echocardiographic speckle-tracking and thus targeting this site for lead placement was thought to result in better synchronization and outcomes.

As compared to the conventional site of LV pacing using anatomic guide, the speckle-tracking guided pacing resulted in a higher responder rates both in terms of LV size regression and clinical end-points such as NYHA class and combined all-cause mortality and heart failure hospitalizations.

However this study has many limitations: (1) speckle-tracking radial strain imaging is neither the best nor the final word in locating the last activation of LV; (2) small sample size with limited follow-up of 6 months from only 2 centres; (3) so-far all echocardiographic studies to guide CRT has had significant inter-observer variability and could not predict outcomes (PROSPECT). Echo studies using advanced software lack reproducibility, requires trained personnel and not readily available for mass practical implementation; (4) in almost one-third patients the targeted site could not be paced because of inaccessible venous anatomy and or presence of scar.

Nonetheless this study is a step-forward in establishing the fact that if we can identify & pace the "sweet-spot" in the LV, the responder rates can be improved.

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Giorgia De Berardis, Giuseppe Lucisano, Antonio D'Ettorre, Fabio Pellegrini, Vito Lepore, Gianni Tognoni, Antonio Nicolucci. Association of aspirin use with major bleeding in patients with and without diabetes. JAMA 307 (21) (2012) 2286–2294

Context: The benefit of aspirin for the primary prevention of cardiovascular events is relatively small for individuals with and without diabetes. This benefit could easily be offset by the risk of hemorrhage.

Objective: To determine the incidence of major gastrointestinal and intracranial bleeding episodes in individuals with and without diabetes taking aspirin.

Design, setting, and participants: A population-based cohort study, using administrative data from 4.1 million citizens in 12 local health authorities in Puglia, Italy. Individuals with new prescriptions for low-dose aspirin (≤300 mg) were identified during the index period from January 1, 2003, to December 31, 2008, and were propensity-matched on a 1-to-1 basis with individuals who did not take aspirin during this period.

Main outcome measures: Hospitalizations for major gastrointestinal bleeding or cerebral hemorrhage occurring after the initiation of antiplatelet therapy.

Results: There were 186,425 individuals being treated with low-dose aspirin and 186,425 matched controls without aspirin use. During a median follow-up of 5.7 years, the overall incidence rate of hemorrhagic events was 5.58 (95% CI, 5.39–5.77) per 1000 person-years for aspirin users and 3.60 (95% CI, 3.48–3.72) per 1000 person-years for those without aspirin use (incidence rate ratio [IRR], 1.55; 95% CI, 1.48–1.63). The use of aspirin was associated with a greater risk of major bleeding in most of the subgroups investigated but not in individuals with diabetes (IRR, 1.09; 95% CI, 0.97–1.22). Irrespective of aspirin use, diabetes was independently associated with an increased risk of major bleeding episodes (IRR, 1.36; 95% CI, 1.28–1.44).

Comments

In a population-based cohort, aspirin use was significantly associated with an increased risk of major gastrointestinal or cerebral bleeding episodes. Patients with diabetes had a high rate of bleeding that was not independently associated with aspirin use.

A meta-analysis based on individual patient data demonstrated that the benefits of low-dose aspirin for the primary prevention of cardiovascular disease are modest. Any benefit of low-dose aspirin might be offset by the risk of major bleeding. It is known that aspirin is associated with gastrointestinal and intracranial hemorrhagic complications. Observational studies suggest an excess of approximately 1–2 major bleeding episodes annually for every 1000 patients treated with low doses of aspirin. The bleeding risk sharply increases in individuals older than 70 years. The bleeding rate was five times higher than the bleeding rate expected based on the results of previously published randomized clinical trials. Diabetics had 36% increased risk of major bleeding episodes irrespective of aspirin use. So, when we have to balance the risk and benefits of aspirin, we have to remember that the baseline risk of bleeding can be very high in some subgroups of patients.

But this study, for the first time, to our knowledge, showed that aspirin therapy only marginally increases the risk of bleeding in individuals with diabetes. The incidence rate of major bleeding was 5.35 per 1000 person-years in those who never took aspirin compared with 5.83 among those taking low-dose aspirin, a nonsignificant difference.

These results can represent indirect evidence that the efficacy of aspirin in suppressing platelet function is reduced in this population. An accelerated platelet turnover in diabetes could explain the reduced incidence of adverse effects related to aspirin, as well as its limited efficacy in preventing major cardiovascular events.

So finally, weighing the benefits of aspirin therapy against the potential harms is of particular relevance in the primary prevention setting, in which benefits seem to be lower than expected based on results in high-risk populations. In this population-based cohort, aspirin use was significantly associated with an increased risk of major bleeding, but this association was not observed for patients with diabetes. In this respect, diabetes might represent a different population in terms of both expected benefits and risks associated with antiplatelet therapy.

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