



Issue 10, September'18

A state of the HEART Update

A monthly cardiology news



STATE OF THE HEART



Dear Reader,

We are grateful to present you the 10th 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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1. ADDITIONAL BENEFIT OF REDUCTION IN CV EVENTS BY LOWERING ALREADY LOW LDLc

Additional Benefit of Reduction in CV events by Lowering Already Low LDLc

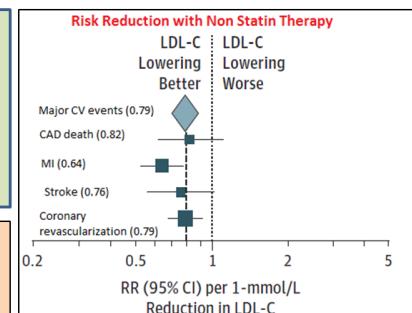
Meta analysis (> 50,000 patients of Non statin therapy)

Inclusion: Randomized, double-blind, controlled CV outcome trial of patients with mean baseline LDL-C levels of 65.7 mg/dL or less

- ❖ Statin data - Cholesterol Treatment Trialists Collaboration &
- ❖ Nonstatin data - Medline database (2015-April 2018)

Results

- Nonstatin therapy added to a statin lowered LDL-C by 11 mg/dL to 45 mg/dL
- 21% RR reduction for major vascular events per 38.7 mg/dL  in LDL-C.
- No increase risk of serious adverse events



Sabatine et al. JAMA Cardiol.
2018.(online), E1-E6



RR= Relative Risk

Further lowering of low-density lipoprotein (LDL) cholesterol (LDL-C) levels in patients with already low LDL-C produced benefit in terms of reduced risk for major vascular events with no serious adverse effects



Importance In the Cholesterol Treatment Trialists Collaboration (CTTC), in patients starting with low-density lipoprotein cholesterol (LDL-C) levels of approximately 131.5 mg/dL, there was a 22% reduction in major vascular events per 38.7-mg/dL lowering of LDL-C. The magnitude of clinical benefit of further LDL-C lowering in patients already with very low LDL-C levels remains debated.

Objective To evaluate efficacy and safety of further lowering LDL-C levels in patient populations presenting with median LDL-C levels of 70 mg/dL or less.

Data Sources and Study Selection The CTTC was used for statin data. For nonstatin therapy, Medline database was searched (2015-April 2018). Key inclusion criteria were a randomized, double-blind, controlled cardiovascular outcome trial of LDL-C lowering with data in populations starting with LDL-C levels averaging ≤ 70 mg/dL.

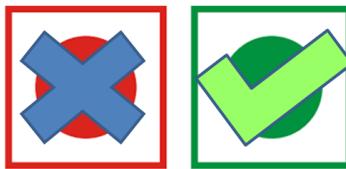
Main Outcomes and Measures The risk ratio (RR) of major vascular events (a composite of coronary heart death, myocardial infarction, ischemic stroke, or coronary revascularization) per 38.7-mg/dL reduction in LDL-C level.

Results In the subgroup of patients from the CTTC meta-analysis of statins with a mean LDL-C in the control arm of 65.7 mg/dL, 1922 major vascular events occurred and the RR for major vascular events per 38.7-mg/dL reduction in LDL-C was 0.78 (95% CI, 0.65-0.94). For 3 trials of nonstatin LDL-C-lowering therapies added to statins, there were 50,627 patients, the median LDL-C in the control arms ranged from 63 mg/dL to 70 mg/dL, and 9570 major vascular events occurred. Nonstatin therapy lowered LDL-C by 11 mg/dL to 45 mg/dL, and the RR for major vascular events per 38.7-mg/dL reduction in LDL-C was 0.79 (95% CI, 0.70-0.88). For statins and nonstatins combined, the RR was 0.79 (95% CI, 0.71-0.87; $P < .001$). *LDLc lowering was not associated with an increased risk of serious adverse events, myalgias and/or myositis, elevation in the level of aminotransferases, new-onset diabetes, hemorrhagic stroke, or cancer.*

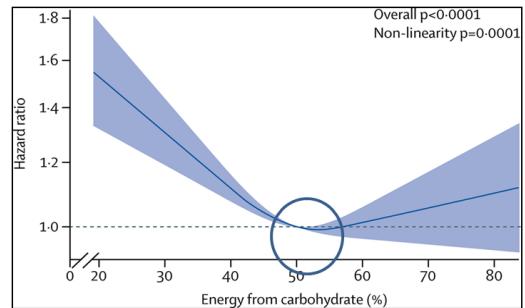
“FURTHER LOWERING OF LDL-C BEYOND THE LOWEST CURRENT TARGETS IS ASSOCIATED WITH FURTHER REDUCED CARDIOVASCULAR RISK WITH NO OFFSETTING SAFETY RISKS.”

2. MODERATION IS KEY FOR CARBS IN LONG-TERM HEALTH

Moderation Is Key for Carbs in Long-term Health



Prospective cohort study and Meta-analysis
15,428 people & 25 years of follow up



Lancet Public Health. 2018 Aug 16.
doi: 10.1016/S2468-2667(18)30135-X



- ❖ 50–55% carbohydrate intake → Lowest Risk
- ❖ High and low percentages of carbohydrate intake- Increased mortality.
- ❖ Plant-derived protein and fat intake (i.e. vegetables, nuts, peanut butter and whole-grain breads) were associated with lower mortality compared to animal sources (i.e. beef, pork and chicken)

Background Low carbohydrate diets, which restrict carbohydrate in favour of increased protein or fat intake, or both, are a popular weight-loss strategy. However, the long-term effect of carbohydrate restriction on mortality is controversial and could depend on whether dietary carbohydrate is replaced by plant-based or animal-based fat and protein. Study aimed to investigate the association between carbohydrate intake and mortality.

Methods Studied 15, 428 adults aged 45–64 years, in four US communities, who completed a dietary questionnaire at enrolment in the Atherosclerosis Risk in Communities (ARIC) study (between 1987 and 1989), and who did not report extreme caloric intake (4200 kcal per day for men and 3600 kcal per day for women). The primary outcome was all-cause mortality. Study investigated the association between the percentage of energy from carbohydrate intake and all-cause mortality, accounting for possible non-linear relationships in this cohort. In this, further examined the association, combining ARIC data with data for carbohydrate intake reported from seven multinational prospective studies in a meta-analysis. Finally, Investigator assessed whether the substitution of animal or plant sources of fat and protein for carbohydrate affected mortality.

Findings Median follow-up of 25 years, 6283 deaths in the ARIC cohort, and 40 181 deaths across all cohort studies. In the ARIC cohort, after multivariable adjustment, there was a U-shaped association between the percentage of energy consumed from carbohydrate (mean 48·9%, SD 9·4) and mortality: a percentage of 50–55% energy from carbohydrate was associated with the lowest risk of mortality. Results varied by the source of macronutrients: mortality increased when carbohydrates were exchanged for animal-derived fat or protein (1·18, 1·08–1·29) and mortality decreased when the substitutions were plant-based (0·82, 0·78–0·87).

