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ARTICLE

Evaluation of the effectiveness of the tuba uterina tubular flap in the peripheral nervous system regeneration in rats

Mehmet Emin Cem Yildirim[a,b], Mehmet Dadaci[a], Bilsev Ince[a], İlker Uyar[a,c], Serhat Yarar[a,d], Pembe Oltulu[e] and Recep Aygul[f]

[a]School of the Medicine, Department of Plastic, Reconstructive and Aesthetic Surgery, Necmettin Erbakan University, Konya, Turkey; [b]Plastic Reconstructive and Aesthetic Surgery Department, Bilecik State Hospital, Bilecik, Turkey; [c]Plastic Reconstructive and Aesthetic Surgery Department, Tokat State Hospital, Konya, Turkey; [d]Plastic Reconstructive and Aesthetic Surgery Department, Konya Numune Hospital, Konya, Turkey; [e]School of the Medicine, Department of Pathology Konya, Necmettin Erbakan University, Konya, Turkey; [f]School of the Medicine, Department of Neurology, Selcuk University, Konya, Turkey

ABSTRACT

Nerve conduits could be used to provide a bridge between both nerve endings. In this study, the tuba uterina of female rats were prepared in a vascularized pedicled flap model and it used as a nerve conduit. The aim was to investigate the effectiveness of a vascularized pedicle nerve conduit and its ciliated epithelium in a sciatic nerve defect. The study was conducted between May and August 2018, and used a total of 60, 14–16-week-old female Wistar albino rats. Six groups were created; Cut and Unrepaired Group, Nerve Graft Group, Flap-Forward Group (Tuba uterina tubular flap, forward direction), Flap-Reversed Group (Tuba uterina tubular flap, reverse direction), Graft-Forward Group (Tuba uterina tubular graft, forward direction) and Graft-Reverse Group (Tuba uterina tubuler graft, reverse direction). Nerve regeneration was evaluated 3 months (90 days) after the surgery by the following methods: (1) *Sciatic Functional Index (SFI) measurement,* (2) *Electromyographic (EMG) assessment,* (3) *Microscopic assessment with the light microscope* and (4) *Microscopic assessment with the electron microscope.* According to the SFI, EMG and microscopic assessments with the light and electron microscope, it was observed that the transfer of tuba uterina tubular conduit as a graft was statistically better in its effect on nerve regeneration than flap transfer, but also indicated that the direction of the ciliated structures had no significant effect. We believe that as this model is improved with future studies, it will shed light on new models, ideas and innovations about nerve conduits.

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Nerve regeneration; nerve conduits; tuba uterina conduit; plastic surgery repair; tissue defect; Microvascular

Introduction

Peripheral nerve injury (PNI) is a significant clinical problem which severely affects the quality of patients' lives. It is a condition that is common in all types of extremity trauma.

Vehicle accidents, occupational accidents, falls, and gunshot wounds are among the main reasons for PNI [1]. Many patients with PNI who undergo nerve repair may often return to their physicians again due to complications such as incomplete recovery, neuropathic pain, or partial or total loss of nerve function [2], because, there are a number of challenges and areas of obscurity in nerve repair.

Tension-free primary nerve coaptation is the gold standard technique in nerve repair [3–6]. When primary repair of the nerve is not possible, the use of nerve grafts is the most common surgical technique for nerve defects. However, nerve grafting can lead to morbidity in the donor area. In addition, there is a limited size of nerve that can be grafted.

Therefore, nerve conduits could be used to provide a bridge between both nerve endings. This procedure can reduce the morbidity that may occur [7,8]. The conduits can be obtained from an artery, vein, nerve sheath or organic-inorganic absorbed or non-absorbable biomaterials. In the literature there are many studies on peripheral nerve repair and nerve conduits. Furthermore, some advantages and disadvantages of autologous nerve conduits and biomaterials have been presented [9–12]. All autogenous materials described in the literature as nerve conduits were used as grafts. A nerve conduit in the form of a vascularized pedicled flap has not been used in any clinical or experimental study. In this study, the tuba uterina of female rats were prepared in a vascularized pedicled flap model and it used as a nerve conduits.

