The Correlation Between Body Weight and Intraocular Pressure

Shawn Khan; Abirami Kirubarajan; Michael Lee; Ian Pitha; Jay C. Buckey Jr.

INTRODUCTION: Preflight body weight is a strong predictor of visual changes in spaceflight. To understand the effect of body weight on the eye, we examined the effect of increased body mass index on intraocular pressure on Earth.

METHODS: We conducted a systematic review to summarize the relationship between weight parameters (including body mass index (BMI) and obesity indices), and intraocular pressure (IOP). Study selection and data extraction were performed in duplicate using EMBASE, MEDLINE, and CENTRAL, from database inception to the second week of April 2020.

RESULTS: A total of 66 individual studies were included for qualitative analysis from the 1364 studies eligible for title and abstract screening. A total of 39 studies were available for quantitative analysis. The average BMI was 25.9 (range, 20.1–48.8) and the average IOP was 14.9 mmHg (range, 11.6–27.8). The overall pooled RR between BMI and elevated intraocular pressure (IOP) was 1.06 (95% CI, 1.04–1.07), meaning for each unit increase in BMI one is 6% more likely of having higher IOP than baseline. Two studies assessed the effects of bariatric surgery, and both showed significant decreases in IOP postoperatively.

CONCLUSION: A higher BMI was associated with increased IOP in ground-based studies. IOP also decreased with weight loss. These data support the idea that alterations in body weight affect intraocular pressures. Further research is needed to understand the relationship between body weight, IOP, and microgravity-induced visual changes. This finding may also be useful clinically.

KEYWORDS: body mass index, BMI, intra-ocular pressure, IOP, spaceflight-associated neuro-ocular syndrome, SANS.

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Why some astronauts experience visual changes in long duration spaceflight is unclear. Past studies in astronauts have documented optic disc edema, globe flattening, and choroidal folds. Clinically, these changes can manifest as a shift toward hyperopia and have been described collectively as spaceflight-associated neuro-ocular syndrome (SANS).[7]

SANS was first characterized by Mader et al. who noted that after 3 wk into a spaceflight mission to the International Space Station, six out of seven astronauts reported difficulty with near vision. This phenomenon has further documented in NASA postflight surveys where 20–50% of astronauts noted visual changes. The shift toward hyperopia typically resolves upon return to Earth over the course of several weeks to months. Some changes, such as choroidal folds and optic disc edema, have been found to persist years after astronauts returned to Earth. These anatomic changes have been found to result in a predisposition for further development of SANS in future missions.[67]

A recent study by Buckey et al. has identified body weight as a strong predictor of these visual changes in spaceflight.[7] In particular, they noted a higher risk of developing these changes for astronauts in the highest weight quartile in comparison to

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the lowest weight quartile. The weight of tissue exerts a compressive force on the outside of blood vessels throughout the body, limiting their ability to expand when internal pressure increases. Increases in body weight either due to obesity or centrifugation cause venous pressures to increase.[7] Central venous pressure and peripheral venous pressure are reduced in weightlessness[7,35,41] consistent with reduced venous pressure due to the loss of tissue compressive forces. In microgravity, astronauts who weigh more experience a greater change in weight when they become weightless, and as such, may experience a greater reduction of tissue compressive forces in comparison to those who weigh less. This relationship between body weight and vision may be mediated by alterations in blood distribution with weightlessness that could alter parameters such as episcleral venous pressure and choroidal thickness over time.

Although data show a strong relationship between preflight body weight and the development of SANS, no published data exist on the effect of body weight on IOP in weightlessness. Also, comparing preflight IOP values to spaceflight results is often difficult because preflight measurements are usually done seated. Seated values are lower than supine values due in part to the hydrostatic column that exists between the eye and heart that is not present either supine or in weightlessness.[2] Nevertheless, data that exist on IOP during spaceflight show that it stabilizes around the seated preflight value (i.e., likely below the preflight supine values) consistent with reduced venous pressures.[19] These venous pressures might be reduced even further in those with higher body weights.

To characterize the effect of body weight on visual function in space, this study sought to understand the relationship between these two parameters on Earth. Specifically, this systematic review was conducted to summarize the results of body mass index (BMI) and obesity index on intraocular pressures (IOP) and/or primary open angle glaucoma (POAG). In addition to the application to spaceflight, this review may also be useful clinically. A better understanding of the contributors to a high intraocular pressure may allow for the identification of new therapeutic targets for glaucoma.[61]

METHODS

The authors conducted an initial systematic search of three databases from database inception to January 10, 2019 with an update on April 18, 2020: 1) the Ovid versions of MEDLINE and MEDLINE Daily including e-publications, in progress, and nonindexed citations; 2) Embase Classic and Embase; and 3) the Cochrane Central Register of Controlled Trials (CENTRAL). A complete search strategy is provided below:

Search Strategy

1. exp Body Weight/or exp Obesity/or exp Body Mass Index/
2. exp OVERWEIGHT/
3. BMI.mp.
4. exp ADIPOSITY/
5. 1 or 2 or 3 or 4
6. exp Intraocular Pressure/
7. IOP.mp.
8. Exp Ocular Hypertension/
9. Eye pressure.mp.
10. 6 or 7 or 8 or 9
11. 5 and 10

This review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.[57] Systematic article screening was performed through an independent double selection and extraction process, from titles to full text review. Throughout the title and abstract screening stages, any article with discordance between reviewers was included to ensure that no relevant articles were prematurely excluded. The reviewers discussed any disagreements at the full text stage and study eligibility was resolved through a third reviewer. The reference lists of all included studies were additionally screened for relevant articles. The results of the systematic search and data collection are presented as a PRISMA flow chart in **Fig. 1**. The search included all original observational studies and randomized control trials (RCTs) in any language investigating the association of BMI on intraocular pressures.

