Patients in the pretreatment group received 30 mg of prasugrel at the time of diagnosis and if angiography confirmed an indication for PCI, an additional 30 mg of prasugrel was administered. Patients in the control group received placebo initially and a 60-mg prasugrel dose was administered following angiography in patients for whom PCI was indicated and performed.

From randomization to Day 7, there was no difference in the primary endpoint with prasugrel pretreatment compared with prasugrel after angiography (HR with pretreatment, 1.02; 95% CI, 0.84 to 1.25; p=0.81). However, there was a significant, nearly 2-fold increase in the rate of TIMI major bleeding in patients receiving prasugrel pretreatment (HR, 1.90; 95% CI, 1.19 to 3.02; p=0.006). The rate of life-threatening bleeding unrelated to coronary artery bypass graft was increased by a factor of 6. Among the 69% of patients who underwent PCI, pretreatment with prasugrel reduced death from cardiovascular causes, MI, stroke, urgent revascularization, or glycoprotein IIB/IIIa inhibitor rescue therapy; however, the rate of TIMI major bleeding at 7 days was significantly increased.

Overall, ACCOAST showed an increased risk of bleeding and demonstrated no benefits with prasugrel pretreatment prior to angiography in patients with NSTEMI, and Prof. Montalescot noted that a re-examination of antiplatelet pretreatment strategies in patients with NSTEMI is necessary.

LINC: Manual and Mechanical CPR Produce Equivalent Outcomes

Written by **Rita Buckley**

Effective manual cardiopulmonary resuscitation (CPR) can be difficult to perform. After 2 to 3 minutes of attempting to compress the chest 100 times each minute, only ~20% to 30% of the compressions may achieve the needed depth of 5 to 6 cm. In addition, interruptions in chest compressions (eg, to analyze heart rhythm) are detrimental to re-initiating circulation. The LUCAS system is a piston-driven device with a suction cup (for adequate chest recoil) designed to deliver compressions according to resuscitation guidelines (100 compressions/minute) at a depth of 4 to 5 cm. In contrast to manual CPR (M-CPR), defibrillation can be delivered during LUCAS CPR (L-CPR), to minimize interruptions to compressions.

A Comparison of Conventional Adult Out-of-Hospital Cardiopulmonary Resuscitation Against a Concept With Mechanical Chest Compressions and Simultaneous Defibrillation study [LINC; NCT00609778] presented by Sten Rubertsson, MD, Uppsala University, Uppsala, Sweden, sought to examine the efficacy and safety of the LUCAS device in contrast with M-CPR.

The prospective, multicenter, randomized, controlled LINC study screened ~5000 patients from six European sites who had suffered an out-of-hospital cardiac arrest and needed resuscitation; 2593 were ultimately randomized. Of these, 1300 were randomized to L-CPR and 1289 to M-CPR. Patients in the L-CPR arm received M-CPR until the device could be applied. Baseline characteristics between the L-CPR and M-CPR groups were similar.

The primary endpoint was survival (defined as return of spontaneous circulation [ROSC]) at 4 hours after CPR. The secondary endpoint was survival up to 6 months with a good neurological outcome (defined as cerebral performance category [CPC] 1 or 2). The inclusion criterion was unexpected adult out-of-hospital cardiac arrest where an attempt of resuscitation was considered appropriate. Exclusion criteria were traumatic cardiac arrest, including hanging; age <18 years; known pregnancy; and patient body size not fitting the LUCAS. Those patients who were defibrillated prior to the arrival of LUCAS or those with ventricular fibrillation/ventricular tachycardia that were defibrillated leading to ROSC were also excluded. Prof. Rubertsson noted that these last criteria may have excluded patients most likely to survive for at least 4 hours. Approximately 50% of subjects had asystole and 20% had pulseless electrical activity at randomization in each arm.

There was no difference in the primary outcome of survival at 4 hours (23.6% with L-CPR vs 23.7% with M-CPR; 95% CI, –3.32 to 3.23; p=1.00). The secondary outcomes were similar between groups.

Poor neurologic outcomes, CPC 3 or 4 (excluding those with brain death [CPC 5]) were infrequent in both groups. Rates of poor neurologic outcomes were low after hospital discharge and similar between groups.

The overall results indicate that LUCAS-aided CPR is not superior to manual CPR for 4 hours post CPR survival. Prof. Rubertsson noted that this was a somewhat surprising outcome given the difficulty of M-CPR. Further analyses by initial rhythm, time to CPR, and by whether the arrest was witnessed by the emergency medical services team will be important.

Home-Monitoring Technology Suggests an Improvement in Survival in Heart Failure Patients

Written by **Nicola Parry**

Gerhard Hindricks, MD, University of Leipzig, Heartcenter, Leipzig, Germany, discussed results from the Influence of Home Monitoring on the Clinical Status of Heart Failure Patients With an Impaired Left Ventricular Function trial [IN-TIME; NCT00538356], a randomized controlled

trial that demonstrated a significant improvement in a composite of heart failure (HF) status and clinical events by using implant-based remote-monitoring to assist physicians in the management of patients with advanced HF.

