

Age-Stratified Phenotypes of Pediatric Pseudotumor Cerebri: Lower Opening Pressure and Atypical Presentation in Younger Children

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Abstract

Purpose.

Pediatric pseudotumor cerebri (PTC), or idiopathic intracranial hypertension, has been described as two phenotypes separated approximately by puberty, but contemporary data comparing them within a single, ethnically diverse population are limited. We compared younger and older children with PTC.

Methods.

In this retrospective cohort study, all children aged 0–18 years presenting to a tertiary pediatric emergency department with a first diagnosis of PTC between 2018 and 2023 were identified. Children aged ≤ 10 years were compared with those aged > 10 years across three pre-specified primary comparisons: sex, opening pressure, and headache.

Results.

Among 117 children (mean age 11.8 years, 50.4% female), 31 were aged ≤ 10 years. Female sex was markedly less common in the younger group (22.6% vs 60.5%, $p < 0.001$). Opening pressure was lower in younger children (31.8 ± 9.2 vs 39.3 ± 12.5 cm H₂O, $p < 0.001$) and remained lower after excluding the 28 sub-threshold cases (36.5 ± 7.5 vs 43.1 ± 10.8 cm H₂O, $p = 0.003$). Adjustment for obesity attenuated this age difference ($p = 0.06$). Headache was less frequent as the presenting complaint in younger children (58.1% vs 80.2%, $p = 0.029$), the weakest of the three comparisons.

Conclusion.

Younger children with PTC showed a more balanced sex distribution and lower opening pressure than older children, with a less certain reduction in headache. The classic profile of obesity, female sex, and headache, and adult opening-pressure thresholds, should not be used to exclude PTC in this age group, and pediatric opening-pressure reference values may need to account for body size as well as age.

Introduction

Pseudotumor cerebri (PTC), also termed idiopathic intracranial hypertension (IIH), is characterized by raised intracranial pressure in the absence of an intracranial mass, hydrocephalus, infection or venous sinus thrombosis and with normal cerebrospinal fluid (CSF) composition.[1] In adults, IIH predominantly affects women of childbearing age with obesity and has an estimated annual incidence of 1–3 per 100 000 in the general population, rising to over 10 per 100 000 in women with obesity.[2] Pediatric PTC is considerably less common and its incidence rises with age, with the highest rates among adolescents.[3]

Pediatric PTC is recognized to encompass two broadly distinct phenotypes, separated approximately by the onset of puberty.[4, 5] Younger children typically show an equal or near-equal sex distribution, a weaker association with obesity, a higher proportion of secondary and identifiable causes, and a more insidious or atypical onset, including some whose papilledema is found incidentally. Older, post-pubertal children, particularly girls with overweight or obesity, tend to resemble the adult disease, with a female predominance and stronger obesity association. These distinctions matter for diagnosis and management, yet they remain incompletely characterized in single-center, ethnically diverse cohorts.

Diagnostic criteria were revised in 2013 and emphasize compatible symptoms (headache, visual obscuration, pulsatile tinnitus), papilledema or sixth cranial nerve palsy, normal neuroimaging, normal CSF composition, and elevated lumbar puncture (LP) opening pressure. LP opening pressure thresholds differ between subgroups: ≥ 25 cm H₂O is generally required in children without obesity who are not sedated, while ≥ 28 cm H₂O is applied in children with obesity or under sedation. A minority of clinically diagnosed pediatric PTC cases fall below these thresholds, posing diagnostic challenges that are not well described in the literature.[1, 6]

Secondary causes of raised intracranial pressure are common in children and must be excluded; recognized triggers include tetracyclines, retinoids, and recombinant growth hormone, as well as endocrine and nutritional disturbances. Their prevalence in emergency department (ED)-based cohorts is not well documented.[7]

The primary objective was to compare demographic and clinical characteristics between children aged ≤ 10 years and those aged > 10 years with PTC. Secondary objectives were to describe the cohort's presenting symptoms, LP opening pressure, secondary triggers, and ethnic composition. Contemporary data directly comparing these two age groups in a single, ethnically diverse population remain sparse.