The tuba uterina has some important features which include being a paired organ, having a tubular anatomical structure and offering a reliable pedicle in terms of its use as a nerve conduit by its design as a tubular flap. In addition, since the sciatic nerve generally is used for nerve repair models in rats, the anatomical proximity of the tuba uterina to the sciatic nerve region and the fact that it is a paired organ are other advantages of the tuba uterina tubular flap.

Since the tuba uterina is a paired organ, the fact that it will not affect the metabolism of the rat in nerve regeneration is another important factor in the selection of the tuba uterina as a conduit. We consider the design of an organ section which is a new nerve conduit model with these unique features as an

CONTACT Mehmet Emin Cem Yildirim dr.cem_yildirim@hotmail.com Plastic Reconstructive and Aesthetic Surgery Department, Bilecik State Hospital, Bilecik 42080, Turkey

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opportunity for a new research area and for clinical studies in nerve regeneration.

Thus, the aim was to investigate the effectiveness of a vascularized pedicle nerve conduit and its ciliated epithelium in a sciatic nerve defect.

Methods

The study was conducted between May and August 2018, and used a total of 60, 14–16-week-old female Wistar albino rats. The study was approved by the Necmettin Erbakan University, Meram Faculty of Medicine, Experimental Medicine Research and Training Center Ethics Committee (reference number: 2017-010). All rats were housed in separate cages and supplied with rat food and tap water. The animals were killed by anesthesia overdose. The same suture materials were used in all groups, and surgical techniques were performed by a single surgeon (MECY). 8.0 Nylon sutures (Etilon, Monofilament polyamide suture W2850, Ethicon Ltd, U.K) were used for coaptations, and 3.0 propylene sutures were used for skin suturing.

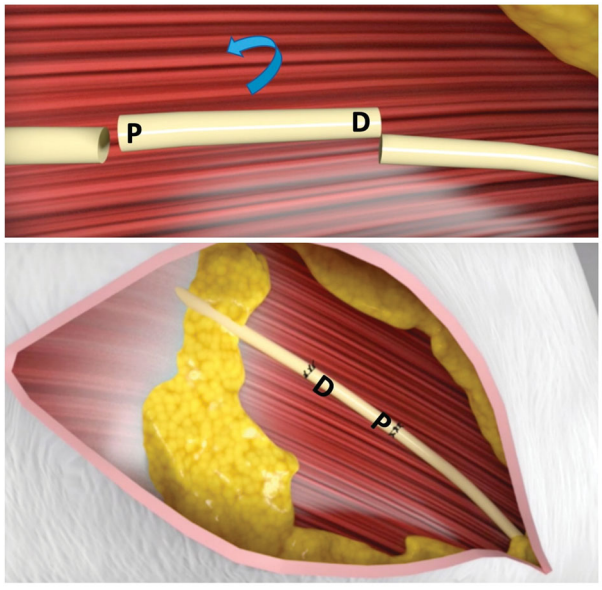

Figure 1. An illustration of the Nerve Graft group.

In this study, six groups were created, and there were 10 randomly selected rats in each group.

The right sciatic nerve of the rats was used, and a 1-cm nerve segment was resected for each rat. Cut and Unrepaired Group; a 1-cm sciatic nerve segment was resected without any repair. Nerve Graft Group; a 1-cm sciatic nerve segment was resected, reversed, placed in the defect and end-to-end coaptation was performed (Figure 1). Flap-Forward Group; the direction of the intramural fimbriae, which are in the histological structure of the rat tuba uterina, was assumed to be the forward direction in the direction from ovary to uterus. The pedicle of a 1.4-cm tuba uterina segment was dissected and protected. This segment was harvested with its pedicle. The tuba uterina tubular flap was passed through a tunnel that was established between the right side of the abdomen and the sciatic nerve region. It was placed on the defect in the proximal-distal direction of nerve trace in its forward direction (ovary-uterus). The proximal and distal nerve stumps were placed inside intubating by 2-mm the tuba uterina tubular flap (Figures 2 and 3). Flap-Reverse Group; Unlike the surgical procedure performed in the Flap-Forward group, the tuba uterina tubular flap was reversed and placed on the defect in the proximal-distal direction of the nerve trace in its reverse direction (uterus-ovary, Figure 4). Graft-Forward Group; the tuba uterina tubular conduit was completely separated from its pedicle and placed on the defect in the proximal-distal direction of the nerve trace in its forward direction as a graft. Graft-Reverse Group; unlike the surgical procedure performed in the Graft-Forward group, the tuba uterina tubular conduit was reversed and placed to the defect in the proximal-distal direction of nerve trace in its reverse direction (uterus-ovary).

