



Issue 13, December'18

State of the HEART

A monthly cardiology news



STATE OF THE HEART



Dear Reader,

We are grateful to present you the 13th issue of “State of the Heart”, which explores the clinical evidence supporting the new understandings and happenings in the field of cardiology.

In India, the epidemiological transition from predominantly infectious disease conditions to non-communicable diseases has occurred over a rather succinct period of time. Despite wide heterogeneity in the prevalence of cardiovascular risk factors across different regions, CVD has emerged as the leading cause of death in all parts of India, including poorer states and rural areas. In this research driven time, management of these disorders is also constantly evolving towards the betterment whether it's pharmacological or non-pharmacological.

Being a healthcare custodian of the society, clinicians are constantly thriving to be abreast with the novel understandings of disease and its management. In this context, this is our initiative to provide you a compiled and to the point information.

Present booklet comprises of recent and latest deeds in the field of cardiovascular diseases like dyslipidemia, coronary artery disease, heart failure and its management. We hope that it will facilitate increased cooperation and innovation, and enthuse commitment to prevent these life-threatening and disabling disorders and providing the best possible care for people who suffer from these conditions.

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1. 2018 ESC GUIDELINES FOR THE MANAGEMENT OF CARDIOVASCULAR DISEASES DURING PREGNANCY

2018 ESC Guidelines for the Management of Cardiovascular Diseases During Pregnancy

Pre-pregnancy risk assessment and counseling is indicated in all women with known or suspected congenital or acquired cardiovascular and aortic disease or pulmonary hypertension.

Echocardiography is recommended in any pregnant patient with unexplained or new cardiovascular signs or symptoms.

Before pharmacological treatment in pregnancy is started, it is recommended to **check drugs and safety data**.

Low molecular weight heparin (LMWH) is recommended for the prevention and treatment of venous thromboembolism (VTE) in pregnant patients and therapeutic doses of LMWH should be based on body weight.

Immediate electrical cardioversion is recommended for any tachycardia with haemodynamic instability and for pre-excited atrial fibrillation (AF), for sustained both unstable and stable ventricular tachycardia (VT).

- Hypertension with subclinical organ damage or symptoms - initiate drug treatment at SBP > 140 mmHg or DBP > 90 mmHg.
- In other cases- initiate drug treatment at SBP ≥ 150 mmHg or DBP ≥ 95 mmHg.
- SBP ≥ 170 mmHg or DBP ≥ 110 mmHg in a pregnant woman is an emergency, and hospitalization is recommended.

Pregnancy is not recommended in patients with pulmonary arterial hypertension, in patients with a systemic right ventricle and moderate or severely decreased ventricular function, in patients with dilated aorta, in patients with severe mitral stenosis or with severely decreased left ventricular ejection fraction (LVEF).



Eur Heart J. 2018;39(35):3269

- **Vaginal delivery is recommended as first choice in most patients;** except for patients presenting in labour on oral anticoagulants, with aggressive aortic pathology, in acute intractable heart failure (HF), or with severe pulmonary hypertension.
- Pregnancy is not recommended in patients with pulmonary arterial hypertension, in patients with a systemic right ventricle and moderate or severely decreased ventricular function, after Fontan operation and any associated complication, in patients with vascular Ehlers–Danlos syndrome, in patients with dilated aorta, in patients with severe mitral stenosis or with severely decreased left ventricular ejection fraction (LVEF).
- **Women with mechanical valves are at high risk of complications** (valve thrombosis, bleeding, obstetric, and foetal complications) and should be counseled before pregnancy and managed during their pregnancies in specialized centers by a Pregnancy Heart Team.
- It is recommended **to treat women with HF during pregnancy according to current guidelines for non-pregnant patients, respecting contraindications for some drugs in pregnancy.**
- In all women with gestational hypertension or with hypertension and subclinical organ damage or symptoms, initiation of drug treatment is recommended at systolic blood pressure (SBP) > 140 mmHg or diastolic blood pressure (DBP) > 90 mmHg. In other cases, initiation of drug treatment is recommended at SBP ≥ 150 mmHg or DBP ≥ 95 mmHg. SBP ≥ 170 mmHg or DBP ≥ 110 mmHg in a pregnant woman is an emergency, and hospitalization is recommended.
- Low molecular weight heparin (LMWH) is recommended for the prevention and treatment of venous thrombo-embolism (VTE) in pregnant patients and therapeutic doses of LMWH should be based on body weight. Before pharmacological treatment in pregnancy is started, it is recommended to check drugs and safety data.

2. ATRIAL THROMBUS EXCLUSION SCORE

Atrial Thrombus Exclusion Score

An ATE score of zero was strongly associated with the absence of atrial thrombus. This new score could be useful to rule out a diagnosis of atrial thrombus before catheter ablation of AF.

JACC Clin Electrophysiol 2018;Oct 31



ATE score		Study population (n=2,494)		
		ATE score	Patients	Thrombus
		n	n	%
	History of stroke	1 point	0	911 0 0
	Congestive heart failure	1 point	1	988 23 2.3
	Hypertension	1 point	2	481 14 2.9
	D-dimer level > 270 ng/ml	1 point	3	111 10 9.0
			4	3 1 33.3

This score may be useful in reducing the need to perform a transesophageal echocardiogram on every patient prior to catheter ablation or cardioversion of atrial fibrillation.

Study Questions:

Can the D-dimer blood level and other clinical items predict the absence of atrial thrombus?

