SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics stratified by transplantation status

Demographics	Not Transplanted (n=373)	Transplanted (n=525)	p-value
Age (years)	51.7±11.9	52.1±10.9	0.607
Male sex	234 (63%)	352 (67%)	0.181
BMI (kg/m^2)	27.3±5.7	27.0±5.0	0.412
Cardiovascular risk factors			
Diabetes	141 (38%)	210 (40%)	0.506
Hypertension	319 (86%)	472 (90%)	0.046
Hyperlipidaemia	183 (49%)	238 (45%)	0.270
History of smoking	148 (40%)	155 (30%)	0.002
History of IHD	85 (23%)	113 (22%)	0.652
Previous transplantation	53 (14%)	57 (11%)	0.131
On renal replacement therapy	213 (57%)	409 (78%)	<0.001
Peritoneal Dialysis	65 (17%)	134 (26%)	0.004
Haemodialysis	148 (40%)	275 (52%)	<0.001
Cause of kidney disease			
Diabetes	125 (34%)	130 (25%)	0.004
IgA nephropathy	59 (16%)	91 (17%)	0.548
Reflux nephropathy	25 (7%)	46 (9%)	0.260
Polycystic kidney disease	33 (9%)	70 (13%)	0.038
Glomerulonephritis	73 (20%)	112 (21%)	0.520
Renovascular	26 (7%)	23 (4%)	0.092
Miscellaneous	32 (9%)	53 (10%)	0.444
Exercise stress echocardiography results			

Test during long interdialytic interval	61 (46%)	78 (33%)	0.011
Test performed on beta blockers	170 (46%)	209 (40%)	0.085
Exercise duration (min)	7.1±2.9	7.9±2.5	<0.001
Reached ≥85% MPHR	209 (56%)	326 (62%)	0.068
METs	8.8±2.9	9.5±2.7	<0.001
Achieved 4 METs	364 (98%)	520 (99%)	0.082
Achieved 7 METs	280 (75%)	454 (86%)	<0.001
Achieved predicted METs	150 (40%)	279 (53%)	<0.001
Baseline LVEF <50%	70 (19%)	71 (14%)	0.033
Abnormal Stress Echocardiogram	68 (18%)	75 (14%)	0.111
Non-diagnostic	19 (5%)	15 (3%)	0.265
Global failure in LV contractile reserve	28 (8%)	23 (4%)	0.190
Inducible regional wall motion abnormalities	21 (6%)	37 (7%)	0.025
Underwent coronary angiography	27 (40%)	29 (39%)	0.899
Non-MI revascularization	11 (3%)	17 (3%)	0.806
Outcomes			
MACE	43 (12%)	50 (10%)	0.331
Cardiac Death	14 (4%)	7 (1%)	0.018
Non-fatal MI	23 (6%)	30 (6%)	0.777
Stroke	16 (4%)	16 (3%)	0.323

Values are mean ± standard deviation, median (Q1-Q3) or n (%).

BMI – body mass index, IHD – ischaemic heart disease, LV – left ventricular, LVEF – left ventricular ejection fraction. MACE – major adverse cardiovascular outcomes, METs – metabolic equivalents, MI – myocardial infarction, MPHR – maximum predicted heart rate.

Table S2. Population characteristics stratified by 7 metabolic equivalents

Demographics	<7 METs (n=164)	≥7 METs (n=734)	p-value
Age (years)	56.4±9.8	50.9±11.4	<0.001*
Male sex	91 (55%)	495 (68%)	0.004
BMI (kg/m^2)	28.9±5.7	26.7±5.1	<0.001
Cardiovascular risk factors			
Diabetes	96 (59%)	255 (35%)	<0.001
Hypertension	148 (90%)	643 (88%)	0.345
Hyperlipidaemia	77 (47%)	344 (47%)	0.984
History of smoking	66 (40%)	237 (32%)	0.051
History of IHD	54 (33%)	144 (20%)	<0.001
Previous transplantation	18 (11%)	92 (13%)	0.582
On renal replacement therapy	118 (72%)	504 (69%)	0.410
Peritoneal Dialysis	45 (27%)	154 (21%)	0.072
Haemodialysis	73 (45%)	350 (48%)	0.462
Cause of kidney disease			
Diabetes	82 (50%)	173 (24%)	<0.001
IgA nephropathy	18 (11%)	132 (18%)	0.030
Reflux nephropathy	9 (5%)	62 (8%)	0.204
Polycystic kidney disease	8 (5%)	95 (13%)	0.003
Glomerulonephritis	22 (13%)	163 (22%)	0.012
Renovascular	11 (7%)	38 (5%)	0.435
Miscellaneous	14 (9%)	71 (10%)	0.691