Surgical technique

50 mg/kg intraperitoneal ketamine (Ketalar 2%, Pfizer, Istanbul, Turkey) and 10 mg/kg xylazine (Rompun, Bayer, Istanbul, Turkey) injections were used for all surgical procedures.

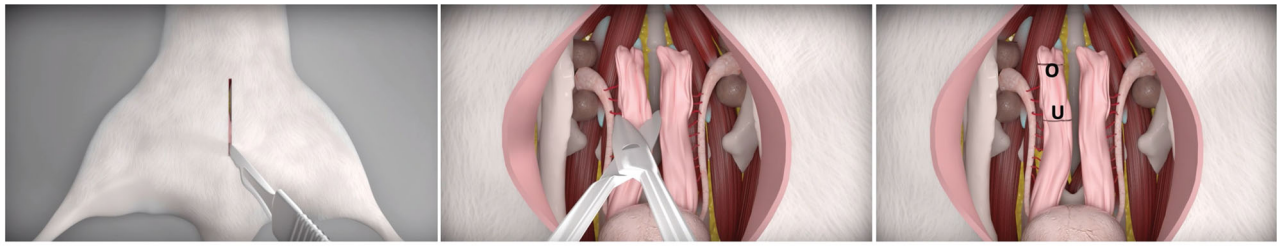

Figure 2. An illustration of the surgical technique stages of the Flap-Forward group. A 2–3 cm long incision was made in the abdominal midline (left); A tubular uterina extending in the form of a strip was found on each side. Tuba uterina tubular conduit was prepared in the form of a flap, preserving the pedicle in the flap groups (middle); The view of direction on the flap. O, Ovary; U, Uterus (right).

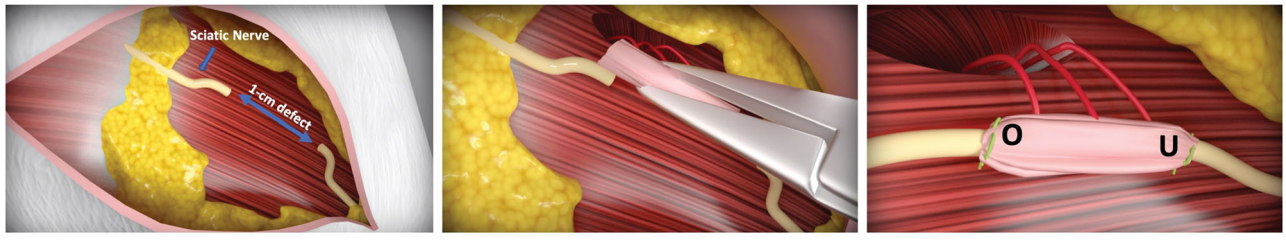

Figure 3. Continuation of the Flap-Forward group. The rat was inverted and laid face down, and an incision was made to reach the sciatic nerve (left); A tunnel was formed from the right abdominal region to the sciatic nerve for flap transposition (middle); the view of direction on the flap O, Ovary; U, Uterus (right).

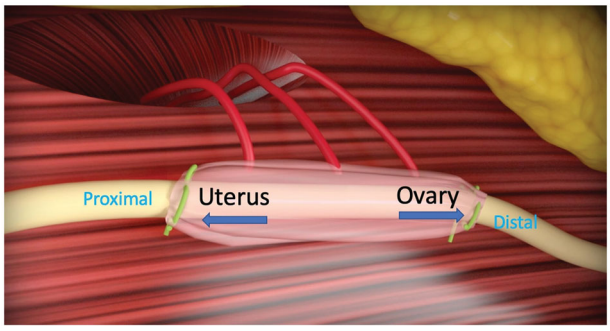

Figure 4. An illustration of the Flap-Reverse group.

In all rats, the right sciatic nerves and right tuba uterina were used. The right posterior leg, gluteal and abdominal regions were shaved.

The rats were first laid on their back on the operation board (Supplementary Video 1). In order to reach the tuba uterina, a 2–3 cm long incision was made in the abdominal midline. The abdomen was reached by crossing the skin and subcutaneous tissue. A tuba uterina extending in the form of a strip was found on each side. The right tuba uterina was dissected. The pedicle of the tuba uterina was clearly explored (Figure 5). The pedicle of the tuba uterina in the graft groups was tied and cut. The tuba uterina's tubular conduit was prepared in the form of a flap, preserving the pedicle in the flap groups.

