Highlights from ACC 15 Scientific Sessions: Part 1

Cihangir Kaymaz, Lale Tokgözoğlu[1]

Clinic of Cardiology, Kartal Koşuyolu Yüksek İhtisas Education and Research Hospital; İstanbul-*Turkey*
[1]Department of Cardiology, Faculty of Medicine, Hacettepe University; Ankara-*Turkey*

The 64th Annual scientific Sessions of the American College of Cardiology took place in San Diego in March 15 to 17. There were close to 14000 attendees from different countries. 103 physicians from Turkey attended. The congress was interactive, innovative and informative with a high scientific quality and the chosen theme for the congress was 'more learning, less lecturing'.

One day before the offical program, the 7th ACC Annual Cardiovascular Conference on the Middle East Conference took place featuring a plenary lecture by Dr. Valentin Fuster. The main focus of the conference was acute coronary syndromes and electrophysiology. Speakers from different countries in the Middle East held a joint session. In this session, Dr. Alev Arat spoke about ACS in the young.

In the opening ceremony, the President of the College Dr. Patrick O'Gara highlighted the innovations in Cardiology and the new things on the horizon like 3-D printers, bioengineering, PCSK9 inhibitors and the big data (1). He also expressed concern about decreased funding and increased external regulations. He emphasised the importance of the human touch in a world of electronic health records and technology and gave examples like the fact that 47% of the time of an emergency medicine doctor is spent in front of the computer (1). Following the end of ACC.15, Patrick T. O'Gara, MD, MACC, immediate past president of the ACC, passed the presidential chain to Kim Allan Williams, Sr., MD, FACC, at the time honored Convocation Ceremony. Williams is currently the James B. Herrick Professor and chief of the division of cardiology at Rush University Medical Center in Chicago, IL. He is board certified in internal medicine, cardiovascular diseases, nuclear medicine, nuclear cardiology and cardiovascular computed tomography. *"Each president has the privilege of inheriting the foundation of past leaders,"* Williams said (2) . *"Following on Pat's year of building new leaders and ensuring continued focus on educational funding and research, I hope to focus on increasing our ongoing effectiveness as advocates for patient access to the best cardiovascular care, regardless of race, gender, income or geography."* (2) *"This past October the* New England Journal of Medicine *published a survey quantifying the declining standing of U.S. physician leaders in the public eye since the 1960s.* (3) *In 1966, 75 percent of Americans surveyed had great confidence in physicians, but by 2012 only 34 percent shared this outlook. This lack of trust places the U.S. well behind other developed countries like Turkey, France, Great Britain, Switzerland and many others.* (3)*"* Williams said. (2)

During the congress, the Turkish Society of Cardiology / İstanbul Consortium Chapter held a joint session with the Indonesian Heart association on the topic of clinical pathways and outcomes in acute coronary syndromes. Dr. Barış Kaya, Dr. Oktay Ergene and Dr. Lale Tokgözoğlu represented the Turkish Society in this session where the similarities and differences in approach between two countries and ways to improve care were discussed. At the end of this session, Dr. Cihangir Kaymaz received the best abstract award for the highest ranking abstract from Turkey. His work was entitled '*The Ekosonic endovascular system provides improvements in thrombotic burden, pulmonary arterial pressures and right atrial and ventricular functions in patients with acute pulmonary embolism at high or intermediate risk".*

In another debate session, Dr. Bülent Görenek discussed the topic of cardioversion of atrial fibrillation with or without anticoagulation very succesfully. He emphasised the importance of individual approach for each patient.

An out of the ordinary session was 'A conversation with the legends' where Dr. Braunwald, Dr. De Maria and Dr. Fox discussed candidly their major successes, failures and lessons learnt in research throughout the years.

On the last day of the meeting, the convocation took place. Many scientists received awards for research, education and

Address for Correspondence: Dr. Cihangir Kaymaz, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi Kardiyoloji Kliniği, 34656, Kartal, İstanbul-*Türkiye* Phone: + 90 216 500 15 00 Fax: +90 216 459 63 21 E-mail: cihangirkaymaz2002@yahoo.com

Accepted Date: 12.5.2015

DOI:10.5152/akd.2015.153201

service. It was impressive to see how many young scientists were motivated by these awards. This was followed by the announcement of the new fellows. From Turkey, Dr. Aylin Yıldırır, Dr. Birhan Yılmaz and Dr. Cihangir Kaymaz became fellows of the ACC. Overall, the congress was succesful in expanding knowledge and generating new insights as Dr. O'Gara stated. I sincerely hope that the scientific contributions from the Turkish Cardiologists will increase even more over the years.

