Influence of Blood Flow on the Neuroma Formation after Transposition of the Nerve Stump into Vein: Experimental and Clinical Study

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Abstract

We study the influence of blood flow on the neuroma formation after transposition of the nerve stump into a vein. A total of 30 rats were divided into two groups. In group (I), a 10-mm segment of the femoral vein was excluded from the blood stream. A venotomy was performed in the middle of this segment. The proximal nerve stump of femoral nerve was transposed into the lumen of the femoral vein via a venotomy and held with an epineural suture through the venous wall. In group (II), the same technique was used as in group (I) but without exclusion of the vein segment from blood flow. The control side of the femoral nerve was transected and then was left in place. All animals were sacrificed after 28 weeks. Histopathological evaluation was performed postoperatively; serial transverse sections were made to find the largest diameter of the neuroma. Selected specimens were processed for electron microscopy examination. The following parameters were assessed in both the groups: cross-sectional area of neuromas; myelinated axons; and neural tissue to connective tissue ratio. In group (I), the proximal end of the tibial nerve formed a nonclassic neuroma. In group (II), the proximal end of the tibial nerve formed a nonclassic neuroma smaller in diameter than group (I). The proximal end of the femoral nerve of the control sides in both groups formed a classic neuroma larger in diameter than the experimental sides in both the groups. A Kruskal–Wallis H test showed that there was a statistically significant difference in myelinated axons between the different groups, $X^2(3) = 36.19$, $p < 0.001$. The average neural tissue to connective tissue ratio in the control group (I) ranged from 39.2 to 85.8%, but on the experimental side, it was more or less equalized. The average of a neural tissue to connective tissue ratio of the group (II) ranged from 59.1 to 63.9% in the treatment sides as compared to 28.6 to 82.4% in the control sides. The clinical experience utilizing the same technique in the treatment of 10 patients of painful neuromas of the superficial radial nerve and digital nerves were presented with encouraging results. The blood flow has a considerable effect on neuroma formation. We recommend a further study to know the fine details about the exact role of blood as the bloodstream may carry away neurotrophic factors that may also be released by the nerve stump itself.

Keywords

- influence of blood flow on the neuroma formation
- transposition of the nerve stump into vein on neuroma
- management of neuroma

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Introduction

Neuromas result from abnormal proximal nerve regeneration after a peripheral nerve lesion. According to Herndon¹ 30% of all neuromas are painful and may lead to disuse atrophy of an extremity. Although 30% of neuromas cause pain, there is no universally successful method of prevention and treatment of painful neuromas. Yüksel et al² mentioned that the undamaged perineurium is an impenetrable barrier for regenerating axons, but when it is damaged, fascicular escape can occur.

Chiu et al³ in their experimental work on interpositional vein grafts for nerve defects, they observed that growth of the axonal was more rapid and more organized along the inner surface of the vein wall.

Tada et al⁴ were utilizing the principles of on nerve-to-vein transfer for neurotization of denervated muscles; they observed that there was no axonal regeneration inside the blood-filled muscle vein, but the axonal regeneration occurred outside the vein through the scar tissue.

According to the researchers mentioned above, there is an interaction between the vessel endothelium and the regenerated axons. Also, there is an adverse effect of the blood on the regenerating axons.

Herbert and Filan⁵ reported a dramatic, immediate pain relief, with 86% success after the initial surgery and 100% success after revision. Also, Koch et al⁶ reported that there are interactions between regenerating axons and the vessel endothelium, with an adverse effect of blood on nerve regeneration. According to the above-mentioned encouraging results, the current work was undertaken to study the influence of blood flow and transposition of the proximal nerve stump into an adjacent vein on the formation of a neuroma.

Material and Methods

This study was divided into two main parts:

Experimental Part

The research has been performed at the Medical Experimental Research Center at the Mansoura University from February 2013 to December 2015. A total of 30 adult Sprague-Dawley rats, with an average weight ranging from 350 to 430 g were chosen randomly, as regard their sex, and divided into two equal separate groups (15 rats per group). The rats were anesthetized with 20 mg/kg body weight of intraperitoneal sodium thiopental after induction of anesthesia with halothane inhalation; a maintenance dose of intraperitoneal sodium thiopental was administered if needed. Both the hind limbs were shaved and prepared in a sterile fashion with povidone-iodine solution. The rats were immobilized on a wax dish in a supine position. The operation was performed using the operating microscope.

