Juvenile nasopharyngeal angiofibroma: nationwide study on incidence, diagnosis, treatment, and recurrence

Mohamed El Haddouchi[1], Patrick R.G. Eriksen[1], Rasmus H. Dahl[2], Maria Kongsvad[3], Willy Krone[4], Gyula Gal[4], Markus Holtmannspoetter[5], Goetz Benndorf[6], Giedrius Lelkaitis[7], Christian von Buchwald[1]

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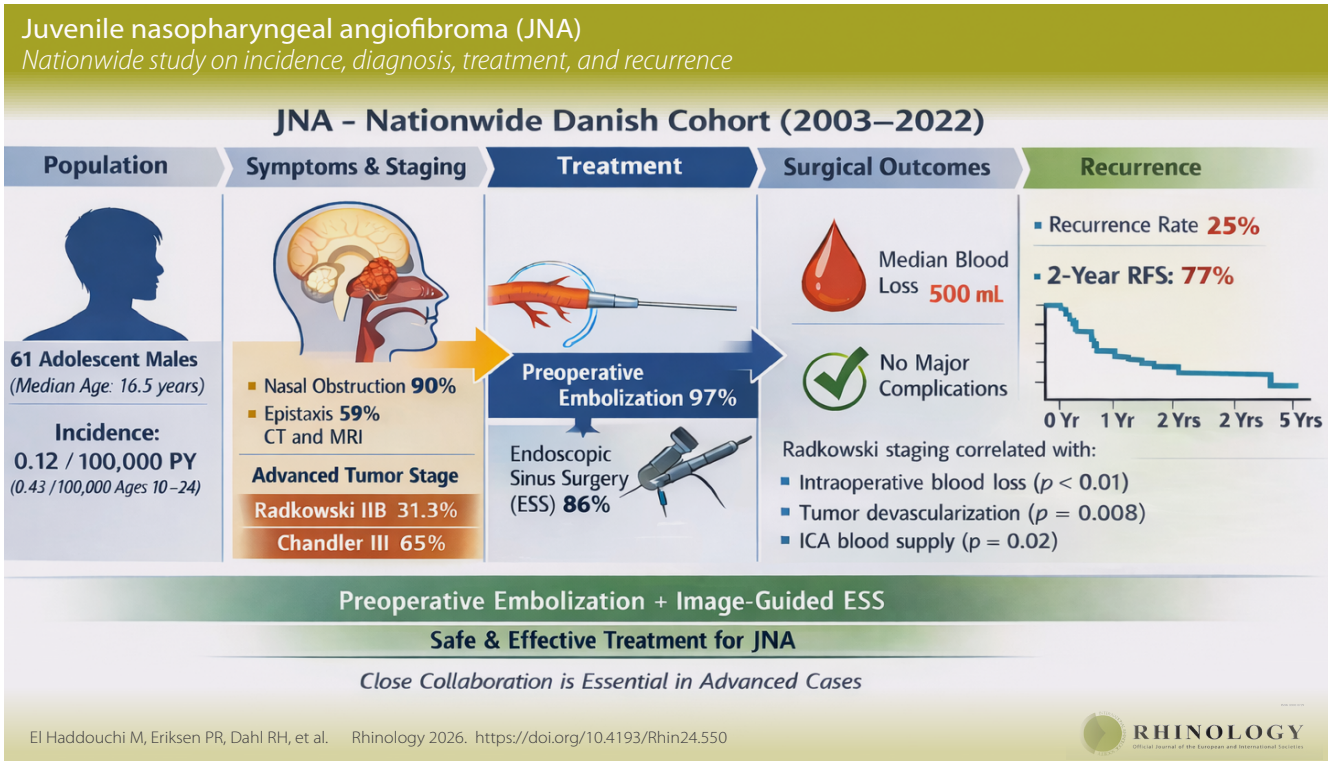

Abstract

Background: Juvenile nasopharyngeal angiofibroma (JNA) is a rare benign tumour affecting adolescent males, originating near the sphenopalatine foramen and often expanding aggressively. This nationwide study examines the clinical presentation, treatment, and prognosis of patients diagnosed from 2003 until mid-2022. **Methods**: Patients were identified in the national pathology database. The Kaplan-Meier estimator calculated event-free survival, and t-test and Fisher's exact test compared variables. The incidence rates were determined using the 2000 World Health Organization World Standard Population. **Results**: Sixty-one male patients were included (median age: 16.5 years). The national incidence was 0.12 per 100,000 male person-years (0.43 per 100,000 men at risk (10-24 years)). Common symptoms included nasal obstruction (90%) and epistaxis (59%). Predominant tumour stages were Radkowski IIB (31.3%) and Chandler III (65%). Most patients (97%) underwent preoperative embolization, with image-guided endoscopic sinus surgery (ESS) as the primary treatment (86%). Median intraoperative blood loss (IBL) was 500 mL. Radkowski staging correlated with IBL, tumour devascularization, and internal carotid artery (ICA) blood supply. No major complications occurred. Recurrence (25%) was associated with Chandler stage III-IV, with a two-year recurrence-free survival rate of 77%. **Conclusions**: Tumour stage correlated with IBL, tumour devascularization, and ICA supply. Recurrence mainly occurred within two years post-surgery, exclusively in advanced-stage cases. With close collaboration between interventionists and rhinologists, preoperative embolization followed by image-guided ESS is recommended as a safe approach with minimal risks.

Key words: angiofibroma, endoscopy, incidence, nasopharyngeal neoplasms, therapeutic embolization

Introduction

Juvenile nasopharyngeal angiofibroma (JNA) is a rare, benign mesenchymal vascular tumour exclusively affecting male adolescents [1–4]. The aetiology is unknown, and reported prevalence ranges from 0.05–0.5% of all head and neck tumours [5,6]. Through immunohistochemical analysis, RNA-sequencing, and gene expression profiling, studies have shown that JNAs express oestrogen- and androgen receptors and elevated vascular endothelial growth factor (VEGF), though no clear association with serum hormone levels has been established [7–10]. Histologically, the tumour is pseudo-encapsulated and consists of thin-walled, branched vessels lacking an intact tunica media [1].
JNAs usually emerge in the sphenopalatine foramen and extend into the nasopharynx, with lateral extension to the pterygopalatine and infratemporal fossae. Despite the benign histology, JNAs can grow aggressively, causing bone-remodelling, and extend into the orbit and intracranial space [1,6,7].

Common presenting symptoms are recurrent epistaxis and nasal obstruction. In patients of appropriate age and clinical findings, magnetic resonance imaging (MRI) and computed tomography (CT) are employed. Subsequently, catheter angiography and histology confirm the diagnosis (Figure 1). Biopsies are relatively contraindicated due to the significant risk of haemorrhage attributed to the thin-walled, non-contractile vessels [5,11]. Various classification systems for JNAs exist; Chandler's and Radkowski's are widely used, with the latter offering a detailed assessment of intracranial extension, which is crucial for surgical planning [5,12,13].

