Evolution in the Treatment of Juvenile Nasopharyngeal Angiofibroma☆

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KEYWORDS
Juvenile angiofibroma; Sinonasal tumours; Surgical approach; Sinonasal endoscopic surgery; Embolisation

Abstract
Introduction: Juvenile nasopharyngeal angiofibroma (JNA) is a rare benign tumour in adolescent males. It may be associated with a significant morbidity because of its anatomical location and its locally destructive growth pattern. Severe haemorrhage constitutes a high risk in JNA and its surgical management could be complex.

Material and methods: We retrospectively analysed the clinical data from 43 patients with JNA surgically treated in our Department from 1993 until 2010. Mean postoperative follow-up time was 85 months.

Results: Analysis was performed on 42 males and one female. Mean patient age was 16 years old. The most common presenting symptoms were unilateral epistaxis (56%) and nasal obstruction (56%). Using the Fisch staging scale, tumours were classified as stage I in 2 patients, stage II in 9, stage III-a in 13, stage III-b in 13 and stage IV-a in 6. Preoperative selective embolisation was performed on 32 patients (74%). Thirty-three patients (77%) underwent an open surgical approach and 10 (23%) were treated by endoscopic approach. Complete resection of the lesion was achieved in 35 patients (81%) and tumour recurrence was observed in 2 (5%). All lesions treated via transnasal endoscopic approach were stage I and stage II lesions.

Conclusion: Surgery is the treatment of choice for JNA. An endoscopic approach is feasible for early-stage lesions (Fisch I and II) and conservative external approaches are still useful in advanced stages (Fisch III and IV). The open approaches proved helpful with respect to exposure, safety, cosmetic outcome and low morbidity. Preoperative embolisation, if possible, is mandatory.

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Introduction

Juvenile nasopharyngeal angiofibroma (JNA) is a vascular tumour arising most often near the sphenopalatine orifice. Although histologically benign, its complex anatomical location, its tendency towards local invasion and towards recurrence and its aggressive growth sometimes make it a sinonasal tumour with specific features.

These JNA tumours have a low incidence (1 case per 150,000 inhabitants) and represent less than 0.5% of tumours arising in the head and neck. They appear almost exclusively in males and are usually diagnosed during adolescence (between 14 and 25 years). Nevertheless, isolated cases have been reported in males older than 25 years and in adolescent females.

A JNA initially occupies the nasal fossae and cavum and its vascular afferents originate from terminal branches of the internal maxillary artery. Subsequently, the tumour erodes the surrounding bone and can spread widely into the paranasal sinuses, pterygopalatine and infratemporal fossae and the oral cavity or even penetrate into the orbit or become intracranial.

Symptoms of JNA depend on tumour location, size and extent. Nasal obstruction, initially unilateral and subsequently bilateral, and unilateral and recurrent epistaxis are the most frequent symptoms.

The diagnosis of JNA is carried out by computed tomography (CT) and nuclear magnetic resonance (NMR) imaging. There are many classifications for the staging of JNA, based on the extent of the tumour, which help to plan the best surgical approach. One of the most used is the Andrews–Fisch classification, which divides the pathology into 4 stages (Table 1).

The treatment of choice in JNA is surgical, after angiography and selective embolization centred on the arteries that nourish the tumour. Sinonasal endoscopic surgery (SNES) is a good alternative in patients with early-stage tumours. For JNA with extensive spread to the infratemporal fossa and skull base, carrying out open approaches is preferable to achieve a proper removal.

The purpose of this study is to present our experience in the treatment of JNA, primarily focusing on the type of surgical approach used, and to review the disease based on the literature and our own experience.

Material and Methods

We reviewed the surgical registry of the Otolaryngology Service at our hospital from 1993 until May 2010, collecting data from medical records pertaining to patients diagnosed with JNA. The study population consisted of 43 patients undergoing surgery. Of these, 23 patients were referred from hospitals in other regions.

