The risk of MACE associated with elevated Lp(a) in a primary prevention population

EPH58

Harriet Benbow[1], Anas Al Zabiby[2], Hannah Byrne[1], Madlaina Costa-Scharplatz[3]

[1]Novartis Ireland, Dublin, Ireland; [2]Novartis, Kuala Lumpur, Salangor, Malaysia; [3]Novartis, Stockholm, Kista, Sweden

Introduction

- Elevated lipoprotein(a) [Lp(a)] is an independent, inherited risk factor for atherosclerotic cardiovascular disease (ASCVD)[1]
- Guidelines now recommend Lp(a) to be measured at least once per lifetime for all adults[2]

Aim: To characterize the impact of elevated Lp(a) on the risk of first and recurrent major adverse cardiovascular event (MACE) in a United Kingdom (UK) Biobank primary prevention population

Methods

- This UK Biobank study, conducted under approved project number 59456, included a primary prevention cohort of 441,896 individuals with an Lp(a) measurement and no ASCVD diagnosis prior to enrollment (**Table 1**)
- Lp(a) was measured in a single accredited biochemistry centre using a Randox assay traceable to the WHO/IFCC reference material
- The UK Biobank contains linked hospital episode statistics (HES) from 1991–2020, with enrollment and Lp(a) measurement from 2006–2010, giving an available follow-up period of 2006–2020
- ASCVD (defined as MI, IS, stable or unstable angina, transient ischemic attack, peripheral artery disease, revascularization procedures, and other coronary artery disease diagnoses) and MACE (defined as myocardial infarction [MI], ischemic stroke [IS], and cardiovascular [CV] death) were identified from the linked HES data
- Associations of serum Lp(a) levels with incidence of and time to first MACE were analysed by calculating incidence rates (per 100 person-years), and Cox proportional hazard models, adjusted for age, sex, and ethnicity

Results

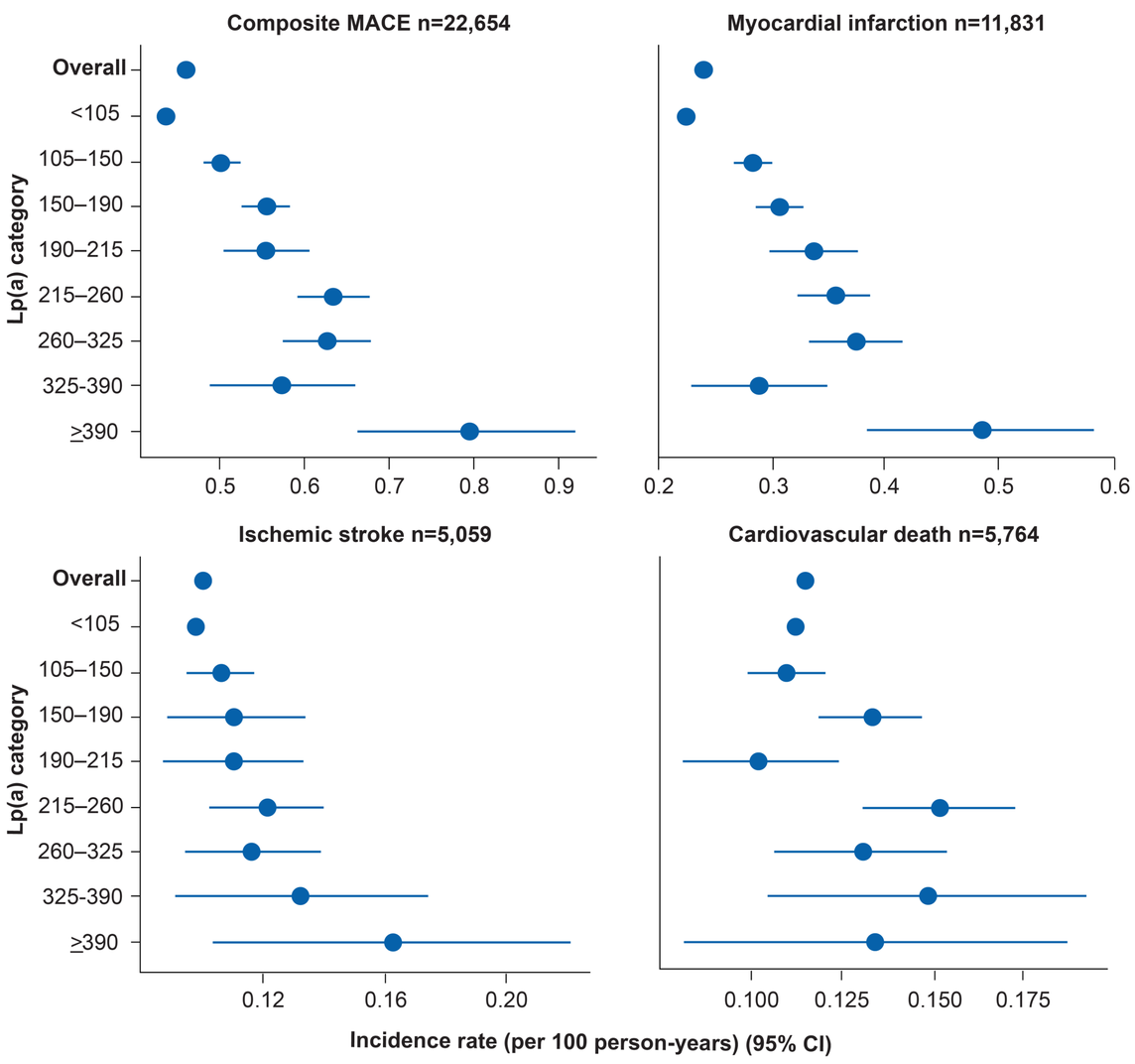
Table 1. Demographics and clinical characteristics

