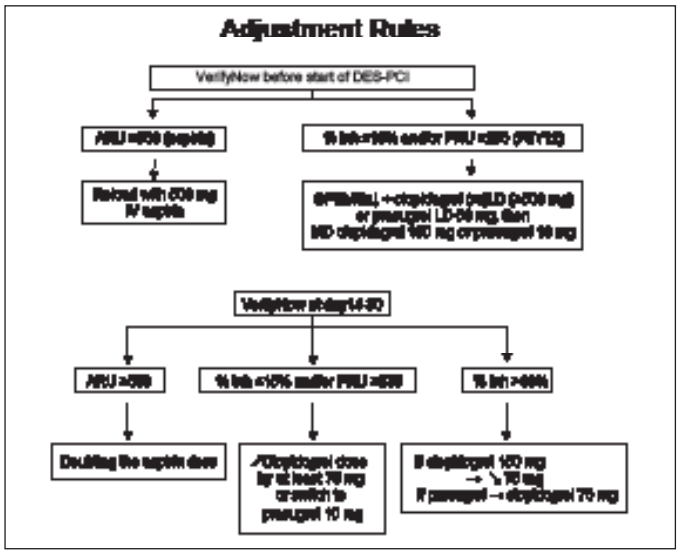
Figure 1. Antiplatelet Dose Adjustment Rules.



DES=drug-eluting stent; inh=inhibition; LD=loading dose; MD=maintenance dose; PCI=percutaneous coronary intervention; PRU=platelet reactivity units. Reproduced with permission from G Montalescot, MD.

At 1 year, the primary endpoint rate was not different between the PFT (34.6%) and conventional therapy groups (31.1%; HR, 1.13; 95% CI, 0.98 to 1.29; p=0.096). The majority of events that comprised the primary endpoint were periprocedural MIs. No significant difference was seen in the 1-year rate of MI between treatment strategy groups (30.3% with PFT-guided therapy vs 28.4% with conventional therapy; HR, 1.08; 95% CI, 0.93 to 1.25; p=0.32), and these neutral findings drove the primary composite results. There also were no significant differences in the rates of the main secondary endpoints (stent thrombosis or urgent revascularization) with PFT-guided therapy compared with conventional therapy (4.9% vs 4.6%; HR, 1.06; 95% CI, 0.74 to 1.52; p=0.77). Data for other ischemic endpoints are shown in Table 1.

Table 1. Other Ischemic Endpoints.

	PFT-Guided Therapy (%)	Conventional Therapy (%)	Hazard Ratio (95% CI)	p Value
Death or MI	31.7	28.8	1.11 (0.96–1.29)	0.15
Death	2.3	1.6	1.41 (0.79–2.50)	0.24
Stent thrombosis	1.0	0.7	1.34 (0.56–3.18)	0.51
Stroke or TIA	0.7	0.6	1.15 (0.42–3.18)	0.78
Urgent revascularization	4.5	4.2	1.06 (0.73–1.55)	0.76

MI=myocardial infarction; PFT=platelet function testing; TIA=transient ischemic attack.
Adapted from Collet JP et al. Bedside Monitoring to Adjust Antiplatelet Therapy for Coronary Stenting. *N Engl J Med* 2012; 367:2100-9.

Key safety outcomes were not significantly different with PFT versus conventional therapy: major bleeding (2.3% vs 3.3%; HR, 0.70; 95% CI, 0.43 to 1.14; p=0.15), minor bleeding (1.0% vs 1.7%; HR, 0.57; 95% CI, 0.28 to 1.16; p=0.12), and major or minor bleeding (3.1% vs 4.5%; HR, 0.69; 95% CI, 0.46 to 1.05; p=0.08).

The ARCTIC study results show that PFT with antiplatelet adjustment before and after stenting does not improve clinical outcomes versus conventional treatment without PFT. These results do not support the routine use of PFT in patients undergoing stenting. The ARCTIC-2 study, in which a second randomization was performed at 1 year after the initial randomization to determine the effect of continuation versus interruption of clopidogrel is ongoing. The Tailored Antiplatelet Therapy Versus Recommended Dose of Prasugrel [ANTARCTIC; NCT01538446] study will evaluate the value of PFT in elderly patients, with a focus on bleeding events. Whether PFT-guided antiplatelet therapy provides benefit for specific types of ischemic events such as spontaneous MI or stent thrombosis is unclear, as the ARCTIC trial was not powered for these individual endpoints and primary findings were largely driven by periprocedural events.

CARRESS-HF: Ultrafiltration Not Superior to Pharmacologic Therapy in the Treatment of Acute Heart Failure

Written by ***Rita Buckley***

Bradley A. Bart, MD, Hennepin County Medical Center, Minneapolis, Minnesota, USA, presented the Cardiorenal Rescue Study in Acute Decompensated Heart Failure [CARRESS-HF; NCT00608491] trial that was simultaneously published in the *New England Journal of Medicine* [Bart BA et al. 2012].

Acute cardiorenal syndrome (Type 1), defined as worsening renal function in patients with acute decompensated heart failure (ADHF) [Ronco C et al. *J Am Coll Cardiol* 2012], occurs in 25% to 33% of patients with ADHF and is associated with poor outcomes [Ronco C et al. *J Am Coll Cardiol* 2012; Metra M et al. *Circ Heart Fail* 2012].

CARRESS-HF was a multicenter, prospective, randomized controlled trial designed to test whether ultrafiltration was superior to stepped pharmacologic therapy for the treatment of patients with ADHF.