Endovascular tumour devascularization before image-guided endoscopic sinus surgery (ESS) can be a beneficial option for patients with JNA. The management is challenging due to high tumour vascularity, complex skull base anatomy, and proximity to the orbit. Early-stage tumours are primarily supplied by the sphenopalatine artery and other distal branches of the internal maxillary artery. As the tumour progresses, it recruits branches from adjacent territories including the internal carotid artery (ICA), such as ethmoidal branches of the ophthalmic artery and dural branches of the cavernous ICA. Consequently, embolization and surgical resection become increasingly complex, posing significant risks of haemorrhage, stroke, and facial growth disturbances [6,11].

Due to heterogeneity in sample size and treatment strategies (e.g., embolization, endoscopic surgery, follow-up), reported recurrence rates vary from 0% to 57% [6,11,14,15]. The risk increases with higher tumour stage and involvement of critical structures such as the optic nerve or cavernous sinus [7,16–18]. As recurrences typically occur within a few years post-surgery, they likely reflect incomplete resection rather than new tumour growth and should be considered residual tumours [19,20].

Preoperative embolization is predominantly performed using a transarterial approach, though some patients undergo additional or stand-alone direct tumour puncture. Given the rarity of JNA and variability in approaches among radiologists, definitive embolization guidelines are lacking, and outcomes such as recurrence, intraoperative blood loss (IBL), and complications remain difficult to stratify by intervention [18,21].

Nationwide data on JNA within a socialized healthcare system remain limited, as most studies report single-center experiences or small cohorts. This study aims to address this gap by presenting demographics, incidence, clinical presentation, diagnosis, staging, treatment strategies, complications, and recurrence rates in a retrospective nationwide cohort of patients diagnosed with JNA from 2003 until mid-2022.

Materials and methods

We identified the patients by searching the The Danish National Pathology Registry from January 1, 2003, until June 30, 2022, employing SNOMED-codes for angiofibroma (M91600) and the following location-specific codes: TY0203 and T21* (the nose region, the external nose, the nasal vestibule, and the nasal cavity), T22* (paranasal sinuses), and T23* (nasopharynx). Since no specific SNOMED-code exists for JNA in the Danish National Pathology Registry, we included the code for angiofibroma, which inevitably yielded cases of cutaneous angiofibroma from the external nose, including the nasal vestibule.

Medical records were collected nationwide, and the following data items were extracted: demographics, clinical presentation, surgical and embolization procedures and corresponding complications, and time to recurrence. Diagnostic imaging (CT, MRI, and catheter angiography) was reviewed to extract tumour stage, specific radiological findings, embolization technique, and tumour blood supply, and an experienced interventional neuroradiologist (GB) assessed the degree of tumour devascularization.
Blood loss was categorized using the American College of Surgeons Advanced Trauma Life Support (ATLS) classification for a healthy 60 kg patient [22]. Class I represents blood loss of up to 15% of total blood volume, class II represents 15–30%, class III represents 30–40%, and class IV represents blood loss exceeding 40%.

Ethical approval

This retrospective nationwide study was approved and registered by the Regional Council of the Capital Region of Denmark (Region Hovedstadens Regionsråd, Center for Regional Udvikling; Journal no.: R-22024842) and by the Danish Data Protec-