On the right side exposure of the femoral nerve and vessels via inguinal crease skin incision, and the femoral nerve was identified and traced distally to isolate its medial and lateral branches (►Fig. 1).

Group (I) includes both experimental and control sides in the same animal. The femoral nerve and femoral vein were

dissected using the magnification on both sides. A 10-mm segment of the femoral vein was excluded from the blood stream with two 8-0 nylon ligatures. A venotomy was performed in the middle of this segment with microscopic magnification, and all blood inside this segment was irrigated with saline. The femoral nerve was transected, mobilized, and the proximal nerve stump was transposed into the lumen of the femoral vein (at least 5 mm of the nerve was inserted into the vein) via a venotomy in an end-to-side fashion in this segment of the femoral vein and held in position with an epineural 10-0 nylon suture through the venous wall. The venotomy was closed around the nerve with 10-0 nylon sutures (►Figs. 1 and 2A).

The control side of the femoral nerve was transected, mobilized to the same fashion as for the experimental side, and then was left in place, and the wounds were closed with absorbable sutures (►Figs. 1B and 2B).

Group (II) includes both experimental and control sides in the same animal. The femoral nerve and vein were identified and dissected under magnification on both the sides. All the procedures were followed as in group (I) but without exclusion of femoral vein segment from the bloodstream (►Figs. 1C and 2C). The control side was the same as mentioned in group (I) (►Figs. 1B and 2B).

Postoperative

The animals were allowed to recover, then housed in the cages, and maintained in a 12-hour light-dark cycle with food and water available ad libitum.

The animals were followed up for 28 weeks after the operation and then sacrificed for the harvesting of the specimens. All animals were anesthetized with intraperitoneal sodium thiopental (20 mg/kg). The previous incision was used for exposure of the femoral nerve and vein.

Tissue Preparation for Pathological Examination

The specimens of both experimental and control side were stained with hematoxylin-eosin, Luxol (Sigma-Aldrich) fast, and serial transverse sections were made to find the largest diameter of the neuromas. The largest diameter of the neuromas was measured under the light microscope. Specimens from five rats in each group were fixed in 3% glutaraldehyde and embedded in Epon 812 resin. Semithin sections were stained with toluidine blue, and ultrathin sections were stained with uranyl acetate and lead nitrate for electron microscopy.

Morphometric Study

Ten randomly chosen fields of the cross-sections of each specimen were used to carry out cross-sectional area of neuroma; myelinated axons, and the neural tissue to connective tissue ratio.

Measurements were calculated using image analyzer (Lucia Q500 MC software) as the following:

1. Cross-sectional area of neuromas
2. Myelinated axons
3. Neural tissue to connective tissue ratio

Fig. 1 A schematic drawing of the surgery of both groups and controls. (A) Group (I) diagram showing a 10-mm segment of the femoral vein was excluded from the blood stream. The femoral nerve was transected, mobilized, and the proximal nerve stump was transposed into the lumen of the femoral vein via a venotomy in an end-to-side fashion. (B) In both the groups the nerve was transected in the control sides and left in place. (C) Group (II) diagram showing the femoral vein was implanted into the femoral vein without exclusion from the blood stream group (II).

The results were calculated, and the statistical analysis was performed using one-way analysis of variance (ANOVA) with least significant difference (LSD). Post hoc test for the cross-sectional area of neuromas, and a Kruskal–Wallis H test was used for myelinated axons.

Clinical Study

Ten patients with symptomatic neuromas underwent resection of the neuroma and implantation of the proximal stump into an adjacent vein. Six patients were men; four were women. Patient age ranged from 18 to 48 years (average, 33 years) (–Table 1). Etiologies were trauma, after wrist surgery, laceration, and gunshot injury. The affected nerves were a superficial branch of radial nerves ($N = 5$), and the palmar digital nerves ($N = 5$). The duration of painful symptoms at the time of operation ranged from 3 to 9 months. Diagnosis of painful neuroma was based clinically on the presence of typical neuromatous pain described as an electric shock, sometimes as spontaneous discharge and frequently elicited through any pressure or contact on the area corresponding to the stump of the sectioned nerve. Tinel–

Hoffmann sign positive in all cases. Three patients have previously undergone surgery.

