

PUBLIC HEALTH AND THE EYE

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Obesity and Eye Diseases

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Abstract. The prevalence of obesity has reached epidemic proportions in many countries. Although its impact on overall health is well documented, less is known about the ocular manifestations of obesity. Among different eye diseases, obesity has been linked with age-related cataract, glaucoma, age-related maculopathy, and diabetic retinopathy. Numerous population-based and prospective studies support an association between obesity and risk of age-related cataract. However, the nature and strength of these associations, particularly with the different cataract subtypes, remains to be determined. There is strong evidence that obesity is associated with elevated intraocular pressure, but there is no convincing data to support a more direct association between obesity and glaucomatous optic neuropathy. Studies to date have not found a consistent pattern of association between obesity and risk of age-related maculopathy or diabetic retinopathy. Thus, although obesity may be a risk factor for many ocular conditions, the present literature is inadequate to establish any convincing associations. Furthermore, whether weight loss reduces the risk of eye diseases remains unresolved. Because of the potential public health impact of obesity, there is a greater need to understand its ocular effects. (*Surv Ophthalmol* 52:180–195, 2007. © 2007 Elsevier Inc. All rights reserved.)

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Introduction

Obesity is a major public health problem, with prevalence increasing at staggering rates in many countries.^{50,51,54,55,77,85,97,98} The World Health Organization (WHO) defines obesity as a body mass index (BMI) of 30 kg/m² or greater, and overweight as individuals whose BMI falls between 25 kg/m² and 29.9 kg/m² (World Health Organization: Controlling the global obesity epidemic. Geneva: World Health Organization, 2002). Different classifications are used for some specific populations, such as Asians and children. In Asian populations, it has been proposed that a BMI of 25 kg/m² or

greater should be classified as obesity.⁹⁸ In children, BMI is classified according to percentiles for age and sex, and children with BMI higher than 95th percentiles for age and sex may be considered as overweight.^{30,39,133}

Obesity affects a wide spectrum of age groups, from the young^{39,133} to the elderly.¹⁰⁴ In the United States, the prevalence of obesity was 30% in 1999–2000,⁵¹ with 65% of adults, and 10–15% of children and adolescents, categorized as overweight or obese.^{77,81} The current International Obesity Task Force estimates suggest at least 1.1 billion people are overweight worldwide, and 312 million of them

are obese (World Health Organization/International Association: Redefining obesity and its treatment. Available at www.idi.org.au/obesity_report.htm).

The medical consequences of obesity are numerous. It is an established risk factor for many systemic diseases including coronary heart disease, type 2 diabetes mellitus, hypertension, stroke, dyslipidemia, osteoarthritis, and sleep apnea.^{43,69,77,123,155} Obesity has also been associated with certain types of cancers.^{12,20} One study estimated that obesity is responsible for approximately 40% of endometrial cancers, 25% of renal cancers, and 10% each of colonic and breast cancers.¹² Other obesity-associated comorbidities include polycystic ovary syndrome, fatty liver, as well as depression secondary to social stigmatization and discrimination.¹²³

The impact of obesity on health is widespread, and the deleterious effects of obesity on the cardiovascular and metabolic systems are well known.⁷⁷ Less well documented, however, are the potential ocular effects of obesity. Obesity has recently been reported to be negatively associated with visual acuity,¹⁰ but the ocular conditions underlying this association and the potential implications are unclear. Among different eye diseases, obesity has been associated with cataract,^{1,21,53,63,86,94,107,108,121,129,168,211,222} age-related maculopathy,^{2,28,167,173} diabetic retinopathy,^{8,24,83,114,171,207} and glaucoma.^{60,127,225} However, these associations have not been consistently documented. The purpose of this article is to review the potential ocular effects of obesity.

Obesity and The Eye

OBESITY AND CATARACT

Obesity has been proposed to be a risk factor for cataract development, though the exact underlying mechanisms are unclear. The relationship between obesity and cataract has been investigated in many epidemiological studies,^{10,21,22,53,63,74,86,94,107,108,121,126,129,144,168,197,211,222} but the findings are not universally consistent (Table 1). The strongest evidence is based on prospective data from several large population-based studies demonstrating positive association between obesity and cataract.^{63,73,86,107,168,211} In 1995⁶³ and 2000,¹⁶⁸ the Physicians' Health Study, a randomized trial of 22071 healthy male American physicians aged 40–84 years, reported both overall obesity, measured as BMI, and abdominal adiposity, measured as waist-to-hip ratio (WHR), as independent risk factors for cataract. It was found that at any given level of BMI, a 2-unit higher level predicted a 12% increase risk of cataract.⁶³ The Nurses' Health Study, a large pro-

spective study of female nurses in 1993, also found a higher rate of cataract surgery for women with BMI levels of 23 or greater compared to women with lower levels.⁷³ Subsequently, the Nurses' Health and the Health Professionals Follow-up Study generated further results, reporting that obesity increases risk of cataract overall, but in particular, of posterior subcapsular (PSC) type, even after adjusting for variables such as smoking, age, and diabetes.²¹¹ Prospective data from the Framingham Eye Study also demonstrate an independent association between greater BMI and higher incident of cortical and PSC opacities.⁸⁶ Further support on the positive association between obesity and cataract is derived from cross-sectional data from other population-based,^{1,21,94,121,129,222} and hospital-based studies,^{126,197} although not all studies have been consistent. For example, using standardized photography to grade lens opacities, the Beaver Dam Eye Study, a cohort study of almost 5,000 white Americans, found no significant associations of obesity with either incident cataract or cataract extraction at the baseline or the 5-year follow-up examination.^{108,110} Nonetheless, 10-year prospective data from this study showed an association between higher BMI and increased risk of PSC cataract in persons without diabetes.¹⁰⁷

There have also been inconsistencies regarding the types of cataract associated with obesity in these studies. Cortical and PSC cataracts have been most consistently associated with obesity.^{1,21,121,129,222} Among these studies, the Barbados Eye Study in African Americans found higher WHR to be associated with cortical opacities.¹²⁹ The Blue Mountain Eye Study in white Australians suggested that obese persons (BMI of 30 kg/m² or greater) have about half- and two-fold increase risk of having cortical and PSC cataracts respectively.²²² In the Age-Related Eye Disease Study (AREDS), both higher BMI and weight gain were found to have significant association with moderate cortical cataract, independent of age and sex.¹ But this association was not statistically significant in the fully adjusted model.

Several plausible pathophysiological mechanisms have been proposed to explain the association of obesity and cataract. One theory suggests that leptin, a 16-kDa pleiotropic cytokine expressed and secreted mainly by adipocytes,²²⁷ is involved in the molecular mechanisms underlying cataract formation.⁶⁴ Studies have discovered that individuals with obesity likely exhibit hyperleptinemia and leptin resistance.^{59,78,79,149} Leptin has also been found to increase accumulation of reactive oxygen species in various cellular models.^{14,219} This link between obesity, hyperleptinemia, and increased

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