A sterile moist gauze was then placed on the abdomen. The rat was inverted and laid face down. The fascia lata muscle was harvested along with the cranial part of the biceps femoris muscle, and the sciatic nerve was observed. The sciatic nerve dissection was performed under an operating microscope (Carl Zeiss, f170, Opmi pico, Germany). A tunnel was then formed from the right abdominal region to the sciatic nerve for flap transposition.

Evaluation of nerve regeneration

Nerve regeneration was evaluated three months (90 days) after the surgery by the following methods: *(1) Sciatic Functional Index (SFI) measurement*: Each rat was walked on a $100 \times 40 \times 20$ cm size hiking platform for gait analysis. Footprint images of the rats were used for measurements. SFI was measured with the formula suggested by Bain et al. [13] SFI = –38.3X ((EPL-NPL)/NPL) +109.5 X ((ETS-NTS)/NTS + 13.3 X ((EIT-NIT)/NIT)-8.8. According to this formula, we used three parameters: print length (PL), that is the distance from the heel to the third finger; toe spread (TS), that is the distance between the first and fifth fingers; intermediate toe spread (ITS), that is the distance from the second and fourth fingers.

When the results are evaluated with this formula, a value of −100 means complete impairment, while a value of 0 shows normal function. *(2) Electromyographic (EMG) assessment*; Since muscle contraction would be measured during EMG evaluation, no muscle relaxant was used, and only a ketamine injection was performed. A conventional EMG device (Synergy, Medelec, U.K.) was used for electrophysiological evaluation. The gluteal muscles were exposed through the old incision and the sciatic nerve was exposed. A needle electrode was placed in the gastrocnemius and soleus muscles at 1-cm distal to the tibial tubercle. For nerve stimulation, a pair of 2.5-mm spaced tungsten wire electrodes whit hook-shaped tips were used and the nerve was elevated 1–2 mm from the other tissues. A current of 25–35 mA was given from the proximal side of the nerve. After that, the evoked compound muscle action potential (CMAP) and the area under the CMAP curve were calculated and evaluated statistically. *(3) Microscopic assessment with the light microscope*; 0.5-cm samples were taken from the middle of the nerve conduits and nerve grafts. These preparations were fixed with a 10% formol solution. Following the fixation, four micron sections were taken from the sample tissue with Microtome (Leica SM 2000 R). These sections were stained with Hemotoxylene-Eosin and examined under the Olympus BX-46 light microscope. It was scored between 0 and 3 by two pathologists who were blinded to the groups according to the density of fibrosis, inflammation and vascularity in the region of nerve regeneration. Nerve connections in the regeneration area were evaluated, and the regular progression of the nerve fibers was scored between 0 and 3. The average scores were noted.

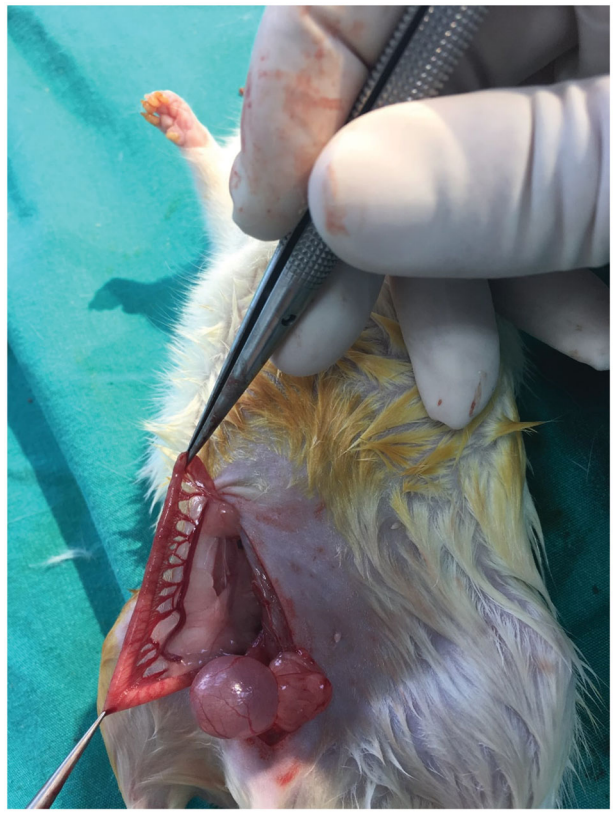

Figure 5. The pedicle of the tuba uterina was clearly explored.

