Journal of the Neurological Sciences 453 (2023) 120801

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Prevalence of pineal cysts in healthy individuals: Emphasis on size, morphology and pineal recess crowding

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ARTICLE INFO

Keywords:
Pineal cyst
Prevalence
Pineal cyst biomarkers

ABSTRACT

The present study aimed to determine prevalence of non-hydrocephalic pineal cysts of different size and morphology in healthy individuals. In a cohort of healthy individuals who as part of research volunteered to undergo magnetic resonance imaging (MRI) of the brain, we performed a systematic search for occurrence of pineal cysts of different sizes, morphology and evidence of crowding of the pineal recess. Degree of crowding in the pineal recess was estimated by the imaging biomarkers anterior-posterior diameter and cyst-tectum-splenium (CTS) ratio at midsagittal MRI. The study included a cohort of 994 healthy individuals, aged 47.0 ± 21.1 years in whom a pineal cyst was demonstrated in 337/994 (37.5%) individuals. A small cyst within a mainly solid gland was observed in 252/994 (25.4%) subjects and a mainly cystic gland in121/994 (12.2%). The pineal cysts were more frequent in women than men, and were associated with age, though not with reduced prevalence in aged individuals, as previously reported. Cysts with maximum anterior-posterior diameter ≥ 10 mm were seen in 51/994 (5.1%) individuals, and with CTS ratio ≥ 0.9 in 16/994 (1.6%) individuals. The occurrence of pineal cysts is frequent and is seen more frequently in women. It usually presents as a small cyst in a predominantly solid gland; however, pineal cysts causing crowding of the pineal recess with a CTS ratio ≥ 0.9 was seen in merely 1.6% of participants.

1. Introduction

Pineal cysts represent an increasing diagnostic challenge to neurologists and neurosurgeons since they are more frequently identified at magnetic resonance imaging (MRI) [1]. Symptomatic individuals with non-hydrocephalic pineal cysts are referred to neurosurgeons for second opinion, but counseling may be hampered by limited information about their occurrence in healthy individuals. The reported prevalence of pineal cysts revealed by MRI is in the range 0.5–4% [2–9]. However, the published series usually refer to pineal cysts above 5 mm in size, and provide limited additional information about size and degree of crowding of the pineal recess.

The vast number of pineal cysts are incidental findings at MRI, and neurosurgery for symptomatic non-hydrocephalic pineal cysts remain highly disputed [1]. It has previously been reported that the degree of cyst-induced crowding of the pineal recess associates with severity and progression of symptoms and clinical outcome of surgery [10–12]. Pineal recess crowding may therefore be a factor to consider during neurosurgical counseling; however, the prevalence in healthy individuals of pineal cysts causing crowding of the pineal recess remains unknown.

On this background, the present study was undertaken to examine the prevalence of pineal cysts of variable size and morphology in a cohort of about 1000 healthy individuals in whom MRI of the brain was

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https://doi.org/10.1016/j.jns.2023.120801
Received 5 July 2023; Received in revised form 8 September 2023; Accepted 9 September 2023
Available online 12 September 2023

