

BACKGROUND Differences in terms of safety and efficacy of percutaneous edge-to-edge mitral repair between patients with functional and degenerative mitral regurgitation (MR) are not well established. We performed a systematic review and meta-analysis to clarify these differences.

METHODS PubMed, EMBASE, Google scholar database, and international meeting abstracts were searched for all studies about MitraClip. Studies with <25 patients or where 1-year results were not delineated between MR etiology were excluded. This study is registered with PROSPERO.

RESULTS A total of 9 studies investigating the mid-term outcome of percutaneous edge-to-edge repair in functional versus degenerative MR patients were included in the meta-analysis (n=2,615). At 1-year there were not significant differences among groups in terms of patients with MR grade ≤2 (719/1,304 vs. 295/504; 58 vs. 54%; RR 1.12; 95% CI: 0.86-1.47; p=0.40), while there was a significantly lower rate of mitral valve re-intervention in patients with functional MR compared with those with degenerative MR (77/1770 vs. 80/818; 4 vs. 10%; RR 0.60; 95% CI: 0.38-0.97; p=0.04). 1-year mortality rate was 16% (408/2,498) and similar among groups (RR 1.26; 95% CI: 0.90-1.77; p=0.18). Functional MR group showed significantly higher percentage of patients in NYHA class III/IV (234/1,480 vs. 49/583; 16 vs. 8%; p<0.01) and re-hospitalization for heart failure (137/605 vs. 31/220; 23 vs. 14%; p=0.03). No differences were found in terms of single leaflet device attachment (25/969 vs. 20/464; 3 vs. 4%; p=0.81) and device embolization (no events reported in both groups) at 1 year.

CONCLUSION This meta-analysis suggests that percutaneous edge-to-edge repair is likely to be an efficacious and safe option in patients with both functional and degenerative MR. Large, randomized studies are ongoing and awaited to fully assess the clinical impact of the procedure in these two different MR etiologies.

CATEGORIES STRUCTURAL: Valvular Disease: Mitral

TCT-581

Impact of severe annular dilatation in the recurrence of mitral regurgitation after percutaneous edge-to-edge mitral valve repair



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BACKGROUND Percutaneous mitral valve repair (PMVR) with MitraClip® has proved to reduce the size and the area of the mitral valve annulus (MVA). However, the impact of severe MVA dilatation in the results of PMVR has not been assessed.

METHODS Prospective registry of all consecutive patients treated with PMVR between June/14 and April/17 in our Institution. MVA diameter (MVAd) and anterior leaflet length (ALL) were determined by transesophageal echo in the LVOT view. Severe MVA dilatation was defined as a ratio MVAd/ALL ≥ 1.5, differencing 2 groups according to this cutting point. Transthoracic echocardiographic (TTE) follow up was performed at 2 and 6 months after the procedure. Successful PMVR was defined as residual mitral regurgitation (MR) I-II.

RESULTS In this period of time, 63 patients (73.6±10.1 years, male 68.3%) underwent PMVR in our center (EuroScore log 21.4±15, LV ejection fraction 38.2±14.9%). Most patients presented functional MR (74.6%) and had been admitted for acute HF within previous year (87.3%). Severe dilatation of MVA was found in 9 patients: 5 with functional MR, 3 with degenerative MR and one with mixed etiology. No significant differences were observed in LV end-diastolic diameter (55.8±5.6 vs 62.2±9.7 mm, p=NS) and left atrial volume in both groups (118.3±45.1 vs 114.3±40.6 ml, p=NS). Acute success of the procedure was similar between groups (88.9% vs 98%, p=NS), as it was the need for more than one clip (44.4% vs 42.0%, p=NS) or the device time (80.8±55.4 vs 69±30.8 minutes, p=NS). A ratio MVA/ALL ≥ 1.5 was related to a higher recurrence of MR grade III-IV at 2- (57.1% vs 18.4%, p=0.043) and 6-month (75% vs 19%, p=0.037) TTE follow up. Logistic binary regression model showed a significant increase of MR grade III-IV at 2 (OR 6.64, CI 95% [1.15-38.4], p=0.035) and 6 (OR 15.04, CI 95% [1.28-176.5], p=0.031) months after PMVR in patients with MVAd/ALL ≥ 1.5.