	Parameters, n (%)	N = 441,896
Sex	**Female**	**243,835 (55.2%)**
	Male	198,061 (44.8%)
Age	**Mean age at enrolment, years (SD)**	**56.32 (8.09)**
Follow-up	**Median, years**	**11.54**
Ethnicity	**White**	**416,561 (94.3%)**
	Asian or Asian British	9,755 (2.2%)
	Black or Black British	6,960 (1.6%)
	Mixed	6,571 (1.5%)
	Unknown	2,049 (0.5%)
Biomarker (mean, SD)	**Lp(a), nmol/L, median (IQR)**	**19.40 (7.6-73.1)**
	Total cholesterol, mg/dL	221.86 (43.5)
	LDL-C, mg/dL	138.77 (33.1)
	HDL-C, mg/dL	56.32 (14.7)
	Triglycerides, mg/dL	154.23 (90.7)
	C-reactive protein, mg/dL	2.57 (4.3)
	BMI	27.34 (4.7)
	SBP, mmHg	139.68 (19.6)

Incidence rates

- Five percent of the cohort experienced a MACE (3% MI, 1% IS, 1% CV death) during the available follow-up
- Incidence rates (IRs per 100 person-years) of first MACE from 0.432 in the Lp(a) <105 nmol/L category by 16–82% in Lp(a) ≥105 nmol/L categories (**Figure 1**)

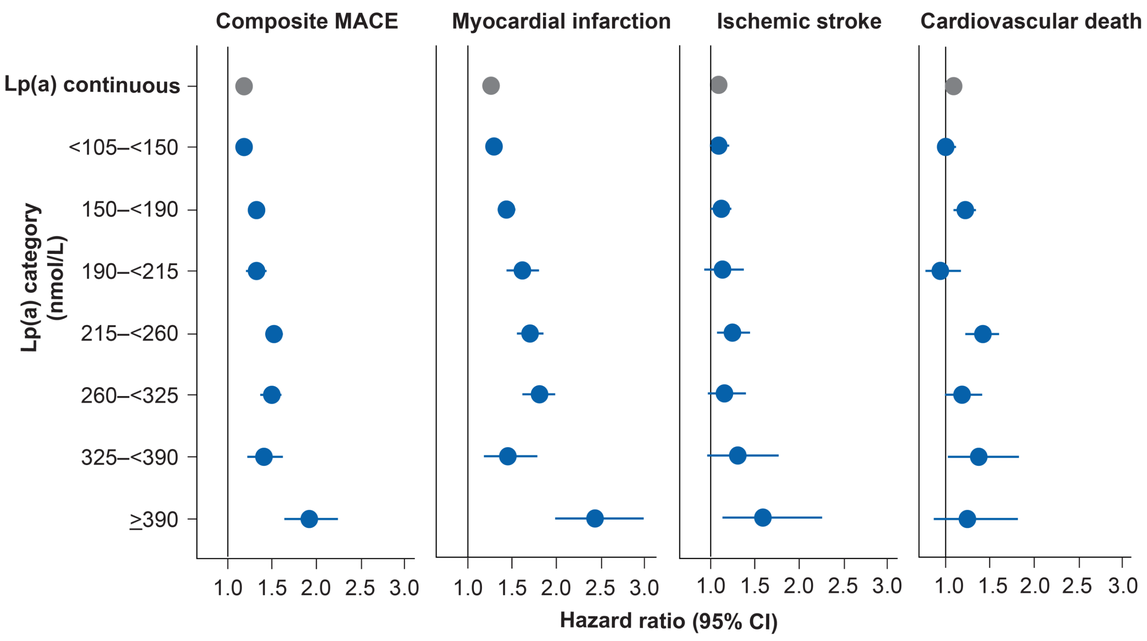
Figure 1. Annualized incidence rates of composite and disaggregated MACE overall and stratified by Lp(a)



Cox hazard ratios

- A 100 nmol/L continuous increase in Lp(a) was associated with an 18% increased risk of first MACE, 24% of MI, 8% of IS and 9% of CV death (**Figure 2**)
- When compared to Lp(a) <105 nmol/L, risk of first MACE increased from 17% up to 91% with increasing Lp(a) categories

