The Laryngoscope

Contemporary Review

Juvenile Nasopharyngeal Angiofibroma: A Systematic Review and Comparison of Endoscopic, Endoscopic-Assisted, and Open Resection in 1047 Cases

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Objectives/Hypothesis: This study is a review of the treatment outcomes of juvenile nasopharyngeal angiofibroma (JNA) specifically comparing endoscopic, endoscopic-assisted, and open surgical approaches.

Study Design: Systematic review of studies using the MEDLINE database.

Methods: A systematic review of studies on JNA from 1990 to 2012 was conducted. A search for articles related to JNA, along with bibliographies of those articles, was performed. Articles were examined for individual patient data (IPD) and aggregate patient data (APD). Demographics, presenting symptoms, surgical approach, follow-up, and outcome were analyzed.

Results: Eighty-five articles were included, with IPD reported in 57 articles (345 cases) and APD in 28 articles (702 cases). For the IPD cohort, average follow-up was 33.4 months (range, 0.5–264 months). Average blood loss was 544.0 mL, 490.0 mL, and 1579.5 mL for endoscopic, endoscopic-assisted, and open surgical cases, respectively ($P < .05$). Recurrence rate following endoscopic surgery and open surgery were significantly less than endoscopic-assisted surgery ($P < .05$). In the APD cohort, the recurrence rate following endoscopic surgery was 4.7% compared to 20.6% in the endoscopic-assisted group and 22.6% in the open surgery group ($P < .05$). Among studies that reported Radkowski/Sessions grading, there was no significant difference in recurrence rates for both the IPD and APD cohorts across each stage between open and endoscopic surgery ($P > .05$).

Conclusions: In this study, endoscopic resection had a significantly lower intraoperative blood loss and lower recurrence rate when compared to open resection. However, there was no difference in recurrence rate when analyzing the IPD and controlling for Radkowski/Sessions grading. Therefore, further large-scale studies may be required to fully elucidate treatment options.

Key Words: Juvenile nasopharyngeal angiofibroma, sinonasal tumors, anterior skull base tumor, endoscopic anterior skull base tumor resection, skull base, infratemporal fossa, angiofibroma, vascular sinonasal tumor, sinonasal tumor.

Level of Evidence: 3a.

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INTRODUCTION

Juvenile nasopharyngeal angiofibroma (JNA) is a rare, benign, and highly vascular tumor that accounts for 0.05% to 0.5% of all head and neck neoplasms.[1] First classified by Chauveau et al.[2] and Friedberg et al.,[3] JNAs are nonencapsulated and composed of an irregular network of blood vessels set in fibroblastic stroma (Fig. 1).[4] Typically, JNA affects adolescent males. The most common presentation of this tumor includes painless nasal obstruction, recurrent unilateral epistaxis, and a nasopharyngeal mass.[5] These tumors originate in the nasopharynx and can be locally aggressive, causing extensive tissue destruction and bone remodeling.[1,6] Expansion of these tumors can occur anteriorly into the nasal cavity, laterally into the pterygopalatine fossa, and superiorly into the intracranial cavity.[7] Due to the vascular nature of these tumors, life-threatening epistaxis and massive intraoperative hemorrhage have been reported.[8]

Currently, there is limited consensus on the ideal staging system for JNAs and there are several criteria

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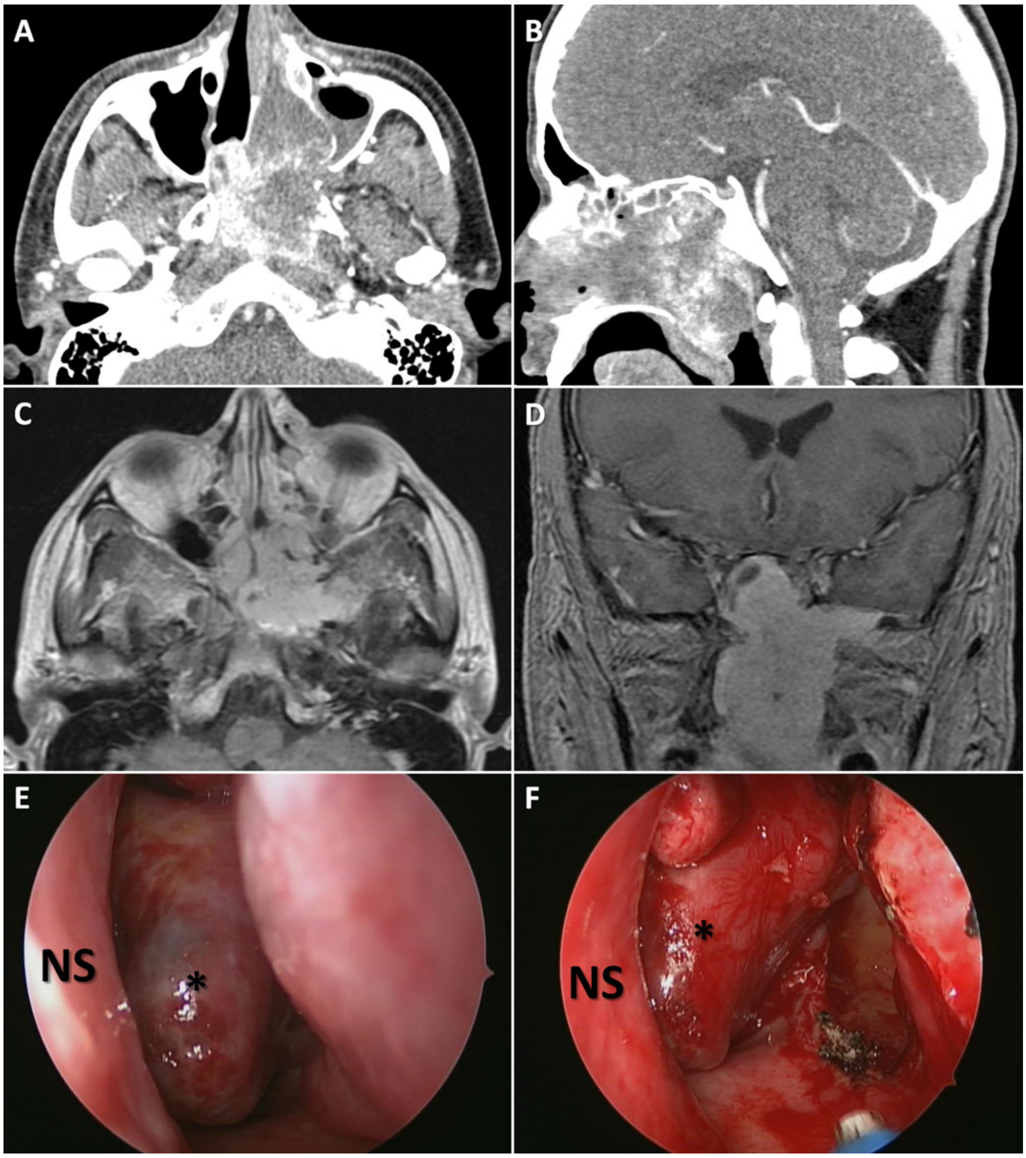

