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Impact of the Valsalva manoeuvre on the choroid: A systematic review with meta-analyses

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Abstract

A variety of daily activities can intentionally or unintentionally cause the Valsalva manoeuvre, which induces a physiological response of elevated peripheral venous pressure. Studies have speculated that it may ultimately affect the choroidal anatomy. This is particularly important from a clinical point-of-view since patients occasionally hold their breath while undergoing macular optical coherence tomography (OCT). In this study, we systematically reviewed the literature to understand the impact of the Valsalva manoeuvre on the choroid and conducted meta-analyses on the changes induced in the subfoveal choroidal thickness (SFCT) and the choroidal vascularity index (CVI). We searched 12 literature databases for studies in healthy participants undergoing Valsalva manoeuvre with choroidal OCT scans before and during the manoeuvre. Seven studies with a total of 444 eyes of 279 individuals were eligible for the review. The Valsalva manoeuvre led to a statistically significant but numerically small increase in the SFCT of 6.5 µm (95% CI: 1.6–11.4 µm; $p=0.01$) and a statistically significant increase in the CVI of 1.48 (95% CI: 1.23–1.73; $p=0.0002$). Thus, the Valsalva manoeuvre has a measurable impact on the choroid, and we recommend careful observation of how the patient sits and behaves behind the OCT scanner while scanning in order to allow accurate measurements of the choroid for diagnosis and monitoring.

KEYWORDS

choroid, choroidal vascularity index, meta-analysis, subfoveal choroidal thickness, systematic review, valsalva manoeuvre

1 | INTRODUCTION

The Valsalva manoeuvre was named after the Italian anatomist Antonio Maria Valsalva, who studied the anatomy of the ear and the heart (Jacobs et al., 2018). The manoeuvre is performed by forcefully exhaling against a closed airway. This induces a variety of changes in the body, which includes the well-characterized changes of the heart rate, the blood pressure, the intracranial pressure,

and the air pressure of the sinuses (Pstras et al., 2016). The Valsalva manoeuvre can be either intentional or unintentional from causes of temporary increase in the intrathoracic pressure, for example, coughing, lifting, blowing musical instruments or holding breath.

From the perspective of the ophthalmologist, the Valsalva manoeuvre is commonly associated with Valsalva retinopathy, which is a condition of preretinal haemorrhage caused by performing the Valsalva

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manoeuvre (Celik Dulger et al., 2021). As the Valsalva manoeuvre leads to elevated peripheral venous pressure, it may also affect the choroidal anatomy and the choroidal perfusion, as exemplified by Valsalva-related subretinal haemorrhages (Conci et al., 2024; Subhi & Sørensen, 2017).

Macular optical coherence tomography (OCT) is routinely used to study macular disease. Increasingly, the choroid is measured for diagnostic and monitoring purposes, which have been enabled through the invention of enhanced depth imaging OCT (EDI-OCT) and swept source OCT (SS-OCT) (Agrawal et al., 2020; Brinks et al., 2022; Feenstra et al., 2024). These modalities have also allowed for image-based analyses of the choroid. The choroidal vascularity index (CVI) is a relatively new parameter introduced by Agrawal et al. (2016), which uses a foveal line scan of an area of 1500 µm centred on the foveola and analyses the choroid in that area outlined by the RPE/Bruch's membrane and the choroid-scleral junction. The analysis includes binarization of the image and identification of the luminal choroidal area, and the ratio between the luminal choroidal area and the total choroidal area is identified as the CVI (Agrawal et al., 2016). Thus, a higher CVI indicates a larger choroidal vascular lumen, and the CVI has been explored as a measure for a variety of chorioretinal diseases (Agrawal et al., 2020; Ambiya et al., 2018; Nicolini et al., 2022; Sacconi et al., 2021).

While performing these OCTs, the patient is advised to rest their face on the chinrest, close their lips and be still while the scans are performed. In our experience, many patients are obliged to do this by holding their breath, and thus, the Valsalva manoeuvre is often performed. In order to understand if this may influence structural choroidal measurements, we performed a systematic review of the literature and conducted meta-analyses on the impact of the Valsalva manoeuvre on the subfoveal choroidal thickness (SFCT) and the CVI.

