

**SUPPLEMENTARY DATA**

**Table 1 of the supplementary data**

Immunoassays used in the study

Abbreviation	Description	Platform	Vendor
CMIA	Chemiluminescent microparticle immunoassay	ARCHITECH	Abbott Diagnostics
ACMIA	Affinity column-mediated immunoassay	DIMENSION	Siemens Healthineers
MEIA	Microparticle enzyme immunoassay	DIMENSION	Abbott Diagnostics
FPIA	Fluorescence polyclonal immunoassay	TDX	Abbott Diagnostics
EMIT	Enzyme multiplied immunoassay	VIVA-E	Dade-Behring Inc

**Table 2 of the supplementary data**

Reported variabilities of the immunoassays used in the study

Method	Drug	Variability	Reference
CMIA	Cyclosporin	< 9%	Vogeser M, et al. <i>Ther Drug Monit.</i> 2014; 36: 640-650 <sup>1</sup>
	Tacrolimus	< 5.8%	Bazin C, et al. <i>J Pharm Biom An.</i> 2010; 53: 997-1002 <sup>2</sup>
ACMIA	Cyclosporin	< 7.2%	Morand K, et al. <i>Ann Biol Clin (Paris).</i> 2003; 61: 713-718 <sup>3</sup>
	Tacrolimus	< 7.3%	Cho EJ, et al. <i>J Clin Lab Anal.</i> 2018; 32: e22357 <sup>4</sup>
MEIA	Tacrolimus	<9.5%	Brunet M. <i>Therapy Drug Monitoring.</i> 1996; 18:706-709 <sup>5</sup>
FPIA	Cyclosporin	<10.4%	Press RR. <i>Eur J Clin Pharmacol.</i> 2010. 66: 579-590 <sup>6</sup>
EMIT	Cyclosporin	<8.7%	Morjana N. The Emit® 2000 Cyclosporine Specific Assay, Extended Range: development of an application protocol for the V-Twin® analyzer. <i>Biotechnol Appl Biochem.</i> 2011; 58: 476-482 <sup>7</sup>

**Table 3 of the supplementary data**

Number (%) of cases with missing data for study variables

Variable	Missing, No. (%)
<b>Recipient characteristics</b>	
<i>Age at transplant, y</i>	0 (0.0)
<i>Female sex</i>	0 (0.0)
<i>Body mass index, kg/m<sup>2</sup></i>	3 (0.2)
<i>Primary diagnosis</i>	0 (0.0)
Dilated	0 (0.0)
Ischemic	0 (0.0)
Others	6 (0.8)
<i>Circulatory support prior to HT</i>	0 (0.0)
<i>Diabetes prior to HT</i>	11 (0.7)
<i>Bilirubin <math>\geq</math> 2 mg/dL</i>	55 (3.5)
<i>Infection prior to HT</i>	10 (0.3)
<i>CMV serology (positive)</i>	31 (2.0)
<i>Mechanical ventilation prior to HT</i>	14 (0.9)
<b>Recipient characteristics at 1 year after HT</b>	
<i>Glomerular filtration rate, mL/min/1.73 m<sup>2</sup></i>	46 (2.9)
<i>LVEF, %</i>	112 (7.1)
<i>History of first-year rejection</i>	0 (0.0)
<b>Treatment at 1 year after HT</b>	
<i>Induction therapy at the time of HT</i>	21 (1.3)
<i>Steroids</i>	0 (0.0)
<i>Steroid daily dose (prednisone equivalent, mg)</i>	0 (0.0)
<i>Antimitotics</i>	10 (0.6)
<i>Antimitotic daily dose</i>	19 (2.2)
<i>m-TOR inhibitors</i>	0 (0.0)
<i>Statins</i>	0 (0.0)
<b>Donor related characteristics</b>	
<i>Age, y</i>	4 (0.3)
<i>Female sex</i>	3 (0.2)
<i>CMV serology (positive)</i>	118 (7.5)
<i>CMV recipient (-)/donor (+)</i>	117 (7.4)
<b>Operating characteristics</b>	
<i>Ischemia time, h</i>	13 (0.8)
<i>Transplant era</i>	0 (0.0)
<b>Calcineurin inhibitor characteristics</b>	
<i>Calcineurin type</i>	0 (0.0)
<i>Number of blood level measurements</i>	0 (0.0)
<i>Coefficient of variation</i>	0 (0.0)

ECMO, extracorporeal membrane oxygenator; HT, heart transplant; LVEF, left ventricular ejection fraction; mTOR, mammalian target of rapamycin.

