

Clinical criteria and the appropriate use of transthoracic echocardiography for the exclusion of infective endocarditis

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Background: Clinical guidelines currently suggest that transthoracic echocardiography (TTE) be carried out in all patients with suspected endocarditis, but the use of TTE where there is a low probability of infective endocarditis has a poor diagnostic yield. This screening approach may no longer be appropriate.

Objective: To examine whether clinical criteria might aid decision making with respect to the use of TTE in possible endocarditis.

Design: A retrospective review of patient records.

Setting: Cardiology department of a tertiary referral centre.

Patients: 500 consecutive hospital inpatients referred for TTE to exclude endocarditis.

Main outcome measures: Evidence of endocardial vegetations on TTE and the presence of predetermined clinical criteria that may predispose to, or be suggestive of, endocarditis.

Results: Evidence of infective endocarditis was detected on echocardiography in 43 of the 500 patients (8.6%). In 239 patients (48%), vegetations and certain prespecified clinical criteria were both absent. These criteria were: vasculitic/embolic phenomena; the presence of central venous access; a recent history of injected drug use; presence of a prosthetic valve; and positive blood cultures. The collective absence of these five criteria indicated a zero probability of TTE showing evidence of endocarditis.

Conclusions: The use of simple clinical criteria during the decision making process may avoid many unnecessary TTE examinations in hospital inpatients with a low probability of endocarditis.

Transthoracic echocardiography (TTE) has a low diagnostic yield in patients referred for "exclusion of infective endocarditis."¹ In spite of this, current American Heart Association guidelines recommend that TTE be carried out in all patients with a high or even a low probability of endocarditis.² As a result, the great majority (more than 80%) of those referred for TTE to exclude endocarditis have no evidence of vegetations on echocardiography—a potentially costly as well as uninformative exercise.^{1,3} The widespread use of TTE in this setting may reflect the results of early studies in which echocardiography showed impressively high positive and negative predictive values for the presence of vegetations; however, those results were influenced by the selection of patients in whom the presence or absence of endocarditis was virtually certain on clinical grounds.^{4–6} In fact, from more recently reported data the sensitivity of TTE for detecting vegetations is only moderate, at between 40–80%.^{4,5,7–11}

In a cost conscious era, therefore, this "screening" approach for infective endocarditis may be inappropriate. While most studies of infective endocarditis have focused on confirming the presence of the disease, there are few published reports that have attempted to identify criteria predicting the *absence* of vegetations on TTE. In this study, therefore, our aim was to identify clinical criteria that might allow the more judicious use of TTE in patients referred for echocardiography on suspicion of infective endocarditis.

METHODS

Between January 1998 and December 1999, we studied 500 consecutive hospital inpatients who had been referred for TTE for suspected endocarditis. From direct interview and review of case records, we recorded the presence of specific predetermined clinical criteria that may predispose to or be suggestive of endocarditis. These were as follows:

- a congenital cardiac structural abnormality (for example, mitral valve prolapse or ventricular septal defect)
- known rheumatic heart disease
- a recent history of injected drug use
- the presence of a prosthetic heart valve
- current central venous access (pacing wire or a pressure line)
- recurrent fevers ($\geq 38.5^{\circ}\text{C}$ for > 2 days, daily)
- organisms grown on blood culture
- recent use of antibiotics (within the past week)
- vasculitic/embolic phenomena.

All patients had standard TTE, and images were acquired in the parasternal long and short axis, and in apical two, three, and four chamber views. Confirmatory evidence of bacterial endocarditis was defined according to the major criteria stated in the Duke classification.¹² Briefly, these are: an oscillating mass on a valve or supporting structures, in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomical explanation; an abscess related to a prosthetic valve; new partial dehiscence of a prosthetic valve; and new valvar regurgitation.

The valve or site of infection within the heart was noted. Studies were undertaken in all cases using a Vingmed System Five (General Electric, Madison, Wisconsin, USA) using a phased array probe (range 1.5 to 3.8 MHz).