2 | METHODS

This study is a systematic review with meta-analyses. We followed the Cochrane Handbook for the design and conduct of our study (Higgins et al., 2023). Our protocol was registered a priori at PROSPERO (protocol no. CRD42024549013). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for the reporting of this study (Moher et al., 2009).

2.1 | Study eligibility and outcomes of interest

Eligible studies were defined as those which measured human foveal choroid in vivo using OCT scans during the Valsalva manoeuvre. We restricted ourselves to studies of healthy eyes. We did not restrict the type of OCT or the protocol of the performed scan. We did not enforce any restrictions on the definition of the Valsalva manoeuvre. However, eligible studies must

have performed the same scan protocol just before and during the Valsalva manoeuvre in order to understand the change that could be attributed to the Valsalva manoeuvre. Outcomes of interest were the changes in the SFCT and the CVI. We did not enforce any restrictions on the definitions of measurement or the methods to obtain the SFCT or CVI.

Single case studies, publications without original data, conference abstracts or animal studies were not considered eligible. We did not restrict studies based on geography/country of publication, journal of publication or time of publication. However, we only considered studies disseminated in English for practical purposes.

2.2 | Information sources, search and study selection

One trained author (Y.S.) searched the literature databases *PubMed*, *Embase*, *the Cochrane Central*, *Web of Science Core Collection*, *BIOSIS Previews*, *Current Contents Connect*, *Data Citation Index*, *Derwent Innovations Index*, *KCI-Korean Journal Database*, *Preprint Citation Index*, *ProQuest™ Dissertations & Theses Citation Index* and *SciELO Citation Index*. All searches were conducted on 18 April 2024. Details of the search in individual databases are available in File S1.

One author (Y.S.) examined the title and abstracts of all identified records to remove duplicates and those deemed obviously irrelevant. The remaining references were retrieved in full-text for evaluation of eligibility in an independent fashion by two authors (A. A-V. and L.C.B-A.). Reference lists were also examined for any other potentially eligible study. Disagreements between the authors were discussed with a third author (Y.S.) to reach a final decision.

2.3 | Data collection, data extraction and risk of bias within studies

Data on study characteristics, population characteristics, methods for diagnosis and study results were extracted from each study using pre-designed data extraction forms. We evaluated the risk of bias of individual studies using the relevant items from the Agency for Healthcare Research and Quality (AHRQ) checklist for Cross-Sectional Studies (Zeng et al., 2015).

Two authors (A. A-V. and L.C.B-A.) independently extracted data and evaluated risk of bias of individual studies. Disagreements between the authors were discussed with a third author (Y.S.) to reach a final decision.

2.4 | Synthesis of results, risk of bias across studies and meta-analyses

Studies were reviewed qualitatively in text and tables. Meta-analyses were performed using MetaXL 5.3 (EpiGear International) for Microsoft Excel 2013

(Microsoft). The random-effects model was employed to account for potential heterogeneity across studies. We will summarize data on the change of outcomes of interest from before the Valsalva manoeuvre, at relaxed state, to during the Valsalva manoeuvre. If data on change is not reported, we will obtain such data by simple subtraction of means and by calculating the standard deviation (SD) of the change (SD_{change}) using the recommended approach by the Cochrane Handbook (Higgins et al., 2023) which includes the use of the following formula that involves SD of the baseline ($SD_{baseline}$) and SD of the measures during Valsalva manoeuvre ($SD_{Valsalva}$):

$$SD_{change} = \sqrt{SD_{baseline}^2 + SD_{Valsalva}^2 - (2 \times C \times SD_{baseline} \times SD_{Valsalva})}$$

The C in this formula states the correlation coefficient of the expected correlation between the values. In other words, how similar baseline values are expected to be to values during the Valsalva manoeuvre. One of the studies in review was able to provide insight into the correlation coefficient between these values (0.99 for SFCT and 0.83 for CVI) (Sevik et al., 2022). Thus, we used these values for C in our calculations. Summary estimates were reported with 95% confidence intervals (95% CI) and p values. Heterogeneity was evaluated using the Cochran's Q and I^2 . Funnel plots were used to evaluate the potential skewness of results and publication bias. Sensitivity analyses were conducted by removing each study in turn and by re-calculating the summary measures to understand the impact of individual studies on the overall summary estimates.