**Table 4 of the supplementary data**

Concomitant immunosuppression in 1581 heart transplant recipients

Regimen at the end of the first posttransplant year	No.	(%)
<i>Tacrolimus</i>		
Tacrolimus + MMF/SMF + steroids	503	32.00
Tacrolimus + MMF/SMF	116	7.38
Tacrolimus + AZA + steroids	41	2.61
Tacrolimus + MTORi + steroids	40	2.54
Tacrolimus + steroids	32	2.04
Tacrolimus + MTORi	30	1.91
Tacrolimus	15	0.95
Tacrolimus + MMF/SMF + MTORi + steroids	10	0.64
Tacrolimus + AZA	2	0.13
Tacrolimus + MMF/SMF + MTORi	1	0.06
<i>Cyclosporine</i>		
Cyclosporine + MMF/SMF + steroids	590	37.53
Cyclosporine + MMF/SMF	28	1.78
Cyclosporine + AZA + steroids	98	6.23
Cyclosporine + MTORi + steroids	36	2.29
Cyclosporine + steroids	13	0.83
Cyclosporine + MTORi	1	0.06
Cyclosporine	5	0.32
Cyclosporine + MMF/SMF + MTORi + steroids	7	0.45
Cyclosporine + AZA	4	0.25
Cyclosporine + MMF/SMF + MTORi	0	0.00
<i>Induction therapy at the time of transplantation</i>		
None	280	17.7
Antithymocyte globulin	104	6.6
OKT3	176	11.1
Daclizumab	83	5.2
Basiliximab	893	56.5
Others	45	2.8

AZA, azathioprine; MMF, mycophenolate-mofetil; MTORi, mammalian target of rapamycin inhibitors (sirolimus, everolimus); SMF, micophenolic acid.

**Table 5 of the supplementary data**

Immunoassays used in the study and their distribution according to calcineurin type, transplant era, inpatient variability, and serum levels

	CMIA	ACMIA	MEIA	FPIA	EMIT
<i>Patients</i>	691 (43.7)	469 (29.7)	173 (10.9)	128 (8.1)	120 (7.6)
<i>Calcineurin inhibitor</i>					
Cyclosporin	316 (45.7)	226 (48.2)	-	128 (100.0)	120 (100.0)
IR tacrolimus	213 (30.8)	142 (30.3)	172 (99.4)	-	-
PR tacrolimus	162 (23.4)	101 (21.5)	1 (0.6)	-	-
<i>Transplant era</i>					
2000-2004	198 (28.7)	132 (28.1)	62 (35.8)	79 (61.7)	107 (89.2)
2005-2009	141 (20.4)	137 (29.2)	105 (60.7)	48 (37.5)	13 (10.8)
2010-2014	352 (50.9)	200 (42.6)	6 (3.5)	1 (0.8)	-
<i>Coefficient of variation</i>	29.0 [20.7, 40.6]	29.9 [20.9, 37.9]	27.0 [19.9, 35.8]	25.3 [18.3, 30.9]	24.5 [17.7, 32.2]
<i>CV &gt; 27.8%</i>	318 (46.0)	220 (46.9)	91 (52.6)	83 (64.8)	79 (65.8)
<i>Mean blood levels &lt; median</i>	395 (57.2)	193 (41.2)	75 (43.4)	64 (50.0)	61 (50.8)

CV, coefficient of variation; IQR, interquartile range, IR, immediate release; PR, prolonged release.

The data are expressed as No. (%) or median (interquartile range)

**Table 6 of the supplementary data**

Univariable analysis of 5-year rejection/graft loss/mortality in 1581 heart transplant recipients

