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HIGHLIGHTS

of the

SCIENTIFIC SESSIONS

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However, addition of fenofibrate to statin therapy showed a trend towards benefit in the subgroup which had high TG (>204 mg/dL) and low HDL

The **ACCORD (Action to Control Cardiovascular Risk in Diabetes) Lipid study,** led by Dr. Henry Ginsberg (Columbia University, New York) presented on March 14, 2010 at the ***American College of Cardiology (ACC) 2010 Scientific Sessions*** *and* published simultaneously online in the *New England Journal of Medicine*, demonstrated the effect of combination therapy with statin plus a fibrate vs. statin monotherapy on the risk of fatal cardiovascular events, nonfatal MI, or nonfatal stroke in patients with type 2 diabetes mellitus.

The ACCORD trial was conducted in 10,251 high-risk patients with type 2 diabetes who were randomly assigned to either intensive or standard glycemic control. In addition, 4733 of the participants were also randomized to either intensive or standard blood-pressure control, the results of which were presented at the ACC, and 5518 patients were randomly assigned to simvastatin plus fenofibrate or simvastatin plus placebo.

After an average follow-up of 4.7 years, there were 291 major fatal or nonfatal cardiovascular events in the fenofibrate-statin-therapy study arm and 310 events in the statin-therapy-alone arm, translating into an annualized rate of 2.2 and 2.4 events per year, respectively, in the two treatment arms. The difference in events was not statistically significant. Among the secondary end points, there was also no statistically significant difference between the two treatments.
It was concluded that the combination of fibrate-statin demonstrated no benefit above the statin monotherapy.

However, there was heterogeneity according to baseline lipid levels: in a pre-specified subgroup with mean baseline HDL 29.5 mg/dl, about 10 mg/dl lower than the rest of the cohort, and mean baseline triglyceride 284 mg/dl, about 120 mg/dl higher than the rest of the cohort, there was a trend towards benefit of adding fenofibrate to statin therapy. This was in contrast to the rest of the patients, in whom the mean HDL cholesterol level was 39.9 mg/dl and the median triglyceride level was 144 mg/dl.

From baseline to 4 months in the fenofibrate group, the HDL cholesterol level rose by 12.9% and the triglyceride level fell by 35.0% among patients in the above mentioned subgroup, as compared to a 7.3% rise in the HDL cholesterol level and a 24.1% decrease in the triglyceride level among all other patients receiving fenofibrate.

Thus, the addition of fenofibrate to statin therapy benefiting only the above mentioned subgroup of patients and not the other subgroups could have diluted the overall effect of fenofibrate.

In view of this subgroup analysis, Dr. Ginsberg said that fenofibrate should be added as that ATP III clinical guidelines indicate- that is, in statin-treated patients with high triglyceride levels and low HDL-cholesterol levels.

"It can be concluded that, the use of statin-fenofibrate combination therapy is consistent with current ATP III guidelines, that recommend adding fenofibrate for patients with hypertriglyceridemia and low HDL cholesterol levels that persist despite statin therapy."

As adapted from www.theheart.org/article/1054681; N Engl J Med. March 14th 2010. As accessed on 18th March 2010.

ACCORD study: Intensive BP lowering beneficial in reducing total stroke and non fatal stroke but does not improve risk for CV events in type 2 diabetes patients

Action to Control Cardiovascular Risk in Diabetes (ACCORD) study presented at the ***American College of Cardiology 2010 Scientific Sessions*** and simultaneously published online in the *New England Journal of Medicine*, showed that **intensive lowering of systolic blood pressure (BP) to a goal of <120 mmHg did not reduce the rate of composite outcome of fatal and nonfatal major cardiovascular events, however it significantly reduced the incidence of stroke.**

ACCORD, a randomized trial, enrolled high-risk type 2 diabetes patients who were further divided to participate into the ACCORD lipid trial or the ACCORD BP trial. In the ACCORD BP trial, 4733 high-risk diabetics were randomized to either intensive BP-lowering regimen (i.e. target systolic BP goal <120 mmHg) or standard BP lowering regimen (i.e. target systolic BP goal <140 mmHg) for the mean follow-up of 4.7 years.

The annual rate of the primary composite outcome of stroke, or death from cardiovascular causes was 1.87% in the intensive-therapy group and 2.09% in the standard-therapy group. **Interestingly, incidence of both total and nonfatal stroke was significantly reduced in the intensive lowering group by 41% and 37% respectively. (Table 1)**

Table 1: Efficacy outcomes in ACCORD-BP trial

Outcome	**Intensive therapy (n=2363), events, n**	**Intensive therapy (n=2363), %/y**	**Standard therapy (n=2371), events, n**	**Standard therapy (n=2371), %/y**	**Hazard ratio**	**p**
Primary outcome	208	1.87	237	2.09	0.88	0.20
Secondary outcomes						
Stroke						
—Any	36	0.32	62	0.53	0.59	0.01
—Nonfatal	34	0.30	55	0.47	0.63	0.03

The study author, Dr William Cushman, Veterans Affairs Medical Center, Memphis, TN, said that the **significant difference in stroke between the intensive and standard BP lowering arms is very interesting because it is consistent with what has been seen in other hypertension trials** with treatment versus placebo, i.e. about a 40% reduction in stroke for a 5 to 10 mmHg reduction in BP.

With an aim to interpret the results, the study discussion mentions certain reasons for the failure to achieve the study endpoints. **Lowering systolic BP from the mid-130s to approximately 120 mmHg does not provide further reduction in most cardiovascular events or the rate of death, while most of the benefits from lowering BP were achieved by targeting a goal of**

<140 mmHg. Alternatively, it is also possible that period of 5 years is not long enough to see significant cardiac benefits from the normalisation of systolic BP among persons with diabetes who have good control of glycemia, especially when other effective treatment such as statins and aspirin, are used frequently.

In an accompanying editorial, **Dr Peter M Nilsson,** University Hospital, Malmö, Sweden, **points that the factorial design of the overall ACCORD study and the inclusion and exclusion criteria that were applied reduced the overall power of study. The current results may have been a consequence of the frequent use of statins and of inclusion criteria that directed participants with dyslipidemia, leaving participants who were at lower risk in the blood-pressure trial.**

There is no reason that high blood pressure in diabetics shouldn't be treated but it is extremely important to get down to the level which has shown benefit i.e. the standard BP lowering regimen in the ACCORD trial.