Statistics

We employed STATA release 5 for all analyses. Univariate analysis was carried out using χ^2 tests. Multivariate analysis was undertaken using logistic regression. Sensitivity, specificity, and predictive values were evaluated according to

Table 1 Clinical criteria in patients with and without evidence of endocarditis on transthoracic echocardiography

| Clinical criteria | TTE evidence of endocarditis | | Total (n=500) |
|------------------------------|------------------------------|---------------------|---------------|
| | Evidence (n=43) | No evidence (n=457) | |
| Congenital heart disease | 4 (9.5) | 4 (0.9) | 8 (2) |
| Rheumatic heart disease | 2 (4.8) | 1 (0.2) | 3 (0.6) |
| Injected drug use | 16 (40) | 41 (9) | 57 (11) |
| Prosthetic heart valve | 6 (14.3) | 44 (9.7) | 50 (10) |
| Central venous access | 7 (16.7) | 11 (2.4) | 18 (4) |
| Recurrent fever | 35 (81.4) | 201 (44) | 236 (47) |
| Positive blood culture | 38 (88.4) | 147 (32) | 185 (37) |
| Recent use of antibiotics | 22 (51.1) | 230 (50) | 252 (50) |
| Vasculitic/embolic phenomena | 33 (74.4) | 9 (2) | 42 (8) |

Values are n (%).
TTE, transthoracic echocardiography.

Table 2 Clinical criteria that are significant independent predictors by multivariate analysis of evidence of endocarditis on transthoracic echocardiography

| Clinical criteria | OR (95% CI) | p Value |
|------------------------|------------------|---------|
| Embolism | 414 (57 to 3028) | <0.0001 |
| Central venous access | 87 (9 to 837) | <0.0001 |
| Injected drug use | 22 (3 to 159) | 0.002 |
| Prosthetic valve | 14 (1.3 to 157) | 0.03 |
| Positive blood culture | 7.4 (1.6 to 34) | 0.01 |

CI, confidence interval; OR, odds ratio.

standard definitions. A probability value of $p < 0.05$ was considered significant.

RESULTS

The mean (SD) age of the patients was 52 (19) years, and 295 (59%) were male. Evidence of infective endocarditis, as defined above, was detected on TTE in 43 (8.6%) of the 500 patients. Vegetations were seen on the mitral valve in 10 of the patients with endocarditis (23%), on the aortic valve in 15 (35%), and on the tricuspid valve in 10 (23%). Four patients (9%) had endocarditis involving more than one valve, one (2%) had Eustachian valve endocarditis, two (5%) had pacemaker wire endocarditis, and one (2%) had a vegetation seen in a conduit for complex congenital heart disease.

Table 1 shows the relative and absolute numbers of patients with each type of clinical criterion for endocarditis. There were 239 patients (48%) in whom both vegetations and certain of the prespecified clinical criteria were absent. These criteria were vasculitic/embolic phenomena; central venous access; a recent history of injected drug use; the presence of a prosthetic

Table 3 Sensitivity, specificity, and predictive values of clinical criteria relating to evidence of endocarditis on transthoracic echocardiography

| Clinical criterion | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|------------------------|-----------------|-----------------|---------|---------|
| Embolism | 77 | 98 | 80 | 98 |
| Central venous access | 17 | 98 | 39 | 93 |
| Injecting drug use | 38 | 91 | 29 | 94 |
| Prosthetic valve | 14 | 90 | 12 | 92 |
| Positive blood culture | 90 | 68 | 20 | 98 |

NPV, negative predictive value; PPV, positive predictive value.

Table 4 Numbers of patients with positive transthoracic echocardiography according to the number of risk factors present*

| Number of risk factors present | Number of patients in each group | Proportion with positive TTE |
|--------------------------------|----------------------------------|------------------------------|
| 0 | 239 (48%) | 0 |
| 1 | 192 (38%) | 6 (14%) |
| 2 | 49 (10%) | 17 (40%) |
| 3–5 | 20 (4%) | 20 (46%) |

*Vasculitic/embolic phenomena, the presence of central venous access, a recent history of injected drug use, presence of a prosthetic valve, and positive blood cultures.

valve; and positive blood cultures. The collective absence of these five criteria indicated a zero probability of demonstrating infective endocarditis on echocardiography.

Univariate analysis was done on all clinical criteria. The significant independent predictors for a positive TTE were vasculitic/embolic phenomena, central venous access, injected drug use, the presence of a prosthetic valve, and positive blood cultures (table 2). None of the other clinical markers was significant. The sensitivity, specificity, and predictive values of a positive TTE for each criterion are shown in table 3, the presence of vasculitic/embolic phenomena having the highest predictive value. Table 4 shows the proportions of patients with a positive TTE according to the numbers of risk factors present.