3 | RESULTS

3.1 | Study selection

Our literature search identified 210 records. Duplicates ($n=89$) and obviously irrelevant records ($n=108$) were discarded. The remaining 13 records were examined in full text. Six of these full text studies were excluded as they did not fulfil our study eligibility criteria. Consensus was reached to include seven studies for both the qualitative and quantitative review (Figure 1).

3.2 | Study characteristics

Studies summarized data from a total of 444 eyes from 279 individuals (Berhuni et al., 2023; Çiçek et al., 2017; Falcão et al., 2012; Kim et al., 2016; Kurultay-Ersan & Emre, 2017; Mete et al., 2016; Sevik et al., 2022). Studies were predominantly from Turkey ($n=5$), apart from Falcão et al. (2012) from Portugal and Kim et al. (2016) from South Korea. All studies were designed as prospective single-centre studies of a cohort of individuals who underwent an intervention of Valsalva manoeuvre. One study recruited patients from the clinic without any apparent ocular disease (Kurultay-Ersan & Emre, 2017),

and the remaining studies recruited healthy volunteers with no ocular or systemic diseases (Berhuni et al., 2023; Çiçek et al., 2017; Falcão et al., 2012; Kim et al., 2016; Mete et al., 2016; Sevik et al., 2022). Mean age ranged between 25 and 37 years, and individuals of female biological sex constituted 17%–73% of the study populations. Study characteristics are summarized in Table 1.

The Valsalva manoeuvre was performed either by covering the mouth and nose with a hand (Berhuni et al., 2023; Çiçek et al., 2017; Falcão et al., 2012; Kurultay-Ersan & Emre, 2017; Sevik et al., 2022) or by using expiratory devices that could measure expiratory pressure (Kim et al., 2016; Mete et al., 2016). Where measured, the expiratory pressure level defined for a Valsalva manoeuvre was either a minimum of 30 mmHg (Kim et al., 2016) or within a range of 35–40 mmHg (Mete et al., 2016). Imaging was made before the Valsalva manoeuvre and at 2–5 s (Kurultay-Ersan & Emre, 2017), 10 s (Mete et al., 2016) or 15 s (Berhuni et al., 2023; Çiçek et al., 2017; Falcão et al., 2012; Kim et al., 2016; Sevik et al., 2022) of sustained Valsalva manoeuvre. All scans were made using spectral domain optical coherence tomography (SD-OCT) with enhanced depth imaging (EDI) mode. Further details of the Valsalva manoeuvre and the imaging protocols are summarized in Table 2. The CVI was measured in two studies (Berhuni et al., 2023; Sevik et al., 2022), which in both cases were performed by a single investigator without any statistics on repeatability.

3.3 | Results of individual studies

Berhuni et al. (2023) found that the Valsalva manoeuvre induced a statistically significant increase in the SFCT and the CVI. This study also reported a statistically significant increase in central macular thickness and intraocular pressure (Berhuni et al., 2023). Çiçek et al. (2017) reported a statistically significant increase in the SFCT as well as the choroidal thickness in the nasal and temporal areas from the Valsalva manoeuvre. Falcão et al. (2012) found no change in the SFCT from the Valsalva manoeuvre, but reported an increase in the intraocular pressure and speculated that choroidal changes may be more profound in the anterior part of the choroid. Kim et al. (2016) found an increase in the SFCT, which did not reach statistical significance. The authors found that the Valsalva manoeuvre induced anterior displacement of the lamina cribrosa and increased the intraocular pressure (Kim et al., 2016). Kurultay-Ersan and Emre (2017) found an increase in the SFCT from the Valsalva manoeuvre in both high myopia and hyperopia. Mete et al. (2016) reported no change in the SFCT from the Valsalva manoeuvre, but instead an increase in the intraocular pressure, optic disc morphology, lower central corneal thickness and anterior chamber depth. Sevik et al. (2022) reported that during the Valsalva manoeuvre, SFCT did not change but CVI increased. The authors reported an increase in the choroidal luminal area and a decrease in the choroidal stromal area (Sevik et al., 2022). The Valsalva manoeuvre also increased the intraocular pressure as well as the systemic blood pressure.

