Figure S1 Relationship between underlying disease, body mass index (BMI), age (circle size), and presence or absence of PGD3 and sRAGE concentration. CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease.

Table S1 Baseline cytokines using 2005 and 2016 guidelines (n=60; HLA samples)

Cytokines	2005 Guidelines			2016 Guidelines		
	Non-PGD (n=46)	PGD (n=14)	P	Non-PGD (n=39)	PGD (n=21)	P
MIP-1B	41.34±53.42	44.15±29.18	0.208	43.41±57.58	39.36±25.85	0.540
IL-6	7.91±18.17	2.31±3.87	0.703	7.59±17.77	4.62±9.25	0.591
IL-1RA	761.51±1,847.38	842.36±1,961.00	0.442	626.86±1,454.63	1,065.47±2,455.67	0.296
TNF-α	12.36±14.83	12.90±8.61	0.287	12.86±15.77	11.80±8.54	0.967
Rantes	6,035.28±8,018.89	7,970.43±9,654.13	0.207	5,736.44±8,027.56	7,794.98±9,060.21	0.158
IL-2	3.00±2.30	6.65±6.45	0.048	2.94±2.47	4.55±3.69	0.018
IL-1β	0.42±0.55	0.59±0.55	0.351	0.37±0.46	0.63±0.65	0.090
Eotaxin	77.19±93.28	77.66±83.15	0.766	63.16±77.53	103.57±107.42	0.196
Basic FGF	12.77±11.97	15.70±12.18	0.270	12.49±12.41	15.33±11.19	0.175
PDGF-BB	1,438.74±1,528.00	1,834.37±1,524.54	0.311	1,268.99±1,446.40	2,017.75±1,578.12	0.045
IP-10	366.63±440.70	473.87±465.75	0.421	378.85±471.79	415.43±400.43	0.403
IL-13	1.08±1.04	1.49±1.72	0.828	0.90±0.57	1.60±1.78	0.389
IL-4	1.56±1.31	1.51±1.18	0.877	1.38±1.17	1.90±1.40	0.139
MCP-1	38.96±75.08	26.63±17.58	0.354	38.34±80.34	31.45±23.14	0.097
IL-8	157.01±243.76	122.74±211.38	0.943	145.14±228.98	156.15±252.77	0.433
MIP-1A	2.36±3.73	3.04±2.39	0.120	2.47±4.01	2.59±2.12	0.181
G-CSF	118.82±73.74	138.54±59.74	0.174	109.84±66.38	148.24±73.55	0.028
IL-12p70	4.54±7.21	5.11±8.68	0.759	4.39±7.77	5.18±7.70	0.366
IL-17A	7.76±6.21	12.36±12.90	0.431	7.73±6.61	11.03±10.98	0.204
IL-9	28.91±11.41	36.94±38.65	0.637	28.93±9.81	34.23±33.11	0.278
sRAGE	1,102.88±721.34	807.87±544.27	0.108	1,170.43±753.84	780.77±476.07	0.024

Values are mean ± standard deviation. FGF, fibroblast growth factor; G-CSF, granulocyte colony-stimulating factor; IL, interleukin; IP, interferon-inducible protein; MCP, monocyte chemotactic protein; MIP, macrophage inflammatory protein; PDGF, platelet-derived growth factor; sRAGE, soluble form of the receptor for advanced glycation end-products; TNF, tumor necrosis factor.

Table S2 Demographics and risk factors for patients who had preoperative HLA samples tested for cytokine analysis using 2005 and 2016 guidelines