“Restrict carbohydrate intake to 50-55% to reduce risk. Plant-derived protein and fat intake (i.e. vegetables, nuts, peanut butter and whole-grain breads) were associated with lower mortality compared to animal sources (i.e. beef, pork and chicken)”

3. LIMIT LOW-CALORIE SODAS AND DRINKS - STICK TO WATER INSTEAD; AHA HEALTH ADVISORY

Limit low-calorie sodas and drinks - stick to water instead; AHA Health Advisory

Health Advisory on Cardio-metabolic Health

Low-calorie sweetened drinks are associated with weight gain, dementia, stroke and other cardio-metabolic health problems

Recommendation by Committee of nutritionists, doctors and researchers who spent **2 years** and reviewed **> 12 studies**

Replace sugary and diet drinks with plain, carbonated or unsweetened flavored water for better cardio-metabolic health



Circulation. 2018;138:00–00. DOI: 10.1161/CIR.0000000000000569

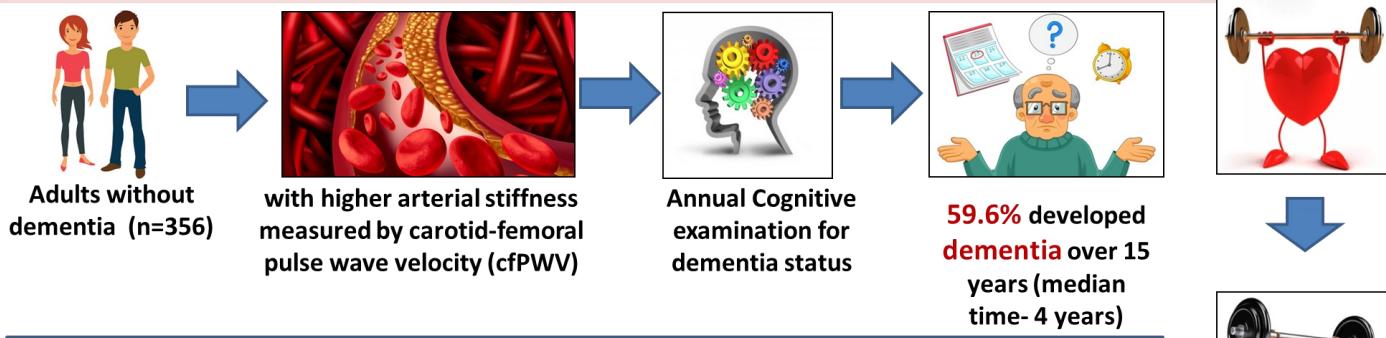
In the United States, 32% of beverages consumed by adults and 19% of beverages consumed by children in 2007 to 2010 contained low-calorie sweeteners (LCSs). Among all foods and beverages containing LCSs, beverages represent the largest proportion of LCS consumption worldwide. The term LCS includes the 6 high-intensity sweeteners currently approved by the US FDA and 2 additional high-intensity sweeteners for which the US FDA has issued no objection letters. This advisory reviews evidence from observational studies and clinical trials assessing the cardiometabolic outcomes of LCS beverages. It summarizes the positions of government agencies and other health organizations on LCS beverages and identifies research needs on the effects of LCS beverages on energy balance and cardiometabolic health.

The use of LCS beverages may be an effective strategy to help control energy intake and promote weight loss. Nonetheless, there is a dearth of evidence on the potential adverse effects of LCS beverages relative to potential benefits. On the basis of the available evidence, the writing group concluded that, at this time, it is prudent to advise against prolonged consumption of LCS beverages by children. (Although water is the optimal beverage choice, children with diabetes mellitus who consume a balanced diet and closely monitor their blood glucose may be able to prevent excessive glucose excursions by substituting LCS beverages for sugar-sweetened beverages [SSBs] when needed.) For adults who are habitually high consumers of SSBs, the writing group concluded that LCS beverages may be a useful replacement strategy to reduce intake of SSBs. This approach may be particularly helpful for persons who are habituated to a sweet-tasting beverage and for whom water, at least initially, is an undesirable option. It is feasible to reduce SSB intake without necessarily substituting LCS beverages for SSBs. Thus, the use of other alternatives to SSBs, with a focus on water (plain, carbonated, and unsweetened flavored), should be encouraged.

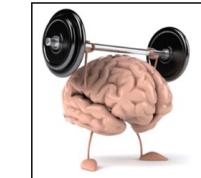
“REPLACE SUGARY AND DIET DRINKS WITH PLAIN, CARBONATED OR UNSWEETENED WATER FOR BETTER CARDIOMETABOLIC HEALTH.”

4. HEALTHY HEART -HEALTHY BRAIN

Healthy Heart -Healthy Brain



Lower physical activity, higher systolic blood pressure, increased heart rate, and higher waist circumference measured about 5 years before cfPWV measurement were significantly associated with greater arterial stiffness.



Conclusion: Preventive interventions directed at risk factors may lower dementia risk by reducing arterial stiffness

Alzheimer's Association International Conference (AAIC) 2018. Abstract 25170. Presented July 24, 2018.



Background: Arterial stiffness occurs with aging and is associated with cognitive decline, cerebral small-vessel arteriosclerotic disease, and brain amyloid deposition and therefore may predict incident dementia.

Methods: Study was carried out in 356 CHS-CS participants (59% women) without dementia at baseline (1998 - 1999) who had annual cognitive exams through 2013 and cfPWV measured between 1996 and 2000.

Results: Participants had a mean age of 78 years at baseline. Of the 356 participants, 212 (59.6%) developed dementia over 15 years. The median time to dementia onset was 4 years. Lower physical activity intensity and higher systolic blood pressure, heart rate, and waist circumference measured about 5 years before cfPWV measurement were significantly associated with greater arterial stiffness.

Conclusion: This suggests that preventive interventions directed at these risk factors may lower dementia risk by reducing arterial stiffness. These findings "fit in with the whole concept of heart health being tied to brain health makes sense, "The brain is hungry for oxygen and nutrients, which involve the cardiovascular system and having healthy blood vessels to bring oxygen and nutrients to brain cells that need them so much. If anything is happening to compromise the cardiovascular system, it seems fairly obvious that it's going to compromise the brain."

"The brain is hungry for oxygen and nutrients, which involve the cardiovascular system and having healthy blood vessels to bring oxygen and nutrients to brain cells that need them so much. If anything is happening to compromise the cardiovascular system, it seems fairly obvious that it's going to compromise the brain."



