

# TOP Journal Club

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## Cilostazol Prevents the Progression of the Symptomatic Intracranial Arterial Stenosis. The Multicenter Double-Blind Placebo-Controlled Trial of Cilostazol in Symptomatic Intracranial Arterial Stenosis.

Ref: *Stroke* 2005;36:782.

**BACKGROUND AND PURPOSE:** Cilostazol, a phosphodiesterase inhibitor, has been reported to reduce restenosis rate after coronary angioplasty and stenting. This study was performed to investigate the effect of cilostazol on the progression of intracranial arterial stenosis (IAS). **METHODS:** We randomized 135 patients with acute symptomatic stenosis in the M1 segment of middle cerebral artery or the basilar artery to either cilostazol 200 mg per day or placebo for 6 months. Aspirin 100 mg per day was also given to all patients. Patients with potential embolic sources in the heart or extracranial arteries were excluded. IAS was assessed by magnetic resonance angiogram (MRA) and transcranial Doppler (TCD) at the time of recruitment and 6 months later. The primary outcome was the progression of symptomatic IAS on MRA and secondary outcomes were clinical events and progression on TCD. **RESULTS:** Thirty-eight patients were prematurely terminated. Dropout rates and reasons for dropouts were similar between the cilostazol and placebo groups. There was no stroke recurrence in either cilostazol or placebo group, but there was 1 death and 2 coronary events in each group. In cilostazol group, 3 (6.7%) of 45 symptomatic IAS progressed and 11 (24.4%) regressed. In placebo group, 15 (28.8%) of symptomatic IAS progressed and 8 (15.4%) regressed. Progression of symptomatic IAS in cilostazol group was significantly lower than that in placebo group ( $P=0.008$ ). **CONCLUSIONS:** Our study suggests that symptomatic IAS is a dynamic lesion and cilostazol may prevent its progression.

## Comparison of cilostazol and clopidogrel after successful coronary stenting.

Ref: *Am J Cardiol.* 2005 Apr 1;95(7):859-62.

This study compared the safety and efficacy of cilostazol and clopidogrel after coronary stenting. Patients ( $n = 689$ ) who underwent successful stenting were randomly assigned to receive cilostazol (group 1,  $n = 344$ , 612 lesions) or clopidogrel (group 2,  $n = 345$ , 628 lesions). The incidence of subacute stent thrombosis or major adverse cardiac events, including death, myocardial infarction, and target lesion revascularization within 30 days (2.6% in group 1 vs 2.0% in group 2,  $p = 0.61$ ) and side effects that required cessation of study drug (0.6% each) did not differ statistically between groups. These results indicate that cilostazol is as safe and effective as clopidogrel in preventing thrombotic complications after stenting.

## Lacunar stroke in patients with intermittent claudication.

Ref: *Acta Neurol Scand.* 2005 Apr;111(4):253

**OBJECTIVES:** To compare the characteristics of lacunar stroke (LS) in patients with and without intermittent claudication. **MATERIAL AND METHODS:** Data of 484 consecutive patients with LS were collected from a prospective hospital-based stroke registry in which 2500 patients are included. **RESULTS:** Of the 142 patients with ischemic stroke and intermittent claudication, 39 (27.5%) had LS (8% of all lacunes). In the multivariate analysis, small centrum ovale topography (odds ratio 7.35), carotid stenosis  $>50\%$  (odds ratio 3.17), and absence of limitation at discharge (odds ratio 2.01) were independent variables significantly associated with LS in patients with intermittent claudication. **CONCLUSION:** Only 8% of patients with LS had intermittent claudication. The short-term prognosis is good with a spontaneous early neurological recovery at discharge in 51.3% of patients. LS patients with intermittent claudication showed a striking similarity in risk factors and clinical syndromes in comparison with the LS patients without intermittent claudication.