Variable	Total (n=60)	2005 Guidelines			2016 Guidelines		
		Non-PGD (n=46)	PGD (n=14)	P	Non-PGD (n=39)	PGD (n=21)	P
Recipient characteristics							
Female	30 (50.0)	25 (54.35)	5 (35.71)	0.360	21 (53.85)	9 (42.86)	0.589
Age (years)	53.08±15.87	52.65±15.93	54.5±16.18	0.706	52.1±16.7	54.4±14.56	0.519
BMI (kg/m²)	25.06±5.21	24.21±5.08	27.85±4.75	0.021	23.46±4.95	28.03±4.38	0.0008
Blood type				0.280			0.222
A	24 (40.0)	16 (34.78)	8 (57.14)		14 (35.90)	10 (47.62)	
B	5 (8.33)	5 (10.87)	0 (0.0)		5 (12.82)	0 (0.0)	
AB	3 (5.0)	3 (6.52)	0 (0.0)		3 (7.70)	0 (0.0)	
O	28 (46.67)	22 (47.83)	6 (42.86)		17 (43.59)	11 (52.38)	
Rh group negative	8 (13.33)	5 (10.87)	3 (21.43)	0.374	4 (10.26)	4 (19.05)	0.433
Primary disease				0.418			0.138
Restrictive lung disease	32 (53.33)	22 (47.83)	10 (71.43)		17 (43.59)	15 (71.43)	
Cystic fibrosis	11 (18.33)	10 (21.74)	1 (7.14)		10 (25. 64)	1 (4.76)	
COPD	13 (21.67)	11 (23.91)	2 (14.29)		9 (23.08)	4 (19.05)	
Other	4 (6.67)	3 (6.52)	1 (7.14)		3 (7.70)	1 (4.76)	
Primary disease				0.140			0.058
Restrictive lung disease	32 (53.33)	22 (47.83)	10 (71.43)		17 (43.59)	15 (71.43)	
Non-restrictive lung diseases	28 (46.67)	24 (52.17)	4 (28.57)		22 (56.41)	6 (28.57)	
Diabetes	10 (16.67)	8 (17.39)	2 (14.29)	1.000	7 (17.95)	3 (14.29)	1.000
Hypertension	26 (43.33)	20 (43.48)	6 (42.86)	1.000	16 (41.03)	10 (47.62)	0.785
History of smoking	28 (46.67)	22 (47.83)	6 (42.86)	0.770	18 (46.15)	10 (47.62)	1.00
LAS	42.24±12.26	41.34±10.44	45.22±17.10	0.304	41.14±10.14	44.29±15.53	0.347
Baseline creatinine (mg/dL)	0.83±0.19	0.81±0.18	0.87±0.23	0.323	0.81±0.18	0.85±0.21	0.427
Condition at time of transplant				0.905			0.759
Not hospitalized	52 (86.67)	40 (86.96)	12 (85.71)		33 (84.62)	19 (90.48)	
Hospitalized (not in ICU)	5 (8.33)	4 (8.70)	1 (7.14)		4 (10.26)	1 (4.76)	
In ICU	3 (5.0)	2 (4.35)	1 (7.14)		2 (5.13)	1 (4.76)	
Life support before transplant	4 (6.67)	2 (4.35)	2 (14.29)	0.230	2 (5.13)	2 (9.52)	0.606
Pre-operative ECMO	2 (3.33)	1 (2.17)	1 (7.14)	0.415	1 (2.56)	1 (4.76)	1.00
Pulmonary hypertension	49 (81.67)	38 (82.61)	11 (78.57)	0.708	32 (82.05)	17 (80.95)	1.00
Prior thoracic surgery*	10 (16.67)	7 (15.22)	3 (21.43)	0.685	4 (10.26)	6 (28.57)	0.143
Prior cardiac surgery	1 (1.67)	1 (2.17)	0 (0.0)	1.000	1 (2.56)	0 (0.0)	1.00
Prior pleurodesis	6 (10.0)	3 (6.52)	3 (21.43)	0.133	3 (7.70)	3 (14.29)	0.655
Donor characteristics							
Age (years)	33.6±12.73	33.87±12.73	32.71±13.89	0.769	33.15±12.87	34.43±12.71	0.714
Extended criteria donor†	19 (31.67)	12 (26.09)	7 (50.00)	0.092	11 (28.21)	8 (38.10)	0.432
Smoker ever	31 (51.67)	24 (52.17)	7 (50.0)	1.000	21 (53.85)	10 (47.62)	0.788
Smoker >20PYH	5 (8.33)	4 (8.70)	1 (7.14)	1.000	4 (10.26)	1 (4.76)	0.649
DCD	5 (8.33)	3 (6.52)	2 (14.29)	0.582	2 (5.13)	3 (14.29)	0.332
Operative characteristics							
Bilateral type of transplant	60 (100.0)	46 (100.0)	14 (100.0)		39 (100.0)	21 (100.0)	
Type of intraoperative support				1.000			1.000
Off-pump	1 (1.67)	1 (2.17)	0 (0.0)		1 (2.56)	0 (0.0)	
ECLS	59 (98.33)	45 (97.83)	14 (100.0)		38 (97.44)	21 (100.0)	
Type of ECLS				1.000			1.000
ECMO	4 (6.67)	3(6.67)	1(7.14)		3 (7.89)	1 (4.76)	
CPB	55 (93.22)	42 (93.33)	13 (92.86)		35 (92.11)	20 (95.24)	
Total ischemic time (min)	295.77±63.59	290.15±66.33	314.2±51.41	0.218	296.15±65.34	295.05±61.77	0.949

Values are n (%) or mean ± SD. *Prior thoracic surgery (non-transplant). †One or more of the following: age >55 years, anticipated ischemia >6 hours, DCD, PaO2/FiO2 <300, donor is >20PYH smoker. COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; PGD, primary graft dysfunction; PYH, pack-year history; CPB, cardiopulmonary bypass; DCD, donor after cardiac death; LAS, lung allocation score.

