CLINICAL SCIENCE

Cardiovascular risk assessment in patients with retinal vein occlusion

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Aim: Patients with retinal vein occlusions (RVO) are at increased risk of cardiovascular disease (CVD). The risk of future CVD was determined using the Framingham algorithm and this risk estimate was used to guide decisions about preventative treatment for CVD in RVO patients.

Methods: 107 unselected RVO patients were studied. After excluding 18 patients because of age, missing data, or pre-existing cardiovascular disease, the calculated coronary heart disease risks (cCHDR) and calculated cardiovascular disease risks (cCVDR) were calculated on the 89 remaining and compared with both the standardised risk and the published incidence of CHD in England by *t* test or χ^2 test.

Results: The mean 10 year cCVDR was significantly higher than the Framingham standardised risk for all RVOs (20.6% (1.2%) *v* 15.7% (1.1%), p = 0.009) and female RVOs (17.8% (1.2%) *v* 12.7% (1.0%), p = 0.022) in particular. The 10 year cCHDR, compared to the actual incidence of CHD in England between the ages of 30 and 74 years, was > 15% in twice as many males than expected (62% *v* 28%, p <0.0001). This rose to almost six times when cCHDRs greater than 30% were compared (17% *v* 3%, p = 0.002). There was a fourfold increase in the proportion of female RVO patients with a cCHDR above 15% (40% *v* 9%, p <0.0001) and at a cCHDR of 30% and above (10% *v* 0%, p = 0.004). There were also significant differences in the cCHDR between central and branch RVO (both sexes). The branch form of RVO (BRVO) having higher cCHDRs because of systolic hypertension (164.1 (21.6) mm Hg *v* 149.5 (23.5) mm Hg, p = 0.003) and age (61.7 (8.3) years *v* 56.7 (10.6) years, p = 0.017).

Conclusions: RVO is the presenting complaint in a group of patients at increased risk of CVD and is in agreement with the long term follow up data demonstrating an increased mortality from CVD in patients with RVO. The Framingham algorithm can accurately determine the cCHDR (or cCVDR) to assist the clinician in deciding who to treat in accordance with the Joint British Societies' guidelines, with particular regard to hypertension, lipid lowering, and the use of aspirin therapy.

Patients with retinal vein occlusion (RVO) are known from long term follow up to be at increased risk of cardiovascular disease (CVD).[1 2] In the majority of RVO patients, there is no evidence of CVD at the time of presentation, but, as the reduction of coronary heart disease (CHD) is one of the UK Department of Health's main goals, the clinic attendance allows the opportunity to evaluate the risk of the patient developing CVD/CHD. The Joint British Societies have published guidelines for the primary prevention of CHD,[3] advocating the introduction of antihypertensives and aspirin when the absolute risk of developing CHD is 15% over 10 years or more. At a 10 year risk of 30% and above, lipid lowering therapy should also be added. The absolute risk of CHD can be calculated using the Framingham algorithm,[4] which is widely available on floppy disk and is also available on the Telepath laboratory information system (ISoft, Manchester). Reasonable estimates of the Framingham risk can also be derived from widely available tables. We calculated the 10 year CHD and CVD risks in an unselected group of patients presenting with RVO and compared their calculated risk with the incidence data for CHD in England used by the Joint British Societies.[5]

PATIENTS AND METHODS

The case notes from 107 patients with RVO attending the medical ophthalmology services in Birmingham were studied. The patients had all previously undergone a thorough examination involving complete ophthalmological and medical examinations with particular emphasis on cardiovascular status, diabetes, and smoking history. Clinical parameters, including blood pressure and, where performed, the presence or absence of ECG evidence of left ventricular hypertrophy were recorded. The diagnosis was confirmed by dilated slit lamp biomicroscopy and/or fluorescein angiography. Routine biochemical measurements of renal and liver function were performed, together with serum lipids, high density lipoprotein (HDL) cholesterol, glucose, and thyroid function.