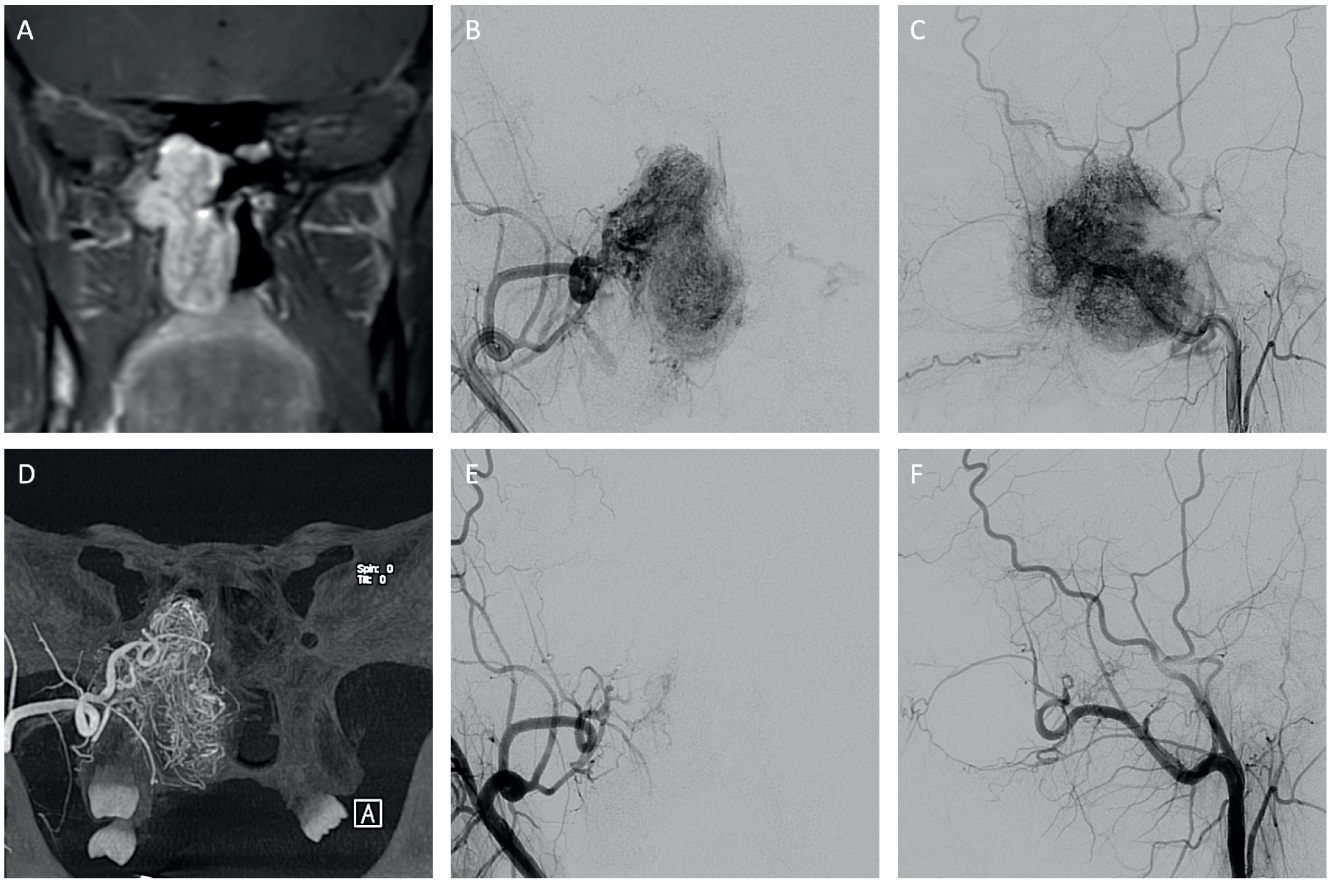

Figure 1. A) Coronal contrast-enhanced T1-weighted image of a JNA* in the right nasal cavity (Radkowski IIB, Chandler III) showing intense contrast enhancement, sphenopalatine foramen enlargement, and extension into the nasopharynx and sphenoid sinus. B-C) Catheter angiography with a left ECA** injection in frontal (B) and lateral (C) views reveals an intense tumour blush, supplied by both ECAs, but not the ICA***. D) Cone-beam CT (right ECA injection, coronal view) shows the tumour blush; transarterial embolization (both ECAs) with particles and deployment of a single coil in the right sphenopalatine artery were performed. E-F) Right ECA control runs (frontal (E) and lateral (F) views) show near-complete devascularization. *Juvenile nasopharyngeal angiofibroma, **External carotid artery, ***Internal carotid artery.

tion Agency (Datatilsynet, Videnscenter for Dataanmeldelser, Pactius; Journal no.: P-2022-121). The study was conducted in accordance with national regulations and the Declaration of Helsinki.

Statistical analyses

The date of diagnosis was defined as the date of tissue extraction for histological verification. Recurrence-free survival was defined as the period from diagnosis until recurrence. The recurrence-free survival was calculated using the Kaplan-Meier estimator. Competing risks were not taken into account, as no patients died during the follow-up period, and no censored observations were noted. The log-rank test was employed to compare curves. The t-test and Fisher's exact test were employed to compare continuous and categorical variables, respectively. The age-adjusted incidence rate was calculated using the World Health Organization (WHO) new World Standard Population from 2000 [23].

Results

The initial search identified 150 patients. After excluding duplicates and cases of cutaneous angiofibroma, 61 cases of JNA were histologically confirmed by our pathologist (GL). The majority of patients were Caucasian, reflecting the predominantly homogeneous Danish population [24]. Four patients were of non-Caucasian origin; Afghanistan (2), Pakistan (1), and Somalia (1). In Denmark, all suspected JNA cases are referred to Copenhagen University Hospital, Rigshospitalet, or Odense University Hospital. CT and/or MRI scans were unavailable for ten patients, and medical records were inaccessible for three, leaving 48 cases with complete data. The 13 patients with incomplete data were excluded from tumour staging and subsequent data analyses.

Patient characteristics

The mean age at diagnosis was 16.9 years (SD: 4.01), and the median age was 16.5 years (range: 9.35 to 29.4; interquartile range: 14.3 to 18.7; Table 1, Figure S1). The JNA cases corres-

Table 1. Characteristics (age for all patients [n = 61] and distribution of tumour stages for patients with accessible imaging [n = 48]) of patients with juvenile nasopharyngeal angiofibroma diagnosed in Denmark from 2003 to 2022.

Characterisitc	Value
Age (N=61)	
Mean (SD)	16.9 (4.01)
Median [IQR]	16.5 [14.3, 18.7]
Min	9.35
Max	29.4
Chandler Classification (N=48)	
IV	7 (14.6%)
III	31 (64.6%)
II	9 (18.8%)
I	1 (2.1%)
Radkowski Staging (N=48)	
IIIB	0 (0%)
IIIA	7 (14.6%)
IIC	9 (18.8%)
IIB	15 (31.3%)
IIA	10 (20.8%)
IB	2 (4.2%)
IA	5 (10.4%)

pond to a crude and age-adjusted incidence rate for the entire population of 0.06 and 0.08 per 100,000 person-years. In the male population, this computes to a crude and age-adjusted incidence of 0.12 and 0.16 per 100,000 person-years, respectively. Specifically for the risk population, men aged 10 to 24 years, the age-adjusted incidence was 0.43 per 100,000 person-years. The predominant tumour stages according to Radkowski's classification were IIA (20.8%) and IIB (31.3%), indicating extension into the pterygopalatine fossa alongside involvement of the paranasal sinuses, nasal cavity, and nasopharynx. In relation to Chandler's classification, the majority of patients were categorized as stage III (65%), denoting tumour extension beyond the nasal cavity, sphenoid sinus, and nasopharynx without intracranial involvement (Table 1).

Symptomatology

Nasal obstruction was the most prevalent symptom (90%), followed by epistaxis (59%). Nasal secretion occurred in 20% of the patients, always in conjunction with nasal obstruction, epistaxis, or both. The mean duration of symptoms until diagnosis was 10.3 months (range: 2.5 to 48). A smaller percentage of patients experienced headache (12%), snoring (7%), anosmia (5%), and recurrent acute or secretory otitis media (5%). Additionally, some patients presented with weight loss (6.6%), fatigue (4.9%), reduced appetite (3.3%), and night sweats (1.6%), raising suspicion of sinonasal malignancy.

Tumour characteristics and diagnostics

Of the 48 patients with available imaging, 37 (77%) showed enlargement of the sphenopalatine foramen. Bone-thinning adjacent to the tumour (excluding bone-thinning of the enlarged sphenopalatine foramen) was present in 30 (63%), and bone destruction in 25 (52%). Tumour extension into the paranasal sinuses was observed in 36 patients (75%). Orbital and intracranial extension were each identified in seven patients (15%).

Information on embolization technique was obtainable in 55 cases; nearly all patients were treated with a transarterial approach (n=52, 95%), while 6% (n=3) underwent a combination of transarterial and direct transnasal embolization. All tumours were supplied from branches of the external carotid artery (ECA) with bilateral supply in 46% (n=25) of cases. Supply from ICA branches was unilateral in 53% (n=29) and bilateral in 9% (n=5) of patients.

Adverse events of endovascular treatment

The majority of patients (83%) experienced no complications following embolization. Facial pain was the most common complication (n=3, 5%). Noteworthy were four cases of cranial nerve (CN) involvement; one patient exhibited a temporary left-sided oculomotor nerve palsy, while another had transient sensory and motor function impairment on the left side of the face (CN V and VII) after transarterial embolization (TAE). Additionally, two patients experienced transient paresthesia of the tongue (CN V3) and of the ala nasi and upper palate (CN V2), respectively, after combined TAE and direct puncture. The oculomotor nerve palsy had nearly resolved after three months, leaving a mildly dilated pupil, which was still present at the five-year follow-up. The other CN affections resolved within 1-2 days.