Materials and methods

Study design and setting

A retrospective cohort study was conducted at the Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Haifa, Israel, a tertiary academic center and the principal pediatric referral hospital for northern Israel, serving an ethnically diverse population (Jewish, Muslim, Druze and Christian Arab). The pediatric ED provides 24-hour acute care for children aged 0–18 years. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies.[8]

The study period extended from 1 January 2018 to 31 December 2023. Ethics approval was granted by the local institutional review board on 30 April 2024. Informed consent was waived given the retrospective design and use of de-identified data (IRB No.: 0047-24-RMB-D).

Participants and case ascertainment

Data were extracted from the institutional electronic medical record system (Prometheus integrated computer system). This computerized system is a mandatory working tool for ED physicians and nursing staff. Potential cases were identified by searching discharge diagnoses coded as "pseudotumor cerebri" or "idiopathic intracranial hypertension" using the MDClone query interface. This returned 303 records spanning all available years (2000–2024). Two trained reviewers independently verified each case against the full clinical documentation, confirming that the working diagnosis of PTC was made by the treating pediatric neurologist and/or ophthalmologist, with supporting clinical, ophthalmological and neuroimaging information. The participant screening and selection process is summarized in Fig. 1.

Of the 303 identified records, 171 were excluded as falling outside the study period (160 pre-2018, 11 post-2023). Of the remaining 132 records within the study period, 15 were excluded after manual chart review: 6 were recurrent or follow-up admissions for a previously established PTC diagnosis and therefore not incident cases. 5 had PTC diagnoses that were subsequently overturned on full clinical review (including 2 in whom papilledema was excluded and attributed to drusen, 1 with a non-PTC surgical diagnosis, 1 with a lymphoproliferative disorder, and 1 with papilledema attributed to an alternative retinal condition). 4 lacked sufficient documentation to confirm the diagnosis. The final cohort comprised 117 incident PTC cases.

Inclusion criteria

- Age 0–18 years at index ED visit.
- Presentation via the pediatric ED with subsequent ward admission.
- Discharge diagnosis of PTC as a primary or major diagnosis.
- First (incident) PTC diagnosis during the study period.

Exclusion criteria

- PTC not accessed via the pediatric ED (e.g., elective or direct inter-hospital transfers)
- Non-incident admissions (recurrent episodes, follow-up admissions)
- Age > 18 years

Age group classification

Children were classified a priori into two age groups using a cut-off of 10 years, following comparative studies in the pediatric PTC literature.[5, 9] Because pubertal status was not assessed clinically, age was used as the stratifying variable rather than a direct measure of pubertal stage, bearing in mind that a single age threshold does not capture sex differences in the timing of puberty.

Data collection and variables

Data were extracted from the electronic medical record into a structured spreadsheet (one row per patient) using a predefined case report form. The following variables were collected:

- Demographics: age at diagnosis (years), sex, religion (categorized as Jewish, Muslim, Druze, or Christian Arab), country of birth, and calendar year of diagnosis.
- Obesity was ascertained from the medical record, based on a documented diagnosis of obesity or, where height was available, a body mass index at or above the 95th percentile for age and sex (WHO 2007 growth reference).[10] Body weight (kg) was recorded where available and used as a continuous variable.
- Clinical variables comprised the chief presenting complaint(s), LP opening pressure (cm H₂O), and known secondary triggers identified from the medication history and documented medical background. Presenting complaints, taken from the ED and admission notes, were grouped into headache, visual symptoms (blurred vision, diplopia, transient visual obscuration), vomiting, incidental presentation via ophthalmology referral, and other (including seizure). Sex was recorded as documented in the medical record (male or female). Gender was not assessed.
- Outcome: in-hospital mortality.

Definitions

All LPs were performed under sedation, as is standard pediatric practice at the study center. The applicable Friedman 2013 diagnostic threshold is therefore ≥ 28 cm H₂O for every patient, and an opening pressure below 28 cm H₂O was classified as sub-threshold. All children meeting the clinical diagnosis of PTC were included in the primary analysis, including those with a sub-threshold opening pressure, and a separate sensitivity analysis tested whether the findings held when these children were excluded. LP opening pressure was recorded as measured at the time of procedure and was available for every child.

Secondary triggers were defined as documented medications known to have a recognized association with raised intracranial pressure, including recombinant growth hormone, tetracycline-class antibiotics (including minocycline), isotretinoin, all-trans retinoic acid (ATRA), and high-dose vitamin A. These were identified from the structured medication and medical background fields in the record.