Methods:

The authors studied 2,494 patients admitted for catheter ablation of atrial fibrillation in a multicenter study. A transesophageal echocardiogram was performed routinely before the ablation procedure. D-dimer levels, CHADS₂ score, left ventricular ejection fraction, preoperative anticoagulation, and medical history details were collected for all patients. The authors used logistic regression to develop a risk prediction score for the absence of atrial thrombus.

Results:

The incidence of atrial thrombus was 1.92%. CHADS₂ and D-dimer levels were associated with the presence of atrial thrombus. A CHADS₂ = 0 had a sensitivity of 90% and a specificity of 52% for excluding atrial thrombus. Patients with an "Atrial Thrombus Exclusion" (ATE) score of zero (no history of stroke, congestive heart failure, hypertension, or an elevated D-dimer level) had no atrial thrombi identified (sensitivity 100%, specificity 37%).

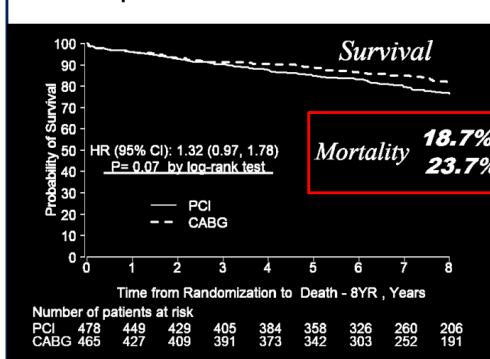
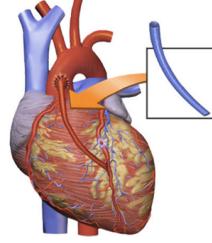
Conclusions:

An ATE score of zero was strongly associated with the absence of atrial thrombus among patients with atrial fibrillation.

“While the D-dimer has long been used to help rule out venous thromboembolism, this study uses the D-dimer along with some clinical characteristics of the CHADS₂ score to rule out atrial thrombus in patients with atrial fibrillation. If replicated and validated, this score may be useful in reducing the need to perform a transesophageal echocardiogram on every patient prior to catheter ablation or cardioversion of atrial fibrillation.”

3. CABG WAS SUPERIOR TO PCI-DES IN REDUCING ALL-CAUSE MORTALITY IN DM PATIENTS WITH CAD

CABG Was Superior To PCI-DES In Reducing All-Cause Mortality In DM Patients With CAD

Methods	Results	Conclusion																														
<ul style="list-style-type: none"> Objective: To evaluate the long-term survival of DM patients with MVD undergoing coronary revascularization in the FREEDOM trial. Median follow-up: 7.5 years <p></p>	<ul style="list-style-type: none"> 943 patients from 25 center  <table border="1"> <caption>Estimated Survival Data from Kaplan-Meier Curve</caption> <thead> <tr> <th>Time (Years)</th> <th>PCI-DES Survival (%)</th> <th>CABG Survival (%)</th> </tr> </thead> <tbody> <tr><td>0</td><td>100</td><td>100</td></tr> <tr><td>1</td><td>98</td><td>99</td></tr> <tr><td>2</td><td>95</td><td>97</td></tr> <tr><td>3</td><td>90</td><td>94</td></tr> <tr><td>4</td><td>85</td><td>91</td></tr> <tr><td>5</td><td>80</td><td>88</td></tr> <tr><td>6</td><td>75</td><td>85</td></tr> <tr><td>7</td><td>70</td><td>82</td></tr> <tr><td>8</td><td>65</td><td>78</td></tr> </tbody> </table> <p>Number of patients at risk PCI: 478, 449, 429, 405, 384, 358, 326, 260, 206 CABG: 465, 427, 409, 391, 373, 342, 303, 252, 191</p> <p>JACC. Nov 2018; 25705; DOI:10.1016/j.jacc.2018.11.001</p>	Time (Years)	PCI-DES Survival (%)	CABG Survival (%)	0	100	100	1	98	99	2	95	97	3	90	94	4	85	91	5	80	88	6	75	85	7	70	82	8	65	78	 <p>CABG was superior to PCI-DES in reducing all-cause mortality in the long-term.</p>
Time (Years)	PCI-DES Survival (%)	CABG Survival (%)																														
0	100	100																														
1	98	99																														
2	95	97																														
3	90	94																														
4	85	91																														
5	80	88																														
6	75	85																														
7	70	82																														
8	65	78																														

Background The FREEDOM trial demonstrated that for patients with diabetes mellitus (DM) and multivessel coronary disease (MVD), coronary artery bypass grafting (CABG) is superior to percutaneous coronary intervention with drug-eluting stents (PCI-DES) in reducing the rate of major adverse cardiovascular and cerebrovascular events after a median follow-up of 3.8 years. It is not known, however, whether CABG confers a survival benefit after an extended follow-up period.

Objective To evaluate the long-term survival of DM patients with MVD undergoing coronary revascularization in the FREEDOM trial.

Methods The FREEDOM trial randomized 1,900 patients with DM and MVD to undergo either PCI with sirolimus or paclitaxel eluting stents or CABG on a background of optimal medical therapy. After completion of the trial, enrolling centers and patients were invited to participate in the **FREEDOM Follow-On** study. Survival was evaluated using Kaplan-Meier analysis, and Cox proportional hazards models were used for subgroup and multivariate analyses.