Operative Technique

Tinel sign localized preoperative marking of the site of neuroma pain. Surgery was performed under general anesthesia or regional nerve block, the patient in prone position, and using tourniquet control. Exploration and identification of the neuromas were done through the previous incision. The neuromas appear grossly as ovoid, firm mass at the proximal nerve stumps, and adherent to the surrounding structures even to the periosteum by fibrous tissues. After identification and mobilization of the neuromas, the neuromas and scar tissue were excised back to healthy nerve tissue to prevent new scar tissue formation in the proximal and distal nerve stumps. Then the appropriate mobilization and transposing of the nerve stump into an adjacent subcutaneous vein were done under loupe magnification using microsurgical instruments. All the nerve stumps were mobilized to approximately 3 to 4 cm. The nerve was transposed into the vein in end-to-side fashion via a lateral venotomy. The vein segment was not excluded from the

Fig. 2 (A) Photograph showing the experimental side of group (I), showing a 10-mm segment of the femoral vein was excluded from the blood stream. The femoral nerve was transected, mobilized, and the proximal nerve stump was transposed into the lumen of the femoral vein via a venotomy in an end-to-side fashion. (B) Photograph showing the control sides in both groups. (C) Photograph showing the femoral vein was implanted into the femoral vein without exclusion from the blood stream group (II).

bloodstream (► **Figs. 3** and **4**). Suitable part of the proximal nerve stump (5–10 mm) was held in position inside the vein with an epineural 10–0 nylon suture through the venous wall. The venotomy was closed all around the nerve with 10–0 nylon sutures. Finally, the anastomosis was buried in the surrounding muscle if possible. Closure of the incision in two layers was done using vicryl 4/0 for the subcutaneous layer and prolene 3/0 for the skin. Systemic prophylactic antibiotic continued for 5 days, analgesic anti-inflammatory drugs for 3 days. All the excised neuromas were subjected to tissue diagnosis and revealed the typical histological picture of the neuroma. The follow-up period ranged from 24 months to 5 months (average 14.6 months).

Assessments of the results were done subjectively and objectively by using the labored grading system (► **Table 2**).⁷ Some minor complications occurred such as wound dehiscence, infection and improved with conservative treatment.

Results

Experimental Study

In group (I), specimens from 12 rats were only studied but 2 rats died before collection of the samples, and the nerve stump was avulsed in 1 rat. In group (II), specimens from 12 rats were studied, 1 rat died, and the nerve stump was displaced in 2 rats.

On gross examination of the control side, marked fibrosis was noted surrounding the femoral nerve with a round to ovoid mass at the proximal nerve stump.

Histological examination of the all the control specimens showed neuroma formation which consists of round to ovoid mass of disorganized nerve fascicles of haphazardly arranged axons, Schwann cells and spindle cells that were a mixture of Schwann cells and fibroblasts in dense collagenous matrix, without the parallel organization which is seen in normal nerve (► **Figs. 5C** and **6A**).

Table 1 Patient's data and follow-up period

Patient no.	Age (y)	Sex	Type of injury and nerve involved	Follow-up time (mo)
1	25	M	Painful neuroma in superficial radial nerves after previous arthroscopy of the right hand at wrist joint	24
2	35	M	Posttraumatic painful neuroma in digital nerve of left middle finger after	22
3	40	F	Posttraumatic painful neuroma in digital nerve of left ring finger	21
4	36	M	Painful neuromas in left superficial radial nerves after gunshot injury	18
5	18	M	Painful neuromas in both digital nerve of right index finger nerves after previous amputation of the distal phalanx	15
6	27	F	Painful neuromas in digital nerve of right middle finger nerves after previous amputation of the distal phalanx	12
7	45	M	Painful neuromas in digital nerve of left ring finger after direct trauma to the finger	11
8	48	M	Painful neuroma in superficial radial nerves after previous surgery of wrist joint of the right hand	10
9	36	F	Painful neuroma in right superficial radial nerves after direct trauma of the hand at wrist joint	8
10	20	F	Painful neuroma in superficial radial nerves after previous gunshot of the left hand at wrist joint	5
Average	33			14.6

Histopathology studies of the nerve stumps in the experimental sides of both groups (I) and (II) showed more organized neural tissues. The small fascicles were organized and arranged in a parallel direction, and there were more myelinated axons and less connective and fibrous tissue in comparison with the control side (►Figs. 5A, B and 6B).

Electron microscopic examination of the neuroma revealed that there are abundant small myelinated fibers with thin irregular myelin sheath scattered in dense collagen fibers. Also, there are a plenty of the newly growing regenerated groups of unmyelinated axons. The fibers are arranged haphazardly (►Fig. 7A).