Exercise stress echocardiography results			
Test during long interdialytic interval	24 (37%)	115 (38%)	0.891
Exercise duration (min)	3.7±1.4	8.5±2.1	<0.001
Reached ≥85% MPHR	44 (27%)	491 (67%)	<0.001
METs	5.2±1.0	10.1±2.3	<0.001
Baseline LVEF <50%	44 (27%)	97 (13%)	<0.001
Abnormal Stress Echocardiogram	54 (33%)	89 (12%)	<0.001
Non-diagnostic	24 (15%)	4 (1%)	<0.001
Global failure in LV contractile reserve	11 (7%)	40 (5%)	0.003
Inducible regional wall motion abnormalities	18 (11%)	40 (5%)	0.170
Non-MI revascularization	10 (6%)	18 (2%)	0.015*
Transplanted	71 (43%)	454 (62%)	<0.001
Median time to transplantation	1.5 [0.9-2.3]	1.5 [0.7-2.9]	0.964

Values are mean ± standard deviation, median (Q1-Q3) or n (%).

BMI – body mass index, IHD – ischaemic heart disease, LV – left ventricular, LVEF – left ventricular ejection fraction. METs – metabolic equivalents, MI – myocardial infarction, MPHR – maximum predicted heart rate.

Table S3. Univariate associations of clinical factors, echocardiographic parameters, ability to achieve predicted metabolic equivalents and major adverse cardiovascular events

Variable	Hazard ratio	95% CI	p-value
Age	1.01	0.99-1.03	0.327
Sex (female referent)	0.58	0.34-0.96	0.035
Diabetes	2.40	1.54-3.74	<0.001
Hypertension	2.43	0.89-6.63	0.084
Hyperlipidemia	2.25	1.42-3.57	0.001
History of smoking	1.97	1.27-3.05	0.003
History of ischaemic heart disease	1.92	1.23-3.01	0.004
Previous kidney transplantation	0.49	0.20-1.21	0.123
Body mass index	1.03	0.99-1.07	0.200
Current renal replacement therapy	1.22	0.72-2.07	0.451
LV hypertrophy	1.25	0.80-1.95	0.330
LV ejection fraction<50%	2.04	1.25-3.33	0.004
Abnormal stress echocardiogram	1.52	0.92-2.52	0.105
Non-MI revascularization	3.08	1.48-6.40	0.003
Achieved Predicted METs	0.41	0.25-0.66	<0.001
Kidney Transplant*	0.48	0.28-0.81	0.006

Hazard ratio for age was calculated per one year. Hazard ratio for body mass index was calculated per 1kg/m^2 increase.

* Transplantation was treated as a time-dependent covariate

CI – confidence interval, LV – left ventricle, METs – metabolic equivalents, MI – myocardial infarction

Table S4. Multivariable associations of clinical factors, echocardiographic parameters, metabolic equivalents as a continuous variable and major adverse cardiovascular events

Variable	Hazard ratio	95% CI	p-value
Age	0.99	0.97-1.01	0.336
Sex (female referent)	0.62	0.35-1.09	0.093
Diabetes	1.72	1.06-2.78	0.027
Hypertension	1.55	0.55-4.36	0.406
Hyperlipidaemia	1.73	1.05-2.86	0.031
History of smoking	1.41	0.89-2.23	0.144
History of ischaemic heart disease	1.11	0.67-1.82	0.689
Previous kidney transplantation	0.53	0.21-1.34	0.179
Body mass index	1.00	0.95-1.04	0.846
LV ejection fraction<50%	1.41	0.81-2.44	0.220
Abnormal stress echocardiogram	0.94	0.53-1.63	0.815
Non-MI revascularization	1.92	0.89-4.11	0.095
METs	0.88	0.80-0.96	0.007
Kidney transplant*	0.53	0.30-0.92	0.024

Hazard ratio for age was calculated per one year. Hazard ratio for body mass index was calculated per 1kg/m^2 increase.

