Overweight, Obesity, and Age-Related Cataract: A Meta-analysis

Chen-Wei Pan* and Yi Lin†

ABSTRACT

Purpose. To examine the longitudinal association of overweight/obesity with age-related cataract.

Methods. A systematic review of the literature was performed using PubMed and Embase from their inception until June 2013 for prospective data on body mass index categories identical or similar to the World Health Organization recommended classifications of body weight and age-related cataract including nuclear, cortical, and posterior subcapsular (PSC) cataract. Meta-analyses were conducted using random-effects models with results reported as adjusted relative risks (RRs).

Results. A total of 163,013 subjects aged 40 to 84 years from six prospective cohort studies were included in the meta-analysis. Obesity was associated with an increasing risk of nuclear cataract (pooled RR, 1.12; 95% confidence interval [CI], 1.02 to 1.25), cortical cataract (pooled RR, 1.34; 95% CI, 1.07 to 1.66), and PSC cataract (pooled RR, 1.52; 95% CI, 1.31 to 1.77). Overweight was only associated with an increasing risk of PSC cataract (pooled RR, 1.23; 95% CI, 1.09 to 1.40).

Conclusions. The longitudinal associations of obesity with incident age-related cataract are confirmed by the findings in this six-study meta-analysis. The association of obesity with PSC cataract is stronger than that with nuclear or cortical cataract. Randomized control trials are warranted to examine the effectiveness and cost-effectiveness of weight reduction in obese populations to decrease the risk of age-related cataract.

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Key Words: overweight, obesity, cataract, meta-analysis

Age-related cataract, including its subtypes, nuclear, cortical, and posterior subcapsular (PSC) cataract, is a leading cause of visual impairment worldwide. With longer life expectancies and an aging population throughout the world, the burden and impact of age-related cataract tend to increase. Although numerous epidemiological studies tend to identify the risk factors for age-related cataract, especially modifiable ones, few risk factors have been consistently associated with age-related cataract such as smoking1 and ultraviolet exposure.2

Overweight/obesity is a huge public health problem with tremendous socioeconomic impact as they are associated with a wide range of chronic diseases including diabetes mellitus3 and cardiovascular diseases.4 Recently, a few case-control or cross-sectional studies have indicated that overweight/obesity may be associated with a higher risk of age-related cataract.5–7 However, case-control or cross-sectional studies are limited to establish a temporal relationship or causal association between an exposure and an outcome.

Clinically, it is important to understand if overweight/obesity is associated with a specific subtype of cataract because the pathophysiology, treatment, and impact on visual functioning of the three subtypes of cataract tend to be different.8 As the prevalence of obesity continues to increase worldwide, it is also worth understanding if obesity would increase the global burden of cataract from a public health perspective. Therefore, a systematic approach to combine the results of all available studies evaluating the longitudinal association of overweight/obesity with subtypes of age-related cataract would be informative. To address this gap, we conducted a systematic review and meta-analysis of the literatures to examine whether overweight/obesity is an independent risk factor for nuclear, cortical, and PSC cataract.

METHODS

Search Strategy and Inclusion Criteria

We conducted a systematic review and meta-analysis to examine the association of overweight/obesity with incident age-related cataract.
3652 published papers were identified using PubMed and Embase to June 2013. 3612 papers excluded after abstract review. 40 reports retrieved after abstract review for more detailed evaluation. 34 excluded: & were case-control or cross-sectional designs; only reported body mass index as continuous covariate; & did not provide summary estimates or 95% CI; & were published in languages other than English.

6 prospective cohort studies reporting the longitudinal associations between overweight/obesity and age-related cataract were included in the meta-analysis.

FIGURE 1.
Flow chart describing the selection of studies.

cataract based on the Meta-analysis of Observational Studies in Epidemiology guidelines. We searched the electronic databases of PubMed and Embase for relevant articles reporting the longitudinal association of overweight/obesity with age-related cataract published up to June 2013 with the following search terms: ("cataract" OR "lens opacity") AND ("body mass index" OR "BMI" OR "obesity" OR "overweight" OR "fat" OR "body weight"). In addition, the reference lists of all identified studies were examined. Titles and abstracts of the studies were independently scanned by two authors. The extracted studies were compared, and inconsistencies were resolved by consensus. Duplicate articles from the two databases were deleted.