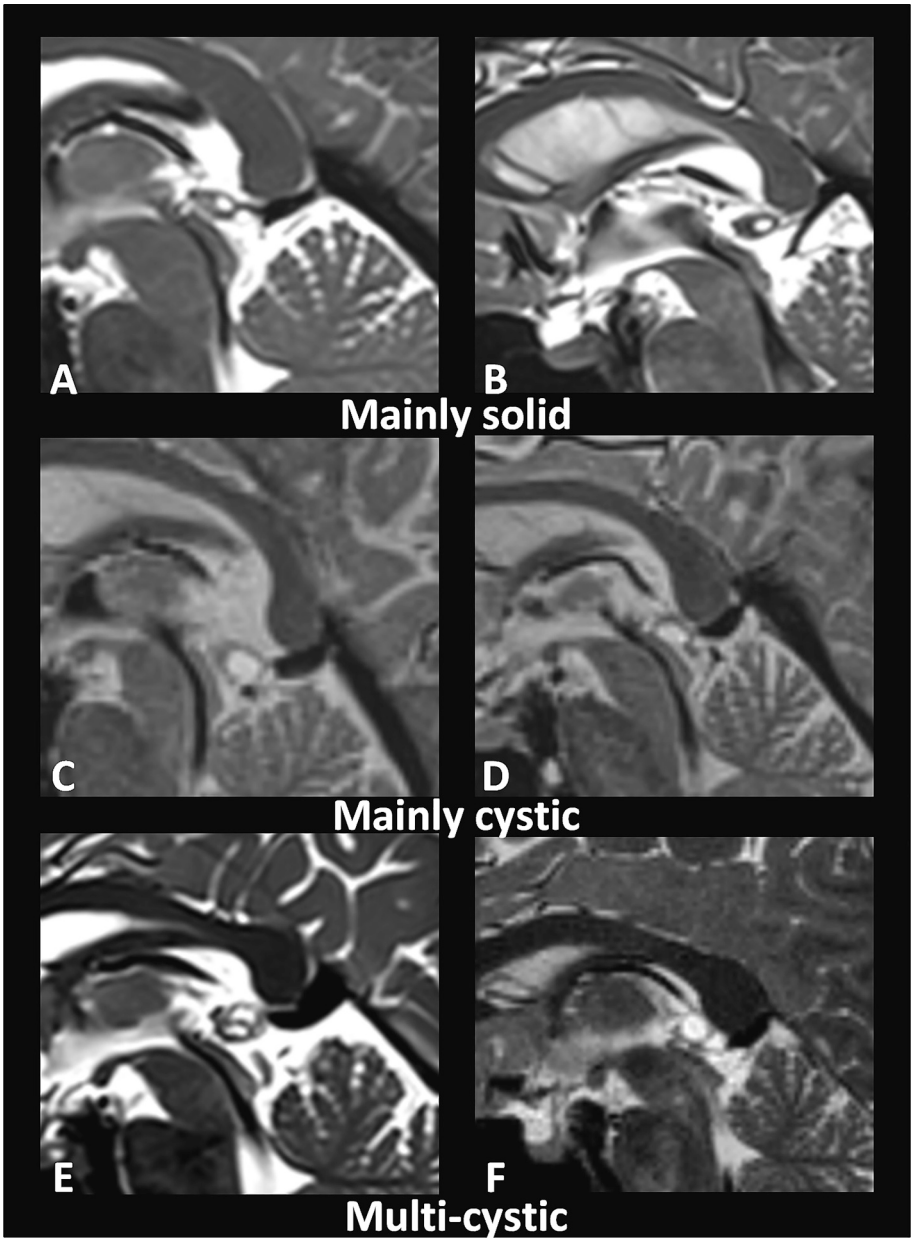


Fig. 1. A-B: Mainly solid pineal glands with small cysts were observed in 252/994 (25.4%) of healthy individuals, here illustrated by mainly solid cysts with anterior-posterior (AP) diameter < 5 mm. C-D: Mainly cystic pineal glands occurred in 121/994 (12.2%) of individuals. *E*-F: Multi-cystic pineal cyst were observed among 73/121 (60.3%) individuals with mainly cystic pineal glands.

done in the absence of known neurological or psychiatric disease.

2. Methods

2.1. Study approval

The study cohort was obtained from two ongoing longitudinal research projects at the Center for the Study of Human Cognition at the University of Oslo (Neurocognitive Development and Cognition and Plasticity through the Life-Span). The studies were approved by The Regional Committee for Medical and Health Research Ethics (REK) of Health Region South-East, Norway. Written informed consent was obtained from all patients older than 12 years and from parents/guardian of volunteers under 18 years of age. Oral informed consent was obtained from participants under 12 years of age. Volunteers were recruited by newspaper advertisements and through local schools and work places. Participants were healthy individuals without prior neurological or psychiatric illness.

2.2. Patient cohort

The patient cohort consists of healthy individuals with no known neurological or psychiatric illness who underwent MRI of the brain as part of research.

2.3. MRI acquisition

Imaging data were acquired on a 1.5 and 3 Tesla Siemens scanner (Siemens Medical Solutions, Erlangen, Germany) at Oslo University Hospital, Rikshospitalet. 3D T1-weighted MP-RAGE (Magnetization

