Acute Severe Hypertension Often Poorly Managed

BY BRUCE JANCIN
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MUNICH — Acute severe hypertension is a common, suboptimally treated condition with a high recurrence rate and surprisingly high morbidity and mortality.

These are the principal lessons of the just-completed large national Studying the Treatment of Acute Hypertension (STAT) registry, Dr. Christopher B. Granger said at the annual congress of the European Society of Cardiology.

The STAT observational registry documented 90-day mortality and readmission rates following an episode of acute severe hypertension (ASH), rates comparable with those typically encountered in patients with acute heart failure or an acute coronary syndrome.

These and other sobering STAT findings "reinforce the major need to improve prevention and treatment of this understudied condition," said Dr. Granger, a cardiologist at Duke University, Durham, N.C., and chairman of the STAT steering committee.

ASH involving blood pressures in excess of 180/110 mm Hg, or greater than 140/90 mm Hg with subarachnoid hemorrhage, occurs in 1%-2% of the 72 million Americans with chronic hypertension. At some busy urban emergency departments, ASH accounts for up to 25% of all patients seen. Yet little contemporary information is available about the characteristics of affected patients, their treatment, or outcomes. This was the impetus for STAT.

Dr. Granger reported on 1,588 adults who received intravenous antihypertensive agents for ASH within 24 hours of presenting at 25 nationally representative participating U.S. hospitals.

The mean age of STAT registry participants was 58 years. About one-half were women, and 56% were African American. Overall, 89% of participants had a history of chronic hypertension, 35% were diabetic, 31% had chronic kidney disease, 15% had a history of drug abuse, and 27% had previously been hospitalized for ASH. Nonadherence to medications for chronic hypertension was deemed a contributing factor in 25% of ASH episodes.

Roughly one-quarter of patients were admitted for acute hypertension, another quarter for stroke or other neurologic complications, and one-quarter for heart failure or other cardiovascular conditions.

The median hospital length of stay was 5 days. Roughly half of patients were admitted to the intensive care unit. During their stay, 48% of patients had brain imaging by CT or MRI and 45% had an echocardiographic examination—yet disturbingly, a mere 13% had a documented funduscopic exam, Dr. Granger noted.

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DR. GRANGER

Among the key STAT findings:

► **Poor outcomes.** In-hospital mortality was 6.9% and 90-day mortality was 11%. The 90-day readmission rate was 37%, and 9.3% of patients were rehospitalized within 90 days for recurrent ASH.

► **Lengthy time to blood pressure control.** The median time to drive systolic blood pressure below 160 mm Hg was 4 hours. Moreover, following initial control, fully 60% of patients experienced a rebound to greater than 180 mm Hg. Also, 4% of patients had iatrogenic hypotension, in most cases requiring vasopressors.

► **Variable treatment approaches.** Intravenous antihypertensive therapy was administered within 1 hour in 47% of patients and within 3 hours in 74%. Two-thirds of patients required two or three intravenous antihypertensive drugs. The first intravenous drug employed was labetalol in 32% of cases and metoprolol in 17%, followed in descending order by nitroglycerin, hydralazine, nicardipine, and sodium nitroprusside. Nicardipine was the only drug that served as monotherapy in the majority of treated patients.

► **Inadequate follow-up.** ASH is a life-threatening condition, yet 65% of patients had no documentation in the medical record of a follow-up appointment being scheduled or attended.

"Although this may be an overestimate of the true degree of the problem, I think it does illustrate what is probably the single most important opportunity to improve care that we've seen in this study," Dr. Granger noted.

Ongoing STAT analyses include efforts to identify risk factors for recurrence, as well as the most effective ways to lower high blood pressure without exacerbating damage to the kidneys and other organs.

"We're trying to analyze the relationship between patterns of control and outcome. There are interesting data from the ECLIPSE [Evaluation of Clevidipine in the Postoperative Treatment of Hypertension Assessing Safety Events] trial showing that it appears patients with perioperative hypertension who get into and stay within a target blood pressure range have better outcome; it was an independent predictor. Whether that's the case in this population with acute severe hypertension is a very important question we currently lack information on," he continued.

Dr. Jeffrey S. Borer, session cochair, commented, "The thing that jumps out at me is the extraordinarily low rate of follow-up.

"It would be easy to blame the doctor, but my guess is that's not what happened. My guess is that it has to do with a lack of effort on the part of the patient. Perhaps they don't realize how important it is to follow up," said Dr. Borer, professor of cardiovascular medicine at Cornell University, New York.