Statistical analysis

All eligible incident cases were included, so no sample size or power calculation was performed; precision is conveyed by 95% confidence intervals (CIs). Children aged ≤ 10 years were compared with those aged > 10 years using Welch's t-test (continuous variables) and Fisher's exact or chi-square tests (categorical variables), with differences in proportions reported as risk differences with 95% CIs.

Opening pressure was correlated with age (Pearson) and modelled by linear regression on age group, sex, and either documented obesity or body weight, to test whether the age difference was independent of body size. As opening pressure was non-normally distributed in the older group, Spearman correlation and the Mann-Whitney U test confirmed these results.

Sex, opening pressure, and headache were pre-specified as primary comparisons, and all other comparisons were exploratory. Two sensitivity analyses tested the opening-pressure finding: excluding sub-threshold cases (< 28 cm H₂O) and applying sex-specific cut-offs (girls ≤ 9 , boys ≤ 11 years). No correction for multiple comparisons was applied, so borderline findings should be interpreted cautiously. Data are summarized as mean $\pm$ SD (range) or n (%). Body weight was missing for two children. Analyses used IBM SPSS Statistics 28.0 (IBM Corp., Armonk, NY, USA).

Results

Cohort overview

One hundred and seventeen children (mean age 11.8 ± 3.9 years, range 1.5–17.8) were diagnosed with incident PTC over the six-year period. Fifty-nine (50.4%) were female. No in-hospital deaths occurred.

Religious background was documented for 111 children (95%): 58 Jewish, 40 Muslim, 7 Druze, and 6 Christian Arab. Most were born in Israel (112, 96%).

Thirty-one children (26.5%) were aged ≤ 10 years and 86 (73.5%) were aged > 10 years.

Age-stratified characteristics

Table 1 summarizes the comparison of demographic and clinical variables by age group. Female sex was significantly less common in the younger group (risk difference – 37.9%, 95% CI – 55.9 to – 19.9). LP opening pressure was also lower in younger children (mean difference – 7.5 cm H₂O, 95% CI – 11.8 to – 3.3) and rose with age across the cohort ($r = 0.25$, $p = 0.008$; Fig. 2). Nonparametric tests gave concordant results.

Sub-threshold opening pressure (< 28 cm H₂O) was present in 28 children (23.9%), more often in the younger group, and all were included in the primary analysis. Ophthalmological assessment was documented for 24 of these 28, most with optic disc findings consistent with papilledema. One 4-year-old had a normal opening pressure (11 cm H₂O), confirmed on repeat measurement with normal cerebrospinal fluid. The diagnosis rested on bilateral papilledema and symptomatic improvement after LP, and the case was retained.

Headache was the most frequent presenting complaint overall (74.4%), followed by visual symptoms (32.5%), vomiting (11.1%), incidental ophthalmological diagnosis (10.3%), and seizure (1.7%). Many children had more than one symptom. As the presenting complaint, headache was significantly less frequent in younger children (risk difference – 22.2%, 95% CI – 41.5 to – 2.9), and incidental diagnosis

through ophthalmology was more common in the younger group without reaching significance. Visual symptoms and vomiting did not differ between age groups.

Obesity was documented in 39 of 117 children (33.3%) and was more frequent in older children (risk difference 36.6%, 95% CI 23.0 to 50.1). Body weight correlated with opening pressure ($r = 0.35$, $p < 0.001$). In multivariable models, the age-group difference in opening pressure attenuated after adjustment for documented obesity and sex (from the unadjusted -7.5 to -5.0 cm H₂O, $p = 0.06$) and was abolished after adjustment for body weight and sex (-1.2 cm H₂O, $p = 0.72$), while obesity ($+6.6$ cm H₂O, $p = 0.008$) and body weight ($+0.12$ cm H₂O/kg, $p = 0.01$) were themselves associated with a higher opening pressure.

Sensitivity analyses

When the 28 sub-threshold children were excluded, opening pressure remained significantly lower in the younger group ($n = 20$ vs 69 ; 36.5 ± 7.5 vs 43.1 ± 10.8 cm H₂O, $p = 0.003$). The age-group difference was therefore not driven by inclusion of diagnostically borderline cases. Applying sex-specific age cut-offs (girls ≤ 9 years, boys ≤ 11 years) likewise did not change the findings: opening pressure remained lower in the younger group (32.0 ± 9.4 vs 39.5 ± 12.5 cm H₂O, $p < 0.001$), as did female predominance ($p < 0.001$).