Statistical Analysis

Data extraction occurred in duplicate. The year of publication, author, location of study, and study design were recorded. All studies included in the meta-analysis evaluated the association between a weight parameter and IOP and/or reported risk ratios (RR) and their respective 95% confidence intervals (95%CI). Using Review Manager 5.3 and STAT 13 to perform the meta-analysis we estimated pooled RR estimates for BMI using the inverse variance method through random-effects analysis, as opposed to fixed effects analysis as the studies were only a sample of a larger population. The effect of participant sex on the relationship between weight parameters and IOP was an a priori defined subgroup analysis used to consider any residual heterogeneity between study outcomes. We evaluated between-study heterogeneity using the I^2 statistic and visual inspection of forest plots. The magnitude of heterogeneity was assessed through consistency of point estimates and extent of overlap of confidence intervals.

Between-study heterogeneity was calculated and evaluated based on the Cochrane Collaboration criteria with 0–40%, 30–60%, 50–90%, 75–100%, representing unimportant, moderate, substantial, and considerable heterogeneity, respectively.

RESULTS

The search strategy yielded 348 results from MEDLINE, 1014 from EMBASE, and 18 from CENTRAL, totaling 1364 articles. Upon removing duplicate articles, 1144 records remained. There were 123 records after title screening and abstract screening. The full text papers of the remaining 123 papers were

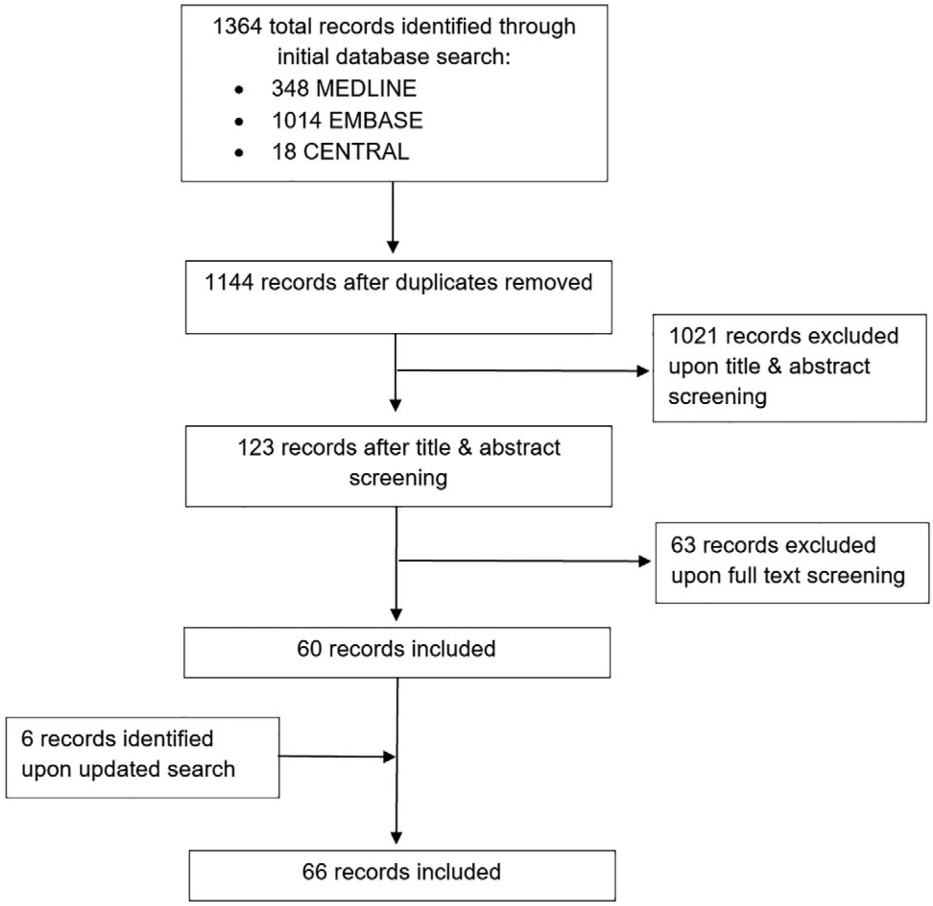

Fig. 1. PRISMA flow chart of included studies.

reviewed, of which 60 articles met the inclusion criteria (Fig. 1). An additional 6 studies were added upon the updated search, after screening 528 more records.

A total of 66 individual studies (39 cross sectional studies, 19 prospective cohort studies, 4 case control studies, 3 retrospective cohort studies, and 1 RCT), were included from the 1364 studies eligible for title and abstract screening. The studies included 1,071,932 participants with an average age of 46.1 (range, 14–100). This study includes data from the Rotterdam and Barbados study.[59,68] However, the Blue Mountains Eye Study did not consider the role of BMI in IOP and was excluded.[47]

A total of 58% (38/66) of the studies were from Asia (11 South Korea, 10 Japan, 7 China, 5 India, 3 Taiwan, 1 Thailand, and 1 Singapore), with 12% (8/66) studies from the United States (**Table I**).

The most common method of measuring IOP was Goldmann applanation tonometry (N = 38), followed by non-contact tonometry (N = 19). A total of 2 studies used mixed methods, 2 studies did not report their method of measurement, and 5 studies used other techniques.

The average BMI was 25.9 (range, 20.1–48.8) and the average IOP was 14.9 mmHg (range, 11.6–27.8). A total of 76% (50/66) of studies found a statistically significant increase in IOP and/or POAG with higher BMI and/or obesity index (**Table II**).

The pooled RR between BMI and average IOP was 1.06 (95% CI, 1.04–1.07, $P < 0.001$; $I^2 = 96.1\%$) (**Fig. 2**). This considerable heterogeneity signifies that 96.1% of the variation across the studies can be due to heterogeneity in the populations rather than by chance alone. To attempt to explain this heterogeneity, we stratified by the a priori variable of sex and performed subgroup analysis.