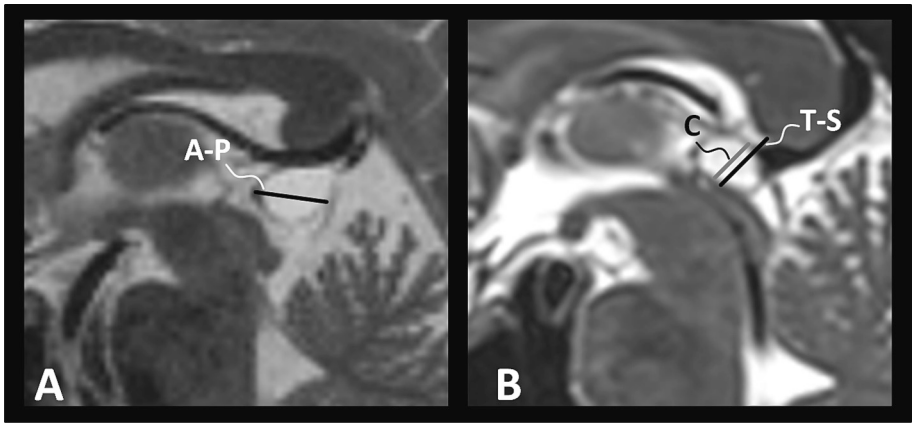


Fig. 2. A: The AP diameter of the pineal cyst is the maximum anterior-posterior (AP) diameter in millimeter using the midsagittal MRI, which in this case was 12.7 mm. B: The cyst-tectum-splenium (CTS) ratio, indicative of crowding of the pineal recess, was measured from the midsagittal MRI as the ratio between the pineal cyst (C) diameter drawn at the shortest distance from the tectum to splenium of corpus callosum divided by the length of the tectal-splenial (T-S) distance, drawn along the same line. In this case, cyst (C) diameter was 7,0 mm, T-S diameter 9.1, which provides CTS ratio equal to 0.77 (=7.0 mm / 9.1 mm).

Prepared Rapid Gradient Echo) (all participants), 3D T2-weighted SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution) (most of the participants). The protocol also included a 25 slices coronal T2-weighted fluid-attenuated inversion recovery (FLAIR) to aid the radiological examination.

In some cases, T2-weighted CISS (Constructive Interference Steady State), T2*-weighted imaging and DWI (diffusion weighted imaging) were acquired. Intravenous contrast-enhanced MRI was not done in these cases.

2.4. Pineal cyst assessment

The assessment of pineal cysts was performed by a single reader, board-certified radiologist (BW), who in cases of doubt consulted another board-certified radiologist (GR) with 16 years of experience in neuroradiology, where consensus was reached in all cases.

The morphology of the pineal gland was characterized as either mainly solid or mainly cystic (Fig. 1). Further, the morphology of the cyst was defined as simple or multicystic. Simple cysts are defined as thin-walled, unilocular cystic lesions without solid components or internal septations. Multicystic were on the other hand defined as multiple small cysts within a solid pineal gland or multilocular cysts with internal septations.

For assessment of pineal cyst size and crowding the following measures were used:

- ***Anterior-posterior (AP) diameter of the cyst.*** The maximum anterior-posterior (AP) diameter (millimeter) of a pineal cyst was measured using the midsagittal plane in MRI (Fig. 2A). In multicystic cysts, the outer diameter of the whole cystic complex was measured.
- ***Tectal compression with aqueduct stenosis.*** The compression of tectum was graded as absent, moderate or severe from the midsagittal MRI. Aqueduct stenosis was dichotomized as absent or present, provided there was a visually recognizable narrowing of the aqueduct lumen at sagittal T1. The combined tectum compression and aqueduct stenosis was dichotomized as No/Moderate/Severe.
- ***Cyst-tectum-splenium (CTS) ratio.*** The ratio between cyst diameter and the shortest distance from splenium to tectum in the same midsagittal image plane was measured along the same line defining the shortest distance between tectum and splenium (Fig. 2B). This ratio was introduced because it may be applied readily to reproducibly assess to which degree the pineal cyst occupies the supra-pineal recess/quadrigeminal cisternal space where the central veins of the brain traverse. This imaging marker was found to differentiate mild from severe symptoms [11], intracranial pressure (ICP) scores [13] and outcome of surgery [14]. A CTS ratio $\geq$ 0.9 was found clinically useful as an index of pineal recess crowding and clinical presentation as well as outcome after surgical cyst removal [10,11,13,14]. Examples of CTS ratio $\geq$ 0.7, $\geq$0.8, $\geq$0.9 and = 1.0 are shown in Fig. 3.

2.5. Statistical analyses

Data are presented as numbers of subjects with percentage occurrence compared with total cohort in parenthesis. Rate ratio was determined Poisson regression with robust standard error and prevalence within age categories and gender was determined by logistic regression analysis and estimation of margins. Significance was accepted at 0.05 level.

3. Results

3.1. Patient cohort

Information about the study cohort is given in Table 1. The study included 994 patients with comparable distribution between male and female. Age range was 4 to 93 years of age (mean 47.0 years, median 46 years). The age distribution of healthy individuals with pineal cysts of any size is shown in Fig. 4A, and the numbers of subjects with pineal cysts above 5 mm in size in Fig. 4B.

3.2. Prevalence of pineal cysts

A pineal cyst was observed in 373/994 (37.5%; 95CI 34.5% to 40.6%) of patients. Pineal cysts were more frequently seen in women, with a female/male relative risk (RR) of 1.55 (95CI 1.31 to 1.84) ($P < 0.001$). The occurrence of a pineal cyst was significantly associated with age (RR 1.004 (95CI 1.0005 to 1.008), $P = 0.026$. Fig. 5 shows prevalence of pineal cysts depending on age and gender.