Adapted from http://www.theheart.org/article/1054543.do. As accessed on 18th March 2010

Intensive BP control increases mortality vs the usual control in patients with diabetes and CHD

A new analysis, presented at the ***American College of Cardiology*** *(ACC)* ***2010 Scientific Sessions***, showed that **intensive blood pressure (BP) control in patients with diabetes and cardiovascular disease was associated with a higher mortality rate than usual control.**

International Verapamil SR-Trandolapril (INVEST) randomly assigned 6400 patients with diabetes and CAD to the two BP lowering strategies starting with verapamil SR or atenolol, with both groups adding trandolapril and hydrochlorothiazide to achieve the target of <130/85 mmHg. Patients were categorized according to the degree of BP control achieved. Patients with a systolic BP of ≥140 mmHg were classified as "not controlled." Those with a systolic BP<130 mmHg were classified as "tight control" and those with a systolic BP between 130 and 140 mm Hg were classified as "usual control."

During the follow-up period, **patients in the uncontrolled group had nearly a 50% higher combined risk of death/MI/stroke when compared with the usual-control group. Patients in the tight-control group had a similar risk of the combined end point as in the usual-control group. However, further analysis revealed an increase in the risk of all-cause death in the tight-control group vs usual-control group.** This increase became apparent about 30 months into the study and persisted for an additional five years of follow-up.

When analysis was done for BP in 5-mmHg-increment reductions in the tight-control group, it was observed that **increase in mortality became apparent only at a systolic BP of 115 mmHg and increased further as BP was lowered beyond this level**.

Results of the current study are in line with those from the ACCORD-BP lowering trial. The two trials had slightly different populations. In INVEST all diabetics also had coronary heart disease, whereas in ACCORD only around 30% had heart disease. However, the results point that we **should not aim to lower systolic BP <130 mmHg in these patients, instead, more attention should be paid to other advices for these patients, like concentrating on better diet and lifestyle modification.**

Dr William Cushman, VA Medical Center, Memphis, TN, the ACCORD investigator further pointed that the JNC-7 recommends a systolic BP target of <130 mmHg for diabetic patients, but this been based on epidemiology rather than outcome studies however he feels that the **target of < 140 mmHg is reasonable**. He further advised **not to give extra drugs to get the BP down to levels below 120 to 130 mmHg. It often requires ≥ 3 antihypertensive drugs to get BP down to 120 or below.**

Patients who were uncontrolled in INVEST were on more antihypertensive drugs than those who were controlled. This may **indicate that the results of the trial may not be broadly applicable**. It **may be a heterogeneous effect like, patients with triple-vessel disease may not tolerate a BP of <120 mmHg, but those with single-vessel disease may be fine with BP as low as 110 mmHg.**

Cushman further added that **if patients are on ACE inhibitors or other antihypertensive agents for other reasons, such as for heart failure, and their BP is <130 mmHg, it is fine. The result of the study just raises a concern to push the patients down just for the BP reduction.**

The results thus concludes that **patients whose systolic BP was lowered to 130-140 mmHg had a better outcome than those with systolic BP >140 mmHg. While those whose systolic BP was reduced to <130 mmHg did not appear to receive any additional benefit and had a higher mortality rate.**

Adapted from http://www.theheart.org/article/1055859.do. As accessed on 18th march 2010.

Effect of Nateglinide and Valsartan on the incidence of diabetes and cardiovascular events

The NAVIGATOR Study Group

Presented at ACC 2010, Atlanta, USA

Daily therapy with an angiotensin receptor blocker (valsartan) had a significant but weak dampening effect on the risk of incident diabetes in a population with impaired glucose tolerance and either cardiovascular disease or cardiovascular risk factors, but no such effect was seen in the same group with a short-acting insulin secretagogue(nateglinide).

The NAVIGATOR study was a double-blind study that involved 9306 participants with impaired glucose tolerance and either cardiovascular disease or cardiovascular risk factors, who were randomized in a 2-by-2 factorial design, to receive nateglinide (up to 60 mg three times daily) or placebo, with valsartan (up to 160 mg daily) or placebo, in addition to participation in a lifestyle modification programme.

The following results were reported:

- Nateglinide, as compared to placebo, did not significantly reduce:
  - Cumulative incidence of diabetes (36% and 34%, respectively; hazard ratio, 1.07; P=0.05)
  - Core cardiovascular outcome* (7.9% and 8.3%, respectively; hazard ratio, 0.94; P=0.43)
  - Extended composite cardiovascular outcome** (14.2% and 15.2%, respectively; hazard ratio, 0.93; P=0.16).
- Valsartan, as compared to placebo, significantly reduced the cumulative incidence of diabetes (33.1% and 36.8% respectively; hazard ratio, 0.86; P<0.001).
- Valsartan, as compared to placebo, did not significantly reduce the incidence of:
  - Extended cardiovascular outcome** (14.5% vs. 14.8%; hazard ratio, 0.96; P=0.43),
  - Core cardiovascular outcome* (8.1% vs. 8.1%; hazard ratio, 0.99; 0.86 to 1.14; P=0.85).

** Core cardiovascular outcome: composite of death from cardiovascular sources, nonfatal MI, non fatal stroke or hospitalization for heart failure.*

*** Extended cardiovascular outcome: composite of death from cardiovascular sources, nonfatal MI, non fatal stroke or hospitalization for unstable angina, heart failure or arterial revascularization.*

The NAVIGATOR study could not definitively answer whether lowering postprandial glycemia reduces the cardiovascular disease or diabetes, since the mean glucose levels 2

hours after a glucose challenge in the annual oral glucose-tolerance tests were higher in the nateglinide group as compared to placebo group. The authors described this paradoxical finding as a rebound effect, since nateglinide was not administered on the mornings that the oral glucose-tolerance tests were done.

Also, no data is available to support the contention that nateglinide was regularly administered on the other days of year. Provision of a lifestyle intervention program for all participants might have also masked the beneficial effect of nateglinide in development of diabetes or cardiovascular disease.

In this study, the high rates of loss to follow-up (13%), use of off-study ACE-inhibitors or ARBs among patients assigned to placebo (24%) and non-adherence to valsartan (34% by study end) could explain the absence of effect of valsartan on cardiovascular disease. The investigators also acknowledge that significantly greater use of diuretics and beta blockers in placebo group ($p<0.001$) may have had something to do with apparently positive diabetes prevention effect from valsartan.