Fig. 1. Axial (A) and sagittal (B) contrast-enhanced computed tomography angiogram of a patient with a mostly left sinonasal juvenile nasopharyngeal angiofibroma. Axial (C) and coronal (D) T1-weighted gadolinium enhanced magnetic resonance imaging of the same patient demonstrating the nasopharyngeal angiofibroma. (E) Thirty-degree endoscopic view of the left sinonasal mass. (F) Endoscopic view of the lesion after endoscopic modified left medial maxillectomy. Asterisks depict lesion. NS = nasal septum.

utilized such as those established by Radkowski et al.,[9] Andrews et al.,[10] Sessions et al.,[11] Chandler et al.,[12] Fisch,[13] Onerci et al.,[14] and Snyderman et al.[15] Staging is based on tumor spread, which is frequently assessed by computed tomography (CT) and magnetic resonance imaging (MRI). CT is best utilized for determining bony changes and MRI for soft tissue destruction.[16] Due to the vascular nature of JNA, angiography is often performed to identify the primary vessels that feed the tumor and allow for embolization to reduce intraoperative blood loss.[17]

The primary treatment for JNA is surgical excision, either by endoscopic, endoscopic-assisted, or open surgical approaches.[7,18,19] Open approaches include lateral rhinotomy, transpalatal, transmaxillary, midfacial degloving, Le Fort I, Denker, infratemporal, and various combinations of approaches.[20–25] With the advent of minimally invasive endoscopic techniques, there have been several studies assessing the effectiveness of endoscopic resection of JNA.[26–28] Although prior studies have elucidated the benefits of the endoscopic approach, they have been limited by the number of patients. We present a systematic review of the literature on JNA, comparing endoscopic, endoscopic-assisted, and open surgical approaches for this rare but potentially life-threatening condition.

MATERIALS AND METHODS

Search Strategy

The MEDLINE database was searched for “nasopharyngeal angiofibroma,” “sinonasal angiofibroma,” and “nasal

