a meta-analysis that showed a significant reduction in bleeding events with radial access, with a trend toward fewer ischemic events, among patients with ACS [Jolly SS. *Am Heart J* 2009].

The RIVAL trial first enrolled patients as part of the ACS trial CURRENT-OASIS 7 [CURRENT–OASIS 7 Investigators. *N Engl J Med* 2010]. Patients were included in RIVAL if an invasive approach was planned and if the interventional cardiologist was willing to proceed with either radial or femoral access and had expertise for both (at least 50 radial procedures for coronary angiography or intervention within the previous year). The original sample size of 4000 was increased to 7000 by the RIVAL steering committee during the trial due to a lower-than-expected overall event rate for the primary outcome and because a sample size of 7000 would provide 80% power to detect a 25% relative risk reduction with a control event rate of 6% and a 30% relative risk reduction with a control event rate of 4% to 5%.

RIVAL enrolled 7021 patients at 158 hospitals in 32 countries. The patients were randomly assigned to radial access (n=3507) or femoral access (n=3514). The primary outcome was a composite of death, myocardial infarction (MI), stroke, or noncoronary artery bypass graft (non-CABG)-related major bleeding at 30 days. Secondary outcomes included death, MI, or stroke at 30 days; non-CABG-related major bleeding at 30 days; and major vascular access site complications.

There were no significant differences between the two groups with respect to either the primary or secondary outcomes that were related to death, MI, stroke, or non-CABG-related bleeding. The primary outcome occurred in 3.7% of the patients in the radial group and 4.0% of the patients in the femoral group (HR, 0.92; 95% CI, 0.72 to 1.17; p=0.50). There was, however, a difference in the rate of major vascular site complications, with fewer complications that were associated with radial access (1.4% vs 3.7%; HR, 0.37; 95% CI, 0.27 to 0.52; p<0.0001).

The researchers compared the two approaches in six prespecified subgroups: age (<75 and ≥75 years), gender, body mass index, PCI volume by operator, radial access volume by center, and diagnosis at presentation (non-STEMI and STEMI). The results were similar in all subgroups with two exceptions: a significant difference was observed in favor of radial access when performed at centers with the highest volume of radial access procedures (HR, 0.49; 95% CI, 0.28 to 0.87; p=0.015) and in patients with STEMI (HR, 0.60; 95% CI, 0.38 to 0.94; p=0.026).

Overall, RIVAL showed no significant benefit for radial access compared with femoral access in patients who presented with ACS. Reasons for this neutral result may include inadequate power to detect a difference of the magnitude that was observed. In the associated manuscript, the authors state, "RIVAL was underpowered to conclusively rule out moderate but important differences in the primary outcome. On the basis of the reported event rate of 4%, a sample of size of 17,000 patients would be needed to have 80% power to detect a 20% relative risk reduction in the primary outcome." Although the findings are neutral overall, clinicians may find the observations that radial access was associated with reduced rates of major vascular complications compared with femoral access and that the effectiveness of radial access appeared to be associated with expertise and volume to be helpful in clinical decision-making.

Further Reading: Jolly SS et al. *Lancet* 2011.

EVEREST Trial 2-Year Results Show Stability of Percutaneous MV Repair Between Years 1 and 2

Ted Feldman, MD, North Shore University Health System, Evanston, Illinois, USA, reported the 2-year results from the Endovascular Valve Edge-to-Edge Repair trial (EVEREST; NCT00209274), showing that percutaneous mitral valve (MV) repair is safe and durable with measurable clinical benefits and is a therapeutic option for select patients with significant mitral regurgitation (MR) [Feldman T et al. *New Engl J Med* 2011].

The EVEREST trial comprised patients with moderate/severe (3+) or severe (4+) MR who were candidates for MV surgery and compared percutaneous MV repair using the MitraClip device with MV surgery. The primary composite endpoint was freedom from death, surgery for mitral valve dysfunction, and grade 3+ or 4+ MR at 12 months, using an intention-to-treat (ITT) analysis. The primary safety endpoint was a composite of major adverse events within 30 days.

A total of 279 patients were randomly assigned in a 2:1 ratio to percutaneous repair (n=184) or surgery (n=95). At 2 years, 12 patients in the percutaneous arm (7%) and 12 patients in the surgical arm (12%) had missing data. Patients were well matched in terms of age and comorbidities, with the exception of history of congestive heart failure, which was more frequent in the percutaneous arm (91% vs 78%; p=0.005). About three-fourths of subjects had degenerative MR, and 27% had functional etiology. Ejection fraction was well preserved in both groups.

