

Risk assessment and risk reduction by perindopril in patients with normal left ventricular function or previous revascularization in the EUROPA study

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BACKGROUND

In the EUROPEAN trial on Reduction Of cardiac events with Perindopril in stable coronary Artery disease (EUROPA), perindopril 8 mg daily significantly reduced the primary endpoint (cardiovascular death, non-fatal myocardial infarction and resuscitated cardiac arrest) by 20%, compared to placebo, after a follow-up of 4.2 years in patients with stable coronary artery disease (CAD). Subsequent risk profiling showed a consistent risk reduction among low, intermediate and high risk patients, respectively, with relative risk reductions of 17%, 32% and 12% in the perindopril group (interaction p-value = 0.15). Whether this pertains in patients with a normal left ventricular function or previous revascularisation is unknown.

METHODS

Of the 12218 patients included in EUROPA, 6878 had a quantified left ventricular ejection fraction (LVEF) \geq 40% and 6709 had a previous revascularization at baseline. For each patient, a risk score was composed of 12 independent risk factors identified by multivariate analysis (table). According to risk score, the population was divided in tertiles of risk level: low, intermediate or high.

To develop a risk scoring system, univariate and multivariate analyses were performed. Significant variables in the univariate analysis were then entered into a multivariate analysis using a stepwise backward selection procedure until the removal of a variable caused a significant change between consecutive models. Interaction by treatment was investigated for each variable.

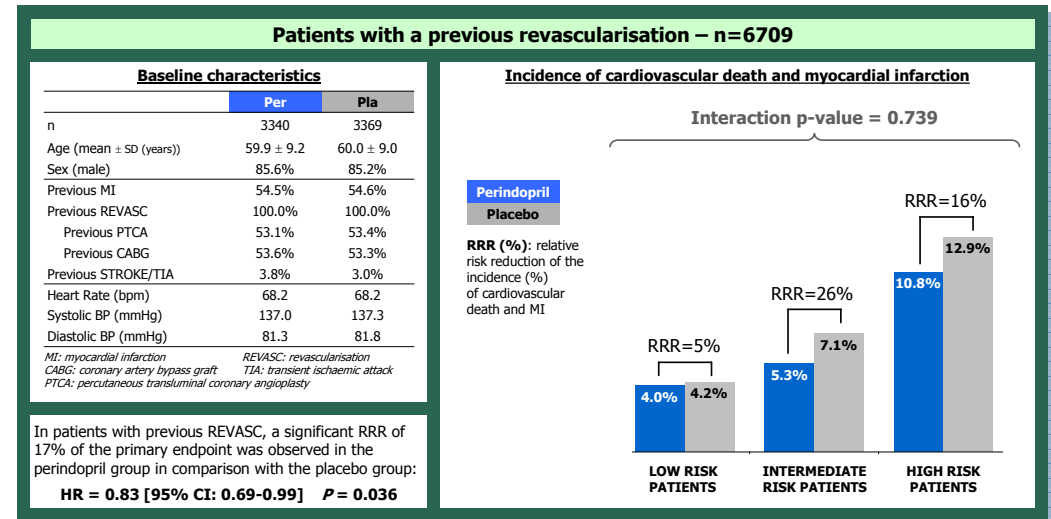
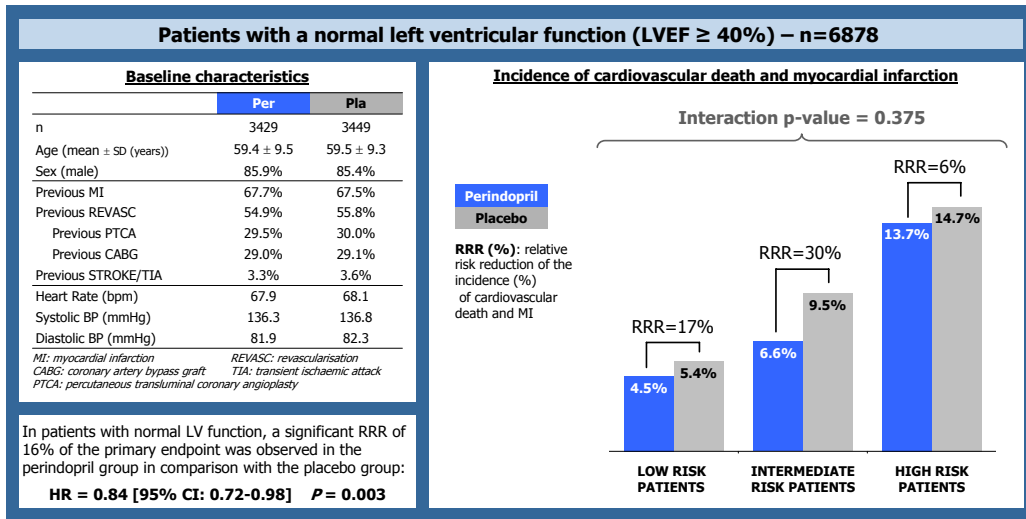
Table: Independent risk factors and score associated

-Age 67-69 years	+1	-Previous Myocardial Infarction	+2	-Current smoker	+2
70-72 years	+2	-Previous stroke or PVD	+3	-Symptomatic CAD	+2
73-76 years	+3	-Family history of CAD	+1	-Diabetes	+2
77-79 years	+4	-Cholesterol >3.5-5.0 mmol/L	+1	-Systolic BP 130-160 mmHg	+1
80-82 years	+5	>5.0-6.5 mmol/L	+2	>160 mmHg	+2
83-85 years	+6	>6.5-8.0 mmol/L	+3	-Creatinine >55-≤70 mL/min	+1
>85 years	+7	>8.0 mmol/L	+4	Clearance >35-≤55 mL/min	+2
-Male	+2	-Obese (BMI>30 kg/m ²)	+2	≤35 mL/min	+3

PVD: peripheral vascular disease BMI: Body Mass Index

RESULTS

Treatment benefit associated with perindopril in 3 risk strata varied from 6% to 30% of relative risk reduction in patients with preserved LVEF and from 5% to 26% in revascularized patients. Test for heterogeneity of treatment effect was negative indicating that treatment benefit was not modified by risk level.



CONCLUSION

Treatment benefit with perindopril is consistent among low, intermediate and high risk patients with normal left ventricular function or previous revascularization without heterogeneity of treatment effect.