5. TOO MUCH SLEEP (>8 HOURS) COULD BE WORSE FOR HEALTH THAN TOO LITTLE

Too much sleep (>8 hours) could be worse for health than too little



Meta-analysis (>3 million people)



Sleeping for **9 hours** → carries a **14 percent higher risk of death**

Sleeping for **10 hour** → carries a **30 percent higher risk of death**

Sleep of **Poor-quality** → carries a **44 percent higher risk of CHD**



- Duration of **sleep >8 hours** was associated with **increased risk of mortality**
- No significant effect was identified for periods of sleep < 7 hours

Conclusion
Attention to **optimizing the duration and quality of sleep** may help reduce the burden of cardiovascular disease



J Am Heart Assoc. 2018;7:e008552. DOI: 10.1161/JAHA.118.008552

Background: There is growing evidence that sleep duration and quality may be associated with cardiovascular harm and mortality.

Methods: Investigators conducted a systematic review, meta-analysis, and spline analysis of prospective cohort studies that evaluate the association between sleep duration and quality and cardiovascular outcomes. Investigators searched MEDLINE and EMBASE for these studies and extracted data from identified studies. Investigators utilized linear and nonlinear dose-response meta-analysis models and used DerSimonian–Laird random-effects meta-analysis models of risk ratios, with inverse variance weighting, and the I² statistic to quantify heterogeneity.

Results: Seventy-four studies including 3 340 684 participants with 242 240 deaths among 2 564 029 participants who reported death events were reviewed. Findings were broadly similar across both linear and nonlinear dose-response models in 30 studies with >1 000 000 participants, and reported results from the linear model. Self-reported duration of sleep >8 hours was associated with a moderate increased risk of all-cause mortality, with risk ratio, 1.14 (1.05–1.25) for 9 hours, risk ratio, 1.30 (1.19–1.42) for 10 hours, and risk ratio, 1.47 (1.33–1.64) for 11 hours. No significant difference was identified for periods of self reported sleep . No significant effect was identified for periods of sleep.

Attention to optimizing the duration and quality of sleep may help in reducing the burden of cardiovascular disease.

**“DURATION
OF SLEEP
>8 HOURS
WAS
ASSOCIATED
WITH
INCREASED
RISK OF
MORTALITY.
”**

6. MORNING HYPERTENSION & DYSLIPIDEMIA: RISK FACTOR OF MACROVASCULAR EVENTS FOLLOWING CEREBRAL INFARCTION

Morning Hypertension & Dyslipidemia: Risk Factor of Macrovascular Events Following Cerebral Infarction

Variables	OR	OR 95% CI lower limit	HR 95% CI upper limit	P
Gender	0.733	0.496	1.084	.120
Morning hypertension	1.821	1.155	2.871	.010*
Diabetes	1.39	0.934	2.068	.104
Dyslipidemia	1.769	1.171	2.675	.007*



Morning hypertension & dyslipidemia:
Increase the risk of macrovascular events following cerebral infarction.

Improving morning blood pressure management and drug compliance (antithrombotic drugs and statins) may reduce the risk of macrovascular events following cerebral infarction

Medicine (Baltimore). 2018 Aug;97(34):e12013.



Aims and Objective: To investigate risk factors (such as morning hypertension, drug compliance, and biochemical parameters) of macrovascular events after cerebral infarction.

Methods: This was a retrospective study of patients with cerebral infarction admitted between May 2015 and April 2016 at the Fengxian Branch, 6th People's Hospital of Shanghai. They were divided into the macrovascular events and control groups according to the diagnosis of macrovascular events following cerebral infarction.

Results: Among the 702 patients included for analysis, 122 patients were with macrovascular events and 580 were without macrovascular events (controls). Morning hypertension ($P = .01$), dyslipidemia ($P = .007$), atrial fibrillation ($P = .039$), carotid artery plaque ($P = .014$), inflammatory infection ($P = .005$), high homocysteine ($P = .032$), antithrombotic compliance ($P < .001$), statins compliance ($P < .001$), morning diastolic blood pressure ($P < .001$), morning systolic blood pressure ($P < .001$), and morning heart rate (morHR) ($P = .033$) were associated with macrovascular events. Multivariable analysis showed that morning hypertension ($P = .021$, odds ratio [OR] = 1.753, 95% confidence interval [CI] [1.088, 2.826]), dyslipidemia ($P = .021$, OR = 1.708, 95% CI [1.085, 2.687]), and inflammatory infection ($P = .031$, OR = 2.263, 95% CI [1.078, 4.752]) were independent risk factors for macrovascular events, while antithrombotic compliance ($P < .001$, OR = 0.488, 95% CI [0.336, 0.709]), statin compliance ($P = .02$, OR = 0.64, 95% CI [0.44, 0.931]), and morHR ($P = .027$, OR = 0.977, 95% CI [0.958, 0.997]) were independent protective factors against macrovascular events. Atrial fibrillation showed a tendency to be associated with macrovascular events ($P = .077$, OR = 1.531, 95% CI [0.955, 2.454]).

“Improving morning blood pressure management and drug compliance (antithrombotic drugs and statins) may reduce the risk of macrovascular events following cerebral infarction.”

7. RISK PREDICTION MODEL FOR 1-YEAR MAJOR CARDIOVASCULAR EVENTS AFTER DISCHARGE FOR ACUTE MYOCARDIAL INFARCTION

Risk Prediction Model for 1-Year Major Cardiovascular Events After Discharge for Acute Myocardial Infarction

- The risk model and its corresponding risk scores (mentioned in table) allow clinicians to identify patients who are at heightened risk of 1-year cardiovascular events.
- Identifying the individuals with the highest risk of long-term cardiovascular events after AMI helps in targeted, intensive, and higher-quality longitudinal care following discharge.

Low risk (0-10)
Average risk (11-30)
High risk (≥ 31)

JAMA Network Open. 2018;1(4):e181079.
doi:10.1001/jamanetworkopen.2018.1079

Risk Factor	Training Data		
	Regression Coefficient	Hazard Ratio (95% CI)	Points ^a
Age, y			
65-74	0.773	2.17 (1.50-3.14)	6
75-84	1.223	3.40 (2.26-5.10)	9
≥ 85	1.906	6.73 (2.83-15.96)	14
No college degree	0.525	1.69 (1.00-2.86)	4
No prearrival medical assistance	0.462	1.59 (1.12-2.26)	3
Prior angina	0.716	2.05 (1.17-3.58)	5
Prior acute myocardial infarction	0.494	1.64 (1.07-2.52)	4
Prior ventricular tachycardia or ventricular fibrillation	0.767	2.15 (0.99-4.70)	6
Hypertension	0.267	1.31 (0.94-1.81)	2
Symptoms to admission >4 h	0.360	1.43 (1.03-2.00)	3
Renal dysfunction (blood urea nitrogen >40 mg/dL or creatinine >2.5 mg/dL)	0.487	1.63 (1.18-2.25)	4
Ejection fraction value			
<40%	1.051	2.86 (1.89-4.34)	8
Unmeasured	0.737	2.09 (1.43-3.06)	6
White blood cell count			
6000/ μ L-12 000/ μ L	0.493	1.64 (1.08-2.47)	4
$>12 000/\mu\text{L}$	0.975	2.65 (1.53-4.61)	7
Fasting blood glucose >216 mg/dL	0.599	1.82 (1.13-2.93)	5
Heart rate >90 beats/min	0.702	2.02 (1.43-2.84)	5
Systolic blood pressure <100 mm Hg	0.529	1.70 (1.05-2.74)	4
Each in-hospital complication	0.213	1.24 (1.09-1.40)	2

Objectives: To identify risk factors and develop and evaluate a risk model that predicts 1-year cardiovascular events after AMI.