The 10 year CHD/CVD risk was calculated as part of clinical management using a proprietary version of the Framingham algorithm for personal computers (CHD Risk Analyser v 2.0.1, WA Bartlett and AF Jones, Heartlands Hospital, Birmingham).[6] This algorithm uses the dichotomous variables sex, smoking status (ex-smoker for 12 months or more = non-smoker), presence or absence of diabetes (or impaired glucose tolerance), and the presence or absence of left ventricular hypertrophy (unknown = no). Additionally, the following continuous variables are required—age (within the range 30–74 years inclusive), systolic blood pressure (mean of two readings), and both total and HDL cholesterol levels. Comparisons were made with a standardised Framingham risk (assuming the same age and sex, but for a non-smoker with a systolic blood pressure of 140 mm Hg, a total

Abbreviations: BRVO, branch RVO; CHD, coronary heart disease; cCHDR, calculated coronary heart disease risks; CRVO, central RVO; CVD, cardiovascular disease; cCVDR, calculated cardiovascular disease risks; RVO, retinal vein occlusion

Table 1 Demographic data for the retinal vein patients studied (n=89)

Age (mean (SD))	59.8 (9.7)
SBP (mean (SD))	157.7 (24.3)
Total cholesterol (mean (SD))	6.1 (1.1)
HDL cholesterol (mean (SD))	1.36 (0.36)
% smokers	21.5
% diabetics	13.1
% hypertensives	43.0
% with LVH	4.7
% with AF	2.8

Table 2 The 10 year calculated cardiovascular disease risk (cCVDR) in RVO, percentage (SD)

	cCVDR	Std risk	p Value*
All (n = 89)	20.6 (1.2)	15.7 (1.1)	0.009
Males (n = 47)	23.5 (1.1)	19.1 (1.1)	0.120
Females (n = 42)	17.8 (1.2)	12.7 (1.0)	0.022

**t* test after logarithmic transformation to normalise the data.
% males with cCVDR ⩾20 = 66%.
% females with cCVDR ⩾20 = 54.8%.

Table 3 The 10 year calculated coronary heart disease risk in RVO compared to the CHD Incidence in England (1991–4)

	cCHDR	Recorded incidence	p Value
>15% risk , males (n = 29)	62%	28%	<0.0001
>20% risk , males (n = 22)	47%	16%	<0.0001
>30% risk, males (n = 8)	17%	3%	0.002
>15% risk, females (n = 17)	40%	9%	<0.0001
>20% risk, females (n = 12)	29%	4%	<0.0001
>30% risk, females (n = 4)	10%	0	0.004

p values determined by χ^2.

cholesterol of 6.0 mmol/l, and an HDL cholesterol of 1.15 mmol/l for males or 1.4 mmol/l for females). The data were compared with the incidence data for CHD risk in the 30–74 year age group recorded for England 1991–4 by the Framingham algorithm. Statistical significance was established by χ^2 or *t* test after logarithmic transformation to normalise the data.

RESULTS

A total of 107 subjects were sequentially included but 18 subjects were excluded because of pre-existing cardiovascular disease (n = 9), missing data (n = 5), already established on statin therapy (n = 3) and age (one patient was older than 74 years). Table 1 shows the demographic data of the 89 patients in whom medical therapy was being given as primary prevention of cardiovascular disease.

The 10 year CVD risks (cCVDR) calculated on the RVO patients compared with the Framingham standardised risk shown in Table 2, demonstrate that patients with RVO (p = 0.009), and especially females (p = 0.022), had significantly higher CVD risks than expected. Two thirds of the males and over 50% of the females had a cCVDR exceeding 20%. When the 10 year CHD risks (cCHDR) for RVO patients were compared with the age matched incidence of CHD risk in England, as shown in Table 3, the RVO patients were noted to have significantly higher cCHDR than would be expected from their age alone. Sixty two per cent of males with RVO and 40% of females had a 10 year cCHDR of 15% or more. Seventeen per cent of males and 10% of females had a 10 year cCHDR of 30% or more, much higher percentages than would be expected from the actual 10 year incidence of CHD in English men and women in the Framingham age range of 30 to 74 years.

Comparisons were also made between the 10 year cCHDR for branch RVO (BRVO, n = 48) and central RVO (CRVO, n = 41), separately. The BRVO patients had higher systolic blood pressures, 164.1 (21.6) mm Hg *v* 149.5 (23.5) mm Hg; p = 0.003 and were older, 61.7 (8.3) years *v* 56.7 (10.6) years; p = 0.017, than the CRVOs and this was reflected in the cCHDR, 16.5% (1.1%) *v* 9.7% (1.2%): p = 0.004 (Table 4A). There were no other significant differences between the groups (not shown). The Heartlands Medical Ophthalmology Clinic has a special interest in young (<50 years) RVO patients and it was considered that this might bias the calculated risks. Therefore, only the data for those patients aged 50 years or older are shown in Table 4B. The previous significant differences disappeared, but the systolic blood pressure remained higher in the BRVO group, as expected,[7] although it did not quite reach statistical significance (p = 0.054).

