

Original Article

Occupational Lifting Tasks and Retinal Detachment in Non-Myopics and Myopics: Extended Analysis of a Case-Control Study

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Objectives: Lifting heavy weights involves the Valsalva manoeuvre, which leads to intraocular pressure spikes. We used data from a case-control study to further investigate the hypothesis that occupational lifting is a risk factor for retinal detachment.

Methods: The study population included 48 cases (patients operated for retinal detachment) and 84 controls (outpatients attending an eye clinic). The odds ratios (OR) of idiopathic retinal detachment were estimated with a logistic regression model (adjusted for age, sex and body mass index). Three indexes were used to examine exposure to lifting; 1) maximum load lifted, 2) average weekly lifting, 3) lifelong cumulative lifting.

Results: For all indexes, the most exposed subjects showed an increased risk of retinal detachment compared with the unexposed (index 1: OR 3.57, 95% confidence interval [CI] 1.21-10.48; index 2: OR 3.24, 95% CI 1.32-7.97; index 3: OR 2.23, 95% CI 1.27-8.74) and dose-response relationships were apparent.

Conclusion: These results reinforce the hypothesis that heavy occupational lifting may be a relevant risk factor for retinal detachment.

Key Words: Retinal detachment, Lifting, Occupational exposure, Occupational diseases, Case-control studies

Introduction

Retinal detachment is a separation of the neurosensory retina from the retinal pigmental epithelium, which can lead to blindness. Identification of the risk factors and predisposing lesions for retinal detachment is important both for primary and secondary prevention.

Lifting of heavy weights involves the Valsalva manoeuvre,

which is characterized by forced holding of breath against a closed glottis [1]. The accompanying rise in intrathoracic and intraabdominal pressure leads to a generalized increase in venous pressure, and ultimately in intraocular pressure (via the episcleral veins draining the anterior segment of the eye) [2-6]. This phenomenon is considered to be responsible for Valsalva hemorrhagic retinopathy, a generally self-resolving condition characterized by various vision disturbances due to rupture of retinal capillaries after the Valsalva manoeuvre [7].

Using a case-control study which initially focused on retinal detachment among myopic people, we identified an increased risk of retinal detachment for subjects with a history of substantial occupational lifting [8]. Analysis of our dataset suggested that in our study population the degree of myopia (measured in dioptres) was not a strong confounder of the relationship between lifting and retinal detachment (unpublished

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data). Findings from a supplementary case-case [9] analysis of available data (in which we compared myopic retinal detachment cases with non-myopic retinal detachment cases) then led us to hypothesize that occupational heavy lifting tasks may increase the risk of retinal detachment regardless of myopia (i.e., there is an absence of effect modification) [10]. Taken together, these findings suggested that; 1) the degree of myopia may not be a major confounder of the relationship between occupational lifting and retinal detachment, 2) the effect of occupational lifting in determining retinal detachment may not be modified by myopia. To explore these issues further, this study comprises an extended case-control analysis of our dataset, incorporating information on both myopic and non-myopic cases. Given the larger number of cases available for the present analysis, we were able to restrict the case definition to idiopathic retinal detachment, thereby eliminating possible effect modification due to trauma or surgery. We were also able to evaluate the existence of a dose-response relationship between occupational lifting and the risk of idiopathic retinal detachment.

Materials and Methods

Study design and participants

The present analysis was conducted using data originally collected for a case-control study reported elsewhere [8]. Although data were originally collected for both non-myopic and myopic cases, analysis was initially restricted to the myopic set, due to a lack of non-myopic controls and the physiologically plausible hypothesis that heavy lifting may interact with myopia in the onset of retinal detachment [8]. To provide additional information on the possible etiologic role of myopia, the present report provides an extended case-control analysis of the original dataset, in which eligibility has been extended to the non-myopic cases that were excluded from the initial analysis. The larger number of available cases has also allowed us to restrict the present analysis to cases of idiopathic retinal detachment, thereby avoiding concerns of effect modification by trauma or prior surgery. Thus, the case definition used in the present analysis is surgically treated idiopathic retinal detachment. Cases with history of cataract surgery, coexisting aphakia or onset presenting after external trauma were excluded. As described elsewhere [8], we had initially screened all patients who received surgical treatment for retinal detachment at the Department of Ophthalmology of Ospedale Maggiore in Bologna between October 2000 and December 2001 (with an extension period of January to March 2002). Of note, since the original case definition did not consider myopia, we collected data on cases both with and without myopia. Identification of cases/

controls and data collection have been reported in detail elsewhere [8]. In brief, a total of 120 cases with or without myopia were identified (overall response: 89%). To meet our case definition, we excluded 71 subjects who reported with ocular/head trauma ($n = 42$) and/or eye surgery ($n = 46$). Thus, 49 cases were considered eligible for the present analysis. For the control group, we screened subjects examined as outpatients in January-September 2002 at three National Health Service ophthalmologic surgeries located within the hospital's catchment area (west Bologna). We selected 99 consecutive patients affected by some degree of myopia, not matched by any factor to cases; all of these subjects agreed to participate and provided informed consent for anonymous publication of data. After the exclusion of one case due to missing information on occupational lifting (listwise deletion), 48 cases and 99 controls were entered in the main analyses.