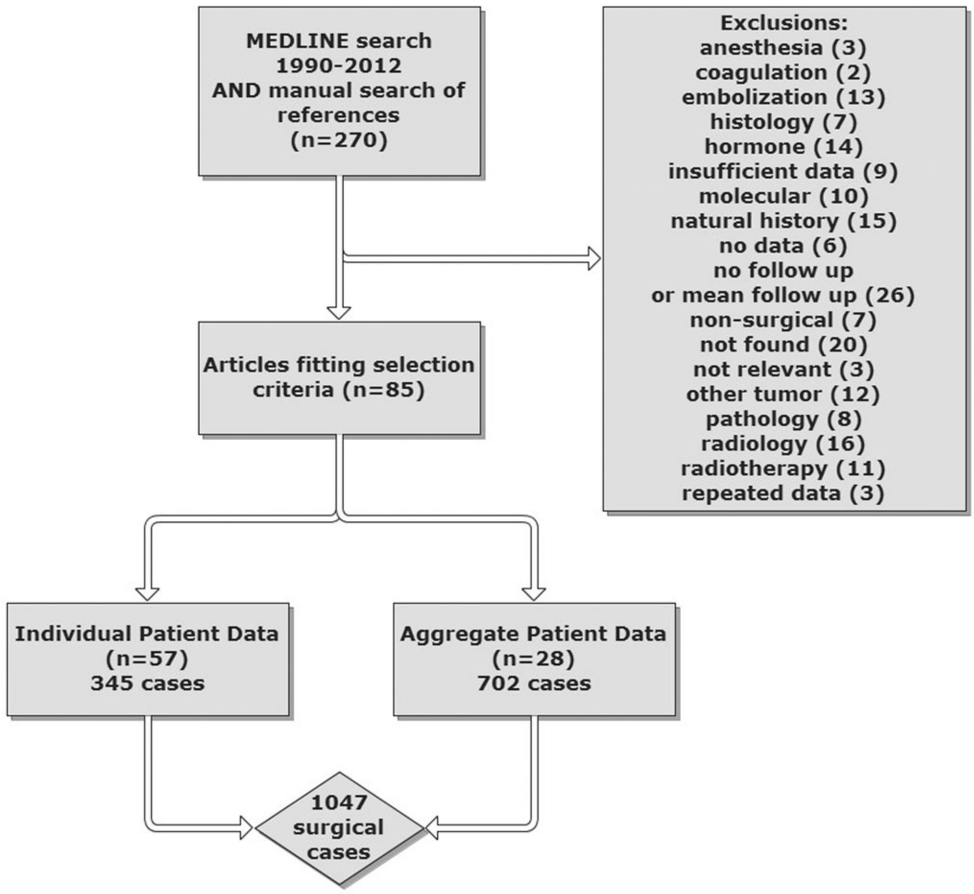

Fig. 2. Flow diagram of identified, excluded, and included studies.

angiofibroma," with a date range of January 1, 1990 to the present. Titles and abstracts were reviewed by two authors for pertinence to the topic of surgical management of JNA. Additionally, the references of included articles were searched manually to gather any studies that may not have been found through the initial search.

Inclusion Criteria

We included all English-language articles, which included case reports, case series, retrospective studies, and nonrandomized prospective studies that pertained to the surgical management of JNA. Patients of all ages and both sexes were included. Cases of recurrent JNA were also included in this review. Articles were included if they reported the diagnosis of JNA, surgical approach, outcome, and follow-up. The articles were then separated into two broad categories: aggregate patient data (APD) and individual patient data (IPD). Articles that presented outcome and follow-up for each individual patient (typically case reports and case series) were included in the IPD set. A second dataset, APD was constructed from articles that presented mean follow-up for an entire patient cohort (typical of larger case series, institutional reviews, or prospective studies).

Exclusion Criteria

Articles that were non-English or animal studies were excluded during the MEDLINE search. Articles pertaining to anesthesia, coagulation, embolization, histology, hormone, nonsurgical management, natural history, other tumors, pathology, radiology, and radiotherapy were excluded. Articles that had no data, insufficient data, and no follow-up or mean follow-up were also excluded. Articles from the same institution by the same set of authors were screened for study time-period overlap, and if repetitive information was presented, duplicated data were excluded. Articles with unobtainable full text were excluded.

Data Extraction

All data were extracted by two independent authors and included patient age, sex, presenting symptoms, tumor location, grading system utilized, grade, surgical approach (purely endoscopic, endoscopic-assisted, or open), outcome (remission/disease free, residual tumor/recurrence, or death), and follow-up. The data were reported per case, not per patient due JNA's tendency to recur and for patients to have repeat surgeries. Any discrepancies were addressed following discussion.

Data Analysis

This analysis utilized Microsoft Excel (Microsoft Corp., Redmond, WA) for data aggregation and analysis, and SAS Software (SAS Institute Inc., Cary, NC) for χ^2 tests, Fisher exact tests, and analysis of variance (ANOVA). Recurrence rates were compared with χ^2 tests or Fischer exact tests where appropriate. Intraoperative blood loss was compared using ANOVA.

RESULTS

Searching the MEDLINE database using the keywords and manual bibliography search identified 270 studies (Fig. 2). Exclusion criteria included no follow-up OR no mean follow-up (26), radiology (16), natural history (15), hormone therapy (14), embolization (13), other tumors (12), radiotherapy (11), insufficient data (nine), pathology (eight), nonsurgical (seven), histology (seven), no data (six), anesthesia (three), not relevant (three), repeat data (three), and coagulation studies (two). Twenty articles were not found. After applying the aforementioned criteria, 85 articles were included in the systematic review.

These 85 studies were composed of 57 studies with IPD and 28 studies with APD (Table I). The studies with IPD spanned from 1992 to 2011, totaling 345 surgeries. Information on age, sex, location of tumor, associated symptoms, staging system, tumor stage, surgical approach, outcome, and follow-up were recorded if available. The aggregate studies spanned from 1996 to 2011, totaled 702 surgeries, and at minimum included the diagnosis, surgical approach, recurrence, and mean follow-up.

Patient Demographics

The average age of the individual patients in this review was 17.2 years (range, 1.25 to 64 years). The vast majority of patients in the IPD cohort were male (98.7%). Age was reported for 303 patients and gender was reported for 305 patients. Presenting symptoms were included in 130 cases; the most common presenting symptoms of JNA were nasal obstruction (76.2%), epistaxis (76.2%), headache (16.9%), vision changes (12.3%), eustachian tube dysfunction (9.2%), and cheek swelling (8.5%). JNAs were most commonly located in the nasopharynx (85.2%), followed by the nasal cavity (66.1%), sphenoid sinus (49.8%), pterygopalatine fossa (48.6%), and infratemporal fossa (29.2%) (Table II).