In this subgroup analysis, ten studies each analyzed the effect of BMI on IOP on men and women, respectively, and the RRs were 1.10 (95% CI, 1.08–1.13, $I^2 = 84.8\%$) and 1.10 (95% CI, 1.08–1.11, $I^2 = 93.2\%$), respectively (**Fig. 3**).

Considerable unexplained heterogeneity (Men: 84.8% and Women: 93.2%) remained even after stratification by sex and there were no significant differences in effect between subgroups ($P = 0.37$). Based on The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) formula the quality of evidence for this predictor on the outcome is moderate due to serious inconsistency (unexplained heterogeneity) and publication bias (asymmetrical funnel plot).

Two studies examined the effect of obesity index, defined as weight divided by height minus 100 times 90, on IOP. There was no statistically significant relationship between these two variables with an RR of 6.66 (95% CI 0.17, 256.99, $P > 0.05$) (**Fig. 4**).

Table I. Study Characteristics of Included Studies.

STUDY	LOCATION	STUDY DESIGN	SAMPLE SIZE	MEAN AGE (RANGE)	SUMMARY OF MAIN FINDINGS
Shiose et al. (1984)[60]	Japan	Cross sectional	192,138	44.7 (NR)	Obesity is associated with higher IOP
Klein et al. (1992)[37]	USA	Cross sectional	4856	NR (43–86)	Association of higher IOP with higher BMI
Wu et al. (1997)[68]	Barbados	Cross sectional	3752	57 (40–84)	Higher BMI associated with higher IOP
Nomura et al. (1999)[52]	Japan	Cross sectional; longitudinal	69,643; 68,998	NR (20–79)	BMI was positively correlated to IOP in both the cross-sectional and longitudinal studies.
Mori et al. (2000)[48]	Japan	Cross sectional	70,139	46.2 (14–94)	Higher BMI associated with higher IOP after adjustments to the cross-sectional and longitudinal analysis
Jaen Diaz et al. (2001)[26]	Spain	Cross sectional	870	54.66	Higher BMI associated with ocular hypertension (OR ≥ 4.2) after adjustment for age and sex
Kaimbo et al. (2001)[29]	DRC	PC	144	52.9 (28–80)	Body mass index conferred a significantly greater risk of OAG
Lee et al. (2002)[42]	South Korea	Cross sectional	13,212	47.6 (20–70)	Higher BMI associated with higher IOP after controlling for age, sex, and mean blood pressure in men ($P < 0.05$), but association not significant in women
Yoshida et al. (2003)[73]	Japan	PC	649	NR (29–79)	BMI was positively associated with the IOP in both sexes
Chen et al. (2005)[13]	Taiwan	RC	1271	50.0 (NR)	No significant association between IOP and BMI
Nakano et al. (2005)[49]	Japan	PC	2330	35.9	IOP trend was significantly positively associated with the trends of systemic factors, including BMI
Oh et al.[53] (2005)	Japan	Cross sectional	943	M: 44.8F: 47.1 46	Men with abdominal obesity and women with high triglyceride also had elevated IOP levels; insulin resistance may play a role
Xu et al. (2007)[70]	China	Cross sectional	3253	60.4 (NR)	Body mass index was not significantly associated with IOP
Kawase et al. (2008)[31]	Japan	Cross sectional	2563	57.0 (40–92)	Higher body mass index was significantly correlated with higher IOP.
Lima et al. (2008)[41]	Brazil	PC	41	68.5 (NR)	There was a significant correlation between IOP fluctuation and BMI
Memarzadeh et al. (2009)[46]	USA	Cross sectional	5958	54.9 (NR)	Body mass index, a measure of obesity was positively correlated with IOP, independent of BP and diabetes
Tan et al. (2009)[62]	Singapore	Cross sectional	3278	58.7	IOP was higher in persons with higher BMI
Pasquale et al. (2010)[56]	USA	PC	78,777	NR	Among women, higher BMI was associated with a lower risk of POAG with IOP ≤ 21 mmHg at diagnosis.
Tomoyose et al. (2010)[63]	Japan	Cross sectional	2838	58.4 (NR)	Higher BMI was significantly correlated with higher IOP
Jonas et al. (2011)[28]	India	Cross sectional	4686	49.5 (30–100)	BMI was associated with IOP, independent of BP
Ramdas et al. (2011)[59]	The Netherlands	PC	3939	65.3 (NR)	In multivariate analysis, BMI has a protective effect on OAG in women, but not in men; BMI was associated with a higher IOP in women
Wang et al. (2011)[65]	China	Cross sectional	1348	65.1 (NR)	Higher IOP was significantly associated with higher BMI
Karadag et al. (2012)[30]	Turkey	PC	140	42.1 (NR)	There were no statistically significant differences between BMI groups in terms of IOP.
Lin et al. (2012)[44]	Taiwan	Cross sectional	10,491	49.5	BMI had a positive association with intraocular pressure in young adults and middle-aged men
Zhou et al. (2012)[75]	China	Cross sectional	6101	NR	In the multivariate analysis higher body mass index was associated with higher IOP
Hoehn et al. (2013)[25]	Germany	Cross sectional	4335	54.7 (35–74)	There is a positive association between IOPs and BMI
Nangia et al. (2013)[57]	India	Cross sectional	4570	48.5 (30–100)	In multivariable analysis, glaucoma was associated with lower body mass index
Ngo et al. (2013)[51]	USA	PC	115	NR	Overweight and obese patients displayed a negative correlation between OPP and IOP.
Panchami et al. (2013)[54]	India	PS	120	46.4 (40–55)	There was a significant positive correlation with BMI in postmenopausal women.

