Clinical future of antimyosin imaging in noncoronary heart disease

Is There a Clinical Role for Antimyosin Imaging?

This rather pessimistic question is raised because, in general, there is not a clinical need for an additional imaging test in acute myocardial infarction. The utility of any imaging test to visualize the area of necrosis would be confined only to some infrequent and equivocal presentations.[1] There are solid arguments, however, for the clinical use of antimyosin in the management of other pathologic conditions of the heart. The clinical utility of antimyosin imaging in these situations is based on direct benefit to the patient in terms of diagnostic efficiency, noninvasiveness, and relatively low cost compared with diagnostic alternatives. We offer in this editorial a review of the pros and cons of antimyosin imaging in several diffuse heart diseases, as well as our perception of its potential impact on patient management. The final result with respect to use will depend on the particular characteristics of each medical institution with regard to specific patient population, professional habits and mentality, and flexibility of the health-care system.

Rejection After Heart Transplantation

Survival rates after heart transplantation have become acceptable in part because of the use of cyclosporine and the early detection of rejection with repeat endomyocardial biopsies.[2-4] Diagnosis of rejection and criteria for treatment are based on the identification of cell damage at endomyocardial biopsy.[5-7] Search for alternative procedures has led to the use of antimyosin antibodies to detect such damage.

Antimyosin uptake is invariably detected shortly after heart transplantation,[8-11] and a steady long-term decrease in its intensity reflects progressive development of tolerance.[12] Individual rejection activity curves allow unique noninvasive visualization of the phenomenon of rejection.[10] In some patients a normal antimyosin study result (tolerance) is eventually attained; its rate of development varies among individuals and can take from several months to years.[11] Other patients show long-term antimyosin uptake reflecting smoldering rejection. Comparison of antimyosin study results with those of endomyocardial biopsy reveals that (1) uptake correlates directly with biopsy score, (2) sensitivity of antimyosin to detect rejection approaches 100%, and (3) positive scans often coexist with endomyocardial biopsy not showing myocardial damage; this discrepancy probably reflects biopsy sampling error.[11] Therefore antimyosin studies probably provide the more sensitive technique available to detect rejection.[12]

Individual patient management can profit from both techniques: antimyosin imaging and biopsy. During the first year after transplantation, the exquisite sensitivity of antimyosin precludes management of patients based only on results of antimyosin scans (risk of overimmunosuppression); endomyocardial biopsies are mandatory in this interval, especially in the presence of early, persistent antimyosin uptake. After the first year of surgery, patients can be withdrawn from biopsy and patient management be adjusted individually on the basis of antimyosin studies. At this time, patients with normal study results receive no treatment for rejection episodes,[10] whereas those with antimyosin uptake are treated yearly with antirejection treatment (a positive antimyosin scan is equivalent to 1.09 biopsy specimens showing myocyte damage/yr) in addition to maintenance immunosuppression.

This strategy allows a more rational patient management without the small but definite risk imposed by repeat endomyocardial biopsy procedures.[13] This not only improves the perception of well-being in patients who have undergone transplantation but also dramatically reduces the cost of a transplantation program and allows better allocation of resources. As a research tool, the sensitive, noninvasive, nature of antimyosin imaging permits assessment of the efficacy of new immunosuppressive regimens or drugs.

Myocarditis and Dilated Cardiomyopathy

Because myocardial cell damage is part of the definition of myocarditis, it seemed reasonable to use antimyosin imaging in its detection. In patients with acute onset of myocardial disease, a high diagnostic sensitivity has been described,[14] making antimyosin studies a first-line procedure to evaluate the presence

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of myocardial damage and to rule out myocarditis.[15,16]

The clinical relevance of myocardial cell damage alone has to be elucidated. In patients with chronic idiopathic dilated cardiomyopathy, it has been described that (1) ongoing myocardial damage is detected in 70% of these patients[17]; (2) antimyosin uptake is not due to heart failure, because patients with stable coronary disease and similar degrees of left ventricular dilation and dysfunction do not show uptake[17]; and (3) uptake is not necessarily due to myocarditis (as evaluated through cardiac explants[18]). In acute onset of myocardial disease, detection of myocardial damage approaches 100%. In addition, evolving patterns of antimyosin uptake occur that correlate with changes in left ventricular function.[19] The nature of myocardial cell damage in these patients is uncertain. The possibility that enteroviruses are implicated[20] has not been fully explored.

The precise clinical relevance of myocardial cell damage in patients with acute or chronic myocardial disease must be understood before antimyosin studies are used to guide patient management. In fact, antimyosin studies do not detect the inflammatory component of myocarditis, which is precisely part of its definition.[18] Intensity of uptake in dilated cardiomyopathy provides prognostic information that allows a more precise risk stratification for death or the need for transplantation.[19] Availability of this technique opens the possibility to the detection of environmental agents or drugs deleterious to the myocardium or for assessing the efficacy of potential therapies destined to halt myocardial damage.