* Transplantation was treated as a time-dependent covariate

CI – confidence interval, LV – left ventricle, METs – metabolic equivalents, MI – myocardial infarction

Table S5. Multivariable associations of clinical factors, echocardiographic parameters, ability to achieve 7 metabolic equivalents and major adverse cardiovascular events

Variable	Hazard ratio	95% CI	p-value
Age	0.99	0.97-1.01	0.447
Sex (female referent)	0.64	0.36-1.13	0.126
Diabetes	1.75	1.08-2.84	0.023
Hypertension	1.50	0.53-4.21	0.444
Hyperlipidaemia	1.78	1.08-2.95	0.024
History of smoking	1.42	0.89-2.24	0.138
History of ischaemic heart disease	1.06	0.64-1.74	0.822
Previous kidney transplantation	0.53	0.21-1.33	0.177
Body mass index	1.01	0.96-1.05	0.808
LV ejection fraction<50%	1.50	0.86-2.61	0.151
Abnormal stress echocardiogram	0.97	0.55-1.71	0.903
Non-MI revascularization	1.94	0.90-4.18	0.092
Achieved ≥7 METs	0.55	0.32-0.95	0.033
Kidney transplant*	0.52	0.30-0.91	0.021

Hazard ratio for age was calculated per one year. Hazard ratio for body mass index was calculated per 1kg/m^2 increase.

* Transplantation was treated as a time-dependent covariate

CI – confidence interval, LV – left ventricle, METs – metabolic equivalents, MI – myocardial infarction

Table S6. Population characteristics comparing patients who achieved predicted metabolic equivalents who did and did not receive transplantation

Demographics	Achieved Predicted METs and not transplanted (n=150)	Achieved Predicted METs and transplanted (n=279)	p-value
Age (years)	53.7±11.8	53.7±10.2	0.952
Male sex	85 (57%)	170 (61%)	0.391
BMI (kg/m^2)	25.5±4.9	25.7±4.4	0.716
Cardiovascular risk factors			
Diabetes	26 (17%)	104 (37%)	<0.001
Hypertension	127 (85%)	250 (90%)	0.135
Hyperlipidemia	69 (46%)	130 (47%)	0.906
History of smoking	49 (32%)	74 (27%)	0.180
History of IHD	26 (17%)	63 (23%)	0.201
Previous kidney transplantation	23 (15%)	32 (11%)	0.254
On renal replacement therapy	69 (46%)	222 (80%)	<0.001
Peritoneal Dialysis	20 (13%)	79 (28%)	<0.001
Hemodialysis	49 (33%)	143 (51%)	<0.001
Cause of kidney disease			
Diabetes	23 (15%)	58 (21%)	0.169
IgA nephropathy	35 (23%)	46 (16%)	0.084
Reflux nephropathy	15 (10%)	26 (9%)	0.819
Polycystic kidney disease	19 (13%)	38 (14%)	0.781
Glomerulonephritis	40 (27%)	73 (26%)	0.910

Renovascular	9 (6%)	15 (5%)	0.789
Miscellaneous	9 (6%)	23 (8%)	0.267
Test during long interdialytic interval	19 (46%)	44 (37%)	0.290
Test performed on beta-blockers	56 (37%)	100 (36%)	0.759
Baseline LVEF <50%	17 (11%)	27 (10%)	0.590
Abnormal Stress Echocardiogram	18 (12%)	24 (9%)	0.259
Non-diagnostic	2 (1%)	1 (0%)	0.387
Global failure in LV contractile reserve	11 (7%)	8 (3%)	0.073
Inducible regional wall motion abnormalities	5 (3%)	15 (5%)	0.026
Underwent coronary angiography	8 (5%)	8 (3%)	0.463
Non-MI revascularization	1 (1%)	5 (2%)	0.344

Values are mean ± standard deviation or n (%).