Regarding the morphology of pineal glands, mainly solid glands with small cysts were twice as common as mainly cystic glands. Among the 121 mainly cystic pineal glands, the occurrence of multicystic cysts was 60% ($n = 73$). The different morphological types are illustrated in Fig. 1. However, the occurrence of small cysts within mainly solid pineal glands was not statistically significantly associated with gender with a female/male RR of 0.99 (95CI 0.86 to 1.14), $P = 0.871$ or age RR of 1.002 (95CI 0.999 to 1.006), $P = 0.154$.

Pineal cysts with AP diameter 10–15 mm were observed in 46/994 (4.6%) of individuals with a female/male RR of 1.26 (95CI 0.72 to 2.24), $P = 0.413$ and age RR of 0.99 (95CI 0.98 to 1.002), $P = 0.100$ while cysts with AP diameter > 15 mm were only observed in 5/995 (0.5%).

None presented with severe tectal compression while 14/994 (1.4%) with moderate tectal compression. Aqueduct stenosis was not observed, but two individuals presented with hydrocephalus (one without a pineal cyst and one with a pineal cyst <5 mm in AP direction).

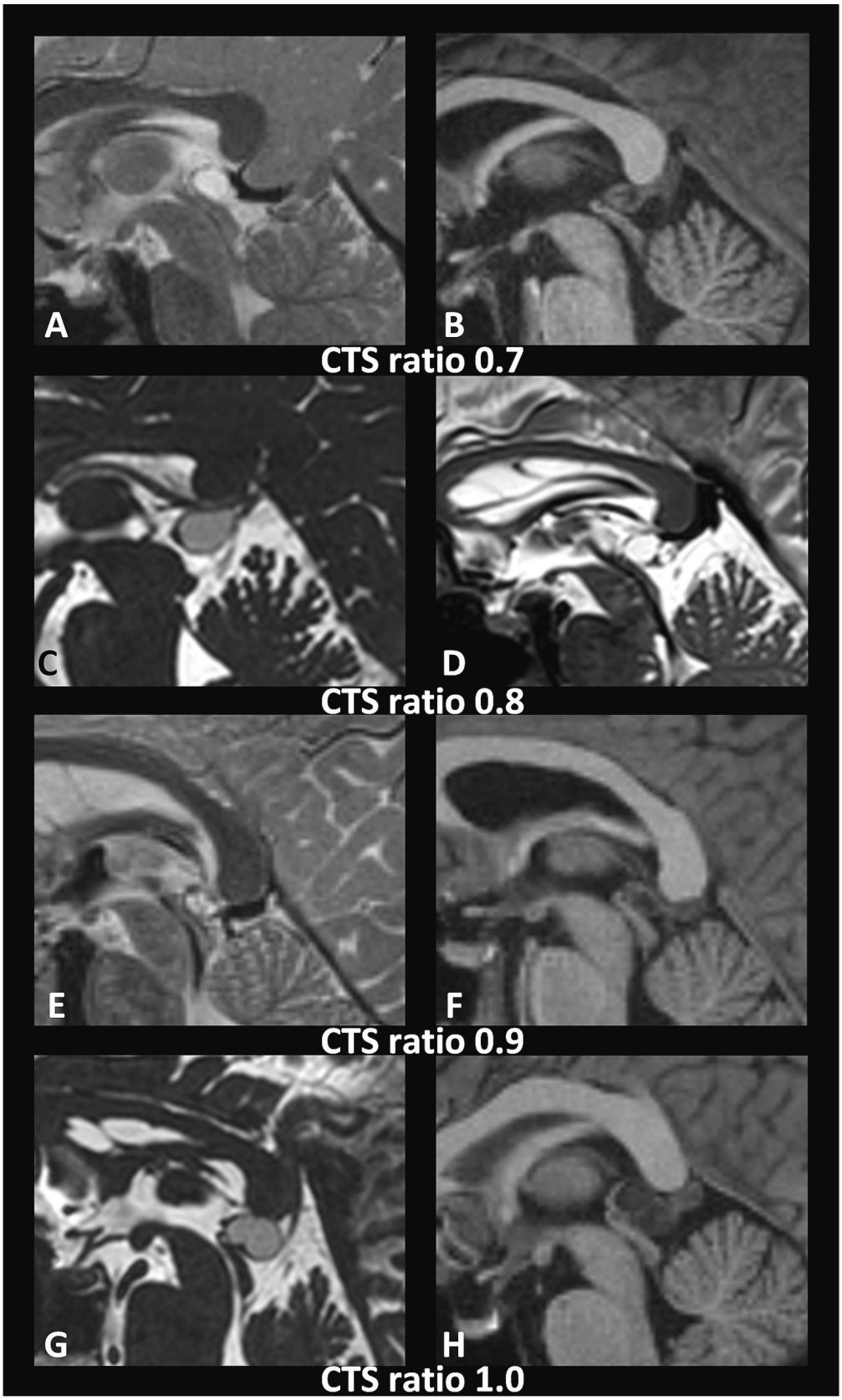


Fig. 3. Examples of individuals with different CTS ratios. A-B: CTS ratio 0.7. C-D: CTS ratio 0.8. E-F: CTS ratio 0.9. G-H: CTS ratio 1.0.

