Using Non-Opioid Medications: NSAID Cardiovascular Risk

All NSAIDs including nonprescription products have prothrombotic effects that could increase the risk of stroke, transient ischemic attack (TIA), myocardial infarction (MI) and symptomatic coronary artery disease or peripheral vascular disease.¹

Meta-analysis of individual patient data involving almost a half-million individuals found that all NSAIDs were associated with an increased risk of MI.² Risk was greatest during first month of use and with higher doses.

Use of COX-2 inhibitors or nonselective NSAIDs is associated with persistently increased coronary risk regardless of time elapsed after a first-time MI.³,⁴

Among patients with stable atherothrombosis, NSAID use is associated with a higher risk of myocardial infarction, stroke, and hospitalizations for both ischemia and heart failure.⁵

NSAIDs can also exacerbate hypertension, which in turn increases the risks associated with these outcomes, as well as congestive heart failure.⁶,⁷,⁸,⁹ Nonselective NSAIDs are more likely to increase blood pressure resulting in hypertension.¹⁰

Differences among drugs in the incidence of the various types of cardiovascular (CV) toxicity exist, but have been difficult to quantify.¹¹,¹²,¹³
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Some important risk factors for CV side effects include hypertension, heart failure, unstable angina, MI, and recent bypass surgery or stent insertion. Although the overall incidence of these adverse events is low, the potential for toxicity should be considered before any of these drugs are prescribed for chronic use. It is likely that older patients, who have a higher rate of cardiovascular comorbidities than other populations, are predisposed to these toxicities. Risk if duration and dose-dependent.

The prevailing opinion had been that naproxen may be the safest from this perspective; however, the FDA refused to approve labeling that would endorse this view. A recent trial in patients with arthritis found elevated risk for celecoxib, naproxen and ibuprofen, with celecoxib being noninferior to the nonselective NSAIDs for cardiovascular death, nonfatal myocardial infarction and non-fatal stroke. The most prudent position for a clinician is to accept that all NSAIDs, including COX-2 selective agents, increase the risk of cardiovascular events, related to prothrombotic effects and a sustained adverse effect of blood pressure, and this risk can be a strong relative contraindication to long-term therapy in some patients.

Key takeaways

• The risk of heart attack or stroke:
  • can occur as early as the first weeks of using an NSAID
  • may increase with longer use of the NSAID
  • appears greater at higher doses
• It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.
• NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied.
• In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
• Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients not treated with NSAIDs after their first heart attack.
• There is an increased risk of heart failure with NSAID use.
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Citations