Highlights from ACC15;

5-year outcomes of transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR) for high surgical risk patients with aortic stenosis (PARTNER 1) (4). Michael Mack, MD, presented 5-year results of PARTNER1 trial on March 15 at the late breaking clinical trial session and 5-year findings of this study were published simultaneously in *The Lancet.* Overall 699 were enrolled (348 assigned to TAVR, 351 assigned to SAVR) in PARTNER 1,and mean Society of Thoracic Surgeons Predicted Risk of Mortality score was 11.7%. At 5 years, risk of death was 67.8% in the TAVR group as compared to 62.4% in the SAVR group (hazard ratio 1.04, 95% CI: 0.6–1.24; p=0.76). No structural valve deterioration requiring surgical valve replacement was noted in either group. Moderate or severe aortic regurgitation (AR) occurred in 14% in the TAVR group and 1% of the patients in the SAVR group (p<0·0001), and was found to be associated with an increased 5-year risk of mortality in the TAVR group (72.4% for moderate or severe AR *vs* 56.6% for those with mild AR or less; p=0·003). In summary, five-year follow-up results of PARTNER1 showed that TAVR results in similar clinical outcomes compared with surgery for patients with high surgical risk (4).

TAVR improves 5-year survival as compared to standard treatment in patients with inoperable aortic stenosis (5). In other study from PARTNER1 trial, 5-year outcomes of TAVR were compared with standard treatment for patients with inoperable aortic stenosis (AS) (5). 358 were enrolled (mean age 83 years, Society of Thoracic Surgeons Predicted Risk of Mortality 11.7%, 54% female). 179 were assigned to TAVR treatment and 179 were assigned to standard treatment. The risk of all-cause mortality at 5 years was 71.8% in the TAVR group vs 93.6% in the standard treatment group (hazard ratio 0.50, 95% CI: 0.39–0.65; p<0.0001). At 5 years, 86% survivors in the TAVR group had New York Heart Association class 1 or 2 symptoms compared with 60% in the standard treatment group. Echocardiography after TAVR showed sustained haemodynamic benefit (aortic valve area 1.52 cm^2 at 5 years, mean gradient 10.6 mm Hg at 5 years), without structural deterioration (5).

The first report of SAPIEN3 in the United States, and the first report on intermediate-risk TAVR patients (6). Susheel Kodaly, M.D. presented the 30-day clinical and echocardiographic outcomes with the SAPIEN 3 TAVR System in inoperable, high-risk and intermediate-risk AS patients. The SAPIEN3 valve approved in Europe in January 2014 for treatment of high-risk and inoperable patients with severe AS, but not approved for the treatment of intermediate - risk severe AS in Europe. The US experience of SAPIEN 3 was analysed in two single-arm, non-randomized cohorts of the PARTNER 2 trial. The high-risk cohort and intermediate- risk cohort enrolled 583 and 1076 patients, respectively. The mortality was lower than predicted 30-day mortality, and was 2.2% and 1.1% in high-risk and intermediate-risk cohorts, respectively. Significant paravalvular AR was 3.0% for high-risk, and 4.2% for intermediate-risk AS consistent with meaningful improvements over earlier generation devices (6).

Two-year results from the CoreValve US Pivotal Trial: TAVR *with CoreValve provides a better survival rate than SAVR in patients with high-risk aortic stenosis:* The difference in all-cause mortality was 4.8% at 12 months and 6.5% at 2 years favoring TAVR (*log rank p*=0.04). For all strokes, the difference was 3.8% at 12 months and 5.7% at 2 years favoring TAVR (*log rank p*=0.05). TAVR patients had less AR between 30 days and 1 year, and the low level of paravalvular AR was maintained at 2 years. Two years after implant, TAVR with CoreValve continues to outperform SAVR in high-risk patients with symptomatic AS (7, 8).

DEFLECT III trial: *The TriGuard embolic protection device may provide fewer 'silent' strokes, possible memory benefits after TAVR* (9). Alexandra Lansky, M.D. reported the early results of the *TriGuard* device, mesh on a nitinol frame that fits across the three arteries that feed the brain. One-third of patients received a CoreValve TAVR, the remainder were treated with a Sapien 3 device. The device related with a longer fluoroscopy time by 10 minutes. The success of TriGuard device deployement was 94%, and coverage of all three vessels was maintained until CoreValve deployment in 87% of patients. The intent-to-treat analysis showed that TAVR with TriGuard as compared to unprotected TAVR resulted in 17 % reduction in the volume of new lesions in (73 vs 88 mm^3). The incidence of the absence of new lesions on diffusion-weighted MRI following the procedure was 21.9% with the TriGuard compared with 12.5% without it in the same analysis. Scores on the Montreal Cognitive Assessment (MoCA), improved from baseline to discharge in TriGuard cohort but deteriorated over that time in the patients without protection. The MoCA scores was maintained in 73.7% of the TriGuard patients and 63.3% of patients without protection. The Visual learning and short-term memory on the CogState (*p*=0.043 and *p*=0.028), but not clinical stroke rates, were found to be significantly improved with TriGuard (p=NS). The rates of in-hospital major adverse cardiovascular and cerebrovascular events were too low for comparison (9).

