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Quantitative detection and follow-up of intracranial hypertension in craniosynostosis: an optical coherence tomography study.

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Approval and consent

This study was approved by the Ethics Committee of the Erasmus MC **(MEC-2015-638 (OCT; MEC-2017-1143)** . Patient consent was not required for this study.

Disclosure informatics

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Running head/short title

Optical coherence tomography and intracranial hypertension

Abstract

Background/purpose To evaluate in craniosynostosis: 1) the diagnostic accuracy of fundoscopy and optical coherence tomography (OCT) to detect intracranial hypertension (ICH); 2) the time course of retinal thickness after treatment of ICH; and 3) the relation between high hyperopia (HH) and fundoscopy/OCT scan findings.

Methods Syndromic, multisuture, unicoronal, unilambdoid and sagittal synostosis patients visiting our national center were included in this longitudinal cohort study and formed a consecutive series. Retinal layers on OCT, OCT fundus image and fundoscopy were evaluated. ICH was scored according to presence of abnormal intracranial pressures, hydrocephalus, progressive cerebellar tonsillar herniation or fingerprinting and growth arrest. Diagnostic accuracy of OCT, fundoscopy and fundus image, the time course of retinal thickness after ICH and interference of HH were analyzed using linear mixed models.

Results 577 OCT scans in 307 patients were included. ICH was found in 7.2%. Combining total retinal thickness (TRT), OCT fundus image and fundoscopy resulted in a sensitivity of 76% and 81% specificity to detect signs of ICH. TRT was increased in patients who have had signs of ICH versus patients who never had signs of ICH (β+44.9 µm in patients who have had ICH, 95%CI 9.0-80.8,P=0.01). TRT decreased to normal in the years after surgery (β -3.6 µm/year, 95%CI -7.2 - -0.05, P=0.047). There were greater odds of having increased TRT in patients with HH (OR 2.9, 95%CI 1.1-7.6,P=0.03).

Conclusions The correlation between TRT, OCT fundus image, fundoscopy and particularly for the combination of these parameters with ICP surrogate markers is fair. Increased TRT in the presence of a clinical suspicion of ICH warrants further screening.

Introduction

The detection of intracranial hypertension (ICH) in craniosynostosis is one of the main challenges in managing these patients. Untreated ICH causes developmental problems and may even lead to loss of vision. Therefore, early detection and treatment of ICH is necessary.[1-3]

The best technique for diagnosing ICH in craniosynostosis is 24-hour invasive intracranial pressure (ICP) monitoring.[4] However, this investigation needs a surgical procedure, thereby making it unfeasible for routine screening. Alternative methods for detecting ICH include evaluating the presence of risk factors for, and indirect indicators of ICH. Risk factors include craniocerebral disproportion, hydrocephalus, obstructive sleep apnea (OSA) and cerebral venous hypertension.[5-7] Indirect indicators include symptoms such as morning headaches and behavioral changes, fingerprinting on skull X-ray [8-11] and papilledema on fundoscopy. Unfortunately, the assessment of fingerprinting is observer-dependent. There are also problems with the diagnostic accuracy of what may appear to be "papilledema" [4,9-14]. For example, the presence of high hyperopia (HH) may interfere with the detection of papilledema, resulting in a mimic, so-called pseudopapilledema. However, the distinction between papilledema and pseudopapilledema may be evident on fundoscopy and by using optical coherence tomography (OCT) images of the fundus.[15-17] In fact, recent studies in isolated craniosynostosis show a high correlation between the presence of papilledema on fundoscopy and OCT-scans.[15-19]

Therefore, we aimed to evaluate the following in children with craniosynostosis: 1) the diagnostic accuracy of fundoscopy and OCT in detecting the presence of ICH; 2) the time course of retinal thickness after the treatment of ICH; and 3) whether the presence of HH interfered with fundoscopy/OCT findings of papilledema.

Methods

All patients with syndromic, multisuture, unicoronal, unilambdoid and sagittal synostosis who were managed between 2016-2020, and who were able to comply with OCT scanning, were prospectively included. We also added patients who underwent OCT scanning before 2016 because of a clinical suspicion of ICH. All patients underwent cranial vault expansion in the first year of life, except for patients with a late referral.[6] Patients with a late referral only underwent surgery when signs of ICH were present, or in case of severe distortion of the skull shape. The Erasmus MC IRB approved this study (MEC-2015-638; MEC-2017-1143).

