

Dear Reader,

We are honoured to present you the 2nd issue of “The 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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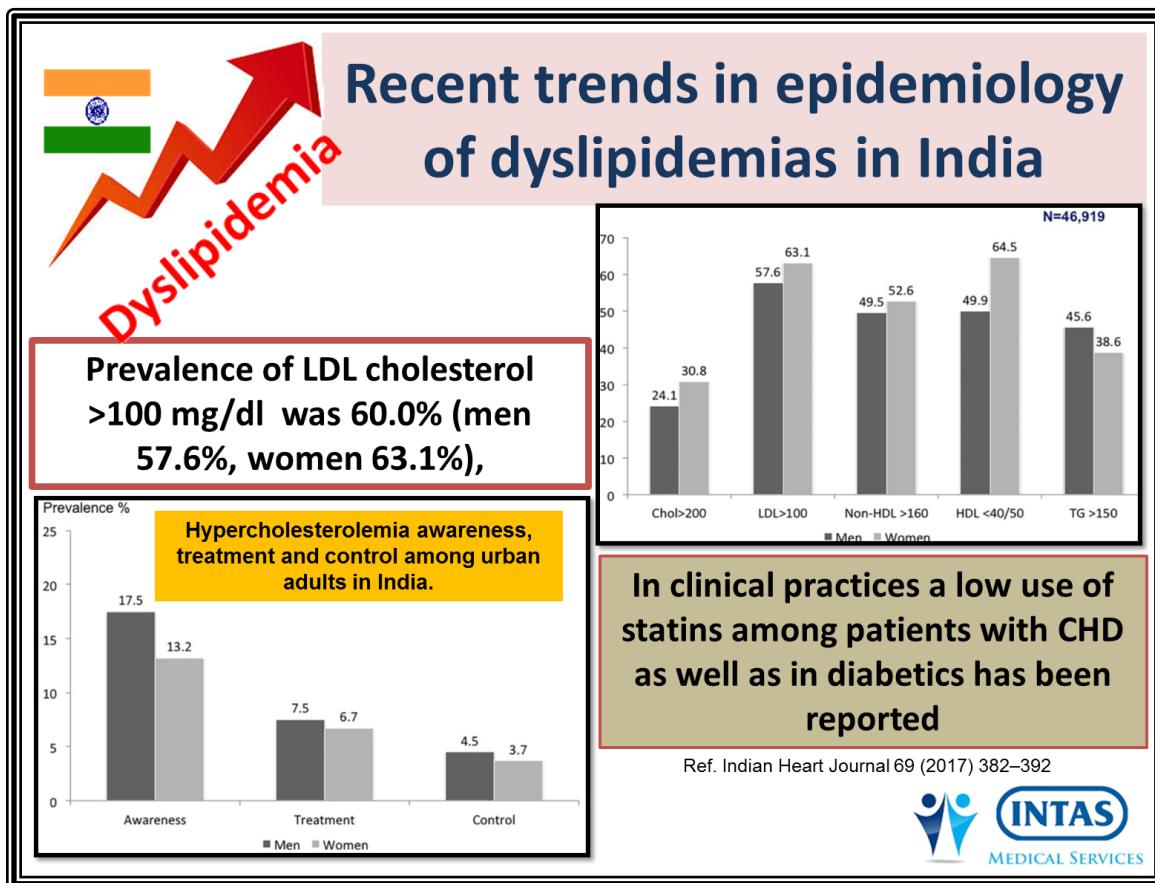
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1. Recent trends in epidemiology of dyslipidemias in India



Dyslipidemia is the most important atherosclerotic risk factor. Review of population based studies in India shows increasing mean total cholesterol levels. Recent studies have reported that high cholesterol is present in 25-30% of urban and 15-20% rural subjects.

This prevalence is lower than high-income countries. The most common dyslipidemia in India are borderline high LDL cholesterol, low HDL cholesterol and high triglycerides. Studies have reported that over a 20-year period total cholesterol, LDL cholesterol and triglyceride levels have increased among urban populations. Case-control studies have reported that there is significant association of coronary events with raised apolipoproteinB, total cholesterol, LDL cholesterol and non-HDL cholesterol and inverse association with high apolipoproteinA and HDL cholesterol. Prevalence of suspected familial hypercholesterolemia in urban subjects varies from 1:125 to 1:450. Only limited studies exist regarding lipid abnormalities in children.

There is low awareness, treatment and control of hypercholesterolemia in India.

2. Frequency of Familial Hypercholesterolemia in Patients With Premature ACS

FREQUENCY OF FAMILIAL HYPERCHOLESTEROLEMIA IN PATIENTS WITH PREMATURE ACS



- Assessed the frequency of FH in 172 patients with premature ACS (age < 55 years for men and < 60 years for women)
- The diagnosis of FH was estimated using phenotypic Dutch Lipid Clinic Network Criteria

The frequency of FH:

- Definite FH was 2 (1.2%),
- Probable FH e 12 (7.0%),
- Possible FH e 32 (18.6%)

Optimizing long-term lipid treatment of these patients is required, including statins in high doses, if necessary ezetimibe

Table 1. Baseline characteristics of patients with and without FH.

	With FH (n=46)	Without FH (n=126)
Age, years	49.0±7.4	48.5±6.0
Female/male, n (%)	12 (26.1)/34 (73.9)	13 (10.3)/113 (89.7)
Family history of premature CAD, n (%)	21 (45.7)	17 (13.5)
LDL-cholesterol *, mmol/l	4.90±0.95	2.60±0.89
Arterial hypertension, n (%)	35 (76.1)	85 (67.5)
Obesity (BMI>30), n (%)	18 (39.1)	47 (37.3)
Diabetes mellitus, n (%)	7 (15.2)	18 (14.3)
Smoking, n (%)	24 (52.2)	80 (63.4)
Use of statins, n (%)	13 (28.3)	23 (18.3)

* - LDL-cholesterol was measured on the first day of ACS.



Ref. Atherosclerosis 263 (2017) e111ee282

Aim:

To assess the frequency of clinical FH and non-lipid risk factors in patients admitted for ACS to our clinic in 2015.

Methods:

We assessed the frequency of FH in 172 patients with premature ACS (age < 55 years for men and < 60 years for women). Clinical data were collected from electronic health records. The diagnosis of FH was estimated using phenotypic Dutch Lipid Clinic Network Criteria.