Among patients with impaired glucose tolerance and established cardiovascular disease or cardiovascular risk factors, assignment to valsartan for 5 years, along with lifestyle modification, led to a 14% relative reduction in incidence of diabetes but did not reduce the rate of cardiovascular events but no such effect was seen with nateglinide.

Presented at ACC 2010 and simultaneously published online in N Engl J Med.

Variability in BP is a stronger determinant of CV outcomes & supplements mean BP very well as a risk factor

Analysis of ASCOT-BPLA trial showed that **variability in blood pressure (BP) is a much stronger determinant of both stroke and coronary disease outcome than average BP**. The trial results were reported by the senior author, Dr Peter Sever, Imperial College, London, UK, at the ***American College of Cardiology 2010 Scientific Sessions*** and it is published in the online March 12, 2010 issue of *Lancet Neurology*.

The current study is based on 1.1 million measurements of BP and therefore it is hugely powerful. The trial showed that **within-visit BP variability and variability assessed by 24-hour ambulatory BP monitoring (ABPM) predicted cardiovascular outcomes. Variation in BP as measured between visit i.e. visit-to-visit variability over a period of five years was the strongest predictor of cardiovascular outcomes. While there was no effect of mean BP on coronary outcomes and a very small effect of average BP on stroke.**

It was observed that **calcium channel blockers (CCB) cause a reduction in BP variability, whereas beta blockers increase BP variability**. Adjusting for BP variability completely explained the differences in stroke and CHD outcomes between amlodipine-based and atenolol-based treatment in ASCOT.

Another systematic review and meta-analysis published in March 13, 2010 issue of Lancet showed that **CCBs and diuretics brought about the greatest reduction in visit-to-visit BP variability and were associated with the best stroke prevention, independently of mean systolic BP**. On the other hand **beta-blockers which dose-dependently increased the variability of BP were the least effective in stroke prevention**. **Interindividual variation in systolic BP was also increased by angiotensin converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs). The strongest effect was seen with CCBs.**

Interestingly, **older age, history of smoking, diabetes, and a prior history of vascular disease all seemed to be associated with higher BP variability, and all those things are indicators of stiff blood vessels.** The relation between long-term visit-to-visit variability in BP and arterial stiffness should be explored to investigate whether these two variables measure the same underlying vascular pathological changes

As per the ASCOT-BPLA analysis, **if an individual had a lower intrapressure and higher variability, he was worse off than if he had a higher pressure in the trial with low variability. Hence random variations in BP cannot be ignored. If the individual is not on CCBs he/she should be switched to receive one. This particularly applies to patients with hypertension who are aged over 55 yrs. In these patients, CCBs and diuretics are more effective, and they should be used, as mentioned in the British guidelines, first**. **The current data points that, CCBs are probably better than diuretics.**

Current hypertension guidelines recommend avoiding use of beta-blockers as first-line drugs if there is no other compelling indication. **The new data strengthens this recommendation and might prompt reconsideration by those who keep beta blockers as first-line treatment**.

However, more studies need to be done to better characterize the effects of different classes of antihypertensive drugs on long-term blood-pressure variability.

Many believe that clinic BP accounts for most of the risk and for the benefits of antihypertensive drugs. The current data does not question the importance of mean BP; rather, it makes a strong argument for also measuring BP variability, because it supplements BP very well as a risk factor.

Adapted from http://www.theheart.org/article/1058005.do. As accessed on 18th March 2010.

Triple Antiplatelet Therapy with Cilostazol Achieves Lower Post-treatment Platelet Reactivity Compared to Dual Antiplatelet Therapy in Patients Undergoing DES Implantation

Results from CILON-T trial, presented at ACC 2010, Atlanta, USA**.**

The ***CIL****ostazol-based triple anti-platelet therapy* ***ON*** *Ischemic Complication after drug-eluting sten****T*** *implantation* (CILON-T) trial, led by Dr. Hyo-Soo Kim (Seoul National University Hospital, Korea) was presented at the recently concluded **American College of Cardiology (ACC) 2010 Scientific Sessions.** It showed that triple antiplatelet therapy with cilostazol improved post-treatment platelet reactivity (PPR) as compared to dual antiplatelet therapy.

The CILON-T trial was conducted in 960 coronary disease patients. They were randomized to receive either standard dual antiplatelet therapy (aspirin and clopidogrel) or a triple antiplatelet therapy (addition of cilostazol to dual antiplatelet therapy) for 6 months after drug-eluting-stent (DES) placement.

Results of CILON-T showed that **cilostazol achieved lower PPR (Table 1) as measured by P2Y12-receptor reaction units (PRU).**

PRU units	Dual Antiplatelet therapy	Triple Antiplatelet therapy
At discharge	**232.1**	**206.6**
After 6 months	**257.7**	**210.7**

However, triple therapy did not necessarily reduce the occurrence of major adverse cardio-cerebro-vascular events in comparison to dual therapy.

Dr. Kim said he believed the reason that triple therapy did not show a reduction in clinical events was because of the platelet hypo responsiveness (PPR >265 units) even after triple therapy.

He showed data indicating correlation of platelet reactivity with clinical outcomes and that **patients with low PPR (PRU < 210 unit) did not develop any thrombotic event like cardiac death, myocardial infarction or ischemic stroke, irrespective of anti-platelet regimen.**

“PRU measurements may be useful in predicting risks after DES implantation and that if PRU readings are high, a third antiplatelet should be considered”

Dr. Robert Harrington, one of the moderators of the session was of a different view, he said, “Multiple studies have shown association between platelet activity and outcomes. What’s needed is to see if changing therapy based on functional platelet knowledge changes clinical outcomes.”

“Based on these results, we believe that PRU measurements may be useful in predicting risks after drug-eluting-stent implantation and that if PRU readings are high, a third antiplatelet drug should be considered," Dr. Kim concluded.

Tailored decisions on the adjunctive use of cilostazol according to PPR can be helpful to reduce adverse clinical outcomes in patients who undergo DES implantation

Adapted from Cardiosource News and www.theheart.org as accessed on 18th March, 2010.

Warfarin genotyping improves dose precision & significantly lowers hospitalization rates

A new study presented at the ***American College of Cardiology 2010 Scientific Sessions*** suggested that **genotyping of warfarin patients resulted in 30% reduction in all-cause hospitalizations and hospitalizations for bleeds/thromboemboli.** The study is in press at the *Journal of the American College of Cardiology* and is expected to be published shortly.