(*Continued*)

Table I. (*Continued*)

STUDY	LOCATION	STUDY DESIGN	SAMPLE SIZE	MEAN AGE (RANGE)	SUMMARY OF MAIN FINDINGS
Park et al. (2013)[55]	South Korea	Cross sectional	4524	43.0	Intraocular pressure was associated with metabolic syndrome in post- menopausal women, but not in premenopausal women.
Rajalakshmi et al. (2013)[58]	India	Case Control	82	NR (18–21)	BMI was the most important individual parameter in prediction of IOP
Wang et al. (2013)[66]	China	PC	2257	59.5	In the 5-yr follow-up, a change in IOP was strongly associated with a corresponding change in BMI
Yavas et al. (2013)[71]	Turkey	Cross sectional	1533	53.4	Obesity and BMI did not have an influence on the development of POAG.
Yoshida et al. (2014)[72]	Japan	Cross sectional	1113	NR (28–79)	BMI was positively associated with IOP in middle-aged and older Japanese men and women.
Choi et al. (2014)[14]	South Korea	Cross sectional	7277	38.9 (NR)	Higher IOP was associated with BMI
Kim et al. (2014A)[34]	South Korea	Cross sectional	4875	40 (NR)	Cardiovascular risk factors, including BMI, are associated with increased IOP
Kim et al. (2014B)[33]	South Korea	Cross sectional	13,431	49.35	Higher IOP was significantly correlated with higher BMI
Kitamura et al. (2014)[36]	Japan	PC	3785	50.9 (23–80)	Multivariate regression showed that the change in IOP was positively correlated with changes in BMI
Baek et al. (2015)[3]	South Korea	Cross sectional	31,857	45.6 (NR)	When BMI was further evaluated, it was not found to be significantly associated with IOP change with increasing age
Charlson et al. (2015)[12]	USA	Cross sectional, case control	2067	Y	Low BMI was significantly associated with POAG
Chun et al. (2015)[16]	South Korea	Cross sectional	4621	43.1 (NR)	In nonobese women, IOP was found to correlate with BMI; however, no correlation with IOP and BMI in obese men and women
Geloneck et al. (2015)[20]	USA	PC	125	45.3 (NR)	Higher BMI is correlated with higher IOP in both the seated and supine positions. However, BMI has no significant effect on the amount of increase in IOP observed in changing from the seated to supine position.
Gunes et al. (2015)[21]	Turkey	Cross sectional	68	48.9	IOP was significantly higher in the obese group
Jang et al. (2015)[27]	South Korea	Cross sectional	15,271	44.4	IOP showed positive linear associations with BMI
Wygnanski et al. (2015)[69]	Israel	RC	12,747	NR	A statistically significant positive correlation was found in male subjects between high BMI and elevated IOP
Baisakhiya et al. (2016)[4]	India	Cross sectional	300	NR (40–79)	The increasing trend of IOP with age could be because of age related changes in BMI
Chan et al. (2016)[11]	UK	Cross sectional	110,573	57 (40–69)	In the univariable regression model, IOPg and IOPcc had a positive relationship with BMI, but after adjusting for confounders, they were associated with lower BMI
Cohen et al. (2016)[17]	Israel	RC	18,575	46 (20–80)	A positive linear correlation was found between BMI and IOP for both men and women
Hashemi et al. (2016)[24]	Iran	Cross sectional	5171	50.9 (40–64)	High BMI is significantly correlated with high IOP.
Kim et al. (2016)[32]	South Korea	Cross sectional	5008	42.1	In healthy women, greater fat mass was associated with higher IOP
Ko et al. (2016)[38]	USA	Cross sectional	5746	56.8 (NR)	BMI was not associated with glaucoma
Kyari et al. (2016)[40]	Nigeria	Case Control	15,375	NR	In univariate analyses, low BMI (underweight) was associated with OAG
Zhao et al. (2016)[74]	South Korea	PC	273,522	40.1	Increases in adiposity were significantly associated with an increase in IOP, an association that was stronger for central obesity
Cekic et al. (2017)[9]	Turkey	Case Control	59	37.8 (NR)	Obese patients have a higher mean IOP than nonobese patients.
Burgansky-Eliash et al. (2018)[8]	Israel	PC	32	40.5 (20–65)	There was a significant decrease in IOP measured 3–6 mo after sleeve gastrectomy

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Table I. (*Continued*)

STUDY	LOCATION	STUDY DESIGN	SAMPLE SIZE	MEAN AGE (RANGE)	SUMMARY OF MAIN FINDINGS
Cekic et al. (2018)[10]	Turkey	PC	32	35.8	Morbidly obese patients who undergo bariatric surgery have statistically significantly lower IOP values than in the preoperative period
Han et al. (2018A)[22]	China	PC	2653	60.8	People with increasing BMI are more likely to have IOP elevation over time
Han et al. (2018B)[23]	China	PC	602	60.9	A small increase in IOP over 10 yr was positively related to the longitudinal change in BMI.
Lin et al. (2018)[45]	South Korea	Cross sectional	10,978	53.8 (NR)	Lower BMI was associated with increased odds of OAG
Viljanen et al. (2018)[64]	Finland	Case Control	22	43	IOP is significantly higher in obese women than in nonobese age-matched controls. Obese subjects had a decrease in IOP after bariatric surgery with no change in IOP in the control group.
Banik et al. (2019)[a]	USA	RCT	165	29	There was no correlation between the amount of weight loss from acetazolamide and change in IOP
Bikbov et al. (2019)[b]	Russia	Cross sectional	5519	58.5	Higher IOP was significantly associated with higher body weight and BMI
Chen et al. (2019)[c]	Taiwan	Cross sectional	14,037	46.9	Hepatic steatosis is a better index for assessing the relationship with increased IOP than BMI
Chua et al. (2019)[d]	Singapore	PC	3188	54.4	BMI was associated with IOP change
Cui et al. (2019)[e]	China	Cross sectional	2112	55	Higher IOP was associated with a higher BMI
Panon et al. (2019)[f]	Thailand	Cross sectional	120	47	A higher BMI strongly correlated with IOP and anterior chamber depth

Notes: BMI, body mass index; IOP, intraocular pressure; NR, not reported; PC, prospective cohort study; RC, retrospective cohort study.