Results:

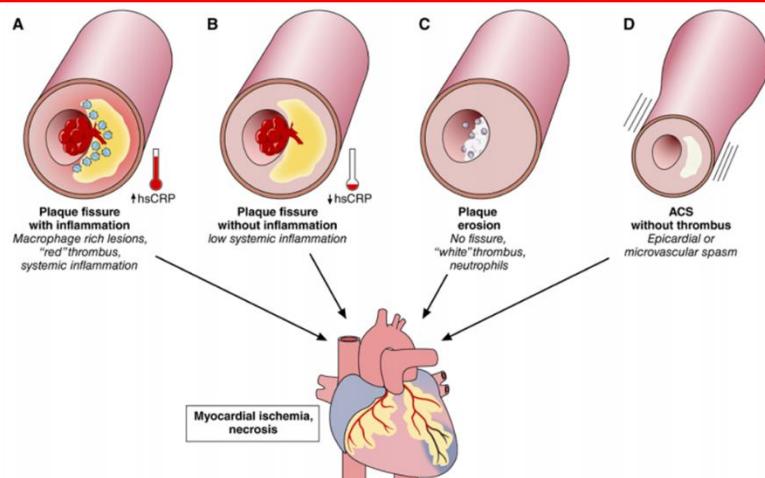
The frequency of definite FH was 2 (1.2%), probable FH e 12 (7.0%), possible FH e 32 (18.6%). Age, LDL-cholesterol (pretreatment level if patient took statin was estimated by use a correction coefficient), non-lipid cardiovascular risk factors and use of statins in patients with and without FH are presented in Table . There were no difference by age, gender and nonlipid risk factors in patients with and without FH. LDL-cholesterol level and statins intake before admission were significantly higher in FH patients.

Conclusions:

A phenotypic diagnosis of definite and probable FH occurs in 8% patients hospitalized for premature ACS. Optimizing long-term lipid treatment of these patients is required, including statins in high doses, if necessary ezetimibe, or new lipid-lowering drugs (PCSK9 inhibitors).

3. Four diverse mechanisms cause acute coronary syndromes

Four diverse mechanisms cause acute coronary syndromes



A. Plaque rupture, also referred to as fissure, traditionally considered the dominant substrate for ACS, usually associates with both local inflammation, as depicted by the blue monocytes, and systemic inflammation, as indicated by the gauge showing an increase in blood C-reactive protein (CRP; measured with a high-sensitivity [hsCRP] assay).

B. In some cases, plaque rupture complicates atheromata that do not harbor large collections of intimal macrophages, as identified by optical coherence tomography criteria, and do not associate with elevations in circulating CRP. Plaque rupture usually provokes the formation of fibrin-rich red thrombi.

C. Plaque erosion appears to account for a growing portion of ACS, often provoking non-ST-segment-elevation myocardial infarction. The thrombi overlying patches of intimal erosion generally exhibit characteristics of white platelet-rich structures.

D. Vasospasm can also cause ACS, long recognized as a phenomenon in the epicardial arteries but also affecting coronary microcirculation.



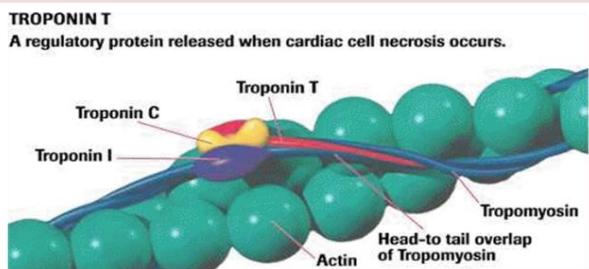
Circulation. 2017;136:1155–1166

ABSTRACT:

Well into the 21st century, we still triage acute myocardial infarction on the basis of the presence or absence of ST-segment elevation, a century-old technology. Meanwhile, we have learned a great deal about the pathophysiology and mechanisms of acute coronary syndromes (ACS) at the clinical, pathological, cellular, and molecular levels. Contemporary imaging studies have shed new light on the mechanisms of ACS. They propose segmenting coronary artery thrombosis caused by plaque rupture into cases with or without signs of concomitant inflammation. This distinction may have substantial therapeutic implications as direct anti-inflammatory interventions for atherosclerosis emerge. Coronary artery thrombosis caused by plaque erosion may be on the rise in an era of intense lipid lowering. Identification of patients with ACS resulting from erosion may permit a less invasive approach to management than the current standard of care. We also now recognize ACS that occur without apparent epicardial coronary artery thrombus or stenosis. Such events may arise from spasm, microvascular disease, or other pathways. Emerging management strategies may likewise apply selectively to this category of ACS. We advocate this more mechanistic approach to the categorization of ACS to provide a framework for future tailoring, triage, and therapy for patients in a more personalized and precise manner.

4. High-Normal Troponin Levels May Signal Risk for Fatal CVD

High-Normal Troponin Levels May Signal Risk for Fatal CVD



The highest third of cardiac troponin levels detected by high-sensitivity cardiac troponin T or troponin I (hs-cTNT/cTNI) assays had a >60% increase in risk for fatal CVD events,

154,052 participants in 28 prospective, long-term studies of patients without a history of CVD

Risk of a First-ever CVD Event

Relative risk comparing top vs. bottom third

CVD	+43%
Fatal CVD	+67%
CHD	+59%
Stroke	+35%



Ref. J Am Coll Cardiol 2017; 70:558-568.

OBJECTIVES : The goal of this study was to assess associations of cardiac troponin concentration with cardiovascular disease (CVD) outcomes in primary prevention studies.

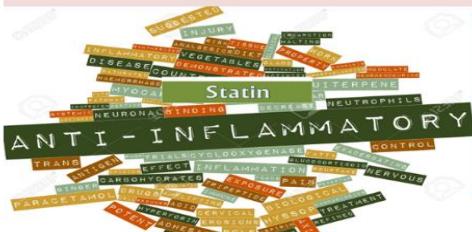
METHODS: A search was conducted of PubMed, Web of Science, and EMBASE for prospective studies published up to September 2016, reporting on associations of cardiac troponin concentration with first-ever CVD outcomes (i.e., coronary heart disease [CHD], stroke, or the combination of both). Study-specific estimates, adjusted for conventional risk factors, were extracted by 2 independent reviewers, supplemented with de novo data from PROSPER (Pravastatin in Elderly Individuals at Risk of Vascular Disease Study), then pooled by using random effects meta-analysis.

RESULTS: A total of 28 relevant studies were identified involving 154,052 participants. Cardiac troponin was detectable in 80.0% (hs-cTnI: 82.6%; hs-cTnT: 69.7%). In PROSPER, positive associations of log-linear shape were observed between hs-cTnT and CVD outcomes. In the meta-analysis, the relative risks comparing the top versus the bottom troponin third were 1.43 (95% confidence interval [CI]: 1.31 to 1.56) for CVD (11,763 events), 1.67 (95% CI: 1.50 to 1.86) for fatal CVD (7,775 events), 1.59 (95% CI: 1.38 to 1.83) for CHD (7,061 events), and 1.35 (95% CI: 1.23 to 1.48) for stroke (2,526 events). For fatal CVD, associations were stronger in North American studies ($p \leq 0.010$) and those measuring hs-cTnT rather than hs-cTnI ($p < 0.027$).

