▥ *AFP* Journal Club

The Story Behind the Study

Is Intensive Blood Pressure Control Beneficial in Patients with Acute Intracerebral Hemorrhage?

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Purpose

In *AFP* Journal Club, three presenters review an interesting journal article in a conversational manner. These articles involve "hot topics" that affect family physicians or "bust" commonly held medical myths. The presenters give their opinions about the clinical value of the individual study discussed. The opinions reflect the views of the presenters, not those of *AFP* or the AAFP.

Article

Anderson CS, Heeley E, Huang Y, et al.; INTERACT2 Investigators. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *N Engl J Med.* 2013;368(25):2355-2365.

For more information on evidence-based medicine (EBM) terms, see the EBM Toolkit at http://www.aafp.org/afp/ebmtoolkit.

A collection of *AFP* Journal Club published in *AFP* is available at http://www.aafp.org/afp/jc.

What does this study say?

Mark: In this study, 2,839 patients with a spontaneous intracerebral hemorrhage were randomized within six hours of symptom onset to standard care (systolic blood pressure target of 180 mm Hg) or intensive blood pressure control (systolic blood pressure target of 140 mm Hg). The goal was to maintain the blood pressure at experimental levels for seven days. Exclusion criteria included a Glasgow Coma Scale score of 3 to 5, a structural cerebral cause of the hemorrhage, a massive hematoma with a poor prognosis, or a planned early surgery. Only nontraumatic hemorrhage was studied.

Follow-up was performed in person or by phone after 90 days. The primary outcome was death or disability at 90 days, with disability defined as a modified Rankin Scale score of 3 to 5 (the Rankin Scale ranges from 0 [no symptoms] to 6 [death]). Interestingly, they calculated a National Institutes of Health (NIH) Stroke Scale score for every patient at baseline and at seven days, but used only the modified Rankin Scale score when reporting 90-day outcome. This will become important later in the discussion.

What did they find?

Mark: The average systolic blood pressure was 150 mm Hg in the intensive treatment group and 164 mm Hg in the standard care group. Only 33% of the intensive treatment group reached the goal of 140 mm Hg. There was no difference between the two groups in hematoma size at 24 hours. There was also no difference in the primary outcome of death and major disability, with an odds ratio of 0.87 (95% confidence interval, 0.87 to 1.01; $P = .06$). There was a small benefit in disability, with an odds ratio of 0.87 (95% confidence interval, 0.77 to 1.0; $P = .04$). However, this was a secondary outcome not considered when the study was originally designed. And, as we will discuss later, there are significant problems with the way this result is reported.

Bob: What is an odds ratio? The odds ratio is defined as the odds of an outcome occurring in one group divided by the odds of an outcome occurring in another group. The term "odds" is used differently in statistics than in the vernacular, where it usually means chance.[1]

To get the odds ratio, we first need to calculate the odds in both groups. Let's say that the probability of a positive outcome in group A is 25/100 (25%). The probability of a negative outcome is 75/100 (75%). So, the odds of a positive outcome are 25/75 (33%). This *seems* pretty good, yet our patient still has only a 25% probability of having a positive outcome. Now, let's look at the odds ratio.

Let's say that the probability of a positive outcome in group B is 50/100 (50%). The probability of a negative outcome is also ▶

50/100 (50%). The odds of each outcome are 50/50 (1).

The odds ratio between the two groups is calculated as 0.33/1.0 = 0.33. However, the actual difference in *probability* of a positive outcome between the two groups is only 50% − 25% = 25%. So, you can see how the odds ratio can make it seem as though the difference between groups is greater than it actually is.

In this study, the odds ratio for a positive outcome is 0.87. It looks pretty good *if* it was a relative risk: perhaps a 13% decrease in disability. Yet, the absolute risk reduction is only 55.6% − 52% = 3.6%. The odds ratio is not the same as the relative risk.

Mark: Odds ratios should really be used only in case-control studies and when the probability of an outcome is less than 10% (where the odds ratio approximates the *relative* risk reduction). So, the odds ratio was the wrong statistic to bring to this table.

Jill: It is also important to note that the odds ratio does not give us a measure of the magnitude of difference between the two groups, only the relative odds of each outcome.

Mark: There is another troublesome aspect to this study. The results table in the appendix reports that the odds ratio adjusts for, among other things, the NIH Stroke Scale score. After appropriately adjusting for baseline imbalances, there was no difference in outcomes (i.e., death or disability). Why hide this in a supplement?

Jill: Most of us assume that all of the important information will be published in the main article, but that's not always the case.

What should the family physician do?

Mark: I think this article reassures us that lowering blood pressure in patients with

Main Points

- It seems to be safe to lower systolic blood pressure to a target of 140 mm Hg in those with an acute hemorrhagic stroke. However, there seems to be no clinical benefit to this approach when the data are adjusted for baseline NIH Stroke Scale scores.

EBM Points

- An odds ratio tells us the odds of an outcome in one group compared with another group, but does not give us the magnitude of this changed outcome. It is usually used in case-control studies and not, as in this article, in randomized trials.

- More and more information is being hidden in online supplemental protocol information or in appendices.

hemorrhagic stroke is at least not harmful. The lack of any difference in outcomes when the data were adjusted for baseline NIH Stroke Scale score makes it difficult to routinely recommend intensive blood pressure control. On the other hand, except for the time involved, there seems to be no downside.

Jill: It is unfortunate that journals choose to bury the "real" results and "real" protocols of studies in supplemental materials online. In this case, some prominent abstract aggregators didn't even mention the online material.

If you conduct a journal club and would like to know the next article that will be discussed, or if you would like to suggest an article for discussion, e-mail afpjournal@aafp.org with "*AFP* Journal Club notification" in the subject line.

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REFERENCE

1. Goldin R. Odds ratio. George Mason University. http://www.stats.org/faq_odds_ratios.htm. Accessed October 5, 2013. ∎