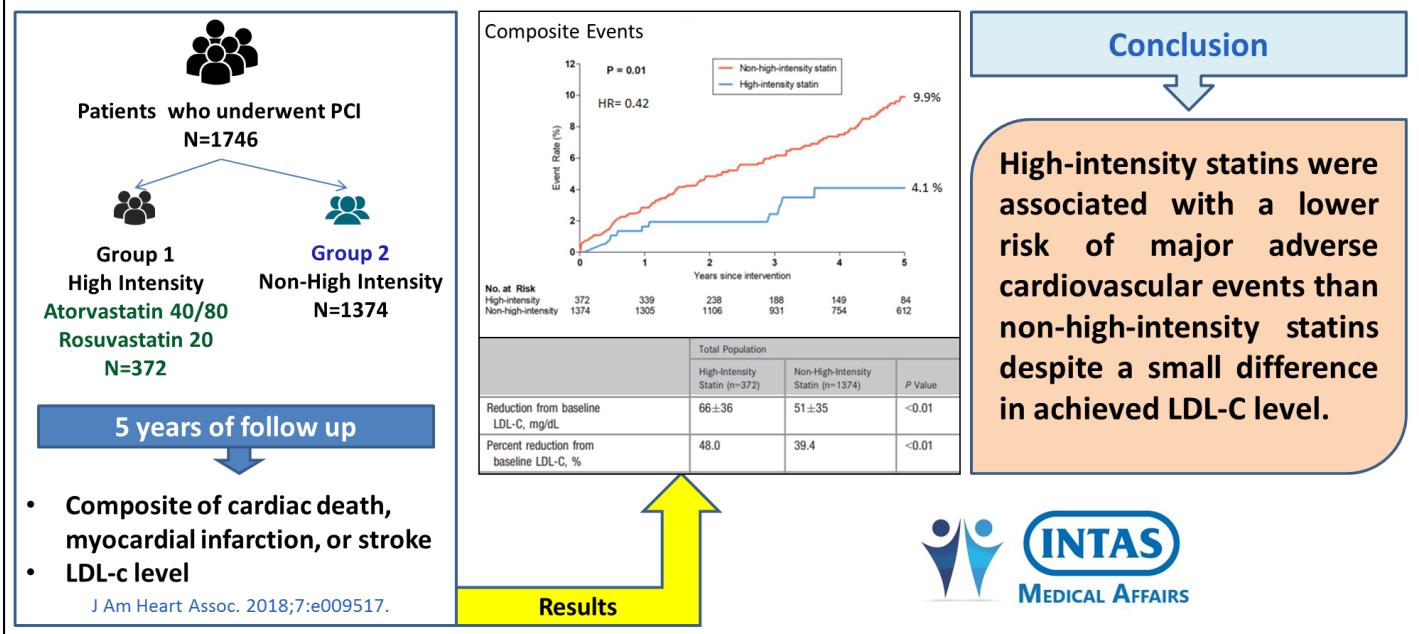
Results Twenty-five centers (out of 140 original centers) agreed to participate in the FREEDOM Follow-On study and contributed a total of 943 patients (49.6% of the original cohort) with a median follow-up of 7.5 years (range, 0 to 13.2). Of the 1,900 patients, there were 314 deaths during the entire follow-up period (204 deaths in the original trial and 110 deaths in the FREEDOM Follow-On). The all-cause mortality rate was significantly higher in the PCI-DES group than in the CABG group (24.3% [159 deaths] vs. 18.3% [112 deaths]; hazard ratio[HR], 1.36; 95% confidence interval[CI], 1.07 to 1.74; p=0.01). Of the 943 patients with extended follow-up, all-cause mortality rate was 23.7% (99 deaths) in the PCI-DES group and 18.7% (72 deaths) in the CABG group (HR, 1.32; 95%CI, 0.97 to 1.78; p= 0.076).

"IN PATIENTS WITH DM AND MVD, CORONARY REVASCULARIZATION WITH CABG LEADS TO LOWER ALL-CAUSE MORTALITY THAN WITH PCI-DES IN LONG-TERM FOLLOW-UP."

4. STATIN THERAPY-HIGHER IS BETTER: ANOTHER EVIDENCE

Statin Therapy-Higher is Better

Another Evidence



Background

Whether use of high intensity statins is more important than achieving low density lipoprotein cholesterol (LDL-C) target remains controversial in patients with coronary artery disease. Study aimed to investigate the association between statin intensity and long term clinical outcomes in patients achieving treatment target for LDL-C after percutaneous coronary intervention.