Table 1
Study cohort of 994 individuals.

N	994
Sex (F/M)	502/492
Age (years)	47.0 ± 21.1
Pineal cyst present (N; %)	373 (37.5%)
Morphology of cyst pineal gland	
Mainly solid (N; %)	252 (25.4%)
Mainly cystic (N; %)	121 (12.2%)
Anterior-posterior diameter of cyst (mm)	
< 5.0 mm (N; %)	195 (19.6%)
≥ 5.0 / < 10.0 mm (N; %)	127 (12.8%)
≥ 10.0 / < 15.0 mm (N; %)	46 (4.6%)
≥ 15.0 mm (N; %)	5 (0.5%)
Tectal compression	
No (N; %)	35 (3.5%)
Moderate (N; %)	14 (1.4%)
Severe (N; %)	0
Aqueduct stenosis	
Present (N; %)	0
Hydrocephalus	
Present (N; %)	2 (0.2%)
Cyst-Tectum-Splenium (CTS) ratio	
< 0.6 (N; %)	322 (32.4%)
≥ 0.6 /< 0.7	8 (0.8%)
≥ 0.7 / <0.8 (N; %)	8 (0.8%)
≥ 0.8 / < 0.9 (N; %)	19 (1.9%)
≥ 0.9 (N; %)	16 (1.6%)

Values are presented as numbers with percentages of total cohort in parenthesis or mean ± SD, unless otherwise indicated.

3.3. The cyst-tectum-splenium (CTS) ratio

The CTS ratio is used as a marker of crowding in the pineal recess [10,11]. A CTS ratio < 0.6 was seen in 322/994 (32.4%) individuals with a female/male RR if 1.60 (95CI 1.33 to 1.93; $P < 0.001$) and age RR of 1.006 (95CI 1.002 to 1.01; $P = 0.004$), while a cyst ratio of 0.8 in 19/949 (1.9%) and a cyst ratio ≥ 0.9 in 16/994 (1.6%) individuals (Table 1).

The distribution of cyst ratios is further shown in Table 2. It can be seen that a CTS ratio ≥ 0.8 occurs in mainly cystic glands while smaller cysts <5 mm are usually seen in mainly solid glands. As expected, a cyst ratio ≥ 0.8 is more frequently associated with larger AP diameter of cyst and a higher occurrence of moderate tectal compression (Table 2).

4. Discussion

The main observation of this study is that the prevalence of pineal cysts is much higher than previously reported with size-independent pineal cysts seen in 373/994 (37.5%) healthy individuals. However, the prevalence varies significantly when specific classes of size and morphological characteristics are considered. Pineal cysts causing crowding of the pineal recess, here shown by a CTS ratio ≥ 0.9, were seen in 16/994 (1.6%) of the individuals.

The present observations differ substantially from previous reports. Pineal cysts with maximum diameter < 5 mm have usually not been reported and were here seen in 195 /994 (19.6%) of the healthy subjects. On the other hand, we identified a pineal cyst ≥5 mm in diameter in 178/994 (17.9%) healthy individuals. This prevalence differs markedly from previously reported series that found a prevalence at MRI in the range 0.5–4% [2–9]. For example, some previous MRI studies including a high number of patients reported pineal cysts >5 mm to occur in 478 of 48,417 (0.99%) subjects [3], 56 of 9546 (0.59%) individuals [8], 281 / 42,099 (0.67%) patients [9]. While the present series refer to healthy subjects, previous studies report on hospital MRI series. One may speculate about the major discrepancy between studies. Possible causes relate to study population, MR image quality and way of radiological assessment.

One obvious question is whether the present individuals volunteering for research with MRI represents a selected cohort? This appears, however, less likely as one inclusion criterion for participation was no diagnosed neurological or psychiatric illness. We therefore see no reason to dispute that the present participants represent a cohort of healthy subjects.