Medco-Mayo Warfarin Effectiveness Study (MM-WES) is the first study to evaluate the role of genetic testing in assisting physicians to gauge the best warfarin dose and monitor intensity during the early dose-adjustment phase of treatment. Researchers recruited 896 patients who were beginning warfarin therapy between 2007 and 2009. Blood sample or buccal swab were collected shortly after starting warfarin therapy, which was analyzed for the genetic expression of two genes, *CYP2C9* and *VKORC1*, polymorphisms in either of which can signal the need for higher or lower doses of warfarin. Results and interpretation of these tests were sent to the doctors treating the individual patients, who had the option to adjust warfarin dosing based on the patient's genotype test results.

The efficacy endpoint of reduction in hospitalization rates was compared with historical control group of similar patients who were new to warfarin treatment but began treatment during the preceding year. To allow for any other changes that might have occurred between the different times that the intervention and control groups were recruited, there were two additional external control groups; one beginning warfarin therapy during the same time period as the intervention group and one starting warfarin treatment during the prior year.

During the six-month follow-up period it was observed that **the genotyped cohort had 31% fewer all-cause hospitalizations** ($p<0.001$) **and 28% fewer hospitalizations for bleeding or thromboembolism** ($p=0.029$) **vs historical control group**. **There was no difference in outcomes between the two external control groups.** The hospitalization curves started to diverge at about 40 days after the start of warfarin treatment and that the whole process of genotyping and getting the results to the doctors/patients took between 11 and 60 days. **It was observed that the earlier the results were attained, the more outcomes improved.**

The study discussant, Dr Mandeep Mehra, University of Maryland School of Medicine, Baltimore, however was critical of the trial on several levels. He argued that the design of the trial was far from ideal and that the question of whether genotyping warfarin patients actually reduces hospitalizations has not been answered. He mentioned that the control group of the study leaves a lot to be desired and leaves a doubt as to whether the reduction in hospitalization seen in the genotyping group was actually due to the genotyping results or just because the doctor paid closer attention to these patients. He also suggested that the primary end point of the study was not the best measure to use, as it was not directly clinically relevant to warfarin. Besides it was also questioned whether genotyping, at a cost of $200 to 400 per test, was an expensive way of making physicians manage their warfarin patients more closely

In response to these comments, Dr. Epstein Medco Research Institute, Franklin Lakes, NJ, the presenter of study said, "**Regardless of whether it is the genotyping or it is just extra attention paid to these patients, if we can reduce hospitalizations in the numbers we showed, it would be more than cost-saving**." He further added, "**Warfarin has been in use for 50 years, and we have been taking about how to achieve better control for all that time, but we still have a 22% hospitalization rate within six months of starting treatment. So if we have a new technology that brings more precision to dosing, then that's got to be good**."

He further concluded, "Our study shows that **genetic testing is a tool clinicians can use to more accurately predict the best warfarin dose early on. Patients may get to a stable dose more quickly and therefore have a lower risk of negative outcomes.**"

Adapted from http://www.theheart.org/article/1058617.do. As accessed on 18th March 2010.

Addition of aliskiren to RAAS blockers has no additional benefit on heart structure or function in post MI patients

According to the results of The Aliskiren Study in Post-MI Patients to Reduce Remodeling (ASPIRE) presented at the ***American College of Cardiology 2010 Scientific Sessions***, **adding aliskiren to the best medical therapy, including an angiotensin converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB), had no additional beneficial effect on left ventricular remodeling after myocardial infarction (MI).**

For the current study researchers' recruited 820 patients two to six weeks post MI. All patients had evidence of left ventricular dysfunction; with at least 20% of the heart unable to contract because of scarring. The average ejection fraction in the study was 38%. Patients were randomly assigned to receive aliskiren, starting with 75 mg daily and increased to 300 mg daily within two weeks, or a matching placebo. All patients also received the best available medical therapy, including an ACE inhibitor or an ARB.

A total of 672 patients had interpretable baseline and follow-up echocardiograms at 36 weeks to evaluate the change in the heart's size and function. **Left ventricular end-systolic volume was reduced in size by an average of 4.4 mL in the aliskiren group and 3.5 mL in the placebo group but the difference was not significant**. There was **no difference between the two groups with respect to change in end-diastolic volume or in the ejection fraction**. During the follow-up, the **combined rates of cardiovascular death, hospitalization for heart failure, recurrent heart attack, stroke and resuscitated sudden death were also similar in the two groups**. However, in patients receiving aliskiren there was a higher rate of hyperkalemia, more hypotension, and more kidney dysfunction, when compared to the placebo group.

The current results are consistent with previous studies that showed no benefit, and potentially greater risk of adverse events, when combining two inhibitors of the renin-angiotensin system. Due to these results, aliskiren currently is not recommended in addition to other inhibitors of the renin-angiotensin system in this specific patient population. However, additional ongoing morbidity and mortality studies with aliskiren are well underway in patients with heart failure and diabetic kidney disease to determine the role for this agent in these populations.

Adapted from
http://www.acc.org/media/acc_scientific_session_2010/press/tuesday/ACC10_Solomon8am.pdf.
As accessed on 18th March 2010.

High-Dose Furosemide May be Better for Fluid Overload

DOSE Study

Diuretic Optimization Strategies Evaluation (DOSE) trial presented at the ***American College of Cardiology Sessions*** on March 17, 2010, showed that in patients with acute heart failure, there is no significant difference in overall symptom relief or change in kidney function whether a diuretic is delivered at high or low doses or by continuous or intermittent infusion, however, **high dose furosemide may be more effective than low-dose furosemide at improving several individual measures of fluid overload and symptom severity.**

The randomizations were "double-blind, double-dummy," in that 308 patients received both continuous and intermittent dosing every 12 hours. Of the 156 patients assigned to intermittent dosing, 74 and 82 received low-and high-dose furosemide, respectively; of the 152 assigned to continuous dosing, 77 received the low dose and 75 the high dose.

"Low dose" corresponded to the patient's oral dose, and "high dose" meant 2.5 times the oral dose.