Surgical treatment, complications, recurrence, and IBL

In three cases, data on treatment were unavailable. The majority of patients (50/58, 86%) underwent image-guided ESS, which became the primary surgical approach in Denmark from 2000. However, seven high-stage tumours (four Radkowski IIIA, three Radkowski IIC) were treated with open approaches in the early study period. These approaches included midfacial degloving (n=4 ,7%), frontal craniotomy (n=2, 3%), and transpalatal surgery (n=1, 2%). Tumours confined to the nasal cavity were resected en bloc. For those extending into adjacent structures such as the paranasal sinuses or orbit, piecemeal resection in two to three segments was performed based on size and location. Dissection followed the pseudo-capsular plane, with bipolar electrocautery used to coagulate visible vessels. Partial resection of the inferior and/or middle turbinate was often required to improve access

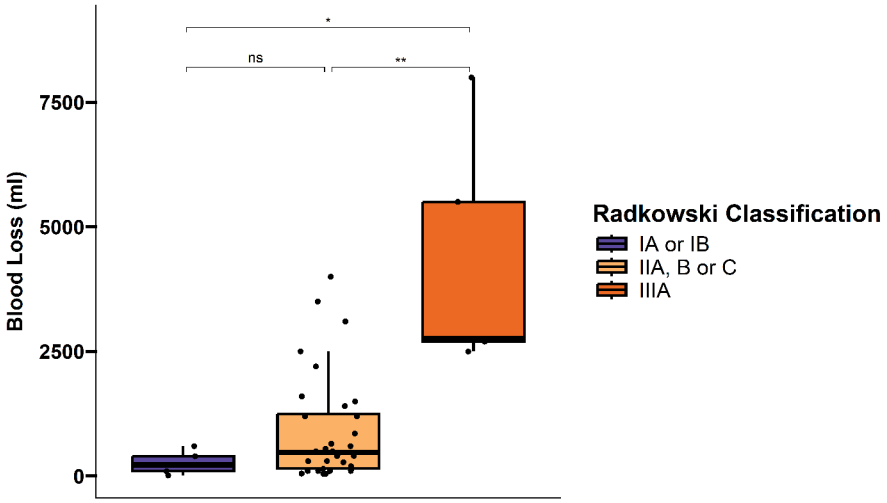

Figure 2. Box plots depicting intraoperative blood loss correlated with Radkowski staging. The plots reveal blood loss amounts for combined stages 1A and 1B (blue), stages IIA, IIB, and IIC (yellow), and stage IIIA (red). Notably, no patients presented with stage IIIB. *The plots show a significant association between higher tumour stages and increased intraoperative blood loss with a p-value of 0.008. **p=0.002, ns: Non significant (p=0.168).

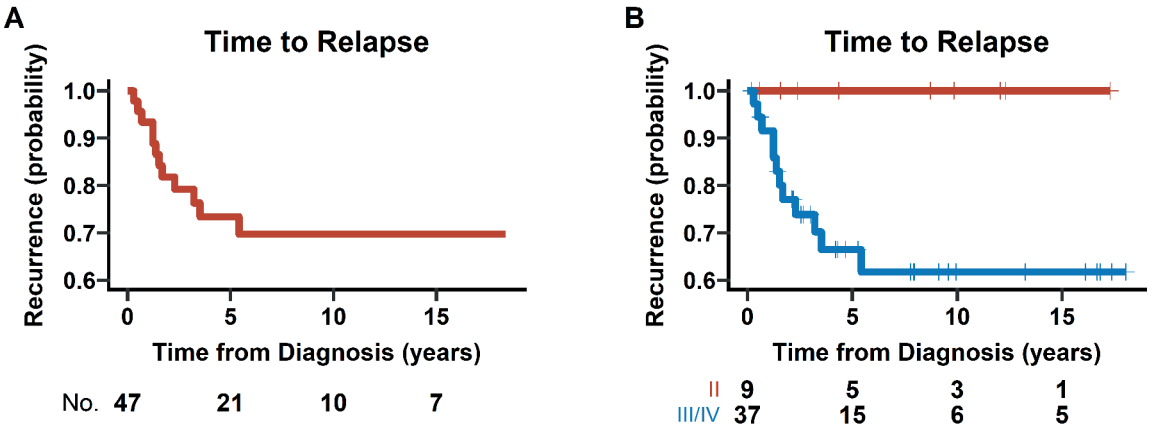

Figure 3. Kaplan-Meier Plots of Recurrence-Free Survival. (A) Encompasses all patients. (B) Contrasts patients with Chandler Stage II tumours (red curve) with those having Chandler Stage III and IV tumours (blue curve), showing a statistically significant difference (log-rank test, p=0.048).

to the tumour. Extension into the maxillary and ethmoid sinuses necessitated middle meatal antrostomy, ethmoidectomy, and widening of the maxillary ostium (1–1.5 cm). Sphenoidotomy was performed when the sphenoid sinus was involved. For tumours extending into the infratemporal or pterygopalatine fossa, part of the posterior maxillary wall was resected. In large tumours with both ECA and ICA supply, ECA-fed segments were removed first to minimize bleeding risk. Within each anatomical region, en bloc resection was preferred; debulking with cutting forceps was used only when necessary. Microdebriders were rarely employed due to the generally high tumour viscosity. In cases with intracranial extension, relevant skull base areas were drilled—typically the vidian canal or adjacent sphenoid bone—to allow safe dissection. One patient received adjuvant chemotherapy, pazopanib, due to a large intracranial residual tumour component in proximity to the cavernous sinus, resulting in a partial response after two years of treatment and subsequent progression after discontinuation. The patient was additionally treated with stereotactic radiotherapy with 36 Gy in 20 fractions resulting in a complete response. Another patient with a large tumour with blood supply from the ophthalmic artery received neo-adjuvant chemotherapy due to the tumour's proximity to the optic canal. The treatment protocol involved two courses of ifosfamide and weekly vincristine over six weeks, proving non-efficacious. The tumour was successfully removed by midfacial degloving, followed eight months later by a zygomaticotemporal approach.

No postoperative complications were experienced in 63% (n=36) of patients. The most common postoperative complica-

Table 2. Relevant variables correlated with Radkowski tumour stage (along with corresponding p-values) among patients treated for juvenile nasopharyngeal angiofibroma in Denmark from 2003 to 2022.

