Accuracy of visible retinal emboli for the detection of cardioembolic lesions requiring anticoagulation or cardiac surgery

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Abstract

Aim—To determine the accuracy of visible retinal emboli as a diagnostic “test” for the likelihood of receiving anticoagulation or cardiac surgery based on the results of transthoracic echocardiography, in the setting of acute retinal arterial occlusion.

Methods—A multicentre retrospective diagnostic study at Kingston Eye Centre, Queen’s University, Kingston, Ontario; Wills Eye Hospital, Philadelphia; Ottawa Eye Institute, Ottawa, Ontario; and the Halifax Infirmary, Halifax, Nova Scotia of 104 patients with both embolic and non-embolic acute retinal arterial obstruction who underwent transthoracic echocardiography was performed, to determine the accuracy of visible retinal emboli as a diagnostic “test” for anticoagulation or cardiac surgery. Anticoagulation or surgical intervention on the basis of abnormalities was detected solely through the technology of transthoracic echocardiography.

Results—41 patients had visible retinal emboli (calcific, cholesterol, or fibrin). The remaining 63 had no evidence of embolic disease. The sensitivity of emboli for the likelihood of a patient receiving anticoagulation or cardiac surgery was 50%. The specificity, positive predictive value, and negative predictive value were 62%, 15%, and 90%, respectively. The likelihood ratio (LR=1.31) obtained given the presence of a visible retinal embolus was neither clinically nor statistically significant (LR+ve = 1.31; 95% CI (0.91, 3.16)). This likelihood ratio, when applied to a patient with a pretest probability of 50%, results in a post-test probability of 56.7%. **Conclusions**—These results demonstrate that the presence of a visible retinal embolus should not be the sole determinant of whether to order transthoracic echocardiography, as the likelihood ratio for a patient receiving anticoagulation or cardiac surgery, given the presence of a visible retinal embolus was only 1.31.

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Patients with acute retinal arterial obstruction commonly present with sudden visual loss. Embolic retinal arterial obstruction is associated with a higher risk in overall mortality when compared with non-embolic occlusion.¹ Retinal emboli may be of cardiac origin, repre-

sent material derived from carotid artery stenosis, or may represent platelet fibrin aggregation.²

The following cardiac pathology has been reported in cases of acute retinal arterial obstruction: aortic and mitral valve disease,³⁻⁵ atrial myxomas,⁶ valvulotomy,⁷ angioplasty,⁸ acute myocardial infarction,⁹ subacute bacterial endocarditis, intravenous drug related talc embolisation,¹⁰ prosthetic valves,¹¹ and mitral valve prolapse.^{12,13} The prevalence of cardiac valvular disease in cases presenting with acute retinal arterial obstruction has been reported to be approximately 25%.^{3,6} Accordingly, it has been recommended that transthoracic echocardiography be performed in the evaluation of acute retinal arterial obstruction, especially in the presence of visible retinal emboli.^{2,4}

By modifying the probability of disease, historical facts, and physical findings act in a fashion similar to a diagnostic test.^{14,15} In fact, the accuracy of physical findings can be quantitated in terms of sensitivity, specificity, and predictive values. In this report we determine if the presence of a visible retinal embolus increases the probability of an acute retinal arterial occlusion patient receiving anticoagulation or cardiac surgery.

Patients and methods

The charts of 243 patients with acute retinal arterial obstruction were consecutively reviewed. The charts were obtained from four tertiary, North American hospital centres. From the initial 243, 104 met the following inclusion criteria:

- (i) Acute central retinal or branch retinal arterial obstruction on the basis of clinical examination (either clinical cloudy swelling or an arterial dye front on angiography).
- (ii) Clear documentation of the presence of retinal emboli (patients’ charts or fundus photographs). We documented the presence or absence of emboli. Qualitative assessment regarding the nature of the emboli was not undertaken, because of its subjective nature.¹⁶
- (iii) A clinical cardiac evaluation on the basis of past history for relevant cardioembolic high risk factors including presence of any of the following: subacute bacterial endocarditis, rheumatic heart disease, mitral valve prolapse, recent myocardial infarction, a prosthetic valve, cardiac tumour, intravenous drug use, congenital heart

Table 1 Anticoagulation or cardiac surgery in acute retinal arterial occlusion patients, given embolic status

	Anticoagulation or cardiac surgery	No anticoagulation or cardiac surgery	Totals
Visible retinal embolus	6	35	41
No embolus	6	57	63
Totals	12	92	104

disease, or valvular heart disease, the presence of a murmur detected at presentation and any electrocardiographic risk factors for embolisation (atrial fibrillation, acute ST elevation or Q-waves).

- (iv) Transthoracic echocardiographic evaluation.
- (v) The decision to anticoagulate (heparin or coumadin) or to surgically intervene based on an echocardiographic result was recorded.

