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Evaluation of mean arterial pressure as a risk factor for missed ophthalmoscopic findings in the emergency department

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An abstract of
A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science
in Clinical Research
2010

Abstract

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By Beau Benjamin Bruce

Background: The objective of this study was to examine risk factors for the failure to diagnose acute ophthalmoscopic findings in patients presenting to the emergency department (ED).

Methods: Consecutive, adult patients presenting to the Emory University ED with a chief complaint of headache, acute focal neurologic deficit, visual changes, or a diastolic blood pressure $\geq$120 were included. Photographs of the ocular fundus (optic disc and macula) were obtained from both eyes using a commercially available non-mydriatic ocular fundus camera. ED physicians were masked to the results of the photographs during their care of these patients and were asked to proceed with their routine evaluation of patients. Photographs were reviewed by experts for the presence or absence of ocular fundus abnormalities. The outcome of interest was *missed findings* defined as the presence of relevant findings not identified during routine care of patients. Presenting complaints, systolic and diastolic blood pressure, heart rate, height, weight, age, race, gender, and the patients ED diagnoses were recorded. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were used to calculate mean arterial pressure (MAP). MAP$\geq$125 was the exposure of interest. Univariate, stratified, and logistic regression analyses were performed.

Results: 350 were enrolled in the study. Forty-four patients (13%) had an relevant abnormality and 27 (61%) of these were missed. Stratified analyses indicated evidence of interaction between MAP and age, BMI, black race, and sex. Logistic regression analyses showed that MAP$\geq$125 was the primary, independent risk factor for missed fundus abnormalities after controlling for age, BMI, race, and sex.

Conclusions: There is a substantial burden of relevant ophthalmoscopic findings in the ED and the majority of these findings are missed. Mean arterial pressure was the most important determinant of whether a patient would have a missed ophthalmoscopic finding during the ED evaluation, and our findings suggest that defining the blood pressure threshold for hypertensive emergency as DBP$\geq$120 is too high to be used as a screening criteria for end organ damage and that a lower threshold may be more appropriate.

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Table of Contents

Introduction 1
Background 2
Methods 7
  Hypothesis 7
  Study Conduct 7
  Analysis 9
Results 10
Discussion 16
References 19
Appendix 24

List of Tables

1	Univariate analyses of potential risk factors for missed findings.	12
2	Odds ratios for missed by exposure.	13
3	Association between missed diagnosis and mean arterial pressure $\geq$125 controlled by covariates.	14
4	Logistic regression model with missed findings as outcome and mean arterial pressure $\geq$125 as exposure of primary interest controlled by covariates.	15
5	Log-linearity assumption checking and cutoff determination for mean arterial pressure.	24
6	Log-linearity assumption checking and cutoff determination for body mass index.	24
7	Log-linearity assumption checking and cutoff determination for age.	25
8	Evaluation of alternate age cutoff to avoid complete separation in stratified analyses.	25
9	Evaluation of confounding regarding the association between mean arterial pressure and missed findings through various logistic regression models.	26

Introduction

Abnormalities in the ocular fundus can be critical indicators of underlying vision- or life-threatening conditions. Therefore, visualization of the ocular fundus is a key part of the screening physical examination in the emergency department (ED). Despite its importance, ophthalmoscopy is often underperformed by physicians due to several factors:

1. limited training in performing the technical skill (1–2),
2. inability to recognize important ophthalmoscopic findings and to interpret their relevance (3–4), and
3. increasing demands on physician's time, coupled with under appreciation of the prognostic value of the examination (5).

Failure to adequately examine the ocular fundus in the ED leads to missed diagnoses with the risk of catastrophic outcomes for the patient and the risk of serious medico-legal liability for the physician.

The objective of this case-control study was to examine risk factors for the failure to diagnose acute ophthalmoscopic findings in patients presenting to the ED.

