Application of Echocardiography to Population-Based Research Projects

JAMES A. SCHOENBERGER

SUMMARY  The value of echocardiography as a tool for the epidemiologic investigation of hypertension has not yet been determined. Since echocardiography is considerably more sensitive than electrocardiography in the detection of left ventricular hypertrophy, the development and regression of left ventricular hypertrophy assessed by echocardiography may be extremely useful in determining prognosis in hypertension and the efficacy of therapeutic interventions. It may free clinical trials of dependence on total mortality and coronary incidence as the only end points. (Hypertension 9 [Suppl II]: II-45-II-46, 1987)

KEY WORDS • echocardiography • left ventricular hypertrophy • hypertension

C L I N I C A L trial methodology has been handicapped by dependence on total mortality as the major end point. In any population free of clinical disease at baseline, the annual death rate in prospective studies is low. Only when patients with far advanced disease are recruited, as, for example, with congestive heart failure, is the annual mortality high. The consequence of a low event rate is the need to obtain a large number of subjects in order to be able to anticipate a high likelihood of a statistically significant result (type I error, \( p < 0.05 \)) and a good probability that a difference will be detected if one exists (type II error or power of 0.9).

The use of other end points, such as cause-specific mortality or nonfatal disease (e.g., myocardial infarction), or of various combinations of fatal and nonfatal end points (e.g., coronary incidence), invariably softens the data because of uncertainty over the precise diagnosis or questions of completeness of ascertainment of the events. Even sophisticated methods of adjudicating the diagnosis by having blinded observers review all pertinent data does not fully solve the problem. Reliance on death certificate classification of cause of death, as classified by experienced nosologists, also fails to yield adequately precise data. In the final analysis, total mortality with all the demands it creates on sample size requirements and the resultant cost of the study has been the gold standard of end points.

It would be highly desirable, then, if intermediate end points could be identified that are closely related to mortality and can be precisely measured. Such end points might greatly reduce the sample size requirements and cost of clinical trials even though they would not completely replace the end point of total mortality. For instance, the assessment of left ventricular hypertrophy (LVH) could be made with a high degree of reliability and consistency, its development or regression would be a useful index by which to judge the success of antihypertensive regimens. It would be reasonable to infer that an antihypertensive regimen that prevented the development of, or hastened the regression of, LVH might prolong the life of hypertensive patients.

An example of how LVH contributes to the probability of developing coronary heart disease can be seen in the Framingham Study. LVH was based on the electrocardiographic changes of tall R waves from the left chest leads accompanied by ST depression and T-wave inversion. For a 50-year-old man with an average cholesterol of 210 mg/dl and a systolic blood pressure of 135 mm Hg, who is not diabetic and does not smoke cigarettes, the probability of developing coronary heart disease in a 6-year period is 4.4%. If LVH is present, the probability doubles to 8.7%.

The use of LVH and other intermediate end points would reduce the sample size that might be required in a full-scale clinical trial if total mortality were the only end point. LVH is an ideal intermediate end point for these purposes because its prevalence in hypertension is quite high and it can be assessed by a repetitive noninvasive procedure. It is not known, however, whether LVH defined by echocardiographic techniques carries with it the same unfavorable prognosis as LVH determined by electrocardiography. This question is currently under investigation.

LVH is considered to be an adaptive process to maintain cardiac output in the face of the increased afterload imposed by hypertension. A price is paid, though, in a decrease in diastolic function as the left ventricle loses its compliance. Therefore, LVH cannot be considered to be a physiologic response in its more severe forms. Further, it creates an imbalance in blood supply and demand because the vasodilator capacity of the coronary arteries may fail to increase in parallel with the increase in muscle mass.

The precise pathophysiologic mechanisms for the development of LVH are not completely understood. Although elevated blood pressure may be the chief instigating factor, adrenergic stimulation of the heart may be the underlying mechanism for...
cardiac hypertrophy. This may have profound therapeutic implications since those antihypertensive drugs that do not interrupt the sympathetic stimulation of the heart may lower blood pressure but may not prevent the development of LVH or its regression. The value of regression of LVH is also incompletely understood since it is possible that normal cardiac function may not be restored.

Therefore, the availability of echocardiography as a more sensitive and specific method of detecting LVH may add considerable understanding to the epidemiologic relationships between LVH and the cardiovascular complications of hypertension.

References
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