CONCLUSION Severely dilated MVA, defined as a ratio MVAd/ALL ≥ 1.5, was related to a higher recurrence of significance MR at 2 and 6

months follow up after PMVR. These patients might require annuloplasty techniques to achieve a permanent reduction in MR.

CATEGORIES STRUCTURAL: Valvular Disease: Mitral

TCT-582

30-Day Readmission and Cost-effectiveness of Percutaneous Mitral Valve Repair in the United States, 2011-2014



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BACKGROUND Percutaneous mitral valve repair (Mitraclip) has been demonstrated to provide a suitable minimally invasive treatment modality for patients with severe mitral regurgitation and high surgical risk. In this analysis we compare mortality, cost, and impact on 30-day readmission between percutaneous and conventional mitral repair in clinical practice.

METHODS Patients undergoing isolated mitral valve repair or mitral clip in the 2011-2014 National Readmission Database (NRD) were identified using ICD-9 CM procedure codes. The NRD is an all-payer inpatient database with discharge data from 1,045 hospitals in the United States sponsored by the Agency for Healthcare Research and Quality. Mortality, readmission, and cost were evaluated using multilevel linear regression to control for patient-level demographics and comorbidities measured by Elixhauser Index, and hospital factors.

RESULTS 2,751 percutaneous and 43,690 conventional repairs were performed during the study period. Patients undergoing percutaneous modality were more likely male (56% vs 43%, P<0.001), to have Medicare (74% vs 56%, P<0.001), elderly (73 vs 64 years, P<0.001), with similar Elixhauser Comorbidity Index (5.5 vs 5.7, P=0.10). Percutaneous repair was associated with lower adjusted mortality at discharge (3.6% vs 5.0% OR=0.54, P<0.001), lower cost of surgery (\$49,564 vs \$65,105, β=-0.38, P<0.001), and shorter index stay (7.9 vs 14.4 days, IRR=-0.58, P<0.001). 30-day readmission rate in percutaneous patients, most commonly for atrial fibrillation (6.8%), was significantly lower (14.7% vs 19.1%, OR=0.77, P<0.002).

CONCLUSION In this study of 46,441 U.S. patients who underwent mitral repair from 2011-2014, the percutaneous approach was 24% less expensive, had 23% lower odds of readmission within 30-days, 45% shorter length of stay, and 28% lower odds of mortality. Based on our findings, investigation of percutaneous mitral repair in lower risk cohort patients is warranted to assess durability and improvements in cardiac function.

CATEGORIES STRUCTURAL: Valvular Disease: Mitral

TCT-583

Abstract Withdrawn



ADJUNCT PHARMACOLOGY AFTER PCI: NON-DAPT DECISIONS

Abstract nos: 584 - 587, 840

TCT-584

A randomized, pharmacodynamic comparison of low dose ticagrelor to clopidogrel in patients with prior myocardial infarction: The ALTIC study



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BACKGROUND In patients with prior myocardial infarction (MI) long-term treatment with clopidogrel reduced ischemic events, with an increase in bleeding. In the Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin

-Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trial-ticagrelor 60mg bid also reduced the ischemic events, at the cost of increased bleeding events. There is no data on the pharmacodynamic efficacy of ticagrelor 60mg bid over clopidogrel.

METHODS The ALTIC (A randomized, pharmacodynamic comparison of Low dose Ticagrelor to Clopidogrel) study was a prospective, single-center, randomized, crossover study involving patients on aspirin 100mg od and PEGASUS-TIMI 54 characteristics: >50 years old with MI 1-3 years earlier and at least one high risk feature (age >65 years, diabetes mellitus, a second MI, multivessel disease, or renal dysfunction). After a 14-day washout period -if on P2Y12 receptor antagonist therapy-, patients were randomized to either ticagrelor 60 mg bid or clopidogrel 75 mg od for 14 days, with a crossover directly to the alternate treatment for another 14 days. Platelet reactivity (PR) was assessed by the VerifyNow P2Y12 reaction assay in platelet reactivity units (PRU) at baseline, pre and post-crossover, 2 hours post last study-drug dose.