Design, Setting, and Participants : Prospective cohort study. Patients with AMI (n = 4227), aged 18 years or older, discharged alive from 53 acute-care hospitals across China from January 1, 2013, to July 17, 2014. Patients were randomly divided into samples: training (50% [2113 patients]), test (25% [1057 patients]), and validation (25% [1057 patients]). Risk factors were identified by a Cox model with Markov chain Monte Carlo simulation and further evaluated by latent class analysis. Analyses were conducted from May 1, 2017, to January 21, 2018.

Main Outcomes and Measures: Major cardiovascular events, including recurrent AMI, stroke, heart failure, and death, within 1 year after discharge for the index AMI hospitalization.

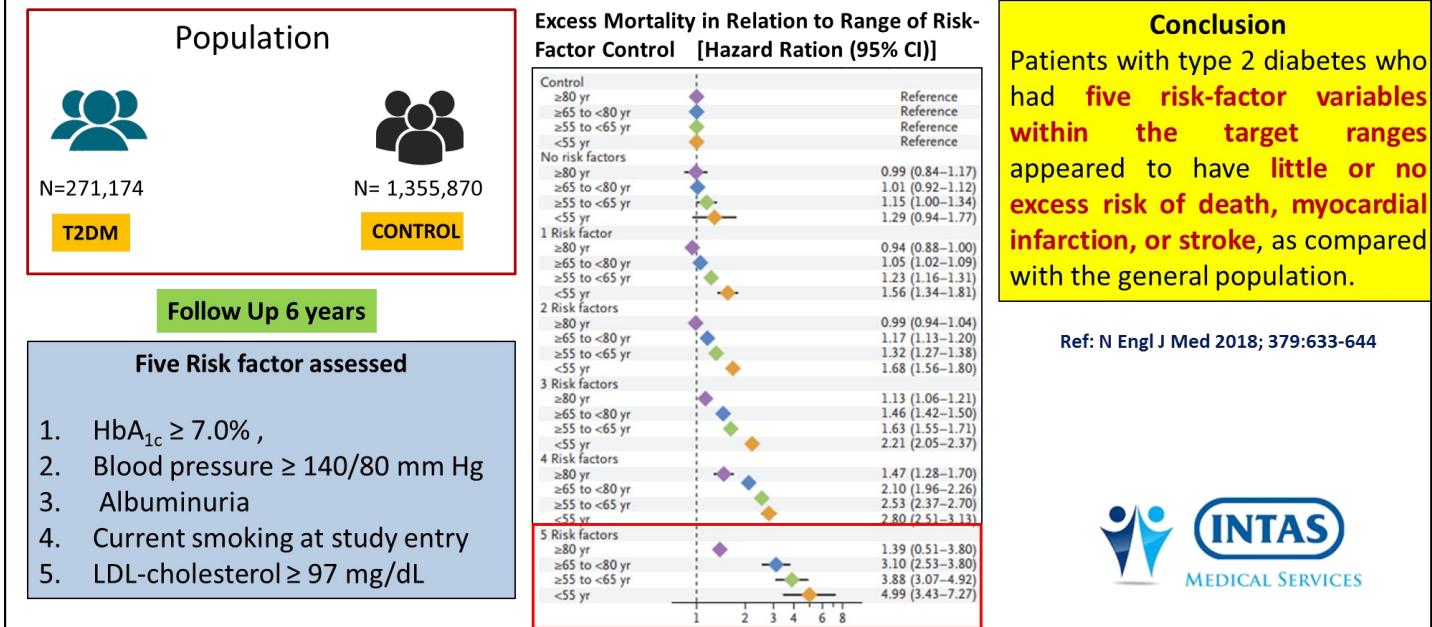
Results The mean (SD) age of the cohort was 60.8 (11.8) years and 994 of 4227 patients (23.5%) were female. Common comorbidities included hypertension (2358 patients [55.8%]), coronary heart disease (1798 patients [42.5%]), and dyslipidemia (1290 patients [30.5%]). One-year event rates were 8.1% (95% CI, 6.91%-9.24%), 9.0% (95% CI, 7.22%-10.70%), and 6.4% (95% CI, 4.89%-7.85%) for the training, test, and validation samples, respectively. Nineteen risk factors comprising 15 unique variables (age, education, prior AMI, prior ventricular tachycardia or fibrillation, hypertension, angina, prearrival medical assistance, >4 hours from onset of symptoms to admission, ejection fraction, renal dysfunction, heart rate, systolic blood pressure, white blood cell count, blood glucose, and in-hospital complications) were identified. In the training, test, and validation samples, respectively, the risk model had C statistics of 0.79 (95% CI, 0.75-0.83), 0.73 (95% CI, 0.68-0.78), and 0.77 (95% CI, 0.70-0.83) and a predictive range of 1.2% to 33.9%, 1.2% to 37.9%, and 1.3% to 34.3%. The C statistic was 0.69 (95% CI, 0.65-0.74) for the latent class model in the training data. The risk model stratified 11.3%, 81.0%, and 7.7% of patients to high-, average-, and low-risk

“NINETEEN RISK FACTORS BASE MODEL HELPS CLINICIANS IN IDENTIFYING HIGH-RISK PATIENTS WHO WOULD BENEFIT MOST FROM INTENSIVE FOLLOW-UP AND AGGRESSIVE RISK FACTOR REDUCTION”



8. RISK FACTOR REDUCTION CUTS EXCESS CV RISK IN DIABETES

Risk Factor Reduction Cuts Excess CV Risk in Diabetes



Conclusion

Patients with type 2 diabetes who had **five risk-factor variables within the target ranges** appeared to have **little or no excess risk of death, myocardial infarction, or stroke**, as compared with the general population.

Ref: N Engl J Med 2018; 379:633-644



BACKGROUND: Patients with diabetes are at higher risk for death and cardiovascular outcomes than the general population. We investigated whether the excess risk of death and cardiovascular events among patients with type 2 diabetes could be reduced or eliminated.

METHODS: In a cohort study, we included 271,174 patients with type 2 diabetes who were registered in the Swedish National Diabetes Register and matched them with 1,355,870 controls on the basis of age, sex, and county. We assessed patients with diabetes according to age categories and according to the presence of five risk factors (elevated glycated hemoglobin level, elevated low-density lipoprotein cholesterol level, albuminuria, smoking, and elevated blood pressure). Cox regression was used to study the excess risk of outcomes (death, acute myocardial infarction, stroke, and hospitalization for heart failure) associated with smoking and the number of variables outside target ranges. We also examined the relationship between various risk factors and cardiovascular outcomes.