OCT protocol

The Spectralis OCT scanner (Heidelberg Engineering, Dossenheim, Germany, Heyex software v6.7.13) was used to obtain OCT scans. For each OCT scan, two parameters were evaluated: 1) TRT; and 2) OCT fundus image. The image of the optic nerve head (ONH) was evaluated by an experienced ophthalmologist (SL). Papilledema was defined as 360 degrees of edema of the optic disc or blurring of the optic disc margins with obscuration of blood vessels. To measure the TRT of the ONH, the ONH was centered, after which the retinal image was focused to optimize scan quality.[19,20] An automatic segmentation algorithm included in the Heyex software detected the TRT reference layers (inner limiting membrane and Bruch's membrane). A circular chart with concentric rings at 1, 2 and 3 mm was positioned over the ONH, dividing the ONH in 8 equal quadrants. The mean thickness of the TRT was calculated with a precision of 0.2 µm. OCT scans in which less than 75% of the areas were available were excluded. According to a previous study using the same OCT device on children (age 4-10 years), a TRT of > 503.6 µm was considered as increased, and thus as papilledema.[19] Since no TRT normative values exist for the Spectralis device in adults, the adults were scored according to these values as well.

Fundoscopy

Results of all fundoscopies performed during follow-up were extracted from the medical records. Fundoscopies were scored by experienced ophthalmologists (SL) as either "papilledema" or "no papilledema". Presence of HH or optic disc drusen was considered with the interpretation of the fundoscopy.

Patients underwent fundoscopy regularly according to our follow-up protocol:

- Sagittal synostosis: preoperatively, and yearly from the age of 2-6 years
- Unicoronal and unilambdoid synostosis: preoperatively, and at the age of 2, 3 and 4 years
- Crouzon syndrome: preoperatively, every 3 months from the age of 1-2 years, biannual from the age of 2-5 years, and annual from the age of 5-10 years
- Apert and Saethre-Chotzen syndrome and multisuture craniosynostosis involving the lambdoid suture(s): preoperatively, biannual from the age of 1-5 years and annual from the age of 5-10 years
- Muenke syndrome, complex craniosynostosis without lambdoid synostosis, *IL11RA* and *HUWE1* gene mutation craniosynostosis: preoperatively, biannual from the age of 1-2 years, and annual from the age of 2-10 years.

Irrespective of age, additional fundoscopy was performed when ICH was suspected.

Refractive error

The spheric cycloplegic refractive error (RE) was measured by an experienced orthoptist and was expressed in diopters (D). HH was defined as a spheric equivalent of >+4 D.

Intracranial hypertension

Presence of ICH was scored as being absent or present, which was determined by the following criteria:

A) Invasive 24-hour ICP monitoring. The baseline findings were classified as: <10mmHg, normal; 10-15mmHg, borderline abnormal depending on the height and duration of abnormal plateau waves (see below); >15mmHg, abnormal. The trend in ICP values were also checked for any increase overnight. Abnormal ICP plateau waves were categorized as: plateau height <25mmHg (normal), or 25-35mmHg (borderline), or >35mmHg (abnormal); and plateau duration <10 minutes (normal), or 10-20 minutes (borderline) or >20 minutes (abnormal). [21,22]

B) Progressive ventriculomegaly (i.e., hydrocephalus) and obliterated subarachnoid spaces on cerebral magnetic resonance imaging (MRI) scans.

C) Progressive cerebellar tonsillar herniation (and/or syrinx) and obliterated subarachnoid spaces on cerebral MRI scans.

D) Progressive fingerprinting on skull X-rays or scalloping of the inner cranial cortex on CT scans, and reduced size of the ventricles and/or obliterated subarachnoid spaces.

E) Occipitofrontal head circumference (OFC) growth curve deflection, indicating craniocerebral disproportion. [6]

Presence of ICH was determined in one of three ways: if Criterion A was abnormal; or if Criterion B or Criterion C were abnormal; or if Criterion D and Criterion E were abnormal. Since the diagnostic accuracy of papilledema was evaluated, papilledema itself was not taken into consideration for the evaluation of the presence of ICH.