Symptoms as gauged by patient global assessment at 72 hours, the primary efficacy end point, weren't significantly different between the intermittent and continuous dosing groups (p=0.47). ***The high-dose strategy trended toward greater symptom improvement (p=0.06) and improvement in multilple other domain viz. weight loss & net volume loss, proportion free from signs of congestion, reduction in NT-proBNP etc.***

Secondary outcomes at 72-hour assessment, low-dose vs. high-dose groups

Outcome	Low-dose, n=151	High dose, n=157	p
Dyspnea self-assessment, AUC	4478	4668	0.041
Congestion-free (%)	11	18	0.091
Change in weight (lbs)	-6.1	-8.7	0.011
Net volume loss (mL)	3575	4899	0.001
Change in NT-pro BNP level (pg/mL)	-1194	-1882	0.06
Cr increase >3 mg/dL (%)	14	23	0.041

The secondary end-point advantages in the high-dose group came at the cost of a greater risk of worsening renal function, defined as a >3 mg/dL rise in creatinine. However, the deterioration in the renal function appeared to be transient and the differences between the groups diminished over time and there was no significant elevated risk at 60 days.

Dr. G Michael Felker (Duke Clinical Research Institute, Durham, NC) said, “These finding suggest that high-dose furosemide may be preferable to low-dose. The price seems to be a transient and relatively small deterioration in kidney function.”

Co-principal investigator Dr Christopher O'Connor (Duke University Medical Center, Durham, NC) said that the "very proper statistical conclusion from this study is that there was no difference." But he also agreed that the promising secondary findings suggest some possible advantages for the high-dose approach that are actionable right away. “Given that there has been no adequately sized clinical trial of diuretic dose or route of administration to date- and because of the encouraging trends in the high-dose group-these results may have an immediate impact on the care of hospitalized heart failure patients,” said Christopher O’Conner.

In an interview, ACC program chair Dr James Mc Clurken (Temple University, Philadelphia, PA), said that, to be safe, he would exclude diabetics with acute heart failure from receiving high-dose diuretics. "I think the other group where there should be caution would be those who come in with acute heart failure for the first time, and they wind up being catheterized.”

"Cardiac catheterization with radiographic contrast would entail hydration to help protect the kidneys. So now you want to hydrate them, but also give diuretics. It can become a bit of a juggling act," he said. “High- rather than low-dose diuretics would only make that situation trickier.”

As a panelist assigned to discuss Felker's presentation, Dr Mandeep R Mehra (University of Maryland School of Medicine, Baltimore) said firmly that the appropriate conclusion from the trial, based on the primary end-point outcomes, "is that there is no difference in either low or high [dosing] or continuous vs. bolus infusion."
“That conclusion could be interpreted as suggesting that, it's perhaps better start low and go slow. This important study tells us that, in this narrow group of heart-failure patients who are on high background doses of diuretics at the time of inception, a strategy of a low initial dose of diuretics, given as a bolus, works just fine as long as you have the opportunity to reevaluate the dosing structure at the two-day time point," Mehra added.

As adapted from http://www.theheart.org/article/1058939;
http://www.acc.org/media/acc_scientific_session_2010/press/tuesday/ACC10.
As accessed on March 18, 2010.

Patients with psoriasis at increased risk of CV events

Presenting the data of a new study at the ***American College of Cardiology 2010 Scientific Sessions*** the lead investigator, Dr Ole Ahlehoff, Copenhagen University Hospital, Denmark, pointed that **patients with psoriasis, particularly those with severe psoriasis, have increased cardiovascular risk**. He further added that such patients should thus be prioritized for lifestyle changes and screening should be done for dyslipidemia and hypertension and they should be considered for earlier medical risk-factor intervention for heart disease.

Dr. Ahlehoff and his colleagues tracked the rates of psoriasis, atrial fibrillation, stroke, myocardial infarction (MI), percutaneous coronary intervention (PCI), and death in the entire adolescent and adult population of Denmark between 1997 and 2006. The data was evaluated for the incidence of cardiac events in 40,000 patients with mild to severe psoriasis and it was compared against those without psoriasis.

Patients with severe psoriasis were more likely to experience all of the adverse cardiac events while patients with mild psoriasis were more likely to experience atrial fibrillation, stroke, and PCI, even after adjustment for other risk factors. (Table 1)

Table 1: Relative risk of cardiac events in patients with psoriasis vs those without psoriasis

Event	Mild psoriasis	Moderate-to-severe psoriasis
AF	1.22	1.51
Stroke	1.19	1.45
MI	1.10	1.24
PCI	1.29	1.59
All-cause mortality	1.04	1.67

The **increased risk of atrial fibrillation and stroke was found to be age-dependent, with the risk in patients with moderate/severe psoriasis higher in those who were younger than 50 years old at the beginning of the study in 1997.**

These novel findings, including the higher risk for younger patients, indicate that psoriasis patients should not only be treated for the symptoms of that disorder but should also take steps to monitor and prevent cardiovascular problems.

Ahlehoff said that the mechanism behind this association is believed to be coincident inflammation. "Both psoriasis and atherosclerosis are inflammatory diseases, and they probably have a large overlap in markers and mediators," he said. He further added, "I believe that our **results call for increased awareness of psoriasis as a contributor to cardiovascular disease and for a discussion of future medical management**." He concluded that **since psoriasis is a common disease, affecting 2% to 3% of people worldwide, reducing cardiovascular risk in this large group of patients would have a considerable impact.**

Adapted from http://www.theheart.org/article/1055235.do. As accessed on 18th March 2010.

ABDOMINAL CT SCANS USEFUL IN TRACING PATIENTS AT HIGH RISK FOR CARDIOVASCULAR DISEASE

Abdominal aortic calcification (AAC) is a predictor of obstructive coronary disease and all-cause mortality, and the absence of AAC is a predictor of no obstructive coronary disease, according to research presented at the ***American College of Cardiology 2010 Scientific Sessions.***

Non-contrast abdominal scans of 367 patients who were asymptomatic for coronary disease but had a coronary angiography within one year of the CT were analyzed. The abdominal scans had been ordered for a variety of reasons, such as abdominal pain. Exclusion criteria were previous known CAD, acute ST-elevation MI at the time of angiography, or previous abdominal aortic surgery.

After a median follow-up of 27 months, 65 of the patients had died. Univariate analysis showed increasing abdominal aortic calcification was associated with increased mortality. Multivariate analysis showed that AAC adds incremental prognostic information over clinical variables, coronary anatomy, and left ventricular function.

A second analysis found that 134 of the patients had obstructive CAD. The patients with obstructed coronaries were older and more likely to have hypertension, diabetes, and high cholesterol and take aspirin and statin therapy than the group overall. AAC scores were significantly higher in subjects with obstructive CAD.