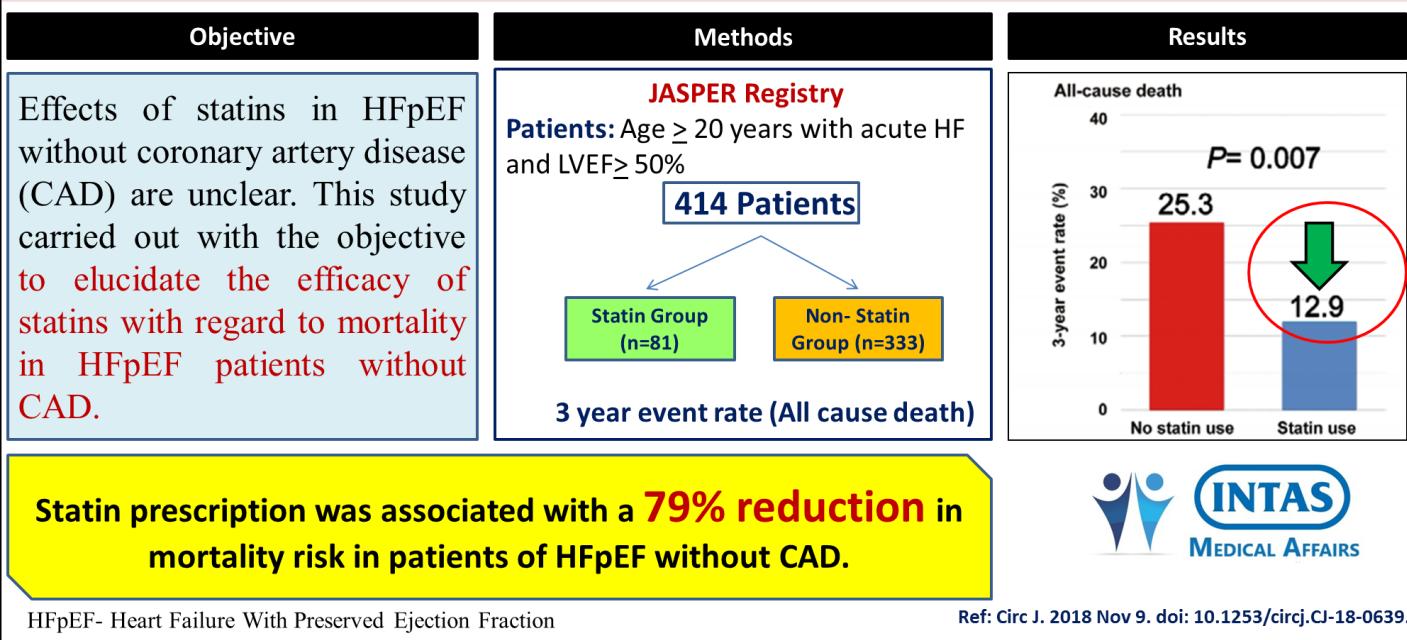
Methods and Results

Between February 2003 and December 2014, 1746 patients who underwent percutaneous coronary intervention and achieved treatment target for LDL-C (<70 mg/dL or >50% reduction from baseline level) were studied. Patients were classified into 2 groups according to an intensity of statin prescribed after index percutaneous coronary intervention: high intensity statin group (atorvastatin 40 or 80 mg, and rosuvastatin 20 mg, 372 patients) and non high intensity statin group (the other statin treatment, 1374 patients). The primary outcome was a composite of cardiac death, myocardial infarction, or stroke. Difference in time averaged LDL-C during follow up was significant, but small, between the high intensity statin group and non high intensity statin group (59±13 versus 61±12 mg/dL; P=0.04). At 5 years, patients receiving high intensity statins had a significantly lower incidence of the primary outcome than those treated with non high intensity statins (4.1% versus 9.9%; hazard ratio, 0.42; P<0.01). Results were consistent after propensity score matching (4.2% versus 11.2%; hazard ratio, 0.36; P<0.01) and across various subgroups.

“Among patients achieving treatment target for LDL-C after percutaneous coronary intervention, high-intensity statins were associated with a lower risk of major adverse cardiovascular events than non-high-intensity statins despite a small difference in achieved LDL-C level.”

5. STATIN USE HAS A BENEFICIAL EFFECT ON MORTALITY IN HFpEF WITHOUT CAD

Statin Use Has A Beneficial Effect On Mortality In HFpEF Without CAD



HFpEF- Heart Failure With Preserved Ejection Fraction

Ref: Circ J. 2018 Nov 9. doi: 10.1253/circj.CJ-18-0639.



Background: Statins might be associated with improved survival in patients with heart failure with preserved ejection fraction (HFpEF). The effect of statins in HFpEF without coronary artery disease (CAD), however, remains unclear.

Methods and Results: From the JASPER registry, a multicenter, observational, prospective cohort with Japanese patients aged \geq 20 years requiring hospitalization with acute HF and LVEF \geq 50%, 414 patients without CAD were selected for outcome analysis.