Assessment of Cardiotoxicity

Conventional management of patients with cancer treated with potentially cardiotoxic chemotherapy is performed by serial ejection fraction measurements. If patients are treated up to a fixed maximal dose, and if well-known guidelines are applied, the incidence and severity of congestive heart failure are minimized.[21] However, an important number of surviving patients have permanent cardiac functional abnormalities at follow-up.[22] This poses a problem of prevention rather than just detection of adverse effects. Furthermore, there is sometimes a need for additional chemotherapy in patients with responding tumors (i.e., remissions of the disease could be prolonged with additional chemotherapy). Antimyosin may provide a tool for improved patient management because it provides early detection of cell damage before functional impairment occurs,[23] relates to the cumulative dose,[24] and allows early identification of patients at risk for significant cardiotoxicity.[25] It seems that a complementary approach with antimyosin studies and functional assessment could provide a more accurate management of patients, especially those with previous risk factors or those who are candidates for future repeat doxorubicin administration.[26,27] In these circumstances, individually tailored drug administration could reduce the incidence and severity of cardiotoxicity, preventing early and late undesirable effects.

In addition to the well-known consistent cardiotoxic effects of doxorubicin, evaluation of other potentially cardiotoxic drugs may be difficult without the aid of a noninvasive tool to detect the impact of acute or chronic drug administration. We have recently used antimyosin to study the capability of tricyclic antidepressant drugs to elicit myocardial damage.[28] In a prospective study involving young patients with major depression taking chronic tricyclic antidepressant drugs, normal scans were seen in imipramine- and clomipramine-treated patients, but antibody uptake was detected in several patients receiving chronic amitriptyline treatment that disappeared after drug withdrawal, suggesting early myocardial toxicity.[28]

Effects of Alcohol on the Heart

In idiopathic dilated cardiomyopathy and dilated cardiomyopathy of alcoholic origin, left ventricular morphology and function are similar[29]; differentiation is often made by clinical criteria.[30] Several reports suggested the deleterious effect of alcohol on the myocardium,[31] but direct evidence of such effect has only been recently been provided by antimyosin studies.[19] Patients with dilated cardiomyopathy who actively consume alcohol have a prevalence and intensity of antimyosin uptake significantly higher than those who have dilated cardiomyopathy of similar severity and are past consumers. Reduction or disappearance of uptake after alcohol abstention is also accompanied by an increase in ejection fraction.[19] These findings link improvement of left ventricular function after cessation of alcohol consumption to reduction or disappearance of alcohol-induced myocardial damage.

Availability of an objective, albeit nonspecific, marker of the myocardial effect of heavy alcohol intake provides the basis for monitoring the effects of ethanol withdrawal in individual patients. Noninvasive evaluation of the effects of ethanol on the myocardium opens a path for future research.

Cautions and Limitations in Antimyosin Scan Interpretation

The importance of interpreting an antimyosin study in a clinical context must be emphasized. A positive scan simply implies that myocardial damage of some kind is detected, be it the result of ischemia, myocarditis, rejection, alcohol abuse, or drug toxicity. Therefore the results of antimyosin studies should be interpreted jointly with the clinical information.

The high sensitivity of antimyosin in the detection of the mildest spectrum of myocardial damage merits caution in deciding patient management solely on the basis of scans. As stated above, a simplistic view of a positive scan after transplantation as rejection activity that should be treated vigorously could lead to excessive immunosuppression. On the other hand, accurate interpretation of single antimyosin studies in certain conditions (rejection, alcohol intake, and acute-onset myocardial disease) requires knowledge of the natural history of myocardial damage and the temporal variations of antimyosin uptake. For example, normalization of antimyosin studies after acute myocarditis can take several months, and a single antimyosin study performed soon after the acute episode would reveal antimyosin uptake; however, repeat studies would show decreasing or absent antimyosin uptake.

Conclusions

Antimyosin studies provide sensitive, noninvasive means for detection of myocardial cell damage and constitute an alternative to endomyocardial biopsy. In some cases (cardiac rejection and cardiomyopathy), antimyosin studies are more sensitive than endomyocardial biopsy (sampling error or myocardial damage not related to myocarditis).

Traditionally, the impact of several agents (e.g., rejection, infection, and drugs) on the myocardium has been evaluated through the presence or absence of functional ventricular abnormalities. Antimyosin studies in various settings have revealed that detectable myocardial cell damage may coexist with normal ventricular function. Therefore the possibility of independently assessing the presence of myocardial damage by antimyosin opens the possibility to a more accurate and early detection of myocardial involvement.

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