

MONOGRAPH

Clinical Utility:

Haptoglobin genotype is a screening for diabetic patients at risk for cardiovascular disease (CVD). Haptoglobin (Hp) is an acute phase protein that binds to freely circulating hemoglobin to prevent iron-mediated oxidative damage to blood vessels. Haptoglobin exists as two distinct forms, Hp1 and Hp2. The longer Hp2 form has been associated with cardiovascular (CVD) events and mortality in individuals with type 2 diabetes (T2DM). Haptoglobin allele frequency in European populations is 40% for Hp1 and 60% for Hp2.

Useful For:

- Identification of diabetic patients who are most at risk for cardiovascular disease for risk stratification purposes
- Identification of those diabetic patients who may benefit from Vitamin E therapy to prevent oxidative vascular damage
- May aid in the evaluation of new therapies to prevent CVD in the diabetic patient

Assay Interpretation:

In patients with diabetes, the antioxidant capacity of Hp for glycosylated hemoglobin is reduced. Hp1 has a smaller molecular weight that allows Hp to enter the extravascular space. The increased size of Hp2 prevents its entrance into the extravascular space and prolongs clearance of free hemoglobin from the circulation. The Hp2 genotype predicts the highest risk for CVD in diabetes, Hp1-2 predicts intermediate risk and Hp1-1 predicts the lowest risk. The genotype of Hp does not predict CVD risk in the general population. Hp2-2 has been associated with a 2–3 fold increased incidence of atherothrombosis in individuals with diabetes (DM) in 10 longitudinal studies compared to DM individuals not homozygous for this duplication (Hp1-1/1-2).

Haptoglobin genotype is a predictor of CVD in the diabetic population but not in the general population. Diabetic patients with the Hp2-2 are 5x more likely to have a CVD than patients with Hp1-1. Patients with an Hp1-1 genotype are at decreased risk for retinopathy, nephropathy and microvascular complications. Consider the implementation of 400U of vitamin E (daily) for diabetic patients with Hp2-2 genotype to provide additional antioxidant coverage for prevention of CVD, as demonstrated in the ICARE study.

Risk Levels by Genotype

- **Hp2-2** genotype—predicts highest risk for CVD in diabetics.
- **Hp1-2** genotype—predicts intermediate risk for CVD in diabetics.
- **Hp1-1** genotype—predicts lowest risk for CVD in diabetics.

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References:

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