Table S3 Clinical characteristics, outcomes, and biomarkers in patients with PGD according to 2005 and 2016 guidelines and in those downgraded to PGD1 using the 2005 guidelines

Variable	PGD 2016 & 2005 (n=33)	PGD 2016 not 2005 (n=14)	P
Recipient characteristics			
Women	10 (30.30)	6 (42.86)	0.406
Age	54.45±15.85	55.50±12.81	0.828
BMI (kg/m^3)	26.15±5.15	27.41±4.13	0.423
Primary disease			0.243
Restrictive lung disease	24 (72.72)	7 (50.50)	
Non-restrictive lung diseases	9 (27.28)	7 (50.50)	
Diabetes	11 (33.33)	4 (28.57)	1.00
Hypertension	17 (51.52)	9 (64.29)	0.421
History of smoking	16 (48.48)	9 (64.29)	0.321
Lung allocation score	45.35±14.17	41.03±9.43	0.302
Baseline creatinine (mg/dL)	0.85±0.20	0.89±0.21	0.639
Condition at time of transplant			0.582
Not hospitalized	28 (84.85)	14 (100.0)	
Hospitalized (not in ICU)	2 (6.06)	0 (0)	
In ICU	3 (9.09)	0 (0)	
Life support before LTx	4 (12.12)	0 (0)	0.302
Pre-operative ECMO	1 (3.03)	0 (0)	0.7
Pulmonary hypertension	23 (69.70)	13 (92.86)	0.181
Prior thoracic surgery (non-transplant)	6 (18.18)	3 (21.43)	1.00
Prior cardiac surgery	0 (0)	1 (7.14)	0.298
Prior pleurodesis	3 (9.09)	0 (0)	0.544
Prior lung transplant	1 (3.03)	1 (7.14)	0.879
Donor characteristics			
Age (years)	33.67±12.88	38.21±10.39	0.249
Extended criteria donor	16 (48.48)	4 (28.57)	0.334
Smoker ever	19 (57.58)	7 (50.00)	0.633
Sex mismatch	12 (36.36)	5 (35.71)	0.772
Sex mismatch, female-male	9 (27.28)	2 (14.29)	0.559
Donor after cardiac death	6 (18.18)	1 (7.14)	0.657
Ex-vivo lung perfusion	3 (9.09)	1 (7.14)	1.00
Operative characteristics			
Type of transplant			0.627
Bilateral	30 (90.91)	12 (85.71)	
Single	3 (9.09)	2 (14.29)	
Type of intraoperative support			0.298
Off-pump	0 (0)	1 (7.14)	
ECLS	33 (100.0)	13 (92.86)	
Type of ECLS			0.849
Cardiopulmonary bypass	28 (84.85)	12 (92.31)	
Modified bypass	5 (15.15)	1 (7.69)	
Total ischemic time (min)	346.30±118.45	301.5±128.44	0.253
Outcome			
Postoperative length of stay (days)	46.30±40.97	20.93±13.47	0.029
ICU length of stay (days)	37.33±36.07	11.71±13.33	0.135
Peak creatinine within 48 hours (mg/dL)	1.23±0.59	0.93±0.19	0.073
Peak creatinine value <1.5 mg/dL	25 (75.76)	14 (100.0)	0.084
Peak creatinine value ≥1.5 mg/dL	8 (24.24)	0 (0)	0.084
Max creatinine (mg/dL)	1.96±1.40	1.48±0.85	0.260
Max creatinine <1.5 mg/dL	15 (45.45)	11 (78.57)	0.055
Max creatinine ≥1.5 mg/dL	18 (54.55)	3 (21.43)	0.055
Discharge creatinine (mg/dL)	1.05±1.05	0.98±0.89	0.420
Peak lactate within 72 hours (mg/dL) (n=115)	9.02±3.64	5.49±3.16	0.004
Postoperative ECMO	15 (45.45)	0 (0)	0.002
Mechanical ventilation ≥48 hours	29 (87.88)	3 (21.43)	0.000
Mechanical ventilation ≥5 days	22 (66.67)	1 (7.14)	0.000
Reintubated	11 (33.33)	2 (14.29)	0.288
Tracheostomy	18 (54.55)	1 (7.14)	0.003
Airway dehiscence	3 (9.09)	0 (0)	0.544
Dialysis	12 (36.36)	0 (0)	0.009
Discharge disposition			0.164
Home	18 (54.55)	11 (78.57)	
Rehabilitation facility	8 (24.24)	3 (21.43)	
Death	7 (21.21)	0 (0)	
90-day mortality	4 (12.12)	0 (0)	0.302
1-year mortality	11 (33.33)	1 (7.14)	0.077
Biomarkers			
IL-2 (n=11 *vs.* 5)	6.65±6.45 pg/mL	3.30±1.06 pg/mL	0.276
IL-1β (n=12 *vs.* 6)	0.59±0.55 pg/mL	0.69±0.88 pg/mL	0.771
PDGF-BB (n=14 *vs.* 7)	1834.37±1524.54 pg/mL	2384.50±1740.78 pg/mL	0.457
G-CSF (n=14 *vs.* 7)	211.20±377.85 pg/mL	166.25±97.02 pg/mL	0.685
sRAGE (n=14 *vs.* 7)	807.87±544.27 pg/mL	726.56±329.39 pg/mL	0.722

