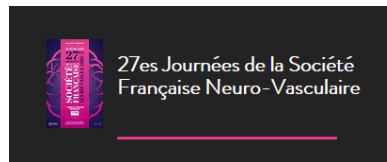


Lien Lp(a) et risque d'AVC

Pr David Calvet

Service de Neurologie Hôpital Sainte-Anne,
Université de Paris, INSERM UMR 1266

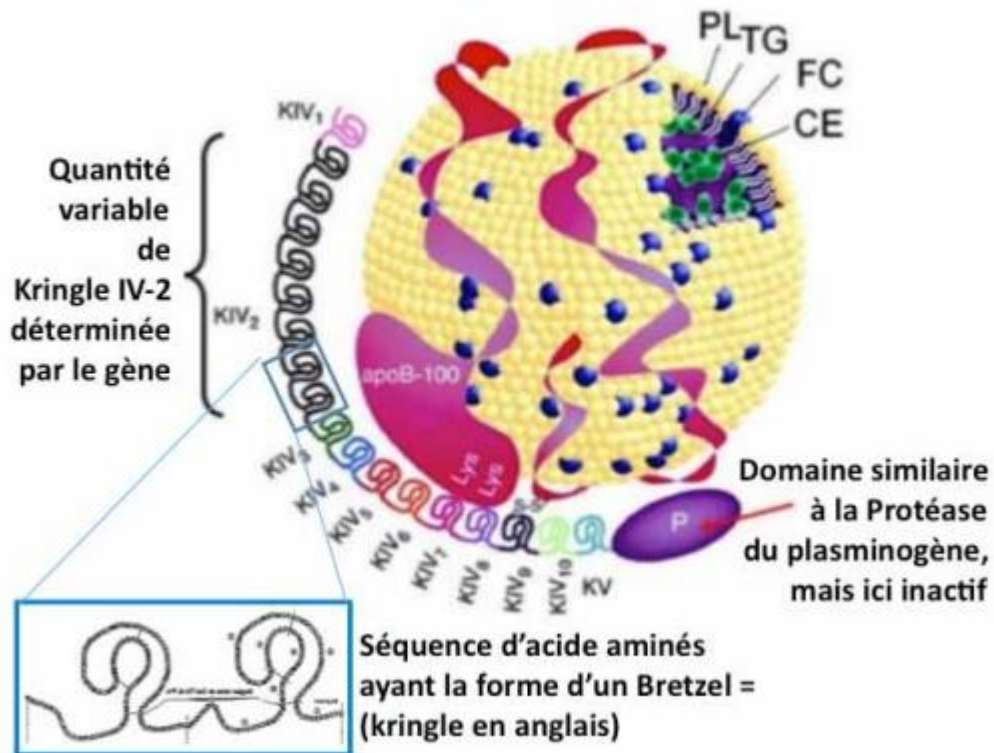
Evaluation du risque lipidique – Symposium Novartis



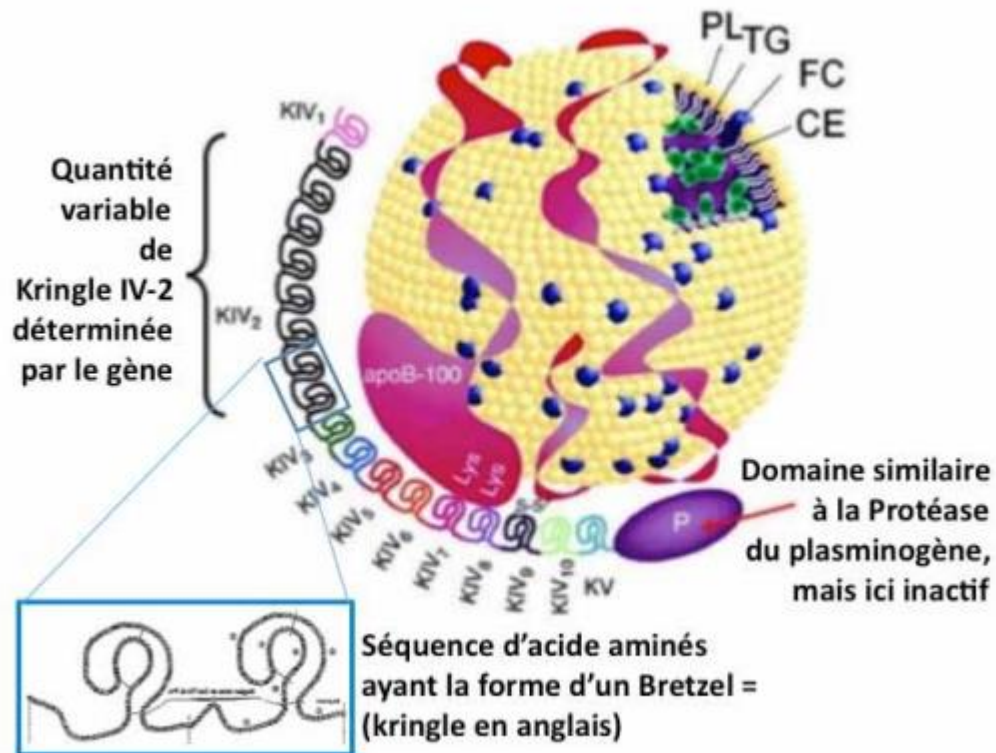
Liens d'intérêts

- ❑ Participation essai thérapeutique en tant qu'investigateur
 - Boehringer Ingelheim (RESPECT-ESUS)
 - Bayer (Navigate-ESUS)
- ❑ Activité de conseil et conférences: AstraZeneca
- ❑ Prise en charge déplacement : Daiichi Sankyo

Qu'est ce que la lipoprotéine (a) ou Lp(a)?

