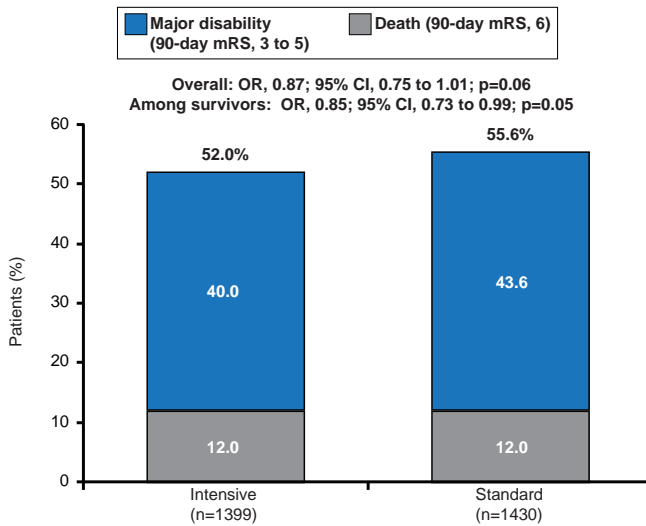




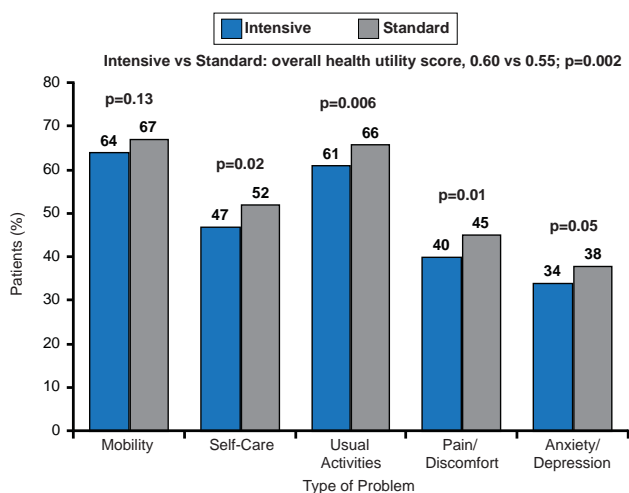
CLINICAL TRIAL HIGHLIGHTS

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

Written 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.



The researchers found that the ratio of the CV event rates to the CV death rate varied with disease severity, with CV death representing a larger fraction of major CV events when the risk of CV mortality was higher (Table 1). When the rate of CV death was 2.5 per 1000 patient-years, the rate of major CV events was 3.86, but when the rate of CV death rose to 7.5 per 1000 patient-years, the rate of major CV events decreased to 2.69. Furthermore, when the CV death rate was 12.5 per 1000 patient-years, the rate of major CV events declined to 2.28.

Table 1. Ratios of Various Types of Events to CV Mortality According to Level of CV Risk

CV mortality rate per 1000 person-years	Outcome/CV Mortality Rate Ratio With 95% CIs		
	2.5	7.5	12.5
Total mortality			
≤65 years	2.17 (2.13 to 2.20)	1.91 (1.89 to 1.94)	1.81 (1.78 to 1.84)
>65 years	3.07 (3.00 to 3.13)	2.24 (2.21 to 2.26)	1.93 (1.91 to 1.95)
Major CV events	3.86 (3.80 to 3.93)	2.69 (2.67 to 2.72)	2.28 (2.25 to 2.31)
Extended CV events			
Active as reference	8.39 (8.17 to 8.62)	5.56 (5.45 to 5.68)	4.59 (4.48 to 4.71)
Placebo as reference	15.78 (5.53 to 6.05)	3.83 (3.70 to 3.97)	3.16 (3.05 to 3.28)

CV=cardiovascular.

Determining Inter-Arm Blood Pressure Is Important in New Patients with Diabetes

Written by Muriel Cunningham

Christopher E. Clark, PhD, University of Exeter Medical School, Devon, United Kingdom, presented results from a study of inter-arm differences (IAD) in systolic blood pressure (BP) in patients with diabetes. Simultaneous measurements, often impractical in a clinical setting, were obtained and compared with calculated sequential pairs. Associations between IAD and vascular disease and mortality were also explored.

Once they had provided informed consent, patients with diabetes and nondiabetic control patients underwent 4 pairs of bilateral simultaneous automated BP measurements. After 2 simultaneous measurements were conducted in a random order, cuffs were switched to the opposite arms and another pair of measurements was obtained. For the simultaneous measurements, IADs were calculated for each pair by subtracting the left BP from the right BP. Sequential pairs were modeled by subtracting the second or fourth left BP from the first right BP, for best

and worst case sequential pairs. Demographic information was collected from each participant. Patient records were flagged in the National Health Service Information Centre to acquire mortality data from death certificates.

A total of 727 patients with diabetes and 285 controls were enrolled. Of these, 514 (71%) of the patients with diabetes and 238 (84%) of the controls had 4 pairs of BP results ($p < 0.001$). Prof. Clark attributed the smaller number of diabetes patients with complete results to the larger number of patients with atrial fibrillation in the diabetes group.

The control group was younger and two-thirds were hypertensive versus 90% of the patients with diabetes. In the diabetes population, 8.6% had a systolic IAD ≥ 10 mm Hg compared with 2.9% of the controls. Prof. Clark stated that he and his colleagues could not attribute the reason for this difference in systolic IAD entirely to diabetes. Both the simultaneous and sequential single pair measurements were significant ($p < 0.001$ for both) in a receiver operating characteristics curve, indicating that a sequential single pair is a useful way to determine IAD in place of simultaneous measurements.

A systolic IAD ≥ 10 mm Hg was associated with peripheral artery disease (OR, 3.1; 95% CI, 1.2 to 8.0; $p = 0.03$) and retinopathy (OR, 1.8; 95% CI, 1.0 to 3.4; $p = 0.056$). A systolic IAD ≥ 15 mm Hg was associated with retinopathy (OR, 6.5; 95% CI, 1.7 to 24.4; $p = 0.003$) and chronic kidney disease (OR, 5.4; 95% CI, 1.4 to 21.1; $p = 0.033$). Additionally, preliminary survival data showed a significant difference in cardiovascular mortality in patients with systolic IAD ≥ 10 mm Hg (HR, 4.6; 95% CI, 1.2 to 17.6; $p = 0.028$) and systolic IAD ≥ 15 mm Hg (HR, 10.9; 95% CI, 2.3 to 51.3; $p = 0.003$).

Prof. Clark emphasized that “there [were] relatively few [adverse] events included in this [study and that they] intend to return to this in the future when a significant number of events have been collected.” He advised clinicians to measure BP in both arms when initially evaluating patients with diabetes as systolic IADs are associated with vascular disease and possibly related to increased cardiovascular mortality.

Success With Self-monitoring: Results From the TASMIN-SR Trial

Written by Muriel Cunningham

The Telemonitoring and Self-Management in the Control of Hypertension trial [TASMINH2], a large study of patients with hypertension, found that those randomized to self-management had significantly lower blood pressure (BP) than controls [McManus RJ et al. *Lancet* 2010]. Subgroup analyses from TASMINH2 suggested a smaller treatment effect in higher risk patients. The purpose of the subsequent Targets and Self-Management for the Control