

# Is pseudoexfoliation syndrome associated with coronary artery disease?

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## Abstract

**Background:** Pseudoexfoliation syndrome (PEX) is recognised by chronic deposition of abnormal pseudoexfoliation material on anterior segment structures of the eye, especially the anterior lens capsule. In recent years, several studies have shown the presence of vascular, cardiac and other organ pseudoexfoliative material in patients with ocular pseudoexfoliation. **Aims:** The purpose of this study is to determine whether an association exists between ocular pseudoexfoliation and coronary artery disease, aortic aneurysms and peripheral vascular disease. **Patients and Methods:** 490 patients who underwent coronary angiography (CAG) at Kosuyolu Cardiovascula Research and Training Hospital were included in the study. Patients were evaluated for conventional risk factors such as age, sex, family history, hypertension, diabetes, dislipidemia and smoking. Detailed eye examinations including evaluation of lens were done in all patients. The presence of PEX material in the anterior segment was best appreciated by slit lamp after pupillary dilation. The patients were divided into two groups according to the presence of PEX, and compared for the presence of CAD and other risk factors. **Results:** CAD was present in 387 patients. 103 patients had normal coronary angiography. 20 (5.2 %) of CAD patients and 4 (3.9%) of normal CAG patients were found to have PEX ( $p>0.05$ ). There was no significant relationship between CAD and the presence of PEX ( $p>0.05$ ). When patients were grouped according to the presence of PEX, only age was significantly different between the two groups ( $r: 0.25, p<0.001$ ). **Conclusion:** There is no significant relationship between the presence of PEX and CAD. Further studies in larger scales with elderly population may be more valuable.

**Keywords:** Pseudoexfoliation syndrome, coronary artery disease, aortic aneurism, peripheral artery disease.

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## Introduction

Pseudoexfoliation syndrome (PEX) is a common, age-related fibrillopathy of unknown cause. It is characterized by the deposition of a distinctive fibrillar material in the anterior segment of the eye and first described in 1917 by Lindberg [1]. The prevalence increases markedly with age. The proportion of people worldwide affected by this syndrome ranges from 0.5% in those younger than 60 years to 15% in people aged 60 years and

older [2]. It is recognised by chronic deposition of abnormal pseudoexfoliation material on anterior segment structures of the eye, especially the anterior lens capsule. Ocular synthesis and deposition of this abnormal fibrillar pseudoexfoliation material can lead to many ocular complications, including open-angle glaucoma as well as an increase in complications in intraocular surgery [3]. Pseudoexfoliation syndrome affects all the tissues of the anterior segment of the eyes, and has been acknowledged as a generalized disorder involving connective tissue of

various visceral organs, such as heart, lung, liver, kidney, and meninges [4].

Although deposition of pseudoexfoliative fibers in cardiovascular system has been documented, data about significance and outcome are limited and conflicting. Some studies have proposed that PEX was related to coronary artery disease (CAD), aortic aneurysm and cardiovascular mortality [5-8], while some others indicated the opposite [9-11]. We aimed to study the relationship between CAD and PEX.

## Patients and Methods

490 successive patients who underwent coronary angiography at Kartal Kosuyolu Cardiovascular Research and Training Hospital between December 5, 2005 and January 20, 2006 were included in the study. Those who had previous bilateral cataract operation, patients younger than 18 years old and those who denied inclusion in the study were excluded from the study. Conventional risk factors for cardiovascular disease were assessed. Family history was defined as the presence of CAD in a first degree male relative younger than 55 years or a female younger than 65 years. Being under treatment for hypertension or blood pressure over 140/90 mmHg was regarded as hypertension. Those who were under treatment for diabetes mellitus or a fasting blood glucose level of  $\geq 126$ mg/dl was taken as diabetic. Being under treatment for dislipidemia, low density lipoprotein (LDL)  $\geq 130$  mg/dl or high density lipoprotein (HDL)  $\leq 35$  mg/dl for males and  $\leq 45$  mg/dl for females was regarded as dislipidemia. Those who had smoked in the last 10 years were regarded as smokers. Written informed consent was taken from all patients and the study was approved by the local ethic committee.

### Angiographic and ophthalmologic examination

Coronary angiography was performed using Axiom Artis (Siemens AG, Germany). The results were evaluated by two experienced cardiologists. Stenosis  $< 50\%$  in epicardial coronary arteries was defined as non-critical, and those  $\geq 50\%$  were regarded as critical lesions. Ectatic coronary arteries (1.5-2 times reference diameter) were evaluated for the presence of aneurysms ( $\geq 2$  folds of reference diameter). Aortography and peripheral angiography was done when indicated. Detailed ophthalmic examinations including visual acuity, fundus examination, tonometer examination and gonioscopic examination were done in Kartal Lutfi Kirdar Research and Training Hospital by two ophthalmologists who were blinded to the patient's clinical history. The presence of PEX material in the anterior segment was best appreciated by slit lamp after pupillary dilation.