Data collection was based on the review of clinical records, noting data on age, gender, performance of previous surgery, tumour size and staging, clinical presentation, mean time from the start of symptoms until the patient had surgery and surgical approach, complications and monitoring. The classification of JNA was carried out based on the Fisch classification. In addition, we evaluated the performance of preoperative embolisation, and the description of the main feeding arteries of the tumour. We also quantified mean blood loss during surgery and transfusion requirements.

The mean follow-up time was 85 months (range, 10–252 months).

We used the SPSS 15.0 program to analyse the data.
Table 1  Andrews–Fisch Classification.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Limited to the nasal cavity and cavum without bone destruction</td>
</tr>
<tr>
<td>II</td>
<td>Invasion of the pterygopalatine fossa, maxillary sinus, ethmoid or sphenoid, with bone destruction</td>
</tr>
<tr>
<td>IIIa</td>
<td>Involvement of infratemporal fossa or orbital fossa, without intracranial involvement</td>
</tr>
<tr>
<td>IIIb</td>
<td>Stage IIIa with extradural intracranial involvement (parasellar)</td>
</tr>
<tr>
<td>IVa</td>
<td>Intralateral extension without involvement of the cavernous sinus, hypophysis or optic chiasm</td>
</tr>
<tr>
<td>IVb</td>
<td>Involvement of cavernous sinus, hypophysis or optic chiasm</td>
</tr>
</tbody>
</table>

Table 2  Presentation Symptoms in the 43 Patients With JNA.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epistaxis</td>
<td>24 (56)</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>24 (56)</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>7 (16)</td>
</tr>
<tr>
<td>Smell alterations</td>
<td>6 (14)</td>
</tr>
<tr>
<td>Hypoacusis</td>
<td>6 (14)</td>
</tr>
<tr>
<td>Facial swelling</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Otitis media</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Cephalalgia</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Epiphora</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Rhinolalia</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Snoring</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Diplopia</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Exophthalmos</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Unilateral amaurosis</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

* Patients usually present more than one symptom.

Results

The sample consisted of 42 male patients and one female, whose mean age at diagnosis was 16 years (median, 16; range, 8–26 years). A total of 12 patients had undergone surgery (20 surgical interventions) prior to being operated on at our service, performing a subtotal resection of the tumour, a biopsy of the tumour or a reduction of the tumour without achieving its total resection. These interventions were carried out by SNES or else by a lateral rhinotomy. On 4 occasions, more than one intervention by SNES had been performed before referral to our centre.

A total of 28 tumours originated in the right nostril (65%) and 15 in the left nostril (35%).

The mean time from onset of symptoms until surgery was 12 and half months (1–60 months). The most frequent symptoms were nasal obstruction and epistaxis in 24 patients (56%), followed by rhinorrhea in 7 (16%) and hearing loss and smell alterations in 6 (14%). One patient referred from another centre, who was later intervened by infratemporal approach and currently has residual tumour, attended our service with loss of vision in one eye due to parasellar infiltration of the tumour (Table 2).

The patients were examined by nasofibroscopy and an MRI and CT scans with contrast were requested before surgery to study tumour extension. An angiography was performed 24–48 h before surgery, aiming to achieve preoperative tumour embolisation, in 39 of the 43 patients (91%). In 34 patients, the primary tumour irrigation system came from the external carotid artery; in one case, the tumour was irrigated by circulation from only the internal carotid artery. In the remaining 8 cases, the tumour received its vascular supply through both arterial systems. In 3 patients, we confirmed the existence of bilateral irrigation from the external carotid artery. A total of 32 patients were embolised (74%) with polyvinyl alcohol microparticles (Fig. 1). Embolisation was not carried out in patients in whom we failed to

![Figure 1](http://www.elsevier.es)  Angiography image before (A) and after (B) embolisation, showing the vascular supply from the internal maxillary artery in a sagittal view.
perform angiography and in whom irrigation was obtained mainly through branches of the internal carotid artery.

According to the Fisch classification, 2 JNAs belonged to Stage I, 9 to Stage II, 13 to Stage IIIa, 13 to Stage IIIb and 6 to Stage IVa. Intraoperative samples of the mass were sent in all cases to the Anatomical Pathology Service to confirm the diagnosis of JNA.

