The rate of freedom from complications related to the CRT-D system at 6 months was 89.6% for all patients who underwent attempted device implantation. Total serious adverse events (939 vs 732) and CRT-D-system related events (74 vs 32) were higher in the CRT arm.

The results of EchoCRT study confirm that patients with a narrow QRS complex should not receive CRT. Even following current guidelines (QRS ≥120 msec), the rate of "nonresponders" to CRT is very high and further research is needed to better identify those patients with moderate QRS widening (120 and 150 msec) who are most likely to benefit.

Cangrelor Reduces Thrombotic Events Among Patients Undergoing PCI

Written by Nicola Parry

Christian W. Hamm, MD, PhD, Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany, presented pooled data from three clinical trials of cangrelor, an intravenous adenosine diphosphate (ADP)-receptor antagonist in patients undergoing percutaneous coronary intervention (PCI) demonstrating significant reductions in thrombotic complications without an increase in major bleeding.

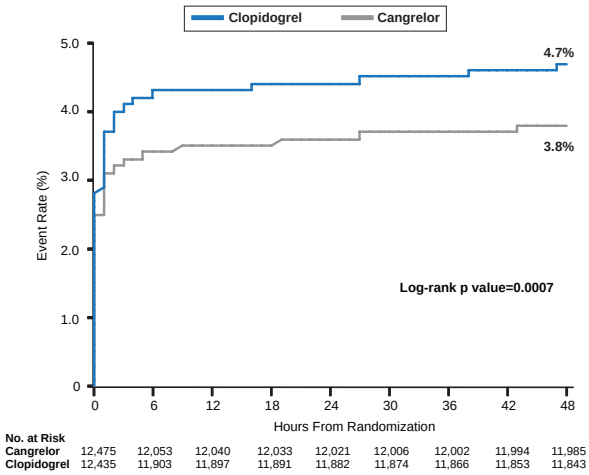
The efficacy of the novel, investigational agent cangrelor, a potent intravenous ADP-receptor antagonist with fast onset and short half-life of 3 to 6 minutes, has been evaluated in three randomized, double-blind, clinical trials against clopidogrel or placebo in patients during and after PCI: CHAMPION PHOENIX [Bhatt DL et al. *N Engl J Med* 2013]; CHAMPION PLATFORM [Bhatt DL et al. *N Engl J Med* 2009]; and CHAMPION PCI [Harrington RA et al. *N Engl J Med* 2009].

Prof. Hamm discussed the results of a meta-analysis of 24,910 patients enrolled in the CHAMPION program. The primary endpoint of the study was the composite of death from any cause, myocardial infarction (MI), ischemia-driven revascularization (IDR), or stent thrombosis (ST) at 48 hours. Secondary endpoints included ST at 48 hours and the composite endpoint of death/MI/IDR at 48 hours. The primary safety endpoint was GUSTO severe bleeding at 48 hours [Steg PG et al. *Lancet* 2013].

The efficacy analysis included patients (72% male; mean age 63 years) undergoing PCI for ST-elevation myocardial infarction (STEMI; 11.6%), non-ST elevation acute coronary syndromes (ACS; 57.4%), and stable coronary artery disease (31.0%) [Steg PG et al. *Lancet* 2013].

Among patients undergoing PCI, cangrelor was associated with a significant 19% relative reduction in the death/MI/IDR/ST at 48 hours compared with control (clopidogrel or placebo; 3.8% vs 4.7%; OR, 0.81; 95% CI, 0.71 to 0.91; p=0.0007; Figure 1) [Steg PG et al. *Lancet* 2013].

Figure 1. Rate of Primary Efficacy Endpoint in Cangrelor Versus Clopidogrel Groups



Reproduced from Steg PG et al. Effect of cangrelor on periprocedural outcomes in percutaneous coronary interventions: a pooled analysis of patient-level data. *Lancet* 2013. With permission from Elsevier.

The rate of ST at 48 hours was reduced by 41% with cangrelor compared with control (0.5% vs 0.8%; OR, 0.59; 95% CI, 0.43 to 0.80; p=0.0008). There was no significant difference in GUSTO severe bleeding, the primary safety endpoint, GUSTO moderate bleeding, or in the rate of blood transfusions between cangrelor and control groups. The rate of GUSTO mild bleeding, however, was increased with cangrelor treatment (16.8% vs 13.0%; p<0.0001) [Steg PG et al. *Lancet* 2013].

Prof. Hamm noted that follow-up was limited to 30 days because this corresponded to data that were available from the CHAMPION PHOENIX study [Bhatt DL et al. *N Engl J Med* 2013]. Despite this minor limitation in the dataset, he concluded that the results of this analysis suggest intravenous cangrelor may represent a viable treatment option to reduce periprocedural thrombotic complications across the range of PCIs, including patients with STEMI, non-ST elevation ACS and stable angina [Steg PG et al. *Lancet* 2013].