BMI – body mass index, IHD – ischaemic heart disease, LVEF – left ventricular ejection fraction, METs – metabolic equivalents, MI – myocardial infarction.

Table S7. Population characteristics comparing patients who achieved predicted metabolic equivalents who did not receive transplantation and patients who did not achieve predicted metabolic equivalents and received transplantation

Demographics	Did Not Achieve Predicted METs and transplanted (n=246)	Achieved Predicted METs and not transplanted (n=150)	p-value
Age (years)	50.1±11.4	53.7±11.8	0.003
Male sex	182 (74%)	85 (57%)	<0.001
BMI (kg/m^2)	28.5±5.2	25.5±4.9	<0.001
Cardiovascular risk factors			
Diabetes	106 (43%)	26 (17%)	<0.001
Hypertension	222 (90%)	127 (85%)	0.096
Hyperlipidemia	108 (44%)	69 (46%)	0.684
History of smoking	81 (33%)	49 (33%)	0.957
History of IHD	50 (20%)	26 (17%)	0.463
Previous kidney transplantation	25 (10%)	23 (15%)	0.126
On renal replacement therapy	187 (76%)	69 (46%)	<0.001
Peritoneal Dialysis	55 (22%)	20 (13%)	0.026
Hemodialysis	132 (54%)	49 (33%)	<0.001
Cause of kidney disease			
Diabetes	72 (29%)	23 (15%)	0.002
IgA nephropathy	45 (18%)	35 (23%)	0.226
Reflux nephropathy	20 (8%)	15 (10%)	0.525
Polycystic kidney disease	32 (13%)	19 (13%)	0.922

Other glomerulonephritis	30 (12%)	35 (23%)	0.004
Renovascular	8 (3%)	9 (6%)	0.191
Vasculitides	9 (4%)	5 (3%)	0.865
Miscellaneous	30 (12%)	9 (6%)	0.025
Test during long interdialytic interval	34 (29%)	19 (46%)	0.040
Test performed on beta-blockers	109 (44%)	56 (37%)	0.172
Baseline LVEF <50%	44 (18%)	17 (11%)	0.080
Abnormal Stress Echocardiogram	51 (21%)	18 (12%)	0.026
Non-diagnostic	14 (6%)	2 (1%)	0.158
Global failure in LV contractile reserve	15 (6%)	11 (7%)	0.017
Inducible regional wall motion abnormalities	22 (9%)	5 (3%)	0.251
Underwent coronary angiography	21 (9%)	8 (5%)	0.809
Non-MI revascularization	12 (5%)	1 (1%)	0.023

Values are mean ± standard deviation or n (%).

BMI – body mass index, IHD – ischaemic heart disease, LVEF – left ventricular ejection fraction, METs – metabolic equivalents, MI – myocardial infarction.

Table S8. Population characteristics comparing patients who achieved <7 metabolic equivalents and received transplantation with patients who achieved ≥7 metabolic equivalents and did not receive transplantation

