

## **Duration of Treatment With Nonsteroidal Anti-Inflammatory Drugs and Impact on Risk of Death and Recurrent Myocardial Infarction in Patients With Prior Myocardial Infarction      A Nationwide Cohort Study**

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**Background**—Despite the fact that nonsteroidal anti-inflammatory drugs (NSAIDs) are contraindicated among patients with established cardiovascular disease, many receive NSAID treatment for a short period of time. However, little is known about the association between NSAID treatment duration and risk of cardiovascular disease. We therefore studied the duration of NSAID treatment and cardiovascular risk in a nationwide cohort of patients with prior myocardial infarction (MI).

**Methods and Results**—Patients  $\geq$ 30 years of age who were admitted with first-time MI during 1997 to 2006 and their subsequent NSAID use were identified by individual-level linkage of nationwide registries of hospitalization and drug dispensing from pharmacies in Denmark.

Risk of death and recurrent MI according to duration of NSAID treatment was analyzed by multivariable time-stratified Cox proportional-hazard models and by incidence rates per 1000 person-years.

Of the 83 677 patients included, 42.3% received NSAIDs during follow-up. There were 35 257 deaths/recurrent MIs.

Overall, NSAID treatment was significantly associated with an increased risk of death/recurrent MI (hazard ratio, 1.45; 95% confidence interval, 1.29 to 1.62) at the beginning of the treatment, and the risk persisted throughout the treatment course (hazard ratio, 1.55; 95% confidence interval, 1.46 to 1.64 after 90 days). Analyses of individual NSAIDs showed that the traditional NSAID diclofenac was associated with the highest risk (hazard ratio, 3.26; 95% confidence interval, 2.57 to 3.86 for death/MI at day 1 to 7 of treatment).

**Conclusions**—Even short-term treatment with most NSAIDs was associated with increased risk of death and recurrent MI in patients with prior MI. Neither short- nor long-term treatment with NSAIDs is advised in this population, and any NSAID use should be limited from a cardiovascular safety point of view.

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**Key Words:** antiinflammatory agents, nonsteroidal  $\gamma$ -cyclooxygenase 2 inhibitors  $\gamma$  mortality  $\gamma$  myocardial infarction  $\gamma$  prognosis