Detecting patients with a previously unknown risk of cardiovascular disease

For a more accurate assessment of cardiovascular risk

Test early. Treat right. Save lives.
Traditional risk factors fail to identify all individuals at risk of CVD

Cardiovascular disease (CVD) is a major health burden: a high proportion of patients are not classified correctly or even missed entirely for cardiovascular (CV) risk assessment
- More than 60% of those who develop coronary events have only one, or even none of the traditional risk factors, and more than half have either normal or mildly increased lipid values
- European Society of Cardiology’s (ESC) guidelines on CV risk prevention use the SCORE risk charts to estimate 10-year risk of fatal CV disease, which takes into consideration age, smoking status, systolic blood pressure and total cholesterol
- Additional factors can be added to help further improve overall risk assessment

Additional biomarkers improve current CV risk assessment
- Lp(a) predicted CV events in both the control and placebo group, suggesting that Lp(a) still contributes to residual CV risk in patients achieving target LDL-C levels with statin therapy

Lp(a) is a major contributor to CVD and residual risk
- Epidemiologic studies and meta-analyses have demonstrated a robust and specific association of elevated Lp(a) levels with an increased risk of CHD
- Almost 20% of the population possess elevated levels of Lp(a) who place them at an increased risk for CVD
- CVD events persisted in subjects with high Lp(a) levels who’s LDL cholesterol had been lowered <1.8 mmol/L by statin therapy
- Lp(a) has been found to be responsible for this phenomenon
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The addition of Lp(a) to risk models for CVD can improve patient risk classification
- With addition of Lp(a) to risk models, 39% and 25% of patients with lipoprotein(a) levels >90th percentile could be reclassified for myocardial infarction (MI) events and coronary heart disease (CHD), respectively
- Extreme Lp(a) levels substantially improve risk prediction for MI and CHD risk
- The European Atherosclerosis Society Consensus Panel recommends screening for elevated lipoprotein(a) in individuals at intermediate or high CVD/CHD risk

hsCRP is a strong predictor of cardiovascular disease
- High sensitive C-reactive protein (hsCRP) has been shown to be a predictor of CVD in multiple studies
- Large scale prospective studies in the US and Europe have consistently shown the predictive value of CRP in CVD
- C-reactive protein has been shown to be a better predictor of the risk of cardiovascular events than low-density lipoprotein (LDL) cholesterol
- In a meta-analysis of 22 studies with an average follow-up of 12 years, the top CRP tertile showed a 58% increased cardiac risk compared to the bottom CRP tertile

Risk prediction models can be improved by the addition of hsCRP
- The addition of hsCRP to the Framingham risk score led to a net classification of 11.8% and 5.6% for CHD and CVD respectively
- More than 20% of all participants with intermediate risk could be reclassified with the addition of hsCRP

The use of hsCRP in risk prediction is recommended by various guidelines
- ESC guidelines recommend that hsCRP may be measured as part of refined risk assessment in patients with an unusual or moderate CV risk profile
- If risk is intermediate (19% – 20%) and uncertainty remains as to the use of preventive therapies such as statins or Aspirin, then hsCRP measurement might be useful for further stratification into a higher or lower risk category
- The optional use of hsCRP to identify patients without known CVD who may be at higher absolute risk than estimated by major risk factors, specifically, those patients at intermediate risk (e.g., 10% to 20% risk of coronary heart disease over 10 years) Result can guide physicians in evaluation further diagnosis or treatment decisions

Homocysteine is a strong, independent risk factor for cardiovascular disease
Numerous clinical and epidemiologic studies have established elevated blood homocysteine (Hcy) as a potent independent risk factor for vascular disease
- Subsequent observations from approximately 80 clinical and epidemiologic studies have demonstrated that hyperhomocysteinemia is an independent, dose-dependent risk factor for atherosclerotic vascular disease and for arterial and venous thromboembolism
- For example, moderate-to-intermediate hyperhomocysteinemia is present in 12–47% of patients with coronary, cerebral, or peripheral arterial occlusive diseases

Homocysteine is an early risk marker for high-risk patients with proven positive patient outcome
- Meta-analysis of 72 studies has demonstrated significant associations between homocysteine and the risk of ischaemic heart disease, deep vein thrombosis, pulmonary embolism and stroke. The results of the meta-analysis provide further strong evidence for a causal relationship between elevated homocysteine and CVD
- Modest reduction of homocysteine is predicted to lower the risk of CVD up to 25%

Lowering homocysteine reduce the risk up to 25% for CVD

Homocysteine provide additive prognostic information over cholesterol
A 5 µmol/L increase in Hcy is equivalent to approx. 20 mg/dl increase in total cholesterol levels. Numerous studies have shown that the connection between Hcy levels and atherosclerosis is even stronger than the connection between atherosclerosis and cholesterol. A concentration-dependent correlation between HCY and CV risk has been established from the Framingham study.

Homocysteine as a risk factor for coronary heart disease
Boushey, et al., performed a meta-analysis of 27 clinical studies, and summarized the odds ratio between elevated HCY and development of vascular disease. The authors found an OR of 1.8 (95% CI 1.4 to 1.7) for men and 1.8 (95% CI, 1.3 to 1.9) for women for a 5-mol/L HCY increment, suggesting that about 10% of the population’s CHD risk appears attributable to HCY. The results of the meta-analysis provide further strong evidence for a causal relationship between elevated homocysteine and CVD

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<td>Low CRP - low LDL</td>
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- Lp(a) levels are associated with future CV disease and CHD events\(^1\)
- hsCRP levels can identify the risk of future heart attack and stroke\(^2\)
- Homocysteine is a strong, independent risk factor for CV disease\(^3-5\)
- Lp(a), hsCRP and HCY improve cardiovascular risk assessment allowing for better treatment decisions\(^6\)

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