Participants were aware that the research regarded possible risk factors for retinal detachment, but were blind to the study hypothesis. The questionnaire [8] collected information on the individual factors that might influence the onset of retinal detachment, including age, body mass index (BMI), non-Caesarean deliveries, alcohol consumption, smoking, sport and hobbies, family history of retinal detachment, head/eye trauma, whiplash, eye surgery, diabetes, hypertension, cardiovascular disease, chronic respiratory pathologies or constipation, and prostate hypertrophy and glaucoma. Regarding lifting, subjects were asked to report all past/present job tasks (specifying periods in calendar years) and describe the manual handling activities undertaken: for each separate task, subjects were required to specify whether they regularly lifted weights greater than 10 kg, and if so the approximate weight (kg) regularly lifted, and the number of manoeuvres per hour.

Statistical analysis

In the descriptive table, the homoscedastic and normally distributed variables were compared using Student's t-test, while the categorical variables were compared using Pearson's chi squared test.

To quantify exposure, we considered 3 different indexes; 1) the maximum load (kg) lifted in a typical working day, 2) the average lifting performed in 1 week, calculated as the product of load and frequency, 3) lifelong cumulative lifting exposure, calculated as the average lifting performed in 1 week multiplied by the number of lifting years. Subjects who reported "no lifting" were considered as unexposed (reference category); exposed subjects were divided into 2 categories based on the median value of exposure among controls (i.e., below or above the median value). The correlation between the exposure indexes

was evaluated with Spearman's rank correlation coefficient (Spearman Rho). Summary statistics are expressed as numbers (percentages) or mean \pm standard deviation, as appropriate. We examined the associations between idiopathic retinal detachment and lifting by calculating odds ratios (OR) and relative 95% confidence intervals (CI) with prospective logistic regression models, according to the method of Breslow and Day [11]. Due to the small number of cases we decided to include in each logistic multivariate model no more than three covariates other than occupational exposure. Based on results from the previous report [8] and on preliminary analysis of the present dataset, we selected age, gender and BMI. Of note, the degree of myo-

pia was not considered in the present analysis since cases could only be non-myopic. In order to study the different metrics of exposure, we needed to define a basic model containing the selected covariates (gender, age and BMI) parameterized in a fixed way. In order to select a parsimonious logistic regression model (saving degrees of freedom), the parameterization of the two continuous covariates (age and BMI) was chosen by first applying fractional polynomials and then selecting the parameterization that minimized the deviance of the model [12]. For age, two parameters were selected (age^{-2} and age^{-1}), while BMI was retained untransformed (BMI^1); to avoid collinearities, the continuous covariates were centered on their means. Linear trends for categorical exposure variables were evaluated using a Wald test, treating the variable as a continuous variable (introduced in the model with 1 degree of freedom). Logistic regression models adopting different indexes for occupational exposures to lifting were compared using Akaike information criterion (AIC) and Bayesian information criterion (BIC) [13]. The Stata 11.2 SE software package (Stata Corporation, Texas, TX, USA) was used for analysis (with $p < 0.05$ being considered significant). Based on p-values, we evaluated the level of evidence against the null hypothesis using the following scale (in line with the interpretation of p-values suggested by Sterne and Davey Smith [14]): $p > 0.10$, 'no evidence'; $0.05 < p < 0.10$, 'weak evidence'; $0.01 < p < 0.05$, 'moderate evidence'; $0.001 < p < 0.01$, 'strong evidence'; $p < 0.001$, 'very strong evidence'.