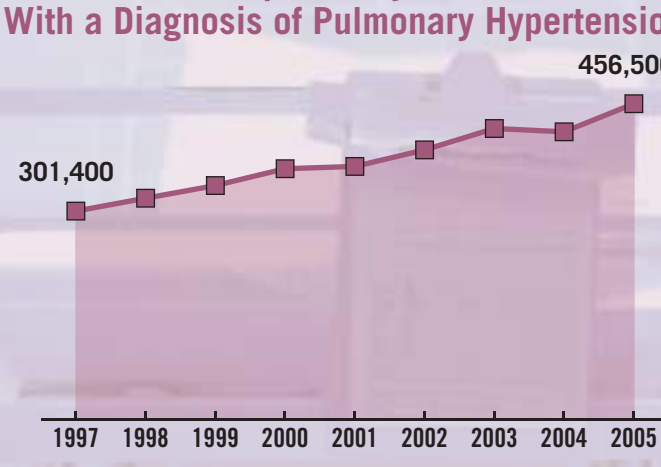
Dr. Granger replied that while it's true ASH is more common in low-income patients having relatively few resources, that's only part of the story. Chronically overtaxed emergency departments are a bigger factor, in his view.

"I think the problem relates largely to the fact that in the [United States]—and this may be an issue worldwide as well—the emergency departments where acute severe hypertension is largely being managed are really overburdened and unable to deal with the issues of longer-term care, follow-up, and prevention of recurrences," Dr. Granger observed.

Both the STAT registry and ECLIPSE were funded by the Medicines Company. Dr. Granger has received research grants and served as a paid consultant to the company. ■

DATA WATCH

Number of Hospital Stays Increased 50% With a Diagnosis of Pulmonary Hypertension*



* Includes ICD-9-CM codes for cases of primary pulmonary hypertension, kyphoscoliotic heart disease, and chronic pulmonary heart disease.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

Killip Class III/IV Doubles Risk of Sudden Cardiac Death

BY BRUCE JANCIN
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MUNICH — Killip class is a powerful predictor of sudden cardiac death risk in post-MI patients with heart failure, according to a secondary analysis of the landmark EPHESUS trial results.

The double-blind EPHESUS (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study) involved 6,632 patients who were randomized to 25-50 mg/day of the selective aldosterone blocker eplerenone (Inspra) or placebo, in addition to standard background medical therapy, beginning 3-14 days after an MI complicated by left ventricular systolic dysfunction. All subjects had a left ventricular ejection fraction (LVEF) of 40% or less at randomization.

During a mean follow-up of 16 months, sudden cardiac death (SCD) occurred in 9.2% of the 1,298 participants who were baseline Killip class III or IV. In contrast, the incidence of SCD in patients who were Killip class I/II at baseline was 4.6%, Dr. Bertram Pitt reported at the annual congress of the European Society of Cardiology.

After adjustment for treatment and LVEF in a Cox proportional hazards model, patients who were baseline Killip class III, defined as severe heart failure with frank pulmonary edema, or Killip class IV, which is cardiogenic shock, had a twofold higher risk of SCD than those who were Killip class I/II, added Dr. Pitt, professor of internal medicine at the University of Michigan, Ann Arbor.

A lower baseline LVEF was also associated with an increased rate of SCD, with an LVEF of 30% proving to be a useful cutoff. The 1,105 patients who were baseline Killip class I/II with an LVEF of less than 30% had a 7.7% rate of SCD, compared with a 3.8% rate in those with a baseline LVEF of 30% or more. Among patients who were Killip class III/IV with an LVEF below 30%, the rate of SCD was 11.1%, compared with 8.5% in Killip class III/IV patients with an LVEF of 30% or above.

These findings underscore the importance of determining LVEF and Killip class in order to predict SCD risk in patients with heart failure following an MI, Dr. Pitt stressed.

EPHESUS is considered a landmark study because it resulted in the addition of aldosterone blockade with eplerenone to the short list of lifesaving therapies in patients with heart failure. During 16 months of follow-up, eplerenone reduced all-cause mortality by 15%, cardiovascular mortality by 17%, and SCD by 21%.

A particularly striking finding was the 37% reduction in the risk of SCD within the first 30 days post randomization; the importance of that result lies in the fact that one-quarter of all deaths in the placebo arm during the entire study occurred in the 30 days after randomization (J. Am. Coll. Cardiol. 2005;46:425-31).

Dr. Pitt led EPHESUS and has served as a consultant to Pfizer Inc., which sponsored the main trial as well as the new post hoc analysis. ■