Electron microscopic examination of experimental sites in both groups' reveals, both myelinated and unmyelinated nerve fibers were present with the near normal appearance in shape with a thin myelin sheath. The axons appeared in groups with marked vasculature and well evident Schwann cells in between. The axons were arranged with each other in a more orderly fashion than in controls. The electron microscopy confirmed the light microscopic findings (►Fig. 7B).

Morphometric Study

Measurements of 10 randomly chosen fields were calculated using Lucia Q500 MC software as the following:

Cross-Sectional Area of Neuromas

The statistical analysis was performed using one-way ANOVA with LSD. Post hoc test for the cross-sectional area of the neuroma was done. The results were reported as a mean $\pm$ standard error of the mean. Values were considered significant at $p < 0.05$. The software SPSS, version 18 was used (IBM Corporation).

1. As regard to the cross-sectional area of neuromas, larger neuromas were apparent in the control sides than the experimental sides in both groups (►Fig. 8).

In group (I), the mean of the cross-sectional area of the regenerated masses was $2.11 \pm 0.15 \text{ mm}^2$ (range, 0.8–2.7 mm^2). However, in the group (II), the mean of the cross-sectional area of the regenerated masses was $0.92 \pm 0.08 \text{ mm}^2$ (range, 0.4–1.4 mm^2).

Comparing the means of the cross-sectional area of the neuroma in control and experimental sides of the group (I) reveals no statistically significant differences $p < 0.06$. Comparing the mean of the cross-sectional area of the neuroma in control and experimental sides of the group (II) reveals statistically significant differences $p < 0.001$.

Comparing the mean of the cross-sectional area of the neuroma in the experimental side in both groups reveals statistically significant differences $p < 0.05$ (►Table 3).

2. Myelinated axons: A Kruskal–Wallis H test showed that there was a statistically significant difference in myelinated axons between the different groups, $X^2(3) = 36.19$, $p < 0.001$ with mean ranks as shown in ►Table 4.

3. The ratio of neural tissue to connective tissue

In group (I), the average neural tissue to connective tissue ratio in the control side was 39.2 to 85.8%, but on the experimental side, it was more or less equalized. In group (II), the average of neural tissue to connective tissue ratio in the treatment side was 59.1 to 63.9% versus 28.6 to 82.4% in the control sides.

Fig. 3 (A) Preoperative photograph showing, scar after previous arthroscopy of the right wrist joint. (B) Intraoperative photograph showing the neuroma in SRN. (C) Intraoperative photograph showing the implantation of the SRN into adjacent superficial vein. SRN, superficial radial nerve.

Results of the Clinical Study

Ten patients with symptomatic neuromas underwent resection of the neuroma and implantation of the proximal stump into the adjacent vein without exclusion from the blood stream. The entire patients were subject to the

postoperative evaluation by using the Laborde et al⁷ grading system.

Subjectively six patients (60%) experienced excellent results. This means complete permanent relief of pain. Three patients (30%) experienced good results (mild sensitivity to

Fig. 4 (A) Intraoperative photograph showing the exploration of left digital nerve neuroma of the left ring finger. (B) Intraoperative photograph showing the implantation of the digital nerve into adjacent superficial vein.

Table 2 Grading system

Grade	Meaning
Pain	
I	None
II	Mild, no interference with daily activities
III	Moderate, work is possible but there is some limitation in the use of the extremity
IV	Severe, cannot work or use extremity
Patient acceptance of surgery	
I	Improved, no interference with daily activities
II	Improvement, slight interference but work is possible
III	Improvement, interference in daily activities unable to work
IV	No change
V	Worse
Tinel's sign	
I	None
II	Mild, slight paresthesia
III	Moderate very uncomfortable
IV	Severe, in ability to use the extremity
Objective (function outcome)	
I	Normal, no interference with daily work
II	Some interference with daily work
III	In ability to use the hand

Source: Adapted from Laborde et al.⁷

direct percussion at the site of nerve implantation, not interference with daily work). In one patient (10%) experienced bad results (painful symptom recurred 3 months after surgery). We attributed this to disruption of the nerve union due to forcible trauma to the site of implantation postoperative. Subjective patient acceptance of surgery, nine patients accept the results of surgery except for one patient who did not accept that results. Objectively for Tinel's sign and function, six patients (60%), revealed no hyperesthesia, or pain but three patients (30%), revealed mild pain and hyperesthesia, and one patient was moderately uncomfortable (10%) (► **Table 5**).