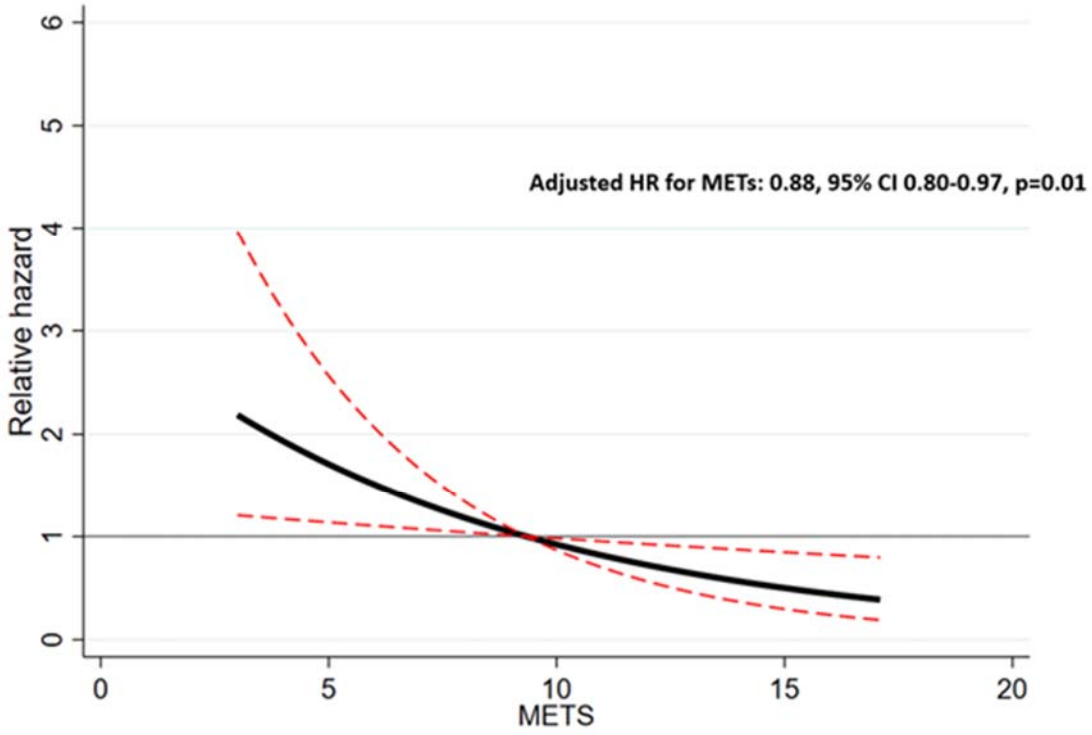
Demographics	<7 METs and transplanted (n=71)	≥7 METs and not transplanted (n=280)	p-value
Age (years)	57.1±10.3	50.2±12.2	<0.001
Male sex	43 (61%)	186 (66%)	0.354
BMI (kg/m^2)	28.4±4.4	26.7±5.2	0.013
Cardiovascular risk factors			
Diabetes	41 (58%)	86 (31%)	<0.001
Hypertension	70 (99%)	241 (86%)	0.003
Hyperlipidaemia	32 (45%)	138 (49%)	0.526
History of smoking	24 (34%)	106 (38%)	0.527
History of IHD	19 (27%)	50 (18%)	0.092
Previous renal transplantation	7 (10%)	42 (15%)	0.264
On renal replacement therapy	55 (77%)	150 (53%)	<0.001
Peritoneal Dialysis	21 (30%)	41 (15%)	0.003
Haemodialysis	34 (48%)	109 (39%)	0.170
Cause of kidney disease			
Diabetes	29 (41%)	72 (26%)	0.012
IgA nephropathy	10 (14%)	51 (18%)	0.412
Reflux nephropathy	6 (8%)	22 (8%)	0.869
Polycystic kidney disease	5 (7%)	30 (11%)	0.356

Glomerulonephritis	11 (15%)	62 (22%)	0.218
Renovascular	4 (6%)	19 (7%)	0.726
Miscellaneous	6 (8%)	24 (9%)	0.948
Test during long interdialytic interval	7 (25%)	44 (46%)	0.044
Baseline LVEF <50%	15 (21%)	41 (15%)	0.183
Abnormal Stress Echocardiogram	23 (32%)	37 (13%)	<0.001
Non-diagnostic	10 (14%)	4 (1%)	0.004
Global failure in LV contractile reserve	3 (4%)	20 (7%)	0.001
Inducible regional wall motion abnormalities	10 (14%)	13 (5%)	0.518
Underwent coronary angiography	11 (15%)	15 (5%)	0.580
Non-MI revascularization	5 (7%)	6 (2%)	0.034

Values are mean ± standard deviation or n (%).