IPD Surgical Approaches and Recurrence Rates

We found 345 cases of JNA that were treated by either purely endoscopic, endoscopic-assisted, or open approaches (Table III). Of these 345 surgeries, 158 were purely endoscopic, 15 were endoscopic-assisted, and 172 were completed through an open surgical approach. The recurrence rate in the purely endoscopic approach was 10.8%, and there were no deaths reported in this group. The open surgical approach yielded a recurrence rate of 14.5%, and there were two deaths reported, both occurring intraoperatively. In total, 27 of the 172 (15.7%) surgeries completed by the open approach yielded a negative outcome (recurrence 14.5% or death 1.2%). Endoscopic-assisted cases had the highest recurrence rate at 46.7%. There was a significant difference in recurrence rates among these approaches ($P < .05$). Recurrence rates were significantly lower in cases completed by the purely endoscopic approach or open approach compared to endoscopic-assisted approaches ($P < .05$). There was no significant difference in recurrence rates between purely endoscopic and open surgical approaches ($P > .05$) (Table IV). The entire IPD cohort had a recurrence rate of 14.2% with an average follow-up of 33.4 months.

Of the 345 JNA included in the IPD cohort, 105 were staged using the Radkowski et al.[9] or Sessions et al.[11] staging criteria (Table V). There was no significant difference in recurrence rate when utilizing the purely endoscopic approach or open surgical approach regardless of stage ($P > .05$). There was only one case completed by the endoscopic-assisted approach, and as such it was excluded from the statistical analysis. The total recurrence rate for JNA resected by the purely endoscopic approach in this group was 6.7% compared to a recurrence rate of 18.2% when utilizing the open surgical approach ($P > .05$).

In the IPD, in those cases where Radkowski/Sessions staging was used (105/345 cases), there was no preference in surgical approach based on stage ($P > .05$). Within the APD, where Radkowski/Sessions staging was used (183/705 cases), there was also no preference in surgical approach used based on stage ($P > .05$).

Blood Loss and Preoperative Embolization

Blood loss was reported in 138 cases, 89 of these cases were completed purely endoscopically, five cases were endoscopic-assisted, and 44 cases were completed with an open surgical approach (Table VI). The mean blood loss for the purely endoscopic group was 544.0 mL (range, 20–2,000 mL) compared to 1,579.5 mL (range, 350–10,000 mL) in the open surgical group. Endoscopic-assisted cases had a mean blood loss of 490.0 mL (range, 100–950 mL). Using ANOVA, mean blood loss was found to be significantly different among these three groups ($P < .05$).

Of the 138 cases where blood loss was reported, data on preoperative embolization were available for 131 cases. Preoperative embolization was completed in 60 pure endoscopic cases, 29 open cases, and two endoscopic-assisted cases; no preoperative embolization was done in 40 cases. For usage of preoperative embolization, there was no statistical difference between open and pure endoscopic cases ($P > .05$). In purely endoscopic cases, preoperative embolization led to significantly lower amounts of blood loss with a mean estimated blood loss of 406.7 mL for embolized cases compared to 828.3 mL for nonembolized cases ($P < .05$). In open surgical cases, there was significantly more blood loss with preoperative embolization (1912.1 mL) compared to nonembolized cases (685.0 mL) ($P < .05$).

APD Surgical Approaches and Recurrence Rates

There were 702 total procedures reported in the APD cohort, of which 150 were completed purely endoscopically, 34 were endoscopic-assisted, and 518 were open surgical procedures (Table VII). Recurrence rate varied from 0.0% to 23.1% for purely endoscopic procedures, with a weighted average of 4.7% for all endoscopic cases. There were 34 endoscopic-assisted cases with a weighted average recurrence rate of 20.6% (range, 15.0%–50.0%). Open surgical procedures had a recurrence rate that ranged from 0.0% to 50.0%, with a weighted average of 22.6%. Analysis revealed that there was a significant difference among recurrence rates in

TABLE I.
Studies Meeting Criteria for Systematic Review.

Author	Year	No. of Patients
Individual patient data		
Ahmad[41]	2008	5
Albuquerque[42]	2009	1
Antoniades[43]	2002	1
Avelar[44]	2011	2
Aziz Sultan[45]	2011	1
Borghei[46]	2006	23
Browne[47]	2000	1
Browne[48]	1994	5
Dare[49]	2003	2
de Brito[50]	2006	9
Donald[51]	2004	5
Dubey[52]	2011	16
Eloy[53]	2007	6
Fagan[54]	1997	16
Fonseca[55]	2008	15
Gaffney[56]	1997	1
Gallia[57]	2010	1
Goel[58]	1994	1
Gullane[20]	1992	14
Gupta[8]	1997	7
Handa[59]	2001	1
Hardillo[23]	2004	28
Hazarika[60]	2002	9
Hofmann[61]	2005	25
Kamel[62]	1996	1
Khalifa[63]	2001	1
Koshy[64]	2008	1
Lin[22]	2008	6
Mair[65]	2003	7
Moschos[66]	1998	1
Murray[67]	2000	1
Nakamura[68]	1999	1
Naraghi[69]	2003	12
Newlands[70]	1999	12
Nicolai[71]	2003	15
Nomura[72]	2006	1
Ochi[73]	2002	1
Patrocinio[74]	2002	1
Patrocinio[75]	2005	1
Peloquin[76]	1997	1
Powell[77]	2002	5
Ramos[78]	2011	2
Reddy[79]	2002	1
Rha[80]	2003	1
Riggs[81]	2010	1
Robinson[82]	2005	4
Romani[83]	2010	1
Rong[84]	2008	3
Schick[85]	1998	1

(Continues)

TABLE 1.
(*Continued*).