Background

Funduscopy is a key element of the physical examination. Despite the rapid progress that has been made in various diagnostic medical technologies, such as neuroimaging, visualization of the ocular fundus is often the only diagnostic clue to the identification of potentially serious ophthalmic and neuro-ophthalmic diseases. Examination of the fundus is necessary for the diagnosis of various disorders causing acute visual loss that require urgent management (e.g., retinal detachment), the detection of warning signs of impending visual loss and potentially catastrophic neurologic complications (e.g., papilledema, central retinal artery occlusion, anterior ischemic optic neuropathy), and to determine the severity of certain medical conditions (e.g., hypertensive crisis). Despite its importance, funduscopy is often neglected by physicians due to several factors: limited training in performing the technical skill (1–2), inability to recognize important ophthalmoscopic findings and to interpret their relevance (3–4), and increasing demands on physician's time, coupled with under appreciation of the prognostic value of the examination (5), Many life-threatening intracranial disorders, such as intracranial mass, cerebrospinal fluid shunt malfunction, hydrocephalus, meningitis, and cerebral vein thrombosis often present to the ED with isolated headache and can also produce papilledema (6–7), which in the absence of funduscopic exam, often go undetected. For example, in idiopathic intracranial hypertension (IIH), a condition that affects primarily young, obese women and leads to permanent severe visual loss in up to 10% of cases (8–9), headache is the most common presenting symptom (over

90% of cases) and the visual loss is typically insidious with patients often becoming severely visually impaired from papilledema before recognizing visual changes (6,10).

Many of these neuro-ophthalmic disorders cannot be easily diagnosed by routine neuroimaging studies and thus require vigilant ED care, including ophthalmoscopic examination. Therefore, failure to correctly examine the ocular fundus in the ED has both important clinical and medical-legal ramifications. Studies of headache management in the ED have found documented ophthalmoscopy in only 37-48% of cases suggesting that there is significant room for improvement in diagnosis, provider education, and technology in order to avoid missing important ocular pathology. In addition, lack of adequate specialty care in the ED is an increasingly important healthcare problem in the United States (11), and poor access to ophthalmologic specialty care in the ED is especially concerning (12). Although the problem is greater in rural areas, even in urban areas there are significant delays in obtaining emergency ophthalmologic consultations (13). These issues pose major roadblocks to the acute management of devastating ocular vascular disease such as central retinal artery occlusion and giant cell arteritis. Because ophthalmology is primarily a specialty where pathology is visible, telemedicine using ocular fundus photography may provide part of the solution to the triage of these patients for further consultation and evaluation. Indeed, many ophthalmologists cover multiple sites while on call. By allowing an on-call ophthalmologist the ability "examine" the patient without traveling to these various sites, ophthalmic telemedicine can lead to better distribution of limited eye care resources.

Numerous projects, such as ORBIS International's Cyber-Sight project, have demonstrated the ability to perform Internet tele-ophthalmologic consultations among local, national, and international physicians and surgeons (14–15), As of August 2007, over 3,300 consults had been performed using ORBIS's telemedicine program (16). Although telemedicine has been explored in an ophthalmic ED as a means for resident physicians to consult with their senior physicians overnight (17), it has not, to our knowledge, been applied to patient care in a large, general ED.

There are very few studies that have investigated the prevalence of ocular findings in patients with neuro-ophthalmic complaints despite the consequences of omitting this important diagnostic evaluation. One study prospectively examined cancer patients presenting with headache to determine risk factors (including papilledema) for the presence of intracranial metastases (18), and two other retrospective studies, one designed to look for new brain tumor diagnoses in the ED and another designed as a neuroimaging study of headache (19–20)have examined specific sub-populations and the prevalence of papilledema. These studies found significant rates of papilledema (9-28%) among these patients. These findings suggest that there is likely to be a large proportion of undiagnosed ocular disease, especially given the barriers to funduscopy discussed above.

The use of ocular fundus photography overcomes many barriers to an adequate funduscopic examination in the ED because many physicians are reluctant to perform routine dilation of patients for funduscopic examination, pupillary dilation takes up

to 30 minutes, and most patients prefer not to have their pupils dilated (4). In addition, neurologic patients represent a unique population in which pupillary reflexes can be critical for monitoring clinical status. Thus, undilated views of the ocular fundus may prove to be extremely useful in overcoming important obstacles to appropriate patient examination.