	HR	95%CI	P
<i>Recipient age at transplant &gt; 56 y</i>	1.375	1.062-1.782	.016
<i>Female sex</i>	0.746	0.528-1.052	.095
<i>Body mass index &gt; 25 kg/m<sup>2</sup></i>	1.154	0.890-1.496	.280
<i>Primary diagnosis</i>			
Dilated	1.000		
Ischemic	1.084	0.819-1.436	.572
Others	0.862	0.585-1.270	.451
<i>Circulatory support prior to HT</i>			
None	1.000		
Intra-aortic balloon	1.011	0.715-1.431	.950
ECMO	1.909	1.009-3.613	.047
Ventricular assist device	0.725	0.321-1.636	.439
<i>Diabetes prior to HT</i>	1.525	1.124-2.070	.007
<i>Bilirubin ≥ 2 mg/dL</i>	1.261	0.871-1.826	.219
<i>Infection prior to HT</i>	1.233	0.835-1.820	.293
<i>CMV serology (positive)</i>	1.132	0.798-1.605	.488
<i>Mechanical ventilation prior to HT</i>	1.219	0.826-1.800	.318
<i>One-year GFR &lt; 61 mL/min/1.73 m<sup>2</sup></i>	1.365	1.050-1.775	.020
<i>One-year LVEF &lt; 64%</i>	1.320	1.008-1.727	.043
<i>History of first-year rejection</i>	1.400	1.080-1.814	.011
<i>Induction therapy at the time of HT</i>	1.146	0.819-1.603	.427
<i>Steroids</i>	1.302	0.853-1.987	.221
<i>Antimitotics</i>			
None	1		
Azathioprine	0.992	0.570-1.724	.977
MMF/mycophenolic acid	0.905	0.601-1.364	.633
<i>m-TOR inhibitors</i>	0.968	0.590-1.586	.896
<i>Statins</i>	0.932	0.697-1.245	.633
<i>Donor age &gt; 39 y</i>	1.484	1.142-1.926	.003
<i>Donor sex (female)</i>	0.904	0.678-1.205	.490
<i>Donor CMV serology (positive)</i>	0.982	0.730-1.321	.906
<i>CMV recipient (-)/donor (+)</i>	0.974	0.655-1.448	.896
<i>Ischemia time &gt; 3.38 h</i>	0.992	0.766-1.285	.953
<i>Transplant era</i>			
2000-2004	1		
2005-2009	0.773	0.561-1.066	.116
2010-2014	0.912	0.671-1.239	.556
<i>Calcineurin inhibitor type</i>			
Cyclosporine	1		
Tacrolimus (immediate)	0.714	0.533-0.956	.024
Tacrolimus (prolonged)	0.540	0.344-0.847	.007
<i>Number of measurements</i>	0.981	0.758-1.271	.886
<i>Mean blood levels &lt; median value</i>	0.867	0.669-1.123	.279
<i>Coefficient of variation &gt; 27.8%</i>	1.342	1.034-1.743	.027

CAV, cardiac allograft vasculopathy; CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenator; HT, heart transplant; LVEF, left ventricular ejection fraction; MMF, mycophenolate mofetil; mTOR, mammalian target of rapamycin.

**Table 7 of the supplementary data**

Univariable analysis of 5-year all-cause mortality/graft loss in 1581 heart transplant recipients

	HR	95%CI	P
<i>Recipient age at transplant &gt; 56 y</i>	1.504	1.081-2.093	.016
<i>Female sex</i>	0.789	0.512-1.215	.283
<i>Body mass index &gt; 25 kg/m<sup>2</sup></i>	1.054	0.758-1.467	.754
<i>Primary diagnosis</i>			
Dilated	1.000		
Ischemic	1.198	0.829-1.731	.335
Others	1.270	0.803-2.007	.307
<i>Circulatory support prior to HT</i>			
None	1.000		
Intra-aortic balloon	0.667	0.401-1.110	.119
ECMO	1.786	0.785-4.061	.167
Ventricular assist device	0.768	0.283-2.081	.603
<i>Diabetes prior to HT</i>	1.976	1.370-2.850	< .001
<i>Bilirubin ≥ 2 mg/dL</i>	1.562	0.940-2.595	.085
<i>Infection prior to HT</i>	1.509	0.949-2.398	.082
<i>CMV serology (positive)</i>	1.050	0.680-1.621	.826
<i>Mechanical ventilation prior to HT</i>	1.298	0.801-2.105	.290
<i>One-year GFR &lt; 61 mL/min/1.73 m<sup>2</sup></i>	1.370	0.980-1.914	.065
<i>One-year LVEF &lt; 64%</i>	1.488	1.049-2.110	.026
<i>History of first-year rejection</i>	1.332	0.957-1.853	.089
<i>Induction therapy at the time of HT</i>	0.728	0.444-1.193	.208
<i>Steroids</i>	1.364	0.786-2.369	.270
<i>Antimitotics</i>			
None	1.000		
Azathioprine	0.738	0.364-1.495	.399
MMF/mycophenolic acid	0.771	0.474-1.256	.296
<i>m-TOR inhibitors</i>	1.024	0.554-1.895	.939
<i>Statins</i>	0.880	0.612-1.265	.490
<i>Donor age &gt; 39 y</i>	1.784	1.273-2.501	.001
<i>Donor sex (female)</i>	0.812	0.558-1.181	.276
<i>CMV serology (positive)</i>	0.994	0.680-1.452	.975
<i>CMV recipient (-)/donor (+)</i>	1.111	0.683-1.806	.671
<i>Ischemia time &gt; 3.38 h</i>	0.953	0.686-1.325	.776
<i>Transplant era</i>			
2000-2004	1.000		
2005-2009	0.825	0.546-1.245	.359
2010-2014	1.088	0.739-1.602	.669
<i>Calcineurin inhibitor type</i>			
Cyclosporine	1.000		
Tacrolimus (immediate)	0.784	0.544-1.130	.192
Tacrolimus (prolonged)	0.557	0.311-0.999	.050
<i>Number of measurements</i>	1.181	0.849-1.642	.323
<i>Mean blood levels &lt; median value</i>	0.878	0.632-1.221	.439
<i>Coefficient of variation &gt; 27.8%</i>	1.418	1.015-1.982	0.041