### Statistics

Statistical analysis was performed with SPSS for Windows, version 16.0 (SPSS Inc. Chicago, Illinois) The two groups separated according to the presence of CAD were compared using Fisher's Exact test in terms of the presence of PEX and other risk factors. The relationship

between the presence of PEX and other risk factors was evaluated by Spearman's correlation coefficient.  $p < 0.05$  was regarded as significant.

## Results

Catheterization was done for evaluation of CAD in 462 patients, preoperative evaluation for rheumatic valvular diseases in 10, peripheral artery diseases in 10, congenital heart diseases in 4, and aortic aneurysms in 4 patients. 387 patients had CAD, 17 had aortic root dilatation and 28 had peripheral artery disease. 333 of CAD patients had critical lesions while 54 had noncritical ones. 103 patients had normal coronary angiograms. PEX was found in 20 (5.2%) of CAD patients and 4 (3.9 %) of normal coronary angiogram patients ( $p > 0.05$ ). No relationship was found between the presence or severity of CAD and PEX (Table 1-3, and Fig. 1). There was no relationship between the presence of PEX and coronary ectasia, aortic root dilatation and peripheral artery disease ( $p > 0.05$ ). When patients were regrouped according to the presence of PEX, a weak relationship was found between PEX and age ( $r: 0.25$ ,  $p < 0.001$ ) (Table 2 and 3, and Fig. 2).

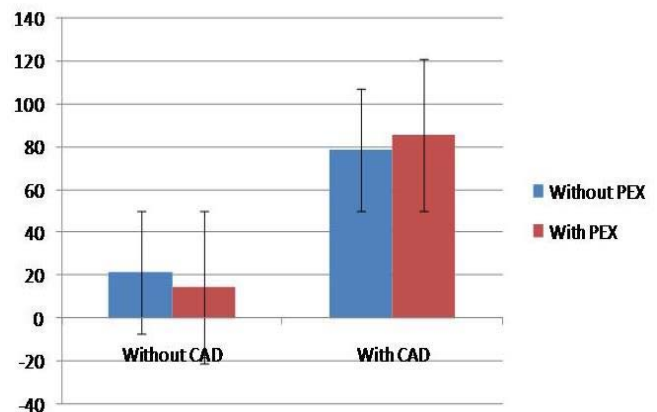


Fig. 1 Relative coexistence of PEX and coronary artery disease

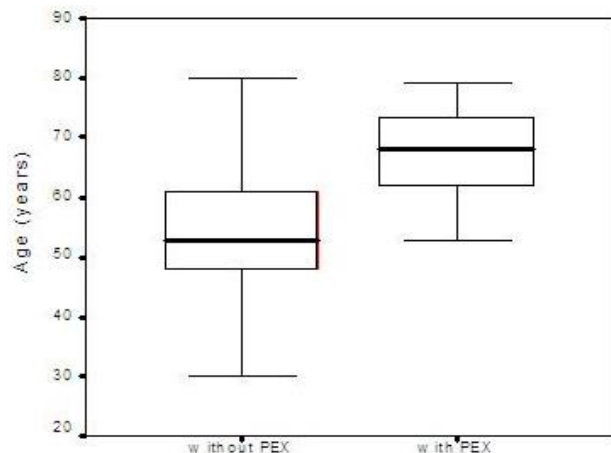


Fig. 2 PEX and age relationship. When patients were regrouped according to the presence of PEX, a weak relationship was found between PEX and age ( $r: 0.25$ ,  $p < 0.001$ )

**Table 1** PEX distribution of patients with and without coronary artery disease

|             | CAD (n=387) | Without CAD (n=103) | Total |
|-------------|-------------|---------------------|-------|
| PEX         | 20(5.2%)    | 4 (3.9%)            | 24    |
| Without PEX | 367 (94.8%) | 99 (96.1%)          | 466   |
| Total       | 387         | 103                 | 490   |