Values are mean ± standard deviation. PGD 2016 & 2005, patients who developed PGD3 at 48-72 hours after transplant using the 2016 and 2005 scoring guidelines; PGD 2016 not 2005, patients who developed PGD3 at 48-72 hours after lung transplant using the 2016 guidelines but not when using the 2005 guidelines. IL, interleukin; PDGF, platelet-derived growth factor; GCSF, granulocyte colony stimulating forming; sRAGE, soluble form of the receptor for advanced glycation end-products.

Table S4 Outcomes for 60 patients who had preoperative HLA samples tested for cytokine analysis using 2005 and 2016 guidelines

Variable	Total (n=60)	2005 Guidelines			2016 Guidelines		
		Non-PGD (n=46)	PGD (n=14)	P	Non-PGD (n=39)	PGD (n=21)	P
Postoperative length of stay (days)				0.047			0.178
≤21	31 (51.67)	26 (56.52)	5 (35.71)		21 (53.85)	10 (47.62)	
22-30	14 (23.33)	12 (26.09)	2 (14.29)		11 (28.21)	3 (14.29)	
>30	15 (25.00)	8 (17.39)	7 (50.0)		7 (17.95)	8 (38.10)	
ICU length of stay (days)	18.85±27.24	15.06±27.24	31.29±35.27	0.050	15.1±24.55	25.81±31.07	0.148
Peak creatinine within 48 hours (mg/dL)	1.05±0.48	1.00±0.48	1.22±0.45	0.140	1.02±0.51	1.11±0.41	0.526
Peak creatinine within 48 hours ≥1.5 (mg/dL)	6 (10.0)	2 (4.35)	4 (28.57)	0.023	2 (5.13)	4 (19.05)	0.171
Max creatinine (mg/dL)	1.46±1.16	1.43±1.16	1.56±0.83	0.710	1.47±1.31	1.47±0.84	0.954
Max creatinine ≥1.5 (mg/dL)	17 (28.33)	10 (21.74)	7 (50.0)	0.040	9 (23.08)	8 (38.10)	0.176
Discharge creatinine (mg/dL)	0.87±0.51	0.87±0.51	0.86±0.37	0.930	0.91±0.59	0.84±0.39	0.479
Peak lactate within 72h (mg/dL) (n=55)	7.12±3.51	6.54±3.51	8.81±3.04	0.036	6.62±3.59	7.99±3.27	0.164
Postoperative ECMO	4 (6.64)	1 (2.17)	3 (21.43)	0.036	1 (2.56)	3 (14.29)	0.119
Mechanical ventilation ≥48 h	28 (46.67)	16 (34.78)	12 (85.71)	0.002	14 (35.90)	14 (66.67)	0.031
Mechanical ventilation ≥5 days	18 (30.0)	9 (19.57)	9 (64.29)	0.003	8 (20.51)	10 (47.62)	0.040
Reintubated	19 (31.67)	15 (32.61)	4 (28.57)	1.000	14 (35.90)	5 (23.81)	0.254
Tracheostomy	15 (25.0)	9 (19.57)	6 (42.86)	0.092	8 (20.51)	7 (33.33)	0.352
Airway dehiscence	1 (1.67)	0 (0.0)	1 (7.14)	0.233	0 (0.0)	1 (4.76)	0.350
Dialysis	6 (10.0)	4 (8.70)	2 (14.29)	0.617	4 (10.26)	2 (9.52)	1.00
Discharge disposition				0.312			0.1743
Home	46 (76.67)	37 (80.43)	9 (64.29)		33 (84.62)	13 (61.90)	
Rehabilitation facility	13 (21.67)	8 (17.39)	5 (35.71)		6 (15.38)	7 (33.33)	
Death	1 (1.67)	1 (2.17)	0 (0.0)		1 (2.56)	0 (0.0)	
Readmission within 1 year (n=59)	50 (84.75)	39 (86.67)	11 (78.57)	0.431	33 (86.84) n=38	17 (80.95)	0.708
ICU readmission within 1 year (n=59)	20 (33.9)	14 (31.11)	6 (42.86)	0.521	11 (28.95) n=38	9 (42.86)	0.390
90-day mortality	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
1-year mortality	4 (6.64)	3 (6.52)	1 (7.14)	1.000	2 (5.13)	2 (9.52)	0.606

Values are n (%) or mean ± SD. ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.