## Update on nutritional supplementation with branched-chain amino acids.

*Ref: Curr Opin Clin Nutr Metab Care. 2005 Jan;8(1):83-7.*

**PURPOSE OF REVIEW:** Branched-chain amino acids (BCAAs) have a peculiar role in whole-body nitrogen metabolism. BCAAs are not only a substrate for protein synthesis, but also modulate several components of the synthetic machinery and help to conserve muscle mass; accordingly, several conditions, characterized by protein loss and catabolic status, are likely to benefit from amino acid administration. In addition, the competitive action of BCAAs on amino acid transport across the blood-brain barrier may ultimately alter the synthesis of brain neurotransmitters, involved in neurological diseases. **RECENT FINDINGS:** Both putative actions of BCAAs have been tested in controlled clinical studies in the last few years. The beneficial effects on nutrition were reported to improve muscle performance, reduce protein loss during bed-rest, favor weight loss in obesity, reduce catabolism in trauma patients and improve clinical outcomes in patients with advanced cirrhosis. In this last area, the effects on nutrition might be coupled with the effects on hepatic encephalopathy mediated by improved neurotransmission, successfully tested in mania, tardive dyskinesia and spinocerebellar degeneration. **SUMMARY:** After 30 years of investigation with BCAAs, new studies each year provide further evidence supporting their beneficial effect in a variety of diseases. There is a need for long-term, randomized clinical studies, both in the prevention and in the treatment of various pathological conditions.

## How to select BCAA preparations.

*Ref: Hepatol Res. 2004 Dec;30S:30-35.*

In Japan, oral branched-chain amino acid (BCAA) preparations are used in nutritional therapy for correcting disorders of protein and amino acid metabolism in patients with liver cirrhosis. There are two forms of oral BCAA preparations: enteral nutrition products for liver failure (or elemental nutrition products for liver cirrhosis) and oral BCAA granular products. Granular products are indicated for patients with uncompensated liver cirrhosis who have no dietary restriction and hypoproteinemia.

Enteral nutrition products are indicated for patients who have a history of hepatic encephalopathy and exhibit protein intolerance. In clinical practice, the existence of protein intolerance in patients with uncompensated liver cirrhosis should be determined based on a history of hepatic encephalopathy and blood ammonia concentration. When patients exhibit protein intolerance, they are given a low protein diet (approximately 0.5-1.0g/kg/day) with enteral nutrition products for liver failure. However, when patients consume adequate amounts of a well-balanced diet and ammonia concentration does not increase, it is possible to control their condition with granular products. However, when patients cannot achieve an adequate dietary intake, it is recommended that enteral nutrition products should be used in order to improve nutritional status, even if these patients do not have a history of encephalopathy.

## Update on branched-chain amino acid supplementation in liver diseases.

*Ref: Curr Opin Gastroenterol. 2005 Mar;21(2):197.*

**PURPOSE OF REVIEW:** Branched-chain amino acids (BCAAs) have a peculiar role in whole-body nitrogen metabolism. BCAAs are a substrate for protein synthesis, and have been used to conserve or restore muscle mass in advanced liver disease. In addition, the competitive action of BCAAs on amino acid transport across the blood-brain barrier may improve hepatic encephalopathy. **RECENT FINDINGS:** The effects of branched-chain amino acids on nutrition and ultimately on prognosis of patients with advanced cirrhosis have been confirmed in a large multicenter, long-term trial. Similarly, BCAA treatment improved the prognosis of patients with hepatocellular carcinoma, treated by chemoembolization. The mechanism for the beneficial effects of BCAA is likely to depend on the stimulating activity of BCAA on hepatocyte growth factor, favoring liver regeneration. **SUMMARY:** After an experience of 25 years with branched-chain amino acids, new data supports their beneficial effect in liver diseases. Although the number of patients who cannot tolerate dietary proteins in amounts sufficient to meet their increased catabolism is probably low, in this specific setting BCAAs remain the sole treatment of proved efficacy.

<http://www.thai-otsuka.co.th/pxnews/index.html> Opinions and suggestions are welcomed Dr. Shwe Win, [shwewin@thai-otsuka.co.th](mailto:shwewin@thai-otsuka.co.th)