

Value of routine funduscopy in patients with hypertension: systematic review

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Abstract

Objective To evaluate the additional value of funduscopy in the routine management of patients with hypertension.

Design Systematic review.

Participants Adults aged 19 or more with hypertensive retinopathy.

Data sources Medline, Embase, and the Cochrane Library from 1990.

Review methods Studies were included that assessed hypertensive retinopathy with blinding for blood pressure and cardiovascular risk factors. Studies on observer agreement had to be assessed by two or more observers and expressed as a κ statistic. Studies on the association between hypertensive retinopathy and hypertensive organ damage were carried out in patients with hypertension. The association between hypertensive retinopathy and cardiovascular risk was carried out in unselected normotensive and hypertensive people without diabetes mellitus.

Results The assessment of microvascular changes in the retina is limited by large variation between observers. The positive and negative predictive values for the association between hypertensive retinopathy and blood pressure were low (47% to 72% and 32% to 67%, respectively). Associations between retinal microvascular changes and cardiovascular risk were inconsistent, except for retinopathy and stroke. The increased risk of stroke, however, was also present in normotensive people with retinopathy. These studies did not adjust for other indicators of hypertensive organ damage.

Conclusion Evidence is lacking that routine funduscopy is of additional value in the management of hypertensive patients.

Introduction

Funduscopy is still recommended as part of the routine examination of hypertensive patients, although its value is being questioned.^{1,2} We carried out a systematic search to determine the usefulness of routine funduscopy in hypertensive patients. We excluded studies in patients with hypertensive urgencies and emergencies as this is a separate group in

whom funduscopy provides essential information for diagnosis and treatment.

Methods

We systematically searched Medline, Embase, and the Cochrane Library for articles on hypertension and retinopathy published since 1990 in adults aged 19 or more. Two investigators (BJHvdB and CAAH) independently carried out the search using several terms (see bmj.com).

We defined hypertensive retinopathy as all retinal changes included in the Keith, Wagener, and Barker classification (see bmj.com). We use the term retinal microvascular changes to refer to narrowing of the retinal arterioles and arteriovenous nicking (see figs A and B on bmj.com). The term retinopathy originally denoted soft exudates and flame-shaped haemorrhages only (see fig C on bmj.com), but in the studies reviewed retinopathy also encompasses microaneurysms, blot haemorrhages, and hard exudates.

We included studies on the reliability of detecting changes to the retina if retinal photographs were independently assessed by two or more observers and if variability of detecting changes associated with hypertension could be expressed as a κ statistic.

For the association between retinal changes and hypertensive organ damage we included studies of hypertensive patients only. For the association between hypertensive retinopathy, cardiovascular risk, and blood pressure, we included population based or cohort studies with unselected normotensive and hypertensive people. In all studies, retinal changes had to be assessed without knowledge of blood pressure and cardiovascular risk factors, and diabetes mellitus had to be excluded, analysed separately, or adjusted for in multivariate analysis.

Statistical analysis

We used κ statistics to express the proportion of agreement for the various retinal changes associated with

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Figures showing retinal changes are on bmj.com



This is an abridged version; the full version is on bmj.com

Table 1 Characteristics of studies of retinal changes in patients with hypertensive retinopathy. Values are numbers (percentages) unless stated otherwise

Study	No of participants	Age range (years)	Participants with hypertension*	Retinal changes		
				Focal arteriolar narrowing (%)	Arteriovenous nicking† (%)	Haemorrhages and exudates (%)
Cardiovascular health study ⁷	2056	69-97	1424 (59)	9.6	7.6	8.3
Beaver Dam eye study ⁶	4311	43-84	1479 (34)	13.5	2.2	7.8
Atherosclerosis risk in communities study‡ ⁹	10 358	48-73	4595 (44)	14.9	14.3	7.0
Blue Mountains eye study ¹⁰	3614	43-86	1656 (46)	7.9	8.9	Not reported
Blue Mountains eye study ⁸	3275	≥49	1447 (44)	Not reported	Not reported	9.9

*Use of antihypertensive drugs or a history of hypertension and blood pressure $\geq 140/90$ mm Hg in cardiovascular health study and atherosclerosis risk in communities study and $\geq 160/95$ mm Hg in the Beaver Dam eye study and Blue Mountains eye study.

†Different definitions used.

‡Included patients with diabetes.

hypertension. We included both weighted and unweighted κ statistics.

For the association between blood pressure and retinal changes we considered the various retinal changes as a diagnostic test for hypertension. We calculated sensitivity, specificity, and positive and negative predictive values. Pooled odds ratios were calculated for the association between hypertensive retinopathy and hypertensive organ damage. We used a random effects model to generate summary measures and confidence intervals. Heterogeneity was examined using the I^2 statistic. To assess the association between hypertensive retinopathy and cardiovascular risk, we took the relative risk after multivariate analysis.