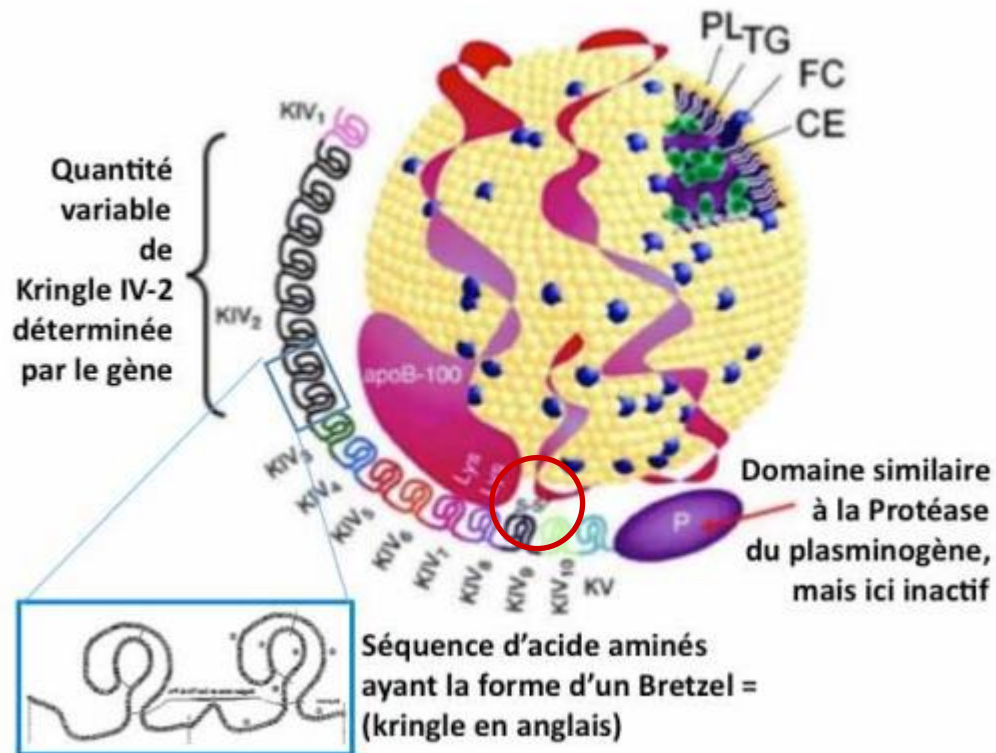


Qu'est ce que la lipoprotéine (a) ou Lp(a)?



« LDL like »
Cholestérol
Autres lipides
Apolipoproteine B

Qu'est ce que la lipoprotéine (a) ou Lp(a)?