We performed an open surgical approach in 33 patients (77%), while the remaining 10 patients (23%) underwent surgery by SNES (Fig. 2). Within the group of open approaches, the most frequently used one was anterior facial translocation (12 patients, 28% of all JNA surgeries), which in 9 cases was done through midfacial degloving (Fig. 3). Secondly, the subtemporal preauricular approach was used in 11 patients (25%), followed by the lateral facial translocation in 6 (14%), transmaxillary approach in 2 (5%) and subcranial approach in another 2 (5%). Table 3 shows the approach used depending on tumour stage. In 8 cases (2 subtemporal approaches, 3 lateral and 3 superior facial translocations) we performed a surgical defect reconstruction using a temporalis muscle flap.

Mean blood loss during surgery was 2300 mL (range, 300–8000 mL). Patients with tumours in advanced stages presented higher intraoperative bleeding ($P < .001$) and perhaps for this reason, patients undergoing SNES bled less (1025 mL on average) than those intervened using open techniques (2833 mL on average) ($P < .001$). A total of 36 patients were transfused during surgery and/or the immediate postoperative period and it was necessary to administer fresh frozen plasma to 8 of them. All patients who underwent open surgery were transfused, as were 5 of the 12 who underwent SNES ($P < .001$).

One patient who underwent lateral facial translocation (Stage IIIb) and another intervened using a subtemporal preauricular approach (Stage IIIa) suffered dehiscence and surgical wound infection, which were treated with antibiotic therapy and conservative measures; another 2 patients, operated on by a preauricular subtemporal approach (Stage

![Figure 2](http://www.elsevier.es) Preoperative sagittal (A) and coronal (B) MRI of Stage II JNA case. Postoperative coronal (C) and axial (D) CT scan of the same patient, after tumour resection through endoscopic sinonasal surgery.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Surgical Approach According to Andrews–Fisch Tumour Stage.</th>
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<tbody>
<tr>
<td></td>
<td>SNES</td>
</tr>
<tr>
<td>Stage I</td>
<td>2</td>
</tr>
<tr>
<td>Stage II</td>
<td>8</td>
</tr>
<tr>
<td>Stage IIIa</td>
<td>0</td>
</tr>
<tr>
<td>Stage IIIb</td>
<td>0</td>
</tr>
<tr>
<td>Stage IVa</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>10 (23%)</td>
</tr>
</tbody>
</table>

SNES, sinonasal endoscopic surgery.
Illob and an anterior facial translocation (Stage Illob), respectively, presented paresis of the 6th cranial nerve, which evolved favourably.

As long-term postoperative sequelae of note, we recorded development of a significant trismus in one patient intervened by subtemporal preauricular approach and a certain degree of epiphora in 2 patients with lateral facial translocation.

The mean hospital stay of all patients was 12 days (range, 3–39 days). The mean hospital stay for patients intervened by SNES was 8 days, while it was 15 days (P<.001) for those who underwent open surgery.

In 35 patients (81%), we achieved complete, macroscopic tumour resection that was objectified during monitoring by image controls. Of the 8 patients in whom tumour resection was incomplete, 2 were patients in Stage Ilia, 3 were patients in Stage Illob and a further 3 had tumours in Stage IIVa. Postoperative radiotherapy was used to treat 3 patients, with 2 of them having stable tumours at present and another being disease-free. Two patients received radiosurgery, one of which responded well and the other remained with a stable tumour. Meanwhile, 3 remained under observation. Progression of the disease was found in one of them, who required a new intervention by preauricular subtemporal approach, while the remaining two presented stable disease (Table 4).

Two patients (5%) presented local recurrence of their disease during follow-up at 28 and 16 months, respectively. Both patients (Stage Illob) had been operated on using open approaches; one of them had undergone a surgical rescue by SNES and another through a preauricular subtemporal approach. Both of them remain free of disease at present.