The exams were scored between from 0 to 3 according to the level of fibrosis, inflammation and vascularity in the nerve regeneration regions. Furthermore, in the regeneration area, the nerve fiber connections and the regular progression of nerve fibers were scored between from 0 to 3.

(4) Microscopic assessment with the electron microscope: The samples were treated with 100 Angstrom thickness and assessed by a SEM ASID-10 scanning electron microscope with an acceleration voltage of 80 kV, and the images were documented. In the evaluation of the full thin sections obtained, the following were examined: axonal structures, the presence of blood vessels, changes in the myelin sheath structure, cytoplasmic edema, nucleus and mitochondria structures.

Statistical analysis

The statistical significance of the differences between mean values was analyzed with the use of SPSS statistical software, version

24.0 (IBM Corp., Armonk, NY) statistical software. Kruskal Wallis Variance Analysis was used to analyze independent variables that did not show normal distribution. A Bonferroni-corrected Mann Whitney U test was used for binary comparisons. The level of significance was accepted as <0.05.

Results

Macroscopic assessment and the SFI measurement

Pressure wounds were not observed in any of the rats. No complications were observed in the surgical region and incision lines. In addition, the old incision lines were difficult to detect due to the normal growth of hairs.

After the exploration of the sciatic nerve and nerve conduits, it was observed that four conduits in the Flap-Forward and Flap-Reverse groups were filled with liquid in the form of a homogeneous gel, and cyst formation developed in these conduits. In macroscopic evaluation of the surgical area with inspection, we detected similar edema, inflammation and fibrosis in all groups. Sciatic nerve dissection was more comfortable in the Nerve Graft, Flap-Forward, Flap-Reverse, Graft-Forward and Graft Reverse groups than in the Graft-Reverse group. At the same time, coaptation lines were easily observed in these groups. Neuroma was not observed in any rats in the Nerve Graft, Flap-Forward, Flap-Reverse, Graft-Forward, Graft- Reverse groups, whereas there are four rats with neuroma formation in the Cut and Unrepaired group.

SFI measurements were calculated for each group as 76.23 ± 6.3, 36.1 ± 7.8, 52.75 ± 12.44, 51.79 ± 12.96, 45.54 ± 6.88, 46.79 ± 7.95 respectively (Table 1). The SFI value was significantly greater in the Nerve Graft group than the other groups ($p < 0.05$). The Graft-Forward group and Graft-Reverse group pair was better than the Flap-Forward group and Flap-Reverse group pair ($p < 0.05$). However, there was no statistical difference between the Graft-Forward and Graft-Reverse groups, or between the Flap-Forward and Flap-Reverse groups ($p > 0.05$).

Electromyographic (EMG) assessment

The CMAP values and the areas under the CMAP curves were analyzed for each individual group and then compared between the groups (Table 1). The CMAP values were measured as 9.3 ± 2.05 ms/mV in the Nerve Graft group, 5.36 ± 2.3 in the Flap-Forward group, 6.97 ± 2.46 in the Flap-Reverse group, 8.36 ± 1.43 in the Graft-Forward group and 8.74 ± 1.56 in the Graft-Reverse group. The areas under the CMAP curves were calculated as 15.51 ± 2.14 m/mV in the Nerve Graft group, 4.73 ± 1.8 in the Flap-Forward group, 5.67 ± 2.17 in the Flap-Reverse group, 10.46 ± 1.81 in the Graft-Forward group and 10.14 ± 1.65 in the Graft-Reverse group. According to this evaluation, nerve regeneration was better in the Nerve Graft group than the other groups ($p < 0.05$). The Graft-Forward and Graft-Reverse group pair was better than the Flap-Forward and Flap-Reverse group pair ($p < 0.05$). However, there was no statistical difference between the Graft-Forward and Graft-Reverse groups or between the Flap-Forward and Flap-Reverse groups ($p > 0.05$).