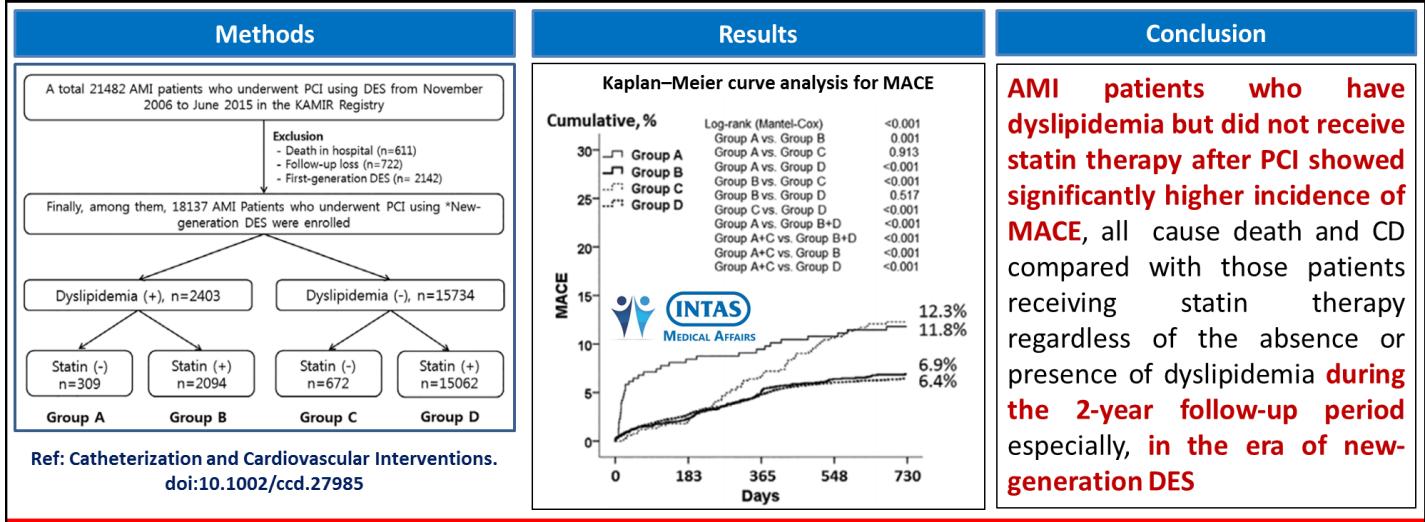
Based on prescription of statins at admission, Patients were divided into the statin group (n=81) or no statin group (n=333). Patients were followed for 25 months. The association between statin use and primary (all-cause mortality) and secondary (non-cardiac death, cardiac death, or rehospitalization for HF) endpoints was assessed in the entire cohort and in a propensity score-matched cohort.

In the propensity score-matched cohort, 3-year mortality was lower in the statin group (HR, 0.21; 95% CI: 0.06–0.72; P=0.014). The statin group had a significantly lower incidence of non-cardiac death (P=0.028) and rehospitalization for HF (P<0.001) but not cardiac death (P=0.593). The beneficial effect of statins on mortality did not have any significant interaction with cholesterol level or HF severity.

"STATIN USE HAS A BENEFICIAL EFFECT ON MORTALITY IN HFpEF WITHOUT CAD. THE PRESENT FINDINGS SHOULD BE TESTED IN AN ADEQUATELY POWERED RANDOMIZED CLINICAL TRIAL."

6. PERSISTENT BENEFIT OF STATIN THERAPY IN THE ERA OF NEW GENERATION DRUG ELUTING STENT

Persistent Benefit Of Statin Therapy In The Era Of New Generation Drug Eluting Stent



Background: Limited studies focused on long-term outcomes of statin therapy in patients with acute myocardial infarction (AMI) with or without dyslipidemia after percutaneous coronary intervention (PCI) in the era of new-generation drug-eluting stents (DES).

Objective: To investigate 2-year clinical outcomes of statin therapy in patients with acute myocardial infarction (AMI) with or without dyslipidemia after percutaneous coronary intervention (PCI).

Methods: A total of 18,137 eligible AMI patients (from the Korea AMI Registry [KAMIR]) were finally enrolled and divided into four groups according to the presence or absence of dyslipidemia and statin therapy (dyslipidemia+/statin- [group A, 309 patients], dyslipidemia+/statin+ [group B, 2094 patients], dyslipidemia-/statin- [group C, 672 patients], dyslipidemia-/statin+ [group D, 15062 patients]). The primary outcome was major adverse cardiac event (MACE) defined as all-cause death, myocardial infarction (MI) and revascularization.

Results: During the 2-year follow-up period, the cumulative incidence of MACE in the group A was higher than the group B (adjusted hazard ratio [HR], 2.207; 95% confidence interval (CI), 1.098–3.743; p = .024) and the group D (adjusted HR, 2.110; 95% CI, 1.240–3.593, p = .006). This significantly increased incidence of MACE caused by the higher cumulative incidences of all-cause death and cardiac death (CD) in the group A compared with groups B and D. However, the cumulative incidences of MI and revascularization were not significantly different among these four groups.

"STATIN THERAPY DEMONSTRATED SIGNIFICANTLY REDUCED INCIDENCES OF MACE, ALL-CAUSE DEATH AND CD COMPARED WITH NON-USERS AFTER PCI IN AMI PATIENTS WITH OR WITHOUT DYSLIPIDEMIA DURING 2-YEAR FOLLOW-UP PERIOD IN THE ERA OF NEW-GENERATION DES."

7. EZETIMIBE MAY PREVENT CEREBRAL AND CARDIOVASCULAR EVENTS IN ELDERLY PATIENTS (> 75 YEARS)

Ezetimibe May Prevent Cerebral And Cardiovascular Events In Elderly Patients (≥ 75 Years)

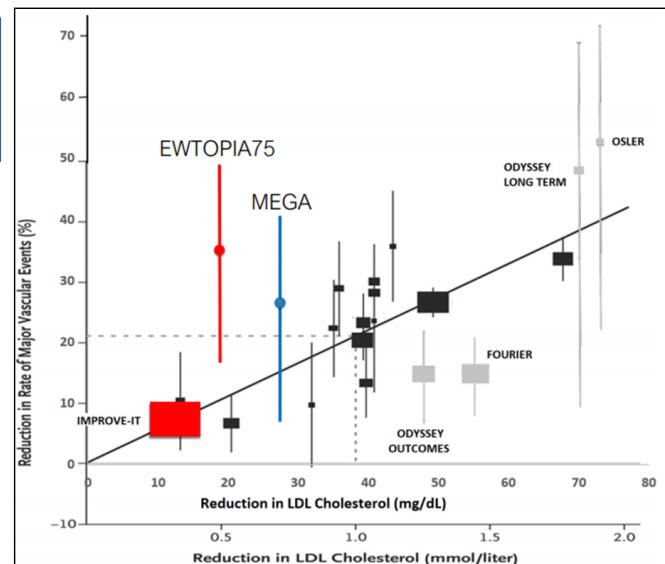
3796 patients

Age : ≥ 75 years, LDL-C > 140 mg/dL with one or more CV risk factors

Ezetimibe 10 mg/Day+
Diet counseling

Diet counseling

13 % more reduction in LDL-C
34% relative risk reduction in MACE



AHA Scientific Session 2018. Late Breaking Trial. LBS 01. EWTOPIA 75

Introduction:

The efficacy of lipid-lowering therapy with statins for high-risk patients is well established. However, there is no evidence about its clinical benefits in Japanese elderly (≥ 75 years old) patients with elevated low-density lipoprotein cholesterol (LDL-C) levels who have no history of coronary artery disease.

Methods:

Between 2009 and 2016, a prospective, multicenter, open-label, blinded end point, randomized controlled trial was conducted in these patients whose LDL-C level was ≥ 140 mg/dL and who had one or more cardiovascular risk factors (e.g., diabetes, hypertension, smoking, low high-density lipoprotein cholesterol levels, and high triglyceride levels). The primary endpoint was a composite of sudden cardiac death, fatal myocardial infarction, nonfatal myocardial infarction, coronary revascularization, fatal stroke, and/or nonfatal stroke.

Results:

A total of 3,796 patients were enrolled, and 1898 patients each were randomly assigned to the ezetimibe group (ezetimibe 10 mg/day plus diet counseling) or the control group (diet counseling alone). Baseline demographic characteristics were as follows: mean age, 80.7 ± 4.8 years; body mass index, 23.4 ± 3.6 ; male, 25.7%; hypertension, 78.0%; and diabetes, 22.8%. Despite the high incidence (78.0%) of concomitant hypertension, systolic and diastolic blood pressures were well controlled (136.1 ± 15.9 mmHg and 74.1 ± 10.5 mmHg, respectively). Mean LDL-C, high-density lipoprotein cholesterol, and triglycerides at baseline were 161.6 ± 19.7 mg/dL, 56.8 ± 14.1 mg/dL, and 131.3 ± 55.3 mg/dL, respectively. Mean LDL-C levels at 1 year after randomization were 126.1 ± 26.2 mg/dL and 144.0 ± 29.2 mg/dL in the ezetimibe and control groups, respectively, and the difference was statistically significant.

"ADDITION OF EZETIMIBE LEADS TO 13 % MORE REDUCTION IN LDL-C AND 34% RELATIVE RISK REDUCTION IN MACE"

8. EZETIMIBE-ATORVASTATIN COMBINATION: BETTER CHOICE THAN ATORVASTATIN ALONE

Ezetimibe-Atorvastatin Combination: Better Choice Than Atorvastatin Alone

Meta-analysis of 11 studies (n=5206)

Compared 4 Common Dose Groups

1. Ezetimibe(10 mg)+ Atorvastatin (10 mg) Vs Atorvastatin (**10 mg**)
2. Ezetimibe(10 mg)+ Atorvastatin (10 mg) Vs Atorvastatin (**20 mg**)
3. Ezetimibe(10 mg)+ Atorvastatin (20 mg) Vs Atorvastatin (**40 mg**)
4. Ezetimibe(10 mg)+ Atorvastatin (40 mg) Vs Atorvastatin (**80 mg**)

Lipids in Health and Disease (2018) 17:239



Results

- Combination therapy [**Ezetimibe + Atorvastatin**] led to significant reduction in **LDL-C** (mean difference, -15.38), **Total Cholesterol** (mean difference, -9.51) and **Triglyceride** (mean difference, -6.42) ($P<0.0001$ for all).
- Combination therapy [**Ezetimibe + Atorvastatin**] was also better in raising the **HDL-C** (mean difference, 0.95, $P=0.002$)

Conclusion

Combination of lipid-lowering agent, **EZETIMIBE with ATORVASTATIN** provides **Better Outcomes** than atorvastatin monotherapy in **lowering LDL-C, TC and TG level and increasing HDL-C.**

Background:

Although there were many studies reporting the combination therapy of Ezetimibe and Atorvastatin's efficacy and Atorvastatin monotherapy's, the conclusions were controversial. Therefore, a systematic review and meta analysis of combination therapy and monotherapy were conducted.

Methods:

PubMed, Cochrane Library and Embase were searched for studies of the combination therapy of Ezetimibe and Atorvastatin and Atorvastatin monotherapy published up to October 20, 2017. Two investigators assessed the articles for eligibility and evaluated quality. The changed values and the efficacy of low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), Total Cholesterol (TC) and Triglyceride (TG) indicators were the outcomes. Four doses of the comparisons were included: the combination therapy of Ezetimibe (10 mg) and Atorvastatin (10 mg) (E10 + A10) versus Atorvastatin (20 mg) monotherapy (A20); E10 + A10 vs. A10; E10 + A20 vs. A40; E10 + A40 vs. A80.