The primary results of the trial showed significantly higher rates of freedom from death, surgery for MV dysfunction, or grade 3+ or 4+ MR at 12 months in those who were randomized to surgery (73%) versus 55% in the percutaneous arm (p=0.007); however, there was no difference in death (a component of the primary endpoint; 6% in each group). Surgery also achieved a greater reduction in MR (p<0.001). When stratified by MR type, patients with degenerative MR did better with surgery, with a significantly higher rate of freedom from the primary endpoint (82% surgery vs 56% percutaneous; p for interaction=0.02). The primary safety endpoint of major adverse events at 30 days was significantly lower in the percutaneous arm (15% percutaneous vs 48% surgery; p<0.001).

The 2-year results showed stability in the outcomes between Year 1 and Year 2. In the 2-year analysis, the rates of the primary composite endpoint were similar to those that were observed in Year 1 (66% surgery vs 52% percutaneous; p=0.04). In addition, the proportion of patients in the percutaneous group who remained free from MV surgery at Year 2 (78.2%) was similar to that at Year 1 (78.8%). There was no difference in mortality between groups at 2 years (11%). MR grade remained stable in both groups, with the more favorable reduction in MR observed in the surgical group at Year 1, persisting through Year 2 (Table 1). Interestingly, NYHA functional class showed a more favorable outcome at both times for the percutaneous group. Importantly, there were no events of device embolization, fracture, erosion, or migration that were reported, and there was no additional occurrence of single leaflet device attachment between 1 and 2 years (6.3% at 1 year).

While the primary ITT analysis favored surgery and counted subsequent MV surgery following percutaneous repair as an "endpoint" event, a second analysis that evaluated the percutaneous strategy was also presented, in which subsequent MV surgery within 90 days of the percutaneous procedure was not considered an endpoint. In this secondary analysis, the differences between treatments were no longer significant (63% percutaneous vs 66% surgery; p=0.67; Figure 1). The presenter observed that "the need for surgery in patients in the clip group was almost entirely in the first several months after therapy, and after 6 months the curves overlapped at 1 and 2 years."

The Year 1 results of this trial showed that percutaneous repair was less effective at reducing MR than conventional surgery but that the procedure was associated with superior safety and similar improvements in clinical outcomes. The Year 2 results demonstrate overall stability in outcomes over the second year of follow-up and are reassuring, in that no device failures were observed over this period. Longer-term follow-up information will be helpful in assessing the durability of catheter-based MV repair.

Figure 1. Primary Effectiveness Analysis at 1 and 2 Years.

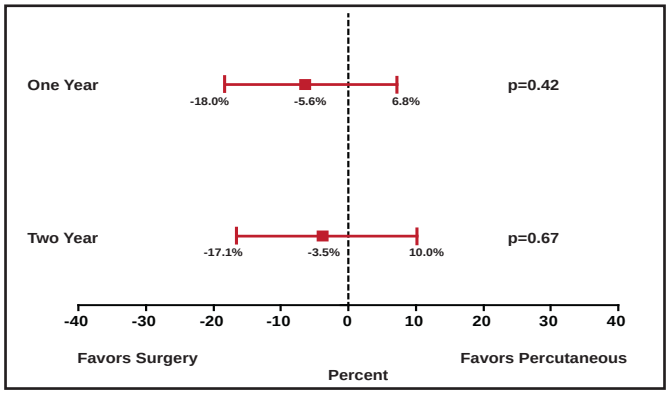

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Table 1. LV Volumes: Intention-to-Treat.

	LV End Diastolic Volume		LV End Systolic Volume	
	Percutaneous	Surgery	Percutaneous	Surgery
Baseline (mL)	157*	158*	62*	60*
Year 1 (mL)	133*†	119*†	57*	55*
Year 2 (mL)	124*‡	110*‡	55*	50*

*within group difference p<0.05; †between group difference at 1 year p<0.05; ‡between group difference at 2 years p<0.05; LV=left ventricular.

Targeted LV Lead Placement Is Feasible and Associated With Enhanced CRT Response

Results from the Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy Study (TARGET; ISRCTN19717943), presented by Fakhar Z. Khan, MD, Addenbrooke's Hospital, Cambridge, UK, show that targeted left ventricular (LV) lead placement not only is feasible but results in enhanced cardiac resynchronization therapy (CRT) response. Concordant LV lead placement, baseline dyssynchrony, and pacing away from areas of the scar are strongly related to improved CRT outcomes.

CRT has become part of the standard treatment for patients with advanced heart failure (HF) symptoms, impaired LV systolic function, and intraventricular conduction delay. Lead placement has emerged as a determinant of response. The objective of the TARGET Study was to prospectively assess the feasibility of a targeted approach to LV lead placement and the impact of LV lead targeting on CRT outcomes. The hypothesis was that targeting LV lead placement to the latest site of