	IA or IB (N=7)	IIA, B or C (N=34)	IIIA (N=7)	Total (N=48)	p-value
Age					0.340
Mean (SD)	19.5 (6.79)	16.9 (3.14)	15.8 (3.85)	17.1 (3.98)	
Median [Min, Max]	17.0 [13.5, 29.4]	16.7 [10.9, 28.4]	16.5 [9.35, 20.5]	16.7 [9.35, 29.4]	
Days from Embolization to Operation					0.786
Mean (SD)	3.00 (1.67)	3.55 (1.73)	4.00 (1.91)	3.54 (1.73)	
Median [Min, Max]	3.50 [1.00, 5.00]	3.00 [1.00, 7.00]	5.00 [2.00, 6.00]	3.50 [1.00, 7.00]	
Missing	1 (14.3%)	1 (2.9%)	0 (0%)	2 (4.2%)	
Precentage of Tumor Devascularized					0.008
Mean (SD)	95.0 (4.08)	85.9 (12.9)	59.0 (29.2)	83.1 (18.1)	
Median [Min, Max]	95.0 [90.0, 100]	90.0 [40.0, 100]	60.0 [30.0, 95.0]	90.0 [30.0, 100]	
Missing	3 (42.9%)	7 (20.6%)	2 (28.6%)	12 (25.0%)	
Internal Carotid Artery Supply					0.020
Uni- or bilateral supply	1 (14.3%)	21 (61.8%)	7 (100%)	29 (60.4%)	
No supply	5 (71.4%)	13 (38.2%)	0 (0%)	18 (37.5%)	
Missing	1 (14.3%)	0 (0%)	0 (0%)	1 (2.1%)	
External Carotid Artery Supply					0.558
Bilateral supply	2 (28.6%)	15 (44.1%)	5 (71.4%)	22 (45.8%)	
Unilateral supply	4 (57.1%)	19 (55.9%)	2 (28.6%)	25 (52.1%)	
Missing	1 (14.3%)	0 (0%)	0 (0%)	1 (2.1%)	

Variables include mean and median values of age at diagnosis, number of days from preoperative embolization to surgery, percentage of tumour devascularization after embolization, presence of tumour blood supply from the external carotid artery, and presence of blood supply from the internal carotid arteries.

tion was infection (n=9, 16%), followed by intranasal synechiae (n=8, 14%), and epistaxis (n=4, 7%).

IBL ranged from 10 mL to 8000 mL (median: 500 mL; mean: 1117 mL). According to the ATLS classification, most of the 52 patients with available blood loss data had class 1 blood loss (62%), while 21% had class 4, and the rest were in the intermediate classes.

Our data revealed a significant association between IBL and Radkowski tumour staging ($p<0.01$; Figure 2).

Patients were followed with annual MRI scans for five years. Endoscopy was performed every three to four months during the first postoperative year and annually thereafter if no recurrence was detected. Among 58 patients with follow-up data, 14 (25%) experienced recurrence; six were symptomatic, while four were detected via endoscopy and four via MRI. The overall 2-year event-free survival was 82%. All recurrences occurred in patients with Chandler Stage III-IV (log-rank test $p = 0.048$; Figure 3), with a 2- and 5-year event-free survival of 77% and 66%, respectively.

Table 2 presents mean and median values of relevant variables correlated with Radkowski tumour stage. The analysis revealed significant associations between tumour stage and the degree of tumour devascularization, as well as blood supply from the ICA. Notably, no significant correlations were found between tumour stage, age, the number of days from embolization to surgery, or the degree of ECA supply.

Discussion

This nationwide retrospective cohort study, covering a period of 19.5 years, stands out as one of the most comprehensive investigations of JNA thus far. It reports on the clinical characteristics, treatment, adverse events, and prognosis and provides a sound estimate of the incidence and patient demographics, offering insights into the disease course.

Our study revealed crude and age-adjusted incidence rates of 0.06 and 0.08 per 100,000 person-years for the Danish population, and 0.12 and 0.16 per 100,000 person-years for men. The age-adjusted incidence among men aged 10–24 years was 0.43 per 100,000 person-years, underscoring the rarity of JNA. These

rates slightly exceed previously reported Danish incidence rates (0.04 [crude] and 0.37 [age- and gender-adjusted] per 100,000 person-years) by Glad et al. in 2007 [6], likely due to incomplete case registrations before the nationwide implementation of electronic health and pathology records in the late 1990s [25,26]. No population-based incidence data exist for other countries, limiting direct comparisons. However, studies suggest lower incidence in Europe and the United States and higher incidence in parts of Asia, possibly reflecting genetic, environmental, or diagnostic differences [17]. Mishra et al. [27] reported 701 cases over 55 years at a single Indian center, with a fourfold increase in recent decades, likely due to improved diagnostics. Similarly, a Chinese study documented 131 cases over 10 years at a Shanghai hospital [28].

The mean age at diagnosis was 16.9 years (range: 9.35–29.4), consistent with literature reporting mean ages ranging from 15 to 17 years [3,20,29,30].
Notably, three patients aged 28 to 29 years suggest that JNAs may occasionally be diagnosed late or develop in early adulthood. These patients reported symptom durations of 6, 7, and 18 months, consistent with the cohort's mean of 10.3 months. Additionally, several studies report patients up to 30 years of age [20,30–32]. Such cases challenge hormonal etiopathogenesis theories linked to adolescence [9]. As residual tumours in critical areas, like the cavernous sinus, tend to regress spontaneously [11], examining recurrence rates relative to age at diagnosis becomes pertinent. Significantly higher recurrence rates have been observed in younger patients [20,29,33], though one study found no correlation [31]. These significant correlations were observed by arbitrarily stratifying patients with cutoffs at 14, 15, and 18 years.

The clinical presentation aligns with previous studies [1,3,20,29], with nasal obstruction and epistaxis as predominant symptoms, though some studies report epistaxis as more prevalent than nasal obstruction [30,35]. These non-specific symptoms, coupled with the contraindication of biopsy, make clinical presentation and imaging crucial for diagnosis. We noted an 77% occurrence of enlarged sphenopalatine foramen, consistent with its identification as an early, pathognomonic CT finding [36–38]. MRI typically reveals internal flow voids and intense contrast enhancement [4,37]. Most patients presented with tumour extension beyond the nasal cavity, nasopharynx, and paranasal sinuses; Radkowski stage IIB (31.3%) and Chandler stage III (65%) were most frequent, indicating aggressive growth. Unlike the earlier Danish study by Glad et al., which found Chandler stage II predominant, our data align with other studies reporting pterygopalatine fossa involvement as common [4,6,30,35].

