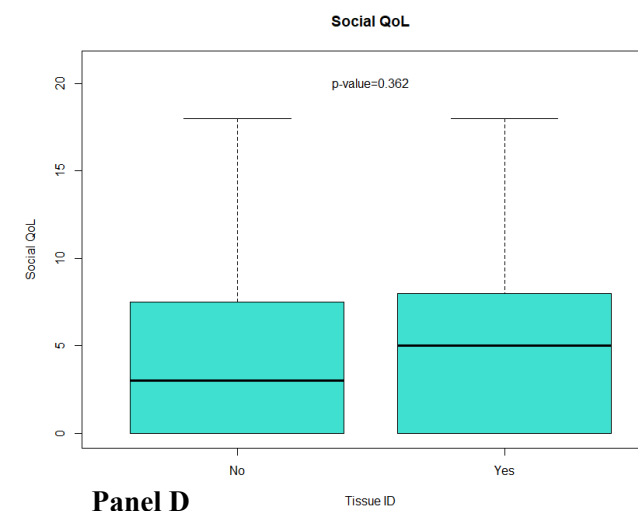
Panel A



Panel B



Panel C



Panel D

Figure S2. Panel A. Boxplots showing the mean and standard deviation of the overall summary score (**Panel A**) and the physical (**Panel B**), emotional (**Panel C**) and social (**Panel D**) dimension scores of the Minnesota Living with Heart Failure Questionnaire (higher scores meaning worse global QoL) according to the presence of tissue ID (Tissue ID [+]) or absence (Tissue ID [-]).

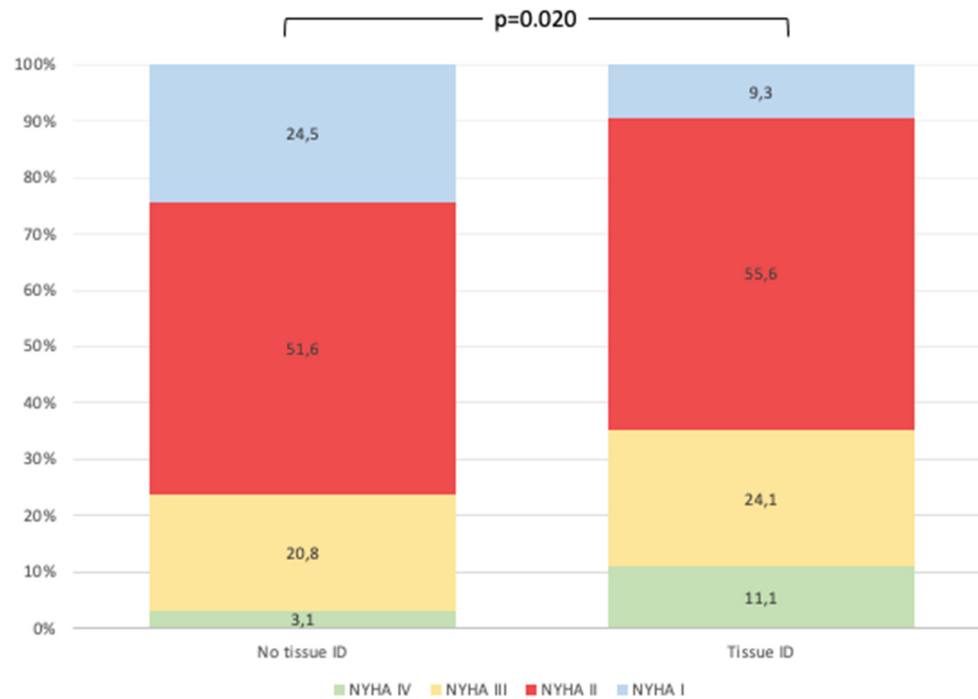


Figure S3. Distribution of patients according to NYHA and impairment in submaximal exercise capacity (defined as 6MWT distance<300 meters) according to tissue ID status.