The patients were then divided into one of two groups, based on the presence or the absence of visible retinal emboli. These two groups were then analysed with respect to whether they received anticoagulation or cardiac surgical intervention based on their echocardiographic result.

The study was designed to detect a likelihood ratio (positive test) of 4, given the presence of a visible retinal embolus. This likelihood ratio was deemed clinically significant, as it is the value at which a pretest probability of 50% translates to a post-test probability of 80%. The study was designed to detect this difference with a power of 80% (type II error = 0.20) and a type I error of 0.05. We summarised our data by way of a contingency table. Likelihood ratios were calculated as described by Sackett *et al.*¹⁵ Ninety five per cent confidence intervals¹⁷ were calculated around likelihood ratios obtained in both the presence and absence of retinal emboli, to assess their statistical significance.

Results

The mean age of our population was 60.9 years. Forty one (39%) of the patients had visible retinal emboli, and the remaining 63 had no evidence of visible retinal emboli.

Forty eight echocardiograms were reported as abnormal. From these, however, only 12 patients (11%) received anticoagulation or cardiac surgery (Table 1). Of these 12 patients, six had visible retinal emboli. Thus, the sensitivity of visible retinal emboli for the likelihood of a patient requiring anticoagulation or cardiac surgery was 50% (Table 2). The specificity was 61.9%.

Table 2 Test variables regarding visible retinal for the outcome of anticoagulation or cardiac surgery

Diagnostic test variable	Visible retinal embolus
Sensitivity	50%
Specificity	62%
Positive predictive value	14.6%
Negative predictive value	90.5%
Likelihood ratio given a positive test	1.31
Likelihood ratio given a negative test	0.807

EMBOLIC GROUP

Forty one patients had visible retinal emboli. Six of 41 embolic patients (15%) required anticoagulation or cardiac surgery based on their echocardiograms. The remaining 35 (85%), required no intervention. The six embolic patients who were anticoagulated or had cardiac surgery had the following cardiac pathology detected—mitral valve prolapse (one case), atrial myxoma (one case), aortic stenosis (one case), a cardiac mural thrombus (two cases), and an acute myocardial infarction (one case). The positive predictive value of the presence of a visible retinal embolus for anticoagulation or cardiac surgery was 14.6% (Table 2).

NON-EMBOLIC GROUP

Sixty three patients with acute retinal arterial obstruction did not have visible retinal emboli. Of these patients, six (8%) received anticoagulation or cardiac surgery based on their echocardiographic results (Table 1). The following pathologies required anticoagulation in the non-embolic group—vegetations on aortic valve (one case), aortic stenosis (two cases), and mitral valve stenosis (three cases). The negative predictive value of the absence of a visible retinal embolus was 90%.

The likelihood ratio for anticoagulation or cardiac surgery, given the presence of visible retinal embolus was 1.31; 95% CI (0.91, 3.16). The likelihood ratio for anticoagulation or cardiac surgery, given the absence of a visible retinal embolus, was 0.807; 95% CI (0.447, 1.45).

Discussion

Acute retinal arterial obstruction has been associated with cardiac valvular disease in approximately 25% of cases.³⁻⁶ Visible retinal emboli are a clinical sign that a retinal arterial obstruction may be associated with carotid or cardiac pathology.¹⁸⁻¹⁹ Accordingly, it has been recommended that acute retinal arterial obstruction in the setting of visible emboli be aggressively investigated to rule out a potential cardiac source for the emboli.² These recommendations have been made on the basis of prevalence figures obtained by historical data, studies with few numbers, or based on deductive reasoning to search for a proximal embolic source.

Our data reveal that 46% (48 of 104) of our patients had detectable abnormalities on their echocardiograms. Owing to the fact that there are numerous abnormalities detected on echocardiography for which no intervention is required, the more important outcome measure is anticoagulation or cardiac surgery, based on these abnormalities. In our series, only 12 of 104 patients (11%) with acute retinal arterial obstruction had findings on their echocardiograms which required anticoagulation or surgical intervention (Table 1). Six of the 12 had visible retinal emboli, whereas the remaining six presented with an acute retinal arterial obstruction which lacked any embolic material. With a sensitivity of 50%, half of the patients with cardiac pathology requiring anticoagulation or cardiac surgery would have

Table 3 Probability of anticoagulation or cardiac surgery given varying pretest probabilities

Patients with hypothetical pretest probabilities	Post-test probability given the presence of a visible retinal embolus	Post-test probability given absence of retinal embolus
Patient A: 10%	12.7% (+2.7)	8.2% (−1.8)
Patient B: 50%	56.7% (+6.7)	44.6% (−5.4)
Patient C: 90%	92.1% (+2.1)	87.9% (−2.1)

been missed if one had not ordered echocardiography in the absence of visible retinal emboli.