RESULTS: The median follow-up among all the study participants was 5.7 years, during which 175,345 deaths occurred. Among patients with T2DM, the excess risk of outcomes decreased stepwise for each risk-factor variable within the target range. Among patients with diabetes who had all five variables within target ranges, the hazard ratio for death from any cause, as compared with controls, was 1.06 (95% confidence interval [CI], 1.00 to 1.12), the hazard ratio for acute myocardial infarction was 0.84 (95% CI, 0.75 to 0.93), and the hazard ratio for stroke was 0.95 (95% CI, 0.84 to 1.07). The risk of hospitalization for heart failure was consistently higher among patients with diabetes than among controls (hazard ratio, 1.45; 95% CI, 1.34 to 1.57). In patients with type 2 diabetes, a glycated hemoglobin level outside the target range was the strongest predictor of stroke and acute myocardial infarction; smoking was the strongest predictor of death.

"Patients with T2DM who had five risk-factor variables within the target ranges appeared to have little or no excess risk of death, myocardial infarction, or stroke, as compared with the general population"

9. CT ANGIOGRAPHY LINKED TO LESS DEATH, NONFATAL MI IN STABLE CHEST PAIN: SCOT-HEART TRIAL

CT Angiography Linked to Less Death, Nonfatal MI in Stable Chest Pain: SCOT-HEART Trial

>4000 patients with stable chest pain

Randomization

CTCA plus standard care (N=2073) or

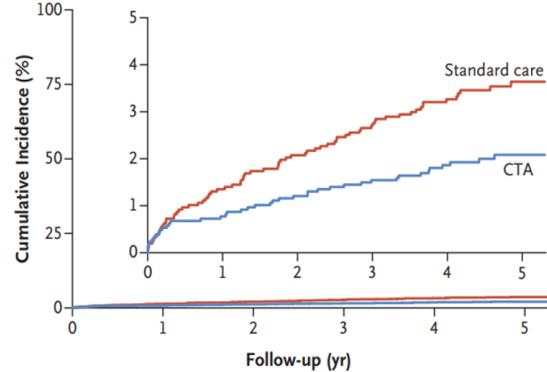
Standard care alone (N=2073)

Followed up for 5 years

Results

Performing CTCA during diagnostic testing was associated with a 41% reduction in the combined primary endpoint: rates of death from CHD and nonfatal MI.

Conclusion :Use of CTA in addition to standard care in patients with stable chest pain significantly lowers the rate of death from coronary heart disease or nonfatal myocardial infarction at 5 years, without resulting in a significantly higher rate of coronary angiography or coronary revascularization.



N engl j med, Aug 2018. DOI: 10.1056/NEJMoa1805971



BACKGROUND: Although coronary computed tomographic angiography (CTA) improves diagnostic certainty in the assessment of patients with stable chest pain, its effect on 5-year clinical outcomes is unknown.

METHODS: In an open-label, multicenter, parallel-group trial, we randomly assigned 4146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2073 patients) or to standard care alone (2073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow-up. The primary end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.

RESULTS: The median duration of follow-up was 4.8 years, which yielded 20,254 patient years of follow-up. The 5-year rate of the primary end point was lower in the CTA group than in the standard-care group (2.3% [48 patients] vs. 3.9% [81 patients]; hazard ratio, 0.59; 95% confidence interval [CI], 0.41 to 0.84; $P=0.004$). Although the rates of invasive coronary angiography and coronary revascularization were higher in the CTA group than in the standard-care group in the first few months of follow-up, overall rates were similar at 5 years: invasive coronary angiography was performed in 491 patients in the CTA group and in 502 patients in the standard-care group (hazard ratio, 1.00; 95% CI, 0.88 to 1.13), and coronary revascularization was performed in 279 patients in the CTA group and in 267 in the standard-care group (hazard ratio, 1.07; 95% CI, 0.91 to 1.27). However, more preventive therapies were initiated in patients in the CTA group (odds ratio, 1.40; 95% CI, 1.19 to 1.65), as were more anti-anginal therapies (odds ratio, 1.27; 95% CI, 1.05 to 1.54). There were no significant between-group differences in the rates of cardiovascular or non-cardiovascular deaths or deaths from any cause.

"USE OF CTA IN ADDITION TO STANDARD CARE IN PATIENTS WITH STABLE CHEST PAIN RESULTED IN A SIGNIFICANTLY LOWER RATE OF DEATH FROM CORONARY HEART DISEASE OR NONFATAL MI AT 5 YEARS, WITHOUT RESULTING IN A SIGNIFICANTLY HIGHER RATE OF CORONARY ANGIOGRAPHY OR CORONARY REVASCULARIZATION."

10. STATIN REDUCES THE RISK OF DEMENTIA: ANOTHER EVIDENCE IN

Statin Reduces The Risk of Dementia: Another Evidence in Patients with Stroke

**14,807 patients of Stroke
(A Nationwide Population-Based Cohort Study)**

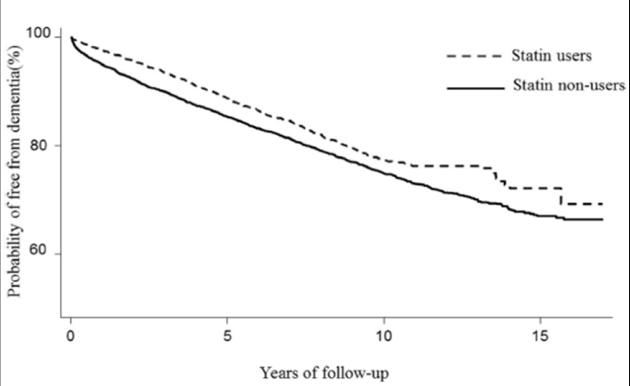
Group 1 Statin User (n=4724)	Propensity Score Matched	Group 2 Statin Non-User (n=4724)
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Results

- Median follow up 7.5 years
- 17% lower risk of dementia** compared to non-statin use

J Stroke Cerebrovasc Dis. 2018 Aug 4.
DOI: 10.1016/j.jstrokecerebrovasdis.2018.06.036.





The graph plots the probability of being free from dementia (%) against the number of years of follow-up. The x-axis ranges from 0 to 15 years, and the y-axis ranges from 60% to 100%. The Statin non-user group (solid line) shows a significantly steeper decline in probability of dementia compared to the Statin user group (dashed line), indicating a higher risk of dementia over time.

Conclusion

Statin use is associated with decreased risk of dementia in patients with stroke. High-potency and prolonged exposure to statins resulted in greater benefit.

Background: Patients with stroke have an increased risk of dementia. Some studies have found that statin use might lower the risk of incident of dementia; however, there is still a lack of data from patients with stroke. Therefore, the aim of this study was to investigate the impact of statin use on the risk of dementia in patients with stroke.

