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A possible paradoxical association between LDL-cholesterol in myocardial infarction patients and relation to major adverse outcomes - a 10-year nationwide cohort study

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Background: Cardiovascular disease (CVD) risk increases with the level of LDL-cholesterol (LDL-C), and LDL-C lowering treatment improves prognosis. Less is known about LDL-C levels at myocardial infarction (MI) admission and long-term prognosis.

Purpose: To investigate admission LDL-C levels in relation to mortality, recurrent MI and baseline characteristics.

Methods: Patients admitted with an MI in Sweden and recorded in the MI-registry (SWEDEHEART) 2006–2016 were included and followed until 2018. Associations between baseline LDL-C, mortality and MI were assessed with Cox regression analysis, adjusting for risk factors (eg. age, diabetes, prior CV events) and lipid lowering therapy.

Results: Of 126,669 patients (median age: 70) admitted with MI, 26.2% (n=32,883) had ongoing statin therapy, and the median LDL-C was 2.96 (interquartile range 2.23, 3.74) mmol/L. During median follow-up of 4.2 years, 31,024 died and 17,896 had an MI (table). Patients with higher LDL-C were younger, had substantially fewer comorbidities such as diabetes and prior CVD ($p<0.001$). In this analysis there was an interaction with ongoing statin-use (p=0.0025). When dividing patients by LDL-C into quartiles, statin naive in the highest LDL-C quartile (3.95 mmol/L) had a lower risk of death compared to patients in the lowest quartile (2.62 mmol/L) HR 0.86 (95% CI 0.83–0.90). For patients with ongoing statin, the risk was also lower with higher LDL-C (2.84 mmol/L) compared to lower LDL-C (1.72 mmol/L) HR 0.88 (95% CI 0.81–0.96). No association was observed between LDL-C and recurrent MI.

Conclusions: In this real-world population with over 126,000 patients and 10 years of follow-up, higher LDL-C at the time of the MI was associated with a markedly better prognosis in patients with and without prior statin therapy. This paradox may, despite adjustment, be caused by a substantially lower CVD baseline risk in patients with higher LDL-C pertaining to a lower burden of risk factors, younger age, and fewer prior CVD events as well as a highly treatable risk factor.

Table 1. Event rate for mortality and myocardial infarction (MI) by LDL quartile groups

		Q1	Q2	Q3	Q4
LDL-C (mmol/L)	Statin naive	<2.62	2.62–3.26	3.26–3.95	>3.95
	Ongoing	<1.72	1.72–2.21	2.21–2.84	>2.84
Mortality	Statin naive	0.074 (6553)	0.049 (4596)	0.037 (3706)	0.030 (2949)
	Ongoing	0.10 (3297)	0.075 (2769)	0.062 (2462)	0.055 (2157)
MI	Statin naive	0.034 (2808)	0.026 (2292)	0.024 (2269)	0.023 (2094)
	Ongoing	0.064 (1796)	0.055 (1792)	0.048 (1694)	0.044 (1557)

Event/year (n of events) stratified by statin treatment at index event.