Statistical analysis

Statistical analyses were performed using R statistical software (v4.0.3) and consisted of two major parts: 1) diagnostic accuracy (primary outcome), and 2) longitudinal follow-up (secondary outcome). The interference of HH was evaluated as a tertiary outcome. Statistical significance was set at a P-value of < 0.05.

Diagnostic accuracy.

To examine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio and negative likelihood ratio for fundoscopy findings, OCT fundus image and TRT to detect ICH, we used data collected from the eye with the thickest TRT. In patients

- who developed ICH, the OCT-scan and fundoscopy at the first moment that ICH was detected were used.
- who never had ICH, who also had identical results for each scan or fundoscopy (i.e., all were true negative or false positive), the first scan or fundoscopy was selected for analyses. In patients with contrasting results (i.e., true negative results in one scan or fundoscopy and false positive results in the other), the false positive scans and fundoscopies were selected.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio and negative likelihood ratios were calculated (contingencytables package v2.0.0).

The odds ratios of an abnormal fundoscopy, OCT fundus image or TRT to detect ICH was analyzed by calculating odds ratios from generalized estimation equation (GEE) models, using the cutoff value from normative values and correcting for age as a covariate and multiple

measurements (geepack package v1.3-1).[19] For this analysis, all OCT-scans were included up until the first moment that ICH was detected. The necessity of interaction terms was tested by evaluation of the quasi-likelihood under independence model criterion (QIC) with and without interaction terms, and interactions were subsequently not entered into the models.

Longitudinal follow-up

The eye with the thickest TRT on the first OCT-scan was selected for all consecutive measurements. Longitudinal time course of retinal thickness after the treatment of ICH was evaluated with 2 linear mixed models (nlme package v3.1-150). Effect plots were generated with the ggplot2 package, v3.3.2. We used three statistical models to examine these data. In the first model, all OCT-scans in all patients who underwent surgery were included. TRT was defined as a continuous outcome variable, whereas a historical finding of ICH (yes/no) and age (continuous) were entered as independent predictors. The necessity of an interaction term between ICH and age was tested by evaluation of the Akaike Information Criterion (AIC) with and without interaction terms, and an interaction was subsequently entered into the first model. In the second model, all patients who had had papilledema and ICH were included. TRT was defined as a continuous outcome, time after surgery in years was included as a continuous independent variable. In the third model, all patients were included. TRT in patients who did not have ICH but underwent surgery according to our protocol was compared to TRT in patients who did not undergo surgery because of late referral and no signs of ICH. In the statistical model, TRT was defined as a continuous outcome variable, whereas surgery (yes/no but no ICH before surgery) and age (continuous) were the independent predictors. Again, the necessity of an interaction term between surgery and age was tested by evaluation of the AIC with and without interaction terms, and an interaction was subsequently entered into the first model.

Interference of HH

The interference of HH on fundoscopy and OCT results was analyzed by calculating odds ratios from GEE models. For this analysis, all OCT-scans were included up until the first moment that ICH was detected. We used three models. In these models, papilledema on fundoscopy (1) or OCT fundus image (2) and increased TRT (3) were defined as a binary outcome (yes/no), and high HH (yes/no) and ICH (yes/no) were the independent predictors.

Results

The total study cohort included 307 patients (46% female) (**Table 1**). An attempt to perform an OCT scan failed in 5 patients: 3 had Apert syndrome, one isolated unicoronal synostosis, and one patient had multisuture synostosis. Reasons to not attempt OCT scanning in children included a lack of focus, intellectual disability and a (time-related) lack of parental consent. 577 OCT scans were carried out, and the median age at OCT scan was 7.7 years (IQR 5.5-11.2). **Figure** 1 depicts the in- and exclusion criteria per individual analysis (i.e. diagnostic accuracy as the primary outcome, longitudinal follow-up as the secondary outcome and the interference of HH as a tertiary outcome) and the numbers of included scans and patients per analysis. A total of 283/307 (92.2%) patients underwent surgery, and the median age at first surgery was 0.7 years (IQR 0.5-1.0). Twenty-four patients did not have ICH and did not undergo surgery, 22 because of late referral and 2 because of parental choice. A subset of 131/307 (42.7%) patients underwent repeated OCT scanning, with the median number of 3 scans in these patients (IQR 2-4, range 2-11), and the median follow-up period between the first and last OCT was 2.1 years in this specific subset of patients (IQR 1.0-4.4, range 0.1-9.8). Manual corrections of the segmentation lines for the TRT were performed in 69/577 (12%) OCT-scans.

