

Supplementary Data

Supplement Table 1: Concentrations and Unadjusted Spearman Correlation Coefficients for Plasma and Urine Concentration of Oxidative Stress Biomarkers in the OPERA Trial*

	Plasma F2- isoprostanes (pg/mL)	Plasma F3- isoprostanes (pg/mL)	Plasma Isofuran (pg/mL)	Urine F2- isoprostanes (ng/mL)	Urine F3- isoprostanes (ng/mL)	Urine isofuran (ng/mL)
Baseline						
Concentration, mean±SD	51.7±38.2	2.7±4.2	62.5±98.5	1.36±0.89	0.19±1.30	1.89±1.26
Plasma F2-isoprostanes	1.00					
Plasma F3-isoprostanes	0.33*	1.00				
Plasma isofuran	0.52*	0.28*	1.00			
Urine F2-isoprostanes	0.18*	0.10*	-0.08	1.00		
Urine F3-isoprostanes	0.02	0.25*	-0.08	0.37*	1.00	
Urine isofurans	0.10*	0.11*	-0.05	0.51*	0.43*	1.00
End of surgery						
Concentration, mean±SD	50.6±52.9	3.9±5.6	66.7±73.6	4.13±4.60	0.58±1.46	7.12±10.96
Plasma F2-isoprostanes	1.00					
Plasma F3-isoprostanes	0.38*	1.00				
Plasma isofuran	0.61*	0.32*	1.00			
Urine F2-isoprostanes	0.12*	-0.05	0.04	1.00		
Urine F3-isoprostanes	-0.01	0.28*	-0.11*	0.48*	1.00	
Urine isofurans	-0.003	-0.06	-0.02	0.72*	0.43*	1.00
Post-op day 2						
Concentration, mean±SD	45.6±37.0	4.0±7.2	55.3±66.3	1.63±1.20	0.40±0.87	2.50±2.16

Plasma F2-isoprostanes	1.00					
Plasma F3-isoprostanes	0.34*	1.00				
Plasma isofuran	0.60*	0.31*	1.00			
Urine F2-isoprostanes	0.18*	0.12*	0.13*	1.00		
Urine F3-isoprostanes	0.08	0.37*	0.04	0.42*	1.00	
Urine isofurans	0.13*	0.10*	0.05	0.59*	0.45*	1.00

* $P < 0.05$

Supplementary Table 2. Multivariable-Adjusted Risk of Post-Operative Atrial Fibrillation According to Plasma Oxidative Stress Biomarkers in the OPERA Trial*

	Quartiles of Oxidative Stress Biomarkers				<i>P</i> for trend [†]
	1 st	2 nd	3 rd	4 th	
Baseline concentrations					
F₂-isoprostanes					
Concentration (pg/mL)	25.5±6.4	38.2±3.1	49.2±3.7	95.2±55.3	
No. of cases/n	46/138	52/145	37/132	36/136	
Odds ratio (95% CI)	1.0 (reference)	1.01 (0.60-1.69)	0.66 (0.38-1.15)	0.72 (0.40-1.32)	0.21
Isofurans					
Concentration (pg/mL)	20.8±5.7	33.8±3.1	46.9±4.8	151±170	
No. of cases/n	45/135	34/137	40/135	48/132	
Odds ratio (95% CI)	1.0 (reference)	0.59 (0.33-1.04)	0.84 (0.48-1.47)	1.31 (0.74-2.33)	0.08
F₃-isoprostanes					
Concentration (pg/mL)	0.5±0.0	1.0±0.1	2.4±0.5	7.5±6.4	
No. of cases/n‡	61/220	17/59	42/132	48/130	
Odds ratio (95% CI)	1.0 (reference)	0.97 (0.50-1.91)	1.23 (0.75-2.02)	1.39 (0.85-2.25)	0.16
End of surgery concentrations					
F₂-isoprostanes					
Concentration (pg/mL)	22.6±4.8	34.1±2.9	47.2±4.9	100±88.4	
No. of cases/n	45/142	46/131	38/139	48/134	
Odds ratio (95% CI)	1.0 (reference)	1.02 (0.60-1.74)	0.75 (0.43-1.31)	1.51 (0.83-2.73)	0.16
Isofurans					
Concentration (pg/mL)	24.9±7.1	42.9±4.4	61.2±6.7	139±118	
No. of cases/n‡	40/138	40/133	42/129	52/133	
Odds ratio (95% CI)	1.0 (reference)	1.18 (0.68-2.06)	1.18 (0.67-2.09)	1.85 (1.04-3.30)	0.03
F₃-isoprostanes					
Concentration (pg/mL)	0.5±0.0	1.6±0.5	3.6±0.8	11.1±7.9	
No. of cases/n‡	54/158	36/127	46/129	38/123	

Odds ratio (95% CI)	1.0 (reference)	0.79 (0.46-1.37)	1.00 (0.59-1.70)	0.86 (0.50-1.47)	0.70
Post-op day 2 concentrations§					
F₂-isoprostanes					
Concentration (pg/mL)	21.6±4.9	31.8±2.6	42.8±4.2	78.8±41.7	
No. of cases/n	14/105	17/103	14/104	25/102	
Odds ratio (95% CI)	1.0 (reference)	1.14 (0.50-2.59)	1.15 (0.49-2.71)	2.53 (1.14-5.58)	0.01
Isofurans					
Concentration (pg/mL)	19.6±6.1	32.6±3.2	46.3±5.4	118±98.0	
No. of cases/n	11/101	14/101	24/102	20/99	
Odds ratio (95% CI)	1.0 (reference)	1.57 (0.63-3.91)	3.07 (1.29-7.31)	2.98 (1.22-7.25)	0.02
F₃-isoprostanes					
Concentration (pg/mL)	0.5±0.0	1.6±0.5	3.2±0.6	12.1±12.0	
No. of cases/n‡	23/138	13/87	18/86	16/93	
Odds ratio (95% CI)	1.0 (reference)	0.77 (0.34-1.72)	1.02 (0.48-2.16)	0.92 (0.43-1.96)	0.93