On the other end of the AAC range, only seven of the 62 patients with an AAC score of zero showed obstructive coronary disease on angiography. AAC's ability to predict obstructive coronary disease had a sensitivity of 96% and a specificity of 31%, with positive and negative predictive values of 58% and 89%, respectively.

Dr. Steven Simpson (Henry Ford Heart and Vascular Institute, Detroit, MI) said, "It's free information, so if somebody is looking at the scan or recording it will probably improve your judgment. Obviously, we're not implying we should order a non-contrast CT of the abdomen for the purposes of a CT coronary calcium score, but since it is free information, we might as well use it."

As adapted from http://www.theheart.org/article/1055507. As accessed on 18th March 2010.

Routine Invasive Strategy In Non-ST-Elevation ACS Superior To Selective Care

A new **meta-analysis of all relevant studies comparing a more aggressive routine invasive strategy with a more conservative selective invasive strategy in patients with non-ST-elevation acute coronary syndrome has clearly shown that the more aggressive treatment approach leads to better long-term outcomes.**

Dr Keith AA Fox (University of Edinburgh, Scotland), the lead researcher said, "The key result is that five years after the randomization, there is a net absolute difference of 3.2% and a 19% relative risk reduction in cardiovascular (CV) death and MI in the routine invasive group, and I don't know of any pharmacological therapy that has that five years from randomization," Fox told.

The analysis, known as the FIR trial collaboration, included the FRISC II, ICTUS, and RITA-3 trials, and Fox said it was performed because "there was ambiguity about the long-term findings of the individual studies. It is only with this combined analysis that we can get a conclusive result." Fox, who was also the lead investigator of RITA-3, explained that a routine invasive strategy is early angiography with subsequent PCI or CABG surgery, whereas a selective invasive strategy means angiography that is performed only if refractory angina or rest ischemia occurs despite optimal medical therapy.

The combined analysis of the three trials consisted of 2721 patients who were randomized to the routine invasive strategy and 2746 patients who received the more conservative selective invasive strategy. The most marked treatment effect was seen for nonfatal MI alone, which occurred in 10% of the routine invasive cohort, compared with 12.9% of the selective invasive cohort, but the researchers also saw a lower number of CV deaths in the routine cohort.

Primary outcomes of combined data set at five years

Outcomes	Selective invasive, % (n=2746)	Routine invasive, % (n=2721)	Hazard ratio	p
MI	12.9	10.0	0.77	0.001
CV death	8.1	6.8	0.83	0.068
CV death/MI	17.9	14.7	0.81	0.002
All-cause mortality	11.7	10.6	0.90	0.190
All-cause mortality/MI	20.9	18.1	0.85	0.008

In addition, Fox and colleagues found that patients in the highest-risk group benefited the most from undergoing the routine invasive strategy. Paradoxically, these patients are usually less likely to receive interventions, he said, explaining that there is evidence from registries that "low-risk people are more likely to be treated aggressively than high-risk people—because, as cardiologists, we are risk-averse. If we think somebody has got increased hazard, we are more likely to stand back. This says think again, there's more to gain than risk. Although the high-risk patients are more difficult and more challenging, they stand to profit most."

Treatment effect by integer risk category, CV death, or MI

Risk category	Low	Mid	High
Risk score	0-4	5-8	>9
Selective invasive, %	10.2	21.1	44.1
Routine invasive, %	8.2	17.3	33.0
Hazard ratio	0.80	0.81	0.68
Absolute risk difference	-2.0	-3.8	-11.1

The findings lend support to the idea of systematically risk-stratifying patients using a simple tool, such as the GRACE or TIMI risk score, to determine who should receive an intervention, he said. "If patients are high risk and without contraindication but they are not going for an invasive strategy, we need to ask why. My recommendation is that patients should be risk-stratified, because clearly there is a most potent benefit in the highest-risk group," Fox told.

Risk stratification is crucial, he said, because although the moderate- to low-risk patients also benefit, "if you just do what we are doing now, people are bypassing the high-risk group. People get stratified now on the basis of troponin, and although troponin is one of the risk markers, it's only one. If you perform more reliable risk stratification, you can identify high-risk people. The most robust algorithm that is recommended as number one by the European Society of Cardiology guidelines and one of the ones recommended by the ACC/AHA guideline is the GRACE score, because it's been validated in independent populations." But Fox explained that the GRACE score was not actually used in this meta-analysis because not all of the studies had collected all of the parameters—age, heart rate, systolic BP, creatinine, heart-failure Killip class, cardiac arrest on admission, ST-segment deviation, and elevated cardiac enzymes/markers; rather, a "shorthand" nomogram was employed by the physician at the bedside.

Adapted from http://www.theheart.org/article/1055735.do. As accessed on 18th May 2010.

No Difference in the Patency for Radial-Artery as compared to Saphenous-Vein Grafts at one year

A new randomized comparison of radial-artery vs saphenous-vein grafts has found no differences in vessel patency at one year. Dr Steve Goldman (Tucson VA Hospital, AZ) as per the results from the CSP-474 trial.

The study results may surprise some surgeons, who have tended to think that the radial artery might perform more like the left internal mammary artery, which has demonstrated superiority to the saphenous vein for CABG procedures. In fact, according to statistics mentioned by Goldman, out of more than 163,000 CABG procedures performed in 2008, 10,319 used radial-artery grafts.

The CSP-474 study, conducted at 11 medical centers between 2003 and 2008, was designed to demonstrate a difference in patency of roughly 10% between the two types of grafts, with the radial artery winning out. Instead, as Goldman showed, patency as assessed by angiography at one year was identical in patients treated by either graft. An analysis based on location of the graft showed no differences based on what type of graft was used. Of note, radial grafts were more likely than saphenous grafts to show early signs of disease, with 8% of radial grafts showing the "string sign" compared with just 1% of saphenous grafts.

A subanalysis looking at the low numbers of patients treated off-pump hinted that patency was no different in radial grafts placed on- or off-pump; by contrast, patency rates were lower in saphenous grafts placed off-pump. And in another intriguing finding, endoscopic harvesting—which has previously been linked to worse patency—was linked to worse patency in the saphenous grafts, but not in the radial grafts.

A cost analysis showed that, overall, costs were nearly identical between the two groups, at around $42 000 to $43 000. Surgical costs, however, were slightly higher in the radial group.
"In conclusion, we saw no differences in the radial-artery graft vs saphenous-vein grafts at one year," Goldman said. "We realize that cardiac surgery is a treatment used for a long-term outcome, so we need to be able to look at long-term patency."