Transcatheter Valve Therapy (TVT) Registry as a r**eal life experience on MitraClip device (10).** This registry presented by

Paul Sorajja, MD, comprised 564 patients at prohibitive surgical risk who underwent transcatheter mitral valve repair using the MitraClip device. Sorajia reported 91.8% procedure success, 7.8% complication rate, 1.8% stroke rate, 2.7% device-related adverse events, 81.9% discharge rate and 5.8% 30-day mortality. In-hospital mortality was 2.3%, and 93% had grade ≤2 residual mitral regurgitation (MR) after MitraClip in TVT registry whereas the EVEREST trials showed 0.9% to 2.6% in-hospital mortality and 74% to 86% grade ≤2 MR (10).

Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) (11): ***Among low- to intermediate-risk patients with chest pain, coronary CT angiography (CTA) was not superior to functional testing*** **but was associated with increased radiation exposure and a trend for increase in total costs.** This study was presented by Dr. Pamela S. Douglas, and Economic comparison analysis was presented by Dr. Daniel B. Mark,and was simultaneously published in the N Engl J Med 2015; Mar 14. The goal of the trial was to evaluate anatomical testing with CTA compared with functional testing among low- to intermediate-risk patients with chest pain suspicious for coronary artery disease (CAD). Low-to intermediate-risk patients (n=10.003) with chest pain were randomized to evaluation with CTA strategy (n=4.996) vs a functional strategy (n=5.007). The mean pretest likelihood of obstructive CAD was 53.3±21.4%. Over a median follow-up period of 25 months, a primary end-point event occurred in 3.3% in the CTA group and in 3.0% in the functional-testing group (adjusted hazard ratio, 1.04; 95% CI: 0.83 to 1.29; p=NS). CTA related to fewer catheterizations showing no obstructive CAD than was functional testing (3.4% vs. 4.3%, p= 0.02): However, more patients in the CTA group underwent catheterization within 90 days (12.2% vs. 8.1%) and overall radiation exposure per patient was higher in this group than in the functional-testing group (mean, 12.0 mSv vs. 10.1 mSv; p<0.001). Coronary CTA was associated with a small, but nonsignificant increase in costs over a median of 2 years vs functional testing. In summary, symptomatic patients with suspected CAD, initial coronary CTA compared with functional testing, did not improve clinical outcomes over a median follow-up of 2 years, but was associated with increased radiation exposure and a trend for increase in total costs (11).

SCOT-HEART: ***Coronary CTA may help to diagnosis and decision for interventions, and may reduce the future risk of myocardial infarction in patients with suspected angina.***In this prospective open-label, parallel-group, multicentre trial the effect of coronary CTA on the diagnosis, management, and outcome of patients referred to the cardiology clinic with suspected angina due to CAD was assessed. 9849 patients referred from 12 cardiology chest pain clinics across Scotland were enrolled and 4146 (42%) of them were randomly assigned (1:1) to standard care plus CTA or standard care alone with a web-based service to ensure allocation concealment. The primary endpoint was certainty of the diagnosis of angina due to CAD at 6 weeks. All analyses were intention to treat. At 6 weeks, CTA reclassified the diagnosis of CAD in 558 (27%) patients and the diagnosis of angina due to CAD in 481 (23%) patients [standard care 22 (1%) and 23 (1%); p<0.0001]. Although both the certainty [relative risk (RR) 2.56, 95% CI 2.33–2,79; p<0.0001] and frequency of CAD increased (1.09, 1.02–1.17; p=0.0172), the certainty increased (1.79, 1.62–1.96; p<0.0001) and frequency tends to decrease (0.93, 0.85–1.02; p=0.1289) for the diagnosis of angina due to CAD. This changed planned investigations (15% *vs.* 1%; p<0.0001) and treatments (23% *vs.* 5%; p<0.0001) but did not affect 6-week symptom severity or admittances to hospital for chest pain. After 1.7 years, CTA was associated with a non-significant 38% reduction in fatal and nonfatal myocardial infarction (26 *vs.* 42, HR 0.62, 95% CI 0.38-1.01; p=0.0527) (12).