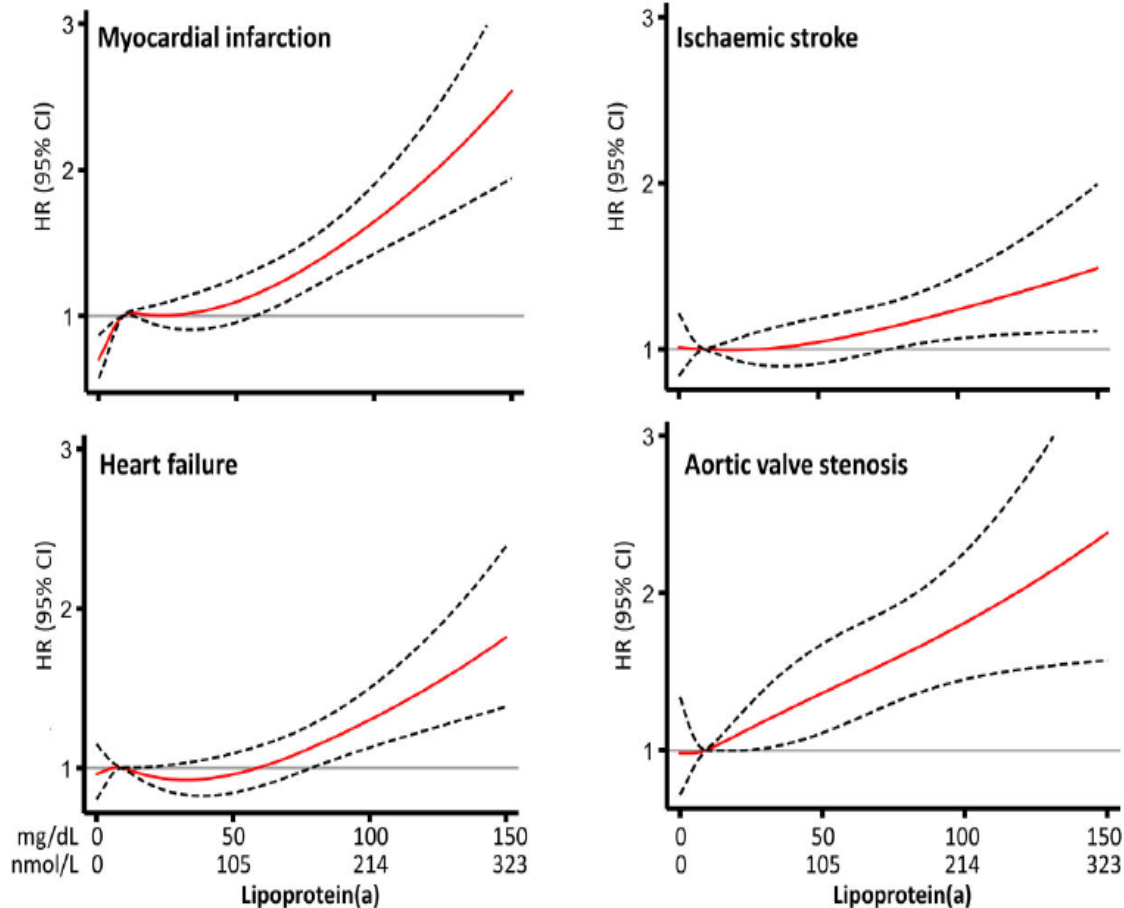
« LDL like »
Cholestérol
Autres lipides
Apolipoprotéine B

Glycoprotéine : **Apolipoprotéine (a)** Apo(a)

Elevated Lp(a) and risk of vascular events

European Heart Journal 2022

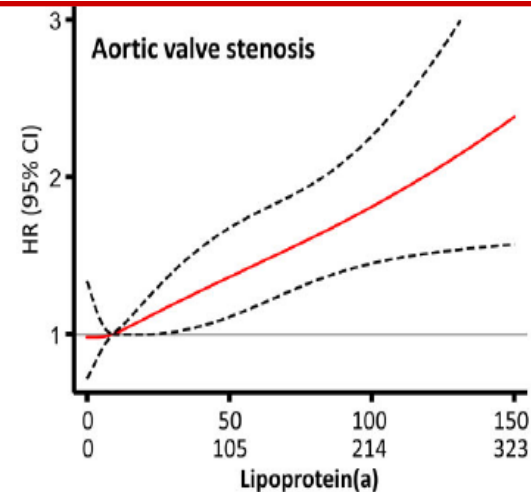
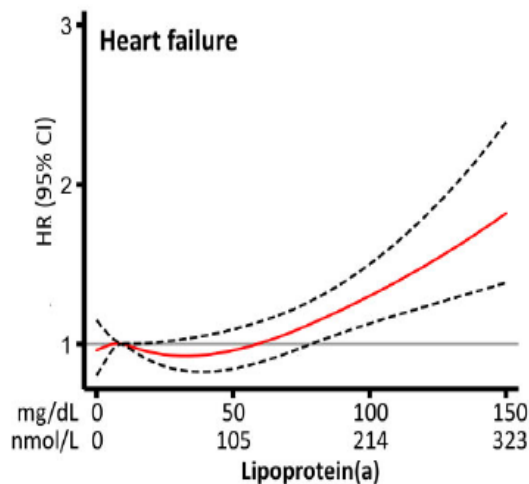
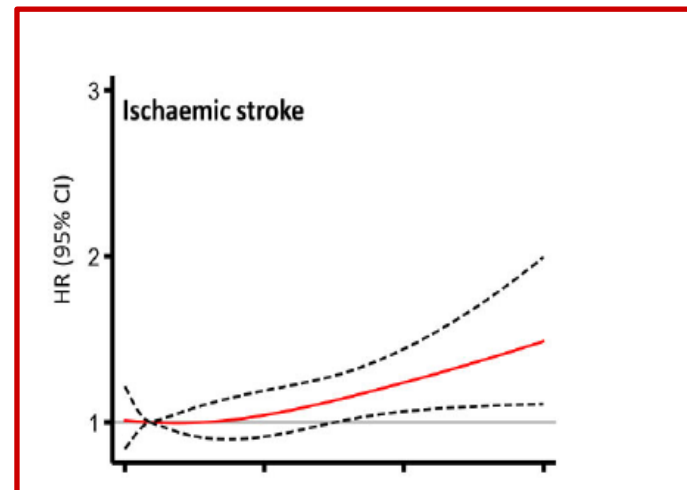
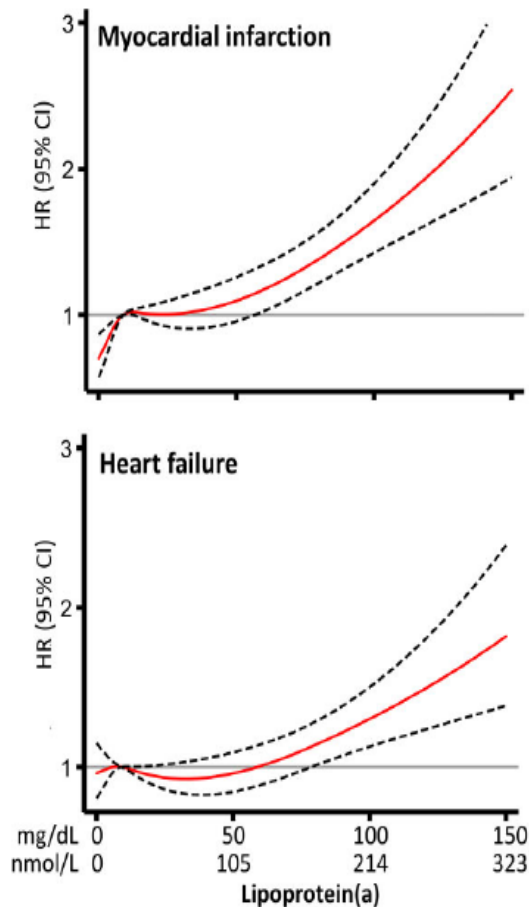
- ❑ Population study : 70286 white individuals (Copenhagen)
- ❑ Median Follow-up : 7.4 years



