the REAL-LATE participants included a broader population that did not limit clinical or lesion characteristics. Exclusion criteria across the studies included contraindications to antiplatelet drugs, concomitant vascular disease or other indications that required the long-term use of clopidogrel, noncardiac comorbidities that limited life expectancy to <1 year, and participation in another drug or coronary device study. Follow-up evaluations were performed every 6 months, and the median duration of follow-up was 19.2 months. The primary endpoint was the first occurrence of MI or death from cardiac causes postrandomization. The secondary endpoints included major bleeding, as defined by Thrombolysis in Myocardial infarction (MI) criteria; a composite of death or MI; a composite of death, MI, or stroke; a composite of cardiac death, MI, or stroke; or individual components, including death, MI, stroke of any cause, definite stent thrombosis, or repeat revascularization.

The risk of cardiac death or MI was similar for both groups (1.8% for dual therapy vs 1.2% for monotherapy; p=0.17). The composite risk of MI, stroke, or death from any cause was slightly higher in the dual therapy group (HR, 1.73; 95% CI, 0.99 to 3.00; p=0.051), as was the composite risk of MI, stroke, or death from cardiac causes (HR, 1.84; 95% CI, 0.99 to 3.45; p=0.06). However, neither of these increases reached statistical significance. The risks that were associated with the individual components of the secondary endpoint were similar in both groups. Overall, the use of dual antiplatelet therapy beyond 12 months post-DES implantation did not significantly reduce the risk of MI or death from cardiac causes compared with aspirin monotherapy.

Dr. Park concluded that this study had insufficient statistical power to determine the safety of clopidogrel discontinuation after 12 months. Therefore, larger clinical trials with a longer-term follow-up are needed to evaluate the risk of clopidogrel discontinuation.

Further Reading: Park S-J et al. Duration of Dual Antiplatelet Therapy after Implantation of Drug-Eluting Stents. *N Eng J Med* 15 Apr 2010;362(15):1374-1382.

Diuretic Optimization Strategies Evaluation in Acute Heart Failure

There is no evidence of benefit for various initial administration or dosing strategies of furosemide therapy in patients with acute decompensated heart failure (ADHF). However, the high-intensification (2.5 x chronic daily oral dose) dosing strategy was associated with improvements or trends toward improvement in multiple areas. Findings from the Diuretic Optimization Strategies Evaluation in Acute Heart Failure (DOSE-AHF; NCT00577135) Study were presented by G. Michael Felker, MD, Duke Clinical Research Institute, Durham, NC.

Intravenous (IV) loop diuretics are commonly prescribed for patients with ADHF. However, there is some debate concerning the risk, benefit, and appropriate use of higher-dose diuretics. There is also an absence of prospective studies and trial evidence to provide clinicians with consistent guidelines for diuretic management. In light of current uncertainty pertaining to the appropriate administration and dosing of diuretics, DOSE-AHF investigators set out to evaluate the safety and efficacy of two administration (bolus Q 12 hours vs continuous infusion) and two dosing (low intensification of 1 x chronic daily oral dose furosemide vs high intensification of 2.5 x chronic daily oral dose furosemide) strategies.

DOSE-AHF was a double-blind, randomized trial with a 2x2 factorial design that included 308 patients with prior clinical diagnosis of acute heart failure (AHF; defined by at least one symptom and one sign) who were identified within 24 hours of hospital admission. All patients were taking oral furosemide 80 mg to 240 mg daily with an anticipated need for IV loop diuretics for at least 48 hours. Patients were excluded from participation if they received or planned to receive IV vasoactive therapy or ultrafiltration therapy for HF; had acute coronary syndrome within 4 weeks; and had systolic blood pressure <90 mmHg, serum creatinine>3.0 mg/dL at baseline, B-type natriuretic peptide (BNP) <250 pg/mL, or N-terminal pro-BNP (NT-proBNP) <1000 pg/mL.

The coprimary endpoints were the efficacy endpoint of patient global assessment by visual analog scale (VAS) over 72 hours using area under the curve (AUC) and the safety endpoint of renal function assessment, defined as change in creatinine from baseline to 72 hours. The study was 88% powered for detecting a creatinine difference of 0.2 mg/dL and a 600-point difference in VAS. Statistical significance for the two primary endpoints was p≤0.25. VAS was assessed at 6, 12, 24, 48, and 72 hours. The secondary endpoints are contained in Table 1.

The difference in global symptom relief and renal function was not statistically significant at 72 hours with regard to administration method (bolus vs continuous infusion) or dose (low vs high intensification). Additionally, results for all secondary endpoints were similar, regardless of the method of furosemide administration. Though transient changes in renal function occurred in patients who received high-intensification therapy prior to 60 days, the difference between the two groups dissipated by Day 60. High-intensification therapy was associated with improvements or trends toward improvement in multiple

domains, including dyspnea, change in weight, change in NT-proBNP, and net volume loss (Table 1).