MATRIX: Reduction in ***Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX: Radial vs. Femoral*** **access.** This randomized parallel blinded trial was presented by Dr. Marco Valgimigli, and was simultaneously published in *Lancet 2015; Mar 16 (13).* This trial was aimed to evaluate radial access compared with femoral access among subjects undergoing cardiac catheterization for acute coronary syndromes (ACS). 8,404 patients with ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) ACS were randomized to radial access vs femoral access. By factorial design, patients were also randomized to bivalirudin versus heparin. Mean age was 66 years, and presentation was STEMI in 48%, and NSTEMI in the remainder. PCI was attempted in 80%, and access was unsuccessful in 5.8% of the radial group vs 2.3% of the femoral group. Duration of follow-up:30 days. The primary outcome of death, MI, or stroke occurred in 8.8% of the radial group vs. 10.3% of the femoral group (p=0.031). The hospitals that performed >80% radial PCIs had better outcomes with radial procedures vs femoral procedures (p for interaction=0.0048), while hospitals with a low and intermediate proportion of radial PCIs had similar outcomes with either radial or femoral procedures. Death, MI, stroke, or BARC (type 3 or 5) major bleeding: 9.8% vs. 11.7% (p=0.0092), respectively, for radial vs. femoral. All-cause mortality was 1.6% vs. 2.2% (p=0.045), Stroke was 0.4% vs. 0.4% (p=0.99), and BARC (type 3 or 5) major bleeding was 1.6% vs. 2.3% (p=0.0128), respectively, for radial vs femoral access. The difference in major adverse cardiovascular events, a co-primary endpoint, was not significant. For catheterization laboratories that have femoral access with low bleeding rates, benefit from radial access may be marginal whereas for catheterization laboratories having high rates of bleeding with femoral access, conversion to radial access would be an appropriate mechanism to lower bleeding and adverse events (13).

MATRIX Antithrombin Program: **Bivalirudin vs heparin:** The antithrombin part of MATRIX included the 7,213 patients who

had PCI planned after diagnostic catheterization. 56% of the pateints had STEMI, 40% had NSTEMI, and 5% had unstable angina. PCI was attempted in 95% of patients, with about 5% ultimately receiving medical treatment. Glicoprotein IIb/IIIa use was 5 times more frequent in the heparin arm than in the bivalirudin arm (25.8% vs. 4.6%). There were no differences between the bivalirudin and heparin groups in either MACE (10.3% vs. 10.9%; RR 0.94; 95% CI 0.81-1.10) or NACE (11.2% vs. 12.4%; RR 0.89; 95% CI 0.78-1.10). However, bivalirudin reduced all-cause mortality (1.7% vs. 2.3%; RR 0.71; 95% CI 0.51-0.99) driven by fewer cardiovascular deaths-and BARC 3 or 5 bleeding (1.4% vs. 2.5%; RR 0.55; 95% CI 0.39-0.78), with an impact on bleeds not related to the access site and both BARC 3 and 5 bleeds individually. TIMI major or minor bleeding and GUSTO moderate or severe bleeding also were less frequent with bivalirudin. The rate of definite stent thrombosis was higher in the bivalirudin group (1.0% vs. 0.6%; RR 1.71; 95% CI 1.00-2.93), with a trend toward more definite/probable stent thrombosis. Findings were consistent across various subgroups and was not related with vascular access site (14).

AJULAR Study: A trans-ulnar approach is noninferior to a transradial approach in the suitable patient and in the hands of experienced operators. In this study, 2600 patients with STEMI, cardiogenic shock, on chronic hemodialysis, or with a history of CABG or Raynaud's disease were excluded. There was no difference in the composite endpoint of major adverse cardiac events, major vascular events, and crossover rates and their individual components (p>0.05) (15).

TOTAL: Randomized Trial of Primary PCI with or without Routine Manual Thrombectomy. In this study, 10.732 patients with STEMI undergoing primary PCI to a strategy of routine upfront manual thrombectomy versus PCI alone. The primary outcome was a composite of death from cardiovascular causes, recurrent myocardial infarction, cardiogenic shock, or New York Heart Association (NYHA) class IV heart failure within 180 days, and safety outcome was stroke within 30 days. This study was published on March 16, 2015, at NEJM.org. The primary outcome occurred in 6.9% in the thrombectomy group vs. 7.0% in the PCI-alone group (hazard ratio (HR) in the thrombectomy group, 0.99; 95% CI: 0.85 to 1.15; p=0.86). The rates of cardiovascular death (3.1% vs. 3.5%; HR, 0.90; 95% CI, 0.73 to 1.12; p=0.34) and the primary outcome plus stent thrombosis or target-vessel revascularization (9.9% vs. 9.8%; HR, 1.00; 95% CI, 0.89 to 1.14; p=0.95) were also similar. Stroke within 30 days was 0. 7% in thrombectomy group versus 0.3% in the PCI-alone group (HR, 2.06; 95% CI, 1.13 to 3.75; p=0.02). ***In patients with STEMI who underwent primary PCI, routine manual thrombectomy, compared with PCI alone, did not reduce the risk of cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or NYHA class IV heart failure within 180 days but was associated with an increased rate of stroke within 30 days*** (16).