Our results reveal that the likelihood for anticoagulation or cardiac surgery was 1.31× higher in the presence of a visible retinal embolus (LR+ve= 1.31). This likelihood ratio was not clinically significant, as it would result in a post-test probability of 56.7%, given a patient with a pretest probability of 50%—an increase in the probability of only 6.7% (Table 3). The value obtained for our positive likelihood ratio was not statistically significant, as its 95% CI (0.91, 3.16) includes 1. Given that our study was designed to detect a likelihood ratio of 4, and that the upper limit of our 95% CI was 3.16, we are able to reject our alternate hypothesis.

The likelihood of a patient receiving anticoagulation or cardiac surgery was 0.807× lower in the absence of a visible retinal embolus (LR−ve=0.807). This likelihood ratio, too, is not clinically significant, as the post-test probability for anticoagulation or cardiac surgery decreases to 45%, given a pretest probability of 50%—a decrease of only 5% (appendix 2). The value obtained for the likelihood ratio obtained in the absence of an embolus is not statistically significant, as the 95% CI (0.447, 1.45) includes 1.

Overall, the presence or absence of a visible retinal embolus, in the setting of acute retinal arterial occlusion, did not significantly alter the probability of anticoagulation or cardiac surgery. This is true for hypothetical patients with varying pretest probabilities (Table 3).

A recent study by our group showed the importance of a careful clinical assessment which included a full functional inquiry and a cardiac auscultatory examination.²⁰ That study demonstrated that, if one or more cardioembolic risk factor was present, a patient was 25 times more likely to require anticoagulation or cardiac surgery than if no risk factors was present (OR = 25, 95% CI (3.04–217.02)).²⁰

In any cross sectional study, there is always the possibility of misclassification of patients with respect to different variables. As this cross sectional study was retrospective in nature, non-differential misclassification may have been introduced. With respect to our “diagnostic” test, that being the presence or absence of emboli, it was unlikely that misclassification of visible emboli occurred, as most clinical assessments were confirmed with fundus photography. However, in the absence of visible emboli, patients were classified as non-embolic. Non-embolic cases could have, in fact, been of embolic pathogenesis, with the emboli disintegrating before ophthalmoscopy. With respect to the outcome variable of anticoagulation or

cardiac surgical intervention, there also was little opportunity to misclassify patients. However, owing to the retrospective nature of the study, the variable of anticoagulation or cardiac surgery actually represents management that was recommended based on the echocardiographic results. These recommendations were made by different cardiologists, based on their own criteria. Certain cardiac pathologies may be handled differently, but without the adoption of various evidence based consensus statements of how to manage different echocardiographic abnormalities, it is difficult to evaluate whether misclassification of our outcome may have occurred.

It should also be noted that the outcome variable of our study (anticoagulation or cardiac surgery) was based on the results of transthoracic echocardiography, as opposed to transoesophageal data. However, there is evidence that certain cardiac pathology detected solely with transoesophageal echocardiography may be associated with acute retinal arterial obstruction.²¹ Given the low prevalence of acute retinal arterial obstruction and the relatively recent use of the technique of transoesophageal echocardiography, a prospective study would have to be undertaken to evaluate this hypothesis.

In summary, the presence of a visible retinal embolus in the setting of acute retinal arterial obstruction did not clinically or statistically increase the likelihood of a patient receiving anticoagulation or cardiac surgery, based on transthoracic echocardiography.

Appendix 1. Calculation of post-test probability, in the presence of a visible retinal embolus

post-test probability = post-test odds/1 + post-test odds

The post-test odds = pretest odds × LR−ve, where the pretest odds = pretest probability/1 − pretest probability

Example: assuming a hypothetical acute retinal arterial occlusion patient has 50:50 chance of having a cardiac lesion which required anticoagulation or cardiac surgery. How much would their probability change if we were to detect an embolus on ophthalmoscopy?

pretest odds = 0.5/1 − 0.5 = 1.0

post-test odds = (pretest odds) (LR+ve test). Given that our data reveal that the LR+ve test = 1.31, the post-test odds = 1.31. Accordingly, the post-test probability is equal to 1.31/2.31 or 57%. Thus, in the presence of a visible retinal embolus, we have gone from a situation where the probability of HSCAS was 50%, to one where it is 57%.

Appendix 2. Calculation of post-test probability, in the absence of a visible retinal embolus

Example: Again, assuming that a patient with acute retinal arterial occlusion who has a 50:50 chance of having cardiac pathology requiring intervention, how much does their probability change if an embolus is not present on ophthalmoscopy?

pretest odds = $0.5/1 - 0.5 = 1$
 post-test odds = pretest odds $\times$ LR-ve.
 Given our data reveals that LR-ve = 0.807,
 post-test odds = $(1) (0.807) = 0.807$. Accordingly,
 the post-test probability is equal to $0.807/1.807$ or 0.446. Thus, we have gone
 from a situation where the probability of HSCAS was 50% to one where it is now
 44.6%.

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