The previous studies on prevalence of pineal cysts did not assess occurrence of cysts causing crowding of the pineal recess. We introduced the CTS ratio as a measure of the degree of crowding, which was found to associate with degree and progression of symptom severity [11], pulsatile ICP [13], clinical outcome of surgical cyst removal [10,14], and measurable physiological changes cyst-associated changes [10]. According to our experience, a CTS ratio ≥ 0.9 is of significance. In the present material, a CTS ratio was seen in 16/994 (1.6%) healthy subjects, high-lightening that signs of cyst-induced crowding are rare in healthy subjects. Furthermore, we found the traditional biomarker "AP diameter" less useful in differentiating symptom severity [11]. Here, we found, a pineal cyst with AP diameter ≥ 10 mm in 51/994 (5.1%) healthy subjects.

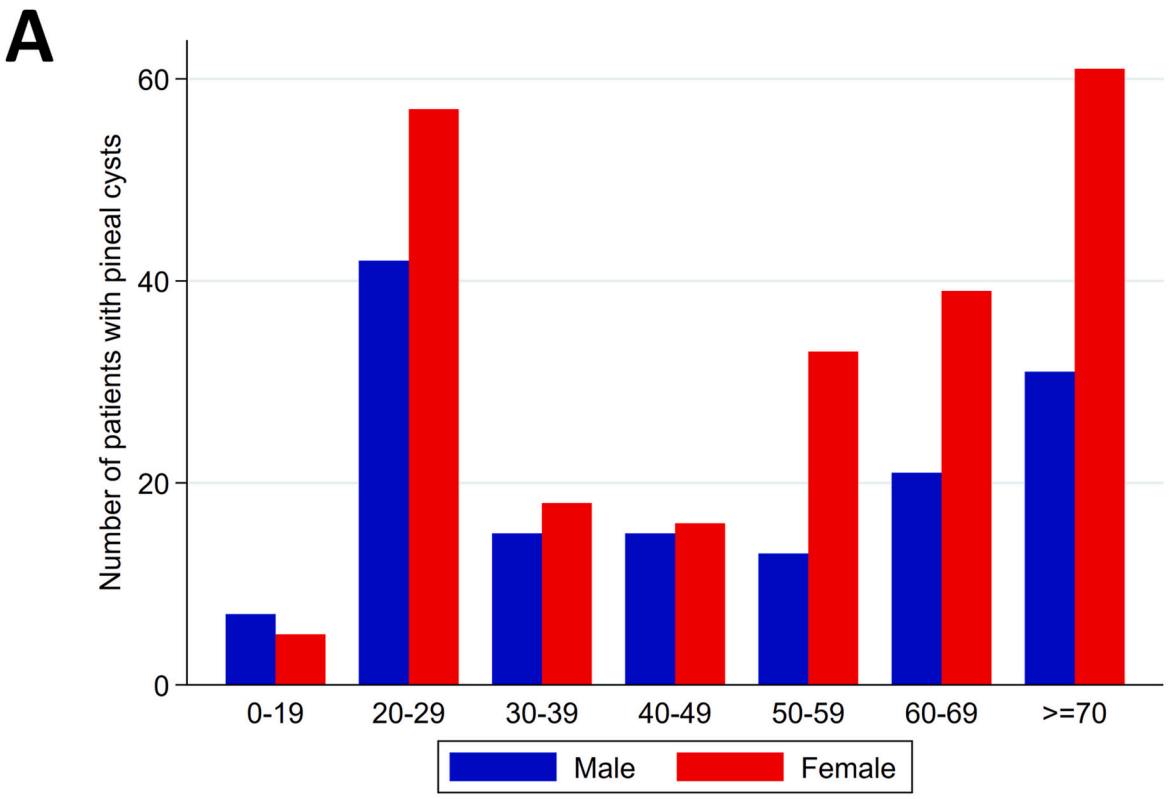
Pineal cysts are more frequent in female than male subjects [1], which was confirmed here by significantly higher relative risk in women than men. This may indicate a hormonal involvement in cyst formation, but further studies are required. We also found a significant association with age, though the distribution differed substantially from previous observations. Hence, in a previous report, prevalence became reduced with increasing age [3], which was not verified here.

None of the present cases presented with hydrocephalus, indicating that hydrocephalic pineal cysts in healthy subjects are rare. On the other hand, non-hydrocephalic pineal cysts in healthy subjects were frequently occurring. An obvious question is which implications these observations may have for counseling of individuals with symptomatic non-hydrocephalic pineal cysts? Currently, there is growing awareness that a small cohort of patients with non-hydrocephalic pineal cysts may benefit from surgical removal of the cyst [12,15], but there is no consensus who might be candidates for surgery. Guidelines are lacking. The present observations might give argument for stressing the importance of size and morphology. We find it of interest that the prevalence of pineal cysts with a CTS ratio > 0.9 was rare, occurring in 1.6% of healthy individuals, given our recent observations on the impact of cyst-induced pineal recess crowding in subjects with symptomatic non-hydrocephalic pineal cysts [10].