"Does TASTE or TOTAL study allow us to rule out the possible benefit from thrombus aspiration in high-risk patients" In the editorial to TOTAL trial published in NEJM, Filippo Crea, M.D. wrote that *" Although the findings of TOTAL are consistent with those of the TASTE trial and together suggest that the time has arrived to prepare a requiem for routine manual thrombectomy, neither study allows us to rule out the possibility that thrombus aspiration might be beneficial in high-risk patients. Indeed, the event rates in both trials were substantially lower than expected, a finding that suggests that the trials didnot enroll high-risk patients. Interestingly, in both trials, the event rates in the placebo group were about half that initially considered for power calculation. Furthermore, in the TASTE trial, mortality was about one-third of that observed in patients who were followed up in a parallel registry", Crea said. " In conclusion, the prevention and treatment of coronary microvascular obstruction remains an unmet need. Four interacting mechanisms cause microvascular obstruction in humans: distal embolization, ischemia-related injury, reperfusion- related injury, and individual susceptibility of the microcirculation to injury. It is likely that the relevance of these mechanisms differs among patients." "Thus, an integrated and personalized approach addressing all mechanisms in different time windows is needed in order to reduce the strikingly increased risk conferred by coronary microvascular obstruction.*" (17).

EMBRACE STEMI trial: ***Administration of a novel mitochondrial targeting peptide, Bendavia, failed to reduce infarct size in STEMI patients.*** In this study, presented by M. Gibson, M.D. at ACC 15, Bendavia (Stealth BioTherapeutics; Newton, MA), a cell-permeable peptide targeted to cardiolipin, a phospholipid found exclusively in the inner mitochondrial membrane was tested in STEMI patients. 297 first-time STEMI patients with proximal or mid LAD lesion from 24 hospitals in 4 countries were randomized to Bendavia infusion (0.05 mg/kg/hr) or placebo administered 15 minutes prior to and 1 hour after PCI. Infarct size, as measured by serum CK-MB, area under the curve (AUC) and sensitive troponins at 6 hours, infarct volume, edema, left ventricular ejection fraction, and angiographic outcomes related to procedural success rates, flow or perfusion were comparable between the two treatment strategy arms. The clinical composite endpoint (death, new-onset congestive heart failure after 24 hours of PCI, or heart failure rehospitalization) was similar between the study arms at 30 days and 6 months (p=NS for both). In a non-prespecified exploratory analysis of patients with hypertension, infarct volume was smaller (35.8 vs. 52.6 mL; p=.03) and edema volume trended smaller (49 vs. 61 mL; p=.053) with the Bendavia compared with placebo. There were no differences in the rate of adverse events or ST-segment resolution. ***In conclusion, Bendavia failed to improve clinical composite endpoint after 24 hours of PCI and heart failure rehospitalizations at 30 days and 6 months in anterior STEMI patients*** (18).

REGULATE-PCI: ***Pegnivacogin (REG-1) in comparison with bivalirudin failed in patients undergoing percutaneous coronary intervention.*** This phase III trial randomized patients undergoing PCI for ACS and non-ACS clinical presentations to pegnivacogin (REG-1), a factor IXa inhibitor (1 mg/kg), at the start of PCI and an active reversal agent (0.5 mg/kg) at the end of PCI or to standard bivalirudin. The trial was designed as a superiority trial for a 20% risk reduction of the composite endpoint of death, nonfatal MI, nonfatal stroke, and urgent target lesion revascularization at day 3, necessitating 13,200 patients. However, because of an unacceptably 10-times higher rate of severe allergic reactions (1 fatal, 9 anaphylactic at 3 days in the REG-1 group), the trial was terminated early. As 3200 patients were enrolled in this trial up to that time, similar outcomes were observed at 3 days and 30 days in the two groups, with more type 4a MIs in the REG-1 group and more stent thrombosis in the bivalirudin arm. There was a significantly lower rate of bleeding events with bivalirudin (19).

DANAMI3-PRIMULTI: The Third DANish Study of Optimal Acute Treatment of Patients With STEMI: PRImary PCI in MULTIvessel Disease: ***FFR-guided complete revascularization is superior to culprit vessel only PCI in patients with multivessel disease presenting with STEMI and undergoing primary PCI.*** This study was presented by Dr. Thomas Engstrøm. The goal of the trial was to compare the utility of infarct-related percutaneous coronary intervention (PCI) versus fractional flow reserve (FFR)-guided complete revascularization in patients with multivessel disease presenting with STEMI. The primary outcome, major adverse cardiovascular events (MACE; all-cause mortality, MI, ischemia-driven revascularization of non-IRA lesions) for IRA only PCI vs. FFR-guided complete revascularization was 22% vs. 13%, HR=0.56 (p=0.004). Benefit was driven by a significant reduction in ischemia-driven revascularization (5% vs. 17%, p<0.001) while mortality (5% vs. 4%, p=0.43); and nonfatal MI (5% vs. 5%, p=0.87) were comparable between two groups. Secondary outcomes were as follows: Periproce-dural stroke: 1.3% vs. 0.3% (p=0.2); urgent PCI: 2% vs. 6% (p=0.03); and nonurgent PCI: 3% vs. 9% (p=0.002), respectively. *In conclusion, the results of DANAMI3-PRIMULTI indicate that FFR-guided complete revascularization prior to hospital discharge is superior to culprit vessel only PCI in patients with multivessel disease presenting with STEMI and undergoing primary PCI* (20).