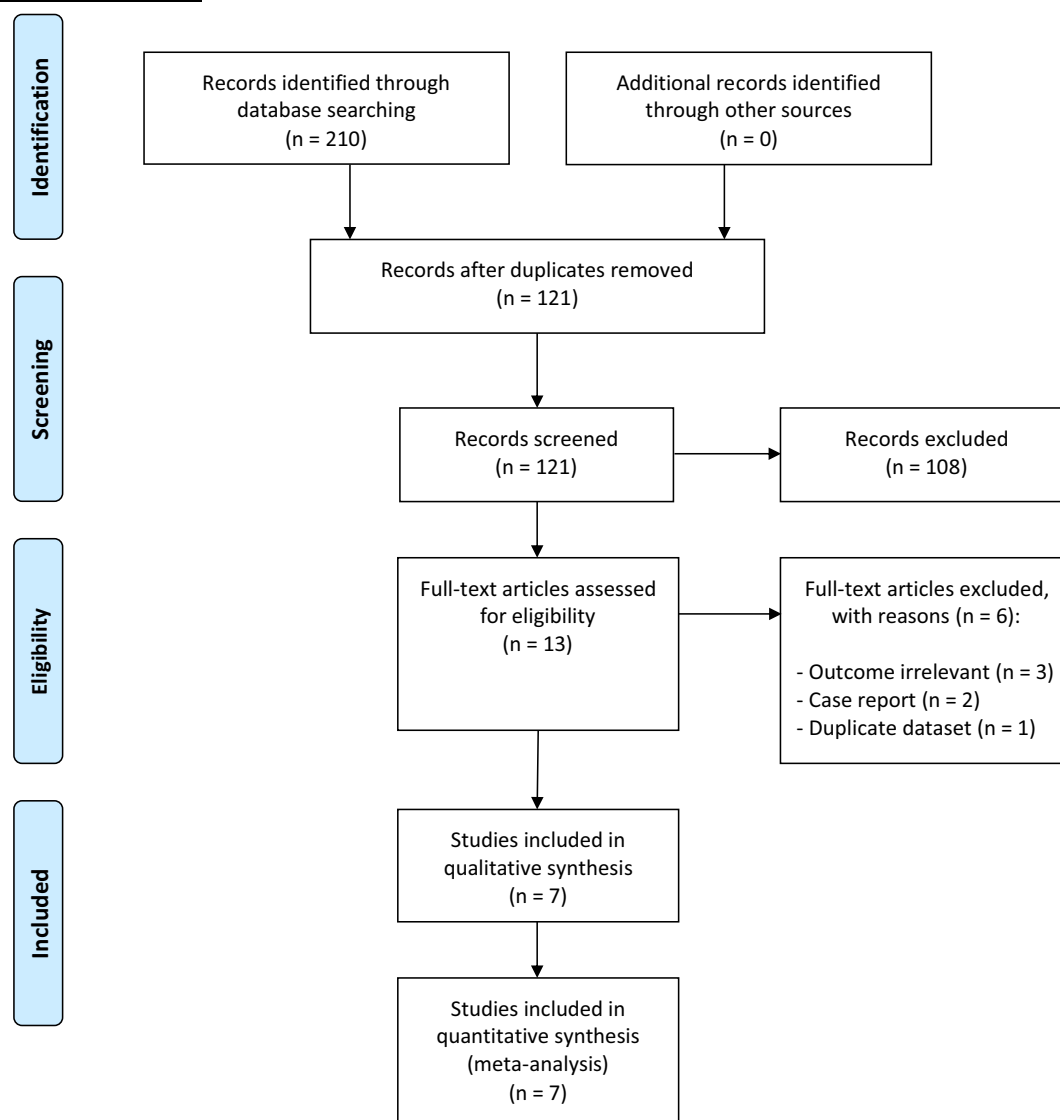


FIGURE 1 PRISMA flow diagram of study selection process.