From a practical standpoint, we proposed that non-physician staff (i.e., trained nurses) could obtain clinically useful ocular fundus photography, thus reducing burdens on limited physician time, an important ED problem. Color, digital photographs can immediately be inserted into the chart or in the electronic medical record, and thus be available to the ED physician during the examination. Several recent studies have used ocular fundus photography to provide population-based studies of vascular disease and perform systematic screening for diabetic retinopathy in primary care settings and retinopathy of prematurity in neonatal intensive care units (21–28). In these studies, trained technicians took photographs of the posterior pole of the eye (which includes the optic nerve, the macula, and the major retinal vessels), often through undilated pupils, showing that it is feasible for non-physician staff to obtain adequate photographs (29). Several studies have already shown high agreement between dilated ocular fundus examinations by an ophthalmologist and ocular fundus photography using table-mounted digital cameras for identifying diabetic retinopathy and other ocular conditions involving the posterior pole of the eye (optic nerve and macula) (30–31). The cost of a non-dilated fundus camera is relatively low and stud-

ies have demonstrated its cost effectiveness in screening for diabetic retinopathy (32). These results are particularly relevant to the present study which primarily aims to diagnose less subtle ocular findings, such as papilledema, and for which the medical morbidities without treatment are often devastating. Although adequate photographs alone in the absence of direct funduscopic exam do not guarantee better recognition of important findings, one small study suggested that internal medicine physicians were considerably better at accurately diagnosing important ocular conditions on photographs compared to examining patients with a direct ophthalmoscope (4). For example, while only 21% of the fourteen physicians correctly identified papilledema with the direct ophthalmoscope, 71% of the physicians did so based on a photograph. Furthermore, it is easier to educate physicians to recognize fundus abnormalities on photographs because the ocular fundus photographs provide a wider field of view than direct ophthalmoscopy and remove the obstacle of simultaneously learning the technical skill of direct ophthalmoscopy. Finally, not only does ocular fundus photography remove the majority of technical barriers to the funduscopic examination by the ED physician, it has the potential to facilitate consultation with specialty physicians, even those located a great distance away, when interpretation difficulties arise (33). Furthermore, because immediate access to an ophthalmologist is often limited, telemedicine may provide a unique opportunity to provide these specialized services to a broader population of patients in a more timely fashion.

Methods

Hypothesis

The null hypothesis for this study is that the odds of exposure to elevated mean arterial pressure in patients presenting to the emergency department with primary complaints of headache, focal neurologic deficits, vision loss, or a diastolic blood pressure $\geq$125 with missed findings is equal to the odds of exposure to elevated mean arterial pressure in patients presenting to the emergency department with primary complaints of headache, focal neurologic deficits, vision loss, or a diastolic blood pressure $\geq$125 with non-missed (found) findings, after controlling for age, sex, race, and body mass index.

Study Conduct

Consecutive patients presenting to the Emory University ED with a chief complaint of headache, acute focal neurologic deficit, visual changes, or a diastolic blood pressure $\geq$120 were included in the first phase of the Fundus photography vs. Ophthalmoscopy Trial Outcomes in the Emergency Department (FOTO-ED) study and were the subjects for this study. Patients who were under the age of eighteen or who were unable to consent were excluded from the study. In the FOTO-ED study, photographs of the ocular fundus (optic disc and macula) were obtained from both eyes of enrolled patients using a commercially available non-mydriatic ocular fundus camera

(Kowa α-D, Torrence, CA). ED physicians were masked to the results of the photographs during their care of these patients and were asked to proceed with their routine evaluation of patients.

Two neuro-ophthalmologists reviewed the photographs for the presence or absence of relevant ocular fundus abnormalities. In the case of disagreement, a third neuro-ophthalmologist made the determination of whether an abnormality was present or absent. In any case in which there remained diagnostic uncertainty, the patient was examined in-person by a neuro-ophthalmologist. The presence or absence of findings determined by the neuro-ophthalmologists in this manner served as the reference standard for the study.