[a]Banik R, Kupersmith MJ, Wang JK, Garvin MK. The effect of acetazolamide and weight loss on intraocular pressure in idiopathic intracranial hypertension patients. J Glaucoma. 2019; 28(4):352–356.

[b]Bikbov MM, Kazakbaeva GM, Zainullin RM, Salavatova VF, Gilmanshin TR, et al. Intraocular pressure and its associations in a Russian population: the Ural Eye and Medical Study. Am. J Ophthalmol. 2019; 204:130–139.

[c]Chen YJ, Chen JT, Tai MC, Liang CM, Chen YY, et al. Examining the associations among intraocular pressure, hepatic steatosis, and anthropometric parameters. Medicine. 2019; 98(43):1–6.

[d]Chua J, Chee ML, Chin CW, Tham YC, Tan N, et al. Inter-relationship between ageing, body mass index, diabetes, systemic blood pressure and intraocular pressure in Asians: 6-year longitudinal study. Br J Ophthalmol. 2019; 103(2):196–202.

[e]Cui Y, Yang X, Zhang G, Guo H, Zhang M, et al. Intraocular pressure in general and diabetic populations from Southern China: the Dongguan Eye Study. Invest Ophthalmol Vis Sci. 2019; 60(2):761–769.

[f]Panon N, Luangsawang K, Rugaber C, Tongchit T, Thongsepee N, et al. Correlation between body mass index and ocular parameters. Clin Ophthalmol. 2019; 13:763.

Two studies explored the role of bariatric surgery on intraocular pressure and found statistically significant reductions in IOP postoperatively. Specifically, in Burgansky-Eliash et al., participant BMI decreased from 42 to 31 and was significantly associated with a decrease in IOP (16.9 mmHg to 14.1 mmHg) ($P < 0.001$), measured 3–6 mo after sleeve gastrectomy.[57] Further, Viljanen et al. (2018) found a higher IOP in those with obesity, and statistically lower IOPs postoperatively (16.5 mmHg to 15.2 mmHg). No differences were noted in the control group or in other ophthalmic parameters, including visual acuity, refraction, or pachymetry.[64]

A total of five of the studies look at the relationship between BMI and glaucoma. Ko et al. found that BMI > 30 was significantly associated with POAG (OR 1.63).[38] Meanwhile, Yavas et al. found that BMI did not have an influence on the development of POAG.[71] Interestingly, Charlson et al. and Kyari et al. noted that POAG cases were more likely to have a lower BMI.[12,40] In addition, Lin et al. noted that a lower BMI was a risk factor for POAG in women and those aged 40–49 yr old in sex and age stratified analysis.[45]

A total of 9 studies adjusted for activity levels in their multivariate analysis.[15,16,27,32,33,45,55,66,72] None of the included studies assessed the role of either age or ethnicity on intraocular pressure.

DISCUSSION

This systematic review and meta-analysis, including 66 studies and 1,071,932 patients, describes the positive relationship between BMI and IOP. The pooled aggregate analysis of included studies suggests a statistically significant relationship between BMI and IOP. The exact reasons for this relationship are not known. Obesity has multiple effects on the body, including increased blood pressure and metabolic changes. However, based on terrestrial studies, higher IOPs in those with higher BMIs may be due to tissue compressive

Table II. Study Characteristics of Included Studies, Continued.