CONCLUSIONS In the general population, high cardiac troponin concentration within the normal range is associated with increased CVD risk. This association is independent of conventional risk factors, strongest for fatal CVD, and applies to both CHD and stroke.

5. Preoperative Statins Cardiac and Inflammatory outcomes following CABG: a Meta-analysis

Preoperative Statins Cardiac and Inflammatory outcomes following CABG: a Meta-analysis

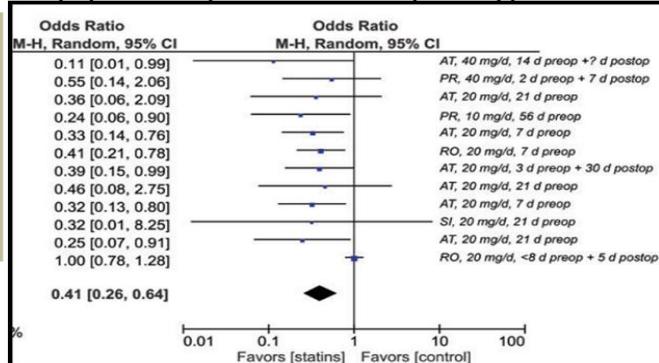


- A meta-analysis was carried out for early cardiac (AF, MI, myocardial injury markers) and inflammatory outcomes.
 - 17 suitable studies that featured data from the total of 2796 patients.

Fig: Forest plot, atrial fibrillation (events) in statin-treated (experimental) versus untreated (control) patients.

Statin pretreatment is associated with beneficially modulation of incidence of atrial fibrillation and rise of inflammatory markers postoperatively.

Ref. Interactive CardioVascular and Thoracic Surgery (2017) 1–8



Background

Early postoperative cardiac complications of coronary artery bypass graft surgery, such as atrial fibrillation (AF) or myocardial infarction (MI), may be beneficially modulated by preoperative statins, involving their anti-inflammatory effects. There is uncertainty on the clinical merit of statin pretreatment.

Method

A search of Medline and Cochrane databases was undertaken to identify suitable studies. A meta-analysis was carried out for early cardiac (AF, MI, myocardial injury markers) and inflammatory (cytokines, C-reactive protein) outcomes.

Results

We identified 17 suitable studies that featured data from the total of 2796 patients. Twelve studies (1260 treated and 1263 untreated patients) reported AF incidence. Statin pretreatment was associated with a significant decrease of AF incidence: odds ratio 0.44 (95% confidence interval: 0.27–0.70; $P = 0.003$). Seven studies (381 treated and 277 untreated patients) reported useful data on MI. Unlike in AF, no significant modulation of postoperative MI in association with statin pretreatment could be observed: odds ratio 0.62 (95% confidence interval: 0.21–1.81; $P = 0.62$). Five studies (248 treated and 245 untreated patients) provided data on postoperative rise of C-reactive protein. This rise was significantly down regulated in statin-pretreated patients: standardized mean difference -0.44 (95% confidence interval: -0.78 to -0.11; $P = 0.02$).

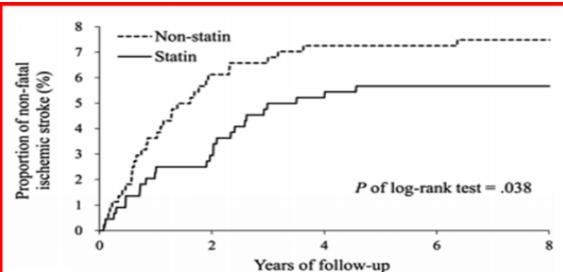
Conclusion

Thus, postoperative AF incidence is the biggest beneficiary of statin pretreatment in coronary artery bypass graft surgery. This effect is associated with beneficial modulation of systemic inflammatory markers.

6. Moderate- to high-intensity statins for secondary prevention in patients with T2DM on dialysis after acute MI

Moderate- to high-intensity statins for secondary prevention in patients with T2DM on dialysis after acute MI

Probability of event rates in each study group for a non-fatal ischemic stroke



- 882 patients with T2DM on dialysis after AMI.
- Compared to non statin group, in statin group
 - Significantly lower risks of non-fatal ischemic stroke by 42%
 - All-cause mortality by 30%.

In T2DM patients on dialysis after AMI, the use of moderate- to high-intensity statins reduce risks of non-fatal ischemic stroke and all-cause mortality



Diabetol Metab Syndr (2017) 9:71

Background: Evidences support the benefits of moderate- to high-intensity statins for patients with acute myocardial infarction (AMI) except for those with type 2 diabetes mellitus (T2DM) on dialysis after AMI. This study was aimed to investigate the safety and efficacy of secondary prevention of cardiovascular diseases using moderate- to highintensity statins in T2DM patients on dialysis after AMI.

Methods: A simulated prospective cohort study was conducted between January 1st, 2001 and December 31st, 2013 utilizing data from the Taiwan National Health Insurance Research Database. A total of 882 patients with T2DM on dialysis after AMI were selected as the study cohort. Cardiovascular efficacy and safety of moderate- to highintensity statins were evaluated by comparing outcomes of 441 subjects receiving statins after AMI to 441 matched subjects not receiving statins after AMI. The primary composite outcome included cardiovascular death, non-fatal myocardial infarction and non-fatal ischemic stroke.

Results: The Kaplan–Meier event rate for the primary composite outcomes at 8 years was 30.2% (133 patients) in the statin group compared with 25.2% (111 patients) in the non-statin group (hazard ratio [HR], .98; 95% confidence interval [CI] .76–1.27). Significantly lower risks of non-fatal ischemic stroke (HR, .58; 95% CI .35–.98) and all-cause mortality (HR, .70; 95% CI .59–.84) were found in the statin group.

Conclusions: In T2DM patients on dialysis after AMI, the use of moderate- to high-intensity statins has neutral effects on composite cardiovascular events but may reduce risks of non-fatal ischemic stroke and all-cause mortality.