Results:

Seventeen studies (11 publications) were included in the meta analysis. Compared with Atorvastatin monotherapy, the overall efficacy of combination therapy of Ezetimibe and Atorvastatin on lowering LDL-C ($MD = - 15.38$; $I^2 = 26.2\%$, $n = 17$), TC ($MD = - 9.51$, $I^2 = 33.7\%$, $n = 17$) and TG ($MD = - 6.42$, $I^2 = 0\%$, $n = 15$) and raising HDL-C ($MD = 0.95$, $I^2 = 0\%$, $n = 17$) was significant. The efficacy of the comparison on HDL-C was largely significant for the different doses.

*"THE OVERALL
EFFICACY AND
SUBGROUP'S EFFICACY
OF COMBINATION
THERAPY OF EZETIMIBE
AND ATORVASTATIN ON
LOWERING LDL-C, TC
AND TG WAS
SIGNIFICANTLY BETTER
THAN ATORVASTATIN
MONOTHERAPY'S."*

9. ADDITION OF EZETIMIBE TO STATIN THERAPY MAY REDUCES THE RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

Addition Of Ezetimibe To Statin Therapy May Reduces The Risk Of Major Adverse Cardiovascular Events (MACE)

Objective	Results	Conclusion
<p>To assess the efficacy and safety of ezetimibe for the prevention of CVD and all-cause mortality.</p> <p>Methods</p> <p>Database accessed: CENTRAL, MEDLINE, Embase and Web of Science on 27 June 2018, and two clinical trial registry platforms on 11 July 2018 without applying language restriction.</p> <p>Selection criteria: Randomized controlled trials (RCTs) that compared ezetimibe versus placebo or ezetimibe plus other lipid-modifying drugs versus other lipid-modifying drugs alone in adults, with or without CVD, and which had a follow-up of at least 12 months.</p>	<p>26 RCTs randomizing 23,499 participants.</p> <p>Ezetimibe with statins further reduces the risk of major adverse cardiovascular events.</p>  <p>Cochrane Library Cochrane Database of Systematic Reviews</p>  	<p>Moderate to high-quality evidence suggests that ezetimibe has beneficial effects on the risk of CVD endpoints.</p> <p><i>Cochrane Database Syst Rev. 2018 Nov 19; 11:CD012502.</i></p> 

Objectives:

To assess the efficacy and safety of ezetimibe for the prevention of CVD and all-cause mortality.

Methods:

CENTRAL, MEDLINE, Embase and Web of Science searched on 27 June 2018, and two clinical trial registry platforms searched on 11 July 2018. Researcher also checked reference lists from primary studies and review articles for additional studies. No language restrictions were applied. Randomised controlled trials (RCTs) that compared ezetimibe versus placebo or ezetimibe plus other lipid-modifying drugs versus other lipid-modifying drugs alone in adults, with or without CVD, and which had a follow-up of at least 12 months were included for analysis.

Results:

26 RCTs randomising 23,499 participants were analyzed. Ezetimibe with statins probably reduces the risk of MACE (risk ratio (RR) 0.94; a decrease from 284/1000 to 267/1000). Trials reporting all-cause mortality used ezetimibe with statin or fenofibrate and found they have little or no effect on this outcome (RR 0.98). Adding ezetimibe to statins probably reduces the risk of non-fatal myocardial infarction (MI) (RR 0.88, a decrease from 105/1000 to 92/1000) and non-fatal stroke (RR 0.83, a decrease 32/1000 to 27/1000). The need for coronary revascularisation might be reduced by adding ezetimibe to statin (RR 0.94, a decrease from 196/1000 to 184/1000). In terms of safety, adding ezetimibe to statins may make little or no difference in the risk of hepatopathy (RR 1.14). It is uncertain whether ezetimibe increase or decrease the risk of myopathy (RR 1.31) and Rhabdomyolysis. For serum lipids, adding ezetimibe to statin or fenofibrate might further reduce the low-density lipoprotein cholesterol (LDL-C), total cholesterol and triglyceride levels and likely increase the high-density lipoprotein cholesterol levels.

“MODERATE TO HIGH-QUALITY EVIDENCE SUGGESTS THAT EZETIMIBE HAS BENEFICIAL EFFECTS ON THE RISK OF CVD ENDPOINTS.”

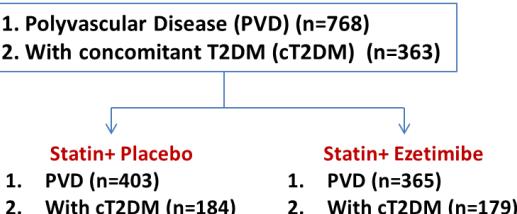
10. ADD-ON EZETIMIBE IS BENEFICIAL FOR DIABETES, POLYVASCULAR DISEASE

Add-on Ezetimibe Is Beneficial For Diabetes, Polyvascular Disease

A Secondary Analysis Of The IMPROVE-IT Trial

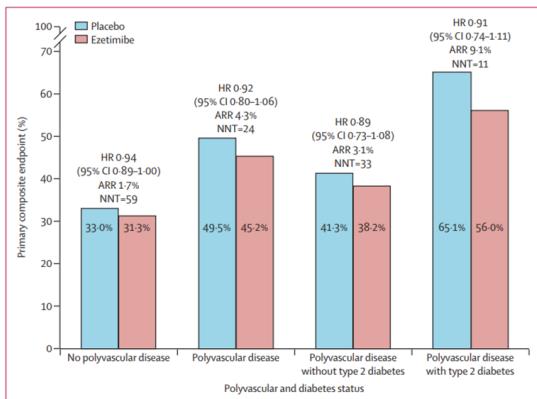
Objective: To assess the effect of ezetimibe given on top of statin therapy in patients with Polyvascular disease and type 2 diabetes.

