健康人の心血管リスクの改善

JUPITER：一次予防としてスタチンを用いてLDLコレステロールおよびC反応性蛋白レベルを低下させることにより心血管リスクが改善する

JUPITER: Lowering LDL and C-reactive protein levels with statins improves cardiovascular risk in primary prevention

スタチン療法開始後に低密度リポ蛋白（LDL）コレステロールおよび高感度C反応性蛋白（hsCRP）が低下した健康な男女は心血管リスクが劇的に低下したとのデータが2009年第58回American College of Cardiology学会で発表され、同時にLancet誌に掲載された。このJUPITERスタディ（一次予防におけるスタチン使用の正当性の証明：ロスバスタチンを評価する介入試験）の解析において研究者らは、LDLおよびhsCRPレベルに関連した心筋梗塞、脳卒中、不安定狭心症による入院、動脈血行再建術、または心血管死発生率に対するロスバスタチン（20mg）とプラセボの効果を評価した。ロスバスタチンを内服しLDLコレステロールレベル70mg/L（1.8mmol/L）未満およびhsCRP2mg/L未満に達した者は心血管リスクが65%低下したのに対し、これらのレベルのいずれか一つを達成した者またはどちらも達成できなかったものにおける低下率は36%に過ぎなかった。無病生存率はLDLコレステロールおよびhsCRPレベルがより強力に低下（LDL<70mg/dLおよびhsCRP<1mg/L）した者においてより高かった；これらの患者は心血管リスクが80%低下した。JUPITERの他の報告によると、ロスバスタチンは静脈血栓塞栓症のリスクを40%以上低下させるとのことである。

Full Text

Healthy men and women who achieved low levels of both low-density lipoprotein (LDL) cholesterol and high sensitivity C-reactive protein (hsCRP) after starting statin therapy dramatically lowered their risk of a future heart attack, stroke, need for bypass surgery, or cardiovascular death, according to new data presented today at the American College of Cardiology's 58th Annual Scientific Session.

The study - the first to prospectively examine clinical benefits of "dual targets" after initiating statin therapy - demonstrates significantly lowered cardiovascular risk of up to 80 percent among patients who achieved more aggressive reductions in on-treatment LDL and hsCRP levels. Researchers suggest that clinicians consider screening for hsCRP, a marker of underlying inflammation, in addition to LDL cholesterol when identifying patients at high risk for heart disease or monitoring the success of treatment among patients starting statin therapy.

"Our data strongly confirms that statins reduce vascular risk by lowering both inflammation and cholesterol, and we found that achieving low levels of both matters for heart health," said Paul Ridker, M.D., Brigham & Women's Hospital, Boston. "Reducing cholesterol is clearly important, but a reduction in hsCRP with statin therapy appears equally important, and patients who lower both simply do better than those who lower only cholesterol or only hsCRP."

In this analysis of 15,548 initially healthy men and women participating in the JUPITER trial, researchers prospectively evaluated the effects of rosuvastatin (20 mg) versus placebo on rates of myocardial infarction, stroke, hospitalization for unstable angina, arterial revascularization, or cardiovascular death according to achieved levels of LDL and hsCRP.

Compared to those given placebo in the JUPITER trial, those taking rosuvastatin who achieved target levels of LDL less than 70mg/L (1.8 mmol/L) and hsCRP less than 2 mg/L experienced a 65 percent reduction in CV risk compared to only a 36 percent reduction among those treated with rosuvastatin who did not achieve one or both of these target levels. Event-free survival was even greater among patients achieving more aggressive LDL and hsCRP levels (LDL less than 70mg/dL and hsCRP less than 1mg/L); these patients had an 80 percent reduction in cardiovascular risk. The effects remained after adjustment for all available baseline characteristics that varied between groups, including pre-randomization levels of both LDL cholesterol and hsCRP.

JUPITER was a randomized, double blind, placebo controlled trial. Study participants were followed for a maximum of five years (median 1.9 years). Enrolled patients had an LDL of less than 130 mg/dL, which meant they did not qualify for statin therapy under current guidelines.

"JUPITER previously showed that statin therapy is highly effective among patients with low cholesterol who are at risk due to increased levels of inflammation as picked up by elevated hsCRP. We now know that the large benefit gained is due not only to reduction in cholesterol, but to reduction in hsCRP as well," Ridker said. "A patient can be at risk for myocardial infarction or stroke even when cholesterol levels are low. Inflammation is a major determinant of CV risk, and statin drugs are 'two-fers' that lower both inflammation and cholesterol."

It is critical to identify new strategies to detect patients at high risk, and then link those strategies to treatment approaches that work and are cost-effective, he added. "For any patient with high cholesterol or a high hsCRP level, the first steps remain diet, exercise, and smoking cessation," Ridker said. "However, for those electing to start drug therapy, both reductions in LDL and hsCRP appear to be indicators of the success of statin therapy."

These results will be simultaneously published in The Lancet.

Another report from JUPITER found that daily therapy with rosuvastatin cut the risk venous thromboembolism (VTE), by more than 40 percent overall.

"The clinical bottom line here is simple," said Ridker. "In addition to reducing risks of myocardial infarction and stroke, we now have hard evidence that aggressive statin therapy reduces life-threatening blood clots in the veins. In contrast to drugs like warfarin and heparin, we got this benefit with no bleeding hazard at all, so the new data are an exciting advance for our patients."

JUPITER was conducted by investigators in 26 countries and was overseen by an academic statistician and an independent Data and Safety Monitoring Board. The study was funded by AstraZeneca.