3.4 | Risk of bias within studies

We found that studies generally were transparent in their source of information obtained, described assessments undertaken for quality assurance purposes, and clearly defined eligibility criteria for their study participants. However, despite having clearly defined eligibility criteria, none of the studies described whether individuals were recruited consecutively and only one study reported the time period of study. Risk of bias evaluations of individual studies are listed in Table 3.

3.5 | Meta-analysis on the effect of the Valsalva manoeuvre on the SFCT and the CVI

All seven studies of 444 eyes in total reported SFCT measures eligible for the meta-analysis. We calculated a summary estimate of an increase of $6.5\mu\text{m}$ (95% CI: $1.6\text{--}11.4\mu\text{m}$; $p=0.01$) in the SFCT due to the Valsalva manoeuvre (Table 4). Heterogeneity statistics found considerable heterogeneity (Cochran's $Q=573$; $I^2=99\%$). The Funnel plot illustrated significantly more spread than what could be expected but without any clear

skewness towards a direction of bias across studies (File S2). Sensitivity analysis showed that omitting Çiçek et al. (2017) or Kurultay-Ersan and Emre (2017) would lead to loss of statistical significance although the direction of the result and the estimated size remained unchanged (File S3).

Two studies of 144 eyes in total reported CVI and were eligible for the meta-analysis. We calculated a summary estimate of an increase of 1.48 (95% CI: $1.23\text{--}1.73$; $p=0.0002$) in the CVI due to the Valsalva manoeuvre (Table 5). Due to the low number of studies in the analysis, it was not meaningful to calculate heterogeneity statistics, generate a Funnel plot or conduct sensitivity analysis.

4 | DISCUSSION

In this systematic review and meta-analysis, we find that the Valsalva manoeuvre leads to a numerically small but statistically significant impact on the SFCT and the CVI. Although the SFCT varies according to various factors, the normal range is considered to be approximately $250\text{--}350\mu\text{m}$ (Kong et al., 2018). Our analyses

TABLE 1 Study characteristics.

Reference	Country	Study design	Participant eligibility	Characteristics
Berhuni et al. (2023)	Turkey	Prospective, single-centre, interventional cohort	Healthy individuals aged 20–50 years, with a BCVA of 20/20, IOP <21 mmHg, and spherical equivalents between −2.00 and +2.00 D. Individuals were required to be cooperative and without any contact lens use, nicotine, alcohol or caffeine addiction or a history of continuous drug use.	84 eyes, 42 individuals Age 35 ± 7 years 38% females
Çiçek et al. (2017)	Turkey	Prospective, single-centre, interventional cohort	Healthy individuals without pregnancy, menstrual irregularity, oral contraceptive use and spherical equivalents between −3.00 and +3.00 D. Individuals had a caffeine consumption of no more than three cups per day.	64 eyes, 32 individuals Age 33 ± 7 years 50% females
Falcão et al. (2012)	Portugal	Prospective, single-centre, interventional cohort	Healthy individuals. Individuals with myopia greater than 6.0 D were not eligible for study.	18 eyes, nine individuals Age 25–38 years 22% females
Kim et al. (2016)	South Korea	Prospective, single-centre, interventional cohort	Healthy individuals without a history of refractive surgery or ocular trauma, without a history of infection, an IOP ≤21 mmHg, a SD-OCT scan of ≥7 and clear visibility of more than one-quarter of the anterior lamina cribrosa surface of the neural canal opening diameter. One eye was randomly selected for the analysis.	48 eyes, 48 individuals Age 25 ± 5 years 17% females
Kurultay-Ersan and Emre (2017)	Turkey	Prospective, single-centre, interventional cohort	Patients without any retinal or choroidal diseases, previous ocular surgery or trauma, glaucoma, systemic diseases or BCVA <20/20. Two categories of eyes were included according to the spherical equivalents, one was those with −6.0 D or more myopia, the other those with +3.0 D or more hypermetropia.	110 eyes, 58 individuals Age 37 ± 15 years 64% females
Mete et al. (2016)	Turkey	Prospective, single-centre, interventional cohort	Healthy individuals with spherical equivalents between −1.00 and +1.00 D. Individuals were required to be cooperative, without any contact lens use or family history of glaucoma, and an IOP ≤21 mmHg. One eye was randomly selected for the analysis.	60 eyes, 60 individuals Age 35 ± 9 years 47% females
Sevik et al. (2022)	Turkey	Prospective, single-centre, interventional cohort	Healthy individuals aged 18–50 years, BCVA 6/6, spherical equivalent between −6.00 and +3.00 D, no history of IOP >21 in either eye, no ocular or systemic medication use, and no media opacity.	60 eyes, 30 individuals Age 31 ± 6 years 73% females