DISCUSSION

In this series of 500 consecutively studied inpatients referred for TTE on suspicion of infective endocarditis, we were able to identify 239 (48%) who had none of five prespecified clinical criteria for likely infective endocarditis and no vegetations or other evidence of endocarditis on TTE. This suggests that nearly half the TTE referrals could have been avoided by the judicious use of appropriate clinical criteria.

The Duke criteria, proposed by Durack and colleagues in 1994, refined the ability to diagnose and classify patients with suspected endocarditis by including both pathological and clinical criteria in the definition of “definite” endocarditis.¹² Recognising the high sensitivity and specificity of echocardiography in the detection of vegetations, the Duke criteria included positive echocardiographic evidence as a major criterion, with the recommendation by the American Heart Association that all patients with suspected endocarditis undergo echocardiography.² Owing to excellent sensitivity and specificity, the Duke criteria have achieved widespread use, but one important question has emerged as a result: is echocardiography necessary in all patients with “suspected endocarditis”? In the current cost conscious era, it may no longer be appropriate to use echocardiography as a screening test if it adds substantial cost with little new information, in an identifiable subset of patients.¹³

Thus we set out to examine whether there were any clinical criteria that might aid decision making with respect to the use of TTE in suspected endocarditis. In this series, absence of vasculitic/embolic phenomena, of central venous access or pacing wire, of recent injected drug use, of a prosthetic valve, and of positive blood cultures indicated a zero probability that TTE would show evidence of infective endocarditis. The application of these criteria might save both time and money for clinicians and patients alike.

Recent American Heart Association guidelines recommend that TTE be carried out in patients with a “low clinical probability” of the disease.³ There is no given definition of this term, but interpretation is guided by an example: “fever and previously known heart murmur.” Consequently, investigators have felt obliged to state their own definitions which can be quite different—for example, one group defined “low clinical

probability" as being less than 2%, where a definite non-cardiac source of infection exists.^{13,14} Absence of a stringent set of defining criteria allows open interpretation of this term, and a knock on effect can be seen in clinical practice whereby a significant number of the TTEs requested are of little practical value.^{1,3}

Other investigators, recognising that there is overuse of TTE in the context of infective endocarditis, have gone so far as to suggest that it is not indicated in patients with a low probability of having this condition.^{1,3,13} Lindner and colleagues, using an adapted version of the Von Reyn criteria, classified 105 consecutive patients with suspected endocarditis as having either a low, intermediate, or high clinical probability of infective endocarditis.^{1,15} The group found that TTE was useful in the intermediate and high risk categories, but had a low diagnostic yield in the low probability group. They concluded that it was of little practical value in these patients. Similarly, Aly and colleagues, studying a cohort of 173 children with varying levels of suspicion of endocarditis, also found that TTE was of limited value in those with a relatively low likelihood of infective endocarditis.³ They proposed an algorithm for the use of TTE in infective endocarditis, and calculated that the number of examinations that their department would have to perform would be reduced by 80%. Both of the above studies help in decision making, but the processes described relied on different and often complicated criteria or flow charts in deciding whether or not TTE was appropriate. As a result clinicians are likely to find them difficult to apply.

Study limitations

We recognise that the sample population may suffer a selection bias in that all subjects were inpatients in a tertiary referral hospital and thus may not be truly representative of the subject group at large. The data collection in this study was prospective, whereas the analysis was retrospective. Ideally, therefore, the criteria proposed by this study should be tested prospectively.

Infective endocarditis may also be present without evidence of vegetations on TTE.¹⁶ In this regard, transoesophageal echocardiography (TOE) may be a more sensitive diagnostic tool in patients in whom the clinical suspicion of infective endocarditis remains high despite a "negative" transthoracic study.² Thus, although the clinical criteria in our series allow physicians to predict a high likelihood of a negative TTE examination in patients with a low probability of infective endocarditis, the diagnosis may ultimately still be established in a small proportion of such patients by a combination of clinical criteria, serial TTE, and TOE.

Conclusions

Guidelines on the use of TTE for screening patients with possible endocarditis are unclear and as a result echocardiography may be an overprescribed diagnostic tool. In this study we

identified five clinical criteria which are easy to remember and simple to apply. Their use may prevent unnecessary echocardiographic investigation in cases with a low probability of endocarditis.

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