SUPPLEMENTAL MATERIAL

Table S1. Effect of fish oil supplementation on biomarkers of bleeding in patients undergoing cardiac surgery in the OPERA trial.

	Fish oil (n=758)†	Placebo (n=758)†	*P* value
Platelet counts, mean (SD)	214 (61)	214 (66)	0.80
median (IQR)	211 (73)	205 (75)	
INR, mean (SD)	1.07 (0.20)	1.09 (0.26)	0.09
PAI-1, ng/ml, median (IQR)	15 (16)	17 (14)	0.95
11-dhTXB2, ng/mg, median (IQR)	0.61 (0.70)	0.53 (0.75)	0.11

Abbreviations: SD, standard deviation; IQR, interquartile range; INR, international normalized ratio; PAI-1, platelet activator inhibitor-1; 11-dhTXB2, 11-Dehydrothromboxane-B2

†Biomarkers were assessed in all 1516 patients except for PAI-1 and 11-dhTXB2 which were only assessed in a subset of 164 and 488 patients respectively

Table S2. Effect of fish oil supplementation on total units of blood transfused in 1516 patients undergoing cardiac surgery in the OPERA trial, according to type of surgery and surgical access

	Fish oil (n=758)	Placebo (n=758)	*P* value†
Type of surgery			
Total units for Valve surgery, mean (SD)	1.65 (2.85)	2.24 (4.18)	**<0.001**
median (25^{th}, 75^{th} percentile)	1 (0, 2.00)	1 (0, 3.00)	
Total units for CABG surgery, mean (SD)	1.43 (2.30)	1.20 (1.88)	0.02
median (25^{th}, 75^{th} percentile)	0 (0, 2.00)	0 (0, 2.00)	
Surgical access			
Total units for mini thoracotomy, mean (SD)	1.10 (1.52)	2.30 (5.03)	**<0.001**
median (25^{th}, 75^{th} percentile)	0 (0, 2.00)	0 (0, 3.00)	
Total units for open thoracotomy, mean (SD)	1.65 (2.60)	1.91 (3.24)	**<0.001**
median (25^{th}, 75^{th} percentile)	1.00 (0, 2.00)	1 (0, 3.00)	

† *Given that interaction analyses were exploratory, alpha level was Bonferroni –adjusted for the six variables (12 hypothesis) tested. Hence, only p<0.004 (in bold) were considered statistically significant. P-interaction by type of surgery <0.001; and p-interaction by surgical access=0.001*

Table S3. Other adverse events in OPERA, according to treatment assignment

Outcome	Placebo (n= 758)	n-3 PUFA (n= 758)	P value†
Adverse events leading to temporary or permanent discontinuation of study drug, no. events / no. patients (% patients)	25 / 20 (2.6)	19 / 19 (2.5)	0.87
Bone marrow or coagulation	0 / 0 (0.0)	0 / 0 (0.0)	--
Bleeding	7 / 7 (0.9)	2 / 2 (0.3)	0.18
Cardiac	3 / 3 (0.4)	6 / 6 (0.8)	0.51
Constitutional symptoms	1 / 1 (0.1)	0 / 0 (0.0)	1.00
Dermatology or musculoskeletal	0 / 0 (0.0)	0 / 0 (0.0)	--
Gastrointestinal, hepatobiliary, or pancreas	2 / 2 (0.3)	8 / 8 (1.1)	0.11
Infection	1 / 1 (0.1)	1 / 1 (0.1)	1.00
Metabolic or laboratory	0 / 0 (0.0)	0 / 0 (0.0)	--
Neurologic	5 / 5 (0.7)	1 / 1 (0.1)	0.22
Pulmonary	3 / 3 (0.4)	1 / 1 (0.1)	0.62
Renal or genitourinary	2 / 2 (0.3)	0 / 0 (0.0)	0.50
Vascular	1 / 1 (0.1)	0 / 0 (0.0)	1.00
Other‡	0 / 0 (0.0)	0 / 0 (0.0)	--
All serious adverse events, no. events / no. patients (% patients)	196 / 147 (19.4)	170 / 136 (17.9)	0.47
Bone marrow or coagulation	0 / 0 (0.0)	6 / 6 (0.8)	0.03
Bleeding	36 / 36 (4.8)	32 / 30 (4.0)	0.45
Cardiac	60 / 54 (7.1)	50 / 44 (5.8)	0.30
Constitutional symptoms	9 / 9 (1.2)	10 / 10 (1.3)	1.00
Dermatology or musculoskeletal	1 / 1 (0.1)	3 / 3 (0.4)	0.62
Gastrointestinal, hepatobiliary, or pancreas	4 / 4 (0.5)	8 / 8 (1.1)	0.39
Infection	27 / 26 (3.4)	16 / 16 (2.1)	0.12
Metabolic or laboratory	1 / 1 (0.1)	2 / 1 (0.1)	1.00
Neurologic	17 / 15 (2.0)	10 / 10 (1.3)	0.31
Pulmonary	25 / 23 (3.0)	18 / 18 (2.4)	0.43
Renal or genitourinary	6 / 6 (0.8)	6 / 6 (0.8)	1.00
Vascular	4 / 3 (0.4)	5 / 5 (0.7)	0.73
Other‡	6 / 6 (0.8)	4 / 4 (0.5)	0.75