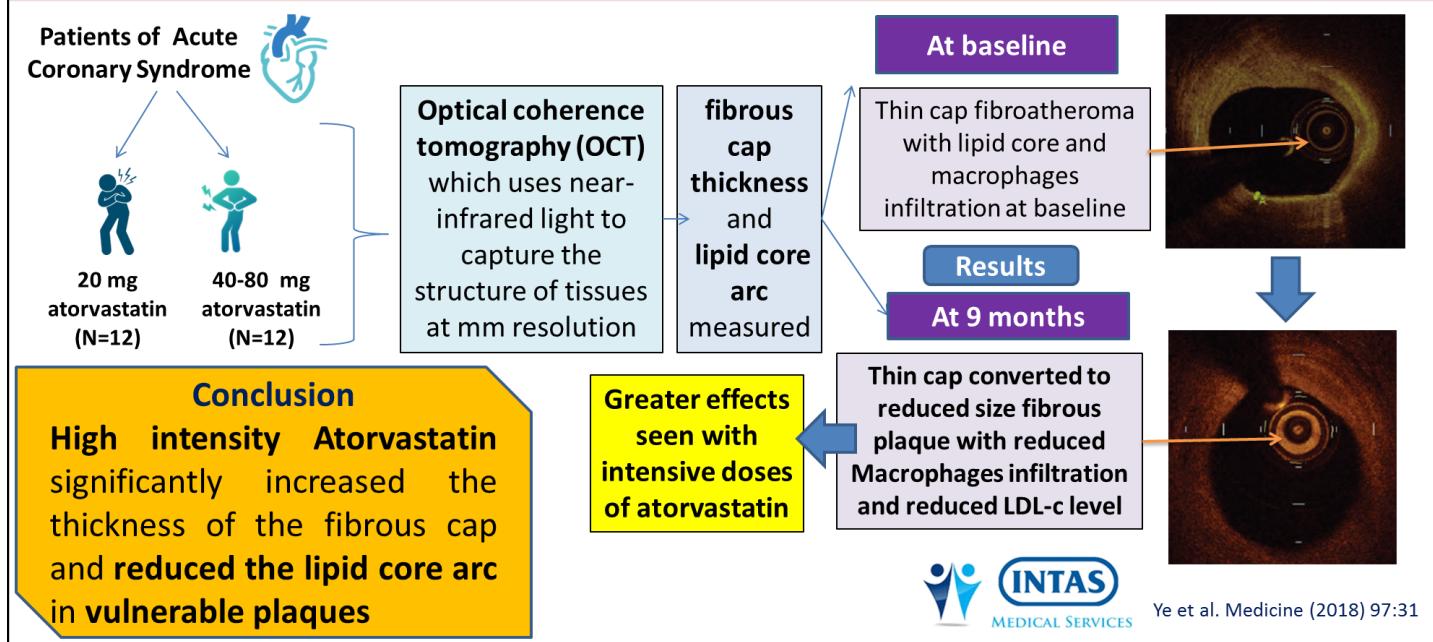
Methods: Investigator used the National Health Insurance Research Database in Taiwan to identify patients diagnosed with stroke from 1997 to 2005. These patients were classified as statin users and nonusers. Propensity score matching was performed to balance selected confounders between the statin users and nonusers. Cox-proportional hazard regression models were used to evaluate the association between statin use and the risk of dementia.

Results: Total 14,807 patients identified with stroke. After propensity score matching, 4724 pairs of statin users and nonusers with comparable age, sex, and comorbidities were used in the analysis of the relationship between risk of dementia and statin use. During the median follow-up period of 7.5 years 1895 patients were diagnosed with incident of dementia. Statin use was associated with a significantly lower incidence of dementia (adjusted hazard ratio, .81; 95% confidence interval, .73-.89) than non user. In particular, lipophilic and high-potency statins were associated with lower risk of dementia. Statin exposure duration was inversely related to the risk of dementia ($P < .001$ for the trend). No significant effect modification for the relationship between statin use and the risk of dementia was found for the age or sex. The potency, solubility, and cumulative duration of statin use were major factors in the reduction of dementia risk.

"Statin use was associated with decreased risk of dementia among patients with stroke. The use of high potency statins, lipophilic statins, and prolonged exposure to statins may be associated with greater benefits."

11. EFFECTS OF ATORVASTATIN ON VULNERABLE PLAQUES: HIGHER IS BETTER

Effects of Atorvastatin on vulnerable plaques: Higher is Better



Aim:

To evaluate optical coherence tomography (OCT) as an assessment of the efficacy of atorvastatin treatment.

Methods:

Twenty-four acute coronary syndrome (ACS) patients were allocated to conventional-dose (20mg atorvastatin, n=12) and intensive-dose (40–80mg atorvastatin, n=12) groups and correlations between changes in the OCT measurements and blood routine indexes were analyzed 9 months post-percutaneous coronary intervention (PCI).

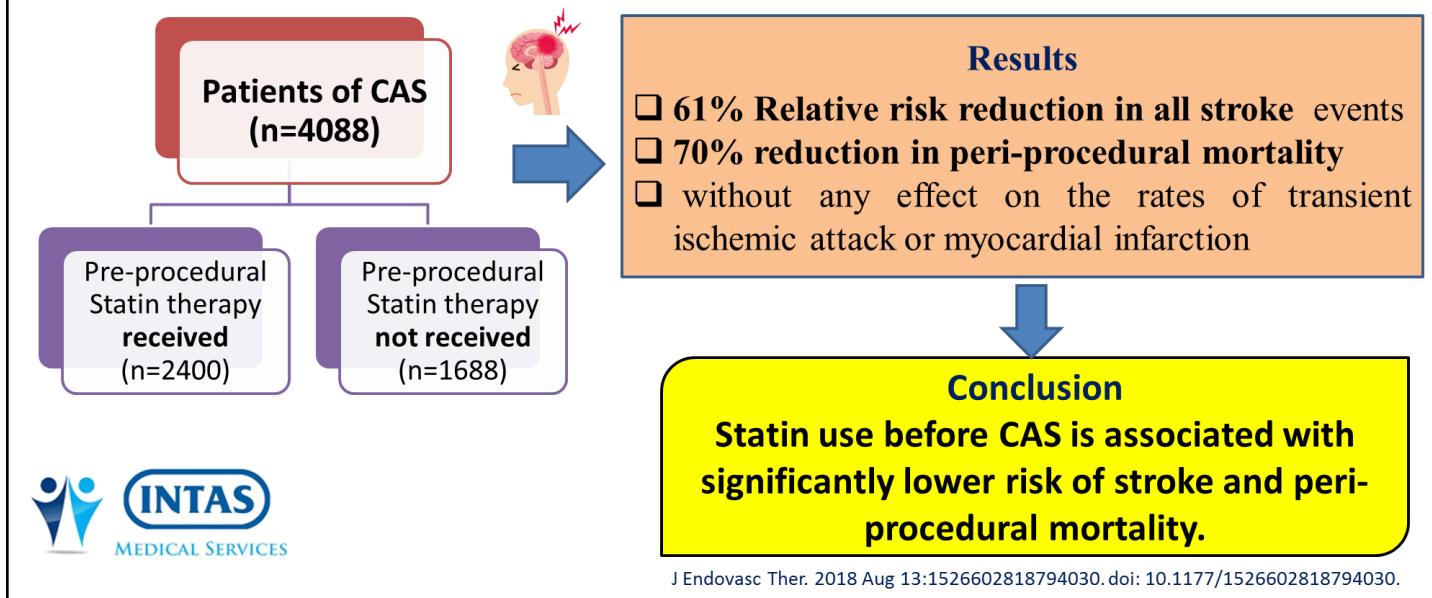
Results:

Treatment with atorvastatin resulted in a significant increase in the target thin cap fibroatheroma (TCFA) fibrous cap thicknesses in both groups. The increase was bigger in the intensive-dose group than in the conventional-dose group (184.1 ± 57.4 mm vs. 125.1 ± 28.6 , P=.005). The TCFA lipid core arc in both groups was significantly decreased compared with baseline (72.9 ± 29.3 vs. 127.6 ± 50.8 , P<.01 and 74.6 ± 32.9 vs. 132.6 ± 51.3 , P<.01, respectively). Correlation analyses showed an inverse relationship between low-density lipoprotein cholesterol (LDL-c) levels and the TCFA cap thickness, and a direct relationship between C-reactive protein (CRP) level and lipid core arc.

"STATINS SIGNIFICANTLY INCREASED THE TCFA FIBROUS CAP THICKNESS AND REDUCED THE LIPID CORE ARC, AND OCT MEASUREMENTS ACCURATELY REFLECTED THE LEVELS OF BLOOD LDL-C AND CRP"

12. STATIN THERAPY PRIOR TO CORONARY ARTERY STENTING (CAS) DECREASES THE RISK OF PERIOPERATIVE STROKE AND DEATH

Statin Therapy Prior to Coronary Artery Stenting (CAS) Decreases The Risk of Perioperative Stroke and Death: A Meta-analysis Report



Background: Carotid artery stenting (CAS), an alternative approach to carotid endarterectomy (CEA), was indicated for patients at high risk for surgery. Emerging endovascular technologies and increasing operator experience has improved CAS outcomes over time. On the other hand, CAS may be associated with higher periprocedural stroke rates. Statins have well-established lipid-lowering effects and have also been shown to reduce the incidence of primary and secondary stroke.

Purpose: To determine through meta-analysis whether administration of statins before carotid artery stenting (CAS) is associated with fewer periprocedural adverse events.

Methods: All randomized and observational English-language studies of periprocedural statin administration prior to CAS that reported the outcomes of interest (stroke, transient ischemic attack, myocardial infarction, and death at 30 days) were included in a random-effects meta-analysis. The I^2 statistic was used to assess heterogeneity. Meta-regression analysis was performed to determine whether an association of statin treatment with risk of outcome events was influenced by other trial-level baseline characteristics of statin-treated and untreated patients.

Results: Eleven studies comprising 4088 patients were included. Patients who received statins prior to CAS had a significantly lower risk of stroke (OR 0.39, 95% CI 0.27 to 0.58, $p<0.01$; $I^2=0\%$) and death (OR 0.30, 95% CI 0.10 to 0.96, $p=0.042$; $I^2=0\%$). Statin use was not associated with a reduced risk of transient ischemic attack or myocardial infarction. In meta-regression analysis, other trial-level baseline characteristics had no significant influence on the association of statin treatment with death or stroke.

"Statin therapy prior to CAS is associated with decreased risk of perioperative stroke and death without any effect on the rates of transient ischemic attack or myocardial infarction."

13. LIPID-LOWERING THERAPY AND GOAL ACHIEVEMENT IN HIGH-RISK PATIENTS

Lipid-lowering Therapy and Goal Achievement in High-risk Patients



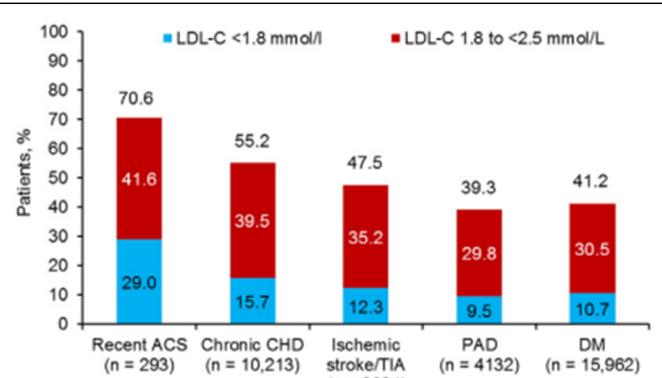
32,924 patients
With ASCVD and DM

Statin Prescribed
55.8% in ASCVD
34.3 % in DM



Achievement of LDL-C levels (<70 mg/dL)

Only **13.9%** for patients with **ASCVD** and
10.7% with **DM**.



Clin Ther. 2018 Aug 17.
doi: 10.1016/j.clinthera.2018.07.008.

Patients with ASCVD and/or DM: Low prescription of statin was associated with suboptimal LDL-C goal achievement relative to current guidelines

Purpose:

The goal of this study was to summarize patterns of lipid-lowering therapy (LLT) usage and achievement of guideline-identified lipid goals in a 2015 general practice cohort of French patients with atherosclerotic cardiovascular disease (ASCVD) and/or diabetes mellitus (DM).

Methods:

From the IMS Health Real-World Data database, patients aged 18 years were classified hierarchically into mutually exclusive categories of ASCVD subgroups and DM. LLT use and lipid goal achievement were assessed on the date of lipid measurement. The data were compared with previously published results of LLT use and lipid goal achievement in a 2014 UK population.