Table 5 shows the comparison between the actual and calculated percentage 10 year CHD risks for males and females with BRVO or CRVO. In both BRVO and CRVO the cCHDRs were higher than expected in both sexes. One half to three quarters of the males had a cCHDR of 15% or more as did one third to a half of the females. Almost 30% of the male BRVOs had a cCHDR of 30% or greater, a 10-fold higher relative risk than for English men in the same age group.

DISCUSSION

When patients present with RVO, this may be the first indication of developing atherosclerosis. Various medical conditions known to cause atherosclerosis have been associated with RVO[7 8] and there is an excess of cardiovascular mortality and morbidity on long term follow up.[1 2] The UK Department of Health has made reducing cardiovascular disease a priority and recommends targeting those individuals at greatest risk. The Joint British Societies have produced guidelines[3] for the identification of individuals at the greatest risk of developing cardiovascular disease based on the Framingham algorithm.

Table 4 The 10 year calculated coronary heart disease risks by diagnosis, % (SD)

	BRVO (n=48)	CRVO (n=41)	BRVO (n=42)	CRVO (n=28)	p Value*
(A) All RVO					
cCHDR	16.5 (1.1)	9.7 (1.2)			0.004
Age	61.7 (8.3)	56.7 (10.6)			0.017
SBP	164.1 (21.6)	149.5 (23.5)			0.003
(B) RVO >50 years					
cCHDR			17.9 (1.1)	13.9 (1.1)	0.175
Age			63.4 (6.8)	62.0 (7.4)	0.405
SBP			164.2 (22.4)	152.8 (25.0)	0.054

**t* test after logarithmic transformation to normalise the data.

Table 5 The 10 year calculated coronary heart disease risk in CRVO and BRVO compared with the CHD incidence in England (1991–4)

	cCHDR	Recorded incidence	p Value
CRVO			
>15% risk , males (n = 11)	48%	28%	0.006
>20% risk , males (n = 8)	35%	16%	0.004
>30% risk , males (n = 1)	4%	3%	ns
>15% risk , females (n = 6)	33%	9%	<0.0001
>20% risk , females (n = 5)	28%	4%	<0.0001
>30% risk , females (n = 1)	6%	0	0.038
BRVO			
>15% risk , males (n = 18)	75%	28%	<0.0001
>20% risk , males (n = 14)	58%	16%	<0.0001
>30% risk , males (n = 7)	29%	3%	<0.0001
>15% risk , females (n = 11)	46%	9%	<0.0001
>20% risk , females (n = 7)	29%	4%	<0.0001
>30% risk , females (n = 3)	12%	0	0.001

p values determined by χ^2.

This was chosen because it has been validated as the best method available for estimating the absolute risk of heart disease (cCHDR) and generalised cardiovascular disease (cCVDR). We calculated both the CVDR and CHDR for the 89 RVO patients with complete data who were candidates for primary prevention and were aged between 30 and 74 years. The results showed that the RVO patients had significantly higher cCVDRs than would be expected for the average age matched person (standardised risk) and that their cCHDR was much higher than the observed 10 year incidence of CHD in England for the same age group. There was also a significant difference in the calculated risks between BRVOs and CRVOs, which disappeared if only patients aged >50 years were studied and was attributed to a number of young (<50 years) CRVOs attending the medical ophthalmology clinic. Inclusion of these younger patients would tend to lower the calculated risk, but even then, the cCHDR was twofold to sevenfold greater than the recorded CHD incidence for England. These results are in agreement with previous long term studies[1 2] where two thirds of the deaths in RVO patients were due to CVD and the incidence of death from myocardial infarction was twice the expected level.[2] Our analysis does not include the nine patients with RVO who had established cardiovascular disease at presentation, in whom secondary prevention treatment targets are appropriate. In terms of the overall cardiovascular risk profile of RVO patients, exclusion of these patients leads to an underestimate of overall population risk.

We have chosen to measure cCHDR in our clinical practice and current guidelines suggest that the CHD risk threshold for intervention in primary prevention should be 15% over 10 years. A calculated risk above this level should alter patient management in that the threshold for blood pressure treatment is lower. Statin therapy may be instituted in many cases and aspirin therapy is appropriate. The latter therapy has been suggested to reduce recurrence of RVO in the fellow eye as well.[2]

This study shows that it is practicable to calculate the 10 year absolute risk of developing CHD using the Framingham algorithm in medical ophthalmology practice with a personal computer and that the cCHDR can be used to inform treatment decisions for the primary prevention of cardiovascular disease in a group of patients at high cardiovascular risk.

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