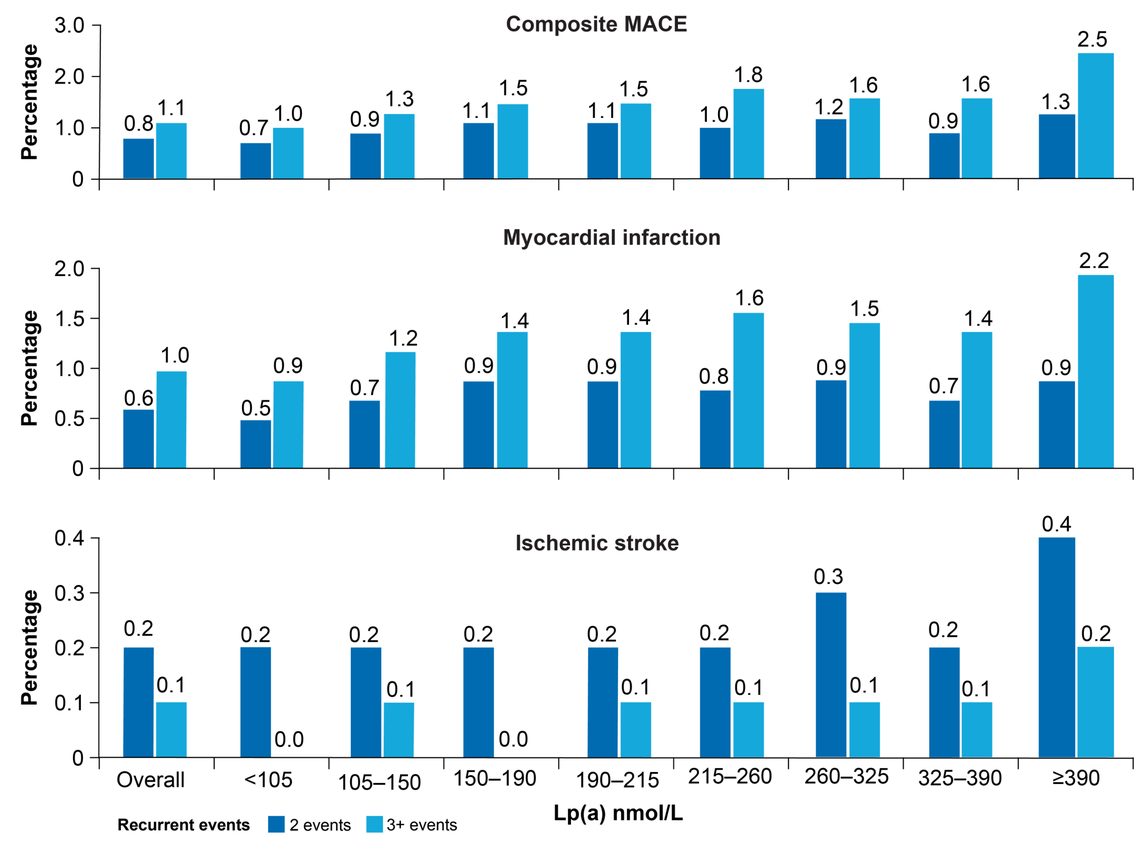
Figure 2. Cox HRs associated with Lp(a) for composite and disaggregated MACE



Recurrent MACE

- Elevated Lp(a) was associated with an increased risk of recurrent MACE (**Figure 3**)
- In the Lp(a) <105 nmol/L category, 0.7% individuals had 2 and 1% had 3+ events
- In Lp(a) ≥105 nmol/L categories, the percentage of individuals with 2 events ranged from 0.9–1.3%, and from 1.3–2.5% for those with 3+ events

Figure 3. Recurrent composite and disaggregated MACE across Lp(a) levels



Conclusions

Individuals with elevated Lp(a) are significantly more likely to experience a first MACE. Within increasing levels of Lp(a), risk of first MACE increases by 18% for every 100 nmol/L. Those at the highest Lp(a) levels have over double the risk of a first MI compared to lower Lp(a) levels. These individuals are also at higher risk of recurrent events and, ultimately, a CV related death. Therefore, Lp(a) testing should be considered in clinical practice for early identification and intervention of high-risk individuals, to mitigate the burden of CV disease

Abbreviations

ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; CV, cardiovascular; HES, hospital episode statistics; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; IS, ischemic stroke; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); MACE, major adverse cardiovascular events; MI, myocardial infarction; n, number of patients; N, total number of individuals in cohort; SBP, systolic blood pressure; UK, United Kingdom

References

1. Tsimikas. *J Am Coll Cardiol.* 2017;69:692–711.
2. Mach, et al. *Eur Heart J.* 2020;41(1):111–188.

Disclosures

All authors are employees of Novartis.

Poster presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) - Europe 2023, 12–15 November 2023, Copenhagen, Denmark.