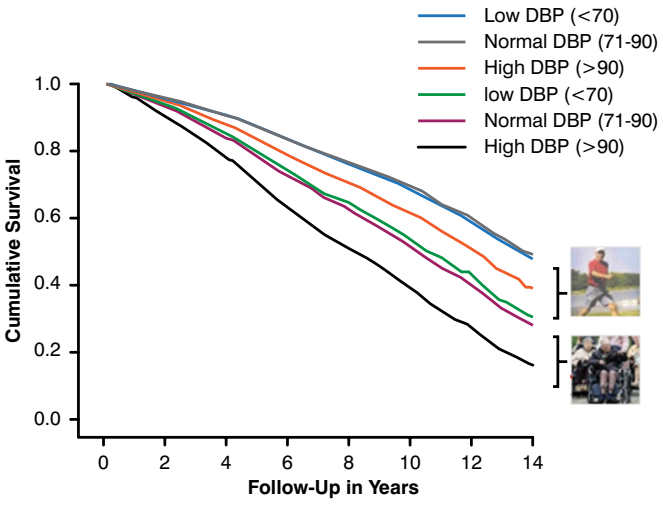
cognitive function was measured by the Mini–Mental State Examination (MMSE). Patients could achieve a biological age combination score of up to 4 points: 0 points for a gate speed of ≥0.8 m/s, 1 for <0.8 m/s, and 2 if the test could not be completed, as well as 0 points for achieving an MMSE score of >28, 1 for 27 to 28, and 2 for ≤26.

In the study, 49% of patients were men; 8% had diabetes; and 37% had cardiovascular disease. Mean (interquartile range) SBP and DBP were 151 mm Hg (134 to 170) and 82 mm Hg (74 to 91), respectively. In addition, 41% of patients were classified as "fit" (combination score of 0 or 1) and 59% as "frail" (combination score of 2 to 4).

Compared with normal DBP (71 to 90 mm Hg), low DBP (≤70 mm Hg) was significantly associated with an increased mortality risk in frail, or biologically old, patients (HR, 1.5; 95% CI, 1.2 to 1.8) (Figure 2). In contrast, high DBP was associated with increased mortality risk in fit, or biologically younger, patients (HR, 1.5; 95% CI, 1.1 to 1.9; trend p=0.01). SBP was not associated with mortality.

Figure 2. Effect of Biological Age on Mortality Risk Stratified by Diastolic Blood Pressure



DBP=diastolic blood pressure.

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Dr. Muller concluded that we need to refine our approach to thinking about optimal BP levels and that data from this study support the use of using markers of biological age to improve our understanding of the association between BP in late life and clinical outcomes.

Simple, Noninvasive Hemodynamic Monitoring Improves Uncontrolled Hypertension

Written by Brian Hoyle

The findings of the multicenter Better Control of Blood Pressure in Hypertensive Patients Monitored Using the HOTMAN System trial [BEAUTY; NCT01482364] of 153 patients has shown the value of the simple and noninvasive monitoring of hemodynamic parameters in improving uncontrolled hypertension. The findings were reported by Tommaso Comotti, MD, Istituto Auxologico Italiano, Milan, Italy.

High blood pressure (BP) remains uncontrolled in up to 20% of those treated for hypertension [de la Sierra A et al. *Hypertension* 2011; Egan BM et al. *Circulation* 2011]. The ultimate control of drug-treated but still uncontrolled hypertension may require more or better-acting drugs [Redón J et al. *J Hypertens* 2010]. Poor adherence due to side effects is also a problem [Ceral J et al. *Hypertens Res* 2011; Gifford RW. *Hypertension* 1988; Klein LE. *Hypertension* 1988].

Another option for BP control is the use of an approach termed *integrated hemodynamic management*. The approach relies on the technique of thoracic electrical bioimpedance, which, by means of externally placed probes, measures the electrical resistance of the thorax to a high-frequency, very-low-magnitude current. The method permits real-time hemodynamic measurements, and the low current used reduces artifacts. The technology is commercially available as the HOTMAN system (Hemo Sapiens, San Ramon, CA, USA).

BEAUTY was a prospective randomized trial designed to explore whether drug selection based on integrated hemodynamic management would improve the hemodynamic status of patients with uncontrolled hypertension during a 6-month follow-up (n=76; patients also received usual hypertensive care; IHM Group), compared with drugs selected conventionally according to the 2007 European Society for Hypertension guidelines (n=77; control group). The primary end point of the study was the absolute change in daytime ambulatory systolic BP. Whether the drug-related changes in hemodynamic parameters are related to BP alterations and whether the improvements in hemodynamic and BP control reduced adverse effects were also assessed.