We included studies if they were prospective cohort studies, with reported body mass index (BMI) categories identical or similar to the World Health Organization recommended classifications of body weight (overweight defined as BMI of 25 to 29.9 kg/m², or obesity as BMI of ≥30 kg/m²) (http://apps.who.int/bmi/index.jsp?introPage=intro_3.html) as an independent variable and any subtypes of age-related cataract as the outcome measure. Furthermore, we included studies only if the summary estimates such as relative risk (RR) and hazard ratios with 95% confidence interval (CI) were reported in the article or allowed for the calculation of the summary estimates based on the data presented in the article. We summarized the measures of association as RR for all the cohort studies. We excluded studies if they were case-control or cross-sectional designs, only reported BMI as a continuous covariate, did not provide summary estimates or 95% CI, or were published in languages other than English.

TABLE 1.
Characteristics of prospective cohort studies evaluating the association between overweight/obesity and age-related cataract

<table>
<thead>
<tr>
<th>First author (publication year)</th>
<th>Study period</th>
<th>Years of follow-up</th>
<th>Design (participants)</th>
<th>Sample size</th>
<th>Age, y</th>
<th>No. cases</th>
<th>Exposure measures (BMI)</th>
<th>Outcome measures (cataract)</th>
<th>Methods for controlling confounding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang (2011)</td>
<td>1992–2008</td>
<td>9.8</td>
<td>Clinic based</td>
<td>4425</td>
<td>NA</td>
<td>Measured</td>
<td>Lens photos</td>
<td>Age, sex, race, education,</td>
<td>Diabetes, smoking, weight change, Centrum use, anti-inflammatory drug use, thyroid hormone use, refractive error, nuclear/cortical/PSC cataract at baseline</td>
</tr>
<tr>
<td>Schaumberg (2000)</td>
<td>1982–1997</td>
<td>13.7</td>
<td>Volunteers</td>
<td>20,271</td>
<td>40–84</td>
<td>1721</td>
<td>Self-reported</td>
<td>Medical record</td>
<td>Age, randomized aspirin and β-carotene assignments, smoking status, daily alcohol consumption, vigorous exercise at least weekly, height, waist-to-hip ratio</td>
</tr>
<tr>
<td>Tan (2008)</td>
<td>1992–2004</td>
<td>10.5</td>
<td>Population based</td>
<td>2564</td>
<td>&gt;49</td>
<td>969</td>
<td>Measured</td>
<td>Lens photos</td>
<td>Age, sex, smoking, myopia, pulse pressure, ever use of steroids, hypertension, sun-related skin damage, diabetes</td>
</tr>
</tbody>
</table>
Data Extraction and Assessment of Study Quality

For each study in the analyses, we extracted the following information: first author, publication year, study name, study design, sample size, age range of the study participants, participation or follow-up rates, definitions of overweight/obesity and age-related cataract, summary estimates and corresponding 95% CI, and confounding factors adjusted for. We assessed the study quality using the tool described by Sanderson et al. The variables examined included the methods for selecting study participants, methods for measuring exposure (overweight/obesity) and outcome variable (age-related cataract), design-specific sources of bias (excluding confounding), methods for controlling confounding, statistical methods (excluding control of confounding), and conflict of interest.

Statistical Methods for the Meta-Analysis

We performed the meta-analysis using Stata version 12.0 (StataCorp, College Station, TX). We meta-analyzed the fully adjusted summary estimates using the random-effects model to account for both within- and between-study variability. Different subtypes of cataract including nuclear, cortical, and PSC cataract were treated as the outcome measure, whereas overweight/obesity was analyzed as the independent variable. For studies that only reported stratified RRs, we pooled the RRs to obtain an overall estimate for overweight/obesity. We treated normal weight as the reference category and converted summary estimates if necessary. Statistical heterogeneity among studies was evaluated using the $I^2$ statistic. Values of 0 to 24%, 25 to 49%, 50 to 74%, and more than 75% denote no, low, moderate, and high heterogeneity, respectively. We evaluated publication bias using the Egger regression asymmetry test and the Begg test. A two-sided p value of less than 0.05 was regarded as significant for all analyses.

RESULTS

We identified 3652 unique titles and abstracts, from which we retrieved 31 full-text articles for review. We included six cohort studies in this meta-analysis (Fig. 1).

The characteristics of the six cohort studies included in the meta-analysis are summarized in Table 1. Among the identified six studies, five were conducted in the United States whereas the other one was conducted in Australia. Two studies assessed BMI using self-reported data. Four studies graded cataract based on standardized protocols such as the Wisconsin grading system or the Lens Opacity Classification System whereas the other two used self-reported data confirmed by ophthalmologists. Although different studies adopt different adjustments of confounders, all studies adjusted for important confounders such as age in the multivariate

![FIGURE 2.](Image)

Random-effects meta-analysis evaluating the association between overweight/obesity and incident nuclear cataract. RR, relative risk; CI, confidence interval; ID, identification.
analysis. All studies reported lost to follow-up rates and described sampling methods, albeit in varying degrees. The follow-up durations varied from 6 to 16 years in all identified studies.