CAD: Coronary Artery Disease, PEX: pseudoexfoliation

**Table 2** Cardiovascular risk factors and PEX distribution according to presence of coronary artery disease

|                              | CAD (n=387) | Without CAD (n=103) | P value |
|------------------------------|-------------|---------------------|---------|
| Sex, male % (n)              | 84 (325)    | 55 (57)             | <0.001  |
| Age (years)                  | 55.7±10.2   | 50.5±10.8           | <0.001  |
| Hypertension % (n)           | 50 (193)    | 34 (35)             | 0.005   |
| DM % (n)                     | 22 (85)     | 17 (18)             | NS      |
| Smoking % (n)                | 37 (143)    | 44 (45)             | NS      |
| Dyslipidemia % (n)           | 50 (194)    | 29 (30)             | 0.001   |
| Family history for CAD % (n) | 41 (159)    | 43 (44)             | NS      |
| PEX % (n)                    | 5.2 (20)    | 3.9 (4)             | NS      |

**Table 3** Cardiovascular risk factors and coronary artery disease distribution according to presence of PEX

|                              | PEX (n=24) | Without PEX (n=466) | P value |
|------------------------------|------------|---------------------|---------|
| Sex, male % (n)              | 83 (20)    | 76 (374)            | NS      |
| Age (years)                  | 65.9±4.2   | 54.7±10.9           | <0.001  |
| Hypertension % (n)           | 50 (12)    | 46.9 (218)          | NS      |
| DM % (n)                     | 4 (1)      | 21 (100)            | NS      |
| Smoking % (n)                | 57 (14)    | 37 (174)            | NS      |
| Dyslipidemia % (n)           | 50 (12)    | 45 (210)            | NS      |
| Family history for CAD % (n) | 25 (6)     | 41 (193)            | NS      |
| CAD % (n)                    | 83.3 (20)  | 78.6 (367)          | NS      |

CAD: Coronary Artery Disease, DM: Diabetes Mellitus

## Discussion

In a prospective single-blind study, Schumacher S et al. ophthalmoscopically examined 55 patients with aneurysms of abdominal aorta and 41 controls with carotid artery occlusion. 24 of 55 patients with aortic aneurysm showed signs of manifest (17 of 55 patients) or early-stage (seven of 55) pseudoexfoliation syndrome. Eight of 41 control patients showed manifest (seven of 41 patients) and early (one of 41) ocular pseudoexfoliation ( $p=0.016$ ). These findings, including histopathological examinations, suggested an association between aneurysms of the abdominal aorta and PEX [6].

On the other hand, in a study conducted by Jaana Hietanen et al., a total of 77 patients recently operated for abdominal aortic aneurysm underwent biomicroscopy under pupillary dilatation to detect the presence of manifest and suspect deposits of exfoliation material. Manifest exfoliation was detected in 11 patients, five of whom were aged 60–69 years and six of whom were aged 70–79 years. Four patients had suspect exfoliation. The prevalence of exfoliation syndrome in patients operated for abdominal aortic aneurysm was similar to that in the general population of the same age in Finland. This finding did not support the proposed connection between PEX and abdominal aortic aneurysm [12].

In a large-population study, Mitchell P et al. proposed that PEX was significantly associated with a history of angina or hypertension or a combined history of angina, acute myocardial infarction, or stroke [5]. In another study designed to investigate the prevalence of glaucoma and CAD in patients with cataract and PEX, Andrikopoulos GK et al. also found that PEX was positively associated with the risk for CAD among subjects 50 years or older [7].

Nevertheless, there are also studies that have contrary results. Shrum KR et al. conducted a study to determine the association between ocular pseudoexfoliation and cardiovascular, cerebrovascular and all-cause mortality. 472 patients who were diagnosed with pseudoexfoliation syndrome or pseudoexfoliative glaucoma at Mayo Clinic from 1976 through 1995 were included in the study. No association was found between ocular pseudoexfoliation and cardiovascular or cerebrovascular mortality [9].

Brajkovic et al. investigated the relationship between PEX and hypertension, CAD, arrhythmia, diabetes and cerebrovascular accidents, and only arrhythmia was found to be higher in PEX patients. No relationship was found between PEX and mortality or other risk factors [11]. Again, in another study, no relationship was noted between PEX and mortality [10]. Interpretation of the results is somewhat compromised in these studies because the control group was generally formed by the population with vascular diseases. In some studies, non-invasive techniques were used to diagnose CAD in PEX patients.

In our study, the presence of PEX was studied in patients with or without CAD, aortic aneurysm or peripheral artery disease. As a result no significant relationship was found between PEX and CAD, aortic aneurysm or peripheral artery disease. PEX and CAD are part of degenerative processes related with aging. The previously found association between PEX and CAD could be the result of increased incidence of both with age. Further detailed study of elderly population may be needed as the presence of PEX is related only with elderly CAD patients in our study.

## Conclusion

No significant relationship was found between PEX and CAD, aortic aneurysm or peripheral artery disease. Further extended study in elderly population may yield more valuable results relating PEX and CAD.

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