RESULTS We recruited 20 eligible patients (95% men, 70% diabetics, 35% smokers, with a mean age of 58.5 ± 10.2 years) for participation in the study (10 in each treatment sequence). The primary end point of PR at the end of the two treatment periods was significantly lower for ticagrelor 60mg (31.8 PRU, 95% CI 3.0-60.5) compared to clopidogrel 75mg (165.6 PRU, 95% CI 136.8-194.3) with a mean difference of -133.8 PRU (95% CI -172.5 to -95.1), $p < 0.001$. The secondary endpoint of high PR (>208 PRU) rate was 0% for ticagrelor and 45.0% for clopidogrel ($p = 0.005$). No patient exhibited a major bleeding event at either treatment group.

CONCLUSION In patients with previous MI and at least one other high-risk feature, low dose of ticagrelor results in a significantly lower platelet reactivity compared to standard dose of clopidogrel.

CATEGORIES CORONARY: Pharmacology/Pharmacotherapy

TCT-585

Effect of high dose of Rosuvastatin on the serum concentration of inflammatory markers in the acute phase of percutaneous coronary intervention with metal stent implantation

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BACKGROUND Preliminary studies have shown that after initial injury with balloon catheter and/or metallic stents, there is endothelial denudation, dissection, platelet deposition and leukocyte attraction as an immediate response, which might limit the late benefits of PCL. Local injury to the arterial wall after stent implantation may promote the gene expression and release of inflammatory mediators which are directly related to the prognosis of cardiovascular disease. Despite their importance, there are few studies that characterize the acute inflammatory response after coronary stent implantation and correlate it to the occurrence of adverse events. **Objectives:** We sought to evaluate the effects of the loading dose of Rosuvastatin (40mg) on the acute inflammatory response after PCI with metallic stents, as well as to correlate the variations in cytokine levels and their respective gene expression.

METHODS Patients with stable coronary disease without statin (≥ 7 days) undergoing elective PCI to de novo lesions in the native coronary artery were randomized to receive a loading dose of 40 mg of rosuvastatin [N = 63] versus a control group (CG) (absence of loading dose); [N = 61]. Blood samples were obtained prior to oral administration of the statin (A), 03 hours after medication (B) and 03 hours after PCI (C). The following laboratory tests were conducted: complete blood count, C-reactive protein (CRP), nitric oxide (NO) and analysis of gene and protein expression by means of RT-qPCR and multiplex luminex, IL-1 mediators, IL-6, IL-8, PAI-1, MCP-1, TNF- α and TGF- β . Clinical follow up was achieved up to 12 months after the procedure.

RESULTS The groups did not significantly differ regarding clinical, angiographic and procedure characteristics, except for the higher amount of bifurcation lesions in the CG (19.7% versus 6.2%, $p = 0.032$). Among patients pre-treated with the statin, there was a reduction in gene expression for IL-6 ($p < 0.001$), IL-1 β ($p = 0.016$) and PAI-1 ($p = 0.002$). For the IL analyses, a progressive decrease in the concentrations of IL-6 0.209 pg/ml (IC 0.156; 0.28 $p < 0.001$), IL-1 β 0.491 pg/ml (IC 0.349; 0.692, $p < 0.001$) and PAI-1 0.986 pg/ml with

paving < 0.001) were observed among patients treated with the statin. Furthermore, a progressive reduction in the concentration of CRP was observed in the three timepoints among patients of the rosuvastatin cohort ($p = 0.04$). An increase in NO concentration was observed from timepoint A to C in the statin group ($p = 0.004$). During the in hospital period, more periprocedural MI occurred among patients in the control group (23% vs 4.7%, $p = 0.004$). Also, 12-month MACE rate was higher in the control group (9.8% vs 1.6%, $p = 0.058$).