Diagnostic accuracy

Sensitivity/specificity of OCT/fundoscopy

Figure 1 shows that 237 patients were included. 17/237 (7.2%) had ICH during the fundoscopy and OCT-scan (**Table 2)**. Of these 17 patients, 9 had syndromic craniosynostosis (Crouzon N=7, Saethre-Chotzen N=1, *IL11RA* N=1), one had multisuture synostosis, and 7 had isolated craniosynostosis (sagittal N=6, unicoronal N=1).

An increased TRT was diagnosed in 43/237 (18.1%) patients. The OCT fundus image was abnormal in 31/237, and fundoscopy in 29/237. Diagnostic accuracy was evaluated for the TRT, OCT fundus image and fundoscopy separately, for all 3 items combined, and for TRT and OCT fundus image combined (**Table 3)**. In this analysis the pre-test probability of signs of ICH was 7.2% (~1-in-14), and the post-test probability of ICH using all three diagnostic evaluations combined was 23.8% (~1-in-4).

Odds ratios OCT/fundoscopy

360 OCT-scans in 237 patients were analyzed. There was a 13-fold, or 15-fold, greater odds of having ICH when TRT was increased, or papilledema present on fundoscopy, respectively (**Table 4)**.

Longitudinal follow-up of TRT after the treatment of ICH

Course of TRT by age in operated patients

A total of 510 OCT-scans were carried out in 278 patients (**Figure 1**). 56 patients had a history of ICH. TRT was increased in patients who have had ICH versus patients who never had ICH (β+44.9 µm in TRT, 95%CI 9.0-80.8). Moreover, the TRT slightly decreased as patients aged (β-4.0 µm/year, 95%CI -5.8 - -2.2, **Figure 2**). The observed decrease by age was not different in patients who have had ICH, versus patients who never had ICH (β+0.4, 95%CI -2.7–3.5).

Course of TRT after surgery in patients who have had papilledema and ICH

A total of 119 scans in 40 patients were used including only patients who have had papilledema and ICH (**Figure 1**). These included 18/119 measurements performed after surgery according to protocol, 77/119 after repeated surgery because of recurrent ICH, and 24/119 because of ICH in patients with a late referral. TRT significantly decreased in the years after surgery (β-3.6 µm/year, 95%CI -7.2- -0.05).

Course of TRT in patients who did not undergo surgery versus patients who did undergo surgery but never had ICH

In this analysis, 412 scans were carried out in 250 patients (**Figure 1**). TRT in the 24 patients who did not undergo surgery was comparable to TRT in patients who underwent surgery according to the protocol, but never had ICH (β +35.2 µm, 95% CI -10.6-81.1), see **Figure 3**.

Interference of HH on fundoscopy and TRT

Last, we analyzed 307 OCT scans carried out in 199 patients (**Figure 1**). In total 46/199 (23.1%) had HH. There was close to 3-fold greater odds of having an increased TRT if HH was present, corrected for the true presence of ICH (OR 2.9, 95%CI 1.4-7.6). In contrast, there did not appear to be greater odds of having papilledema on the OCT fundus image or fundoscopy in patients with HH, corrected for the true presence of ICH (OR 2.3, 95%CI 0.8-6.7, and OR 3.1, 95%CI 0.9-9.8).

Discussion

Our study provides three key observations about quantitative detection and follow-up of ICH in patients with craniosynostosis.

Diagnostic accuracy

Following a sensitivity of 76% for the combination of OCT and fundoscopy, approximately 24% of patients do not develop papilledema and/or an increased retinal thickness in the presence of signs of ICH (false negative measurements).

The sensitivity of 59% for fundoscopy alone is remarkably higher compared to the 11-22% reported in literature.[10,16] In contrast, the sensitivity on OCT parameters seems to be slightly lower compared to the numbers in the study of Swanson et al.[16] Explanations for this difference include the alternative method to diagnose ICH (i.e., the ICP was measured under general anesthesia and for one minute), and the other OCT parameters which were used to evaluate retinal thickness. The difference between the fundoscopy sensitivity reported by Tuite et al and the current study includes the different patient population (i.e. the majority of their population had non-operated isolated craniosynostosis) and the alternative method to assess ICP (i.e. only baseline ICP was evaluated).[10] Besides, the recorded time of the ICP was only 3 hours in some patients, whereas the recommended standard is a 24-hour overnight measurement [4].