7. Effects of statin therapy on platelet reactivity after PCI in patients with ACS

Effects of statin therapy on platelet reactivity after PCI in patients with ACS

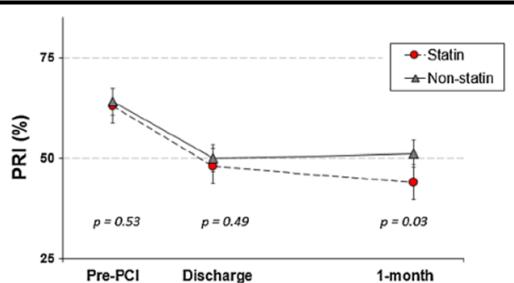


Fig. 1 Platelet reactivity index (PRI) values during study time course according to statin use. *PCI* percutaneous coronary intervention

- In ACS patients undergoing PCI treated with clopidogrel, the use of statins at discharge was associated with significantly lower 1-month HPR rates compared with patients not treated with statins. (39.6 vs 52%, respectively, $p = 0.009$).



J Thromb Thrombolysis 2017 Aug 24

Abstract:

Statin use is associated with enhanced pharmacodynamics response to clopidogrel in patients with stable coronary artery disease undergoing percutaneous coronary intervention (PCI). However, the impact of statin therapy on clopidogrel response profiles in patients with acute coronary syndrome (ACS) undergoing PCI has not been established and represents the objective of this investigation. On-treatment P2Y12 platelet reactivity was measured using the vasodilator stimulated phosphoprotein (VASP) phosphorylation assay before PCI, at hospital discharge, and at 1 month after PCI in ACS patients enrolled in the multicenter, prospective GEn polymorphisms, Platelet Reactivity, and Syntax Score (GEPRESS) study ($n = 962$). High platelet reactivity (HPR) was defined as platelet reactivity index $\geq 50\%$. Statins were prescribed at hospital discharge in 87% ($n = 835$) of patients. All patients were followed for 1 year. The 1-month HPR rate was lower in statin than in non-statin treated patients (39.6 vs 52%, respectively, $p = 0.009$). This finding was confirmed also among statin-treated patients with high Syntax score (≥ 15). After adjustment for differences in baseline characteristics, statin use at discharge was independently associated with 1-month HPR rate (odds ratio, 0.58, 95% confidence interval, 0.38–0.89; $p = 0.015$). In ACS patients undergoing PCI treated with clopidogrel the use of statins at discharge was associated with significantly lower 1-month HPR rates compared with patients not treated with statins.

8. Do not down-titrate the statin dose!

Do not down-titrate the statin dose!

High intensity atorvastatin significantly reduced late adverse events compared with low-intensity statin in Asians

Drug eluting stent

Among clinically stable DES-treated patients, Atorvastatin 40 mg significantly reduced late MACE compared with low-intensity statin

Clinically stable patients who underwent DES implantation were randomly assigned to receive either

- 40mg atorvastatin, n = 1000, or
- Low-intensity-20mg pravastatin, n = 1000
- 12 month follow-up

Late MACE
RR(p=0.1) **42%**

Ref. Rev Esp Cardiol (Engl Ed). 2017 Jul 14. pii: S1885-5857(17)30317-1.

INTAS
MEDICAL SERVICES

Introduction and objectives:

Current guidelines on the treatment of blood cholesterol recommend continuous maintenance of high-intensity statin treatment in drug-eluting stent (DES)-treated patients. However, high-intensity statin treatment is frequently underused in clinical practice after stabilization of DES-treated patients. Currently, the impact of continuous high-intensity statin treatment on the incidence of late adverse events in these patients is unknown. We investigated whether high-intensity statin treatment reduces late adverse events in clinically stable patients on aspirin monotherapy 12 months after DES implantation.

Methods:

Clinically stable patients who underwent DES implantation 12 months previously and received aspirin monotherapy were randomly assigned to receive either high-intensity (40 mg atorvastatin, n = 1000) or low-intensity (20 mg pravastatin, n = 1000) statin treatment. The primary endpoint was adverse clinical events at 12-month follow-up (a composite of all death, myocardial infarction, revascularization, stent thrombosis, stroke, renal deterioration, intervention for peripheral artery disease, and admission for cardiac events).

Results:

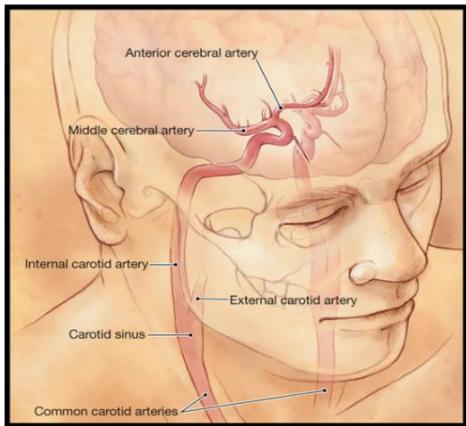
The primary endpoint at 12-month follow-up occurred in 25 patients (2.5%) receiving high-intensity statin treatment and in 40 patients (4.1%) receiving low-intensity statin treatment (HR, 0.58; 95%CI, 0.36-0.92; P = .018). This difference was mainly driven by a lower rate of cardiac death (0 vs 0.4%, P = .025) and nontarget vessel myocardial infarction (0.1 vs 0.7%, P = .033) in the high-intensity statin treatment group.

Conclusions:

Among clinically stable DES-treated patients on aspirin monotherapy, high-intensity statin treatment significantly reduced late adverse events compared with low-intensity statin treatment.

9. Effect of clopidogrel combined with atorvastatin on NIHSS and Barthel score in patients with progressive cerebral infarction

Effect of clopidogrel combined with atorvastatin on NIHSS and Barthel score in patients with progressive cerebral infarction



- 88 patients with progressive cerebral infarction.
- Clopidogrel combined with atorvastatin has a significant effect on the patients with intracranial large artery stenosis and improve the neurological function as measured by NIHSS score and quality of life

NIHSS: National Institutes of Health Stroke Scale



Journal of Hainan Medical University 2017; 23(12): 155-159

Objective: Study the clinical effect of atorvastatin combined with clopidogrel on patients with progressive cerebral infarction of intracranial aortic stenosis.

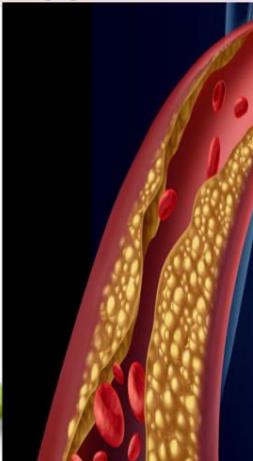
Methods: Chose eighty-eight patients with progressive cerebral infarction in our hospital from June 2014 to October 2015. They were randomly divided into study group and control group, 44 cases in each group. The patients in the control group were treated with oral clopidogrel. On the basis of this, the patients in the study group were treated with atorvastatin; all patients were treated for 4 weeks. Compared the total effective rate, adverse reaction rate, coagulation function index and blood lipid level between the two groups, and compared the NIHSS score and daily life ability (ADL) score between the two groups before and after treatment.