CONCLUSION Pre-loading with high dose of rosuvastatin resulted in a marked reduction in the expression of the main inflammatory markers (IL-1 β , IL-6, PAI-1 and CRP) associated with restenosis after PCI with stents. Additionally, an increase in the NO blood concentration was noticed among these patients.

CATEGORIES CORONARY: Cell Therapy and Angiogenesis

TCT-586

Alirocumab efficacy and safety in patients with prior coronary revascularization

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BACKGROUND Patients with prior revascularization are at high risk of further CV events, and may need additional lipid-lowering therapy beyond statins. We assessed the PCSK9 inhibitor alicumab in patients with prior coronary revascularization (PCI or CABG).

METHODS Efficacy data from 8 Phase 3 trials were analyzed in 3 pools per trial design: alicumab 150 mg every 2 weeks (Q2W) vs placebo; alicumab 75/150 mg (75 mg Q2W with possible dose increase to 150 mg Q2W at Week 12 based on Week 8 LDL-C) vs placebo; alicumab 75/150 mg Q2W vs ezetimibe. All trials included background statin therapy. Primary endpoint was % change in LDL-C from baseline to Week 24.

RESULTS Of 4629 total randomized patients, 2191 (47.3%) had prior revascularization; of these, >50% had history of acute MI, 53-84% were on high intensity statin therapy, mean age was 60-62 years and 71-70% were male (ranges over pooled groups). LDL-C was significantly reduced with alicumab vs controls, with LS mean $\pm$ SE reductions of $63.1 \pm 1.1\%$ with the 150 mg Q2W dose and $51.5 \pm 1.7\%$ and $52.8 \pm 1.4\%$ in pools using 75/150 mg Q2W, respectively; other lipids were also reduced (Table). Alicumab was generally well-tolerated, with a higher injection site reaction frequency vs controls.

Table. Baseline lipids and reductions from baseline to Week 24

Pool	ALI 150 vs PBO (n=1092)	ALI 75/150 vs PBO (n=416)	ALI 75/150 vs EZE (n=655)
Group	ALI	PBO	ALI
LDL-C			
Baseline, mg/dL	119.7 $\pm$ 38.9	120.9 $\pm$ 40.1	115.7 $\pm$ 41.9
% change at W24	-63.1 $\pm$ 1.1	-6.1 $\pm$ 1.5	-51.5 $\pm$ 1.7
W24 achieved, mg/dL	41.4 $\pm$ 1.2	113.1 $\pm$ 1.6	52.9 $\pm$ 1.9
Non-HDL-C			
Baseline, mg/dL	148.9 $\pm$ 43.1	151.4 $\pm$ 43.3	144.4 $\pm$ 46.4
% change at W24	-53.5 $\pm$ 0.9	-0.5 $\pm$ 1.2	-43.7 $\pm$ 1.4
Apo B			
Baseline, mg/dL	100.8 $\pm$ 26.7	101.9 $\pm$ 27.1	100.8 $\pm$ 28.0
% change at W24	-54.7 $\pm$ 0.9	-0.0 $\pm$ 1.2	-40.3 $\pm$ 1.4
Lp(a)			
Baseline, mg/dL	27.4 (9.4-79.3)	26.8 (7.6-78.5)	36.0 (11.0-88.5)
% change at W24	-30.2 $\pm$ 1.0	-3.1 $\pm$ 1.5	-26.4 $\pm$ 1.7

All comparisons are $P < 0.0001$ versus control. "n" values are for the intention-to-treat population. Baseline values are means $\pm$ SD, except for Lp(a), for which median and Q1-Q3 are shown. % change and achieved values are LS means $\pm$ SE, except for Lp(a) for which adjusted means $\pm$ SE are shown. ALI, alicumab; Apo B, apolipoprotein B; EZE, ezetimibe; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); LS, least-squares; non-HDL-C, non-high density lipoprotein cholesterol; PBO, placebo; SE, standard error; W24, week 24. Clinical trial.gov identifiers: NCT01507831, NCT01623115, NCT01709500, NCT01617655, NCT01644175, NCT01644188, NCT01730040, NCT01730053.