It is important to note that this study evaluated only patients with a history of chronic HF and moderate to high diuretic requirements. Therefore, these results may not apply to *de novo* HF patients, concluded Dr. Felker. DOSE protocol also allowed for changes in therapeutic strategy at 48 hours, based on clinical response. This and the study's limited power to detect differences in clinical events may have influenced results with regard to observed differences between the groups.

Table 1. Secondary Endpoints.

Secondary Endpoint	Low Intensification (1 x oral dose/d)	High Intensification (2.5 x oral dose/d)	p value
Dyspnea VAS AUC at 72 hours	4478	4668	0.041
% free from congestion at 72 hours	11%	18%	0.091
Change in weight at 72 hours	-6.1 lbs	-8.7 lbs	0.011
Net volume loss at 72 hours	3575 mL	4899 mL	0.001
Change in NT-proBNP at 72 hours	-1194 pg/mL	-1882 pg/mL	0.06
% Treatment failure (persistent HF, worsening renal failure, or death)	37%	40%	0.56
% with creatinine increase >0.3 mg/dL within 72 hours	14%	23%	0.041
Length of stay, days (median)	6	5	0.55

Reproduced with permission from GM Felker, MD.

Results from the JETSTENT Trial

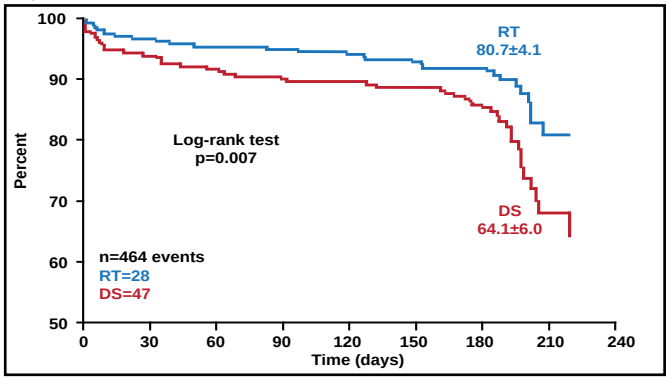
Rheolytic thrombectomy plus stenting is associated with better 6-month outcomes and improved myocardial reperfusion compared with direct stenting alone in patients with ST-elevation myocardial infarction (STEMI). While procedure time was higher in the thrombectomy group (60 minutes) than in the direct stenting group (46 minutes; p<0.001), this did not appear to impact the rate of procedural complications, such as the need for pacing to vessel perforation. David Antoniucci, MD, Careggi Hospital, Florence, Italy, discussed results from the Comparison of Angiojet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting to Direct Stenting Alone in Patients with Acute Myocardial Infarction (JETSTENT; NCT00275990) Trial.

The JETSTENT study included 500 patients with STEMI within 12 hours of symptom onset, at least moderate thrombus burden, and infarct artery vessel diameter ≥2.5 mm. Patients were randomized to either rheolytic thrombectomy (RT) plus stenting (n=256) or direct stenting (DS) alone (n=245). The use of a temporary pacemaker and balloon predilation was strongly discouraged. Patients with recent stroke (≤30 days), recent surgery (≤6 weeks), a prestented infarct-related artery, or lysis were excluded from participation in the study. However, cardiogenic shock was not grounds for exclusion and accounted for 2.7% of patients in the RT group and 5.3% of patients in the DS group. The mean follow-up was 6 months, and the mean age was 63 years. Patients were well matched at baseline.

The primary surrogate endpoints were early ST-segment resolution, defined as ≥50% reduction in ST-segment elevation at 30 minutes, and final infarct size at one month, determined by scintigraphy. Clinical endpoints were major adverse cardiac events (MACEs) at 1, 6, and 12 months and death or readmission for congestive heart failure at 12 months. The secondary surrogate endpoints included Thrombolysis in Myocardial Infarction (TIMI) flow, corrected TIMI frame count, and TIMI blush grade.

There was no significant difference in final infarct size between RT and DS (p=0.40). However, ST-segment resolution at 30 minutes was significantly improved in patients who underwent RT compared with DS (p=0.04). However, anterior acute MI appeared to be a predictor of ST-segment resolution (p<0.001). At one month, there was a 2-fold increase in MACEs in patients who received DS compared with RT (6.9% vs 3.1% for RT; p=0.05). DS was also associated with higher rates of death, MI, total vessel revascularization, and stroke compared with RT at one month. This trend continued at 6 months, with the exception of stroke incidence, which was identical in both groups (0.4% for both). TIMI major bleeding occurred in 3.9% of RT patients versus 1.6% of DS patients (p=0.12). However, this difference did not reach statistical significance. Total MACE rate at 6 months was 20.7% for the DS group versus 12.0% for the RT group (p=0.01). Randomization to RT, age, and bleeding appeared to be predictors of MACEs at 6 months (Figure 1).

Figure 1. 6-Month MACE Kaplan-Meier Estimate.



Reproduced with permission from D. Antoniucci, MD.