Results: The total effective rate (90.90%) was significantly higher in the study group than in the control group (72.73%). After treatment, the NIHSS score of the study group was significantly lower than that of the control group. The levels of LDL-C, TG and TC in the study group were significantly lower than those in the control group, and HDL-C was significantly higher than that in the control group. There was no significant difference between the two groups.

Conclusion: Clopidogrel combined with atorvastatin has a significant effect on the patients with intracranial large artery stenosis and improve the neurological function and quality of life. It is safe and reliable. It is worthy to be popularized.

10. More prominent effect of atorvastatin than Extra Virgin Olive Oil (EVOO) plasma lipids level in Type 2 diabetic dyslipidemia

More prominent effect of atorvastatin than Extra Virgin Olive Oil (EVOO) plasma lipids level in Type 2 diabetic dyslipidemia



Ref. J Ayub Med Coll Abbottabad. 2017 Jan-Mar;29(1):83-86.



Atorvastatin was given to Group One or two tablespoons of extra virgin olive oil orally per day was given to T2DM patients with dyslipidemia

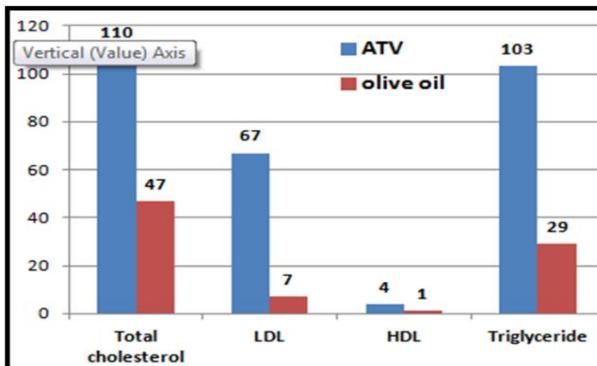


Fig. Mean \pm SD differences among patients of two groups before and after treatment

Background:

Extra virgin olive oil (EVOO) is fruit oil with rich source of monounsaturated fats and powerful antioxidants. The purpose of this study was to determine & compare the lipid lowering effect of EVOO with atorvastatin in type 2 diabetic dyslipidaemia which is leading cause of microvascular diseases.

Methods:

This randomised controlled trial was conducted on 60 already diagnosed cases of type 2 diabetes mellitus with dyslipidaemia. All sixty subjects were divided randomly into 2 groups. Atorvastatin 40 mg was given to Group One and two tablespoons of extra virgin olive oil orally per day was given to Group Two. Blood was collected for estimation of plasma lipids level at base line, 4th week, and 6th weeks in two groups and was compared statistically.

Results:

The present study demonstrated 20–40% lipid lowering effect of atorvastatin on plasma lipids level with 9–16% increase in HDL while extra virgin olive oil showed 14–25% reduction in plasma lipids with 8–12% increase in HDL-cholesterol level.

Conclusion:

This study concludes that both atorvastatin and extra virgin olive oil are effective in reducing plasma lipids level in type 2 diabetic dyslipidaemia with more prominent effect of atorvastatin than EVOO.

11. Atorvastatin in Asian dyslipidemia patients An analysis from the lamp study

Atorvastatin in Asian dyslipidemia patients An analysis from the lamp study



- Total 6,206 were evaluated
- Sixty percent of patients had comorbid diseases
 - 40%-Vascular disorders,
 - 21% Metabolic diseases,
 - 7- Cardiac disorders
- 92% of patients were well tolerated with atorvastatin

Atorvastatin calcium anhydrous is considered as a therapeutic agent for patient with dyslipidemia with few safety concerns. The LAMP Study



Ref. Atherosclerosis 263 (2017) e111ee282

Aim:

The Lipilou sAfery study for Korean dyslipideMia Patients (LAMP) study is an observational study evaluating the safety and tolerability of atorvastatin calcium anhydrous in over 20,000 Korean patients with dyslipidemia.

Methods:

An interim analysis from the LAMP study was conducted for more than 5,000 (25% enrollment) patients who were treated with atorvastatin calcium anhydrous at 348 medical institutions in Korea from the start of surveying of this drug in February 2015. Data was collected and analyzed independently by the independent data monitoring committee (IDMC).

Results:

Of the total 6,212 patients enrolled, 6,206 were evaluated. Sixty percent of patients had comorbid diseases (vascular disorders, 40%; metabolic diseases, 21%; cardiac disorders 7%). Ninety-two percent of patients were well tolerated with treatment of atorvastatin calcium anhydrous and continued the medicine during 12±4 weeks. Twelve of 6,206 patients (0.19%) taking this drug discontinued treatment because of an adverse event (AE). The occurrence of any AE and adverse drug reaction (ADR) were 1.05% and 0.13%, respectively. Serious AEs were observed in six (0.10%) patients.

There was no serious ADRs.

Conclusions:

Based on this result of an interim analysis from the LAMP study reflecting real world treatment, atorvastatin calcium anhydrous is considered as a therapeutic agent for patient with dyslipidemia with few safety concerns.

12. CANTOS: Anti-Inflammatory Drug Cuts CV Events, Cancer

CANTOS
Anti-Inflammatory Drug Cuts CV Events, Cancer

INFLAMMATION at the Root of Most Diseases

CANTOS:
>10,000 high-risk patients who had a prior MI and persistently elevated hs-CRP levels,
• Received subcutaneous canakinumab 150 mg every 3 months

ESC CONGRESS BARCELONA 2017
26 – 30 August

Where the world of cardiology comes together

Canakinumab (Ilaris, Novartis) significantly decreased the risk of

- Recurrent major CV events without any effect on cholesterol.
- Dramatically cut rates of new lung cancer & lung-cancer mortality

Ref. NEJM. 27 Aug 10.1056/NEJMoa1707914

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Primary End Point with Canakinumab, 150 mg, vs. Placebo
Hazard ratio, 0.85 (95% CI, 0.74–0.98)
P=0.021

Years	Placebo (%)	Canakinumab (150 mg) (%)
0	0	0
1	~4	~2
2	~8	~4
3	~12	~6
4	~16	~8
5	~20	~10

BACKGROUND

Experimental and clinical data suggest that reducing inflammation without affecting lipid levels may reduce the risk of cardiovascular disease. Yet, the inflammatory hypothesis of atherothrombosis has remained unproved.

METHODS

Conducted a randomized, double-blind trial of canakinumab, a therapeutic monoclonal antibody targeting interleukin-1 β , involving 10,061 patients with previous myocardial infarction and a high-sensitivity C-reactive protein level of 2 mg or more per liter. The trial compared three doses of canakinumab (50 mg, 150 mg, and 300 mg, administered subcutaneously every 3 months) with placebo. The primary efficacy end point was nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death.