Author	Year	No. of Patients
Schick[86]	1999	5
Scholtz[5]	2001	14
Sinha[87]	2008	2
Szymanska[88]	2006	1
Tosun[21]	2006	24
Tseng[89]	1997	1
Yi[90]	2007	2
Yiotakis[40]	2008	19
Total individual patient data		345
Aggregate patient data		
Andrade[91]	2007	12
Bales[92]	2002	5
Bleier[93]	2009	18
Bosraty[94]	2011	42
Chen[33]	2006	8
Cherekaev[95]	2011	29
Danesi[96]	2008	85
de Mello-Filho[97]	2004	19
Elsharkawy[98]	2010	23
Gaillard[99]	2010	16
Hackman[18]	2009	31
Herman[34]	2011	4
Hosseini[100]	2005	37
Howard[36]	2001	39
Huang[101]	2009	19
Margalit[25]	2009	7
Mattei[102]	2011	20
Midilli[103]	2009	42
Paris[6]	2001	33
Pryor[19]	2005	58
Radkowski[9]	1996	23
Roger[35]	2002	20
Singh[104]	2011	12
Tewfik[105]	1999	14
Ungkanont[106]	1996	36
Wormald[107]	2003	7
Ye[26]	2011	23
Zhang[108]	1998	20
Total aggregate patient data		702

this cohort ($P < .05$). There was significantly lower recurrence in the purely endoscopic group compared to endoscopic-assisted ($P < .05$) and open surgical approaches ($P < 0.05$) (Table IV). There was no significant difference between recurrence rates of endoscopic-assisted and open surgical cases ($P > .05$).

DISCUSSION

JNA is a rare entity, making prospective, randomized, double-blind analysis difficult. Therefore, systematic review of the existing literature can provide valuable information when these optimal studies are not feasible. We conducted a systemic review with the

TABLE II.
Summary of Individual Patient Data: Patient Demographics, Presenting Symptoms, and Tumor Extent From the Sphenopalatine Region.

Presenting Symptoms (n = 130 Cases)	No. Reported	% Reported	Location (n = 257 Cases)	No. Reported	% Reported
Nasal obstruction	99	76.2	Nasopharynx	219	85.2
Epistaxis	99	76.2	Nasal cavity	170	66.1
Headache	22	16.9	Sphenoid sinus	128	49.8
Vision changes	16	12.3	Pterygopalatine fossa	125	48.6
Hyponasality	13	10.0	Infratemporal fossa	75	29.2
Eustachian tube dysfunction	12	9.2	Ethmoid sinus	47	18.3
Cheek swelling	11	8.5	Pterygomaxillary fissure	32	12.5
Proptosis	9	6.9	Maxillary sinus	28	10.9
Nasal discharge	8	6.2	Orbit	26	10.1
Pain	4	3.1	Cavernous sinus	26	10.1
Snoring	4	3.1	Middle cranial fossa	22	8.6
Hearing changes	3	2.3	Cheek	17	6.6
Smell changes	3	2.3	Pterygoid process/plate	16	6.2
Posterior nasal drip	2	1.5	Pterygoid base	14	5.4
Respiratory distress	2	1.5	Clivus	11	4.3
Alopecia	1	0.8	Sella turcica	9	3.5
Epiphora	1	0.8	Basisphenoid	8	3.1
Weight loss	1	0.8	Intracranial (unspecified)	6	2.3
Insomnia	1	0.8	Skull base	6	2.3
Dizziness	1	0.8	Orbital apex	6	2.3
Facial numbness	1	0.8	Parasellar region	5	1.9
Dry eye	1	0.8	Sphenoid bone	5	1.9
			Vomer	3	1.2
Average age (n = 303 patients), yr	17.2		Inferior orbital fissure	2	0.8
Range (1.25–64 years)			Anterior cranial fossa	1	0.4
			Oropharynx	1	0.4
Sex (n = 305 patients), N			Optic chiasm	1	0.4
Male	301	98.7	Optic canal	1	0.4
Female	4	1.3	Vidian canal	1	0.4
			Temporal fossa	1	0.4
			Lacrimal sac	1	0.4
			Superior orbital fissure	1	0.4

largest single series of JNA to apply acquired clinically relevant information toward its current and future management.

Incidence and Demographics

There have been few studies on the incidence of JNA. Glad et al.[1] reported an incidence rate of 0.4 cases per million inhabitants per year, with a median age at diagnosis of 15 years. When considering the population at risk, the incidence rose to 3.7 cases per million. The population that is affected by JNA is overwhelming consisting of adolescent males. In our study, we found 301 males out of the 305 cases where sex was reported. The mean age of this patient cohort was 17.2 (range, 1.25–64

TABLE III.
Individual Patient Data Cohort.