Abbreviations: BCVA, best-corrected visual acuity; D, dioptres; IOP, intraocular pressure; SD-OCT, spectral domain optical coherence tomography.

estimate a 6.5 µm increase during the Valsalva manoeuvre which corresponds to a 2%–3% increase. The normal range of CVI is reported to be 65.61 ± 2.33 (Agrawal et al., 2016). Our analyses estimate an increase of 1.48 during the Valsalva manoeuvre which corresponds to a 2% increase in CVI. Thus, although both the SFCT and CVI increase with the Valsalva manoeuvre, it is important to note that the increase is small. Based on these findings, care should be taken into patient behaviours in relation to the conduct of the OCT scans for diagnosis and monitoring of the choroid. Although the size of the changes attributable to the Valsalva manoeuvre is limited, similar care is recommended when monitoring the choroid in relation to time of scan (the choroid undergoes diurnal variation of the thickness) (Chakraborty et al., 2011; Tan et al., 2012) or recent physical exercise (Insa-Sánchez et al., 2021; Li et al., 2021), coffee intake (Nagasato et al., 2021; Vural et al., 2014; Zengin et al., 2015) or tobacco smoking (Moschos et al., 2016; Zengin et al., 2014).

The Valsalva manoeuvre forces blood out of the pulmonary circulation into the left atrium, which initially increases the cardiac preload and the cardiac output. After a few seconds, this is followed by a reduction of the cardiac preload and output (Pstras et al., 2016).

During the Valsalva manoeuvre, since the venous return to the heart is decreased, the peripheral venous blood pressure increases (Pstras et al., 2016). Rosen and Johnston (1959) demonstrated in dog and rabbit that the Valsalva manoeuvre associated increase in venous pressure was correlated to an increase in the intraocular pressure. Schuman et al. (2000) studied musicians playing wind instruments (trumpet, clarinet and saxophone) to perform a sustained controlled Valsalva manoeuvre. The authors reported a Valsalva manoeuvre related increase in intraocular pressure and a corresponding thickening of the anterior uvea on ultrasound biomicroscopy (Schuman et al., 2000). Based on these findings, it is speculated that the general peripheral increase in the venous blood pressure affects the choroid through an increase in the venous pressure of the jugular, orbital and vortex veins. However, although the effects of the Valsalva manoeuvre on the jugular veins have been studied previously (Seong et al., 2016), the impact of the Valsalva manoeuvre on the orbital veins and the vortex veins is a topic of speculation and remains unexplored. We find that the CVI increases during the Valsalva manoeuvre which may reflect a dilation of the choroidal vessels due to increased venous pressure.

TABLE 2 Valsalva manoeuvre employed in individual studies and time of imaging.