RESULTS

At 48 months, the median reduction from baseline in the high-sensitivity C-reactive protein level was 26 percentage points greater in the group that received the 50-mg dose of canakinumab, 37 percentage points greater in the 150-mg group, and 41 percentage points greater in the 300-mg group than in the placebo group. Canakinumab did not reduce lipid levels from baseline. At a median follow-up of 3.7 years, the incidence rate for the primary end point was 4.50 events per 100 person-years in the placebo group, 4.11 events per 100 person-years in the 50-mg group, 3.86 events per 100 person-years in the 150-mg group, and 3.90 events per 100 person-years in the 300-mg group. The hazard ratios as compared with placebo were as follows: in the 50-mg group, 0.93 (95% confidence interval [CI], 0.80 to 1.07; P = 0.30); in the 150-mg group, 0.85 (95% CI, 0.74 to 0.98; P = 0.021); and in the 300-mg group, 0.86 (95% CI, 0.75 to 0.99; P = 0.031). Canakinumab was associated with a higher incidence of fatal infection than was placebo.

CONCLUSIONS

Antiinflammatory therapy targeting the interleukin-1 β innate immunity pathway with canakinumab at a dose of 150 mg every 3 months led to a significantly lower rate of recurrent cardiovascular events than placebo.

13. DETO2X-AMI: No Mortality Benefit of Supplemental Oxygen in Acute MI

DETO2X-AMI: No Mortality Benefit of Supplemental Oxygen in Acute MI



DETO2X-AMI:
6629 patients with suspected MI & O₂ saturation > 90% were randomly assigned to receive

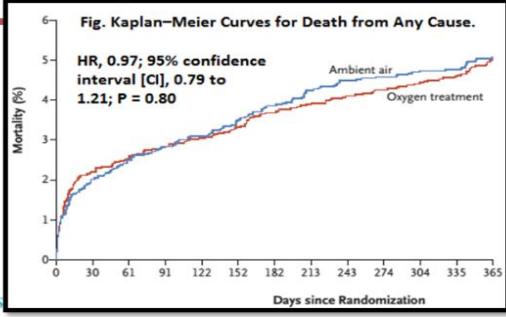
- O₂ (6 liters per minute for 6 -12 hours, through an open face mask) or
- Ambient air

Routine use of supplemental oxygen in patients with suspected myocardial infarction who did not have hypoxemia was not found to reduce 1-year all-cause mortality

Ref. NEJM. 28 Aug DOI: 10.1056/NEJMoa1706222



Fig. Kaplan-Meier Curves for Death from Any Cause.
HR, 0.97; 95% confidence interval [CI], 0.79 to 1.21; P = 0.80



BACKGROUND

The clinical effect of routine oxygen therapy in patients with suspected acute myocardial infarction who do not have hypoxemia at baseline is uncertain.

METHODS

In this registry-based randomized clinical trial, used nationwide Swedish registries for patient enrollment and data collection. Patients with suspected myocardial infarction and an oxygen saturation of 90% or higher were randomly assigned to receive either supplemental oxygen (6 liters per minute for 6 to 12 hours, delivered through an open face mask) or ambient air.

RESULTS

A total of 6629 patients were enrolled. The median duration of oxygen therapy was 11.6 hours, and the median oxygen saturation at the end of the treatment period was 99% among patients assigned to oxygen and 97% among patients assigned to ambient air. Hypoxemia developed in 62 patients (1.9%) in the oxygen group, as compared with 254 patients (7.7%) in the ambient-air group. The primary end point of death from any cause within 1 year after randomization occurred in 5.0% of patients (166 of 3311) assigned to oxygen and in 5.1% of patients (168 of 3318) assigned to ambient air (hazard ratio, 0.97; 95% confidence interval [CI], 0.79 to 1.21; P = 0.80). Rehospitalization with myocardial infarction within 1 year occurred in 126 patients (3.8%) assigned to oxygen and in 111 patients (3.3%) assigned to ambient air (hazard ratio, 1.13; 95% CI, 0.88 to 1.46; P = 0.33). The results were consistent across all predefined subgroups.

CONCLUSIONS

Routine use of supplemental oxygen in patients with suspected myocardial infarction who did not have hypoxemia was not found to reduce 1-year all-cause mortality.

14. Associations of fats and carbohydrate intake with cardiovascular disease: PURE study

Associations of fats and carbohydrate intake with cardiovascular disease: PURE study



Study found a Beneficial effect on mortality

- Fruit, vegetables, and legumes, Fat in diet
- The maximum benefit was seen at 3-4 servings a day (equivalent to 375–500 g/day)

Associated with an increased risk of mortality

- High carbohydrate intake

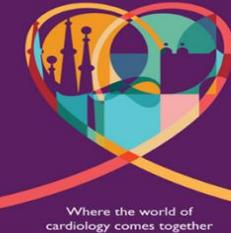
The Lancet, August 2017 DOI: 10.1016/S0140-6736(17)32253-5



The PURE, a study of dietary habits in 135,000 people from 18 countries for 7 yrs

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Hazard Ratio for Total Mortality (Highest Quintile vs Lowest Quintile)

Group	HR (95% CI)	P for trend
Carbohydrate	1.28 (1.12–1.46)	0.0001
Total fat	0.77 (0.67–0.87)	<0.0001
Saturated fat	0.86 (0.76–0.99)	0.0088
Monounsaturated fat	0.81 (0.71–0.92)	<0.0001
Polyunsaturated fat	0.80 (0.71–0.89)	<0.0001

Background The relationship between macronutrients and cardiovascular disease and mortality is controversial. Most available data are from European and North American populations where nutrition excess is more likely, so their applicability to other populations is unclear.

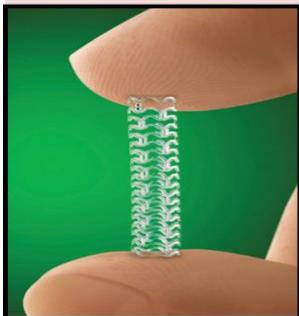
Methods The Prospective Urban Rural Epidemiology (PURE) study is a large, epidemiological cohort study of individuals aged 35–70 years (enrolled between Jan 1, 2003, and March 31, 2013) in 18 countries with a median followup of 7·4 years (IQR 5·3–9·3). Dietary intake of 135 335 individuals was recorded using validated food frequency questionnaires. The primary outcomes were total mortality and major cardiovascular events (fatal cardiovascular disease, non-fatal myocardial infarction, stroke, and heart failure). Secondary outcomes were all myocardial infarctions, stroke, cardiovascular disease mortality, and non-cardiovascular disease mortality. Participants were categorised into quintiles of nutrient intake (carbohydrate, fats, and protein) based on percentage of energy provided by nutrients.