* Adjusted for age (years), gender (male/female), country(Italy, USA, Argentina), body mass index (kg/m²), prevalent hypertension (yes/no), prevalent diabetes (yes/no), prevalent coronary heart disease (yes/no), prevalent chronic renal failure (yes/no), prevalent heart failure (yes/no), smoking (never or former/current), dyslipidemia (yes/no), statin medication use (yes/no), ejection fraction (%), and logistic Euroscore (continuous).

† Linear trend was tested by assigning to participants the median value in each quartile and assessing this as a continuous variable. All findings were similar when biomarker concentrations were evaluated in their natural units as continuous exposures.

‡ Bottom quartile consisted of subjects whose plasma F₃-Isoprostanes were below the detection limit.

§ Excluding subjects who developed PoAF within two days of surgery for these analyses.

Supplementary Table 3. Multivariable-Adjusted Risk of Post-Operative Atrial Fibrillation According to Creatinine Adjusted Urine Oxidative Stress Biomarkers in the OPERA Trial*

	Quartiles of Oxidative Stress Biomarkers				<i>P</i> for trend [†]
	1 st	2 nd	3 rd	4 th	
Baseline concentrations					
F₂-isoprostanes					
Concentration (ng/mg)	0.53±0.17	0.97±0.11	1.38±0.14	2.57±0.89	
No. of cases/n	44/129	43/134	32/122	32/128	
Odds ratio (95% CI)	1.0 (reference)	0.93 (0.54-1.59)	0.69 (0.39-1.22)	0.79 (0.44-1.43)	0.35
Isofurans					
Concentration (ng/mg)	0.77±0.27	1.36±0.16	1.94±0.18	3.51±1.43	
No. of cases/n	36/129	36/126	39/128	40/127	
Odds ratio (95% CI)	1.0 (reference)	1.05 (0.59-1.87)	1.08 (0.60-1.94)	1.49 (0.82-2.72)	0.16
F₃-isoprostanes					
Concentration (ng/mg)	0.01±0.005	0.06±0.02	0.13±0.02	0.58±2.59	
No. of cases/n	33/116	26/115	41/116	38/114	
Odds ratio (95% CI)	1.0 (reference)	0.56 (0.28-1.11)	1.21 (0.63-2.30)	1.11 (0.57-2.17)	0.23
End of surgery concentrations					
F₂-isoprostanes					
Concentration (ng/mg)	1.10±0.37	2.15±0.35	3.63±0.57	9.64±6.38	
No. of cases/n	38/128	34/126	46/127	45/127	
Odds ratio (95% CI)	1.0 (reference)	0.75 (0.42-1.34)	1.39 (0.78-2.47)	1.26 (0.69-2.30)	0.20
Isofurans					
Concentration (ng/mg)	1.45±0.54	3.01±0.53	5.41±1.04	18.6±17.2	
No. of cases/n	35/128	38/127	41/127	50/127	
Odds ratio (95% CI)	1.0 (reference)	1.02 (0.57-1.85)	1.19 (0.66-2.14)	1.95 (1.05-3.62)	0.01
F₃-isoprostanes					
Concentration (ng/mg)	0.01±0.02	0.15±0.05	0.37±0.10	1.80±2.56	
No. of cases/n	29/114	32/113	42/114	42/113	

Odds ratio (95% CI)	1.0 (reference)	1.17 (0.59-2.31)	1.87 (0.94-3.71)	2.10 (1.04-4.25)	0.04
Post-op day 2 concentrations‡					
F₂-isoprostanes					
Concentration (ng/mg)	0.57±0.23	1.10±0.11	1.67±0.23	3.28±1.29	
No. of cases/n	16/97	13/96	16/96	17/96	
Odds ratio (95% CI)	1.0 (reference)	0.91 (0.39-2.16)	1.36 (0.59-3.14)	1.26 (0.53-3.01)	0.48
Isofurans					
Concentration (ng/mg)	0.92±0.27	1.60±0.21	2.42±0.30	5.04±3.0	
No. of cases/n	12/98	16/95	16/96	18/96	
Odds ratio (95% CI)	1.0 (reference)	1.31 (0.53-3.22)	1.25 (0.50-3.13)	1.23 (0.48-3.17)	0.83
F₃-isoprostanes					
Concentration (ng/mg)	0.02±0.02	0.10±0.03	0.22±0.06	1.14±1.17	
No. of cases/n	8/87	14/86	22/87	15/86	
Odds ratio (95% CI)	1.0 (reference)	1.94 (0.70-5.41)	2.92 (1.10-7.80)	1.76 (0.59-5.24)	0.90

* Adjusted for age (years), gender (male/female), country (Italy, USA, Argentina), body mass index (kg/m²), prevalent hypertension (yes/no), prevalent diabetes (yes/no), prevalent coronary heart disease (yes/no), prevalent chronic renal failure (yes/no), prevalent heart failure (yes/no), smoking (never or former/current), dyslipidemia (yes/no), statin medication use (yes/no), ejection fraction (%), and logistic Euroscore (continuous).

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