Longitudinal follow-up

This study shows that TRT slightly decreases as children age, and this was comparable in children who have had ICH versus children who never had ICH. Patients who have had ICH kept a significantly increased TRT compared to patients who never had ICH, which is consistent with a previous study from our group.[20] After surgery, TRT quickly decreases below the upper limit of normal values.[19] We hypothesize that in some patients the retinal thickness remains in the upper bound of normal because of permanent anatomical changes.[23]

We did not identify a difference in TRT in late referred patients without ICH who never underwent surgery and patients who underwent surgery according to the treatment protocol, but

who never had ICH. This finding most likely reflects a mild phenotype in patients with a late referral. It appears that a conservative approach to surgical intervention in this particular group is safe, although long-term assessment of cognition and psychosocial wellbeing should be undertaken.

Influence of HH

HH did not influence the OCT fundus image or fundoscopy outcomes, only TRT was influenced by this refractive anomaly. HH is commonly associated with a crowded optic nerve head, which causes pseudopapilledema.[24] The association between an increased TRT and HH reflects both a strength and weakness of TRT, as the precision of the measurement up to a few microns likely results in earlier detection of retinal changes, but it also causes more false positive measurements. These findings represent an additional argument to combine the OCT scan with fundoscopy. Also, total retinal volume, might be of added value to distinguish papilledema from pseudopapilledema in patients with an increased TRT. [25] Caution with the interpretation of this tertiary analysis is warranted, the confidence intervals of the OR were wide.

Clinical diagnosis of ICH

The practice in our center is to check for signs of ICH at every visit, besides fundoscopy and OCT, including complaints of headaches in the morning, changes in behavior or sleep pattern, and decline of OFC. If ICH is suspected, we proceed with imaging (CT and/or MRI) and, sometimes, invasive ICP measurement. The current study underlines the importance of additional diagnostic aids for accurately screening for ICH. Although the pre- to post-test increase in probability of ICH being present was modest (7.2 to 24%, or 1-in-14 to 1-in-4) for certainty in identifying ICH – they are better than what we have at the moment using clinical

assessment alone. In patients with craniosynostosis, a high sensitivity and NPV are essential to prevent consequences of prolonged ICH.[1-3,26]

Our study does have limitations. First, only 17 patients were diagnosed with ICH, which resulted in pre-test probability for signs of ICH of only 7.2% and limited the evaluation of sensitivity. This low number may be related to our protocol with routine surgery within the first year of life. Also, we only had invasive ICP measurements in 8 patients, and the majority of the cases with ICH were diagnosed based on proxy measurements. Invasive measurements represent the best technique for diagnosing ICH in craniosynostosis, but are unfeasible for routine screening since it requires a surgical procedure and inpatient care for 24 hours. The calculated sensitivity and specificity should therefore be interpreted with caution. However, we did use several other clinical derivatives of and risk factors for ICH to evaluate the presence of ICH, such as ventriculomegaly, Chiari I malformation and skull growth arrest. These individual risk factors potentially suffer from measurement error, but pooling them together reduces the chance of missing or over-diagnosing ICH. Also, we analyzed the diagnostic accuracy based on a group of patients with isolated and syndromic craniosynostosis who are at risk of developing ICH. This may have influenced our calculated parameters, since the risk of ICH varies within these diagnoses. For future studies, we would recommend an analysis per diagnosis, in patients with a low and high risk of developing ICH, within a greater sample size.

Also, we did not have enough data to analyze the diagnostic accuracy and longitudinal follow-up of the peripapillary RNFL, an OCT parameter which has been studied by others.[16,18] However, the TRT and TRV are apparently more accurate in monitoring and diagnosing papilledema/ICH, especially in the pediatric age group.[27-29]

Conclusion

The sensitivity of TRT, OCT fundus image and fundoscopy to detect the presence of signs of ICH is 71%, 59% and 59% respectively and 76% if the three methods are combined. We found that the presence of HH affects the OCT findings and needs to be considered when evaluating OCT results. An increased TRT (after excluding HH) and papilledema on fundoscopy, combined with a clinical suspicion of ICH, warrants further screening for the presence of ICH. During follow-up after surgery, the increased TRT due to ICH remains higher compared to the TRT of age-matched patients without ICH, but falls within the bounds of normative values.