CMV, cytomegalovirus; ECMO, extracorporeal membrane oxygenator; GFR, glomerular filtration rate; HT, heart transplant; LVEF, left ventricular ejection fraction; MMF, mycophenolate mofetil; mTOR, mammalian target of rapamycin.



**Table 8 of the supplementary data**

Predictors of 5-year outcomes after excluding calcineurin-inhibitor type from the models

	Univariable			Multivariable		
	HR	95%CI	P	HR	95%CI	P
<b>Rejection/graft loss/mortality</b>						
<i>Coefficient of variation &gt; 27.8%</i>	1.342	1.034-1.743	.027	1.358	1.041-1.772	.024
<i>Donor age &gt; 39 y</i>	1.484	1.142-1.926	.003	1.563	1.195-2.044	.001
<i>Circulatory support prior to HT</i>				1.000		
None				1.100	0.774-1.562	.596
Intra-aortic balloon	1.011	0.715-1.431	.950	2.497	1.288-4.843	.007
ECMO	1.909	1.009-3.613	.047	0.820	0.354-1.895	.642
Ventricular assist device	0.725	0.321-1.636	.439	1.361	1.046-1.77	.022
<i>History of first-year rejection</i>	1.314	1.011-1.708	.041	1.307	0.994-1.719	.055
<i>One-year LVEF &lt; 64 %</i>	1.320	1.008-1.727	.043	1.341	0.978-1.837	.068
<i>Diabetes prior to HT</i>	1.525	1.124-2.070	.007	0.746	0.527-1.055	.098
<i>Recipient female sex</i>	0.746	0.528-1.052	.095	1.225	0.933-1.609	.143
<i>Recipient age at HT &gt; 56 y</i>	1.375	1.062-1.782	.016	0.826	0.635-1.074	.154
<i>Mean blood levels &gt; median value</i>	0.867	0.669-1.123	.279	1.235	0.939-1.626	.131
<i>One-year GFR &gt; 61mL/min/1.73 m<sup>2</sup></i>	1.365	1.05-1.775	.020	1.000		
<i>Transplant era</i>				0.775	0.56-1.074	.126
2000-2004				0.809	0.582-1.126	.210
2005-2009	0.773	0.561-1.066	.116	1.358	1.041-1.772	.024
2010-2014	0.912	0.671-1.239	.556	1.563	1.195-2.044	.001
<b>Mortality/graft loss</b>						
<i>Coefficient of variation &gt; 27.8%</i>	1.418	1.015-1.982	.041	1.489	1.054-2.105	.024
<i>Donor age &gt; 39 y</i>	1.784	1.273-2.501	.001	1.799	1.266-2.557	.001
<i>Infection prior to HT</i>	1.509	0.949-2.398	.082	1.726	1.076-2.769	.024
<i>Diabetes prior to HT</i>	1.976	1.370-2.850	< .001	1.615	1.102-2.366	.014
<i>One-year LVEF &lt; 64%</i>	1.488	1.049-2.110	.026	1.408	0.985-2.014	.061
<i>History of first-year rejection</i>	1.332	0.957-1.853	.089	1.327	0.946-1.863	.102
<i>Recipient age at HT &gt; 56 y</i>	1.504	1.081-2.093	.016	1.293	0.911-1.835	.150
<i>Bilirubin &gt; 2 mg/dL</i>	1.562	0.940-2.595	.085	0.723	0.433-1.206	.214
<i>Mean blood levels &gt; median value</i>	0.878	0.632-1.221	.439	0.824	0.587-1.156	.262
<i>One-year GFR &gt; 61 mL/min/1.73 m<sup>2</sup></i>	1.370	0.980-1.914	.065	1.155	0.813-1.642	.421
<i>Transplant era</i>				1.000		
2000-2004	1.000			0.842	0.549-1.291	.403
2005-2009	0.825	0.546-1.245	.359	1.027	0.683-1.543	.900
2010-2014	1.088	0.739-1.602	.669	1.489	1.054-2.105	.024