Secondary triggers

Identifiable secondary triggers were present in 9 children (7.7%): minocycline in 3, recombinant growth hormone in 2, ATRA in 2, isotretinoin in 1, and hypervitaminosis A in 1. Their distribution did not differ by age group. Vitamin D deficiency was documented in a further 9 children but was not counted as a trigger, as causality could not be established from the records.

Table 1
Characteristics of 117 children with PTC stratified by age group.

Variable	≤ 10 years (n = 31)	> 10 years (n = 86)	p-value
Age (years), mean ± SD (range)	6.4 ± 2.2 (1.5–10.0)	13.8 ± 2.1 (10.1–17.8)	–
Female, n (%)	7 (22.6%)	52 (60.5%)	< 0.001
LP OP (cm H₂O), mean ± SD	31.8 ± 9.2	39.3 ± 12.5	< 0.001
Sub-threshold LP OP (< 28 cm H ₂ O), n (%)	11 (35.5%)	17 (19.8%)	0.090
Headache as chief complaint, n (%)	18 (58.1%)	69 (80.2%)	0.029
Visual symptoms, n (%)	11 (35.5%)	27 (31.4%)	0.66
Vomiting, n (%)	5 (16.1%)	8 (9.3%)	0.33
Incidental presentation (ophthalmology), n (%)	6 (19.4%)	6 (7.0%)	0.080
Obesity, n (%)	2 (6.5%)	37 (43.0%)	< 0.001
Known secondary trigger medication, n (%)	1 (3.2%)	8 (9.3%)	0.44

Bold indicates pre-specified comparisons ($\alpha = 0.05$). Other p-values are exploratory. Opening pressure was recorded for all 117 children. LP OP, lumbar puncture opening pressure.

Discussion

Principal findings

This six-year study of 117 children identifies three differences between those aged ≤ 10 years and older children: lower female predominance, lower LP opening pressure, and less frequent headache as the presenting complaint. Together they describe a distinct clinical picture in younger children within an ethnically diverse ED population.

Sex and LP opening pressure

The lower female predominance in younger children replicates the pattern described in pediatric PTC series, in which female predominance emerges around the pubertal transition through hormonal and metabolic mechanisms that remain incompletely understood.[5, 9, 11]

The lower opening pressure in younger children bears directly on diagnosis. Because every lumbar puncture was performed under sedation, the applicable Friedman threshold was ≥ 28 cm H₂O, yet just under a quarter of children fell below it, more often in the younger group, though this did not reach

significance. These children were retained, with papilledema documented in most, supporting the diagnosis despite borderline pressures. The single child with a normal opening pressure, diagnosed on papilledema and clinical course, shows the limits of a fixed threshold in young children, in whom papilledema and clinical course are more informative. The age-group difference persisted after excluding all sub-threshold children, so it is not an artifact of borderline cases.

The higher obesity prevalence in older children mirrors the recognized emergence of obesity as a dominant feature after puberty.[9, 12] Multivariable modelling indicated that much of the age-group difference in opening pressure is attributable to body habitus rather than chronological age. Because body size is downstream of age rather than a confounder, these models estimate a direct effect: the unadjusted difference remains the quantity relevant to a diagnostic threshold, but body habitus appears to be its proximate correlate. This argues for reference values indexed to body size as well as age. Obesity was ascertained from documented diagnoses and from BMI where height was available, so residual misclassification is likely and these estimates are provisional.

Presentation: symptoms and incidental diagnosis

The lower frequency of headache in younger children accords with their tendency to present atypically or with incidentally discovered raised intracranial pressure. Incidental diagnosis through ophthalmology was more common in the younger group, though not significantly. These findings suggest that prominent headache should not be required before proceeding to diagnostic lumbar puncture in this age group.[4] Of the three primary comparisons the headache difference was the weakest, and unlike the differences in sex and opening pressure it would not withstand correction for multiple comparisons; it is therefore best read as suggestive.

Visual symptoms and vomiting did not differ between groups and were common at all ages, in keeping with papilledema and its threat to vision throughout the pediatric range.[4]

Secondary triggers and medical context

The prevalence of identifiable secondary triggers (7.7%) matches published pediatric series.[7] Strictly, these represent secondary rather than idiopathic intracranial hypertension, a distinction that could not be applied reliably from routine coding. Vitamin D deficiency documented in a further nine children was likewise not counted as a trigger, as causality could not be established.

