SUPPLEMENTAL MATERIAL

Supplemental Table I: Definitions for histological plaque features in Oxford Plaque Study and Athero-Express

Characteristic	Staining Oxford	Staining AE	Definition used in Oxford Plaque Study	Definition used in Athero-Express	Overall Agreement	Similarities	Differences
Overall plaque stability	H&E EVG CD68	H&E EVG CD68 PSR	0 Stable predominantly fibrous plaque with thick, intact cap OR predominantly stable, some features of instability, eg, inflammation, but thick, intact cap 1 Unstable with intact thin cap, large lipid core, but no definite rupture or surface thrombus OR unstable with ruptured cap or thrombus present	0 Stable/fibrous: small (<10% of plaque area) or absent lipid core, low macrophage infiltration, and high smooth muscle cell and collagen content 1 Unstable/atheromatous: large lipid core (>40% of plaque surface area) and high macrophage infiltration with low smooth muscle cell and collagen content	Good	Assessment includes - Lipid core - Fibrous composition - Inflammation	- Cap rupture (no data in AE) - Thrombus (not included in AE definition)
Fibrous	H&E EVG	H&E EVG	0 Very little fibrous tissue or ≈ 50% fibrous tissue 1 Predominantly fibrous plaque	0 Atheromatous/fibroatheromatous 1 Predominantly fibrous plaque, absent lipid core, or <10% of plaque surface area	Good	Both based on 3-grade scale	
Lipid core	H&E	H&E PSR	0 None or small 1 A large lipid core was considered to occupy ≥ 50% of the thickness of the plaque or ≥ 25% of the total section area.	0 no or smaller than 40% of total plaque surface area 1 >40% of plaque surface area covered by lipid core	Moderate / Good	Both based on 3-grade scale	Different cut off: Oxford >25% AE >40%
Inflammatory plaque (severity of CD68 staining)	CD68 CD 3	CD68	0 No staining OR +: occasional scattered cells or 1 group of >50 cells 1 ++:Several groups (>5) of >50 cells or +++: Many groups (>5) of >50 cells or 1 group of >500 cells	0 Absent or minor CD68 staining with negative or clusters with <10 cells present 1 moderate or heavy staining, cell clusters with >10 cells present or abundance of positive cells	Good	Both based on 4-grade scale	Different cut off for number of positive cells and clusters
Presence of thrombus	H&E	H&E Fibrin	0 No luminal thrombus 1 Thrombus was recorded when there was an organized collection of fibrin and red blood cells in the lumen.	0 No luminal thrombus 1 Thrombus formation at the luminal side of the plaque with positive staining for fibrin	Good	- Comparable definitions - Both binominal	None

Characteristic	Staining Oxford	Staining AE	Definition used in Oxford Plaque Study	Definition used in Athero-Express	Overall Agreement	Similarities	Differences
Presence of intraplaque hemorrhage	H&E	H&E Fibrin	0 None 1 Includes recent or old hemorrhage; is an area of erythrocytes causing disruption of plaque architecture (def: Bassiouny et al.)	0 Absent 1 Hemorrhage within the tissue of the plaque, including fresh and organized haemorrhage	Good	Loose erythrocytes scored negative	Additional fibrin staining in AE
Calcifications	H&E	H&E	0 None or small amounts when there was stippling only 1 considered to be present in large amounts when nodular deposits	0 no or minor staining along part of the luminal border of the plaque or a few scattered spots within the lesion 1 moderate or heavy staining along the entire luminal border or evident parts within the lesion	Good	Both based on 4-grade scale	
Collagen		EVG	No data	0 no or minor staining along part of the luminal border of the plaque 1 moderate or heavy staining along the entire luminal border	None		
Cap rupture	EVG		0 Intact Cap 1 Clear communication between the lipid core and the lumen with a break in the fibrous cap	No data	None		
Smooth muscle cells		α-actin	No data	0 no or minor -actin staining over the entire circumference with absent staining at parts of the circumference of the arterial wall 1 positive cells along the circumference of the luminal border, with locally at least few scattering cells	None		

Supplemental Table II: Odds-ratios for the presence of individual plaque characteristics in the highest versus lowest quartile of 1-year stroke risk for subgroups of patients with and without prior statin use.

Plaque characteristic	No Prior Statin Use (n=678)				Prior Statin Use (n=913)				P-Value for Interaction
	Total N (%)	OR	95% CI	P-value	Total N (%)	OR	95% CI	P-value	
Overall plaque instability	452 (67.6)	1.28	0.83-1.98	0.27	613 (67.2)	1.43	0.97-2.11	0.07	0.71
Thrombus	259 (38.4)	1.24	0.80-1.91	0.34	374 (41.0)	1.57	1.06-2.33	0.03	0.58
Heavy macrophage staining	401 (60.0)	1.57	1.02-2.40	0.04	554 (60.9)	1.11	0.76-1.64	0.59	0.31
High micro-vessel density	179 (31.5)	1.53	0.94-2.46	0.09	190 (33.5)	1.30	0.77-2.18	0.32	0.16
Large lipid core	467 (68.9)	1.28	0.82-2.00	0.29	676 (74.6)	1.23	0.81-1.87	0.33	0.82
Plaque haemorrhage	187 (27.6)	1.25	0.80-1.97	0.33	206 (22.6)	1.14	0.72-1.82	0.58	0.87
Fibrous plaque	206 (30.4)	0.62	0.39-0.97	0.04	301 (33.0)	0.71	0.48-1.05	0.09	0.65
Heavy calcification	360 (53.1)	0.91	0.60-1.38	0.66	459 (50.4)	0.86	0.59-1.26	0.44	0.85

Abbreviations: N, number of cases; OR, odds ratio; CI, confidence interval. Statin use was unknown in 49 patients. All data stratified by study cohort.