After Eighty Study: ***Among elderly patients with NSTE-ACS, invasive therapy reduces adverse cardiovascular events compared with conservative therapy.*** This study was presented by Nicolai Tegn, MD and simultaneously published in the *New England Journal of Medicine.* The goal of the trial was to evaluate invasive versus conservative therapy among the elderly with non-ST-elevation acute coronary syndrome (NSTE-ACS). The study was conducted in 16 health facilities across Norway, and included 458 patients receiving treatment for NSTEMI or unstable angina. Using a randomized 1:1 trial, patients were randomized to receive a conservative protocol of drug therapy, or coronary angiography to determine which course of treatment would result in the best clinical outcomes. The primary outcome of death, myocardial infarction (MI), stroke, or urgent revascularization was significantly reduced in the invasive group compared with those in the conservative group (41% vs. 61%, p<0.0001). Secondary outcomes for invasive vs. conservative therapy were as follows; Death: 25% vs. 27% (p=0.53), MI: 17% vs. 30% (p=0.0003), and Stroke: 3% vs. 6% (p=0.26), respectively,. In summary, the After Eighty Study showed that invasive therapy versus conservative therapy reduced adverse cardiovascular events among the elderly patients with NSTE-ACS. This seems to be driven by a reduction in recurrent MI and urgent revascularizations (21).

PEGASUS-TIMI 54: ***Ticagrelor May Reduce Risk Of Death From Heart Attack Or Stroke Long After Initial MI.*** This study was presented by Sabatini and simultaneously published in N Engl J Med 2015. The efficacy and safety of ticagrelor were investigated in 21,162 patients who had a MI 1 to 3 years earlier randomly assigned, in a double-blind 1:1:1 fashion to ticagrelor at a dose of 90 mg twice daily, ticagrelor at a dose of 60 mg twice daily, or placebo. All the patients were allowed to receive low-dose aspirin. The median follow-up was 33 months, and the primary efficacy end point was the composite of cardiovascular death, MI, or stroke while the primary safety end point was Thrombolysis in Myocardial Infarction (TIMI) major bleeding. The two ticagrelor doses each reduced, as compared with placebo, the rate of the primary efficacy end point, with Kaplan–Meier rates at 3 years of 7.85% in the group that received 90 mg of ticagrelor twice daily, 7.77% in the group that received 60 mg of ticagrelor twice daily, and 9.04% in the placebo group [HR for 90 mg of ticagrelor vs. placebo, 0.85; 95% confidence interval (CI), 0.75 to 0.96; p=0.008; hazard ratio for 60 mg of ticagrelor vs. placebo, 0.84; 95% CI, 0.74 to 0.95; p=0.004]. Ticagrelor related with a higher rate of TIMI major bleeding (2.60% with 90 mg and 2.30% with 60 mg) than with placebo (1.06%) (p<0.001 for each dose vs. placebo). The rates of intracranial hemorrhage or fatal bleeding in the three groups were 0.63%, 0.71%, and 0.60%, respectively. *In conclusion, PEGASUS-TIMI 54 indicates that ticagrelor significantly reduced the risk of cardiovascular death, myocardial infarction, or stroke and increased the risk of major bleeding in patients with a MI more than 1 year previously* (22).

In an editorial on the PEGASUS results in *NEJM,* John F. Keaney Jr., MD wrote that "*These data prompt speculation as to whether dual platelet inhibition with high-potency agents is approaching the point of diminishing returns." "In the study by Bonaca et al., ticagrelor did not significantly affect overall mortality, and the numerical excess of deaths from noncardiovascular causes appeared to be related to cancer, a feature not seen in the Study of Platelet Inhibition and Patient Outcomes (PLATO). Collectively, these data do not support a unified concern with*

respect to excess mortality with dual antiplatelet therapy, but they do remind us of the fragile balance between efficacy and adverse events."(23).

