

Circulating levels of a lung protein found to be 'strongly predictive' of cardiovascular disease

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A blood protein known as surfactant protein-D (SP-D), which is mainly synthesised in the lungs, has been described as "a good predictor" of cardiovascular disease following a large study in North America. Reporting the study online today in the *European Heart Journal*, the investigators said that circulating SP-D levels were clearly associated with CVD and total mortality in patients with angiographically diagnosed coronary artery disease independent of other well established risk factors (such as age, smoking, cholesterol and C-reactive protein levels).

In the lungs SP-D has a role in the body's defensive response to the many microorganisms and antigens inhaled each day, by binding to their surface and prompting their clearance from the body. Blood levels of SP-D increase when the lungs are inflamed and not working well - for example, when someone catches a cold, flu or other [respiratory tract infection](#). Blood levels also increase in those who smoke or develop a chronic lung condition such as asthma, emphysema or obstructive pulmonary disease (COPD).

In healthy people with normal lung function blood levels of SP-D are low, but when lung function is impaired (as with infections, smoking or COPD), SP-D leaks from the lungs into the blood and then into the circulation, increasing the risk of atherosclerosis.

This study aimed to determine whether or not circulating SP-D is related

to [cardiovascular morbidity](#) and mortality in two independent cohorts: first, a large cohort of patients having coronary angiography for suspected coronary artery disease (CAD); and second, a "replication" cohort of ex- and current smokers with mild airflow restriction but without a known history of CVD.

"We've known for a long time that chronic [lung inflammation](#) is associated with an increased risk of cardiovascular and total mortality," said investigator Dr Don Sin from the Providence Heart and Lung Institute at St Paul's Hospital, and University of British Columbia, Vancouver, Canada. "However, apart from lung function tests, there are no universally accepted biomarkers that could clearly predict these events. Recent studies have identified SP-D as a promising biomarker of lung inflammation and injury - for example, circulating SP-D levels are nearly 40% higher in active smokers than in lifetime non-smokers, and rise further in subjects with impaired [lung function](#). It was our hypothesis that in the systemic circulation SP-D may promote atherosclerosis."

Plasma SP-D levels were measured in 806 patients having coronary angiography. These patients were derived from the Vancouver [Coronary Angiography](#) Cohort referred for angiography between 1992 and 1995. [Coronary artery disease](#) (CAD) was defined as any lesion causing at least 20% stenosis (and severe CAD at least 50%). Follow-up continued until 2007, with primary outcome defined as CVD mortality. The replication cohort was derived from the Lung Health Study and included subjects with mild or moderate COPD.

The angiography patients who died during follow-up (30% of the cohort) had significantly higher plasma SP-D levels than those who survived (median 85.4 vs. 64.8 ng/mL; P

Eight per cent of the patients in this group had CAD (verified by

angiography), 71% had severe CAD, and 29% had angiographic evidence of triple vessel disease. CVD accounted for 45% of the total deaths in this group.

In the group of current and ex-smokers serum SP-D levels were higher in those who died or were hospitalised for CVD than in those who did not (median 99.8 vs. 90.6 ng/mL; $P = 0.0001$).

Dr Sin described the association between circulating SP-D levels and CVD as "strong" but emphasised that the study was designed to determine causality. "Based on our data," he said, "we cannot determine whether SP-D was intrinsically involved in the pathogenesis of cardiovascular events or an epiphenomenon of lung inflammation."

However, he agreed that circulating SP-D levels were a strong predictor of future CVD mortality, independent of other risk factors. "Our data certainly implicate lung inflammation in the pathogenesis of heart and blood vessel disease and raise the possibility of using this protein as a biomarker for risk stratification in CVD patients above and beyond the traditional biomarkers of serum cholesterol and [C-reactive protein](#). SP-D may provide a simple blood test to determine who has lung disease and is also at high risk of heart and blood vessel disease. Such patients could be targeted for interventions such as smoking cessation and drug therapy to lower their heart disease risk."

Provided by European Society of Cardiology

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