Preoperative embolization with subsequent ESS is considered a beneficial treatment option for patients with JNA, significantly reducing IBL, recurrence, and complications [2,6,18,39,40]. In our study, 62% of tumours had ICA supply (9% bilateral, 53% unilateral), which was associated with higher IBL compared to ECA-only supply [32]. Embolization of ICA branches has not shown reductions in IBL or recurrence rates in recent studies [32,41,42], likely due to technical challenges and incomplete devascularization, particularly in bilaterally supplied tumours [32]. Most of our patients (95%) underwent TAE, predominantly with particles. While Diaz et al. [18] reported higher complication and recurrence rates with particle embolization, our data showed complications only with liquid emboli material (Onyx), either during TAE alone (n=2) or combined with direct puncture (n=2) in high-stage tumours. CN complications were the most frequent (n=4, 6.8%); three (5%) were transient, and one patient (1.7%) showed a residual deficit at 5-year follow-up (all embolized with Onyx). Transient facial pain occurred in three patients (5%). No CN deficits were observed in patients embolized with PVA particles or embospheres. Although rare, CN palsy has been linked to embolization of cavernous ICA branches supplying CNs, particularly in high-stage tumours [18,43,44]. No minor or major strokes occurred in our series. The largest published JNA series to date included 170 patients undergoing TAE and reported major complications in 2.4% of cases: iliac artery thrombosis (1), pulmonary oedema (1), and necrosis of the tonsil (1) and nasal wing (1), all without functional or aesthetic sequelae. No strokes were reported, and all minor complications (59%) were transient [44].
Particle embolization is a widely used method that results in the temporary occlusion of JNA-feeding arteries. It is generally accepted that surgery should preferably be performed within 24–72 hours, and no more than seven days after the embolization procedure, to ensure sufficient tumour devascularization [40]. However, to our knowledge, an optimal interval based on the timely development of tumour occlusion and revascularization has not been established. The current practice at both institutions aligns with the 24–72-hour time interval, whereas a longer interval was observed in this study, spanning 20 years (median interval of 3–4 days regardless of tumour stage). Several of our patients underwent surgery 6-7 days post-embolization, mainly for logistical and scheduling reasons. While this may be considered a delay by some operators, we did not observe any untoward effects. We strongly believe that close collaboration between neurointerventionalists and surgeons is essential for optimal planning of both the preoperative devascularization and surgical treatment, and that each center should maintain experienced multidisciplinary teams with sufficient JNA case volumes to preserve procedural expertise and optimize patient outcomes.

The majority of our patients (86%) underwent image-guided ESS, with a few early cases treated via open approaches. Most patients (62%) experienced IBL below 600 mL; however, 11

patients had ATLS class IV IBL, all with high Radkowski stage and ICA tumour supply, complicating both embolization and surgery. This supports our finding of a significant association between higher tumour stage, ICA supply, and increased IBL, as reported in multiple studies [6,32,45–47]. As JNAs grow, they appear to gradually recruit branches of the contralateral sphenopalatine artery and branches of the ipsilateral and contralateral ICA [32,46,48].

Glad et al. reported a median IBL of 1200 mL in non-embolized versus 650 mL in embolized patients, demonstrating that embolization significantly reduces IBL [6]. Our median IBL of 500 mL further confirms the importance of preoperative embolization in JNA treatment.

Our recurrence rate of 25% aligns with the literature (20–40%), with most recurrences occurring within two years post-surgery and in advanced-stage tumours [18,20,29,34,49,50]. In Denmark, patients with JNA undergo five-year surveillance with annual MRI scans. Our observations suggest that follow-up could potentially conclude after two years, particularly for patients with low-stage tumours (Chandler I–II, Radkowski IA–IIB), with further follow-up based on the presence of clinical symptoms [49].

Distinguishing new tumour growth from residual tumour is crucial. Seven of our patients (12%) underwent incomplete tumour excision, primarily due to proximity to critical structures such as the ICA, cavernous sinus, or optic nerve. These cases were managed with surveillance, reoperation, or radio- or chemotherapy (n=3). While most incomplete resections were recognized intraoperatively, some were only detected during early postoperative follow-up, complicating recurrence assessment. As noted by others, it is plausible to regard all recurrences as residual tumours, given their frequent occurrence within the first few years post-surgery, particularly in advanced-stage cases where complete excision is challenging [19]. Radiotherapy was effective in one case (a ten-year-old patient), but two patients treated with chemotherapy showed no sustained response. Given the risk of radiation-induced malignancy and malignant transformation of JNA, radiotherapy is preferably avoided [11,19].

A key limitation of this study is its retrospective design, leading to inconsistencies in data reporting and missing specific outcome measures. Additionally, the study spans two centers over a 20-year period, inevitably resulting in some missing data. However, careful data collation from both institutions helped mitigate this issue. For instance, CT and MRI scans were unavailable for 13 patients, limiting information on tumour extension and involvement of surrounding structures. These cases were therefore excluded from tumour staging and subsequent data analyses. Future multicenter studies are needed to validate our findings and enhance our understanding of this rare disease.

Conclusion

This study revealed an insignificant increase in the Danish JNA incidence rate from 0.04 to 0.06 cases per 100,000 person-years. Tumour stage correlated significantly with the degree of tumour devascularization after embolization, increased IBL, and tumour blood supply from the ICA. Preoperative TAE remains a safe and effective procedure for JNA, significantly reducing IBL with minimal complications. Recurrences occurred within the first two years post-surgery, exclusively among patients with advanced-stage tumours, highlighting the need for initial close clinical and imaging follow-ups in these patients. Successful JNA management relies on close collaboration between interventional radiologists and rhinologists while maintaining sufficient case volumes to ensure expertise.

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None.

Author contributions

ME assembled the cohort, extracted data, created figures, analysed data, and wrote the manuscript. PRGE conducted data analysis, performed statistical calculations, created tables and figures, and provided supervision. RHD extracted and reviewed radiological and embolization-related data and contributed to figure creation. MK extracted clinical data from Odense University Hospital. WK extracted radiological and embolization-related data from Odense University Hospital. GG reviewed radiological and embolization-related data from Odense University Hospital and contributed data. MH reviewed radiological and embolization-related data. GB reviewed radiological and embolization-related data, contributed data and interpretation of analyses, supervised, and assisted with study design. GL validated diagnoses and contributed to figure creation. CvB designed the study and supervised.

Conflict of interest

The authors confirm no conflicts of interest or competing financial interests.