Results

We identified 111 reports with possible data on the association between hypertensive retinopathy and blood pressure, hypertensive organ damage, and cardiovascular risk (see bmj.com).

Variability in detecting retinal changes

Six studies had data on interobserver agreement for hypertensive retinopathy using retinal photographs. No such data were found for direct funduscopy. One study was excluded because we could not calculate κ statistics.³ The most extensive study of observer agreement involved three readers grading a random sample of 206 retinal photographs.⁴ See bmj.com for the κ statistics of this and other studies. In these studies, interobserver agreement was fair or moderate for focal arteriolar narrowing (κ 0.3 to 0.4) and arteriovenous nicking (κ 0.4 to 0.6) and excellent for haemorrhages and exudates. A computerised grading method was

used to assess the arteriovenous ratio.⁵ With this method, agreement was good (κ 0.7 to 0.8).

Retinal changes and blood pressure

Four large population based studies examined the association between hypertensive retinopathy and blood pressure (table 1).⁶⁻¹⁰ In one, age and sex standardised prevalence of hypertensive retinopathy was 12% in white Europeans and 18% in people of Afro-Caribbean origin.¹¹

The sensitivity of hypertensive retinopathy for hypertension ranged from 3% to 21%, indicating a low prevalence of retinal abnormalities in hypertensive patients. In contrast, specificity ranged from 88% to 98%, and therefore retinopathy was rarely observed in normotensive patients. The positive predictive value ranged from 47% to 70% for haemorrhages and exudates, 53% to 66% for arteriovenous nicking, and 49% to 72% for focal arteriolar narrowing (table 2). The negative predictive value ranged from 43% to 67% for haemorrhages and exudates, 44% to 66% for arteriovenous nicking, and 32% to 59% for focal arteriolar narrowing.

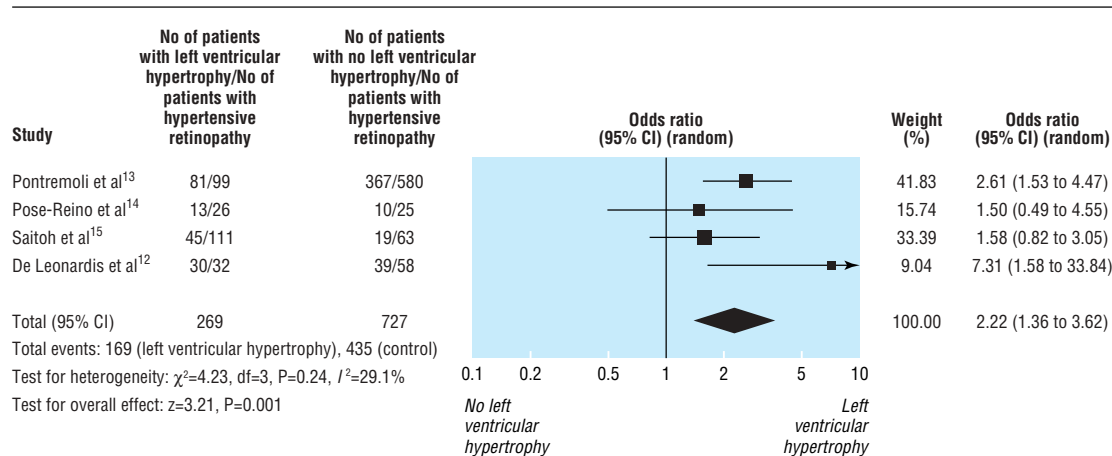
Retinal changes and other indicators of organ damage

Four studies examined the association between hypertensive retinopathy and echocardiographically determined left ventricular hypertrophy.¹²⁻¹⁵ One study failed to give the number of patients with events; when retinopathy was present, the age and sex adjusted odds ratio (95% confidence interval) for left ventricular hypertrophy was 1.92 (1.03 to 3.60).¹⁶ The figure gives details of the other studies. The pooled odds for left ventricular hypertrophy in the presence of hyper-

Table 2 Diagnostic accuracy (%) of retinal changes for hypertension in studies included in systematic review

Study	Generalised or focal arteriolar narrowing				Arteriovenous nicking				Haemorrhages and exudates			
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Cardiovascular health study ⁷	12	94	72	46	9	94	66	44	9	94	70	43
Beaver Dam eye study ⁶	19	89	49	68	3	98	53	66	11	94	47	67
Atherosclerosis risk in communities study ⁹	21	89	61	59	18	88	55	57	10	95	62	57
Blue Mountains eye study ¹⁰	11	95	66	52	12	93	59	56	Not reported	Not reported	Not reported	Not reported
Blue Mountains eye study ⁸	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	13	93	58	57

*People with diabetes included.