Reference	Performed Valsalva manoeuvre	Time of imaging	Imaging protocol for the subfoveal choroid
Berhuni et al. (2023)	Participants covered their mouths with their hands, their noses with their fingers, and exhaled vigorously for 15 s.	1 min before and at 15 s of Valsalva	SD-OCT (Optovue RTVue XR, Optovue Inc., Fremont, California, USA) ($\lambda=840$ nm, 26 000 A-scans/s, 5 μ m axial resolution) was used for choroid and macula imaging. Foveal scans were obtained using the EDI mode. OCT was performed between 09:00 AM and 12:00 PM in a sitting position to avoid diurnal variation. The SFCT was measured as the vertical distance from the lower border of the RPE in the centre for the fovea to the choroido-scleral junction. The CVI was measured using ImageJ and a single central line scan. Measurements were based on a diameter of 1500 μ m area centred on the fovea. Images were converted to 8-bit and image binarization of the region of interest was performed using Niblack autolocal threshold. CVI was calculated as the ratio of the luminal area to the total choroidal area. Calculations were made three times for each image, and average of the measurements were taken.
Çiçek et al. (2017)	Participants blew forcefully against their hands while occluding their noses with their fingers.	Before (not specified) and at 15 s of Valsalva	SD-OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany). EDI mode was used for imaging. The SFCT was measured as the vertical distance from the RPE to the inner surface of the sclera centred on the fovea.
Falcão et al. (2012)	Participants blew forcefully against their hands while occluding their noses with their index fingers and thumbs.	Before (not specified) and at 15 s of Valsalva	SD-OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany) using EDI mode with 100 times averaging. Two perpendicular scans centred on the fovea were obtained. All scans were carried out in a sitting position. The SFCT was measured as the central distance between the RPE and the inner scleral boundary.
Kim et al. (2016)	Participants exhaled into a mouthpiece connected to a handheld differential pressure-meter and were instructed to maintain the expiratory pressure at a minimal level of 30 mmHg.	Before (not specified) and at 15 s of Valsalva	SD-OCT (Cirrus HD-OCT 5000; Carl Zeiss Meditec, Dublin, California, USA). One line scan through the fovea was made using the EDI mode. All scans were performed in a sitting position. Details of the SFCT measurements were not reported.
Kurultay-Ersan and Emre (2017)	Participants were instructed to take a deep breath and hold it until the OCT measurements were over.	Before (not specified) and at 2–5 s of Valsalva	SD-OCT (Cirrus HD-OCT 4000, Carl Zeiss Meditec, Dublin, California, USA). EDI mode scan of the fovea was made. The SFCT was measured as the vertical distance between the posterior edges of the RPE to the choroid/sclera junction at the level of the fovea.
Mete et al. (2016)	Participants maintained an expiratory pressure ranging between 35 and 40 mmHg by blowing through a mouthpiece attached to a manometer.	1 m before and at 10 s of Valsalva	SD-OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany) using EDI mode. The scan pattern used was a line scan of 30° consisting of 768 A-scans per frame and with 100 times averaging of the B-scan with the aid of eye tracking. All scans were carried out in a sitting position. The SFCT was measured from the outer limit of the RPE to the choroidal-scleral junction at the centre of the fovea.
Sevik et al. (2022)	Participants blew forcefully against their hands while occluding their noses with their index fingers and thumbs.	Before (not specified) and at 15 s of Valsalva	SD-OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany) using EDI mode. The scan pattern employed was the horizontal single-line scan of the fovea with 100 times averaging of the B-scan with the aid of eye tracking. All scans were carried out in a sitting position. The SFCT was measured between the outer border of the RPE and the choroid-sclera junction as a perpendicular line at the level of the fovea. The CVI was measured using Fiji and a single central line scan. Measurements were based on a diameter of 1500 μ m area centred on the fovea. Images were converted to 8-bit and image binarization of the region of interest was performed using Niblack autolocal threshold. CVI was calculated as the ratio of the luminal area to the total choroidal area.

Abbreviations: EDI, enhanced depth imaging; OCT, optical coherence tomography; RPE, retinal pigment epithelium. SD-OCT, spectral domain optical coherence tomography; SFCT, subfoveal choroidal thickness.

The time of imaging before and during the Valsalva manoeuvre were slightly different across studies in our review. Since there seems to be a time dependent impact of the Valsalva manoeuvre and the cardiovascular

physiologic response, one can speculate if the impact of the choroid would differ depending on time from onset of the Valsalva manoeuvre. Kurultay-Ersan and Emre (2017) reported results at 2–5 s, Mete et al. (2016)

TABLE 3 Risk of bias within individual studies.