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References

1. Sánchez-Romero C, Carlos R, Díaz Molina JP, Thompson LDR, de Almeida OP, Rumayor Piña A. Nasopharyngeal angiofibroma: a clinical, histopathological and immunohistochemical study of 42 cases with emphasis on stromal features. Head Neck Pathol. 2018;12(1):52–61.
2. Garofalo P, Pia F, Policarpo M, Tunesi S, Valletti PA. Juvenile nasopharyngeal angiofibroma: comparison between endoscopic and open operative approaches. J Craniofac

Surg. 2015;26(3):918–821.
3. Midilli R, Karci B, Akyildiz S. Juvenile nasopharyngeal angiofibroma: analysis of 42 cases and important aspects of endoscopic approach. Int J Pediatr Otorhinolaryngol. 2009;73(3):401–8.
4. Alimli AG, Ucar M, Oztunali C, Akkan K, Boyunaga O, et al. Juvenile nasopharyngeal angiofibroma: magnetic resonance imaging findings. J Belg Soc Radiol. 1. 2016;100(1):63.
5. Alshaikh NA, Eleftheriadou A. Juvenile nasopharyngeal angiofibroma staging: An overview. Ear Nose Throat J. 2015;94(6):E12-22.
6. Glad H, Vainer B, Buchwald C, et al. Juvenile nasopharyngeal angiofibromas in Denmark 1981-2003: diagnosis, incidence, and treatment. Acta Otolaryngol. 2007;127(3):292–9.
7. Szymańska A, Szymański M, Czekajska-Chehab E, Szczerbo-Trojanowska M. Two types of lateral extension in juvenile nasopharyngeal angiofibroma: diagnostic and therapeutic management. Eur Arch Otorhinolaryngol. 2015;272(1):159–66.
8. Schick B, Rippel C, Brunner C, Jung V, Plinkert PK, Urbschat S. Numerical sex chromosome aberrations in juvenile angiofibromas: genetic evidence for an androgen-dependent tumor? Oncol Rep. 2003;10(5):1251–5.
9. Doody J, Adil EA, Trenor CC, Cunningham MJ. The genetic and molecular determinants of juvenile nasopharyngeal angiofibroma: a systematic review. Ann Otol Rhinol Laryngol. 2019;128(11):1061–72.
10. Jones JW, Usman S, New J, et al. Differential gene expression and pathway analysis in juvenile nasopharyngeal angiofibroma using RNA Sequencing. Otolaryngol Head Neck Surg. 2018;159(3):572–5.
11. Safadi A, Schreiber A, Fliss DM, Nicolai P. Juvenile angiofibroma: current management strategies. J Neurol Surg B Skull Base. 2018;79(1):21–30.
12. Radkowski D, McGill T, Healy GB, Ohlms L, Jones DT. Angiofibroma: changes in staging and treatment. Arch Otolaryngol Head Neck Surg. 1996;122(2):122–9.
13. Chandler JR, Goulding R, Moskowitz L, Quencer RM. Nasopharyngeal angiofibromas: staging and management. Ann Otol Rhinol Laryngol. 1984;93(4 Pt 1):322–9.
14. Makhasana JAS, Kulkarni MA, Vaze S, Shroff AS. Juvenile nasopharyngeal angiofibroma. J Oral Maxillofac Pathol. 2016;20(2):330.
15. Reyes C, Bentley H, Gelves JA, Solares CA, Byrd JK. Recurrence rate after endoscopic vs. open approaches for juvenile nasopharyngeal angiofibroma: a meta-analysis. J Neurol Surg B Skull Base. 2019;80(6):577–85.
16. Rogers DJ, Bevans SE, Harsha WJ. Endoscopic resection of juvenile nasopharyngeal angiofibroma. Adv Otorhinolaryngol. 2012;73:132–6.
17. Boghani Z, Husain Q, Kanumuri VV, et al. Juvenile nasopharyngeal angiofibroma: a systematic review and comparison of endoscopic, endoscopic-assisted, and open resection in 1047 cases. Laryngoscope. 2013;123(4):859–69.
18. Diaz A, Wang E, Bujnowski D, et al. Embolization in juvenile nasopharyngeal angiofibroma surgery: a systematic review and meta-analysis. Laryngoscope. 2023;133(7):1529–39.
19. López F, Triantafyllou A, Snyderman CH, et al. Nasal juvenile angiofibroma: current perspectives with emphasis on management. Head Neck. 2017;39(5):1033–45.
20. Fang R, Sun W, Shi J, et al. Risk factors and characteristics of the recurrence of juvenile nasopharyngeal angiofibroma: a 22-year experience with 123 cases at a tertiary center. Clin Exp Otorhinolaryngol. 2022;15(4):364–71.
21. Kothari DS, Linker LA, Tham T, et al. Preoperative embolization techniques in the treatment of juvenile nasopharyngeal angiofibroma: a systematic review. Otolaryngol Head Neck Surg. 2023;169(3):454–66.
22. Galvagno SM, Nahmias JT, Young DA. Advanced trauma life support® update 2019: management and applications for adults and special populations. Anesthesiol Clin. 2019;37(1):13–32.
23. World (WHO 2000-2025) Standard - Standard Populations - SEER Datasets [Internet]. Available from: https://seer.cancer.gov/stdpopulations/world.who.html
24. Publication: Denmark in Figures 2019 [Internet]. Available from: https://www.dst.dk/en/Statistik/nyheder-analyser-publ/Publikationer/VisPub?cid=28924
25. Vyberg M, Bjerregaard B, Bak M, Gram I, Hvolris H. [Pathology database. Danish Society of Pathologic Anatomy and Cytology]. Ugeskr Laeger. 21. 2005;167(12–13):1401.
26. Gjødsbøl IM, Høyer K, Langstrup H, Kayser L, Vrangbæk K. Digitalisering i det danske sundhedsvæsen? Samfundsoekonomen. 2021(1):26–38.
27. Pamuk AE, Özer S, Süslü AE, Akgöz A, Önerci M. Juvenile nasopharyngeal angiofibroma: a single centre's 11-year experience. J Laryngol Otol. 2018;132(11):978–83.
28. Mishra A, Mishra SC. Changing trends in the incidence of juvenile nasopharyngeal angiofibroma: seven decades of experience at King George's Medical University, Lucknow, India. J Laryngol Otol. 2016;130(4):363–8
29. Liu Z, Hua W, Zhang H, et al. The risk factors for residual juvenile nasopharyngeal angiofibroma and the usual residual sites. Am J Otolaryngol. 2019;40(3):343–6.
30. Tang IP, Shashinder S, Gopala Krishnan G, Narayanan P. Juvenile nasopharyngeal angiofibroma in a tertiary centre: ten-year experience. Singapore Med J. 2009;50(3):261–4.
31. Nicolai P, Villaret AB, Farina D, et al. Endoscopic surgery for juvenile angiofibroma: a critical review of indications after 46 cases. Am J Rhinol Allergy. 2010;24(2):e67-72.
32. Overdevest JB, Amans MR, Zaki P, Pletcher SD, El-Sayed IH. Patterns of vascularization and surgical morbidity in juvenile nasopharyngeal angiofibroma: A case series, systematic review, and meta-analysis. Head Neck. 2018;40(2):428–43.
33. Sun XC, Wang DH, Yu HP, Wang F, Wang W, Jiang JJ. Analysis of risk factors associated with recurrence of nasopharyngeal angiofibroma. J Otolaryngol Head Neck Surg. 2010;39(1):56–61.
34. Liu L, Wang R, Huang D, et al. Analysis of intra-operative bleeding and recurrence of juvenile nasopharyngeal angiofibromas. Clin Otolaryngol Allied Sci. 2002;27(6):536–40.
35. Gaillard AL, Anastácio VM, Piatto VB, Maniglia JV, Molina FD. A seven-year experience with patients with juvenile nasopharyngeal angiofibroma. Braz J Otorhinolaryngol. 2010;76(2):245–50.
36. Schick B, Kahle G. Radiological findings in angiofibroma. Acta Radiol. 2000;41(6):585–93.
37. Szymańska A, Szymański M, Czekajska-Chehab E, Szczerbo-Trojanowska M. Invasive growth patterns of juvenile nasopharyngeal angiofibroma: radiological imaging and clinical implications. Acta Radiol. 2014;55(6):725–31.
38. Lloyd G, Howard D, Phelps P, Cheesman A. Juvenile angiofibroma: the lessons of 20 years of modern imaging. J Laryngol Otol. 1999;113(2):127–34.
39. Choi JS, Yu J, Lovin BD, Chapel AC, Patel AJ, Gallagher KK. Effects of preoperative embolization on juvenile nasopharyngeal angiofibroma surgical outcomes: a study of the kids' inpatient database. J Neurol Surg B Skull Base. 2022;83(1):76–81.
40. Lutz J, Holtmannspötter M, Flatz W, et al. Preoperative embolization to improve the surgical management and outcome of juvenile nasopharyngeal angiofibroma (JNA) in a single center: 10-year experience. Clin Neuroradiol. 2016;26(4):405–13.
41. Liu Q, Xia Z, Hong R, et al. Preoperative embolization of primary juvenile nasopharyngeal angiofibroma: is embolization of internal carotid artery branches necessary? Cardiovasc Intervent Radiol. 2023;46(8):1038–45.
42. Gargula S, Saint-Maurice JP, Labeyrie MA, et al. Embolization of internal carotid artery branches in juvenile nasopharyngeal angiofibroma. Laryngoscope. 2021;131(3):E775–80.
43. Tawfik KO, Harmon JJ, Walters Z, et al. Facial palsy following embolization of a juvenile nasopharyngeal angiofibroma. Ann Otol Rhinol Laryngol. 2018;127(5):344–8.
44. Ogawa AI, Fornazieri MA, da Silva LV, et al. Juvenile angiofibroma: major and minor complications of preoperative embolization. Rhinology. 2012;50(2):199–202.
45. Bignami M, Pietrobon G, Arosio AD, et al. Juvenile angiofibroma: what is on stage? Laryngoscope. 2022;132(6):1160–5.
46. Chan KH, Gao D, Fernandez PG, Kingdom TT, Kumpe DA. Juvenile nasopharyngeal angiofibroma: vascular determinates for operative complications and tumor recurrence. Laryngoscope. 2014;124(3):672–7.

