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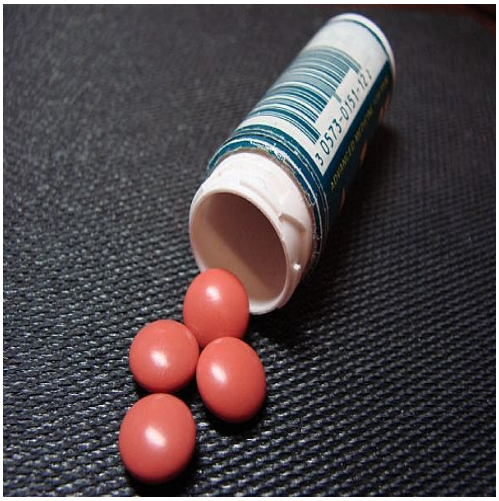
Naproxen Best NSAID for Heart-Disease Patients

One of the first large studies to look at the safety of different nonsteroidal anti-inflammatory drugs (NSAIDs) specifically in patients with heart disease has found that **naproxen** appears to have better cardiovascular safety than **diclofenac**, **ibuprofen**, and higher doses of **rofecoxib** (Vioxx, Merck) and **celecoxib** (Celebrex, Pfizer) [1].The study, published in the May 2009 issue of Circulation: Cardiovascular Quality and Outcomes, was conducted by a group led by Dr Wayne Ray (Vanderbilt University School of Medicine, Nashville, TN).They explain that the cardiovascular safety of NSAIDs is highly controversial, with several studies suggesting increased cardiovascular risk associated with the new COX-2 inhibitors and also some older traditional NSAIDs, and that this issue is particularly important for patients with existing serious coronary heart disease, whose baseline risk of adverse cardiovascular events is increased.



In addition, many of these patients take low-dose aspirin, which may interact with the NSAID. But they note that data on the cardiovascular safety of these drugs in heart-disease patients is limited. They therefore conducted the current retrospective cohort study in which they examined the cardiovascular safety of individual NSAIDs in 48,566 patients with a hospitalization for myocardial infarction (MI), revascularization, or unstable angina that had been recorded in one of three large databases ,

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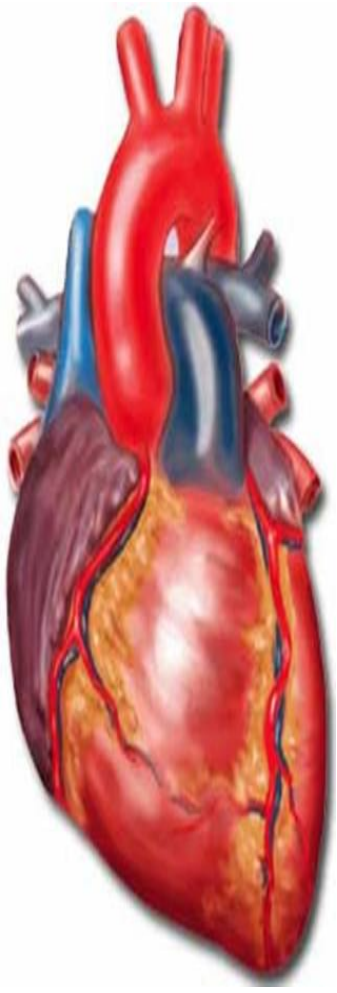

Tennessee's expanded Medicaid program, Saskatchewan Health databases in Canada, and the United Kingdom's General Practice Research Database--between 1999 and 2004. The primary study end point was serious coronary heart disease, defined as MI or out-of-hospital death from CHD [coronary heart disease]. A secondary end point was the composite of serious cardiovascular disease (MI or stroke) and death from any cause. Preplanned analyses were conducted for the most frequently prescribed NSAIDs, which were naproxen, ibuprofen diclofenac, celecoxib, and rofecoxib. Results showed that cardiovascular safety was best for naproxen, which had a lower incidence rate ratio (IRR) for serious cardiovascular disease than non-NSAID users. In contrast, there was evidence that cardiovascular risk was increased for users of the other study NSAIDs.