Findings During follow-up, we documented 5796 deaths and 4784 major cardiovascular disease events. Higher carbohydrate intake was associated with an increased risk of total mortality (highest [quintile 5] vs lowest quintile [quintile 1] category, HR 1·28 [95% CI 1·12–1·46], ptrend=0·0001) but not with the risk of cardiovascular disease or cardiovascular disease mortality. Intake of total fat and each type of fat was associated with lower risk of total mortality (quintile 5 vs quintile 1, total fat: HR 0·77 [95% CI 0·67–0·87], ptrend<0·0001; saturated fat, HR 0·86 [0·76–0·99], ptrend=0·0088; monounsaturated fat: HR 0·81 [0·71–0·92], ptrend<0·0001; and polyunsaturated fat: HR 0·80 [0·71–0·89], ptrend<0·0001). Higher saturated fat intake was associated with lower risk of stroke (quintile 5 vs quintile 1, HR 0·79 [95% CI 0·64–0·98], ptrend=0·0498). Total fat and saturated and unsaturated fats were not significantly associated with risk of myocardial infarction or cardiovascular disease mortality.

Interpretation High carbohydrate intake was associated with higher risk of total mortality, whereas total fat and individual types of fat were related to lower total mortality. Total fat and types of fat were not associated with cardiovascular disease, myocardial infarction, or cardiovascular disease mortality, whereas saturated fat had an inverse association with stroke. Global dietary guidelines should be reconsidered in light of these findings.

15. Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents: BIOFLOW V Trial

Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents



BIOFLOW V Trial

- Randomly assigned (2:1) to either an ultrathin strut (60 µm) bioresorbable polymer sirolimus-eluting stent or to a durable polymer everolimus-eluting stent
- 90 hospitals in 13 countries

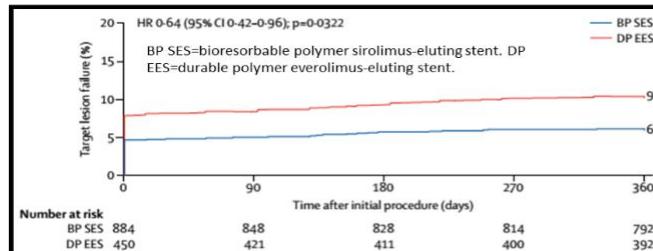


This is the first trial that has demonstrated superior outcomes with bioresorbable stent, which has served as a benchmark or standard for drug-eluting stents

Lancet 2017; DOI:10.1016/S0140-6736(17)32249-3.



Fig. Cumulative incidence of target lesion failure from 0 to 12 months



BACKGROUND:

The development of coronary drug-eluting stents has included use of new metal alloys, changes in stent architecture, and use of bioresorbable polymers. Whether these advancements improve clinical safety and efficacy has not been shown in previous randomised trials. We aimed to examine the clinical outcomes of a bioresorbable polymer sirolimus-eluting stent compared with a durable polymer everolimus-eluting stent in a broad patient population undergoing percutaneous coronary intervention.

METHODS:

BIOFLOW V was an international, randomised trial done in patients undergoing elective and urgent percutaneous coronary intervention in 90 hospitals in 13 countries. Eligible patients were those aged 18 years or older with ischaemic heart disease undergoing planned stent implantation in de-novo, native coronary lesions. Patients were randomly assigned (2:1) to either an ultrathin strut (60 µm) bioresorbable polymer sirolimus-eluting stent or to a durable polymer everolimus-eluting stent.

FINDINGS:

Between May 8, 2015, and March 31, 2016, 4772 patients were recruited into the study. 1334 patients met inclusion criteria and were randomly assigned to treatment with bioresorbable polymer sirolimus-eluting stents (n=884) or durable polymer everolimus-eluting stents (n=450). 52 (6%) of 883 patients in the bioresorbable polymer sirolimus-eluting stent group and 41 (10%) of 427 patients in the durable polymer everolimus-eluting stent group met the 12-month primary endpoint of target lesion failure (95% CI -6.84 to -0.29, p=0.0399), with differences in target vessel myocardial infarction (39 [5%] of 831 patients vs 35 [8%] of 424 patients, p=0.0155). The posterior probability that the bioresorbable polymer sirolimus-eluting stent is non-inferior to the durable polymer everolimus-eluting stent was 100% (Bayesian analysis, difference in target lesion failure frequency -2.6% [95% credible interval -5.5 to 0.1], non-inferiority margin 3.85%, n=2208).

INTERPRETATION:

The outperformance of the ultrathin, bioresorbable polymer sirolimus-eluting stent over the durable polymer everolimus-eluting stent in a complex patient population undergoing percutaneous coronary intervention suggests a new direction in improving next generation drug-eluting stent technology.

16. Adherence to beta blocker drugs and association with long term risk of HF admission and mortality among patients hospitalized for their first MI - SWEDEHEART registry

Adherence to beta blocker drugs and association with long term risk of HF admission and mortality among patients hospitalized for their first MI - SWEDEHEART registry

The graph plots 'Cumulative probability of LOHF/death' on the y-axis (70 to 100) against time in days on the x-axis (0 to 1200). Two lines are shown: a dashed line for 'Non-adherent' patients and a solid line for 'Adherent' patients. The non-adherent group starts at approximately 100% at day 0 and decreases to about 85% by day 1200. The adherent group starts at 100% and decreases more sharply, reaching approximately 75% by day 1200. A red box highlights the text '23 % RRR in all cause mortality' and '16% RRR in composite of HF readmission or death'.

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- Nearly one in three of AMI patients were non adherent to β blockers within the first year.
- Adherence to β blocker treatment was associated with improved long term outcomes at 4 years.

INTAS MEDICAL SERVICES

European Heart Journal (2017) 38 (Supplement), 1063

Aims: To describe the association between adherence to beta blocker treatment after a first myocardial infarction (AMI) and the long term risk of heart failure (HF) admission and/or death.