Relevant ocular fundus abnormalities were defined as optic disc edema, optic disc pallor, retinal vascular occlusion, mass lesion, grade III or IV ischemic retinopathy, and retinal detachment. ED physicians were notified within 24 hours of any relevant findings identified.

The outcome of interest was *missed findings* defined as the presence of relevant findings not identified during routine care of patients in the ED by any means (e.g., ED physician direct ophthalmoscopic examination, consultation requested in the ED, or the relevant finding was known prior to the ED visit).

Presenting complaints, systolic and diastolic blood pressure, heart rate, height, weight, age, race, gender, and the patients ED diagnoses were recorded. Systolic blood pres-

sure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were used to calculate mean arterial pressure (MAP) based on the empirical forumla reported by Razminia *et al.* (34):

$$\text{MAP} = \text{DBP} + (0.0012\text{HR} + 0.33)(\text{SBP} - \text{DBP}).$$

Body mass index was calculated from height in meters divided by weight in kilograms squared.

Analysis

Univariate analyses were undertaken to examine the data, check for outliers, and to evaluate if each variable met the underlying assumptions (log-normal) for logistic regression. For variables that did not appear to meet this assumption, cutpoints were chosen to categorize each continuous variable (see Appendix) for further analyses: MAP$\geq$125 (Table 5), BMI$\geq$30 (Table 6), and age$\leq$40 years (Tables 7 & 8). Although a cutoff of age$\leq$65 was initially considered this led to complete separation in the stratified analyses with respect to outcome and an alternate cutoff of age$\leq$40 was used. Stratified analyses were performed evaluating first for interaction (exact conditional test) and then confounding. Various logistic regression models (see Appendix) were fit to control for interaction and potential confounding effects on the association of interest (Table 9). Statistical significance was considered to be $p < 0.05$.

Results

Three hundred and fifty patients were enrolled in the study. Median age was 44.5 years (interquartile range [IQR]: 31-58.75). One hundred thirty (37%) were men. Median body mass index was 30 (IQR: 24-32). Based on a review of the triage logs, about 1950 patients were eligible to be enrolled in the study. Thus, our 350 patients represent about 18% of the potentially eligible patients. Headache was the presenting complaint in 122 patients (35%), focal neurological deficit in 100 (29%), visual complaints in 92 (26%), and elevated diastolic blood pressure in 21 (6%). Forty-four patients (13%) had an relevant abnormality and 27 (61%) of these were missed. Eleven of the 44 patients were found because they were diagnosed before their ED visit and six additional patients were found by ophthalmology consultation. Although six patients were examined by the ED physicians with direct ophthalmoscopy, no relevant abnormalities were identified in this fashion.

Among the 18 patients with MAP$\geq$125, 7 were enrolled for DBP$\geq$120, 4 for isolated headache, 1 for isolated acute focal neurologic deficit, 3 for isolated acute visual complaints, 1 for an acute neurologic deficit with visual complaints, and two with headache combined with acute focal neurologic deficit. The minimum MAP among the patients enrolled with DBP$\geq$120 was 143 mm Hg, and the blood pressure range for the other 11 patients was 166-201/84-119 (SBP/DBP, mmHg). Only one abnormality among the 18 patients with MAP$\geq$125 would have been considered unrelated

pathophysiologically to elevated blood pressure (anterior optic neuritis).

Univariate analyses (Tables 1 & 2) showed that MAP≥125, BMI≥30, and black race were risk factors for missed findings.

Examining the association between MAP and missed findings in the presence of the other covariates showed evidence of interaction between MAP and age, BMI, black race, and sex (Table 3).

A logistic regression model (Table 4) found that MAP remained a significant, independent predictor of missed findings after controlling for age, BMI, race, sex.