Discussion

There are numerous techniques have been described for treatment of painful neuromas such as epineural barriers, ligation, implantation into muscle or bone, silicone caps, centro-central repair, end-to-side neurorrhaphy concept and injection of steroids or other chemical agents.^{8–20} Until now, there is no universally successful method of prevention and treatment of painful neuromas.

In our study, we found no statistically significant differences of the cross-sectional area of neuroma between control and treatment sides in group (I). There is a statistically significant difference of cross-sectional area of neuroma in the experimental side of groups (I) and (II) but the histo-

morphological criteria of two groups more or less the same. This may indicate that the blood flow has a role in the formation of a nonclassic neuroma. The blood may contain certain neurotrophic factors (interleukins or other growth factors) affecting the neuroma.

Chiu et al³ in their experimental work on interpositional vein grafts for nerve defects, they found that growth of the axonal was more rapid and more organized along the inner surface of the vein wall.

Tada et al⁴ were utilizing the principles of nerve-to-vein transfer for neurotization of denervated muscles; they observed that the axonal regeneration did not occur inside the blood-filled muscle vein, but the axonal regeneration occurred outside the vein through the scar tissue.

Strauch et al²¹ in their study found that there was no extension of the nerve tissue into the lumen of the vein. Also, they think that axons or Schwann cells or both will not grow into the lumen of the vein that already is occupied by flowing blood. Also, reendothelialization of the vessel occurs over the neuroma. No thrombosis was identified, suggesting that either nerve tissues are not thrombogenic. There was no extension of nerve tissue outside the vein, suggesting that accurate sealing of the epineurium to the tunica adventitia could contain the regenerated nerve or prevent the target-derived neurotrophic factors from reaching the nerve endings through the surrounding soft tissue.

Fig. 5 (A) Histological examination of the nerve end in the vein lumen on the experimental side group (I). (B) Histological examination of the nerve end in the vein lumen on the experimental side group (II). The axons and spindle cells were arranged more parallel to each other and more closely resembled normal nerve). (C) Histological examination of a neuroma on the control side (stained with hematoxylin–eosin, $\times 20$).

From the research mentioned above, we can conclude that there is an interaction between the vessel endothelium and the regenerated axons. Also, there is an adverse effect of the blood on the regenerating axons.

Koch et al⁶ utilizing the same theory, there is an interaction between regenerating axons and the vessel endothelium, with an adverse effect of blood on nerve regeneration. In this technique, the affected nerve is identified proximal to

Fig. 6 (A) Semithin section (TS) the control side it shows neuroma with haphazardly arranged spindle cells and axons that are characteristic of neuroma (stained with toluidine blue, $\times 40$). (B) Semithin section (TS) of the experimental side. It shows the regenerating nerve axons. The axons and spindle cells were arranged more parallel to each other and more closely resembled normal nerve (stained with toluidine blue, $\times 40$. TS, transverse section).

Fig. 7 (A) Transmission electron micrograph of the neuroma (control side), showing the newly growing regenerated groups of unmyelinated axons of the femoral nerve. It shows UMNV and MNV and dense collagen fibers. The fibers are arranged haphazardly with thin myelin sheath thickness. Schwann cells are also shown. (B) Transmission electron micrograph of the experimental side, showing the newly growing regenerated groups of axons of the femoral nerve, with near normal MNV and UMNV. The fibers are arranged more orderly (stained with uranyl acetate and lead citrate, magnification $\times 2,800$). MNV, myelinated nerve fibers; UMNV, unmyelinated nerve fibers.

the neuroma and dissected distally to free the neuroma from surrounding scar tissue, resected back to the healthy nerve, and mobilized sufficiently to allow implantation into an adjacent vein without tension. The nerve is then inserted into the vein and held with an epineural suture through the venous wall.^{5,6}

Herbert et al⁵ in their study reported dramatic, immediate pain relief, with 86% successful after the initial surgery and 100% successful after revision. Herbert et al also showed histologically that nerve stumps transposed into a vein lumen showed more organized endoneural architecture, small fascicles oriented in the same direction, and a high

rate of myelinated axons. Advantages of this technique are that subcutaneous veins are readily available throughout the body; suitable veins are usually in proximity, making substantial nerve mobilization unnecessary; and the nerve end is situated well within the vein lumen, preventing regenerating axons from accessing the tissue outside the vein.⁶

In the current study, there are statistically significant differences between the means of cross-sectional area of the neuroma in control and experimental sides of group (I).