Some limitations should be noted. The study cohort includes 994 healthy individuals. A higher number might be preferable. Furthermore, one limitation is that we have no information about symptoms in subjects with large pineal cysts. It therefore remains an unanswered question whether individuals with large cysts were completely asymptomatic. The prevalence of asymptomatic non-hydrocephalic pineal cysts with a CTS ratio ≥ 0.9 may therefore be even lower. Finally, other biomarkers of pineal cyst crowding, such as apparent diffusion coefficient that also associate with symptom severity [11], were not determined since the MRI sequences not allow us to do so in several cases.

5. Conclusions

In conclusion, prevalence of any pineal cyst at MRI was found in >1/3 of subjects, which is more frequent than reported before and may thus be considered a normal variant. However, the prevalence of pineal cysts depends heavily on size and morphology. Cysts with maximum anterior-posterior diameter ≥ 10 mm were seen in approximately 5% of individuals. Pineal cysts with crowding of the pineal recess (CTS ratio ≥ 0.9)were rare, occurring in 1.6% of individuals.



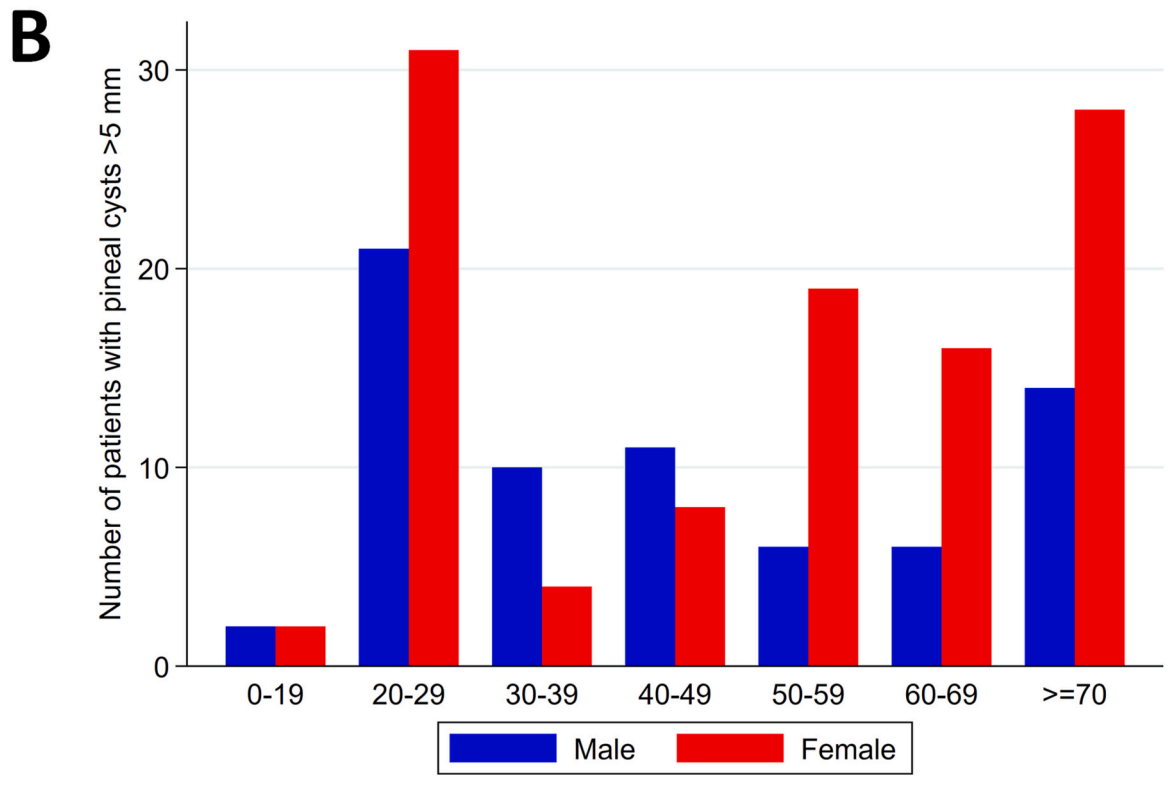


Fig. 4. A: Number of patients with a pineal cyst. B: Number of patients with a pineal cyst ≥5 mm.