	Missed (n=27)		**Non-missed (n=323)**			
Variable	**n**	**%**	**n**	**%**	χ^2	***p*-value**†
MAP≥125	16	23.9	11	3.9	30.4	<0.0001*
BMI≥30	17	14.0	10	4.4	10.3	0.001*
Age≥65	2	3.4	25	8.6	‡	0.28§
Black race	18	10.7	9	4.9	4.1	0.04
Woman	15	6.8	12	9.2	0.7	0.41

Missed was defined as patients with the presence of relevant ophthalmoscopic findings not identified during routine care of patients in the ED by any means (e.g., ED physician direct ophthalmoscopic examination, consultation requested in the ED, or the relevant finding was known prior to the ED visit).

MAP = mean arterial pressure

BMI = body mass index

Age in years

† α=0.05. Significant *p*-values are marked with an asterisk (*).

‡ Fisher's Exact Test

§ Two-tailed *p*-value

Table 1 Univariate analyses of potential risk factors for missed findings.

Variable	**OR**	**(95%CI)**
MAP≥125	7.8	(3.4–18.1)
BMI≥30	0.38	(0.06–1.33)
Age≥65	3.56	(1.6–8.3)
Black race	2.3	(1.03–5.5)
Woman	0.72	(0.32–1.6)

OR = odds ratio

CI = confidence interval

See Table 1 for additional symbol and abbreviation definitions.

Table 2 Odds ratios for missed by exposure.

Variable	**OR$_1$**	**OR$_0$**	***p*-value**
Age≤40	7.8	36.1	<0.001
BMI≥30	3.6	17.2	<0.001
Black race	4.1	24.0	<0.001
Woman	5.0	16.1	<0.001

Crude OR: 7.8

OR$_1$ and OR$_0$ are the odds ratios for the association among those with and without, respectively, the variable criteria in column 1 p-value calculated by exact conditional test for interaction

See Table 1 for additional symbol and abbreviation definitions.

Table 3 Association between missed diagnosis and mean arterial pressure ≥125 controlled by covariates.

Variable	**Estimate**	**SE**	**z**	***p*-value**
MAP≥125	5.1811	1.4143	3.663	0.0002*
BMI≥30	1.5262	0.7492	2.037	0.041*
Black race	1.0825	0.8492	1.275	0.20
Age≤40	2.2112	1.0654	2.076	0.037*
Woman	-0.3416	0.6829	-0.500	0.62
MAP≥125×BMI≥30	-1.1422	0.9757	-1.171	0.24
MAP≥125×Black race	-1.0899	1.0558	-1.032	0.30
MAP≥125×Age≤40	-1.4475	1.2692	-1.140	0.25
MAP≥125×Woman	-0.6637	0.9166	-0.724	0.46

Intercept = -6.0800; -2 log likelihood: -71.43718; Hosmer-Lemeshow: p=0.12

See Table 1 for additional symbol and abbreviation definitions.

Table 4 Logistic regression model with missed findings as outcome and mean arterial pressure ≥125 as exposure of primary interest controlled by covariates.

Discussion

Our study found that more than one in ten patients presenting to the ED with headache, acute focal neurologic deficits, acute visual changes, and diastolic blood pressure of at least 120 mm Hg have relevant ophthalmoscopic findings that should have been identified during their evaluation in the ED. Over 60% of these findings were missed and if one excludes the patients that came to the ED with a known diagnosis over 80% of patients with relevant findings were missed. Thus, there is a substantial burden of relevant ophthalmoscopic findings in the ED and the majority of these findings are missed.

This study identified mean arterial pressure as the most important determinant of whether a patient would have a missed ophthalmoscopic finding during the ED evaluation. Patients with MAP$\geq$125 in isolation had 175 times the odds of being missed compared to patients with a lower MAP. In terms of probability, a patient presenting with any of the eligible complaints who also had a MAP$\geq$125 had a 24% chance of being missed versus only 4% of those who had a lower blood pressure. Male patients with MAP$\geq$125 had a 38% probability of a missed finding.