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European Heart Journal 2022

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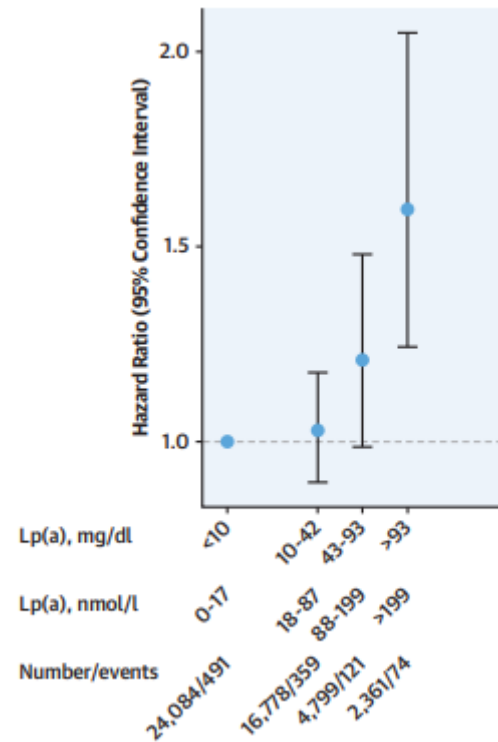
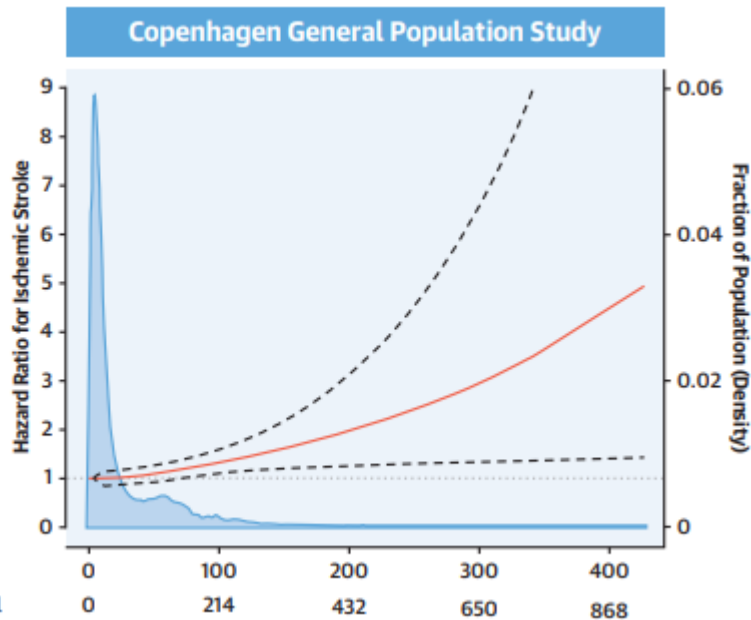
Elevated Lp(a) and risk of ischemic stroke

JACC 2019

- 49,699 individuals (Copenhagen General Population study)
- Plasma levels of Lp(a)
- Analyse génétique (randomisation mandélienne)
 - Kringle-IV type 2 numbers of repeat
 - LPA rs10455872
- Endpoints : ischemic stroke
- Ajustements pour age, sex, smoking, SBP, BMI, lipid lowering therapy, LDL (corrected by subtracting 30% of total Lp(a) mass)