STUDY	WEIGHT PARAMETER	MEAN BMI	MEAN IOP (mmHg)
Shiose et al. (1984)[60]	Obesity index - weight divided by height minus 100 times 0.9 times 100	NR	NR
Klein et al. (1992)[37]	Obesity index - weight divided by height minus 100 times 0.9 times 100	NR	M: 15.3 F: 15.5
Wu et al. (1997)[68]	BMI	NR	17.8 ± 3.5 M: 17.6 ± 3.4 F: 18.0 ± 3.6
Nomura et al. (1999)[52]	BMI	M: 23.1 ± 2.8 F: 21.7 ± 2.9	M: 11.9 ± 2.5 F: 11.5 ± 2.4
Mori et al. (2000)[48]	BMI	22.4 ± 2.8 M: 22.9 ± 2.8 F: 21.6 ± 2.8	11.6 ± 2.6 M: 11.7 ± 2.6 F: 11.4 ± 2.5
Jaen Diaz et al. (2001)[26]	(Obesity) BMI > 30	In Spanish	12.96 in right, 13.27 in left
Kaimbo et al. (2001)[29]	BMI	Case: 27.0 ± 6.0 Control: 25.0 ± 5.0	Case: 27.8 ± 14.9 Control: 16.0 ± 3.4
Lee et al. (2002)[42]	BMI	23.8 ± 3.0 (M: 23.9 ± 2.9 F: 23.7 ± 3.1)	15.5 ± 3.1 (M: 16.0 ± 3.2 F: 15.1 ± 2.9)
Yoshida et al. (2003)[73]	BMI	M: 23.2 ± 2.7 F: 22.2 ± 2.9	M: 13.1 ± 2.7 F: 12.3 ± 2.9
Chen et al. (2005)[13]	BMI	24.5, SD = 3.5 M: 24.8 ± 3.3 F: 24.2 ± 3.8	13.6, SD = 2.9 M: 13.7 ± 2.9 F: 13.5 ± 2.9
Nakano et al. (2005)[49]	BMI	NR	NR
Oh et al.[53] (2005)	BMI	M: 24.7 ± 0.1 F: 23.5 ± 0.2	M: 15.7 ± 0.1 F: 15.1 ± 0.1
Xu et al. (2007)[70]	BMI	NR	15.7 ± 2.9
Kawase et al. (2008)[31]	BMI	22.9 ± 3.3 (SD) (M: 23.2 ± 3.1 F: 22.7 ± 3.4)	14.5 M: 14.6 (SD = 2.7) F: 14.5 (SD = 2.5)
Lima et al. (2008)[43]	BMI	25.4 (SD = 5.1)	16.2 (SD = 3.5)
Memarzadeh et al. (2009)[46]	BMI	NR	14.5 ± 3.2
Tan et al. (2009)[62]	BMI	26.36 (SD = 5.11)	1st quartile = 15.0 2nd quartile = 15.5 3rd quartile = 15.4 4th quartile = 15.7
Pasquale et al. (2010)[56]	BMI	NR	NR
Tomoyose et al. (2010)[63]	BMI	25.1 ± 3.6	15.1 ± 3.1 M: 15.2 ± 3.1 F: 15.1 ± 3.0
Jonas et al. (2011)[28]	BMI	NR	13.6 ± 3.4
Ramdas et al. (2011)[59]	BMI	Incident OAG 25.8 No OAG 26.3	Incident OAG 17.3 No OAG 15.0
Wang et al. (2011)[65]	BMI	23.5 ± 3.4 (SD = 3.4)	15.2 ± 3.1 (SD = 3.1)
Karadag et al. (2012)[30]	BMI	Group 1: 22.1 ± 2.5 Group 2: 27.1 ± 1.3 Group 3: 34.7 ± 3.9	Group 1: 16.8 ± 2.3 Group 2: 16.6 ± 2.1 Group 3: 17.3 ± 1.7
Lin et al. (2012)[44]	BMI	M: 25.0 ± 3.4 F: 23.3 ± 3.6	M: 13.7 ± 3.2 F: 13.8 ± 3.1
Zhou et al. (2012)[75]	BMI	24.5	15.0 ± 2.8 (M: 14.6 ± 2.8 F: 15.4 ± 2.7)
Hoehn et al. (2013)[25]	(Obesity) BMI > 30	27.2 ± 4.8	14.0 ± 2.6 (M: 14.1 ± 2.7 F: 13.9 ± 2.5)
Nangia et al. (2013)[50]	BMI	NR	13.8 ± 4.6
Ngo et al. (2013)[51]	BMI	28.1 ± 0.5	16.1 ± 0.4
Panchami et al. (2013)[54]	BMI	Premenopausal: 22.9 ± 3.84 Postmenopausal: 27.39 ± 4.27	Premenopausal: 15.24 Postmenopausal: 18.48
Park et al. (2013)[55]	BMI	Premenopausal: 21.9 ± 0.1 Postmenopausal: 24.0 ± 0.1	Premenopausal: 13.8 ± 0.1 Postmenopausal: 13.8 ± 0.1
Rajalakshmi et al. (2013)[58]	BMI	Case: 27.63 ± 2.53 Control: 20.09 ± 1.22	Case: 18.50 ± 1.71 Control: 14.24 ± 1.35

(*Continued*)

Table II. (*Continued*)

STUDY	WEIGHT PARAMETER	MEAN BMI	MEAN IOP (mmHg)
Wang et al. (2013)[66]	BMI	NR	NR
Yavas et al. (2013)[71]	BMI	NR	NR
Yoshida et al. (2014)[72]	BMI	M: 23.3 ± 2.4, F: 22.3 ± 2.8	M: 14 ± 2.5 F: 13.7 ± 2.6
Choi et al. (2014)[14]	BMI	23.6 ± 0.1	14.0 ± 0.1
Kim et al. (2014A)[34]	BMI	Stratified	Stratified
Kim et al. (2014B)[33]	BMI	23.62 ± 3.38	OD: 13.99 ± 2.7 OS: 13.99 ± 2.75 M:14.19 ± 2.78, F: 13.79 ± 2.7
Kitamura et al. (2014)[36]	BMI	22.8 ± 2.8 (M: 23.2 ± 27 F: 22.2 ± 2.8) 1999: 22.8 ± 2.8, 2008: 22.9 ± 2.9	13.1 ± 3.0 1999: 13.1 ± 3.0 2008: 12.4 ± 2.9
Baek et al. (2015)[3]	BMI	NR	13.9 ± 3.0 OD: 13.91 ± 2.9 OS: 13.91 ± 3.0
Charlson et al. (2015)[12]	BMI	30.5 Cases: 29.6 (± 6.7) Controls: 31.8 (± 7.4)	NR
Chun et al. (2015)[16]	BMI	NR	NR
Geloneck et al. (2015)[20]	BMI	36.0 ± 10.5	Seated 16.3 ± 2.9 Supine 17.7 ± 3.1
Gunes et al. (2015)[21]	(Obesity) BMI > 30	Case: 39.8 ± 4.1 Control: 21.4 ± 1.7	Case: 15 mmHg Control: 13 mmHg
Jang et al. (2015)[27]	BMI	M: 24.0 ± 0.1 F: 23.2 ± 0.1	M: 14.1 ± 0.1 F: 13.8 ± 0.1
Wygnanski et al. (2015)[69]	BMI	NR	17.3 (SD = 3.9, range - 9 to 32)
Baisakhiya et al. (2016)[4]	Waist-Hip Ratio (WHR)	NR?	F: 16.03 ± 2.9 M: 16.4 ± 2.3
Chan et al. (2016)[11]	BMI	27.4 ± 4.8	IOPg: 15.72 (95% CI - 15.7–15.74) IOPc = 15.95 (95% CI - 15.92–15.97)
Cohen et al. (2016)[17]	BMI	M: 27.2 ± 4.0 F: 25.5 ± 4.9	M: 13.4 ± 2.5 F: 13.0 ± 2.2
Hashemi et al. (2016)[24]	BMI	NR	12.87 ± 2.27
Kim et al. (2016)[32]	BMI	M: 24.2 ± 0.1 F: 23.2 ± 0.1	M: 14.2 ± 0.1 F: 13.8 ± 0.1
Ko et al. (2016)[38]	(Obesity) BMI > 30	NR	NR
Kyari et al. (2016)[40]	BMI	NR	Case: 22 ± 11 Control: 14 ± 4
Zhao et al. (2016)[74]	BMI	23.5 ± 3.2	13.5 ± 2.7
Cekic et al. (2017)[9]	(Obesity) BMI > 30	Case 50.39 ± 8.30 Controls 23.33 ± 1.60	Case 18 ± 6.68 Control 13.71 ± 1.60
Burgansky- Eliash et al. (2018)[8]	BMI	Preop: 42.1 ± 6.4 Postop: 31 ± 8	Preop: 16.9 ± 4 Postop: 14.1 ± 3
Cekic et al. (2018)[10]	(Obesity) BMI > 30	Preop 48.8 ± 2.27 Postop 36.28 ± 5.41	Preop 18.2 ± 2.06 Postop 16.1 + 1.81
Han et al. (2018A)[22]	BMI	24.3 ± 3.0	15.2 ± 2.4
Han et al. (2018B)[23]	BMI	23.7 ± 3.1	15.3 ± 3.0
Lin et al. (2018)[45]	BMI	Case: 23.7 (0.2) Controls: 24.0 (0.1)	Case: 14.9 (0.2) Controls: 14.0 (0.1)
Viljanen et al. (2018)[64]	(Obesity) BMI > 30	Preoperative 40.8 ± 4.0 Postoperative 31.8 ± 4.2 Control 22.6 ± 2.8	Preoperative Case: 16.6 ± 3.0 Control: 14.3 ± 1.5 Postoperative Case/Control: 15.2 ± 2.7
Banik et al. (2019)*	Weight (kg)	NR	15.35
Bikbov et al. (2019)*	BMI	27.9	13.6
Chen et al. (2019)*	BMI	M: 25.22 F: 22.69	M: 14.68 F: 14.8
Chua et al. (2019)*	BMI	26.4	15.4
Cui et al. (2019)*	BMI	24.7	15.58
Panon et al. (2019)*	BMI	23.42	12.3