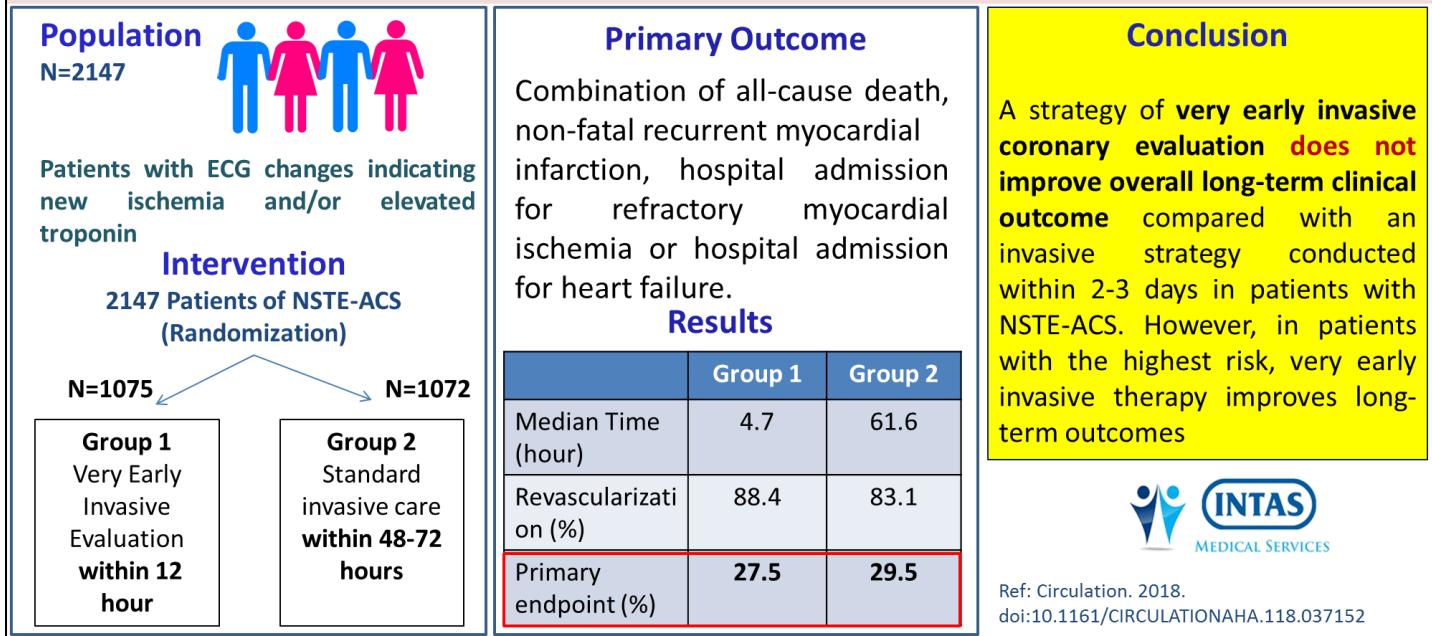
Findings:

Of 32,924 patients meeting the inclusion criteria, only 47.5% were prescribed a statin as of the index date. Hierarchically, the highest rates of use of any statin (73.3%) and high-intensity statins (43.3%) were among patients with recent acute coronary syndrome; rates in DM without ASCVD were 38.7% and 2.3%, respectively. Overall, achievement of LDL-C levels<1.8 mmol/L was higher in the 2014 UK population than in the 2015 French population (37.3% vs. 22.2%, and 36.8% vs. 20.3%, for ASCVD and DM).

"PATIENTS WITH ASCVD AND/OR DM: LOW PRESCRIPTION OF STATIN WAS ASSOCIATED WITH SUBOPTIMAL LDL-C GOAL ACHIEVEMENT RELATIVE TO CURRENT GUIDELINES"

14. NO ADVANTAGE OF EARLY INVASIVE STRATEGY IN NSTE-ACS

No Advantage of Early Invasive Strategy in NSTE-ACS



Background: The optimal timing of invasive coronary angiography (ICA) and revascularization in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is not well defined. We tested the hypothesis, that a strategy of very early invasive coronary angiography (ICA) and possible revascularization within 12 hours of diagnosis, is superior to an invasive strategy performed within 48-72 hours in terms of clinical outcomes.

Methods: Patients admitted with clinical suspicion of NSTE-ACS in the Capital Region of Copenhagen, Denmark were screened for inclusion in the VERDICT trial. Patients with ECG changes indicating new ischemia and/or elevated troponin, in whom ICA was clinically indicated and deemed logistically feasible within 12 hours, were randomized 1:1 to ICA within 12 hours or standard invasive care within 48-72 hours. The primary endpoint was a combination of all-cause death, non-fatal recurrent myocardial infarction, hospital admission for refractory myocardial ischemia or hospital admission for heart failure.

Results: A total of 2147 patients were randomized; 1075 patients allocated to very early invasive evaluation had ICA performed at a median of 4.7 hours after randomization, whereas 1072 patients assigned to standard invasive care had ICA performed 61.6 hours after randomization. Among patients with significant coronary artery disease identified by ICA, coronary revascularization was performed in 88.4% (very early ICA) and 83.1% (standard invasive care) of the patients. Within a median follow-up time of 4.3 (IQR 4.1-4.4) years the primary endpoint occurred in 296 (27.5%) of participants in the very early ICA group and 316 (29.5%) in the standard care group (HR 0.92 [CI95 0.78-1.08]). Among patients with a GRACE risk score >140, a very early invasive treatment strategy improved the primary outcome compared with the standard invasive treatment (HR 0.81 95% CI 0.67-1.01, p-value for interaction = 0.023).

"A strategy of very early invasive coronary evaluation does not improve overall long-term clinical outcome compared with an invasive strategy conducted within 2-3 days in patients with NSTE-ACS. In patients with the highest risk, very early invasive therapy improves long-term outcomes"

15. LONG TERM STATIN THERAPY IS SAFE AND EFFICACIOUS IN CHILDREN WITH FAMILIAL HYPERCHOLESTEROLEMIA

Long Term Statin Therapy is Safe and Efficacious in Children with Familial Hypercholesterolemia



N=131

Children with Familial Hypercholesterolemia



Follow up

4 year and 2 months



Outcome Measures

1. Decrease in LDLc
2. Percentage of Patients received target of LDLc < 160 mg/dL
3. Adverse events

Conclusion

This large cohort confirm the long-term safety and efficacy of statin therapy in children with familial hypercholesterolemia

Results

Mean decrease in LDLc -32%

Target LDLc achieved in 67% of patients

Height, weight and sexual growth not affected

No major side effects

Ref. Abstract MON-P354, Clinical Nutrition 37 (2018)
S46eS314

Rationale: Statins are commonly used in children with familial hypercholesterolemia to prevent cardiovascular risk in adulthood. Their efficacy and tolerance in the short term (less than 2 years) are confirmed by many studies, but long-term data are very rare in children.

Aim: To evaluate the long term efficacy and tolerance of statins in children and adolescents with familial hypercholesterolemia.

Methods: Records of 131 children or adolescents treated with statins for familial hypercholesterolemia were analyzed retrospectively. The efficacy of the treatment was established by the decrease in LDL-cholesterol levels and the percentage of children who managed to achieve LDL-cholesterol levels below 160 mg/dL during treatment. Treatment tolerance was evaluated by the occurrence of clinical or biological side effects, regularity of height and weight growth, and pubertal development.

Results: Mean duration of treatment by statins was 4 years and 2 months. A mean decrease of 32% in LDL-cholesterol was observed ($p < 0.0001$). The therapeutic target (LDL-cholesterol $< 160 \text{ mg/dL}$) was achieved in 67% of cases. Height and weight growth and sexual maturation were not affected by the treatment. Minor side effects were reported in 24 (18%) patients: 3 cases of clinically asymptomatic CPK (creatine phosphokinase) increase, 2 cases of CPK increase with muscular symptoms, 14 cases of myalgia without CPK increase, 3 cases of abdominal pain, 1 case of dysuria, and 1 case of diffuse pain. None of these side effects justified to discontinue the statin therapy, although a change of statin was required in 7 cases. This new statin was tolerated in all the cases. No patients experienced biological disturbance of the liver function during the course of the treatment.

“LONG-TERM STATIN THERAPY IS SAFE AND EFFICACIOUS IN CHILDREN WITH FAMILIAL HYPERCHOLESTEROLEMIA”

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