Two studies comparing everolimus-eluting stents with CABG: BEST trial; Everolimus-eluting stents are not superior to *surgery for multivessel coronary disease.* The BEST study, a randomized Korean trial, was presented by Seung-Jung Park, MD, and was published online in the *New England Journal of Medicine.* After the enrollment of 880 patients (438 patients randomly assigned to the PCI group and 442 randomly assigned to the CABG group), the study was terminated early owing to slow enrollment. At 2 years, the primary end point had occurred in 11.0% of the patients in the PCI group and in 7.9% of those in the CABG group [absolute risk difference, 3.1 percentage points; 95% confidence interval (CI), -0.8 to 6.9; p=0.32 for non-inferiority]. At longer-term follow-up (median, 4.6 years), the primary end point had occurred in 15.3% of the patients in the PCI group and in 10.6% of those in the CABG group (HR, 1.47; 95% CI, 1.01 to 2.13; p=0.04). No significant differences were seen between the two groups for the composite safety end point of death, myocardial infarction, or stroke. However, the rates of any repeat revascularization and spontaneous myocardial infarction were significantly higher after PCI than after CABG. *In summary, among patients with multivessel coronary artery disease, the rate of major adverse cardiovascular events was higher among those who had undergone PCI with the use of everolimus-eluting stents than among those who had undergone CABG* (24).

The real life data for comparison between everolimus-eluting stents with CABG: In a second study based on the propensity-score matching of observational registries of all procedures done in the state of New York, adjustment for confounding factors in physician, and patient selection for one procedure over the other in real-world practice was performed among the 34,819 patients with multivessel disease (48.5% these treated with everolimus-eluting stents). This study was simultaneously published on March 16, 2015, at *New England Journal of Medicine.* The primary outcome was all cause mortality, and secondary outcomes were the rates of MI, stroke, and repeat revascularization. At a mean follow-up of 2.9 years, PCI with everolimus-eluting stents, as compared with CABG, was associated with a similar risk of mortality [3.1% per year and 2.9% per year; HR, 1.04; 95% confidence interval (CI), 0.93 to 1.17; p=0.50], higher risks of MI (1.9% per year vs. 1.1% per year; HR, 1.51; 95% CI, 1.29 to 1.77; p<0.001) and repeat revascularization (7.2% per year vs. 3.1% per year; HR, 2.35; 95% CI, 2.14 to 2.58; p<0.001), and a lower risk of stroke (0.7% per year vs. 1.0% per year; HR, 0.62; 95% CI, 0.50 to 0.76; p<0.001), respectively. The higher risk of MI with PCI than with CABG was not significant among patients with complete revascularization but was significant among those with incomplete revascularization (p=0.02 for interaction). *In this registry based on data from real-world clinical-practice patterns, PCI with everolimus-eluting stents and CABG resulted in similar mortality, and PCI was associated with a higher risk of MI among patients with incomplete revascularization and repeat revascularization but a lower risk of stroke. In contrast to BEST trial didn't show the increased stroke risk frequently reported with CABG versus stent studies, the New York registry also confirmed this trend* (25).

In an *New England Journal of Medicine* accompanying editorial to two studies, Robert A. Harrington, MD, wrote that *"To the extent that the data from these two studies can be relied on, there are clearly tradeoffs between the two revascularization strategies that need to be discussed with patients as part of the shared decision-making process. The early hazard of CABG (the risk of stroke) may be unacceptable to some patients, whereas others might want to avoid the later hazards of PCI (the risk of needing a repeat PCI procedure or having a myocardial infarction). The decision should also take into account the results of coronary angiography, with particular focus on whether complete revascularization with PCI appears to be feasible - a factor that would make PCI more attractive than CABG"."Although these conclusions seem reasonable on the basis of the current data, we should do better than base clinical decisions on flawed observational studies and undersized randomized trials "* , *Harrington said (26).*

References

1. ACC.15 Convocation Speech: Patrick T. O'Gara, MD, MACC. From ACC News.
2. ACC.15 Convocation Speech: Kim Allan Williams, Sr., MD, FACC. From ACC News.
3. Blendon RJ, Benson JM, Hero JO. Public Trust in Physicians-U.S. medicine in international perspective. N Engl J Med 2014; 371: 1570-2. [CrossRef]
4. Mack JM, Leon MB, Smith CR, Miller C, Moses JW, Tuzcu EM, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. Lancet 2015 Mar 15. pii: S0140-6736(15)60308-7. doi: 10.1016/S0140-6736(15)60308-7. [Epub ahead of print]. [CrossRef]
5. Kapadia SR, Leon MB, Makkar RR, Tuzcu EM, Svensson LG, Kodali S, et al. 5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomised controlled trial. Lancet 2015 Mar 15. pii: S0140-6736(15)60290-2. doi: 10.1016/S0140-6736(15)60290-2. [Epub ahead of print].
6. Kodali S, on behalf of The PARTNER Trial Investigators. The first report of SAPIEN3 in the United States,and the first report on intermediate-risk TAVR patients. Presented at the American College of Cardiology's (ACC) 64th Annual Scientific Session in San Diego. March 15, 2015.
7. Barker CM, Reardon MJ. The CoreValve US pivotal trial. Semin Thorac Cardiovasc Surg 2014; 26: 179-86. [CrossRef]
8. Reardon M. A Randomized Comparison of Self-expanding Transcatheter and Surgical Aortic Valve Replacement in Patients

with Severe Aortic Stenosis Deemed at Increased Risk for Surgery 2-Year Outcomes. Presented at the American College of Cardiology's (ACC) 64th Annual Scientific Session in San Diego CA. March 2015.