During follow-up, there were no deaths due to the tumour or complications thereof, nor due to intercurrent causes. At present, 5 patients remain with visible tumours in imaging tests (12%) and 38 patients (88%) are free of disease. All patients who remain with tumours were operated by open techniques (P>.05).

**Discussion**

A JNA tumour is histologically benign, but it can be locally aggressive and destructive. All patients in our study were male except for one case. The mean age at diagnosis was 16 years, which was similar to that reported by other series. Although there have been cases described in females, a comprehensive review of the anatomopathological study and genetic testing are recommended, given its exceptional occurrence. Our female patient underwent a karyotype, which reported her 46XX condition, subsequently confirmed by her motherhood. Interestingly, in addition to presenting this tumour, this patient also had surgery for a pilonidal sinus, a pathology that is also typical of males.

The aetiology and pathogenesis of JNA are nuclear, but genetic and hormonal factors have been implicated and could explain why the prevalence of these tumours is higher in males.

The presence of recurrent unilateral epistaxis and unilateral respiratory failure in a young male is generally the clinical presentation of patients with JNA. In our study, over half of the patients (56%) presented these symptoms at the time of diagnosis, which coincides with reports by other authors. Consequently, it would be recommendable to perform a nasal examination on every adolescent male with recurrent unilateral epistaxis to rule out JNA. Occasionally, these tumours have a mild initial clinical presentation, with conductive hearing loss secondary to unilateral secretory otitis media. Tumour extension produces rhinosinus symptoms and facial swelling. Visual and neurological deficits may also appear when the orbit, skull base or endocranium are affected. At the time of diagnosis, we confirmed the

<table>
<thead>
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<th>Table 4</th>
<th>Treatment of Persistent Disease.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Fisch Stage</td>
</tr>
<tr>
<td>1</td>
<td>IlVa</td>
</tr>
<tr>
<td>2</td>
<td>IlVa</td>
</tr>
<tr>
<td>3</td>
<td>Ilia</td>
</tr>
<tr>
<td>4</td>
<td>Ilb</td>
</tr>
<tr>
<td>5</td>
<td>Ilia</td>
</tr>
<tr>
<td>6</td>
<td>Ilb</td>
</tr>
<tr>
<td>7</td>
<td>Ilb</td>
</tr>
<tr>
<td>8</td>
<td>IlVa</td>
</tr>
</tbody>
</table>
presence of facial swelling in 12% of patients in our series and of neurological involvement in less than 5%. These figures are similar to those described in the literature.\textsuperscript{14} Early diagnosis in initial stages would justify the scarcity of neurological and compressive symptoms. Delay in diagnosis was common before the introduction of imaging methods and when this was obtained, patients presented advanced-stage tumours with frequent intracranial and skull base involvement. In our case, the average delay between symptom onset and surgery was 12.5 months, as in other series.\textsuperscript{13}

The diagnosis of JNA is based on clinical history, physical examination and nasofibroscopy. In the latter, the most common sign is the presence of a reddish mass located at the back of the nasal cavity and the cavum, often lobed and hard. A differential diagnosis should be conducted with other benign tumours such as Killam polyps, meningioma or inverted papilloma, and with malignant tumours such as sarcoma, chordoma and epidermoid carcinoma. However, if the suspected diagnosis is JNA, biopsy should not be performed due to the risk of profuse bleeding.

All patients should undergo imaging studies (CT and MRI) to guide the diagnosis and, above all, to stage the tumour, observe tumour extension and plan treatment, as well as to subsequently assess tumour persistence and recurrence.\textsuperscript{7}

There are several classifications of JNA,\textsuperscript{15,16} but that by Andrews–Fisch\textsuperscript{10} is the most widespread in the literature. In our study, 67% of patients presented JNA corresponding to advanced stages (III or IV in the Fisch classification) and 34% suffered intracranial extension. This figure is slightly higher than that observed by some authors,\textsuperscript{17} who estimate it at between 10% and 20%. This would be partly justified by the fact that 53% of cases were referred from other centres, and these usually coincided with the more advanced cases.