All Surgeries (n = 345)	Total Cases	Remission (%)	Recurrence (%)	Death (%)
Endoscopic	158	141 (89.2)	17 (10.8)	0 (0.0)
Endoscopic-assisted	15	8 (53.3)	7 (46.7)	0 (0.0)
Open surgery	172	145 (84.3)	25 (14.5)	2 (1.2)

Mean follow-up = 33.4, $P < .05$ (χ^2).
Two by three χ^2 analysis revealed that there was a significant difference among recurrence rates based on approach ($P < .05$).

TABLE IV.
The Results of χ^2 or Fisher Exact Tests Comparing Recurrence Rates Between Treatment Groups in the IPD and APD Cohorts.

	IPD	APD
ES vs. OS	$P = .323$ (NS)	$P < .05$ (S)
ES vs. EA	$P < .05$ (S)	$P < .05$ (S)
OS vs. EA	$P < .05$ (S)	$P = 1.000$ (NS)

APD = aggregate patient data; EA = endoscopic assisted group; ES = endoscopic group; IPD = individual patient data; NS = not significant; OS = open surgery group; S = significant.

TABLE V.
Individual Patient Data Cohort That Included Staging by Radkowski or Sessions Staging Criteria.

	Radkowski or Sessions Graded Patients (n = 105 Patients)			
	Stage I	Stage II	Stage III	Total
Endoscopic (ES)	29	28	3	60
ES recurrences (%)	1 (3.4%)	3 (10.7%)	0 (0.0%)	4 (6.7%)
Endoscopic-assisted (EA)	0	1	0	1
EA recurrences (%)	—	0 (0.0%)	—	0 (0.0%)
Open surgery (OS)	13	27	4	44
OS recurrences (%)	1 (7.7%)	6 (22.2%)	1 (25.0%)	8 (18.2%)
ES vs. OS	$P = 1.000$	$P = .295$	$P = 1.000$	$P = .118$

Fisher exact tests were completed to compare recurrence between the endoscopic and open surgery groups; no significant difference was found.

EA = endoscopic assisted group; ES = endoscopic group; OS = open surgery group.

years). Interestingly, four cases of JNA were women with the ages of 14, 31, 57, and 64 years, which may call into question the diagnosis. The tendency for this tumor to occur in adolescent males has led to the hypothesis that sex hormone receptors are present in JNA, although evidence to support this claim remains equivocal.[29–31]

Presenting Symptoms

There are a wide variety of symptoms, including extranasopharyngeal symptoms that can manifest as a result of JNA due to its locally destructive nature. However, there is an agreement on the classic clinical presentation of JNA: an adolescent male with recurrent epistaxis, nasal obstruction, and a nasopharyngeal mass.[20] Our findings were consistent with the current paradigm; 76.2% of patients presented with nasal obstruction and recurrent epistaxis. Prior studies have demonstrated similar proportions of patients who present with these symptoms.[19,21,23,32]

Location and Staging

Advances in imaging have allowed for more accurate localization and staging of JNA, which are essential for selection of the correct approach for resection. CT and MRI are the two most commonly utilized modalities for assessing JNAs. Biopsies can be an effective alternative, but surgeons remain wary due to the vascular nature of JNA and possibility of causing severe epistaxis. The location of JNA is classically in the nose and pterygopalatine fossa, with erosion of bone posteriorly, and the diagnosis can be made solely on the basis of CT.[16] In our study, the most common locations for JNA were the nasopharynx, nasal cavity, sphenoid sinus, and the pterygopalatine fossa. The middle cranial fossa (8.6%) was the most common location for intracranial manifestation of JNA. Most patients with JNA manifest prior to intracranial extension. We found that only seven cases of the 105 with available staging manifested as Radkowski stage IIIa or stage IIIb (with intracranial extension).

Treatment and Recurrence

Consensus has not been reached as to which approach is most appropriate with respect to complications, morbidity, and mortality. With the introduction of endoscopic techniques, both purely endoscopic and endoscope-assisted, further procedures have been developed, but not extensively evaluated. Some may note that a predilection for treating stage I and stage II neoplasms with an endoscopic approach may distort outcome measures. However, when we analyzed for a preference based on stage (albeit only with a subset of the data), we found no significant difference in both the IPD and APD cohorts.

From the individual patient cohort, we found that there is no statistically significant difference between the recurrence rate of JNA after purely endoscopic and open surgery. Both of these approaches had lower recurrence rates compared to the endoscopic-assisted group. Yet, the comparison is of limited value, because only 15 cases were completed with the endoscopic-assisted approach. Purely endoscopic and open surgical techniques were equally as effective regardless of stage. Prior studies have demonstrated that endoscopic approaches may have lower recurrence rate, but statistical analysis is limited by the small power of these studies.[33,34] For example, Pryor et al.[19] found that a purely endoscopic approach had a recurrence rate of 0.0% in five patients, compared to a recurrence rate of 26.4% after open surgical approaches. Renkonen and colleagues[7] demonstrated that a 33.3% recurrence rate was achieved following endoscopic surgery compared to 37.5% in the open surgical group; three patients participated in the endoscopic group. Both of these studies suffer from a limited number of patients included in the endoscopic group. Standardization of staging criteria and multi-institute studies are required to fully elucidate when the endoscopic approach is indicated for resection.