Incidence Rate Ratios (IRRs) for Serious CV Disease or Serious CV Disease and Death for Users of Various NSAIDS vs Non-NSAID Users

Drug	IRR (serious CV disease)	IRR (serious CV disease/death)
Naproxen	0.88	0.91
Ibuprofen	1.18	1.14
Diclofenac	1.27	1.38
Celecoxib	1.03	0.99
Rofecoxib	1.19	1.07

Other results showed that individuals who took diclofenac had a 50% increased risk of MI, stroke, or death from any cause compared with naproxen users. The authors point out that diclofenac is widely used outside the US and has been the reference drug in several COX-2-inhibitor outcome trials and this excess risk was present for low and moderate doses (< 150 mg/day) as well as higher doses. Ibuprofen users had a 25% increased risk for the MI, stroke, or death end point compared with naproxen users. In a comparison with high-dose naproxen use, users of higher doses of celecoxib (> 200 mg/day) and rofecoxib (> 25 mg/day) had increased risk of serious coronary heart disease.Relative to NSAID nonusers, serious coronary heart disease risk increased with short-term (less than 90 days) use for ibuprofen, diclofenac, celecoxib, and rofecoxib, but not for naproxen. The authors note that this is in contrast to a widely publicized post hoc analysis of the APPROVE trial data, interpreted by some as suggesting no risk for use of less than 18 months.

In an accompanying editorial [2], **Dr Daniel Solomon** (Brigham and Women's Hospital, Boston, MA) says that this study breaks new ground in focusing on patients with known cardiovascular disease. As arthritis and cardiovascular disease commonly coexist, studying the cardiovascular safety of NSAIDs in this subgroup is of great public-health value.

Compounded by Noha Gamal

References

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1. **Solomon D H. Searching for a safe analgesic in patients with cardiovascular disease. *Circ Cardiovasc Qual Outcomes* 2009; 2:146-147.**

This study was funded by an unrestricted grant from Pfizer. Ray has consulted with plaintiff's attorneys and insurance companies regarding rofecoxib. Two other authors were employees of Pfizer when this research began, and other authors have received research support from Merck, AstraZeneca, Novartis, and Pfizer.Solomon receives salary support for research from Amgen and Abbott. He serves as an unpaid member of the executive committee of the Pfizer-sponsored PRECISION trial, and he serves as an unpaid member of the data safety monitoring board of a Pfizer-sponsored trial investigating a non-NSAID analgesic for osteoarthritis.

Lifestyle May Counter Blood Pressure Genes

Being born with genes that predispose you to high blood pressure doesn't mean you're doomed to have it, a long-term study shows .It's been known for many years that blood pressure is affected by genes," said Dr. Nora Franceschini, an assistant professor of epidemiology at the University of North Carolina and lead author of a report on the study. "It's also known that lifestyle affects blood pressure. Now we are showing that they interact, and that the effect of those genes varies among individuals who have different behaviors."It's an important finding because high blood pressure is a major risk factor for heart attack, stroke and other cardiovascular diseases. The study, reported online Tuesday in Circulation: Cardiovascular Genetics, "reinforces the message that lifestyle changes can alter the effect of genetics," Franceschini said. That message comes from the Strong Heart Family Study, which has been looking at diabetes and high blood pressure among American Indians in Arizona, North and South Dakota and Oklahoma, an ethnic group in which the incidence of both is high. The study now includes more than 3,600 people aged 14 to 93. The new report shows that different lifestyles and socioeconomic status influence the effect of inherited genetic patterns .

About 15 percent of the variation in diastolic blood pressure, the lower of the two numbers in a blood pressure reading, is because of genes, Franceschini said. The study linked the effects of three behavioral traits -- drinking, smoking and exercise -- with that of the genes. It also looked at education level, a socioeconomic factor. The study found that genes for high blood pressure have a greater effect in smokers than nonsmokers, Franceschini said. It also found a similar effect for physical exercise. And it found that blood pressure among drinkers is affected by different genes than in people who quit drinking or never drank.

Our study shows a comprehensive effect across multiple behaviors," she said. The findings help answer whether genes alone determine high blood pressure, said Dr. Richard A. Stein, a professor of medicine and director of the urban community cardiology program at New York University and a spokesman for the American Heart Association. "The answer is, not by a long shot," Stein said. "The actual effect is explained only by adding behavioral and socioeconomic factors into the equation. It is actually more how you live than what you are born with." The next step in the study is an effort to identify the specific genes that interact with each of the behavioral traits to increase blood pressure, Franceschini said. Analysis of the entire genome "may allow us to identify the particular genes that account for the interaction," she said. Another study reported in the same issue of the journal showed that small changes in measures aimed at controlling high blood pressure can produce significant results. Another study reported in the same issue of the journal showed that small changes in measures aimed at controlling high blood pressure can produce significant results.

References

1. **Nora Franceschini, M.D., research assistant professor, epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, N.C.; Richard A. Stein, M.D., professor, medicine, and director, Urban Community Cardiology Program, New York University, New York City; June 16, 2009, Circulation: Cardiovascular Genetics.**

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