Elevated Lp(a) and risk of ischemic stroke

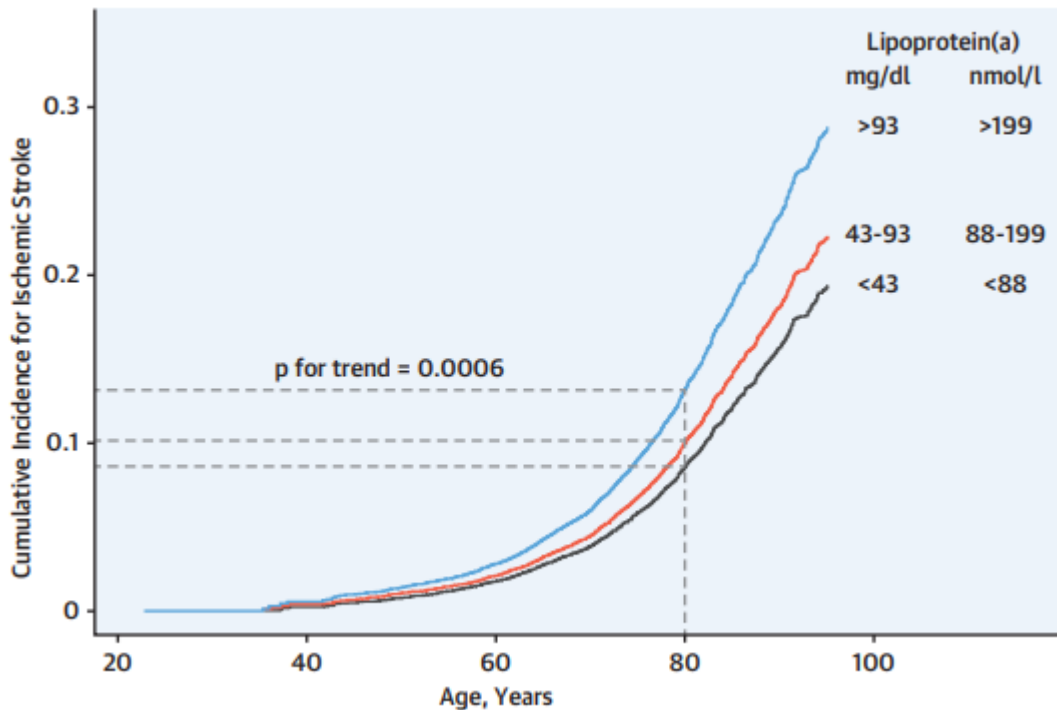
JACC 2019



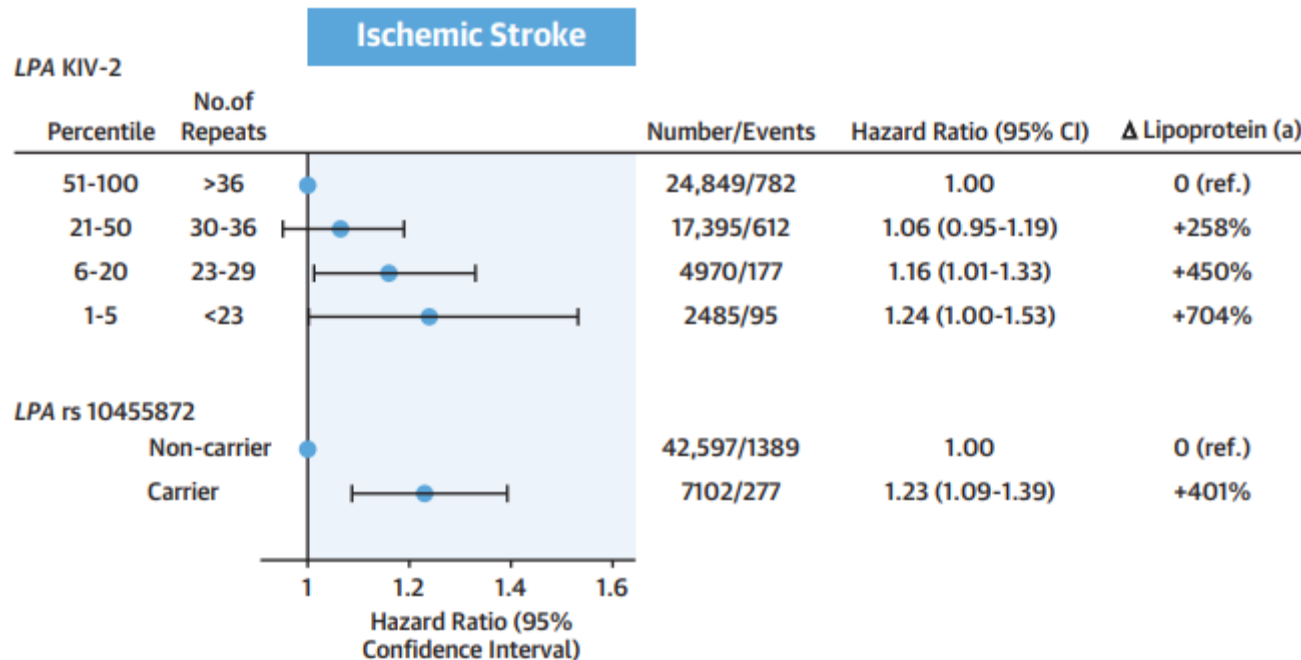
Median : 10 mg/dL

Elevated Lp(a) and risk of ischemic stroke

JACC 2019



Elevated Lp(a) and risk of ischemic stroke



❑ Highest absolute 10-y risk women above 70, active smokers and HTA from 11% to 17% with Lp(a) levels >93 mg/dL (96th to 100th percentile)