Notes: BMI, body mass index; IOP, intraocular pressure; PCT, prospective cohort study; RC, retrospective cohort.
*See references a–f in Table I.

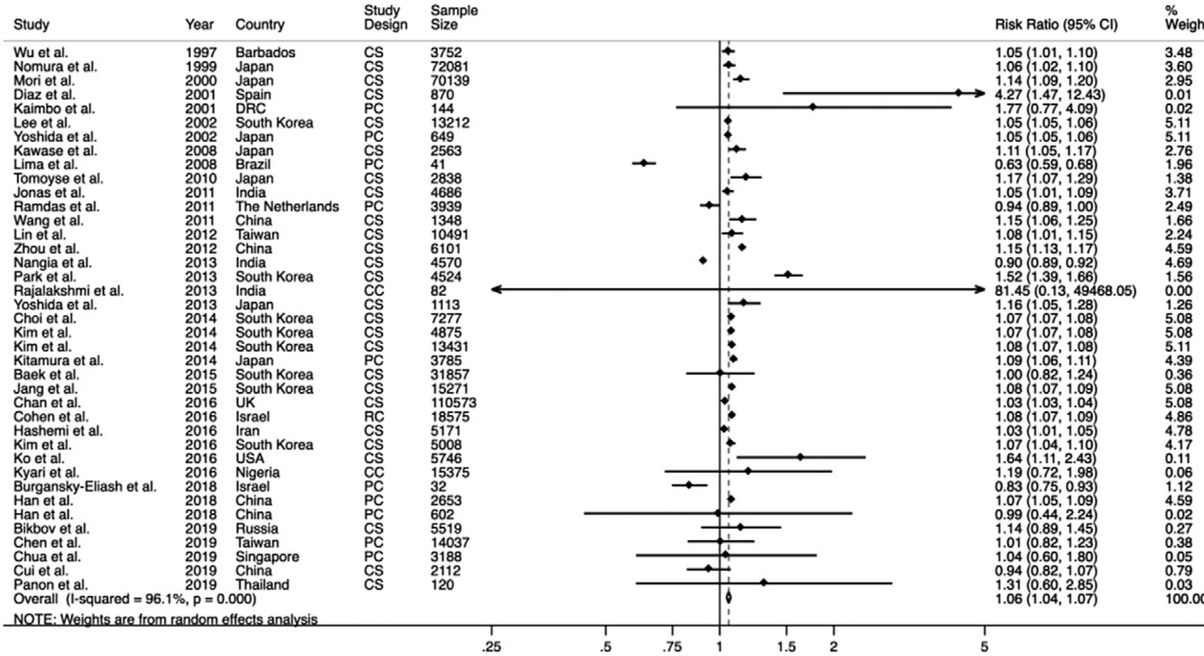

Fig. 2. Meta-analysis on the effect of 1 kg · m^{-2} increase of BMI on IOP and OAG incidence. (I^2: between study variation due to heterogeneity in populations rather than by chance alone.)

forces throughout the body, resulting in increased venous pressures.[1,6,18] These increased venous pressures in turn can increase intraocular pressure through the Goldmann equation.[5] Two studies assessing the effects of bariatric surgery support this idea because they both showed significant decreases in IOP postoperatively.