Table 1. Characteristics of the 48 cases of idiopathic retinal detachment and of the 99 controls

Characteristics	Cases (n = 48)	Controls (n = 99)	p-value
Gender			
Male	24 (50)	49 (49)	0.95*
Female	24 (50)	50 (51)	
Age (year)			
< 40	7 (15)	19 (19)	0.04 [†]
40-54	5 (10)	25 (25)	
55-69	21 (44)	39 (39)	
≥ 70	15 (31)	16 (16)	
Mean \pm SD	60.4 \pm 16.5	54.6 \pm 14.7	
Body mass index (kg/m ²)			
< 18.50	0 (0)	1 (1)	0.0001 [†]
18.50-24.99	21 (44)	69 (70)	
25.00-29.99	20 (42)	27 (27)	
≥ 30.00	7 (15)	2 (2)	
Mean \pm SD	25.8 \pm 3.5	23.5 \pm 3.1	
Myopia			
Non-myopic	26 (54)	0 (0)	NA [‡]
-0.5 to -5.75 diopters	15 (31)	81 (82)	
-6.0 to -9.75 diopters	2 (4)	14 (14)	
-10 diopters or worse	5 (10)	5 (4)	

SD: standard deviation, NA: not available.

*Pearson's chi squared test, [†]Student's t-test, [‡]Statistical testing not appropriate due to study design.

Values are presented as n (%).

Results

Table 1 summarizes the characteristics of the 48 cases of idiopathic retinal detachment and the 99 controls. Cases were older than controls and had higher mean BMI. As shown in Table 2, all the correlations between the exposure indexes were strong (Spearman's rank correlation coefficient always > 0.9). Table 3 reports results from the logistic regression models for the three exposure indexes. The measures of relative goodness of fit, AIC and BIC, were almost the same for each of the 3 adjusted logistic regression models. In the multivariate analysis, all 3 indexes were associated with risk of idiopathic retinal detach-

Table 2. Spearman's rank correlation coefficient (p-value) among exposure indexes, calculated in the entire study population (n=147)

	Maximum load lifted	Average weekly lifting	Lifelong cumulative exposure
Maximum load lifted	-	0.94 (p < 0.0001)	0.96 (p < 0.0001)
Average weekly lifting	0.94 (p < 0.0001)	-	0.97 (p < 0.0001)
Lifelong cumulative exposure	0.96 (p < 0.0001)	0.97 (p < 0.0001)	-

Table 3. Occupational weight-lifting and risk of idiopathic retinal detachment

	Cases	Controls	Univariate	Multivariate*	AIC multivariate* model	BIC multivariate* model
Maximum load lifted in a typical working day (kg)						
No manual lifting	20 (42)	67 (68)	1.00 Ref	1.00 Ref	1.146	-541.2
10-20	13 (27)	21 (21)	2.07 (0.88-4.87)	2.34 (0.93-5.93)		
> 20	15 (31)	11 (11)	4.57 (1.81-11.51)	3.57 (1.21-10.48)		
			P_{trend} 0.001	P_{trend} 0.011		
Average lifting performed in one week (kg × frequency)						
No manual lifting	20 (42)	67 (68)	1.00 Ref	1.00 Ref	1.145	-541.3
< 240	8 (17)	14 (14)	1.91 (0.70-5.21)	2.06 (0.67-6.29)		
≥ 240	20 (42)	18 (18)	3.72 (1.66-8.36)	3.24 (1.32-7.97)		
			P_{trend} 0.001	P_{trend} 0.009		
Cumulative lifting exposure (kg × frequency × years)						
No manual lifting	20 (42)	67 (68)	1.00 Ref	1.00 Ref	1.146	-541.2
< 5,400	11 (23)	17 (17)	2.17 (0.87-5.37)	2.23 (0.81-6.13)		
≥ 5,400	17 (35)	15 (15)	3.80 (1.61-8.93)	3.34 (1.27-8.74)		
			P_{trend} 0.002	P_{trend} 0.010		

AIC: Akaike information criterion, BIC: Bayesian information criterion, Ref: reference category.

*Multivariate adjusted models included age, gender and body mass index.

Results from logistic regression models including different exposure metrics.

Values are presented as n (%) or odds ratio (95% confidence interval).

ment. Subjects in the highest categories of exposure showed a three to fourfold increase, compared with unexposed subjects. For all 3 indexes a dose-response relationship was apparent, as well as moderate to strong evidence supporting a trend.

Discussion

We previously reported an association between cumulative exposure to occupational lifting and the risk of retinal detachment in myopic subjects [8]. In the present analysis we expanded our study population by including non-myopic cases that were previously excluded due to lack of non-myopic controls and focused exclusively on the possible role of occupational lifting after adjusting for BMI (another implicated risk factor and an important confounder). Given the larger number of available cases, we decided to exclude subjects with history of cataract surgery, coexisting aphakia or onset presenting after external trauma. The rationale for this choice was identification of idiopathic retinal detachment cases, which comprise an ideal population in which to study possible causal associations with occupational exposures.