BMI – body mass index, IHD – ischaemic heart disease, LV – left ventricular, LVEF – left ventricular ejection fraction. METs – metabolic equivalents, MI – myocardial infarction

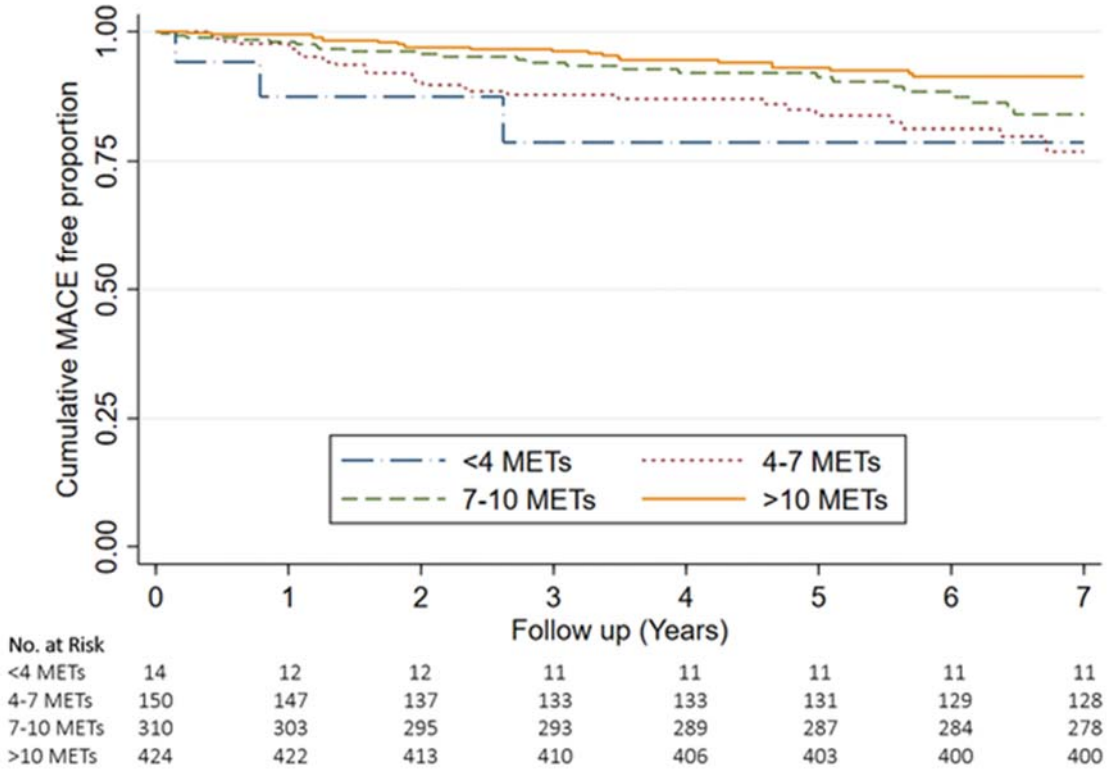
Figure S1. Relationship between relative hazard of MACE with METs



Graph demonstrates relative hazard of MACE with associated 95% CI for METs fitted from multivariable modelling at 7 years, using age, sex, diabetes, hypertension, hyperlipidemia, history of smoking, history of ischaemic heart disease, previous kidney transplantation, body mass index, baseline left ventricular dysfunction, abnormal exercise stress echocardiography result, non-myocardial infarction revascularization prior to transplantation, ability to achieve predicted METs, and transplantation (treated as time-dependent covariable). Results demonstrate a reduction of 12% in hazard for each increasing unit of METs (p=0.01).

CI – confidence interval, HR – Hazard ratio, MACE – Major adverse cardiovascular events, METs – metabolic equivalents

Figure S2. Cumulative MACE free proportion stratified by MET groups



No. at Risk								
<4 METs	14	12	12	11	11	11	11	11
4-7 METs	150	147	137	133	133	131	129	128
7-10 METs	310	303	295	293	289	287	284	278
>10 METs	424	422	413	410	406	403	400	400

With increasing categories of METs, patients have an improved freedom from MACE ($p<0.001$).

MACE – Major adverse cardiovascular events, METs – metabolic equivalents