Recently, due to the important role of endoscopic surgery in the treatment of these tumours, Snyderrmann et al.\textsuperscript{17} have proposed a new JNA staging system based on two factors: the route of intracranial invasion and the vascular supply. These authors reported that tumour size and sinus extent of the disease are less important factors in predicting complete tumour excision, a philosophy which we share. Furthermore, they report that residual tumour vascularisation after embolisation is related to intraoperative bleeding, the rate of recurrences and the need for a second operation.

Angiography is important in determining the pattern of blood supply. Preoperative tumour embolisation promotes a better control of intraoperative bleeding and a possible reduction in tumour size. Both factors are associated with a better visualisation of the surgical field during surgery (especially in endoscopic procedures) which entails a greater likelihood of complete tumour resection, a key factor in the absence of disease recurrence.\textsuperscript{18} Of the two patients who relapsed in our series, one had not been embolised. Vascular supply to the tumour comes mainly from branches of the external carotid artery (internal maxillary or ascending pharyngeal), as observed in our series (79%). Those branches of the internal carotid artery arising from neangiogenesis phenomena that influence tumour growth cannot be embolised. In our study, the internal carotid artery was involved in 21% of cases. In some cases (7% in our series), irradiation is clearly bilateral and both maxillary arteries should be embolised if possible, since backflow by one of them could hinder surgery. Embolisation does not usually cause sequelae, although some cases of amaurosis and hemiplegia have been described,\textsuperscript{19} as well as paralysis of cranial nerve pairs. In the present study, 74% of patients were embolised and there were no notable complications.

In our study, we found no significant overall differences in the requirements for intraoperative and postoperative transfusion of packed red blood cells among those patients who underwent tumour embolisation before surgery and those who did not. These data contrast with the obvious evidence and the data published by other authors, who observed that embolisation reduces the need for transfusions.\textsuperscript{20} However, in procedures on tumours that have not been embolised, blood loss is reduced by controlling and ligating the nutrient vessels (mainly the internal maxillary artery) prior to manoeuvres typical of tumour removal.

Various treatments have been proposed, although the treatment of choice for all stages of JNA is surgery. Spontaneous regression of untreated JNA has been observed only occasionally.\textsuperscript{21}

External stereotactic radiotherapy (RT) as the only treatment is indicated only for certain inoperable tumours, with intracranial extension and involvement of structures such as the cavernous sinus or optic chiasma.\textsuperscript{22} However, in certain occasions, stereotactic RT and radiosurgery are used as an adjunct treatment for surgery in cases of tumour persistence in close proximity to intracranial neurovascular structures. Normally, RT fails to reduce the tumour, but stops its growth. Some authors link the administration of RT with the appearance of facial hypotrophy and cases of JNA becoming malignant.

The use of chemotherapy or hormone treatment is not recommended.\textsuperscript{23} The latter was applied, given the possible involvement of androgen receptors in JNA pathogenesis. However, recent studies have failed to show any usefulness.\textsuperscript{24}

The purpose of surgery is complete tumour resection with the least possible morbidity. The choice of surgical approach should be based on tumour stage, extent and location.\textsuperscript{25} The surgeon’s experience is decisive in the choice of either approach and experienced surgeons may consequently use more limited approaches to remove larger tumours. However, complete resection of the tumour requires sufficient surgical exposure.

External approaches are divided into anterior, inferior and lateral. Except for those cases where an anterior approach is used by degloving, the rest require facial and/or intraoral incisions; with the aesthetic consequences entailed. The inferior approaches (transpalatal, transoral-transpharyngeal) can approach the cavum and the nasal fossae, and have been used in JNA in Fisch Stages I and II. However, given the usefulness of the endoscopic approach, these procedures have become obsolete. The anterior transfacial approaches (or preferably through degloving) expose the nasal fossa and can be extended towards the paranasal sinuses and the pterygopalatine fossa. Due to its sequelae, open facial translocation is hardly ever employed and those cases in our series belong to the early years of the review. If the involvement of the infratemporal fossa or the middle cerebral fossa is broad or intradural, it is safer to access through a lateral approach such as the subtemporal-preauricular approach. With the latter approach, it is possible to expose and control the internal carotid artery.
and the temporal lobe. In our series, 72% of patients underwent open surgery, with anterior facial translocation by degloving and subtemporal-preauricular approaches being the most commonly used. The high frequency of open techniques in our cases might be because 68% of our JNA cases were in advanced stages. Notable complications were recorded in only 4 JNA cases in Stage III, which were resolved without the need for aggressive measures. This complication rate (13%) is acceptable with this type of approaches. If a reconstruction with temporal flap has to be carried out, it must be borne in mind that resections very lateral to the tumour or even embolisation could damage or thrombose deep temporal arteries, making the use of this muscle impractical, due to the danger of its necrosis.