We only considered occupational lifting of at least 10 kg (a cut-off selected to catch the 15-20 kg or more loads that have been reported to produce substantial intraocular pressure spikes [15]). To develop suitable exposure measures, we broadly followed examples provided by studies on lumbar disk

hernia, for which lifting is a prominent risk factor and in which at least three components are thought to contribute; intensity, frequency and long-term duration of lifting manoeuvres [16]. To allow consideration of the different contributions of these three components, we adopted three different exposure indexes for occupational lifting. For each of these we found evidence of an association with idiopathic retinal detachment. Unfortunately, in our study population the three indexes were strongly correlated, thereby precluding any evaluation of the different contributions of intensity, frequency and duration.

Our main pathophysiological hypothesis is that the observed increase in risk could be a consequence of the frequent and prolonged variation in intraocular pressure caused by the Valsalva manoeuvre. The possibility that this may be linked to retinal detachment has been considered in the context of case reports and a case series [1,5,6]. As early as 1921, Edridge-Green [17] noted that “when anyone tries to lift a box which is at the limit of his strength he experiences a great feeling of tension in the eyes.” In 1973, Dambite and Flik [18] presented a case series of 352 myopic workers; the authors highlighted an association between selected comorbidities (i.e., retinal detachment and hemorrhagic retinopathy) and high demand physical work. When Pivovarov et al. [15] measured intraocular pressure in healthy subjects performing static physical efforts associated with various simulated lifting manoeuvres (with or without sudden holding of the breath), it was found that lifting of

weights over 15-20 kg was generally accompanied by an abrupt rise (~25 mmHg) and fall in intraocular pressure, particularly when this exertion was accompanied by a sudden holding of the breath. The authors of this study hypothesized that these hydro-/hemodynamic spikes could eventually cause breaches, triggering retinal detachment. An alternative pathophysiological pathway linking lifting and retinal detachment could be mediated by ciliary muscle spasm; however, an experimental study conducted by Schwab and Gärtner [19] suggests that lifting a 25-kg-heavy weight is unlikely to provoke a considerable ciliary spasm.

Study limitations

We enrolled both myopic and non-myopic cases but only myopic controls. Therefore, we were not able to control for myopia in the present analysis. In the European Prospective Investigation into Cancer and Nutrition - Norfolk (EPIC-Norfolk) cohort, refractive errors were found to be associated with educational level but not with occupational class (manual vs. non-manual) [20], an observation that is in line with the concept that the association between occupational lifting and idiopathic retinal detachment may not be substantially confounded by myopia. Furthermore, a previous analysis of our study population suggested that the association between lifting and risk of retinal detachment is not modified by the presence of myopia [10]. Therefore, we believe that the estimates presented in this article may not be seriously biased due to the absence of the degree of myopia in our multivariate logistic regression models.

The study was vulnerable to the biases inherent in non-population-based case-control studies. Differential severity of underlying eye conditions between the cases (hospital outpatients) and controls (outpatients from a local public health service eye clinic) is possible, and the choice of setting for the control group (myopic subjects) may also have entailed some systematic differences in comparison with the general population, especially in terms of concomitant eye conditions. We expect that such considerations may conceivably have led to an underestimation of the risks associated with lifting, given that blue-collar workers tend to have more concomitant pathologies than white-collar workers [21]. Socioeconomic selection biases require consideration, since more well-to-do patients are less likely to attend public health service facilities. However, since such patients are also unlikely to perform repeated occupational lifting tasks, their underrepresentation (presumably in both cases and controls) is unlikely to have substantially affected the main results.

Recall bias may not have been a major concern, as participants were not aware of the study hypothesis, and the exposure

information was deeply embedded in a lengthy questionnaire, and lifting is not a widely recognized risk factor for retinal detachment.

In the present analysis we used logistic regression models adjusted for BMI (as well for age and gender). Due to the small sample size we were not able to properly test for a possible interaction between BMI and occupational lifting. Since BMI has been reported to influence intraabdominal pressure during physical exercises [22], it is plausible that an overweight person could experience higher Valsalva manoeuvre-related intraocular pressure spikes when lifting heavy weights. Moreover, it has been noted that increases in BMI are associated with increases in intra-abdominal pressure [23]; thus, the Valsalva manoeuvre and BMI could be synergic in determining an increase of intraocular pressure. Future studies, based on larger populations, should properly account for the possible interaction between BMI and occupational lifting. Future studies should also carefully investigate lifelong occupational lifting and try to disentangle the contributions of intensity, frequency and duration of occupation lifting.

