Clinical DIGEST 3

Cardiovascular journals

A meta-analysis provides more evidence to support aspirin for primary prevention of cardiovascular disease



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t is evident that aspirin is beneficial for people who have previously been diagnosed with coronary heart disease (CHD) and is probably beneficial to all people at high risk for developing CHD, on the basis of an appropriate

assessment of known risk factors. Controversy persists, however, regarding the potential benefit of aspirin with respect to primary cardiovascular (CV) disease prevention, which has been further supported by recent clinical trial evidence.

The study by Bartolucci et al (2011; summarised alongside) is a meta-analysis of all trials published to date assessing the effect of aspirin in primary CV disease prevention, including two trials conducted in people with diabetes with no symptoms of CV disease. The analysis compares the effects of taking aspirin as opposed to not taking aspirin or taking placebo in over 90 000 individuals. The results confirm that aspirin decreases the incidence of non-fatal myocardial infarction (MI) and CV events.

Aspirin had no statistically significant effect on CHD, stroke, CV mortality, and all-cause mortality, but was highly significant for overall CV events. In this meta-analysis, there was heterogeneity across the studies for several outcomes. Possible sources of this heterogeneity include patient selection and randomisation, baseline disease

severity, management of intercurrent outcomes (such as bleeding, gastritis, and hypertension), and treatment strategies. However, the overall difference between aspirin and placebo, as shown in this meta-analysis, did not appear to be affected by significant heterogeneity, because similar results were obtained when the analysis was conducted using the so-called "random-effects model" (which accounts for the randomness of the effects across studies and thus controls for possible confounding arising from heterogenicity across studies included in a meta-analysis).

A limitation of this study is that it is a metaanalysis of the results of published studies and may thus be limited by the absence of raw data analysis, which would provide further key insights into this question.

In summary, based on this meta-analysis, primary prevention with aspirin decreased the risk for total CV events and non-fatal MI, but no significant differences in the incidences of stroke, CV mortality, all-cause mortality and total coronary heart disease were seen with the use of aspirin in primary prevention. These data thus support the concept that aspirin use in primary prevention may have outcome benefits in a range of people, particularly those at elevated CV risk. However, the benefits of primary prevention with aspirin must be considered in relation to the potential risks for each individual.

AMERICAN JOURNAL OF CARDIOLOGY

Aspirin reduces risk of total CV events and nonfatal MI

Readability	1111
Applicability to practice	1111
WOW! factor	1111

This meta-analysis looked at data from nine randomised trials that evaluated the benefits of aspirin for the primary prevention of cardiovascular (CV) events.

The nine trials included two trials of participants with diabetes: the POPADAD (Prevention of Progression of Arterial Disease and Diabetes) trial and the JPAD (Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes) trial.

The combined sample from all the trials totalled 90 000 people, of whom approximately half (50 868) took aspirin and half did not, or took a placebo (49 170).

This analysis assessed the following six CV endpoints: total coronary heart disease, non-fatal myocardial infarction (MI), total CV events, stroke, CV mortality and all-cause mortality.

The results suggest that people treated with aspirin had a significantly decreased risk for nonfatal MI (P=0.042) and total CV events (P=0.001).

Results were not significant for a decreased risk of stroke, CV mortality and all-cause mortality. There was no evidence of statistical bias (*P*<0.05).

It was concluded that primary prevention with aspirin decreased the risk for total CV events and non-fatal MI but did not significantly decrease risk for other CV endpoints.

Bartolucci AA, Tendera M, Howard G (2011) Meta-analysis of multiple primary prevention trials of cardiovascular events using aspirin. *Am J Cardiol* **107**: 1796–801

OF CARDIOLOGY

New risk score for heart failure in T2D

Readability / / /
Applicability to practice / / /
WOW! factor / / / /

The authors of this post-hoc analysis aimed to calculate a risk prediction score for the development of heart failure in people with T2D and macrovascular disease.

Out of 4951 people with available baseline data, 233 suffered a

serious adverse heart failure event during a mean follow-up of 34.5 months.

The risk score showed a good calibration and moderate discrimination (area under the curve 0.75).

Participants were accurately stratified with an actual risk of 1.0% for the bottom tertile, 3.2% for the middle and 9% for the top tertile.

The authors concluded that this risk score proved a good stratification for future heart failure.