Lastly, if the involvement of the anterior fossa or planum sphenoidale is very broad or intradural, a craniofacial or subcranial approach with acceptable morbidity can be used. In our case, 2 JNA patients in Stage Iva were intervened, with total excision of the entire tumour in one case and incomplete excision in the other, without notable morbidity.

Endoscopic resection of JNA, alone or in combination with limited external approaches, is the treatment of choice for JNA in early stages; in certain centres with sufficient experience, JNA in advanced stages are also intervened. Due to the rapid development of this surgery, it can be expected that, with the help of neuronavigation, and in expert hands, tumours with intracranial invasion can be resected safely by SNES. This type of surgery allows a radical approach in tumour resection, which is minimally invasive, avoids external scars and is associated with minimal morbidity. Since 1995, 12 of the 42 patients included in our study (28%) underwent endoscopic surgery and they all belonged to Stages I and II. In all of them, it was possible to achieve complete tumour resection without complications and without any recurrence being observed. These results are comparable to those observed in other more favourable patient series. A technical detail to note is the need for drilling the pterygoid canal at its roots (following the vidian nerve), rostrum and ipsilateral sphenoid floor, as well as sufficient lateral exposure of the pterygopalatine fossa to ensure proper removal.

One of the advantages of endoscopic approaches is less intraoperative blood loss, although this also depends on the availability and quality of embolisation, as well as tumour stage and location. In addition, hospital stay for SNES is usually less than for open surgery. By contrast, resection by SNES could represent a disadvantage in relation to the duration of the surgery, a fact remedied by the improvement of the learning curve and which can easily be assumed in light of the advantages it offers.

 Cure rates for JNA by surgical treatment, regardless of the approach route, are generally 80%–100% in exclusively extracranial tumours and 70% in those where intracranial invasion is observed. The percentage of recurrences in patients in our series was 5%, in all cases involving patients who underwent open surgery. This figure is lower than that in other series of patients (up to 50%) including those with endoscopic approaches. Both patients were rescued; one through SNES and another through a subtemporal infratemporal approach, and they are currently free of disease.

Of the 8 patients in whom residual tumour was observed, 3 are currently tumour-free after one surgical rescue, one external RT and one radiosurgery, respectively. In 5 of them, we observed no radiological progression of the tumour or symptoms derived thereof during follow-up (78 months on average). This supports the consideration of conservative surgical treatment in certain JNA cases with extension close to vital structures, along with a possible postoperative RT treatment. At present, it appears that the application of radiosurgery in tumour remains close to these structures would improve disease control without adding significant morbidity.

Conclusions

The treatment of choice in JNA is surgery. The endoscopic approach is the route of choice for early stages (I and II) and, at present, in the hands of experienced surgeons, also for advanced-stage tumours, because it represents lower patient morbidity in relation to external approaches, without increasing the risk of tumour persistence or recurrence. However, open surgery through limited approaches (facial translocation by degloving and subtemporal preauricular approach) continues to play an important role in advanced tumours, without causing significant morbidity or major aesthetic sequelae. Preoperative embolisation is recommended in all cases. Subtotal resection of the tumour, along with postoperative radiosurgery and observation, is a valid strategy for patients with intracranial involvement or involvement of vital structures.

Conflict of Interests

The authors have no conflicts of interest to declare.

References