95%CI, 95% confidence interval; ECMO, extracorporeal membrane oxygenator; GFR, glomerular filtration rate; HR, hazard ratio; HT, heart transplant; LVEF, left ventricular ejection fraction.

**Table 9 of the supplementary data**

Univariable analysis of 5-year rejection/graft loss/mortality in patients without a history of first-year rejection

	HR	95%CI	P
<i>Coefficient of variation &gt; 27.8%</i>	1.679	1.172-2.406	.005
<i>Recipient age at transplant &gt; 56 y</i>	1.578	1.105-2.253	.012
<i>Female sex</i>	0.746	0.458-1.217	.241
<i>Body mass index &gt; 25 kg/m<sup>2</sup></i>	0.919	0.645-1.311	.642
<i>Primary diagnosis</i>			
Dilated	1.000		
Ischemic	1.072	0.724-1.586	.729
Others	1.143	0.696-1.876	.597
<i>Circulatory support prior to HT</i>			
None	1.000		
Intra-aortic balloon	0.760	0.454-1.272	.296
ECMO	2.151	0.997-4.638	.051
Ventricular assist device	0.652	0.206-2.057	.465
<i>Diabetes prior to HT</i>	1.370	0.883-2.124	.160
<i>Bilirubin ≥ 2 mg/dL</i>	1.168	0.707-1.928	.545
<i>Infection prior to HT</i>	1.069	0.613-1.865	.814
<i>CMV serology (positive)</i>	1.018	0.629-1.647	.943
<i>Mechanical ventilation prior to HT</i>	1.185	0.679-2.068	.549
<i>One-year GFR &gt; 61 mL/min/1.73 m<sup>2</sup></i>	1.545	1.076-2.220	.019
<i>One-year LVEF &lt; 64%</i>	1.338	0.936-1.913	.111
<i>Induction therapy at the time of HT</i>	1.289	0.811-2.049	.282
<i>Steroids</i>	1.622	0.894-2.942	.112
<i>Antimitotics</i>			
None	1.000		
Azathioprine	1.056	0.509-2.188	.884
MMF/mycophenolic acid	0.767	0.438-1.346	.356
<i>m-TOR inhibitors</i>	1.329	0.674-2.621	.411
<i>Statins</i>	1.037	0.676-1.589	.868
<i>Donor age &gt; 39 y</i>	1.158	0.813-1.649	.417
<i>Donor gender (female)</i>	0.833	0.557-1.246	.375
<i>CMV serology (positive)</i>	1.069	0.709-1.612	.749
<i>CMV recipient (-)/donor (+)</i>	1.099	0.639-1.890	.733
<i>Ischemia time &gt; 3.38 h</i>	0.997	0.700-1.420	.985
<i>Transplant era</i>			
2000-2004	1.000		
2005-2009	0.792	0.515-1.218	.289
2010-2014	0.829	0.541-1.269	.387
<i>Calcineurin inhibitor type</i>			
Cyclosporine	1.000		
Tacrolimus (immediate)	0.494	0.325-0.752	.001
Tacrolimus (prolonged)	0.255	0.111-0.583	.001
<i>Number of measurements</i>	0.735	0.513-1.053	.093
<i>Mean blood levels &lt; median value</i>	1.061	0.745-1.512	.741

CMV, cytomegalovirus; ECMO, extracorporeal membrane oxygenator; GFR, glomerular filtration rate; HT, heart transplantation; LVEF, left ventricular ejection fraction; MMF, mycophenolate mofetil; mTOR, mammalian target of rapamycin.