9. Lansky AJ. First report of the DEFLECT III trial results: A prospective randomized evaluation of The TriGuardTM HDH embolic DEFLECTion device during transcatheter aortic valve replacement. Presented at the American College of Cardiology's (ACC) 64th Annual Scientific Session in San Diego CA. March 2015.
10. Sorajja P. Transcatheter Valve Therapy (TVT) Registry as a real life experience on MitraClip device. Presented at the American College of Cardiology's (ACC) 64th Annual Scientific Session in San Diego CA. March 2015.
11. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med 2015; 372: 1291-300. [CrossRef]
12. SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet 2015 Mar 13. pii: S0140-6736(15)60291-4. doi: 10.1016/S0140-6736(15)60291-4. [Epub ahead of print]
13. Valgimigli M, Gagnor A, Calabró P, Frigoli E, Leonardi S, Zaro T, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015 Mar 13. pii: S0140-6736(15)60292-6. doi: 10.1016/S0140-6736(15)60292-6. [Epub ahead of print]. [CrossRef]
14. Valgimigli M. Bivalirudin infusion compared to unfractionated heparin in patients with acute coronary syndromes undergoing invasive management: results from the Minimizing Adverse Hemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox (MATRIX) antithrombin program. Presented at American College of Cardiology/i2 Scientific Session; March 16, 2015; San Diego, CA.
15. Gokhroo R, Kishor K, Ranwa B, Bisht D, Gupta S, Avinash A. Ulnar artery intervention non inferior to radial approach: Reality or myth? AJmer ULnar ARtery working group study.A randomized parallel group Non-Inferiority trial. Presented at American College of Cardiology (ACC) 2015 Scientific Sessions March 14 - 16, 2015; San Diego, CA.
16. Jolly SS, Cairns JA, Yusuf S, Meeks B, Pogue J, Rokoss MJ, et al. Randomized trial of primary PCI with or without routine manual thrombectomy. N Engl J Med 2015; 372: 1389-98. [CrossRef]
17. Jolly SS, Cairns JA, Yusuf S, Meeks B, Pogue J, Rokoss MJ, et al. on behalf of TOTAL Investigators. Randomized trial of primary PCI with or without routine manual thrombectomy. N Engl J Med 2015; 372: 1389-98. [CrossRef]
18. Gibson CM. The EMBRACE STEMI Study: a phase 2a, randomized, double-blind, placebo controlled trial to evaluate the safety, tolerability and efficacy of intravenous Bendavia on reperfusion injury in patients treated with standard therapy including primary PCI and stenting for ST-segment elevation myocardial infarction. Presented at: American College of Cardiology/i2 Scientific Session; March 15, 2015; San Diego, CA.
19. Herrmann J, A Randomized, Open-Label, Multi-Center, Active-Controlled, Parallel Group Study to Determine the Efficacy and Safety of the REG1 Anticoagulation System Compared to Bivalirudin in Patients Undergoing Percutaneous Coronary Intervention (REGULATE-PCI) Cardiology. Expert Opinion / Conference Coverage. March 16, 2015.
20. Engstrøm T. The third DANish study of optimal Acute treatment of patients with ST-segment elevation Myocardial Infarction: PRImary PCI in MULTIvessel disease. Presented at: American College of Cardiology/i2 Scientific Session; March 16, 2015; San Diego, CA.
21. Tegn NK, Invasive vs. Conservative Strategy in Patients over 80 Years With Non-ST-Elevation Myocardial Infarctionor Unstable Angina Pectoris- Clinical Trial After Eighty Study. Presented at: American College of Cardiology/i2 Scientific Session; March 16, 2015; San Diego, CA.
22. Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, et al.; PEGASUS-TIMI 54 Steering Committee and Investigators. Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. N Engl J Med 2015; 372: 1791-800. [CrossRef]
23. John F. Keaney, Jr, M.D. Balancing the risks and benefits of dual platelet, nhibition. N Engl J Med 2015; 372: 1854-6. [CrossRef]
24. Park SJ, Ahn JM, Kim YH, Park DW, Yun SC, Lee JY, et al. Trial of Everolimus-Eluting Stents or Bypass Surgery for Coronary Disease. N Engl J Med 2015; 372: 1204-12. [CrossRef]
25. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Xu J, Hannan EL. Everolimus-eluting stents or bypass surgery for multivessel coronary disease. N Engl J Med 2015; 372: 1213-22. [CrossRef]
26. Harrington RA. Selecting Revascularization Strategies in Patients with Coronary Disease. N Engl J Med 2015; 372: 1261-3. [CrossRef]