Also, there are statistically significant differences between the means of cross-sectional area of the neuroma in control and experimental sides of group (II).

Fig. 8 Histogram illustrating the cross-sectional area of neuromas in control and experimental sides in both the groups.

Table 3 The results of one way ANOVA with LSD. Post hoc test on cross-sectional area

Group	Cross-sectional area
Control group (I)	3.08 ± 0.5 ^a 1.5–6
Experimental group (I)	2.11 ± 0.15 ^a 0.8–2.7
Control group (II)	3.12 ± 0.49 ^a 1.3–6
Experimental group (II)	0.92 ± 0.08 ^{bcd} 0.4–1.4

Abbreviations: ANOVA, analysis of variance; LSD, least significant difference.

Note: Data expressed as mean ± standard error of mean.

^aSignificant versus experimental group (II).

^bSignificant versus control group (I).

^cExperimental group (I).

^dSignificant versus control group (II).

Table 4 Results of Kruskal–Wallis H test

Group	Number	Mean rank
(I) Control ligated	12	12.67
(I) Experimental ligated	12	31.17
(II) Control	12	14
(II) Nerve in blood stream	12	40.17

Note: Results showed that there was a statistically significant difference in myelinated axons between the different groups, $X^2(3) = 36.19$, $p < 0.001$ with mean ranks as shown in the table.

Also, there are statistically significant differences between means of cross-sectional area of the neuroma in experimental side in both the groups.

There were statistically significant differences concerning the size of neuroma between the experimental sides of two groups but the histomorphological criteria were more or less the same.

Also, more myelinated axons were present in the experimental sides in both the groups and revealed statistically significance difference for both the groups.

Also, the ratio of neural tissue to connective tissue, in group (I) the connective tissues were more than the neural tissues in the control side, but in the experimental side the

ratio of neural tissue to connective tissue was more or less equal to each other. In group (II), there were more connective tissues than the neural tissues in the control side (28.6–82.4%) but in the experimental side it ranged from 59.1 to 63.9%. Our explanation of these statistically significant differences of the diameter of nonclassic neuroma between the experimental side in both groups may be due to the fact that blood stream carry certain neurotropic factors that are released by the nerve stump itself.

Koch et al²² were using the same technique; they stated that there were significant differences concerning neuroma size between the two groups but not in the histomorphological criteria that were analyzed, and the bloodstream in the veins may be the reason for this difference because the bloodstream may have carried away neurotropic factors that are released by the nerve stump itself. They failed to exactly determine the possible effects of endothelium and of blood in the prevention of neuroma formation in this experiment because they found liquid blood in almost of all the vein lumens. Fortunately, in current study we did not find liquid blood in the lumen of the excluded vein segment as mentioned by Koch et al so we can conclude the significant changes in nonclassic neuroma in group (II) are due to the blood flow.

Low et al²³ implanted the medial branch of the femoral nerve into the femoral vein and fixed it to the adventitia with epineural sutures. Their results concerning the size of neuroma were more or less similar to our results. They found more degenerated nerve fibers in the treatment sides with electron microscopy.

In the current experimental study three nerves were avulsed from the vein, so we advise for proper insertion of enough length of freed nerves and accurate fixation into the vein. This is one of the causes of recurrence of neuroma.

The limitations of the study and potential risks of the technique:

1. Needs learning curve about venotomy site and proper insertion of enough length of freed nerves and accurate fixation into the vein
2. Nearby vein not always available
3. High rate of the nerve avulsion
4. Theoretically, the blood clotting and risk of embolism may occur and why not to administrate a prophylactic anticoagulant therapy, actually no thromboembolic manifestation were recorded. We plan to study this point in the future.

Table 5 Results according to evaluation criteria

	Subjective criteria										Objective criteria						
	Pain				Patient acceptance					Tinel's signs				Functional outcome			
	I	II	III	IV	I	II	III	IV	V	I	II	III	IV	I	II	III	
Preoperative				10				3	6				10		6	4	
Postoperative	6	3		1	9		1			6	3	1		6	3	1	

Strauch et al,²¹ think that axons or Schwann cells or both will not grow into the lumen of the vein that is already occupied by flowing blood. In addition, reendothelialization of the vessel occurs over the neuroma. No thrombosis was identified, suggesting that either nerve tissues are not thrombogenic.

Conclusion

The blood flow has a considerable effect on formation of nonclassic neuroma. A further study is recommended for confirming that the blood stream containing certain neurotropic factors affects the neuroma formation.

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