Strengths and limitations

Strengths. The study captured every incident PTC case admitted through the ED over six consecutive years at a large tertiary children's hospital, in an ethnically diverse population under-represented in the existing literature. All LPs were performed under sedation, so a single opening-pressure threshold applied uniformly and sedation did not confound the between-group comparison. The age-stratified comparison and its three primary hypotheses were pre-specified, and cases were reviewed independently by two investigators. These features support the internal validity of the differences reported here, within the constraints of a retrospective single-center design.

Limitations

First, the retrospective design and reliance on clinician documentation and discharge coding introduce misclassification risk. Second, obesity was drawn from documented records and from BMI where height was available and may be under-recorded, so the body-size adjustment is imprecise and BMI z-scores could not be used. Third, pubertal status was not assessed, and a single age threshold does not capture sex differences in pubertal timing; Tanner staging or sex-specific thresholds would refine this. Fourth, cases were not graded as definite, probable, or possible PTC, and some sub-threshold cases may reflect misdiagnosis or measurement error, though ophthalmologic assessment was documented in most. Fifth, the study is single-center, limited to ED presentations and the index admission, without ophthalmological outcome data to assess visual morbidity.[13] Sixth, only diagnosed cases were captured, so the sex and obesity distributions do not estimate incidence.

Future directions

Prospective, multi-center cohorts with Tanner staging, standardized BMI z-scores, and ophthalmological outcomes are needed to confirm these age-stratified differences and to quantify how much of the age difference in opening pressure reflects body habitus. Age-, sex-, and weight-stratified normative opening-pressure data within the pediatric range also merit dedicated study.

Conclusions

In children with PTC, those aged ≤ 10 years differed from older children in three respects: lower female predominance, lower opening pressure, and less frequent headache. Clinicians should not rely on the classic profile of obesity, female sex, and headache, or on adult opening-pressure thresholds, to exclude PTC in younger children. A lower opening pressure does not exclude the diagnosis when papilledema and the clinical course are consistent. Much of the age difference in opening pressure was attributable to body habitus, so reference values should be indexed to body size as well as age.

Declarations

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

This retrospective study was approved by the Institutional Review Board of Rambam Health Care Campus (approval number 0047-24-RMB-D) and was performed in line with the principles of the Declaration of Helsinki.

Consent to participate

The requirement for informed consent was waived by the Institutional Review Board owing to the retrospective design and the use of de-identified data.

Consent to publish

Not applicable. The manuscript contains no individually identifiable data.

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Author Contribution

All authors contributed to the study conception and design. Data collection was performed by G.A. and N.L. Analysis, tables and figures were performed by N.L. Methodological and clinical supervision were performed by R.A. and N.L. The first draft was written by N.L., and all authors commented on previous versions. All authors read and approved the final manuscript.

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Data Availability

The de-identified data supporting the findings of this study are available from the corresponding author on reasonable request, subject to local ethics committee approval.

