There were also no significant differences from baseline to 3 months in plasma renin activity, which is an indirect measure of angiotensin I production, and the level of the inflammatory markers.

Leptin levels did not significantly change from baseline to 3 months. The levels of nonesterified fatty acid (NEFA), a metabolic biomarker, were significantly reduced (from 1 to 0.4 mEq/L; p<0.001), but there were no significant reductions in body weight, BMI, or waist-to-hip ratio.

In explaining the high baseline NEFA levels in this patient population that has resistant hypertension and high BMI, it should be noted that NEFA has been implicated in elevated BP, particularly in animal studies [Sarafidis PA, Bakris GL. *J Hum Hypertens* 2007]. Furthermore, the levels of NEFA tend to be higher in overweight and obese persons as it is primarily released from adipose tissue [Heptulla R et al. *J Clin Endiocrinol Metab* 2001; Koutsari C, Jensen MD. *J Lipid Res* 2006].

NEFA and insulin levels seem to have an inverse relationship, said Prof. Eikelis. Therefore, it is perhaps no surprise that in the present study, NEFA levels significantly decreased while insulin levels significant increased from baseline (21 uU/mL) to 3 months (28 uU/mL; p<0.01).

Whole body noradrenaline spillover, a measure of whole body sympathetic activity, did not change significantly over the 3 months. However, Prof. Eikelis noted that sympathetic responses are regionalized and global measures lack precision. When looking at regional sympathetic activity, there were significant reductions from baseline to 3 months and to 6 weeks in muscle and kidney sympathetic activity, respectively (p<0.05 for both).

Study findings show that while RDN led to significant reductions in office BP, and muscle and renal sympathetic activity, there were no significant changes in endothelial function and inflammatory markers. There was a significant reduction in NEFA, without changes in body weight, and this may be an indirect measure showing reduction or withdrawal of nervous activity from adipose tissue.

INTERACT2 Results: Intensive BP Lowering Safe and Effective in Acute ICH Patients

Written by John Otrompke

Although physicians have long subscribed to the fear that using intensive methods to lower the blood pressure (BP) of patients who had suffered acute intracerebral hemorrhage (ICH) would result in increased risk of death or neurological deterioration, the technique is safe and effective, and should become the standard of care, according to results of the Second Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial [INTERACT2; NCT00716079; Anderson CS et al. *N Engl J Med* 2013].

While there was no reduction in deaths among acute ICH patients treated with an intensive BP-lowering strategy, functional outcomes and health-related quality of life (QoL) were better in these patients, according to John Chalmers, MD, PhD, Georgia Institute for Global Health, University of Sydney, Sydney, Australia, who presented the results of INTERACT2.

In the study, researchers examined the question of whether patients with acute ICH treated with the goal of reducing the BP to <140 mm Hg within an hour (early intensive group) or those treated with the goal of reducing BP to the current guideline-recommended goal of <180 mm Hg (standard group) would have improved survival free of major disability.

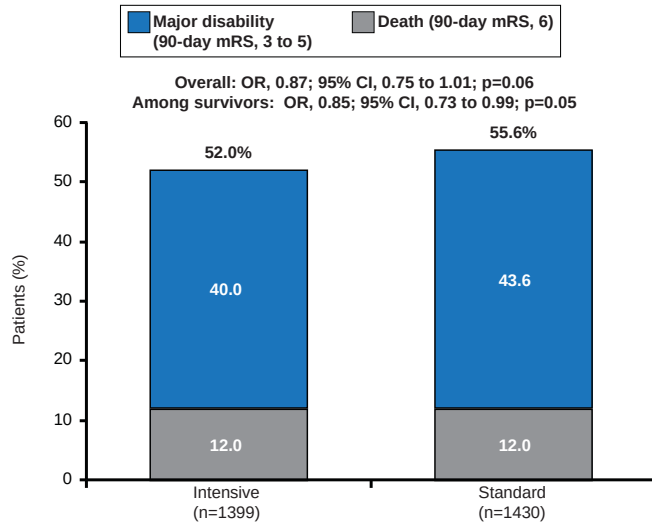
The study was performed across 144 hospitals in 21 countries. Patients (n=2839) with acute spontaneous ICH and systolic BP of 150 to 220 mm Hg were randomized within 6 hours of ICH to the early intensive (n=1403) or standard group (n=1436) and managed in-hospital for 7 days. The locally available intravenous BP-lowering agent used was based on the physician's choice.

Baseline characteristics of the two groups were similar and ~68% of patients in each group were from China. The patient population had a mean age of 64 years, a mean BP of 179/101 mm Hg, and a median ICH volume of 11 mL.

