Aetiologic diagnosis of pericardial disease: worthy efforts may not be applied in the appropriate direction

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This editorial refers to 'Molecular analysis of pericardial fluid: a 7-year experience' by P.-Y. Levy et al., on page 1942

The aetiologic diagnosis of pericardial disease has something of a paradox. On the one hand, the precise aetiology of many, perhaps most, instances of pericarditis remains an enigma in individual patients. Fortunately, for management purposes, such precise diagnosis is virtually irrelevant in most cases, as spontaneous cure is the rule in such patients; however, in a few patients, it may prove crucial. On the other hand, because of the poor specificity of many clinical findings, patients needing aetiologically guided intervention may remain unnoticed until too late.

Not rarely, when concomitant disease does not point at a likely aetiological association, the only means of assessing if pericardial disease is due to specific mechanisms requiring individual therapy is to examine the pericardial fluid or tissue. If often poorly acknowledged as such, the challenge has always been to know in which patients the study of pericardial fluid or tissue is likely to be rewarding in terms of discovering specific, treatable disease. The key issue in acute pericardial disease is whether or when investigation of pericardial fluid or tissue in search of the aetiologic diagnosis is warranted for clinical purposes. To do too many invasive investigations would amount to a number of irrelevant findings, patients needing aetiologically guided intervention may remain unnoticed until too late.

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Levy et al. report9 on the experience developed in a sophisticated microbiological laboratory with the analysis of a sample of pericardial fluids over a 7-year period and its diagnostic yield. These authors have investigated, using conventional and molecular methods of analysis, 106 pericardial fluid specimens. They provide us with small information as to the clinical features of the patients from whom pericardial fluid was obtained and their rates of cardiac tamponade, associated diseases, or prolonged clinical features of infection. Data about the characteristics of the population where the patients with scheduled pericardial drainage came from are also lacking. That is to say, their pretest probability of specific disease cannot easily be known from the data provided by the authors. A positive aetiologic diagnosis of the pericardial disease was obtained in 80 of the 106 patients from whom pericardial fluid was obtained. Sixty-nine of these diagnoses were obtained with the conventional methods commonly used for the assessment of pericardial disease, either invasive (cytologic examination or culture of effusion) or non-invasive (clinical history or general serology), and 11 were the result of positive PCR studies in the 37 specimens of pericardial fluid where conventional culture or cytologic examination had been negative. In four of these 11 patients, specific antibiotic therapy was administered as a consequence of the positive finding and, in the other seven, therapy was withheld, possibly on the grounds of being unavailable or unnecessary. In other words, the implementation of the highly complex molecular diagnosis procedure had a net benefit of four specific treatments being given in a population of 106 patients.
This study brilliantly shows that PCR techniques may represent a useful adjunct to conventional laboratory studies in the investigation of pericardial fluid, permitting the rapid identification of organisms otherwise not easily found, or found with longer delay. In fact, 11 objective diagnoses of infection in 37 specimens with negative conventional culture (30%) represent a remarkable achievement, particularly in pericardial fluid. We believe that these highly sophisticated methods, when indicated in patients in whom a specific infection is a likely diagnosis, may increase the sensitivity of pericardial fluid examination and help to an adequate, early therapeutic decision. However, we cannot agree with the conclusion that the authors derive from their own findings, namely, that pericardiocentesis should be proposed as a second line of investigation in any patient with pericarditis in whom serological tests are negative, although such recommendation is endorsed by the current ESC Guidelines on Pericardial Disease. Indeed, it should be kept in mind that this highly sophisticated approach led to an absolute increase in specific useful diagnoses of not more than 3.8% in an already selected population, the remaining 64% being achieved by conventional methods. Certainly, these conventional methods included pericardiocentesis in some patients; but the criteria on the basis of which pericardiocentesis is likely to have a good or a poor diagnostic yield have been previously defined irrespective of the results of serologic tests.

The study does provide good evidence of the sensitivity of molecular studies in pericardial fluid: it does not say anything about what their results could be (or could lead to) in a population of patients with pericarditis with those features that in other clinical studies have been shown to predict uneventful recovery. If indicated without clinical discrimination, molecular diagnostic techniques, in addition to requiring an invasive procedure such as pericardiocentesis, could lead to a variety of irrelevant findings (such as viral infections for which chemotherapy is not available or even needed, or other findings of questionable meaning) and, maybe, to the institution of unnecessary or dangerous therapeutic approaches.

When pericarditis develops in association with a condition known to frequently cause pericardial disease, such as myocardial infarction, systemic lupus erythematosus, or renal failure, it can usually be assumed that both are pathogenetically related, and no additional studies are necessary for the aetiological diagnosis. The study by Levy et al. provides evidence in favour of this approach, as the sophisticated investigations that were done in the pericardial fluid of their 49 patients in whom a specific diagnosis was made by non-cardiac studies provided no instance of superinfection. In fact, superinfection of pericardial fluid in pericardial diseases of non-infective aetiology is an exceedingly rare observation in clinical practice, in agreement with our own experience.

The study by Levy et al. has the merit of having shown how, in a high-quality microbiological laboratory setting, the use of molecular techniques may be helpful in identifying a small proportion of selected patients with infective pericarditis in which the need for specific therapy could have been missed. However, if not properly interpreted, its findings may point in an inappropriate direction. They may suggest to those physicians unaware of the clinical and epidemiological background of their patients that a thorough aetiological investigation is needed in all but banal cases of acute pericarditis. That such thorough investigation may not, even should not, be needed could sound as outrageous to those persons with a naïve view of scientific medicine. However, as shown even by recent guidelines, the principle of limiting diagnostic tests to those patients in whom a clinical benefit is reliably anticipated as a likely possibility has not yet been so clearly acknowledged in pericardial disease as it has been in other areas of cardiology.

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References