Although the individual patient cohort suggests that purely endoscopic and open surgical approaches are equally as effective, the aggregate patient cohort leads to a different conclusion. In the aggregate patient cohort of 702 cases, we found that purely endoscopic resection had a significantly lower rate of recurrence/residual disease compared to both endoscopic-assisted and open surgical approaches. Recent studies that focus solely on the purely endoscopic approach have come to similar conclusions.[35] Nicolai et al.[27] conducted one of the largest studies that focused on purely endoscopic approaches, consisting of 46 consecutive patients. The authors of this study found that the recurrence rate was

TABLE VI.
Blood Loss Compared Among Endoscopic, Endoscopic-Assisted, and Open Surgery Groups in the Individual Patient Data Cohort.

Blood Loss (n = 138 Patients)	Patients Reported	Mean Blood Loss (mL)	Range (mL)
Endoscopic	89	544.0	20–2,000
Endoscopic-assisted	5	490.0	100–950
Open surgery	44	1579.5	100–10,000

Analysis of variance revealed a statistically significant difference in mean blood loss ($P < .05$).

TABLE VII.
Aggregate Patient Data Cohort of Studies Comparing Endoscopic, Endoscopic-Assisted, and Open Surgery Groups.

All Aggregate Data													
Study	Year	Total Patients	ES Patients	ES Recurrence	ES % Recurrence	EA Patients	EA Recurrence	EA % Recurrence	OS Patients	OS Recurrence	OS % Recurrence	Follow-up
Ye	2011	23	23	0	0.0	0	—	—	0	—	—	58.0
Singh	2011	12	0	—	—	0	—	—	12	0	0.0	12.0
Mattei	2011	20	0	—	—	20	3	15.0%	0	—	—	60.0
Herman	2011	4	4	0	0.0	0	—	—	0	—	—	11.3
Cherekaev	2011	29	0	—	—	0	—	—	29	5	17.2	48.0
Bosraty	2011	42	13	3	23.1	0	—	—	29	9	31.0	43.4
Gaillard	2010	16	2	0	0.0	2	1	50.0%	12	6	50.0	27.6
Elsharkawy	2010	23	0	—	—	0	—	—	23	4	17.4	21.0
Midilli	2009	42	12	0	0.0	0	—	—	30	7	23.3	92.0
Margalit	2009	7	0	—	—	0	—	—	7	0	0.0	42.0
Huang	2009	19	19	0	0.0	0	—	—	0	—	—	34.0
Hackman	2009	31	15	1	6.7	12	3	25.0%	4	1	25.0	48.0
Bleier	2009	18	10	0	0.0	0	—	—	8	4	50.0	24.4
Danesi	2008	85	0	—	—	0	—	—	85	13	15.3	54.9
Andrade	2007	12	12	0	0.0	0	—	—	0	—	—	24.0
Chen	2006	8	8	1	12.5	0	—	—	0	—	—	54.0
Pryor	2005	58	5	0	0.0	0	—	—	53	14	26.4	13.0 ES, 48.0 OS
Hosseini	2005	37	0	—	—	0	—	—	37	10	27.0	46.5
de Mello-Filho	2004	19	0	—	—	0	—	—	19	0	0.0	116.4
Wormald	2003	7	7	0	0.0	0	—	—	0	—	—	45.0
Roger	2002	20	20	2	10.0	0	—	—	0	—	—	22.0
Bales	2002	5	0	—	—	0	—	—	5	1	20.0	38.0
Paris	2001	33	0	—	—	0	—	—	33	8	24.2	56.0
Howard	2001	39	0	—	—	0	—	—	39	8	20.5	24.0
Tewfik	1999	14	0	—	—	0	—	—	14	4	28.6	63.0
Zhang	1998	20	0	—	—	0	—	—	20	5	25.0	25.0
Ungkanont	1996	36	0	—	—	0	—	—	36	13	36.1	61.8
Radkowski	1996	23	0	—	—	0	—	—	23	5	21.7	72.0
Total		702	150	7	4.7	34	7	20.6	518	117	22.6	—

EA = endoscopic assisted group; ES = endoscopic group; OS = open surgery group.

8.7% and suggest that endoscopic techniques can be utilized even in cases of intracranial involvement. Indications for open surgical approaches may include instances when there is significant involvement of internal carotid artery, cavernous sinus, or optic nerve.[27] Ardehali et al.[32] also came to similar conclusion following a study of 47 patients treated by endoscopic or endoscopic-assisted resection; recurrence rate in this cohort was 19.1%. The authors of this study similarly suggested that endoscopic approaches may be utilized in cases of minimal intracranial involvement, but cases where there is a large intracranial component should be reserved for open surgery. Drawing on their experiences with endoscopic resection, the authors recounted one case of a Radkowski stage IIIb JNA. Due to cavernous sinus injury, significant intraoperative hemorrhage occurred leading to 8,500 mL of blood loss.[32]