If we consider using these risk factors as screening tools, using the MAP$\geq$125 criteria alone had a sensitivity of 59% and a specificity of 84%. Adding age$\leq$40 years and BMI$\geq$30 to the criteria increased the sensitivity to 100%, but decreased the specificity to 31%. Although a specificity of 31% may appear modest, the need to screen almost a

third less patients in the ED with these complaints would likely result in substantial time and savings. For example, given that we estimate that about 1950 eligible patients were seen during the approximately 6 months over which the study ran, this could have prevented about 583 patients from being screened.

While it was expected that more obese patients would be at greater risk of missed diagnosis, we were surprised to find that younger age was also a risk factor for missed diagnosis. It is possible that this occurred because ED physicians had a lower concern for serious underlying pathology in younger patients. An alternate hypothesis is that it represents a survivorship bias. It is well established that hypertension is a risk factor for early mortality, thus older patients with hypertension and thus potentially abnormal ocular fundi may not have survived to be included in our source population.

Our study had several notable limitations. First, the study was limited to patients at high risk for ocular findings, and we do not know if the frequency with which malignant hypertensive changes were observed in patients with DBP<120 will be similar in patients presenting to the ED with any complaint. Second, because one must be abnormal before one could be potentially missed and such a large proportion of the patients were missed, these may merely represent risk factors for abnormalities of the ocular fundus. Regardless, this is of clinical relevance. Finally, we were only able to include about one fifth of the potentially eligible patients. While we have no reason to believe there was systematic inclusion of patients with a higher or lower risk of findings this cannot be completely excluded.

In conclusion, our findings suggest that the literature defining the blood pressure threshold for hypertensive emergency is too high to be used as a screening criteria for end organ damage and that a lower threshold such as SBP$\geq$160 may be more appropriate. We plan to validate these findings during the second phase of the FOTO-ED study in which the ED physicians will be provided with the fundus photographs and plan future studies in which we will enroll patients by a less stringent blood pressure criteria.

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Appendix

Quintile	[68,94]	(94,102]	(102,110]	(110,124]	(124,184]
n	70	70	70	70	70
$\hat{\beta}_1$	0.00	0.42	0.42	0.42	2.31
OR	1.0	1.5	1.5	1.5	10

n = number of patients

$\hat{\beta}_1$ = log odds ratio comparing a given quintile to the lowest quintile

OR = odds ratio comparing a given quintile to the lowest quintile

Table 5 Log-linearity assumption checking and cutoff determination for mean arterial pressure.

Groups	[14,20]	(20,25]	(25,30]	(30,40]	(40,64]
n	27	97	104	89	32
$\hat{\beta}_1$	0.00	0.11	0.27	1.19	1.99
OR	1.00	1.12	1.31	3.29	7.32

See Table 5 for symbol and abbreviation definitions.

Table 6 Log-linearity assumption checking and cutoff determination for body mass index.

Quintile	[18,29]	(29,38]	(38,50]	(50,62]	(62,94]
n	72	68	77	67	66
$\hat{\beta}_1$	0.00	0.06	0.09	0.08	-1.07
OR	1.00	1.06	1.09	1.08	0.34

See Table 5 for symbol and abbreviation definitions.

Table 7 Log-linearity assumption checking and cutoff determination for age.

Quintile	[17,40]	(40,94]
n	154	196
$\hat{\beta}_1$	0.00	-0.50
OR	1.00	0.60

See Table 5 for symbol and abbreviation definitions.

Table 8 Evaluation of alternate age cutoff to avoid complete separation in stratified analyses.

Model	**Coef.**	**LRT**	***p*-value**
Selected model	5.18	N/A	N/A
3-way interactions (+7 d.f.)	5.25	3.93	0.78
No sex interaction	4.82	0.53	0.47
No age interaction	4.27	1.53	0.22
No race interaction	4.71	1.12	0.29
No BMI interaction	4.81	1.41	0.23
No interactions (-4 d.f.)	2.52	6.15	0.19

The selected model is the model described in Table 4.

Coef. is the estimate of the coefficient for mean arterial pressure.

BMI = body mass index

LRT = likelihood ratio test with its associated p-value

Table 9 Evaluation of confounding regarding the association between mean arterial pressure and missed findings through various logistic regression models.