Dr Joe Sabik (Cleveland Clinic, OH) pointed out that the modes of failure in different grafts follow different mechanisms for vein grafts vs arterial grafts and as such the grafts are used preferentially for different vessel occlusions. It may be that a bias toward using radial grafts in right heart lesions—where they tend to fare better—might have diluted the ability to detect a difference in outcomes.

Sabik also expressed concern that five and even 10 years might not be long enough follow up to see any differences in patency rates emerge. Dr William O'Neill (University of Miami, FL) made a plug on behalf of interventionalists, noting that, particularly outside the US, interventionalists are increasingly using the radial artery for percutaneous procedures. "I would plead with surgeons: use the left [radial artery], because we want the right for future access for these patients."

Adapted from http://www.theheart.org/article/1058537.do. As accessed on 18th May 2010.

Long-term Concern with Role of DES in STEMI Patients

Long-term results from two studies comparing drug-eluting stents (DES) with bare-metal stents in patients with ST-segment-elevation MI (STEMI) have raised some questions about the long-term risks of the drug-eluting devices.

In the PASSION trial, investigators observed no differences between the two stents in the composite end point of cardiac death, recurrent MI, or target lesion revascularization (TLR) at five years and no significant differences in the incidence of major adverse cardiac events (MACE), but they did observe a trend of very late stent thrombosis in DES-treated patients, and this small risk appeared to persist for several years after stent implantation. **In the DEDICATION trial, investigators report an increased risk of cardiac death at three years in patients treated with a DES compared with patients treated with a bare-metal stent.**

Responding to the increased risk of cardiac death in the DEDICATION trial, lead investigator Dr Peter Clemmensen (Copenhagen University Hospital, Denmark) said they observed more deaths caused by heart failure, but no increased risk of MI or reinfarction. He said that the DEDICATION trial is small, and the increased risk of cardiac death might be the play of chance. Commenting on the results of the studies, Dr David Holmes (Mayo Clinic, Rochester) said the information available from the most recent meta-analyses of STEMI patients suggests no difference in mortality between DES and bare-metal stents. The cardiac death data from DEDICATION will require more study "because the stent-thrombosis rate in that trial was about the same," said Holmes. "So whether this is other disease, whether it's a play of chance—the trial only had 600 patients so it's underpowered and really just hypothesis generating—is unknown."

The results help shed some light on the long-term safety and efficacy of DES in the setting of STEMI. The DEDICATION trial randomized 626 STEMI patients either to a bare-metal stent or a DES. The trial also included patients randomized to distal protection. Eight-month follow-up results hinted at an increased risk of cardiac mortality. During follow-up at three years, this risk was maintained, with a 6.1% cardiac death rate in those treated with the DES and a 1.9% cardiac death rate in the bare-metal-stent arm. Major adverse cardiovascular events (MACE), which included cardiac death, reinfarction, and TLR, were significantly lower in the DES arm, a result that was driven by a reduction in TLR. There was no interaction with distal protection.

DEDICATION: MACE at 3 years

End point	DES (%)	Bare-metal stent (%)	p
MACE	11.5	18.2	0.024
Death	10.5	6.4	0.084
Cardiac death	6.1	1.9	0.013
MI	4.2	5.4	0.58
Reinfarction	1.9	3.2	0.45
TLR	6.1	16.3	<0.001
TVR	8.9	19.8	<0.001
Stroke	3.2	2.6	0.64

Dr David Moliterno (University of Kentucky, Lexington), the moderator during the session, noted that the DEDICATION study is small and that investigators had access only to the patient's

vital status and as such were unable to ascertain numerous variables, such as whether or not the patient received an implantable cardioverter defibrillator (ICD) during follow-up, which might have affected cardiac death. Also, Dr Gregg Stone (Columbia University, New York), the lead investigator of the 3000-patient-plus HORIZONS-AMI study, said that their two-year data showed equivalent mortality—4.4% in the bare-metal-stent arm and 4.1% in the DES arm—and no difference in rates of stent thrombosis. Long-term follow-up from other studies, including the SESAMI trial, did not show an increased mortality risk with the DES.

Dr Maarten Vink (OLVG Hospital, the Netherlands) was the lead researcher of the PASSION study. Conducted in two centers, the researchers enrolled 619 patients with STEMI and followed them for up to five years. All patients were treated with 75 mg of clopidogrel daily for at least six months and 80 to 100 mg aspirin indefinitely. At five years, the composite end point of cardiac death, recurrent MI, and TLR was 22.0% in the bare-metal-stent arm and 18.3% in the DES arm, a nonsignificant difference. Unlike the DEDICATION study, there was no statistically significant difference in the rates of cardiac death—11.5% in the bare-metal-stent and 8.9% in the DES arms. Rates of TLR at five years were 10.5% and 7.3% in the bare-metal-stent and DES arms, respectively. There was a trend toward increased rates of definite stent thrombosis among those treated with the paclitaxel-eluting stent. At five years, stent thrombosis was double that of the bare-metal-stent-treated patients, although this increased risk was not statistically significant. The increased risk appeared between years one and five of follow-up, according to investigators.

PASSION: Stent thrombosis

Stent thrombosis	Drug-eluting stent, n (%)	Bare-metal stent, n (%)	p
	10 (3.6)	5 (1.7)	0.20
Definite or probable	11 (3.9)	10 (3.4)	0.85
Possible	20 (6.8)	19 (6.7)	0.93

During a press conference, Vink said the trend showed that using a bare-metal stent in the STEMI patients could halve the risk of stent thrombosis, and, given the absence of clinical benefit, he sees no reason why the older-generation DES should be used in this setting. **Clemmensen said that the two studies suggest it is equally safe and effective to use a bare-metal stent in the STEMI setting, but there are numerous factors that clinicians must take into account, such as the length of antiplatelet therapy and the patient's economic situation.**

Adapted from http://www.theheart.org/article/1058779.do. As accessed on 18th May 2010.

Taxus Element paclitaxel-eluting stent especially beneficial in small-diameter vessels

PERSEUS trial presented at the ***American College of Cardiology 2010 Scientific Sessions*** by Dr Dean Kereiakes**,** Christ Hospital, Cincinnati, OH Boston, showed that **a new Taxus Element paclitaxel-eluting stent performed as well as older stent platforms and was especially beneficial in small-diameter vessels.**

The Taxus Element is based on a new platinum-chromium alloy that gives it more radial strength and flexibility compared with older stent platforms. It's designed to evenly distribute the drug across the coronary lesion, besides the higher-density alloy is more visible under X-ray.