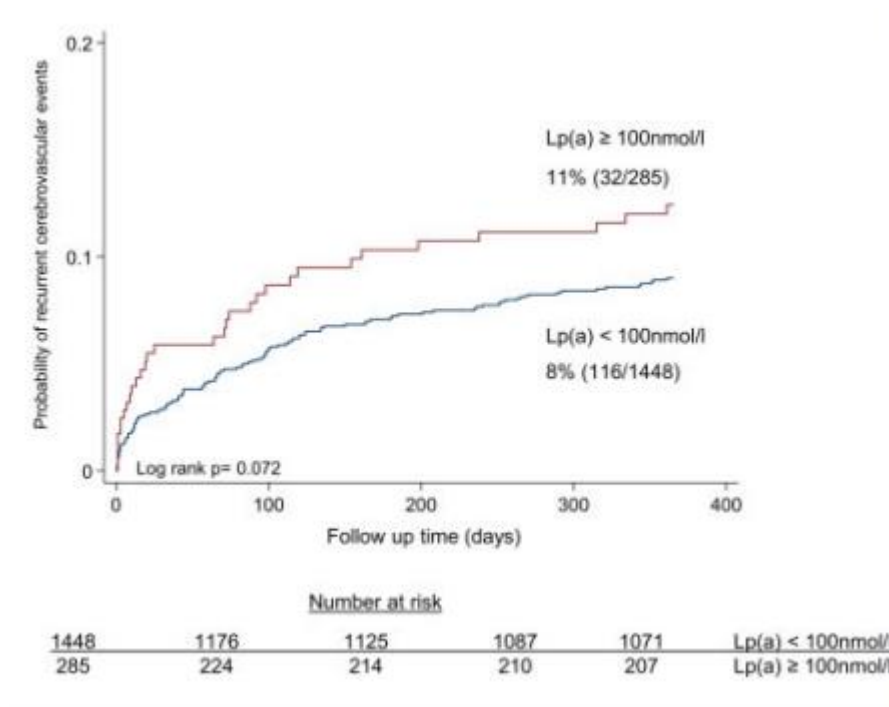
❑ Individuals with Lp(a) levels in the top 5% had a 60% increased risk of IS compared with individuals with levels at or below the median