Ref: *Lancet Diabetes Endocrinol.*
doi:10.1016/s2213-8587(18)30290-0



At 7 Years

Primary End Point: cardiovascular death, major coronary event or stroke



Additional 9% risk reduction observed in the group with vascular disease receiving Ezetimibe at year 7

Background

Polyvascular disease (PWD) and type 2 diabetes (T2DM) are each associated with increased cardiovascular risk, but whether these risks are additive is unknown. In this exploratory analysis of a randomized trial, investigators explored the long-term cardiovascular risk associated with PWD, T2DM and their combination in patients with ACS, and assessed the effect of ezetimibe given on top of statin therapy in patients with these concomitant conditions.

Methods

18 144 patients aged 50 years and older who had been stabilized after an ACS were randomly assigned to 40 mg/day simvastatin plus either 10 mg/day ezetimibe or matched placebo, for a median duration of 6 years. In this post-hoc exploratory analysis, prespecified endpoints of the trial were assessed, including the primary composite endpoint (cardiovascular death, a major coronary event or stroke) by concomitant PWD at baseline and stratified by concomitant T2DM.

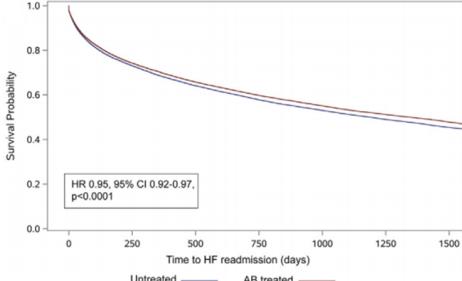
Results:

1005 patients (6%) had peripheral artery disease and 1071 (6%) had stroke or transient ischaemic attack at baseline. Of these, 388 (39%) and 409 (38%) also had concomitant type 2 diabetes, respectively. At 7 years, patients with either polyvascular disease or type 2 diabetes had similar rates of the primary endpoint (39.8% and 39.9%, respectively), which were higher than patients without polyvascular disease or diabetes (29.6%). Polyvascular disease with concomitant type 2 diabetes was associated with further heightened risk (60.0% 7-year Kaplan-Meier rate, HR 1.60; $p<0.0001$). Ezetimibe reduced cardiovascular risk consistently across groups with greater numerical absolute risk reductions in the highest-risk subgroups.

"In patients with coronary artery disease, concomitant polyvascular disease or type 2 diabetes are associated with increased long-term cardiovascular risk. The combination of polyvascular disease and diabetes is additive, resulting in very high risk. The benefit of ezetimibe is consistent in patients with and without polyvascular disease and type 2 diabetes."

11. TREATMENT OF HEART FAILURE (HF) PATIENTS WITH AN ALPHA-BLOCKER WAS ASSOCIATED WITH A LOWER RATE OF HF READMISSION AND DEATH

Treatment Of Heart Failure (HF) Patients With An α -Blocker Was Associated With A Lower Rate Of HF Readmission And Death

Objective	Results	Conclusion
To evaluate whether alpha-blocker (AB) use following an admission for heart HF was associated with an increased risk of HF readmission or death.	<ul style="list-style-type: none"> 35,713 in each group (Matched cohort) AB use was associated with fewer HF readmissions (39.8% vs. 41.7% at 2 years; $p < 0.0001$) and death (42.8% vs. 46.5%, $p < 0.0001$).  <p>HR 0.95, 95% CI 0.92-0.97, $p < 0.0001$</p>	Treatment of HF patients with an AB was associated with a lower rate of HF readmission and death and can be used safely in HF patients where clinically indicated.
Methods		J Am Coll Cardiol HF 2018

Background:

ABs, found to increase the risk of HF in the ALLHAT (Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial) trial, are commonly used for prostatic hypertrophy, including in those with or at risk for HF. Objective is to evaluate whether alpha-blocker (AB) use following an admission for heart failure (HF) was associated with an increased risk of HF readmission or death.

Methods

This propensity score-matched cohort study included patients discharged from a Veterans Affairs hospital between January 2002 and September 2015 with a primary diagnosis of HF and ascertained AB use at discharge. Cox proportional hazards models were constructed to compare time to first HF readmission and death at 2 years between groups. Secondary analyses assessed effects by AB dose and type and by beta-blocker (BB) use.

Results:

Of 169,911 HF patients, 47,638 (28%) were prescribed an AB. In the propensity score-matched cohort, AB use was associated with fewer HF readmissions (39.8% vs. 41.7% at 2 years; hazard ratio: 0.95; 95% confidence interval [CI]: 0.92 to 0.97; $p < 0.0001$) and death (42.8% vs. 46.5%, hazard ratio: 0.93; 95% CI: 0.91 to 0.94; $p < 0.0001$). Nonselective ABs had fewer deaths and HF readmissions ($p < 0.0001$), while higher AB doses reduced mortality ($p < 0.0001$). AB treatment was associated with reduced deaths in both BB-treated and untreated patients, with no increase in HF.



"TREATMENT OF HF PATIENTS WITH AN AB WAS NOT ASSOCIATED WITH A HIGHER BUT INSTEAD WITH A LOWER RATE OF HF READMISSION AND DEATH ."

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