In a previous report we presented evidence supporting the pathophysiologically plausible hypothesis that heavy occupational lifting is a relevant risk factor for retinal detachment in myopics [8]. Findings from the present supplementary analysis provide evidence that lifting could be a risk factor for retinal detachment in both myopic and non-myopic subjects. Although we were not able to study separately the effects of short and long term exposures, we did find a dose response relationship between cumulative lifting and risk of retinal detachment.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Rafuse PE, Mills DW, Hooper PL, Chang TS, Wolf R. Effects of Valsalva's manoeuvre on intraocular pressure. *Can J Ophthalmol* 1994;29:73-6.
2. Harris A, Arend O, Bohnke K, Kroepfl E, Danis R, Martin B. Retinal blood flow during dynamic exercise. *Graefes Arch Clin Exp Ophthalmol* 1996;234:440-4.
3. Qureshi IA. Effects of exercise on intraocular pressure in physically fit subjects. *Clin Exp Pharmacol Physiol* 1996;23:648-52.
4. Qureshi IA, Wu XD, Xi XR, Yang J, Huang YB. Resting intraocular pressure of steel factory workers is related to their physical fitness. *Ind Health* 1997;35:259-63.

5. Dickerman RD, Smith GH, Langham-Roof L, McConathy WJ, East JW, Smith AB. Intra-ocular pressure changes during maximal isometric contraction: does this reflect intra-cranial pressure or retinal venous pressure? *Neurol Res* 1999;21:243-6.
6. Dickerman RD, McConathy WJ, Smith GH, East JW, Rudder L. Middle cerebral artery blood flow velocity in elite power athletes during maximal weight-lifting. *Neurol Res* 2000;22:337-40.
7. Duane TD. Valsalva hemorrhagic retinopathy. *Trans Am Ophthalmol Soc* 1972;70:298-313.
8. Mattioli S, De Fazio R, Buiatti E, Truffelli D, Zanardi F, Curti S, Cooke RM, Baldasseroni A, Miglietta B, Bonfiglioli R, Tassinari G, Violante FS. Physical exertion (lifting) and retinal detachment among people with myopia. *Epidemiology* 2008;19:868-71.
9. Porta M. A dictionary of epidemiology. 5th ed. New York (NY): Oxford University Press; 2008. 289 p.
10. Mattioli S, Curti S, De Fazio R, Farioli A, Cooke RM, Zanardi F, Violante FS. Risk factors for retinal detachment. *Epidemiology* 2009;20:465-6.
11. Breslow NE, Day NE. Statistical methods in cancer research. Vol. 1. Lyon (France): International Agency for Research on Cancer; 1980. 350 p.
12. Royston P, Altman D. Regression using fractional polynomials of continuous covariates: parsimonious parametric modelling (with discussion). *Appl Statist* 1994;43:429-67.
13. Long JS, Freese J. Regression models for categorical dependent variables using Stata. 2nd ed. College Station (TX): Stata Press; 2006. 527 p.
14. Sterne JA, Davey Smith G. Sifting the evidence-what's wrong with significance tests? *BMJ* 2001;322:226-31.
15. Pivovarov NN, Malakhova LA, Bagdasarova TA, Chetvertukhin AP. Role of weight lifting in the development of retinal detachment. *Vestn Oftalmol* 1977;6:50-3.
16. Bernard BP. Musculoskeletal disorders and workplace factors. A critical review of epidemiologic evidence for work-related musculoskeletal disorders of the neck, upper extremity, and low back. Cincinnati (OH): National Institute for Occupational Safety and Health, US Department of Health and Human Services; 1997. 590 p.
17. Edridge-Green FW. Cause and prevention of myopia. *Lancet* 1921;1:469-71.
18. Dambite GR, Flik LP. Effect of different types of work on the development of severe complications in myopia. *Oftalmol Zh* 1973;28:375-8.
19. Schwab B, Gärtner J. Can the lifting of heavy weights provoke a spasm of ciliary muscles conducive in turn to retinal detachment? *Mod Probl Ophthalmol* 1977;18:64-7.
20. Foster PJ, Broadway DC, Hayat S, Luben R, Dalzell N, Bingham S, Wareham NJ, Khaw KT. Refractive error, axial length and anterior chamber depth of the eye in British adults: the EPIC-Norfolk Eye Study. *Br J Ophthalmol* 2010;94:827-30.
21. Peate WF. Work-related eye injuries and illnesses. *Am Fam Physician* 2007;75:1017-22.
22. Cobb WS, Burns JM, Kercher KW, Matthews BD, James Norton H, Todd Heniford B. Normal intraabdominal pressure in healthy adults. *J Surg Res* 2005;129:231-5.
23. Frezza EE, Shebani KO, Robertson J, Wachtel MS. Morbid obesity causes chronic increase of intraabdominal pressure. *Dig Dis Sci* 2007;52:1038-41.