Lp(a) and recurrent stroke

BIOSIGNAL STUDY

Eur Heart J 2021

- 1733 Caucasian IS patients
- Outcomes: LAA etiology and IS/TIA within 1 year

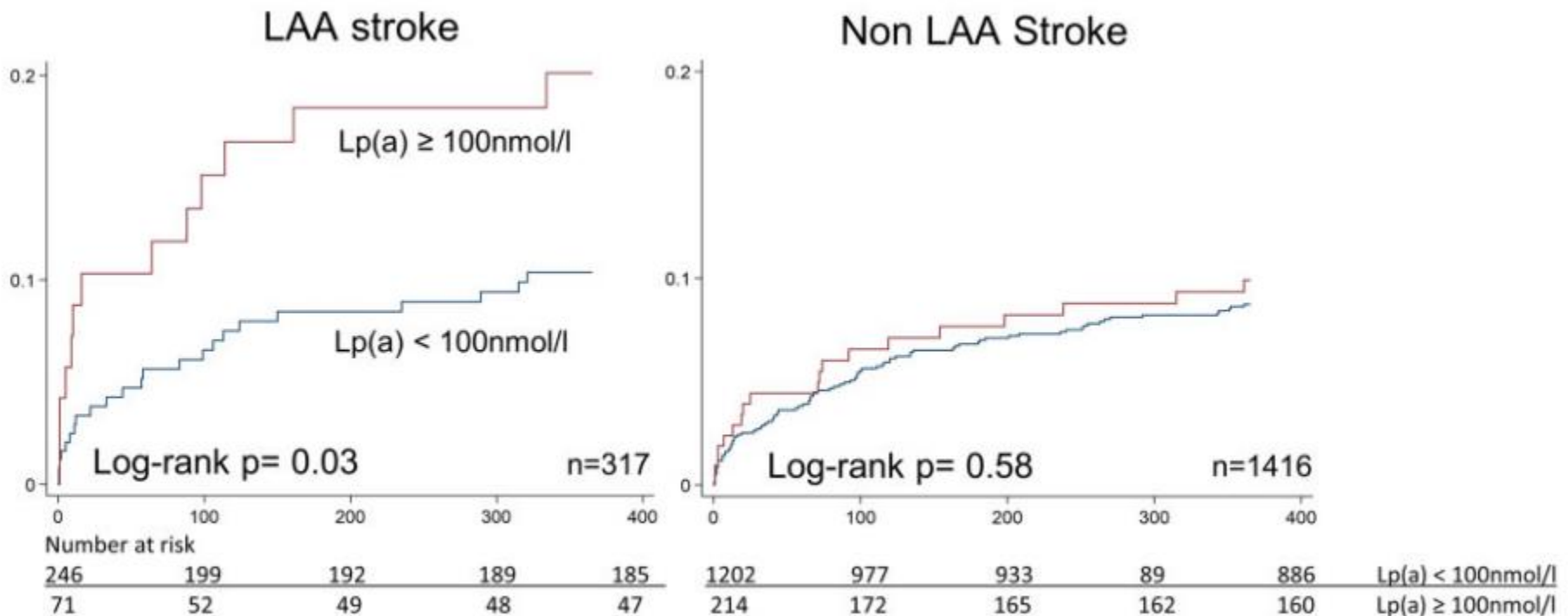


Lp(a) and recurrent stroke

BIOSIGNAL STUDY

Eur Heart J 2021

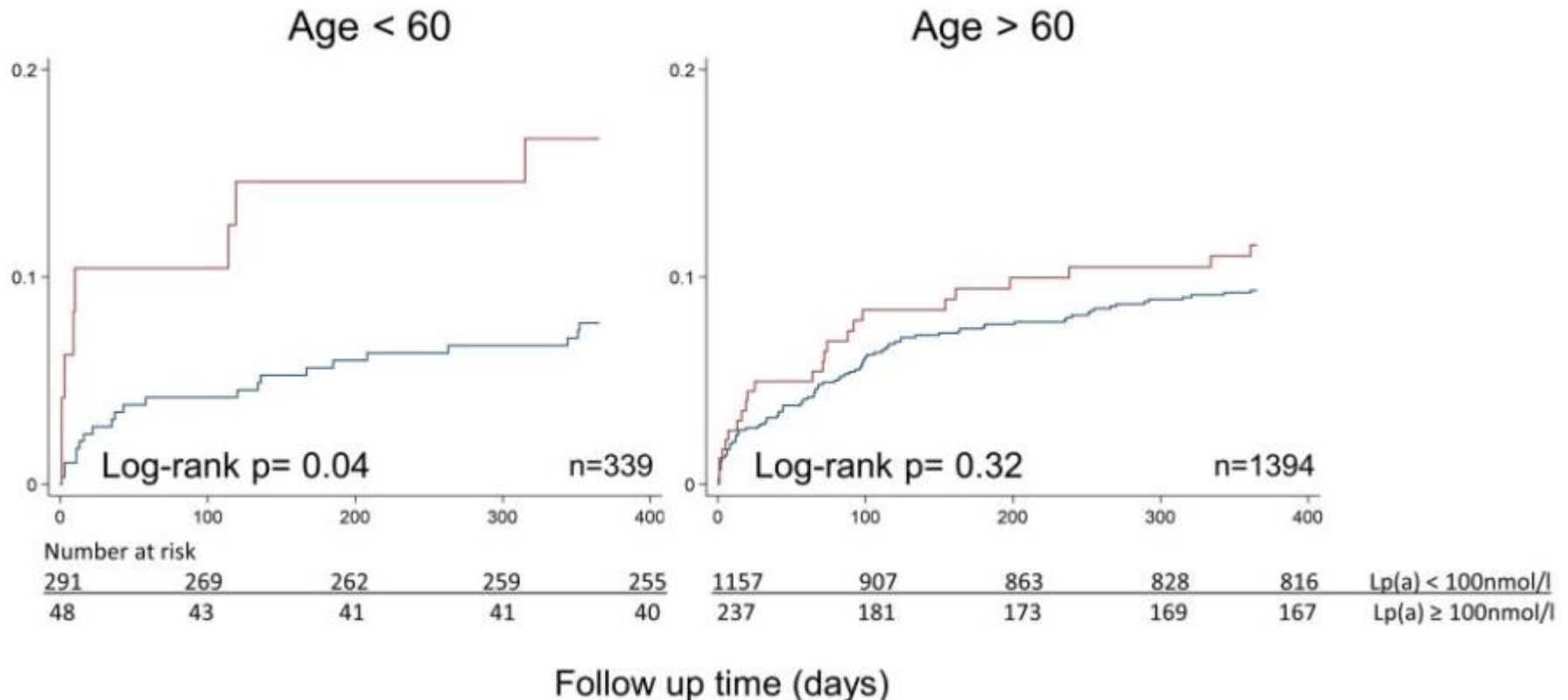
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Lp(a) and recurrent stroke BIOSIGNAL STUDY

Eur Heart J 2021

- 1733 Caucasian IS patients
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REGARDS study

ATVB 2019

- 30239 black and white US adults ≥ 45 y
- Lp(a) in 572 cases of incident IS and 967-person cohort random
- Adjustment for age, sex, stroke risk factors

Table 1. Sex-Race Specific Lp(a) Quartile Values in the REGARDS Cohort Random Sample

Group	Q1	Q2	Q3	Q4
	N=215	N=241	N=265	N=246
Lp(a), black men, mg/dL	<13	13–26	27–56	≥ 57
Lp(a), black women, mg/dL	<17	17–32	33–55	≥ 56
Lp(a), white men, mg/dL	<4	4–8	9–31	≥ 32
Lp(a), white women, mg/dL	<4	4–10	11–39	≥ 40

Lp(a) indicates lipoprotein(a); Q, quartile; and REGARDS, Reasons for Geographic and Racial Differences in Stroke.