**Table 10 of the supplementary data**

Univariable analysis of 5-year mortality/graft loss in patients without a history of first-year rejection

	HR	95%CI	P
<i>Coefficient of variation &gt; 27.8%</i>	1.574	1.000-2.476	.050
<i>Recipient's age at transplant &gt; 56 y</i>	1.532	0.977-2.403	.063
<i>Female sex</i>	0.764	0.413-1.414	.391
<i>Body mass index &gt; 25 Kg/m<sup>2</sup></i>	0.855	0.545-1.342	.496
<i>Primary diagnosis</i>			
Dilated	1.000		
Ischemic	1.440	0.851-2.436	.174
Others	2.096	1.158-3.795	.015
<i>Circulatory support prior to HT</i>			
None	1.000		
Intra-aortic balloon	0.571	0.273-1.193	.136
ECMO	2.500	1.003-6.235	.049
Ventricular assist device	1.081	0.339-3.449	.895
<i>Diabetes prior to HT</i>	1.538	0.899-2.633	.116
<i>Bilirubin ≥ 2 mg/dL</i>	1.327	0.682-2.585	.405
<i>Infection prior to HT</i>	1.585	0.856-2.934	.143
<i>CMV serology (positive)</i>	0.965	0.530-1.756	.907
<i>Mechanical ventilation prior to HT</i>	1.743	0.941-3.226	.077
<i>One-year GFR &gt; 61 mL/min/1.73 m<sup>2</sup></i>	1.676	1.055-2.663	.029
<i>One-year LVEF &lt; 64 %</i>	1.577	0.998-2.492	.051
<i>History of first-year rejection</i>	0.882	0.454-1.712	.711
<i>Induction therapy at the time of HT</i>	1.722	0.792-3.746	.170
<i>Steroids</i>			
<i>Antimitotics</i>	1.000		
None	0.778	0.307-1.973	.597
Azathioprine	0.682	0.348-1.333	.263
MMF/mycophenolic acid	1.666	0.766-3.625	.198
<i>m-TOR inhibitors</i>	1.040	0.607-1.783	.886
<i>Statins</i>	1.268	0.809-1.985	.300
<i>Donor age &gt; 39 y</i>	0.668	0.390-1.144	.142
<i>Donor sex (female)</i>	1.146	0.682-1.927	.607
<i>CMV serology (positive)</i>	1.069	0.531-2.150	.852
<i>CMV recipient (-)/donor (+)</i>	1.084	0.693-1.697	.723
<i>Ischemia time &gt; 3.38 h</i>			
<i>Transplant era</i>			
2000-2004	1.000		
2005-2009	0.762	0.436-1.331	.339
2010-2014	0.959	0.565-1.626	.875
<i>Calcineurin inhibitor type</i>			
Cyclosporine	1.000	-	
Tacrolimus (immediate)	0.632	0.38-1.048	.076
Tacrolimus (prolonged)	0.305	0.11-0.844	.022
<i>Number of measurements</i>	1.214	0.775-1.902	.396
<i>Mean blood levels &lt; median value</i>	1.574	1.000-2.476	.050

CMV, cytomegalovirus; ECMO, extracorporeal membrane oxygenator; GFR, glomerular filtration rate; HT, heart transplantation; LVEF, left ventricular ejection fraction; MMF, mycophenolate mofetil; mTOR, mammalian target of rapamycin.

**Table 11 of the supplementary data**

Predictors of 5-year outcomes for heart transplant recipients without a history of rejection during the first post-transplant year