Reference	Defines source	Eligibility criteria	Time period	Consecutive recruitment	Quality assurance
Berhuni et al. (2023)	Yes	Yes	No	No	Yes
Çiçek et al. (2017)	Yes	Yes	No	No	Yes
Falcão et al. (2012)	Yes	Yes	No	No	Yes
Kim et al. (2016)	Yes	Yes	No	No	Yes
Kurultay-Ersan and Emre (2017)	Yes	Yes	Yes	No	Yes
Mete et al. (2016)	Unclear	Yes	No	No	Yes
Sevik et al. (2022)	Yes	Yes	No	No	Yes

Note: Studies are assessed on relevant items from the Agency for Healthcare Research and Quality checklist: Defines source: Defines the source of information. Eligibility criteria: Lists inclusion and exclusion criteria or refers to previous publications. Time period: Indicates time period used for identifying participants. Consecutive recruitment: Indicates whether or not subjects were consecutively recruited for the study. Quality assurance: Describes any assessments undertaken for quality assurance purposes.

TABLE 4 Meta-analysis on the effect of Valsalva manoeuvre on the subfoveal choroidal thickness (SFCT).

Reference	Eyes, N	Mean change in SFCT	95% CI	Study weight
Berhuni et al. (2023)	84	13.4 µm	13.0–13.8 µm	15.4%
Çiçek et al. (2017)	64	19.3 µm	16.2–22.4 µm	14.5%
Falcão et al. (2012)	18	−5.7 µm	−13.8–2.4 µm	10.9%
Kim et al. (2016)	48	8.9 µm	5.1–12.7 µm	14.1%
Kurultay-Ersan and Emre (2017)	110	5.4 µm	4.6–6.1 µm	15.3%
Mete et al. (2016)	60	0.0 µm	−1.9–1.9 µm	15.1%
Sevik et al. (2022)	60	1.1 µm	−1.8–3.9 µm	14.7%
<i>Summary estimate</i>	444	6.5 µm	1.6–11.4 µm	100.0%

Abbreviations: CI, confidence interval; N, number; SFCT, subfoveal choroidal thickness.

TABLE 5 Meta-analysis on the effect of Valsalva manoeuvre on the choroidal vascularity index (CVI).

Reference	Eyes, N	Mean change in CVI in absolute values	95% CI	Study weight
Berhuni et al. (2023)	84	1.45	1.19–1.72	88.7%
Sevik et al. (2022)	60	1.72	0.98–2.45	11.3%
<i>Summary estimate</i>	144	1.48	1.23–1.73	100.0%

Abbreviations: CI, confidence interval; CVI, choroidal vascularity index; N, number.

at 10s and the other included studies at 15s (Berhuni et al., 2023; Çiçek et al., 2017; Falcão et al., 2012; Sevik et al., 2022). We were unable to find any clear pattern across studies based on the time from the onset of the Valsalva manoeuvre. However, this is in our opinion a topic that deserves further attention.

Limitations should be noted when interpreting the results of our systematic review and meta-analysis. First, the Valsalva manoeuvre was not defined in a uniform manner across studies. This introduces a bias in that the intervention was not uniform across all studies. Moreover, in five of seven studies, the participants were asked to blow forcefully or hold their breath, which does not give any detailed insight into the impact on intrathoracic pressure. Second, the protocol for the scans differed across the studies. Although

different OCT machines and protocols may lead to differences in the thickness measurements or the CVI due to potential differences in general reflectivity, foveal tracking and imaging (Lee et al., 2021), we obtained values from studies reporting differences in images obtained with the same machines. Therefore, this source of bias is not considered to have a significant impact. Third, all study individuals were healthy participants. This means that generalization to eyes with disease that impacts the choroid, for example, central serous chorioretinopathy, can be challenging as the choroidal perfusion may differ in way so that the impact of the Valsalva manoeuvre may be attenuated or enhanced. Fourth, participants had a mean age between 25 and 37 years. Physiologically, this would suggest a relatively good capacity for autoregulation, which may be impaired in older age groups. Fourth, differences in axial length in study groups across studies, to which there was limited insight, may potentially influence the response from the Valsalva manoeuvre. This aspect remains incompletely explored. Finally, only two studies contributed to the meta-analysis of the Valsalva manoeuvre associated impact on the CVI, which is a small sample for conclusive meta-analyses.

In conclusion, we find that the Valsalva manoeuvre has a measurable, statistically significant, numerically small impact on the SFCT and the CVI. We recommend careful observation of patient position and behaviour during OCT acquisition to allow accurate and reproducible measurements of the choroid for diagnosis and monitoring.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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