The occurrence of the primary composite outcome of death or major disability, defined as a 90-day modified Rankin Scale (mRS) score of 3 to 6, was nonsignificantly lower in the intensive group (52%) compared with the standard group (55.6%; OR, 0.87; 95% CI, 0.75 to 1.01; p=0.06; Figure 1).While the rate of death was similar in the two groups (~12%), significantly fewer survivors in the early intensive group (40%) experienced major disability compared with the standard group (43.6%; p=0.05).

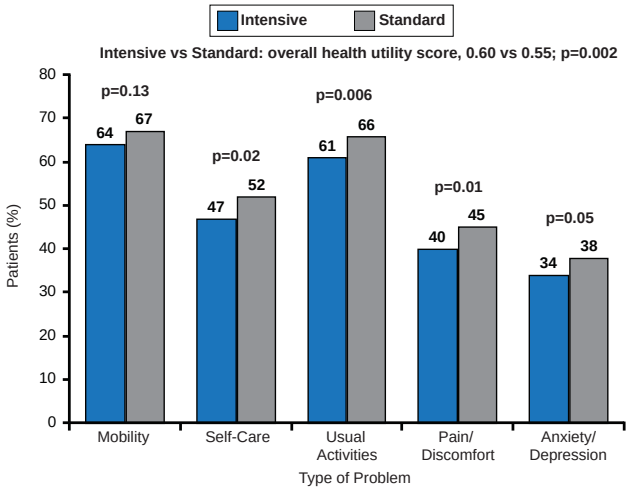
A prespecified subgroup analysis showed that the primary outcome findings did not significantly differ by region (ie, China vs other regions; p=0.97). Ordinal analysis of mRS score distribution showed that mRS scores were significantly lower in the intensive group versus the standard group (pooled OR for shift to higher mRS score, 0.87; 95% CI, 0.77 to 1.00; p=0.04).

Figure 1. Death or Major Disability (90-day mRS Score, 3 to 6)



Health-related QoL, measured using the European QoL-5 Dimensions (EQ-5D) questionnaire, was significantly better in the intensive group versus the standard group (overall health utility score, 0.60 vs 0.55; p=0.002; Figure 2). In particular, the intensive group had significantly fewer problems in the dimensions of self-care, usual activities, pain or discomfort, and anxiety or depression.

Figure 2. Health-Related Quality of Life



There were no significant differences between the groups in the secondary endpoints of median length of hospital stay (20 vs 19 days; p=0.43), 90-day institutional care (9% for both), 24-hour neurological deterioration (66% vs 68%, p=0.22), severe hypotension (0.5% vs 0.6%, p=0.83), nonfatal serious adverse events (23.3% vs 23.6%; p=0.92), and cause-specific mortality.

INTERACT2 findings show that early aggressive BP lowering in acute ICH patients is generally safe and effective compared with standard therapy, and may yield better functional outcomes.

Large Study Suggests That Death Comprises Higher Proportion of Major CV Events in Patients With Greater CV Risk

Wrtten by John Otrompke

A review of 51 clinical trials of antihypertensive agents suggested a method of creating simple equations to determine a patient's risk of suffering death, major cardiovascular (CV) death, or other CV disease once the patient's risk of CV mortality is known, according to Antonella Zambon, PhD, University of Milano-Bicocca, Milan, Italy. The technique incorporated the latest European Society of Hypertension/European Society of Cardiology (ESH/ESC) Hypertension Guidelines [Mancia G et al. *J Hypertens* 2013].

Beginning in 1999, guidelines began stratifying the risk that hypertensive patients will suffer death [WHO-ISH Guidelines Subcommittee. *J Hypertens* 1999], but the guidelines have become more expansive, with European guidelines introduced in 2003 [ESH/ESC Guidelines Committee. *J Hypertens*] and 2007 [Mancia G et al. *J Hypertens*], and the expansive definitions used in the Framingham classification growing to include more adverse events such as organ damage, angina, or coronary insufficiency within the category of major CV events. Accordingly, definitions of major CV events have come to be somewhat mutable, and vary between clinical trials, according to Prof. Zambon. This makes it sometimes difficult to estimate a patient's risk of death based merely on their risk of having a major CV event, he added.

For the risk of CV death within 10 years, the 2013 ESH/ESC Hypertension Guidelines retain the risk stratifications of low (<1% risk), moderate (1% to 5%), high (5% to 10%), and very high (>10%) risk, Prof. Zambon noted. The new guidelines add nonfatal stroke and nonfatal myocardial infarction to the list of what constitutes a major CV event, he said.

The researchers identified 61 clinical trials, of which 51 were retained for analyses. Trials were included if the study population was comprised of ≥40% hypertensive patients and ≥2500 patient-years of observations. This resulted in a database that included 15,164 CV deaths and 1,674,427 patient-years of follow-up.