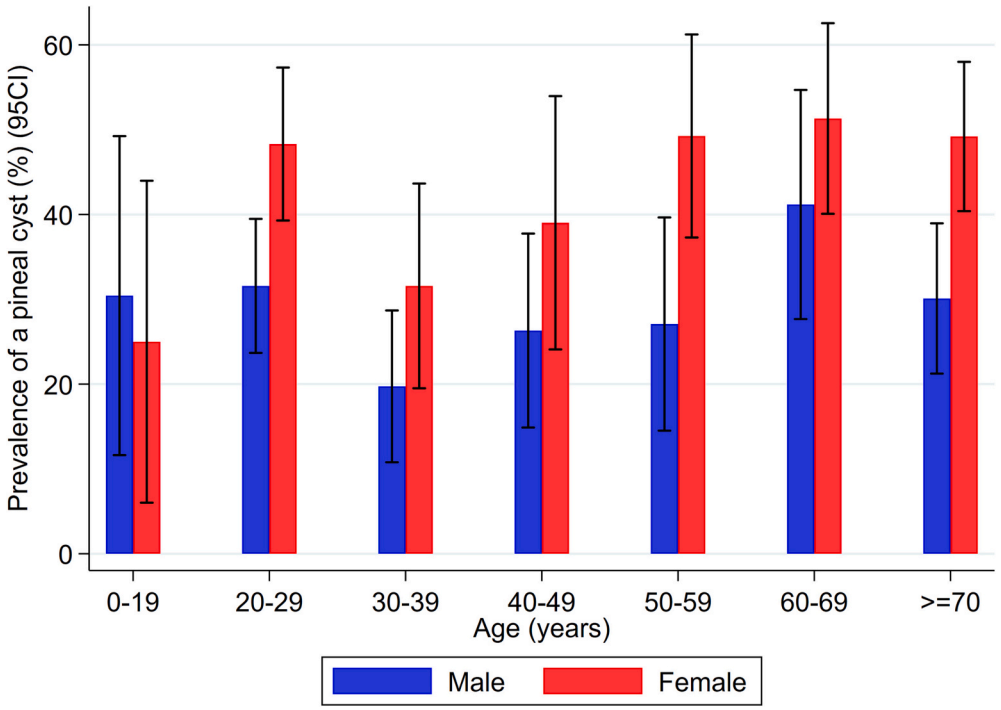


Fig. 5. A: The prevalence of pineal cysts in male and women depending on age in the entire cohort. Results shown as prevalence in percentage with 95% confidence interval (CI).

Table 2
Variables for different categories of Cyst- Tectum-Splenium (CTS) ratio in patients with a pineal cyst ($n = 373$).

	Cyst-Tectum-Splenium (CTS) ratio				
	< 0.6 (N; %)	≥ 0.6 / <0.8 (N; %)	≥ 0.8 / < 0.9 (N; %)	≥ 0.9 (N; %)	Significance
N	322	16	19	16	
Sex (F/M)	200/122	9/7	11/8	9/7	ns
Age (years)	49.8 ± 21.0	46.9 ± 23.9	42.5 ± 18.3	41.8 ± 18.8	ns
Morphology of cyst pineal gland					
Mainly solid (N; %)	250 (78%)	0	1 (5%)	1 (6%)	$P < 0.001$
Mainly cystic (N; %)	72 (22%)	16 (100%)	18 (95%)	15 (94%)	
Anterior-posterior diameter of cyst (mm)					
< 5.0 mm (N; %)	195 (61%)	0	0	0	
≥ 5.0 / < 10.0 mm (N; %)	127 (39%)	0	0	0	$P < 0.001$
≥ 10.0 / < 15.0 mm (N; %)	0	16 (100%)	19 (100%)	12 (75%)	
≥ 15.0 mm (N; %)	0	0	0	4 (25%)	
Tectal compression					
No (N; %)	322 (100%)	15 (94%)	15 (79%)	7 (44%)	
Moderate (N; %)	0	1 (6%)	4 (21%)	9 (56%)	$P < 0.001$
Severe (N; %)	0	0	0	0	
Hydrocephalus					
Present (N; %)	1 (0.3%)	0	0	0	

Values are presented as numbers with percentages of total cohort in parenthesis or mean ± SD, unless otherwise indicated. Statistical testing: Analysis of variance (ANOVA) for age differences; Pearson Chi square test for categorical data. Ns = Non-significant.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions

Conception and design: Ringstad, Eide. Acquisition of data: Warsza, Pernille Due-Tønnessen, Paulina Due-Tønnessen. Analysis and interpretation of data: Warsza, Pripp, Eide. Statistical analysis: Pripp, Eide. Drafting the article: Eide. Critically revising the article: all authors. Approved the final version of the manuscript on behalf of all authors: Eide. Administrative/technical/material support: Ringstad, Eide.

Funding

GR received support from the Clinic for Radiology and Nuclear Medicine Research Fund.

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