

New Inflammatory Marker Linked to Higher Mortality

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TORONTO — An elevated serum level of a novel inflammatory marker, YKL-40, was linked with a significantly increased risk for all-cause death and cardiovascular death in a study of more than 4,000 patients with a history of myocardial infarctions or angina.

"This is the first time that YKL-40 levels were tested in patients with cardiovascular disease," Dr. Jens Kastrup said at the 14th World Congress on Heart Disease. "We're now looking to see how YKL-40 may differ from brain natriuretic protein and C-reactive protein," said Dr. Kastrup, director of angiogenesis research at the Heart Centre of Rigshospitalet in Copenhagen.

YKL-40 is produced by macrophages in early atherosclerotic lesions, and serum levels are elevated in patients with inflammation and tissue remodeling. Results from prior studies showed that serum levels of YKL-40 are high in patients with ST-elevation MIs and in those with stable coronary artery disease. Elevated serum levels following MI eventually subside back close to normal. YKL-40 levels are also elevated in cancer patients, and results from other studies have suggested that YKL-40 may be a prognostic marker in cancer patients.

YKL-40 is measured by an investigational immunoassay made by Quidel Corp. of San Diego. Quidel provided some of the assays used in the current study but did not provide any other research support. Dr. Kastrup said that he and his associates had no other financial relationship with the company and that Quidel had no role in the design or conduct of the study, in the collection, analysis, or interpretation of the results, or in the preparation, review, or approval of the report from the study.