Odds ratios (95% confidence intervals) for association between hypertensive retinopathy and left ventricular hypertrophy

tensive retinopathy was 2.22 (1.36 to 3.62), with little heterogeneity. Two studies examined the association between hypertensive retinopathy and microalbuminuria (odds ratios 1.51, 0.84 to 2.68 and 4.98, 1.97 to 12.60).¹³⁻¹⁷ Three population based studies reported on the association between hypertensive retinopathy and intima-media thickness.¹⁸⁻²⁰ In the cardiovascular health study and atherosclerosis risk in communities study only the presence of haemorrhages and exudates was associated with increased intima-media thickness. In the Rotterdam eye study a lower arteriovenous ratio was associated with an increased intima-media thickness.

Retinal changes and cardiovascular risk

Hypertensive retinopathy as an independent predictor of cardiovascular risk was examined in six different populations, totalling 16 000 participants. We excluded two studies because blood pressure and patient history were known to the investigators before funduscopy.²¹⁻²² See bmj.com for the association between hypertensive retinopathy and cardiovascular risk after adjustment in multivariate analysis. Risks of coronary heart disease, stroke, or death from cardiovascular disease differed with regard to retinal microvascular changes. Data on the association between retinopathy and stroke were more consistent: relative risk of stroke 3.4 (1.0 to 11.3) for men in the Shibata study and 2.6 (1.6 to 4.2) for men and women in the atherosclerosis risk in communities study. In the cardiovascular health study the odds ratio for stroke was 2.0 (1.1 to 3.6).

In the atherosclerosis risk in communities study and the Beaver Dam eye study, associations between retinal abnormalities and stroke were stratified by hypertension status. The relative risk of stroke in the atherosclerosis risk in communities study was 2.6 (1.2 to 5.6) with retinopathy and hypertension compared with 2.0 (0.5 to 8.4) in normotensive people. In the Beaver Dam eye study, the odds ratio for death from cardiovascular disease in people aged 43-74 with retinopathy and hypertension or diabetes, or both was 2.3 (1.2 to 4.2) compared with 1.5 (0.4 to 5.3) for those without hypertension and diabetes. The odds ratio for those aged 75-84 was 2.0 (1.0 to 4.0) if retinopathy and hypertension or diabetes, or both were present and 1.8 (0.4 to 8.4) if only retinopathy was present.

Discussion

In this systematic review we found limited additional value of funduscopy in the routine management of patients with hypertension, except in emergency cases.

The evaluation of hypertensive retinopathy is subject to large variability between observers, especially microvascular changes. Only haemorrhages and exudates can be reliably assessed in retinal photographs. A computerised grading method has been developed to increase reproducibility of retinal microvascular changes, but this method is not widely available.

The low sensitivity of retinal abnormalities associated with hypertension indicates that hypertensive retinopathy is not common in hypertensive people. Less than half the retinal changes associated with hypertension cannot be explained by high blood pressure (low positive predictive value). In both the Beaver Dam eye study and the Blue Mountains eye study little difference was found in the presence of haemorrhages and exudates between normotensive and hypertensive people aged over 65.⁵⁻²³ The high specificity indicates that hypertensive retinopathy is rare in patients with normal blood pressure. Half the people without hypertensive retinopathy, however, still have hypertension (low negative predictive value).

The presence of hypertensive retinopathy doubles the risk of left ventricular hypertrophy. Data on the association between hypertensive retinopathy and microalbuminuria are inconsistent. Patients with haemorrhages and exudates have a higher intima-media thickness.

Evidence that hypertensive retinopathy is an independent predictor of cardiovascular risk is based on two large studies in which hypertensive patients with retinal haemorrhages or exudates had a twofold higher risk of stroke. Neither study, however, examined or adjusted for other indicators of hypertensive organ damage. Furthermore, the association between retinopathy and stroke is also observed in normotensive people, suggesting that besides blood pressure, other factors are important.

A recent paper reported on the associations between hypertensive retinopathy, blood pressure, and mortality from cardiovascular disease.²⁴ Although the

What is already known on this topic

Funduscopy is recommended in the routine management of hypertensive patients

The usefulness of funduscopy is being questioned

What this study adds

Funduscopy is of limited additional value in hypertensive patients, unless a hypertensive emergency is suspected

authors found a significant association between hypertensive retinopathy and hypertension, the low predictive values we calculated indicate that funduscopy cannot reliably determine whether a patient has hypertension. Only for stroke is the association with retinopathy significant and consistent. This association is also observed in people without hypertension and is not corrected for other indicators of hypertensive organ damage.

The included studies have several limitations. Firstly, hypertensive retinopathy was established on a photograph of one eye. Some retinal abnormalities may thus have been a sign of unilateral eye disease instead of hypertension. Secondly, most of the studies used a broad definition for hypertensive retinopathy. Thirdly, hypertension may have been misclassified, as blood pressure was measured only once or twice. Fourthly, two of the studies included people with diabetes. Diabetic retinopathy is a known risk factor for cardiovascular disease. Multivariate analysis may not have totally accounted for this confounding effect. Finally, only middle aged and older people were studied, although the association between hypertensive retinopathy, blood pressure, and risk of cardiovascular disease gets stronger in those under 60.²⁵

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