The findings of this study are relevant for long-duration spaceflight because a strong relationship between body weight and the development of ocular changes in long duration astronauts exists.[7] Those who weigh more preflight may have a more pronounced decrease in tissue compressive forces in flight compared to those who weigh less. In turn, there may also be a

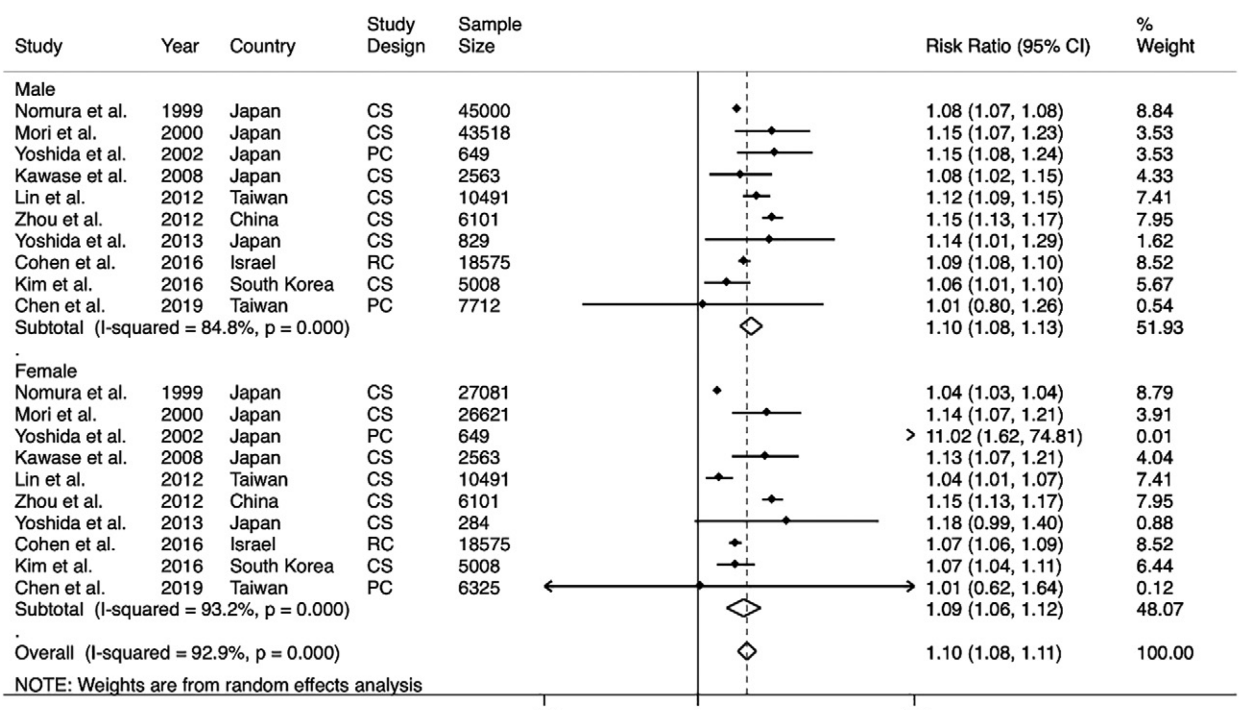

Fig. 3. Subgroup analysis on the effect of 1 kg · m^{-2} increase of BMI on IOP and OAG incidence based on sex. (I^2: between study variation due to heterogeneity in populations rather than by chance alone.)

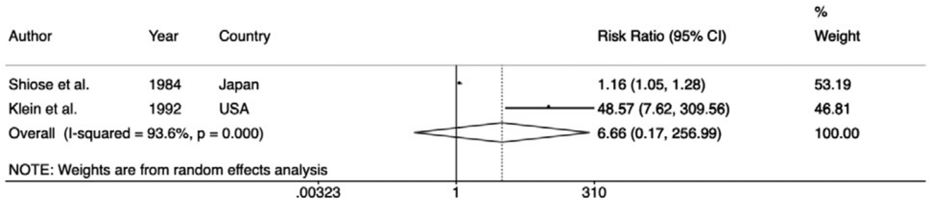

Fig. 4. Meta-analysis on the effect of 1 kg · m^{-2} increase of obesity index on IOP and OAG incidence. (I^2: between study variation due to heterogeneity in populations rather than by chance alone.)

greater drop in IOP experienced in astronauts with a higher preflight body weight. This drop could contribute to changing the pressure gradient across the lamina cribrosa within the eye, which in turn could contribute to the choroidal folds and disc edema seen in long-duration astronauts.[7] An increase in choroidal thickness may also be a contributing factor.

While intraocular pressure is no longer used to define glaucoma, it is one of the largest modifiable risk factors for disease progression.[61] As such, it was reasoned that a study of BMI on IOP would have clear applications to POAG. However, the majority of included studies assessed IOP in healthy participants using a cross sectional study design, excluding patients on glaucoma medication. The studies that did include POAG cases found conflicting results, with some studies describing lower BMI as a risk factor for POAG. Further, another potential consideration is that the majority of included studies were from Asia, including 21 studies from South Korea and Japan. Past studies have noted that Asian populations have a lower baseline IOP than Caucasian patients and develop glaucoma at lower IOPs. Furthermore, other physiologic mechanisms associated with higher body mass, such as hyperlipidemia and hypoventilation, may at least in part be contributing to the observed relationship noted in this study.[32]

Based on the findings of this meta-analysis, there is a clear association between BMI and IOP, including two bariatric studies that found a reduction in IOP following weight loss. However, there is not sufficient evidence to inform clinical decision making as it is unclear whether this reduction in IOP is clinically significant. It remains unclear whether weight loss is truly protective of POAG.

CONCLUSION

A higher BMI is associated with increased IOP in ground-based studies suggesting that a reduction in weight (such as occurs in weightlessness) might reduce IOP. Further research is needed to elucidate a shared mechanism describing the effects of adiposity on IOP, consistent with physiology in both terrestrial and microgravity environments, as well as its clinical implications in POAG development.

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