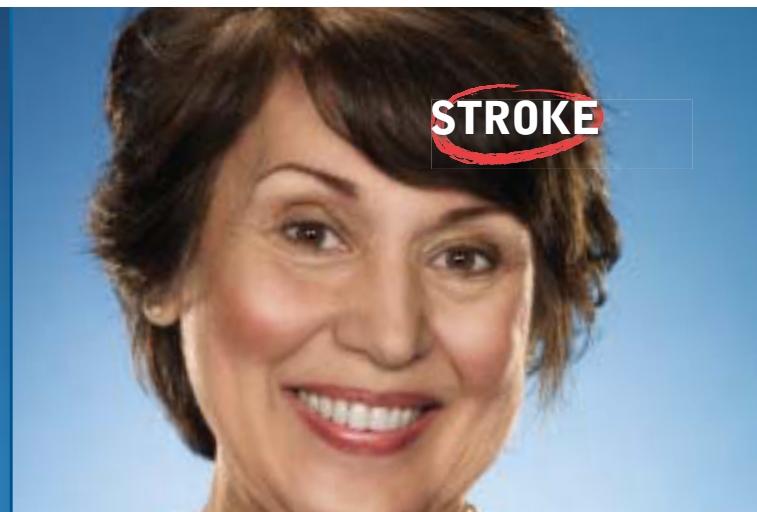
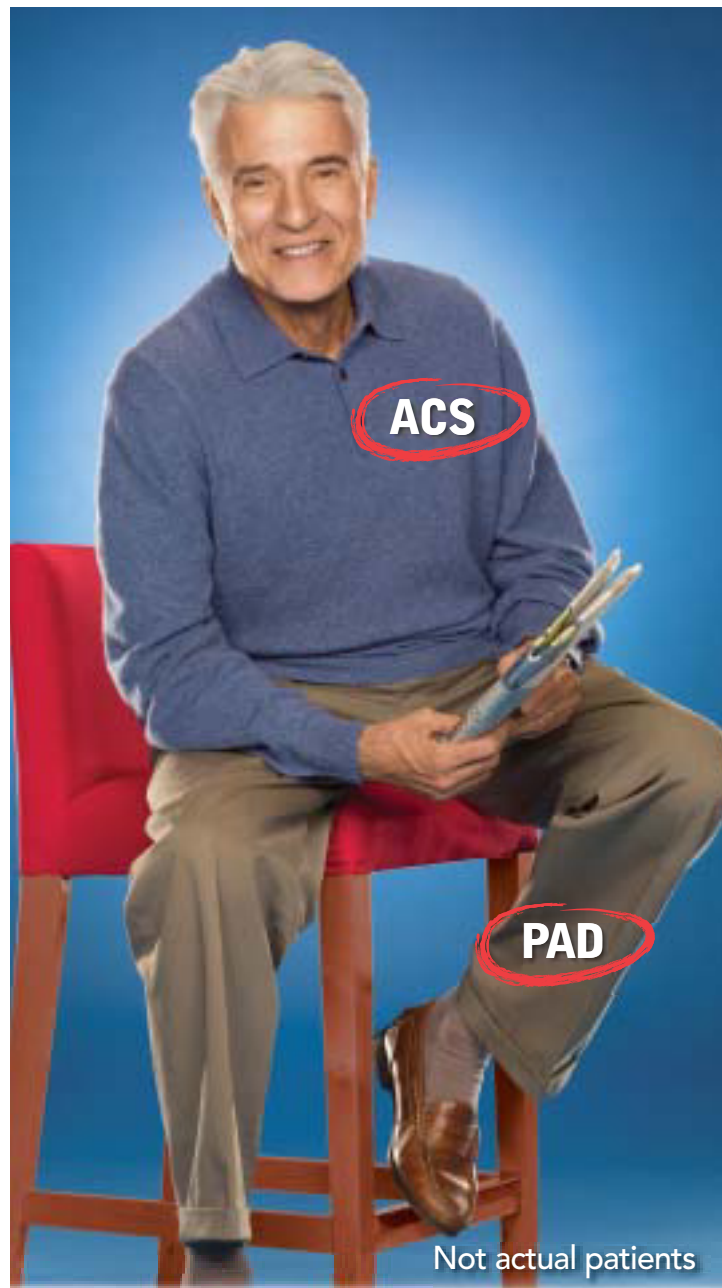
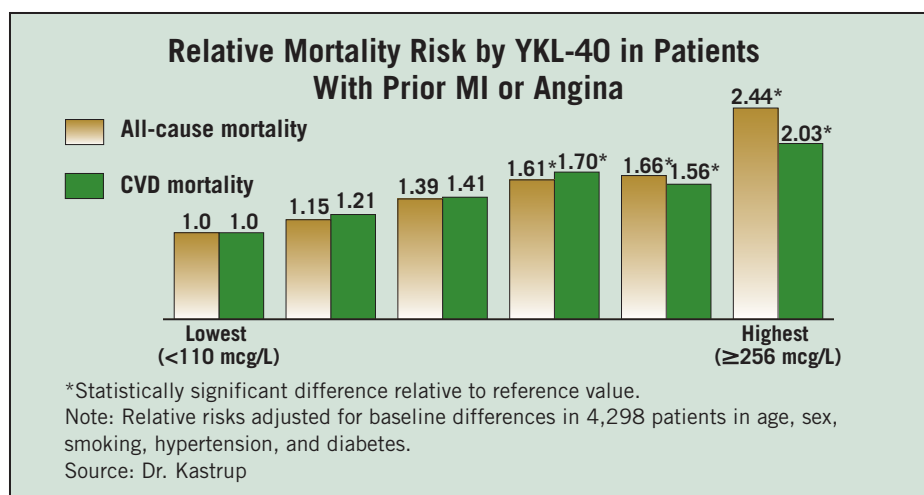
The current study was designed to test the hypothesis that high levels of YKL-40 would predict an increased risk for death. Serum specimens were used from 4,298 patients with a diagnosis of myocardial infarction (about two-thirds of the patients) or angina who had been enrolled in an earlier trial that had compared the efficacy of 2 weeks of treatment with clarithromycin against placebo (BMJ 2006;332:22-7).

The median level of YKL-40 in all patients from this study was 110 mcg/L, compared with a normal value of 30-40 mcg/L, Dr. Kastrup said at the congress, sponsored by the International Academy of Cardiology. The patients were divided into six groups based on their serum levels, ranging from the lowest group, which had serum values of less than 110 mcg/L, up to levels of 256 mcg/L or greater in the subgroup with the highest serum levels.

During an average follow-up of 2.6 years, the rate of all-cause death rose with the serum level of YKL-40, with the highest rate of death in patients in the subgroup with the highest serum level. After adjustment for baseline differences such as age, sex, smoking history, hypertension, and diabetes, patients with the highest

level of YKL-40 were about 2.4-fold more likely to die than were patients in the subgroup with the lowest level of YKL-40, a statistically significant difference.

Similar analyses showed that patients with the highest levels of YKL-40 were also significantly more likely to have a cardiovascular disease death than were patients with the lowest level (see chart). ■



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