Pfister R, Cairns R, Erdmann E, Schneider CA (2011) A clinical risk score for heart failure in patients with type 2 diabetes and macrovascular disease: An analysis of the PROactive study. *Int J Cardiol* [Epub ahead of print]

AMERICAN HEART JOURNAL

Lower burden of coronary artery disease associated with black ethnicity

Readability	1111
Applicability to practice	1111
WOW! factor	1111

- The impact of race or ethnicity on coronary artery disease (CAD) was analysed in Americans and Canadians with long-standing T2D.
- Data from the BARI 2D (Bypass Angioplasty Revascularisation Investigation in Type 2 Diabetes) trial were used for the multivariate regression analysis which was used to determined the independent association of race on the burden of CAD after adjusting for baseline risk factors.
- The main outcome measure was myocardial jeopardy index (MJI) - the percentage of myocardium jeopardised by significant lesion (≥50%).
- People of black ethnic origin with CAD were more likely to be women, have no health insurance, be current smokers, have a longer duration of diabetes and a higher HbA, level.
- After controlling for baseline risk factors, black participants had a significantly lower burden of CAD. The adjusted MJI was 5.43 U lower (95% confidence interval [CI], -9.13 to -1.72), and the adjusted number of lesions was 0.53 fewer (95% CI, -0.88 to -0.18) in black people compared with white.
- The authors concluded that ethnicity was a powerful predictor of the burden of CAD after adjusting for baseline characteristics. Ethnicity was also associated with differences in baseline risk factors.

Beohar N. Davidson CJ. Massaro EM et al (2011) The impact of race/ethnicity on baseline characteristics and the burden of coronary atherosclerosis in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. Am Heart J 161: 755-63

AMERICAN HEART JOURNAL

HbA_{1c} and inpatient mortality in people with AMI

Readability	1111
Applicability to practice	1111
WOWI factor	1111

- The authors of this cohort study investigated whether a J-shaped relationship exists between HbA, and inpatient mortality in people with diabetes and acute myocardial infarction (AMI).
- The study included data from across the USA of people who

were hospitalised with AMI and had pre-existing diabetes and a previous HbA₁₀ measurement.

- No evidence of a J-shaped relationship was found between HbA, level and inpatient mortality (P=0.89).
- Participants with the lowest (<5.5% [<37 mmol/mol]) and highest (\geq 9.5% [\geq 80 mmol/mol]) HbA₁₀ level had a crude mortality rate of 4.6% and 2.8%, respectively.
- The authors found no J-shaped association between HbA, and inpatient mortality in people with diabetes and AMI.

Britton KA, Aggarwal V, Chen AY et al (2011) No association between hemoglobin A1c and inhospital mortality in patients with diabetes and acute myocardial infarction. Am Heart J 161: 657-663

Albuminuria was strongly associated with coronary atherosclerosis in people with and without T2D, independent of other risk factors."

CIRCULATION

Better angina outcomes with initial revascularisation

Readability	////
Applicability to practice	1111
WOW! factor	1111

The authors of this study tested whether initial treatment with coronary revascularisation (CR) was superior to optimal medical treatment with the option of subsequent CR in preventing worsening and new angina and another CR in participants from BARI 2D (Bypass Angioplasty Revascularisation Investigation in T2D).

The initial CR group had a lower rate of worsening angina (8% vs 13%; P<0.001), new angina (37% vs 51%; P=0.001) and subsequent CR (18% vs 33%; P<0.001), compared with those who received optional subsequent CR.

The authors concluded that in these participants a strategy of initial CR reduced the occurrence of worsening angina, new angina and subsequent CRs more than initial optimal medical treatment with subsequent CR.

Dagenais GR. Lu J. Faxon DP et al (2011) Effects of optimal medical treatment with or without coronary revascularization on angina and subsequent revascularizations in patients with type 2 diabetes mellitus and stable ischemic heart disease. Circulation **123**: 1492–500

AMERICAN JOURNAL OF CARDIOLOGY

Albuminuria associated with atherosclerosis

Readability	111
Applicability to practice	1111
WOW! factor	1111

The authors tested whether albuminuria is associated with atherosclerosis among 914 people who had been referred for the evaluation of suspected coronary artery disease.

- People with albuminuria had ≥50% more stenoses than those without (66% vs 51%; P<0.001).
- Adjusted logistic regression analysis confirmed that albuminuria was significantly associated with stenoses \geq 50% (P=0.007).
- The authors concluded that albuminuria was strongly associated with coronary atherosclerosis in people with and without T2D, independent of other risk factors.

Rein P, Vonbank A, Saely CH et al (2011) Relation of albuminuria to angiographically determined coronary arterial narrowing in patients with and without type 2 diabetes mellitus and stable or suspected coronary artery disease. Am J Cardiol 107: 1144-8