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Figure legends

Figure 1. Patient inclusion in the analyses. Note that the sections are not mutually exclusive.

Figure 2. Effect plot of linear mixed model, visualizing the course of total retinal thickness in patients who have had ICH (red line), versus patients who never had ICH (purple line).

Figure 3. Effect plot of linear mixed model, visualizing the course of total retinal thickness in patients who never underwent surgery (purple line) versus patients who did undergo surgery, but never had ICH (red line)

Diagnosis	**No. of patients**
Syndromic craniosynostosis	
Apert	16 (1 unoperated)
Crouzon-Pfeiffer	43 (7 unoperated)
Muenke	22 (1 unoperated)
Saethre-Chotzen	19 (1 unoperated)
Multisuture craniosynostosis	29 (3 unoperated)
IL11RA craniosynostosis	2
HUWE1 craniosynostosis	1
Isolated craniosynostosis	
Unicoronal synostosis	28 (2 unoperated)
Sagittal synostosis	138 (9 unoperated)
Lambdoid synostosis	9
Gender	140 female (46%)
Median age first surgery	0.7 years (IQR 0.5-1.0)
Median age OCT scan*	7.7 years (IQR 5.5-11.2)
Median number of OCT-scans**	3 (IQR 2-4)
Median follow-up time between first and last OCT-scan**	2.1 years (IQR 1.0-4.4)

Table 1 Patient characteristics.

* median age for all 577 OCT scans (thus including multiple measurements)

** in patients who underwent multiple OCT measurements (131 of the 307 patients)

Diagnostic evaluation of intracranial hypertension	No. of patients
Criterion A. Elevated intracranial pressure on 24-hour monitoring	8
Criterion B. Progressive ventriculomegaly and obliterated subarachnoid spaces	4[1]
Criterion C. Progressive cerebellar tonsillar herniation and obliterated subarachnoid spaces	4[1]
Criterion D + E. Progressive scalloping of the inner cranial cortex and reduced size of ventricles and/or obliterated subarachnoid spaces, OFC growth curve deflection	3

Table 2 Classification of intracranial hypertension

[1]Two patients were classified as both criterion B and C

Abbreviations – OFC: occipital frontal head circumference

	Sensitivity[1]	Specificity[1]	Positive predictive value[1]	Negative predictive value[1]	Positive likelihood ratio	Negative likelihood ratio	Pre and post-test probability for ICH (%)
TRT	71% (12/17) 95% CI 64-76%	86% (189/220) 95% CI 81-90%	28% (12/43) 95% CI 23-34%	97% (189/194) 95% CI 95-99%	5.0 95% CI 3.0-7.8	0.3 95% CI 0.12-0.62	7.2 → 28.6
OCT fundus image	59% (10/17) 95% CI 52-65%	90% (199/220) 95%CI 86-94%	32% (10/31) 95% CI 27-38%	97% (199/206) 95% CI 93-98%	6.2 95% CI 3.2-11.0	0.5 95% CI 0.2-0.7	7.2 → 31.5
Fundoscopy	59% (10/17) 95% CI 52-65%	91% (201/220) 95% CI 87-94%	34% (10/29) 95% CI 29-41%	97% (201/208) 95% CI 93-98%	8.2 95% CI 4.7-14.3	0.3 95% CI 0.1-0.6	7.2 → 34
TRT + OCT fundus image	71% (12/17) 95% CI 64-76%	83% (183/220) 95% CI 78-87%	24% (12/49) 95% CI 19-30%	97% (183/188) 95% CI 94-99%	4.2 95% CI 2.6-6.3	0.4 95% CI 0.1-0.6	7.2 → 25
TRT + OCT fundus image + fundoscopy	76% (13/17) 95% CI 71-81%	81% (179/220) 95% CI 76-86%	24% (13/54) 95% CI 19-30%	98% (179/183) 95% CI 95-99%	4.1 95% CI 2.7-5.9	0.3 95% CI 0.1-0.6	7.2 → 24

Table 3 Diagnostic accuracy of total retinal thickness, OCT fundus image and fundoscopy to detect intracranial hypertension.