	Univariable			Multivariable		
	HR	95%CI	P	HR	95%CI	P
<b>Rejection/graft loss/mortality</b>						
<i>Coefficient of variation &gt; 27.8%</i>	1.679	1.172-2.406	.005	1.609	1.129-2.295	.011
<i>Calcineurin inhibitor type</i>						
Cyclosporine	1.000			1.000		
Tacrolimus (immediate)	0.499	0.333-0.747	.001	0.443	0.287-0.685	< .001
Tacrolimus (prolonged)	0.315	0.226-0.440	.001	0.260	0.111-0.608	.003
<i>Circulatory support prior to HT</i>						
None	1.000			1.000		
Intra-aortic balloon	0.760	0.454-1.272	.296	0.772	0.593-1.006	.328
ECMO	2.151	0.997-4.638	.051	2.275	1.067-4.489	.047
Ventricular assist device	0.652	0.206-2.057	.465	1.067	0.584-1.947	.915
<i>Number of measurements</i>	0.735	0.513-1.053	.093	0.613	0.422-0.890	.010
<i>Mean blood levels &lt; median value</i>	1.061	0.745-1.512	.741	0.925	0.643-1.330	.673
<i>One-year GFR &gt; 61 mL/min/1.73 m<sup>2</sup></i>	1.545	1.076-2.220	.019	0.725	0.495-1.061	.098
<i>Transplant era</i>						
2000-2004	1.000			1.000		
2005-2009	0.792	0.515-1.218	.289	0.949	0.756-1.190	.816
2010-2014	0.829	0.541-1.269	.387	1.128	0.699-1.821	.622
<b>Mortality/graft loss</b>						
<i>Coefficient of variation &gt; 27.8%</i>	1.574	1.000-2.476	.050	1.511	0.948-2.407	.082
<i>Recipient age at transplant &gt; 56 y</i>	1.532	0.977-2.403	.063	1.459	0.905-2.352	.121
<i>Primary diagnosis</i>						
Dilated	1.000			1.000		
Ischemic	1.440	0.851-2.436	.174	1.249	0.732-2.132	.415
Others	2.096	1.158-3.795	.015	2.222	1.205-4.097	.011
<i>Circulatory support prior to HT</i>						
None	1.000			1.000		
Intra-aortic balloon	0.571	0.273-1.193	.136	0.477	0.209-1.090	.079
ECMO	2.500	1.003-6.235	.049	1.744	0.549-5.542	.347
Ventricular assist device	1.081	0.339-3.449	.895	1.127	0.306-4.146	.857
<i>Mechanical ventilation</i>	1.743	0.941-3.226	.077	2.363	1.053-5.302	.037
<i>One-year LVEF &lt; 64%</i>	1.577	0.998-2.492	.051	1.683	1.054-2.687	.029
<i>One-year GFR &gt; 61 mL/min/1.73 m<sup>2</sup></i>	1.676	1.055-2.663	.029	0.761	0.476-1.217	.255
<i>Calcineurin inhibitor type</i>						
Cyclosporine	1.000	-		1.000		
Tacrolimus (immediate)	0.632	0.380-1.048	.076	0.543	0.320-0.921	.024
Tacrolimus (prolonged)	0.305	0.110-0.844	.022	0.217	0.071-0.664	.007
<i>Mean blood levels &lt; median value</i>	1.574	1.000-2.476	.050	0.876	0.553-1.387	.571
<i>Transplant era</i>						
2000-2004	1.000			1.000		
2005-2009	0.762	0.436-1.331	.339	0.911	0.522-1.587	.744
2010-2014	0.959	0.565-1.626	.875	1.336	0.749-2.384	.326

ECMO, extracorporeal membrane oxygenator; LVEF, GFR, glomerular filtration rate; HT, heart transplantation; left ventricular ejection fraction.



**Table 12 of the supplementary data**

Predictors of 5-y outcomes with addition of the type of immunoassay to the adjusted model