Catheter-Based Renal Artery Denervation – Sustained Blood Pressure Lowering With Reassuring Safety at 3 Years

Written by Nicola Parry

Catheter-based renal artery denervation appears to result in sustained blood pressure (BP) reduction with a favorable safety profile in patients through 3 years with consistent benefit across age, diabetes status, and renal function, according to Henry Krum, MBBS, PhD,

Monash University, Melbourne, Australia, who presented the final 3-year results from the Renal Denervation in Patients With Refractory Hypertension trial [Symplicity HTN-1; NCT00664638].

Although percutaneous renal denervation (RDN), an endovascular catheter-based procedure using radiofrequency energy, has been shown to successfully reduce BP for 1 year in patients with resistant hypertension [Krum H et al. *Lancet* 2009], its long-term efficacy may potentially be attenuated by sympathetic nerve regrowth and functional re-innervation.

The Symplicity HTN-1 was a series of pilot trials designed to evaluate the safety and BP-lowering efficacy of RDN using the Symplicity catheter system in refractory hypertension. These nonrandomized open-label studies were conducted among 19 centers in the United States, Australia, and Europe. Inclusion criteria were systolic BP (SBP) ≥160 mm Hg, despite full doses of ≥3 antihypertensive agents, and estimated glomerular filtration rate ≥45 mL/min. Exclusion criteria included type 1 diabetes, known secondary causes of hypertension, current clonidine, rilmenidine, or moxonidine therapy, and renovascular abnormalities.

The primary endpoints of the Simplicity HTN-1 were office BP and safety data before and at 1, 3, 6, 9, and 12 months after RDN. The secondary endpoints were the effects of RDN on renal noradrenaline spillover and renal function.

Of the 153 individuals enrolled, 65 patients (42.5%) were not included in the final analytic cohort because of missing baseline BP data, withdrawal of consent, loss to follow-up, or death. Results were presented for the remaining 88 patients (58%) who successfully completed the 36-month study.

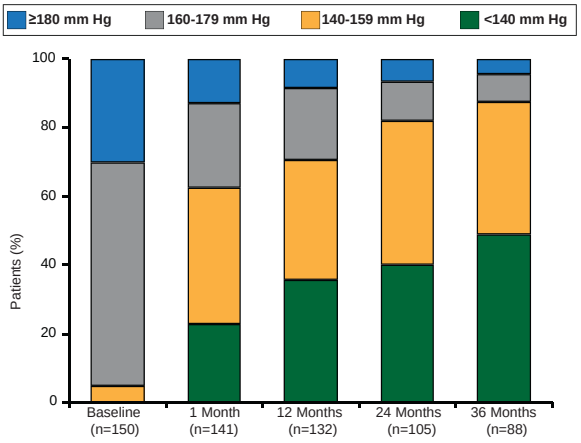
In the 58% of patients who completed the study through to 36 months, renal function was demonstrated to remain stable, and few significant late-stage adverse events were reported (Table 1).

Table 1. Late-Stage Adverse Events

Event	Episodes
Hypotension	2 (renal failure) 1 (diarrhea/dehydration)
Orthostatic hypotension	2 (1 patient)
Renal stenosis	4
Deaths associated with cardiac events	3

RDN was associated with significant ($p<0.01$) and sustained BP reductions (mean −32/−14 mm Hg) in patients who completed the study to 36-month follow-up. Still further, 50% of patients were able to achieve a target SBP <140 mm Hg (Figure 1). The BP reduction associated with RDN was consistent regardless of patient age, diabetes status, and baseline renal function.

Figure 1. Changes in SBP Through 36 Months



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Prof. Krum concluded that Symplicity HTN-1 is the first and longest running clinical trial for RDN to date, comprising the largest cohort of patients. Although the proportion of the cohort with follow up (n=88 of 153) was limited and longer-term evaluation of this therapy in blinded control trials is required, the results of this study suggest that RDN has a favorable safety profile and sustained BP-lowering over 36 months in patients with refractory hypertension.

CLARIFY Registry: Angina and Ischemia in Stable CAD Predicts Worse Outcomes

Written by **Mary Mosley**

The characteristics, management, and outcomes of outpatients with stable coronary artery disease (CAD) are being studied in the multicenter Prospective Observational Longitudinal Registry of Patients with Stable Coronary Artery Disease [CLARIFY; ISRCTN43070564]. Philippe Gabriel Steg, MD, University of Paris, Paris, France, presented data on the prevalence of angina and myocardial ischemia in this cohort and their association with clinical outcomes. He noted that little information is available in the current era of widespread revascularization and increased utilization of effective medical therapies (eg, β-blockers, statins).

The CLARIFY registry provides a dataset of 32,396 patients with stable CAD with at least one of the following at the time of enrollment: prior myocardial infarction (MI), chest pain and evidence of myocardial ischemia, evidence of CAD on coronary angiography, and prior percutaneous coronary intervention or coronary artery bypass surgery. All patients were enrolled in 2009 or 2010 across 45 countries and now have at least 2 years of follow-up.