A major goal after a cardiovascular event, whether a myocardial infarction, exacerbation of heart failure, or revascularization procedure, is return to the community and resumption of normal health and functioning. This process has a number of components. They include making sure that there is adequate social support, that patients understand what medications to take, that patients understand what activities to begin and when, that appropriate disease management programs have been engaged, and that patients have appointments or a least a well-explained path to reestablishing care with their family doctor, internist, or cardiologist. Another component is helping patients who have become debilitated to various degrees because of their illnesses regain sufficient strength and well-being to function as well as possible. Cardiovascular rehabilitation is a critical part of this process.

The ability to function well in society is a difficult goal that is hard to measure. Thus, evaluating outcomes of cardiovascular rehabilitation can be challenging. Mortality is often used as a metric for outcome because it is easy to measure, but it might well be argued that, for rehabilitation, reducing mortality and future events does not address what rehabilitation is principally for and that a decrease in events adds to the overall benefit.

It is in this complicated environment concerning rehabilitation that we must consider the article by Hammill et al. They considered the relationship between the number of rehabilitations sessions and subsequent events in a study performed using the national Medicare 5% sample of beneficiaries. Hammill et al identified 30,161 elderly patients who had cardiac rehabilitation. After correction for baseline differences, they noted that as patients attended more sessions up to a total of 36, they had lower risks of mortality and myocardial infarction. Of interest, the distribution of the number of sessions attended was somewhat unusual, being nearly flat but with some increased numbers at the extremes and a model value of 36.

Although the statistical methods were quite sophisticated, the interpretation of the data is uncertain. Thus, as the authors point out, the data may be confounded. A confounder is a risk factor related to outcome that varies in prevalence between the groups being assessed for another risk factor(s). Statistical methods such as those in this study can account for measured confounders but not for unmeasured confounders. This can be a particular problem in studies such as that by Hammill et al that are based on administrative data. The baseline data in administrative databases are not as detailed or reliable as data from clinical databases. Thus, if sicker patients or disadvantaged patients drop out of rehabilitation early, they may also have increased risk or recurrent events. If such factors cannot be accounted for, the relationship between how many times patients went to rehabilitation and subsequent outcome may not be reliable.

In principle, to evaluate the impact of the number of rehabilitation visits on outcome free of treatment selection bias, it would be necessary to conduct a randomized trial in which patients were randomly assigned to a number of rehabilitation visits. This may or may not be a bit too small an issue to warrant the time, effort, and expense of a randomized trial. Pending such a trial, we will probably have to settle for randomized trial data that show a reduction in cardiovascular events with rehabilitation compared with no rehabilitation plus observational data such as in this study.

How can we assess whether the statistical association found in an observational study such as this is causal? That is, how can we tell in the absence of randomized data whether having a larger number of rehabilitation visits causes a decrease in cardiovascular events rather than just being a statistical association? One approach is to consider the Bradford Hill criteria. The British epidemiologist Austin Bradford Hill devised these criteria in response to the criticism that the observational studies he conducted in the 1950s with Richard Doll concerning the relationship between cigarette smoking and lung cancer did not prove that cigarette smoking caused the lung cancer. The Bradford Hill criteria are as follows: (1) strength of association: an exposure that has a greater statistical and generally statistically significant observed relationship to risk or risk reduction is more likely to be causal than a weak statistical relationship; (2) consistency of the observation: if all or most studies find similar findings, it is more likely to be causal; (3) dose response: the more exposure, the greater the risk, or for therapy, the greater the risk reduction, the more likely it is causal; (4) temporality: the exposure precedes the outcome; (5) biological plausibility: there is a reasonable biological explanation; (6) coherence: the observed relationship between exposure and outcome is consistent with other known facts; (7) consideration of alternative explanations; (8) specificity: a single cause produces a single effect (This is the weakest and generally has
been abandoned); and (9) the relationship has been tested by experiment.

The relationship between rehabilitation and events can be considered reasonably well established by clinical trial data. How does the relationship between the number of visits and outcome, as considered by Hammill et al, fare when considered in light of the Bradford Hill criteria? The results follow: (1) The strength of association is fairly strong with a hazard ratio of 0.53 (47% event reduction) for mortality and 0.68 (32% event reduction) for myocardial infarction comparing 36 sessions to 1 session; (2) these data are consistent with clinical trial data for rehabilitation versus no rehabilitation, but there do not appear to be other studies of this specific relationship to dose; (3) these data are about dose response, and the findings are thus consistent with this criteria; (4) there is clear temporality with the rehabilitation preceding the events; (5) this is biologically plausible; (6) this is consistent with other things we know about the benefit of increased activity; (7) for alternative possibilities, the data in this study may be confounded; (8) specificity is generally not considered; and (9) the dose response could be subjected to a clinical trial but has not been to date.

After consideration of the Bradford Hill criteria, the issue is still uncertain, but it could be a causal relationship and would be worthy of further study. Should prospective studies be considered, the issue should be considered broadly, with outcomes that include health status, functioning measures, and recurrent events. A prospective trial should also include economic and cost-effectiveness analyses. In the meantime, while gathering further data is being considered, it is important to act on making rehabilitation available and reducing barriers. Such barriers include financial and logistical impediments to patients enrolling and remaining in rehabilitation. This involves incorporating rehabilitation into practice, including thorough integration into informatics systems and daily workflow. In the absence of randomized trials, multi-center observational databases with clinical as opposed to currently available administrative data will give a richer understanding of patient outcome. Finally, cardiovascular rehabilitation should be considered in the overall context of returning patients to being as fully functioning in society as possible.

Disclosures

None.

References


Key Words: Editorials • epidemiology • exercise • rehabilitation
Do More Cardiac Rehabilitation Visits Reduce Events Compared With Fewer Visits?
William S. Weintraub

_Circulation_. 2010;121:8-9; originally published online December 21, 2009;
doi: 10.1161/CIR.0b013e3181cd3ce6

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/121/1/8

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/