47. Mehan R, Rupa V, Lukka VK, et al. Association between vascular supply, stage and tumour size of juvenile nasopharyngeal angiofibroma. Eur Arch Otorhinolaryngol. 2016;273(12):4295–303.
48. Snyderman CH, Pant H, Carrau RL, Gardner P. A new endoscopic staging system for angiofibromas. Arch Otolaryngol Head Neck Surg. 2010;136(6):588–94.
49. Carrillo JF, Maldonado F, Albores O, Ramírez-Ortega MC, Oñate-Ocaña LF. Juvenile nasopharyngeal angiofibroma: clinical factors associated with recurrence, and proposal of a staging system. J Surg Oncol. 2008;98(2):75–80.
50. Mishra A, Mishra SC. Time trends in recurrence of juvenile nasopharyngeal angiofibroma: Experience of the past 4 decades. Am J Otolaryngol. 2016;37(3):265–71.

Mohamed El Haddouchi
Department of Otorhinolaryngology Head and Neck Surgery and Audiology
Copenhagen University Hospital Risghospitalet
2100 Copenhagen
Denmark

Tel: +45-4031 8203
E-mail:
mohamedelhaddouchi@outlook.dk

Mohamed El Haddouchi[1], Patrick R.G. Eriksen[1], Rasmus H. Dahl[2], Maria Kongsvad[3], Willy Krone[4], Gyula Gal[4], Markus Holtmannspoetter[5], Goetz Benndorf [6], Giedrius Lelkaitis[7], Christian von Buchwald[1]

[1] Department of Otorhinolaryngology, Head and Neck Surgery & Audiology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

[2] Department of Radiology, Copenhagen University Hospital, Rigshospitalet, Copengagen, Denmark

[3] Department of Otorhinolaryngology, Odense University Hospital, Odense, Denmark

[4] Department of Radiology, Odense University Hospital, Odense, Denmark

[5] Department of Neuroradiology, Nuremberg Hospital, Paracelsus Medical University, Nuremberg, Germany

[6] Department of Radiology, Baylor College of Medicine, Houston, TX, USA

[7] Department of Pathology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

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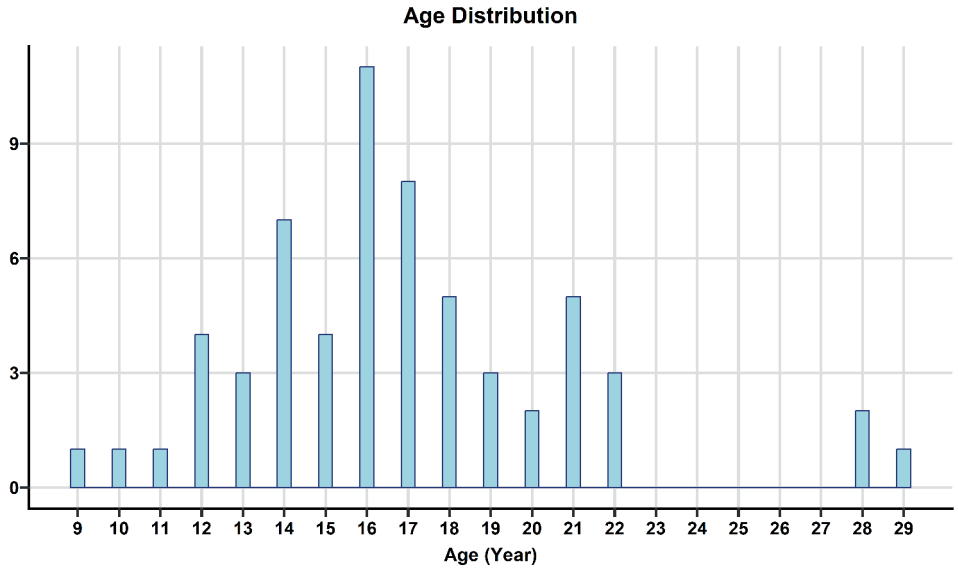

Figure S1. Histogram depicting the number of patients by age at diagnosis in Denmark from 2003-2022.