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.

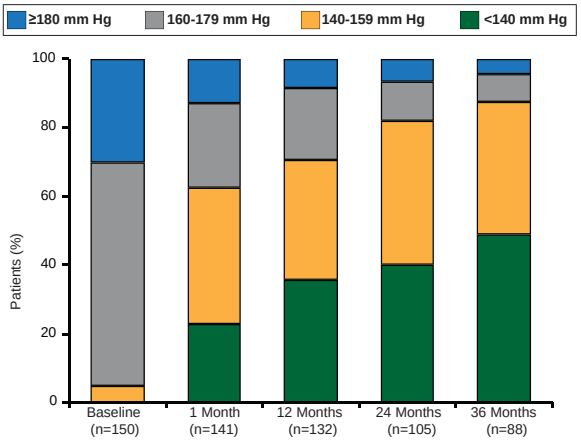
In the 58% of patients who completed the study through to 36 months, renal function was demonstrated to remain stable, and few significant late-stage adverse events were reported (Table 1).

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



Reproduced with permission from H Krum, MBBS, PhD.

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**

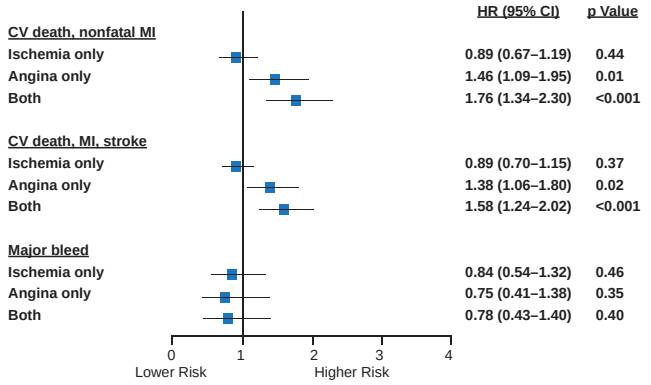
The characteristics, management, and outcomes of outpatients with stable coronary artery disease (CAD) are being studied in the multicenter Prospective Observational Longitudinal Registry of Patients with Stable Coronary Artery Disease [CLARIFY; ISRCTN43070564]. Philippe Gabriel Steg, MD, University 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.

The present analysis found that 20,402 (63%) of these CLARIFY patients underwent a noninvasive test for myocardial ischemia within 12 months prior to enrollment that did not lead to revascularization. Baseline data was used to characterize these patients as having neither angina nor ischemia (n=13,283), angina but no ischemia (n=1843), ischemia but no angina (n=3060), and both angina and ischemia (n=2216). Approximately two thirds of these patients had neither angina nor ischemia.

There was no difference in the primary composite endpoint of cardiovascular death and nonfatal MI between patients with ischemia alone versus those without ischemia and angina (HR, 0.89; Figure 1). Those with angina alone did have an increased risk (HR, 1.46; 95% CI, 1.09 to 1.95) and those with both angina and ischemia appeared to have an even higher risk (HR, 1.76; 95% CI, 1.34 to 2.30).

Figure 1. Outcomes by Ischemia or Angina Status in CLARIFY



CV=cardiovascular; MI=myocardial infarction.

*All outcomes were adjusted for age, sex, geographical region, smoking status, hypertension, dyslipidemia, and diabetes.

Reproduced with permission from PG Steg, MD.

Although the majority of stable CAD outpatients have neither angina nor ischemia, the presence of both appeared to confer higher risk for all of the cardiovascular secondary endpoints. Prof. Steg noted that 60% of the events in this dataset occurred in the subgroup with neither angina nor ischemia at baseline, emphasizing the need to optimize secondary prevention measures even in stable, asymptomatic patients.