	Univariable			Multivariable		
	HR	95%CI	P	HR	95%CI	P
<b>Rejection/graft loss/mortality</b>						
<i>Coefficient of variation &gt; 27.8%</i>	1.342	1.034-1.743	.027	1.538	1.163-2.034	.003
<i>Donor age &gt; 39 y</i>	1.484	1.142-1.926	.003	1.498	1.140-1.969	.004
<i>Calcineurin inhibitor type</i>						
Cyclosporine	1			1		
Tacrolimus immediate release	0.714	0.533-0.956	.024	0.604	0.398-0.918	.018
Tacrolimus prolonged release	0.540	0.344-0.847	.007	0.470	0.275-0.805	.006
<i>History of first-year rejection</i>	1.400	1.080-1.814	.011	1.363	1.036-1.793	.027
<i>Circulatory support prior to HT</i>						
None				1		
Intra-aortic balloon	1.011	0.715-1.431	.950	1.131	0.791-1.617	.500
ECMO	1.909	1.009-3.613	.047	2.047	1.979-4.282	.057
Ventricular assist device	0.725	0.321-1.636	.439	0.969	0.414-2.263	.941
<i>One-year LVEF &lt; 64%</i>	1.320	1.008-1.727	.043	1.454	1.097-1.926	.009
<i>Recipient age at HT &gt; 56 y</i>	1.375	1.062-1.782	.016	1.279	0.967-1.693	.085
<i>Diabetes prior to HT</i>	1.525	1.124-2.07	.007	1.403	1.021-1.927	.037
<i>Mean blood levels &gt; median value</i>	0.867	0.669-1.123	.279	1.221	0.931-1.602	.148
<i>One-year GFR &lt; 61 mL/min/1.73 m<sup>2</sup></i>	1.365	1.05-1.775	.020	1.182	0.891-1.569	.246
<i>Recipient female gender</i>	0.746	0.528-1.052	.095	0.850	0.590-1.226	.385
<i>Transplant era</i>						
2000-2004				1		
2005-2009	0.773	0.561-1.066	.116	0.977	0.689-1.385	.894
2010-2014	0.912	0.671-1.239	.556	1.501	0.994-2.268	.054
<i>Immunoassay type</i>						
CMIA	1			1		
ACMIA	1.00	0.71-1.41	.98	0.901	0.633-1.283	.563
MEIA	1.22	0.79-1.89	.36	1.980	1.128-3.477	.017
FPIA	1.57	1.00-2.45	.05	1.423	0.860-2.356	.170
EMIT	2.35	1.57-3.51	< .001	2.391	1.495-3.824	< .001
<b>Mortality/graft loss</b>						
<i>Coefficient of variation &gt; 27.8%</i>	1.418	1.015-1.982	.041	1.390	0.974-1.984	.069
<i>Donor age &gt; 39 y</i>	1.784	1.273-2.501	.001	1.862	1.307-2.655	.001
<i>Calcineurin inhibitor type</i>						
Cyclosporine	1.000			1		
Tacrolimus immediate release	0.784	0.544-1.130	.192	0.545	0.332-0.894	.016
Tacrolimus prolonged release	0.557	0.311-0.999	.050	0.327	0.169-0.635	.001
<i>Infection prior to HT</i>	1.509	0.949-2.398	.082	1.657	1.031-2.665	.037
<i>Diabetes prior to HT</i>	1.976	1.370-2.850	< .001	1.558	1.058-2.294	.025
<i>One-year LVEF &lt; 64%</i>	1.488	1.049-2.110	.026	1.523	1.058-2.191	.023
<i>History of first-year rejection</i>	1.332	0.957-1.853	.089	1.458	1.029-2.066	.034
<i>Recipient age at HT &gt; 56 y</i>	1.504	1.081-2.093	.016	1.362	0.956-1.940	.087
<i>Bilirubin &gt; 2 mg/dL</i>	1.562	0.940-2.595	.085	0.703	0.420-1.176	.179
<i>Mean blood levels &gt; median value</i>	0.878	0.632-1.221	.439	1.214	0.859-1.716	.271
<i>One-year GFR &lt; 61 mL/min/1.73m<sup>2</sup></i>	1.370	0.980-1.914	.065	1.142	0.801-1.629	.462



<i>Transplant era</i>						
2000-2004	1.000			1		
2005-2009	0.825	0.546-1.245	.359	0.967	0.616-1.517	.884
2010-2014	1.088	0.739-1.602	.669	1.683	1.036-2.733	.036
<i>Immunoassay type</i>						
CMIA	1			1		
ACMIA	1.011	0.675-1.515	.957	0.876	0.573-1.340	.542
MEIA	1.195	0.711-2.008	.502	1.809	0.914-3.582	.089
FPIA	0.918	0.481-1.751	.795	0.742	0.367-1.502	.407
EMIT	1.357	0.768-2.398	.293	1.255	0.638-2.469	.510

ACMIA, affinity column-mediated immunoassay; CMIA, chemiluminescent microparticle immunoassay; EMIT, enzyme multiplied immunoassay; FPIA, fluorescence polyclonal immunoassay; GFR, glomerular filtration rate; HT, heart transplant; LVEF, left ventricular ejection fraction; MEIA, microparticle enzyme immunoassay.

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