Hemodynamic status was assessed as worsened, stable, or improved based on comparison of values obtained at baseline and the final clinic visit. The 2 investigators were blind to patient randomization. Inclusion criteria were age 18 to 75 years, essential hypertension,

sustained hypertension at the baseline visit (systolic BP >140 mm Hg) and during ambulatory BP monitoring (daytime systolic BP >135 mm Hg), treatment with ≥2 antihypertensive drugs, and signed informed consent. Patients were monitored during 6 clinic visits (ambulatory BP monitoring, echocardiography, HOTMAN, and pulse wave velocity; not all performed at each visit); they also maintained a BP diary.

Overall, hemodynamic status of the IHM group improved more (49% and 50%, according to both investigators) than did the control group (27% and 29%; p=0.038 and p=0.008, respectively). Joint improvement of hemodynamic status and BP was superior in the treatment group (42% and 43%) than in the control group (22% and 23%; p=0.014 and p=0.030, respectively). Drug selection according to the HOTMAN responses was associated with fewer investigator-assessed side effects (1.18±1.17) than was the conventional drug-selection process (1.91±2.09).

Data from BEAUTY suggest that the noninvasive HOTMAN approach is associated with more favorable hemodynamic changes in patients with uncontrolled hypertension, better joint control of hemodynamics and BP, and fewer side effects. Future studies are necessary to determine whether treatment strategies guided by integrated hemodynamic management will translate into improved clinical outcomes that are cost-effective.

No Long-Term Benefit of Candesartan for Patients With Acute Stroke

Written by Toni Rizzo

Among patients with acute stroke, approximately 75% have systolic blood pressure (BP) ≥140 mm Hg [Qureshi AI et al. *Am J Emerg Med* 2007; Leonard-Bee J et al. *Stroke* 2002]. Elevated BP in the acute phase of stroke has been associated with poor short- and long-term outcomes [Leonard-Bee J et al. *Stroke* 2002]. The Phase 2, prospective, randomized Acute Candesartan Cilexetil Therapy in Stroke Survivors study [ACCESS] in 500 patients with stroke found that vascular events and mortality were significantly lowered by candesartan, without a significant difference in adverse event rates [Schrader J et al. *Stroke* 2003]. However, large clinical trials have yet to demonstrate a beneficial effect of BP lowering in the acute phase of stroke.

The Scandinavian Candesartan Acute Stroke Trial [SCAST; NCT00120003] did not demonstrate a difference at 6 months between BP lowering with candesartan and placebo for 7 days in the acute phase of stroke (HR, 1.09; 95% CI, 0.84 to 1.41; p=0.52) [Sandset EC et al. *Lancet* 2011]. The aim of this SCAST prespecified secondary analysis, presented by A. G. Hornslien, MD, Oslo University Hospital Ullevaal, Oslo, Norway, was to investigate whether a difference might be observed over longer follow-up.

In total, 2029 patients with acute ischemic or hemorrhagic stroke and systolic BP ≥140 mm Hg were randomly assigned to candesartan versus placebo for 7 days. Of these patients, long-term follow-up data were available in 632 patients who were allocated to candesartan and 624 patients who were allocated to placebo. Follow-up data were collected from national patient, hospital, and death registries in Norway, Sweden, and Denmark. The primary end point was the composite of stroke, myocardial infarction, or vascular death. The secondary end points were recurrent stroke and all-cause death. Time to first event was analyzed by Cox proportional-hazards regression with adjustment for baseline variables (age, stroke type, systolic BP, and Scandinavian Stroke Scale score).

Baseline characteristics were well balanced between the 2 arms. At 3 years, there was no significant difference in the primary end point between the candesartan group (28.2%) and the placebo group (32.5%; adjusted HR, 0.87; 95% CI, 0.71 to 1.07; p=0.19).

There was no significant difference in the recurrent stroke rate between the candesartan group (16.9%) and the placebo group (adjusted HR, 0.83; 95% CI, 0.64 to 1.07; p=0.15) at 3 years. Similarly, no significant difference was observed in the rates of all-cause death in the candesartan group (17.9%) compared with the placebo group (18.8%; adjusted HR, 1.00; 95% CI, 0.77 to 1.30; p=1.00).

In this study, candesartan treatment during the acute phase of stroke in patients with elevated BP had no significant effect on the occurrence of vascular events, recurrent stroke, or death at 3 years. These results are consistent with the 6-month results and support the conclusion that there is no indication for routine BP-lowering treatment with candesartan in the acute phase of stroke.