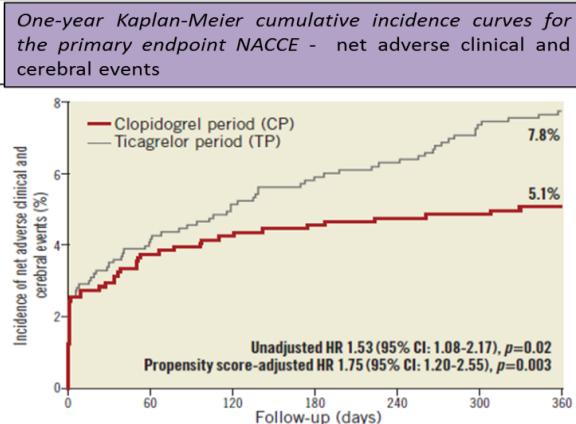
Methods: All patients admitted for a first AMI and included in the Swedish Web system for Enhancement and Development of Evidence based care in Heart disease Evaluated According to Recommend Therapies (SWEDEHEART) registry between 2005–2010 were eligible. Patients who died in hospital and those with unknown left ventricular ejection fraction (LVEF) during admission were excluded. Adherence to prescribed beta blockers was determined for one year using the National register of dispensed drugs.

Results: At discharge 90.1% (N=41,131) of all patients were on a beta blocker. At one year 31.8% of 1year survivors were non adherent to betablockers. Compared to patients with normal EF (NEF) without in hospital HF, patients with reduced EF (REF) with out in hospital HF and patients with in hospital HFREF were more likely to remain adherent to beta blockers at one year. Increasing age, lower income, single civil status, admission systolic blood pressure <90 mmHg and high grade AV block during admission were among factors associated with higher odds for non adherence. Adherence was associated with a lower adjusted all cause mortality (HR 0.77, 95% CI (0.71–0.84)) and lower risk for the composite of HF readmission or death, (HR 0.84, 95% CI (0.78–0.89)) during the subsequent 4 years of follow up

Conclusion: Nearly one in three of AMI patients were non adherent to beta blockers within the first year. Adherence to beta blocker treatment was better in patients with REF with or without in hospital HF and associated with improved long term outcomes.

17. Clopidogrel or ticagrelor in ACS patients treated with newer-generation drug-eluting stents: CHANGE DAPT

Clopidogrel or ticagrelor in ACS patients treated with newer-generation drug-eluting stents: CHANGE DAPT



- 2,062 consecutive real-world ACS patients, treated by PCI.
- Higher NACCE (adj. HR 1.75; p=0.003) and major bleeding risks during Ticagrelor period (adj. HR 2.75; p=0.01) than during Clopidogrel period.

Key Message: The guideline-recommended ticagrelor-based primary DAPT regimen was associated with an increased event risk in consecutive ACS patients treated with newer-generation DES.



EuroIntervention 2017;13-online publish

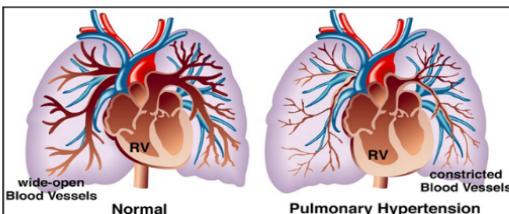
Aims: Acute coronary syndrome (ACS) guidelines have been changed, favouring more potent antiplatelet drugs. We aimed to evaluate the safety and efficacy of a ticagrelor- instead of a clopidogrel-based primary dual antiplatelet (DAPT) regimen in ACS patients treated with newer-generation drug-eluting stents (DES).

Methods and results: CHANGE DAPT (clinicaltrials.gov: NCT03197298) assessed 2,062 consecutive real-world ACS patients, treated by percutaneous coronary intervention (PCI), the primary composite endpoint being net adverse clinical and cerebral events (NACCE: all-cause death, any myocardial infarction, stroke or major bleeding). In the clopidogrel (CP; December 2012-April 2014) and ticagrelor periods (TP; May 2014-August 2015), 1,009 and 1,053 patients were treated, respectively. TP patients were somewhat older, underwent fewer transfemoral procedures, and received fewer glycoprotein IIb/IIIa inhibitors. In the TP, the one-year NACCE rate was higher (5.1% vs. 7.8%; HR 1.53 [95% CI: 1.08-2.17]; p=0.02). Assessment of non-inferiority (pre-specified margin: 2.7%) was inconclusive (risk difference: 2.64 [95% CI: 0.52-4.77]; non-inferiority=0.48). TP patients had more major bleeding (1.2% vs. 2.7%; p=0.02) while there was no benefit in ischaemic endpoints. Propensity score-adjusted multivariate analysis confirmed higher NACCE (adj. HR 1.75 [95% CI: 1.20-2.55]; p=0.003) and major bleeding risks during TP (adj. HR 2.75 [95% CI: 1.34-5.61]; p=0.01).

Conclusions: In this observational study, the guideline-recommended ticagrelor-based primary DAPT regimen was associated with an increased event risk in consecutive ACS patients treated with newer-generation DES

18. Pulmonary arterial hypertension treatment with carvedilol for heart failure PAHTCH Trial

Pulmonary arterial hypertension treatment with carvedilol for heart failure PAHTCH Trial



- Carvedilol-treated groups had no decrease in exercise capacity measured by 6-minute walk
- Also had lower heart rates at peak and after exercise, and faster heart rate recovery.
- Dose-escalating carvedilol was associated with reduction in right ventricular (RV) glycolytic rate and increase in β AR levels.

Carvedilol is likely safe in PAH over 6 months of therapy and has clinical and mechanistic benefits associated with improved outcomes



JCI Insight. 2017;2(16):e95240.

BACKGROUND. Right-sided heart failure is the leading cause of death in pulmonary arterial hypertension (PAH). Similar to left heart failure, sympathetic overactivation and β -adrenoreceptor (β AR) abnormalities are found in PAH. Based on successful therapy of left heart failure with β -blockade, the safety and benefits of the nonselective β -blocker/vasodilator carvedilol were evaluated in PAH.

METHODS. PAH Treatment with Carvedilol for Heart Failure (PAHTCH) is a single-center, doubleblind, randomized, controlled trial. Following 1-week run-in, 30 participants were randomized to 1 of 3 arms for 24 weeks: placebo, low-fixed-dose, or dose-escalating carvedilol. Outcomes included clinical measures and mechanistic biomarkers.

RESULTS. Decreases in heart rate and blood pressure with carvedilol were well tolerated; heart rate correlated with carvedilol dose. Carvedilol-treated groups had no decrease in exercise capacity measured by 6-minute walk, but had lower heart rates at peak and after exercise, and faster heart rate recovery. Dose-escalating carvedilol was associated with reduction in right ventricular (RV) glycolytic rate and increase in β AR levels. There was no evidence of RV functional deterioration; rather, cardiac output was maintained.

CONCLUSIONS. Carvedilol is likely safe in PAH over 6 months of therapy and has clinical and mechanistic benefits associated with improved outcomes. The data provide support for longer and larger studies to establish guidelines for use of β -blockers in PAH.

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