The primary measure of success in the treatment of JNA is the recurrence rate.[16] Howard et al.[36] found that the recurrence rate was reduced from 35.0% to 0.0% when macroscopic removal of JNA was combined with drilling out of the basisphenoid. The working hypothesis in this study was that most recurrences occur as a result of invasion of the sphenoid and incomplete excision. Lund et al.[37] put forth the concept that JNA undergoes a period of rapid growth followed by a stable phase. Therefore, the recurrence of JNA may be due to an incomplete resection during the aggressive growth phase of the JNA.[36] Recognizing this and the fact that not all studies report residual tumor separately from recurrence, we combined residual tumor and recurrence into one category. Comparing the IPD and APD, the total recurrence rates of these series were 14.2% and 18.7%, respectively. The recurrence rates in this study are similar to what has been reported in the literature.[14,18]

The conflicting results between IPD and APD cohorts with respect to recurrence rate is interesting and should be commented on. IPD provides the most effective data when provided in large quantities, as it allows for complete and accurate analysis of outcome measures as well as demographic data. The risk of bias in IPD, however, is introduced when it is provided by case reports and case series, as these are low in quality and therefore high in variability. Meta-analyses are highly effective in high-quality data and most useful in randomized controlled studies. Meta-analyses would also be more rigorous in terms of statistical independence and hidden biases than the techniques used in this study. However, given the rare nature of this tumor, there were not sufficient studies that satisfied the requirements for meta-analyses. The APD group, therefore, was used to examine recurrence rate across studies that generally provided a higher n (average of 25.1 [range, 4–85] cases per study vs. 6.1 [range, 1–28] for IPD studies). Although APD typically only report summary data, the value of these data is higher than that provided by case reports and small case series, as temporal, regional, and interinstitutional biases are not introduced. In addition, smaller studies do not take into account the experience of the surgeon or group of surgeons over time. Because the endoscope is a relatively new tool, there is a learning curve associated with it.[38] This may demonstrate that in larger APD studies, where the surgeons were more experienced with endoscopic techniques, there might be a higher benefit in using the endoscope. This could possibly explain the significance obtained in the APD cohort compared to the IPD cohort.

Recurrence Rates in Endoscopic-Assisted Surgery

Recurrence rate in endoscopic-assisted surgery is of particular interest due to the novelty of this approach. This hybrid technique combines the superior visualization provided by the endoscope with increased maneuverability due to surgical incision. These added benefits make the endoscopic-assisted approach particularly well suited for resection of larger and more technically challenging JNAs. The data from our study suggest that the endoscopic-assisted approach provides limited benefits in terms of recurrence rates. In the IPD cohort, the recurrence rate was significantly higher, and in the APD cohort there was no significant difference between endoscopic-assisted and open surgical approaches. Yet, it is of note that endoscopic-assisted approaches constituted only 49 of 1047 cases reviewed in our study. Other studies by Carrau et al.[39] and Hackman et al.[18] have found that recurrence rates of endoscopic-assisted surgery are higher than purely endoscopic surgery. Yet, endoscopic-assisted approaches are reserved for cases where the purely endoscopic approach would not suffice due size, spread, or complexity of the JNA that must be resected. In all, more studies are required to compare open surgery and endoscopic-assisted surgery.

Blood Loss

Blood loss was found to be significantly less in the purely endoscopic approach compared to the open approach.[32] In our study, the average blood loss from the purely endoscopic approach was 544.0 mL (range, 20–2000 mL) compared to 1579.5 mL (range, 350–10,000 mL) for the open approach. Endoscopic-assisted cases had an average blood loss of 490.0 mL (range, 100–950 mL). Several studies have come to similar conclusions regarding blood loss.[19,32,40] Diminished blood loss leads to fewer transfusions and decreased morbidity and mortality. Intraoperative hemorrhage still occurs with purely endoscopic techniques, especially in cases with significant intracranial extension.[32] In addition, preoperative embolization was found to make a significant impact on blood loss when used in purely endoscopic cases. Preoperative embolization increased blood loss in open surgeries, but there were a limited number of cases with both values included. Additionally, it is possible that the significantly increased blood loss noted in the embolized cases in the open approach may be due to selection bias based on larger tumors being embolized.

Limitations

There are several limitations in this study that should be noted. Assessing studies that span a significant time frame introduces biases with respect to the advancements in diagnosis and treatment. The quality of the data available in the literature was inconsistent, and much of it was taken from case reports and case studies, thus introducing allocation and selection biases. In addition, due to the nonuniform staging systems utilized and heterogeneous reporting of follow-up, recurrence, and residual tumor, the quality of the data was affected. Ideally, there would be a uniform staging method so the endoscopic and open approaches could be effectively compared across stages with respect to outcome measures (recurrence and blood loss). Additionally, the number of endoscopic-assisted cases was limited in the literature both in the IPD and APD cohorts. In the data collection, there were some patients in which the diagnosis of JNA was questioned as they affected individuals who did not fall into the typical affected population (female gender, advanced age). Last, because APD was used, it is possible that there was heterogeneity in these studies and inconsistencies in those datasets that were unknown due to the summation of data.

CONCLUSION

JNA is a rare tumor with aggressive growth, tendency for recurrence, and local tissue destruction, making it particularly difficult to treat. In select cases, purely endoscopic surgery may be more effective than open techniques in resecting JNA, as it may lead to decreased recurrence and blood loss. Because IPD and APD results varied, however, further analysis in large-scale studies should be undertaken to further elucidate treatment modalities.

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