Patients hospitalized with ADHF and worsened renal function (defined as an increase in the serum creatinine level of at least 0.3 mg/dL) 12 weeks before or 10 days after

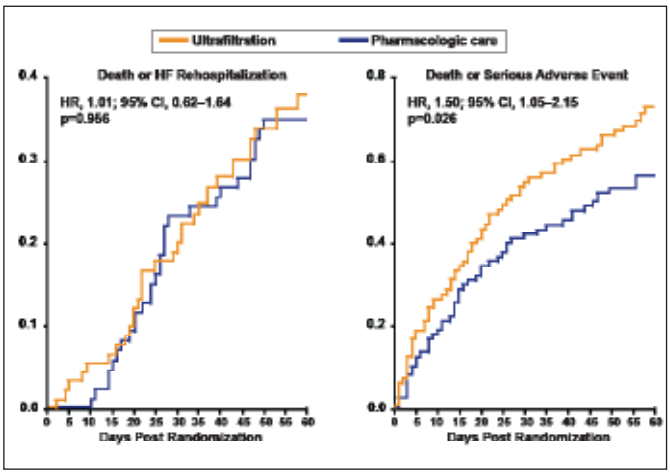
the index admission for heart failure (HF) were eligible for inclusion. Additional inclusion criteria included at least 2 of the following conditions at the time of randomization: at least 2+ peripheral edema, jugular venous pressure greater than 10 cm of water, or pulmonary edema or pleural effusion on chest radiography.

In total, 188 patients were randomized to a strategy of stepped pharmacologic therapy (n=94) or ultrafiltration (n=94). The primary endpoint was a composite of change from baseline in serum creatinine level and body weight at 96 hours. Clinical outcomes were assessed at 60 days.

Results showed that ultrafiltration was inferior to pharmacologic therapy with respect to the primary endpoint of changes in serum creatinine and body weight at 96 hours (p=0.003); this was due primarily to an increase in creatinine levels in the ultrafiltration group.

The mean change in the creatinine level at 96 days was –0.04±0.53 mg/dL in the pharmacologic therapy group compared with +0.23±0.70 mg/dL in the ultrafiltration group (p=0.003). There was no significant difference in weight loss between patients in the pharmacologic therapy group and those in the ultrafiltration group 96 hours after enrollment (a loss of 5.5±5.1 kg and 5.7±3.9 kg, respectively; p=0.58). At 60 days, there was no difference in death (17% vs 14%; p=0.55) or HF hospitalization (26% vs 26%; p=0.97), but serious adverse events (AEs) were more frequent with ultrafiltration (p=0.03) and there was a significant increase in the rate of death or serious AE with ultrafiltration compared with pharmacologic therapy (HR, 1.50; 95% CI, 1.05 to 2.15; p=0.026; Figure 1).

Figure 1. 60-Day Outcomes Post-Randomization.



Reproduced with permission from BA Bart, MD.

Dr. Bart concluded that, compared with pharmacologic therapy, ultrafiltration as administered in this study was associated with deterioration in renal function and worse clinical outcomes, and should not be used routinely in clinical practice. Whether or not ultrafiltration could be useful using slower rates of volume removal or as guided by hemodynamics is unknown. He said, "Treatment of these patients with ADHF, worsened renal function, and persistent congestion remains a challenging clinical problem in need of better therapy."

Long-Term Dabigatran Extension Study for Stroke Prevention in Treatment for Atrial Fibrillation

Written by ***Toni Rizzo***

Previously, the Randomized Evaluation of Long-Term Anticoagulation Therapy [RE-LY] trial evaluated two doses of dabigatran (110 and 150 mg BID; open dabigatran but blinded dose) versus warfarin (open-label) in patients with nonvalvular atrial fibrillation and at least 1 risk factor for stroke [Flaker et al. *J Am Coll Cardiol* 2012]. The goal of the RELY-ABLE extension study [NCT00808067] presented by Stuart J. Connolly, MD, McMaster University, Hamilton, Ontario, Canada, was to describe the long-term efficacy and safety of ongoing dabigatran therapy after the RE-LY trial.

Patients who had been randomized to dabigatran and were still taking it at then end of the the blinded dose of dabigatran taken in RE-LY trial were eligible for the was continued in the RELY-ABLE extension study. Patients continued on the same dose of dabigatran (the dose of dabigatran remained blinded) trial for a mean of 2.3 years. In the RE-LY trial, patients were randomized to dabigatran 110 mg (n=6015) or dabigatran 150 mg (n=6076) in a blinded fashion, or open-label warfarin (n=6022). Among these, 4492 (75%) in the 110-mg arm and 4519 (75%) in the 150-mg arm completed RE-LY and were still receiving dabigatran. Of these, 3395 (76%) in the 110-mg arm and 3397 (75%) in the 150-mg arm were beeing followed at a site participating in RELY-ABLE.

A total of 2914 patients receiving dabigatran 110 mg and 2937 patients receiving dabigatran 150 mg were enrolled in RELY-ABLE, and 2511 and 2508 patients, respectively, completed the study, representing 86% and 85% of the patients.

During 2.3 years of additional dabigatran treatment after RE-LY (total mean follow up of 4.3 years), rates of stroke and major bleeding remained low and comparisons of the 2 doses were consistent with those observed during the main RE-LY trial. The rates of stroke and myocardial infarction (MI) from the RELY-ABLE and RELY trials are compared in Table 1.