[1] Value, absolute numbers and 95% confidence interval

Abbreviations – ICH: intracranial hypertension, OCT: optical coherence tomography, TRT: total retinal thickness

	Odds ratio (95% CI)	P-value
Odds of having intracranial hypertension		
Increased TRT	13.2 (4.3-40.5)	P < 0.001
Papilledema on OCT fundus image	12.3 (4.2-35.7)	P < 0.001
Papilledema on fundoscopy	15.0 (5.0-45.1)	P < 0.001
Increased TRT or papilledema on OCT fundus image or papilledema on fundoscopy[1]	11.9 (3.7-37.6)	P < 0.001
Increased TRT and papilledema on OCT fundus image[2]	9.6 (3.3-28.2)	P < 0.001

Table 4 Odds of having intracranial hypertension in patients with an increased TRT or papilledema on OCT fundus image or fundoscopy (dichotomous outcomes).

[1] Odds of having ICH if one of the following parameters indicated ICH: 1) TRT; 2) OCT fundus image; 3) fundoscopy

[2] Odds of having ICH if one of the following parameters indicated ICH: 1) TRT; 2) OCT fundus image

Abbreviations – ICH: intracranial hypertension, SE: standard error, TRT: total retinal thickness

Fig 1

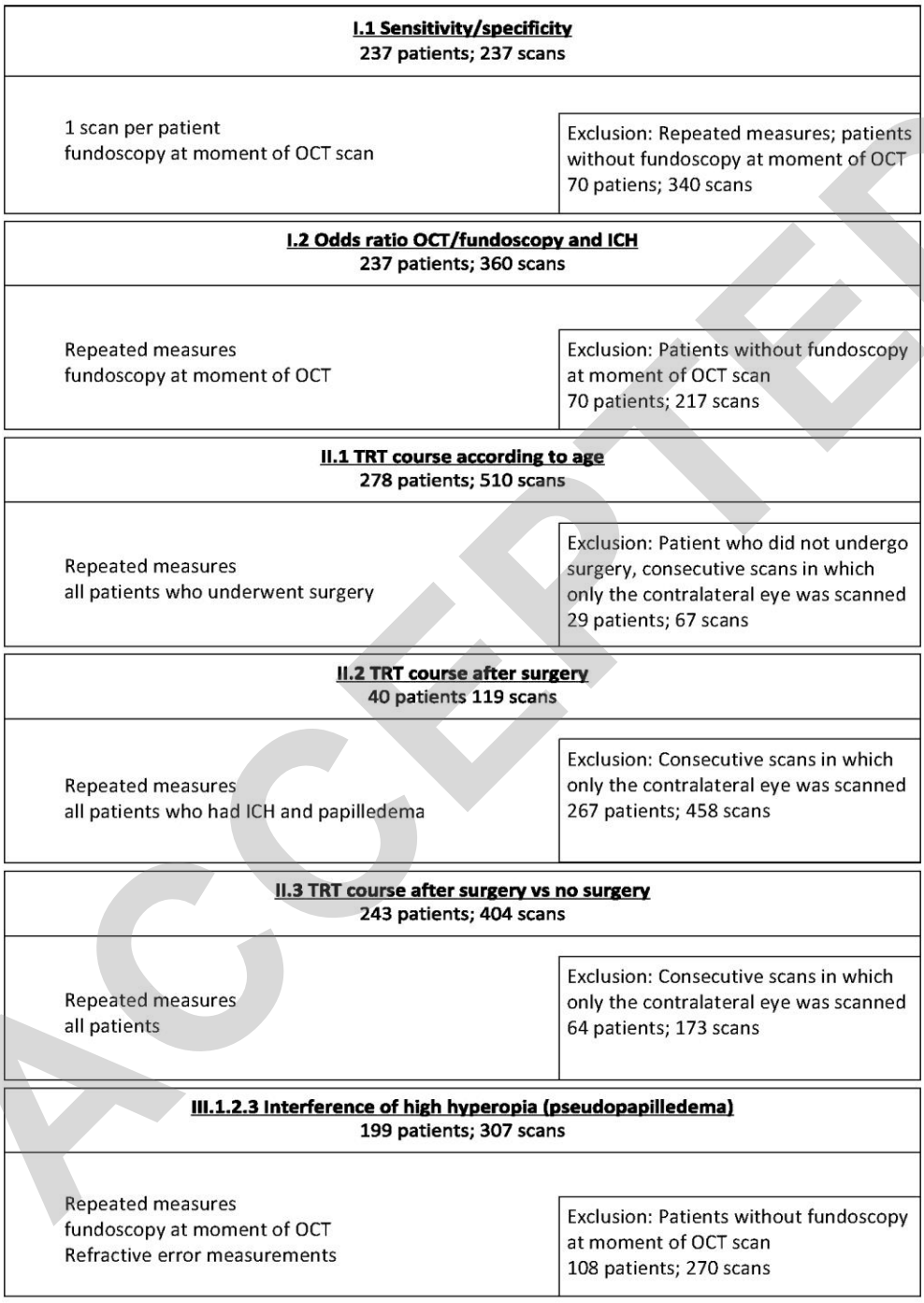

Fig 2

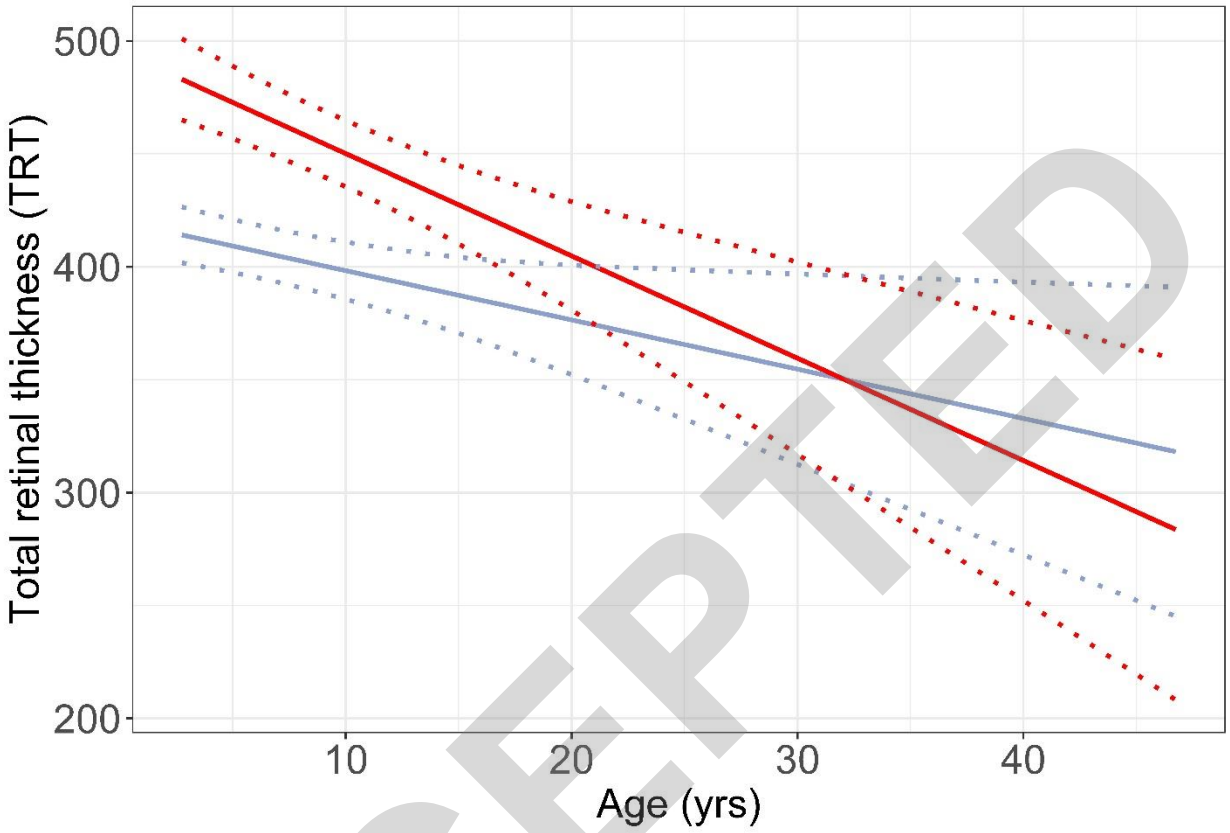

Fig 3