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Figures

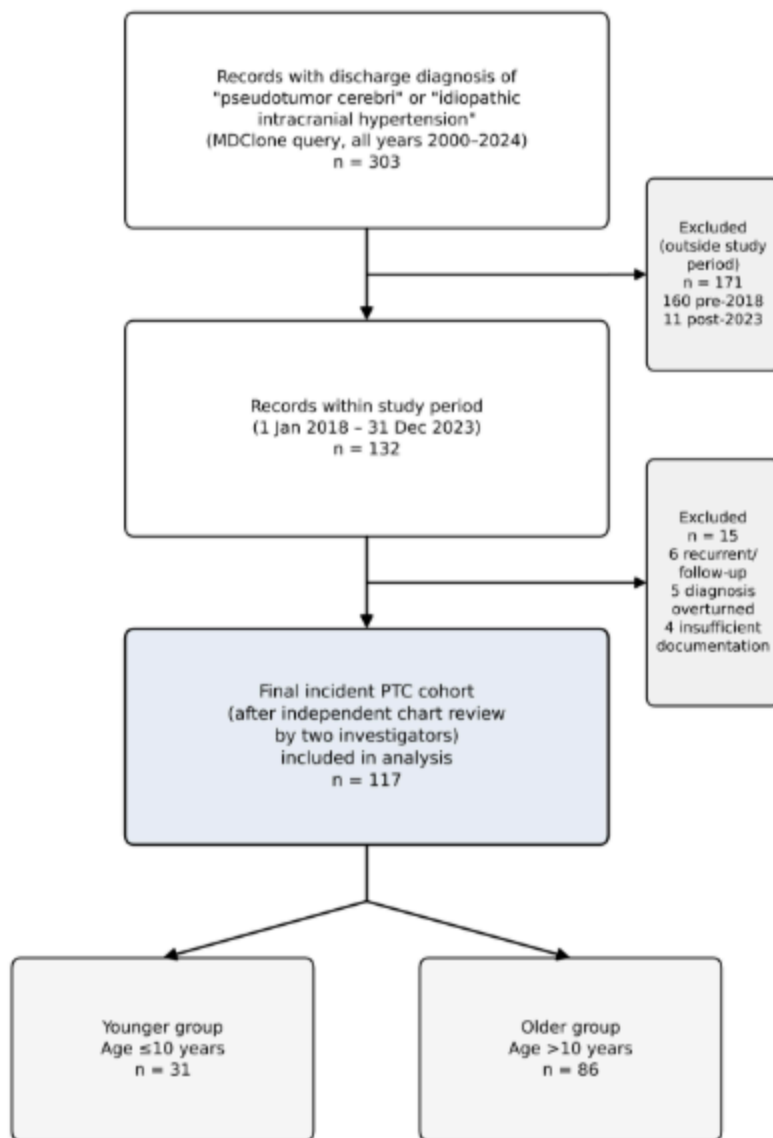


Figure 1

STROBE participant flow diagram. Six-year retrospective cohort of pediatric pseudotumor cerebri (PTC), tertiary pediatric emergency department, 2018–2023. MDCIone is the institutional electronic medical record query system.

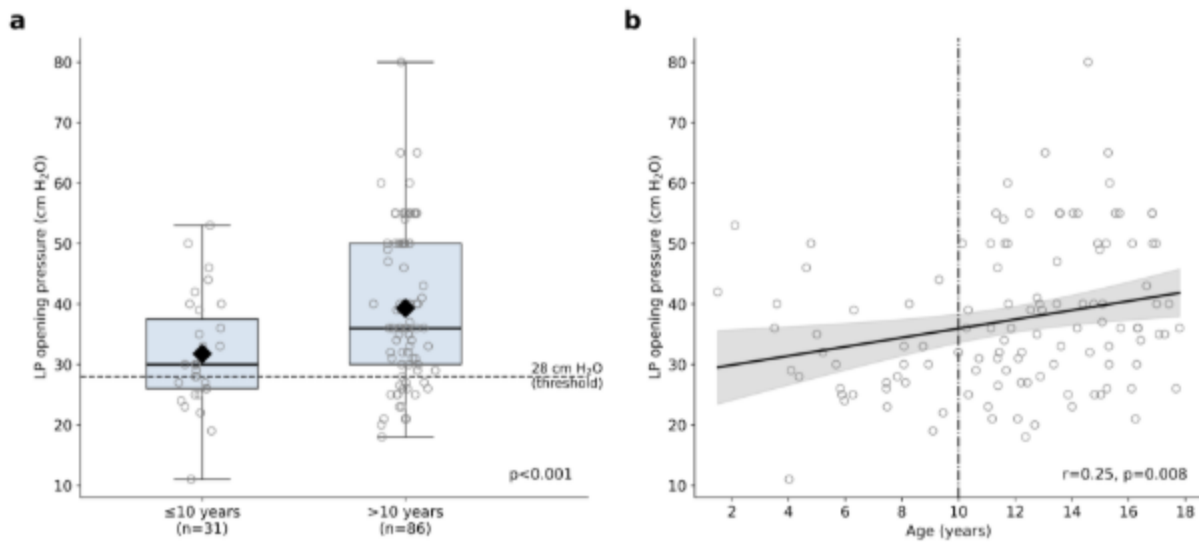


Figure 2

LP opening pressure by age group (a) and as a function of age (b). a Box plots (median, interquartile range, and $1.5 \times \text{IQR}$ whiskers) with individual data points; diamonds mark group means, and the dashed line marks the ≥ 28 cm H₂O diagnostic threshold. b Scatter plot with least-squares regression line and 95% confidence band; the dash-dot line marks the 10-year age cut-off