PERSEUS is a two-part trial. In the **PERSEUS Workhorse** study patients (n = 1262) with lesions $\leq$28 mm in length in coronary vessels between 2.75 mm and 4.0 mm in diameter were randomized in a 3:1 ratio to receive either the Taxus Element or Boston Scientific's first-generation Taxus Express paclitaxel-eluting stent. Taxus Element and Taxus Express had **statistically similar one-year target-lesion failure rates, 5.57% and 6.14%, respectively. The nine-month average percent diameter stenosis was 3.09% and 3.12% respectively; while the one-year stent-thrombosis rates were 0.3% and 0.4% respectively.**

In the **PERSEUS Small Vessel** study, 224 patients with lesions $\leq$20 mm in length in coronary vessels between 2.25 mm to 2.75 mm in diameter received the Taxus Element stent. When the PERSEUS trial had began in 2007 no drug-eluting stents were FDA-approved for these small vessels so the control was a matched historical Express bare-metal-stent control group from the TAXUS V trial for the primary end point of nine-month in-stent late loss. **The Taxus Element's nine-month late loss was 0.38, vs 0.80 for the Taxus Express**.

For the **secondary end point of target lesion failure, the Taxus Element's 7.3% easily beat the prespecified performance goal of 19.5% that was derived from both the bare-metal- and drug-eluting-stent results in the TAXUS IV and TAXUS V trials. The Element was still superior to the bare-metal stent after propensity adjustment for 28 variables to account for the nonrandomized design of the Small Vessel analysis. The one-year stent-thrombosis rate for the Taxus Element in the small vessels was 0.3%, compared with 0.6% in the historical bare-metal-stent control group. A** nonsignificant trend in favor of the Taxus Element in the measures of minimum lumen diameter and acute lumen gain, suggests that the **Taxus Element resists recoil even in tight vessels, despite its thinner struts.**

Adapted from http://www.theheart.org/article/1058345.do. As accessed on 18th March 2010.

MitraClip, not replacement for surgery but, an effective therapeutic option for patients with significant mitral regurgitation

Results from the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) II showed that the novel **MitraClip device, a percutaneous version of edge-to-edge mitral-valve repair, may lead to fewer early adverse events than traditional valve repair or replacement, with noninferior efficacy out to one year.** These results were presented at the ***American College of Cardiology 2010 Scientific Sessions/i2 Summit***.

The MitraClip device emulates the edge-to-edge repair technique in which the free edge of the anterior mitral-valve leaflet is joined to the posterior leaflet, creating a point of permanent coaptation and a double orifice. With the MitraClip, the device is threaded via the femoral vein to the right atrium and passed into the left atrium via transseptal puncture. The device is then passed through the mitral valve into the left ventricle. When the clip is deployed, it essentially clothes-pegs the free edge of the anterior mitral-valve leaflet to the posterior leaflet, creating a point of permanent coaptation.

EVEREST II is the first trial to directly compare outcomes with the device against the gold standard, surgery, in a randomized trial. In the trial, 279 patients with significant mitral regurgitation (3+ to 4+) were randomized 2:1 to the MitraClip procedure or to surgical repair or replacement at the surgeon's discretion. Patients who were symptomatic or, if asymptomatic those with documented LV dysfunction were included in the trial. The trial was conducted at 37 centers and it included patients with both functional mitral regurgitation (27%) and degenerative mitral regurgitation (73%). Primary end points of the study were major adverse events at 30 days (designed to show superiority) and clinical success rate, defined as freedom from a combination of death, mitral-valve surgery or reoperation for mitral-valve dysfunction, and an improvement of at least two grades of mitral regurgitation at 12 months (designed to demonstrate noninferiority of the clip device).

The **primary safety end point (combination of adverse events including death, major stroke, reoperation, urgent/emergent surgery, MI, renal failure, and blood transfusions, among others) in the per-protocol analysis significantly favored the percutaneous procedure at 30 days, with less than 10% of patients experiencing a major adverse event, as compared with 57% of the patients treated surgically**. Need for blood transfusions was the main driver of the safety end point, with a difference of 8.8% vs 53.2%. For the **primary efficacy end point in the per-protocol analysis, the overall clinical success rate was numerically higher in the surgery group, at 87.8% compared with 72.4%, but this difference, statistically, met the prespecified noninferiority hypothesis of 31%. Similar r**esults were observed in the intention-to-treat analysis. (table 1)

Table 1: EVEREST II: Safety and efficacy end points

End point	Clip (%)	Surgery (%)
Safety, per protocol	9.6	57.0
Efficacy, per protocol	72.4	87.8
Safety, intention to treat	15	47.9
Efficacy, intention to treat	66.9	74.2

All between-group differences statistically significant

Individually, the pattern of benefit was similar for the different components of the efficacy end point. While reductions in mitral-regurgitation grade were greater in the surgery group, improvements in left ventricular volume, left ventricular dimension, and NYHA class were similar between the two groups.

For the quality-of-life end point specifically, **12-month improvements were similar between the two groups; the only conspicuous difference between the MitraClip and surgery groups was for the physical quality-of-life scores, which improved significantly within 30 days for the percutaneously treated patients, but, not surprisingly, declined significantly in the surgery group** within this early period, "consistent with the recovery from open-heart surgery," ultimately rebounding to catch up to the clip group at one year. The study investigators saw no differences in outcomes between the degenerative mitral-regurgitation patients vs the functional mitral-regurgitation patients.

Responding to the point that the improvement in mitral-regurgitation grade was unsatisfactory, Dr. Feldman, Evanston Hospital, IL, lead investigator, noted that there were several patients in the study who had 3+ mitral regurgitation after initial therapy and were deemed failures but in fact they did not go on to have surgery and that may be because clinically they were doing really well.

The trial thus concludes that the **MitraClip procedure is an important therapeutic option for patients with significant mitral regurgitation**, given the demonstrated safety, effectiveness, and clinical benefit. **The clip would not supplant surgery but was an additional option for patients deemed suitable for this percutaneous approach**. **The cases that are most likely to be successful are the ones where the jet of the mitral regurgitation is central and relatively discrete and when there is a flail leaflet, where the gap between the two leaflets is not too great.**

Adapted from http://www.theheart.org/article/1054941.do. As accessed on 18th March 2010.