†Evaluated using Pearson chi-square or Fisher exact tests (as appropriate)

‡Ocular/visual, pain, or surgical/intra-operative injury.

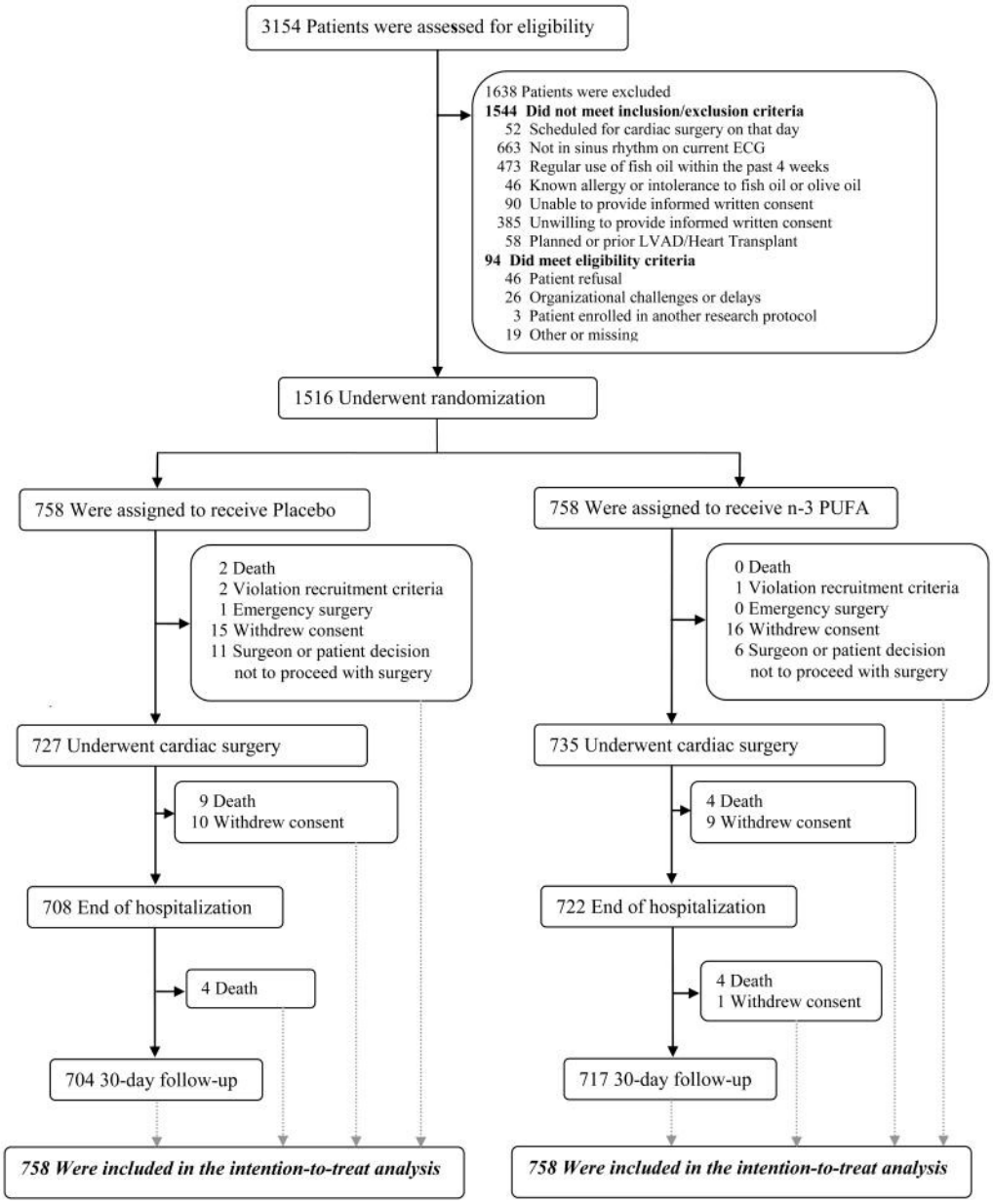

Figure S1. Patients enrollment, randomization and follow up

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