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REGARDS study

ATVB 2019

	First Quartile	Second Quartile	Third Quartile	Fourth Quartile	Interaction P Value
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	
All					
N cases	99	114	174	160	
N controls	215	241	265	246	
Model 1	1.0 (ref)	1.05 (0.72–1.53)	1.43 (1.01–2.03)	1.38 (0.96–1.98)	
Model 2	1.0 (ref)	1.24 (0.81–1.92)	1.49 (0.98–2.25)	1.45 (0.96–2.19)	
Blacks					
N cases	39	43	66	79	
N controls	104	124	122	128	
Model 1	1.0 (ref)	0.90 (0.51–1.59)	1.47 (0.87–2.49)	1.74 (1.03–2.94)†	
Model 2	1.0 (ref)	0.95 (0.50–1.81)	1.48 (0.82–2.67)	1.96 (1.10–3.46)†	
Whites					
N cases	60	71	108	81	
N controls	111	117	143	118	
Model 1	1.0 (ref)	1.14 (0.70–1.86)	1.36 (0.86–2.14)	1.16 (0.72–1.87)	
Model 2	1.0 (ref)	1.59 (0.87–2.90)	1.39 (0.79–2.47)	1.14 (0.64–2.04)	
Race interaction, model 1/2					0.37/0.12

REGARDS study

ATVB 2019

Subtype	N	HR Stroke		
		Second Quartile	Third Quartile	Fourth Quartile
		HR (95% CI)	HR (95% CI)	HR (95% CI)
Cardioembolic	N			
All (107 cases)				
Model 1	1073	1.02 (0.50–2.07)	1.55 (0.82–2.95)	1.76 (0.93–3.34)
Model 2	984	1.43 (0.61–3.34)	1.41 (0.64–3.14)	1.63 (0.73–3.64)
Black (36 cases)				
Model 1	514	1.20 (0.38–3.84)	1.61 (0.53–4.89)	2.04 (0.70–6.00)
Model 2	472	1.71 (0.42–7.03)	1.88 (0.49–7.19)	3.25 (0.92–11.52)
White (71 cases)				
Model 1	559	0.92 (0.38–2.25)	1.49 (0.68–3.25)	1.65 (0.75–3.64)
Model 2	512	1.18 (0.36–3.89)	0.98 (0.33–2.87)	1.02 (0.33–3.16)

REGARDS study

ATVB 2019

Large vessel disease				
All (74 cases)				
Model 1	1040	1.42 (0.61–3.30)	1.98 (0.90–4.32)	2.18 (1.00–4.77)
Model 2	948	1.55 (0.62–3.88)	1.63 (0.69–3.84)	2.00 (0.84–4.75)
Black (26 cases)				
Model 1	504	1.75 (0.41–7.40)	2.74 (0.70–10.74)	2.35 (0.57–9.63)
Model 2	459	1.45 (0.29–7.25)	1.90 (0.39–9.15)	2.15 (0.44–10.43)
White (48 cases)				
Model 1	536	1.29 (0.45–3.71)	1.69 (0.65–4.39)	2.09 (0.81–5.39)
Model 2	489	1.81 (0.48–6.74)	1.47 (0.44–4.97)	2.30 (0.68–7.75)

REGARDS study

ATVB 2019

Small vessel disease				
All (85 cases)				
Model 1	1051	1.13 (0.57–2.24)	1.55 (0.82–2.92)	0.64 (0.30–1.39)
Model 2	962	1.25 (0.56–2.77)	1.99 (0.99–4.00)	0.69 (0.30–1.57)
Black (42 cases)				
Model 1	520	0.65 (0.23–1.86)	1.28 (0.50–3.26)	1.15 (0.44–2.97)
Model 2	476	0.66 (0.18–2.37)	1.50 (0.53–4.23)	1.16 (0.41–3.33)
White (43 cases)				
Model 1	531	1.66 (0.66–4.18)	1.64 (0.67–4.04)	0.10 (0.01–0.86)
Model 2	486	2.75 (0.76–9.95)	2.58 (0.83–7.97)	0.15 (0.02–1.39)

Lp(a) et AVC en pratique

- ❑ Intérêt pour l'identification d'un sous-groupe à très haut risque (athérosclérose)
- ❑ Identifier les « résistants » aux statines
- ❑ Cut-off : top 5%, taux $>100\text{mg/dL}$?
- ❑ Cible thérapeutique à étudier dans des ECR