The ability to more closely monitor these tenuous patients has long been hypothesized as a way to improve a wide variety of HF endpoints. Certain clinical events or characteristics, such as arrhythmia or increased heart rate at rest, may precipitate worsening HF, leading to hospital admission or death [Opasich C et al. *Am J Cardiol 2001*]. Home-monitoring (HM) data provides access to these early predictive changes of worsening HF and thereby may enable intervention prior to hospitalization [Sack S et al. *Eur J Heart Fail* 2011].

IN-TIME was designed to evaluate the impact of physician access to these predictive parameters (eg, heart rate, atrial fibrillation burden) in relative "real-time" to influence changes in therapeutic treatment. No specific guidance was provided to physicians; treatment decisions were left to each physician's clinical judgment. The primary endpoint was the modified Packer score—a clinical composite score based on mortality, overnight hospitalization for worsening HF, NYHA class status, and changes in the patient's global self-assessment score. Secondary endpoints included all-cause total mortality and the number of overnight hospitalizations due to worsening HF.

The trial was conducted among 36 international investigational centers. Inclusion criteria included a history of HF ≥3 months, NYHA Class II or III symptoms for 1 month prior to screening, left ventricular ejection fraction ≤35% within 3 months prior to screening, indication for diuretic therapy and an indication for an implantable cardioverter defibrillator (ICD; with or without cardiac resynchronization therapy). All patients received a device with remote-monitoring capability at the time of ICD implantation. Although remote monitoring data were collected for all patients, these were not available to treating physicians until the study was completed in the control group.

Of the 716 patients enrolled, 52 were excluded during an initial run-in; 664 were subsequently randomized to either HM (n=333) or a control group with standard HF care (n=331). Baseline characteristics were similar in both arms, except for a slightly lower utilization of angiotensin-converting enzyme inhibitors/angiotensin II receptor blocker in the control arm (86.4% vs 92.2%). A total of 82 patients (30 in the HM arm and 52 in the control arm) did not complete 12 months of follow-up. This difference was primarily related to the excess of mortality in the control arm compared to HM arm (control 27 vs HM 10).

At 12 months, significantly fewer patients in the HM group compared with the control group had reached the primary endpoint, worsening of HF according to modified Packer score (18.9% vs 27.5%; p<0.05). A significantly reduced rate was found in the secondary endpoint of all-cause mortality (HR, 0.36; 95% CI, 0.17 to 0.74; p=0.004). The increase in mortality was largely cardiovascular in cause (HR, 0.37; 95% CI, 0.16 to 0.83; p=0.012).

IN-TIME has contributed important data regarding the efficacy of telemonitoring in patients with HF. Further analyses are needed to better understand its impact on how physicians responded to these data and the consequent changes in conventional therapies. Prof. Hindricks summarized by stating that IN-TIME is the first implant-based, telemonitoring, randomized trial to show significant survival benefits of this type of monitoring in advanced HF patients. The decrease in mortality will require further studies for validation since there were a small number of deaths (37 total) in this trial, and it was not powered to evaluate this endpoint.

Losartan Reduces Aortic Dilatation Rate in Adults With Marfan Syndrome

Written by **Maria Vinall**

Results from the Cozaar in Marfan Patients Reduces Aortic Enlargement trial [COMPARE; Groenink M et al. *Eur Heart J* 2013] reported by Maarten Groenink, MD, PhD, Academic Medical Centre, Amsterdam, The Netherlands, demonstrated that the angiotensin receptor blocker, losartan, significantly reduced the rate of aortic enlargement after 3 years in patients with Marfan syndrome (MFS).

MFS is a connective tissue disorder caused by a mutation in fibrillin-1 that is associated with structural dysfunction in the aortic wall and biochemical changes including over expression of TGF β [Cohn RD et al. *Nat Med* 2007]. Patients with MFS are at an increased risk of sudden death due to aortic dissection or rupture. Clinical management includes prophylactic aortic root replacement and pharmacologic therapy (β-blockers and possibly losartan).

COMPARE was a multicenter, open-label, randomized, controlled trial designed to assess the effect of the addition of losartan to the standard of care on the rate of aortic dilatation at any level in adult patients with MFS. The study included adults aged ≥18 years with MFS (as classified by the 1996 Ghent criteria) with an aortic root diameter <50 mm, no aortic dissection and ≤1 vascular prosthesis. Subjects received losartan (100 mg QD) along with their previous medication (n=116) or remained on their previous medication only (n=117). Magnetic resonance imaging was performed at inclusion and after 3 years of follow-up. The primary endpoint was aortic dilatation rate at any of the predefined aortic levels at follow-up. Secondary endpoints included