In the meta-analysis of six longitudinal cohort studies, obesity was associated with an increasing risk of nuclear cataract (pooled RR, 1.12; 95% CI, 1.02 to 1.25; $I^2 = 4.4\%$), whereas no significant association was found between overweight and nuclear cataract (pooled RR, 1.01; 95% CI, 0.91 to 1.12; $I^2 = 24.8\%$) (Fig. 2). Similarly, obesity was also associated with an increasing risk of cortical cataract (pooled RR, 1.34; 95% CI, 1.07 to 1.66; $I^2 = 43.6\%$) and no significant association was found between overweight and cortical cataract (pooled RR, 1.11; 95% CI, 0.93 to 1.34; $I^2 = 43.6\%$) (Fig. 3). Both overweight and obesity were found to be associated with increasing risks of PSC cataract (pooled RR, 1.23; 95% CI, 1.09 to 1.40; $I^2 = 0$ for overweight; pooled RR, 1.52; 95% CI, 1.31 to 1.77; $I^2 = 0$ for obesity) (Fig. 4). There was no evidence of publication bias as indicated by a nonsignificant Egger test (all $p > 0.05$) and Begg test (all $p > 0.05$) in all analyses.

**DISCUSSION**

In this systematic review and meta-analysis of longitudinal studies, obesity was associated with all cataract subtypes whereas overweight was only associated with PSC cataract. The findings indicated that obesity may be an independent risk factor for age-related cataract.

Our study indicate that obesity is associated with a 12% increase in the risk of nuclear cataract, a 34% increase in the risk of cortical cataract, and a 52% increase in the risk of PSC cataract. A previous meta-analysis showed that ever smoking is associated with a 41% increase in risk of cataract among cohort studies (RR, 1.41; 95% CI, 1.23 to 1.62). The magnitude of risk association for obesity with age-related cataract is comparable to that for smoking in longitudinal studies. Moreover, smoking is mostly like to cause nuclear cataract whereas obesity is related to a higher risk of PSC cataract. PSC cataract affects vision more severely and thus leads to surgery sooner than other types of cataract. Thus, clinicians and epidemiologists should not neglect the impact of obesity on cataract.

The biological plausibility of the observed association has not been elucidated, and we offer several possible explanations. First, oxidative stress is well known to be involved in the process of cataract formation. Individuals with elevated plasma levels of leptin, a cytokine expressed mainly by adipocytes, have been found to enhance accumulation of reactive oxygen species in various cellular models. Second, obese people have higher amounts of systemic inflammation with elevated levels of C-reactive protein and proinflammatory cytokines, both of which could promote the development of cataract because of their association with inflammation in the eye. Finally, obesity might be associated with cataract formation because of its systematic complications including diabetes, hyperlipidemia, and hypertension, which are all known risk factors for age-related cataract.

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**FIGURE 3.**

Random-effects meta-analysis evaluating the association between overweight/obesity and incident cortical cataract. RR, relative risk; CI, confidence interval; ID, identification.
There are several strengths of this meta-analysis. Only longitudinal cohort studies were included, which is less susceptible to selection bias than retrospective case-control studies or cross-sectional studies. In addition, the sample sizes of the included studies are large and the follow-up periods are relatively long, which make the evidence more cogent.

The limitations of this meta-analysis should also be acknowledged. First, the potential biases in the original studies, methodological issues, and different strategies for adjusting for confounders could affect the results of this meta-analysis. The observed association may have been confounded by other unadjusted factors or selection bias even if the meta-analysis is based on longitudinal cohort studies. Second, persons with cataract surgery are excluded from analysis, leading to an imprecision in the estimation of associations owing to the reduced number of cases. Third, the number of the contributing prospective studies was small, and therefore, subgroup analysis may not be feasible. Fourth, different studies used different cataract grading systems, which would affect the estimates of incidence. Finally, publication bias could be of concern because studies that report statistically significant results are more likely to get published than studies that report nonsignificant results, and this could have distorted the findings of our meta-analyses. Although the Egger test and the Begg test indicated little evidence of publication bias in this meta-analysis, the estimation may not be accurate enough as the number of the studies is insufficient.

In conclusion, this systematic review and meta-analysis of six prospective cohort studies confirmed a longitudinal effect of obesity on age-related cataract, especially PSC cataract. The results of the meta-analysis suggest that lifestyle changes including healthy diet or more physical activities would help to reduce the incidence and associated costs of cataract, subsequently improving visual functioning and health-related quality of life. Randomized control trials are warranted to examine the effectiveness and cost-effectiveness of weight reduction in obese populations to decrease the risk of age-related cataract.

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REFERENCES


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