Microscopic assessment with the light microscope

Since there was no nerve regeneration in the Cut and Unrepaired group, it was not evaluated. The inflammation score was calculated as 0.9 ± 0.31 in the Nerve Graft group; 2.1 ± 0.56 in the Flap-Forward group; 2.1 ± 0.73 in the Flap-Reverse group; 1.5 ± 0.52 in the Graft-Forward group; and 1.3 ± 0.67 in the Graft-Reverse group. The fibrosis score was calculated as 0.8 ± 0.63 in the Nerve Graft group; 2.4 ± 0.7 in the Flap-Forward group; 2 ± 0.81 in the Flap-Reversed group; 1.3 ± 0.48 in the Graft-Forward group; and 1.2 ± 0.42 in the Graft-Reversed group. The vascular proliferation score was calculated as 2.8 ± 0.42 in the Nerve Graft group; 1.9 ± 0.31 in the Flap-Forward group; 1.9 ± 0.31 in the Flap-Reverse group; 2.5 ± 0.52 in the Graft-Forward group; and 2.3 ± 0.67 in the Graft-Reverse group. The score of regular progression of nerve fibers was calculated as 2.8 ± 0.63 in the Nerve Graft group; 1.3 ± 0.48 in the Flap-Forward group; 1.2 ± 0.63 in the Flap-Reverse group; 2.2 ± 0.63 in the Graft-Forward group; and 2.4 ± 0.51 in the Graft-Reverse Group. In the Graft-Forward and Graft-Reverse groups, myelinated and unmyelinated axons were simpler than in the Flap-Forward and Flap-Reverse groups, and the arrangement of axons was more homogeneous. The scores of vascular proliferation and regular progress of nerve fibers in the Graft-Forward and Graft-Reverse groups were significantly higher than in the Flap-Forward and Flap-Reverse groups ($p < 0.05$). The scores of fibrosis and inflammation in the Graft-Forward and Graft-Reverse groups were significantly lower than in the Flap-Forward and Flap-Reverse groups ($p < 0.05$). There were no statistically significant differences between the Flap-Forward and Flap-Reverse groups or between the Graft-Forward and Graft-Reverse groups ($p > 0.05$) (Table 1). The Nerve Graft group was statistically better in terms of nerve regeneration parameters than other groups (Figures 6 and 7).

Table 1. The results of the SFI measurements, EMG and Microscopic Assessments.

	SFI	CMAP ms/mV	CMAP Area m/mV	Inflammation*	Fibrosis*	Vascular proliferation*	Regular progression of nerve fibers*
Cut and Unrepaired Group	76.23 ($SD = 6.3$)	–	–	–	–	–	–
Nerve Graft Group	36.1 ($SD = 7.8$)	9.3 ($SD = 2.05$)	15.51 ($SD = 2.14$)	0.9 ($SD = 0.31$)	0.8 ($SD = 0.63$)	2.8 ($SD = 0.42$)	2.8 ($SD = 0.63$)
Flap-Forward Group	52.75 ($SD = 12.44$)	5.36 ($SD = 2.3$)	4.73 ($SD = 1.8$)	2.1 ($SD = 0.56$)	2.4 ($SD = 0.7$)	1.9 ($SD = 0.31$)	1.3 ($SD = 0.48$)
Flap-Reverse Group	51.79 ($SD = 12.96$)	6.97 ($SD = 2.46$)	5.67 ($SD = 2.17$)	2.1 ($SD = 0.73$)	2 ($SD = 0.81$)	1.9 ($SD = 0.31$)	1.2 ($SD = 0.63$)
Graft-Forward Group	45.54 ($SD = 6.88$)	8.36 ($SD = 1.43$)	10.46 ($SD = 1.81$)	1.5 ($SD = 0.52$)	1.3 ($SD = 0.48$)	2.5 ($SD = 0.52$)	2.2 ($SD = 0.63$)
Graft-Reversed Group	51.79 ($SD = 7.95$)	8.74 ($SD = 1.56$)	10.14 ($SD = 1.65$)	1.3 ($SD = 0.67$)	1.2 ($SD = 0.42$)	2.3 ($SD = 0.67$)	2.4 ($SD = 0.51$)

SFI: Sciatic Functional Index; CMAP: evoked compound muscle action potential. *The pathologic examinations were performed and scored by 2 pathologists who were blinded to the groups.

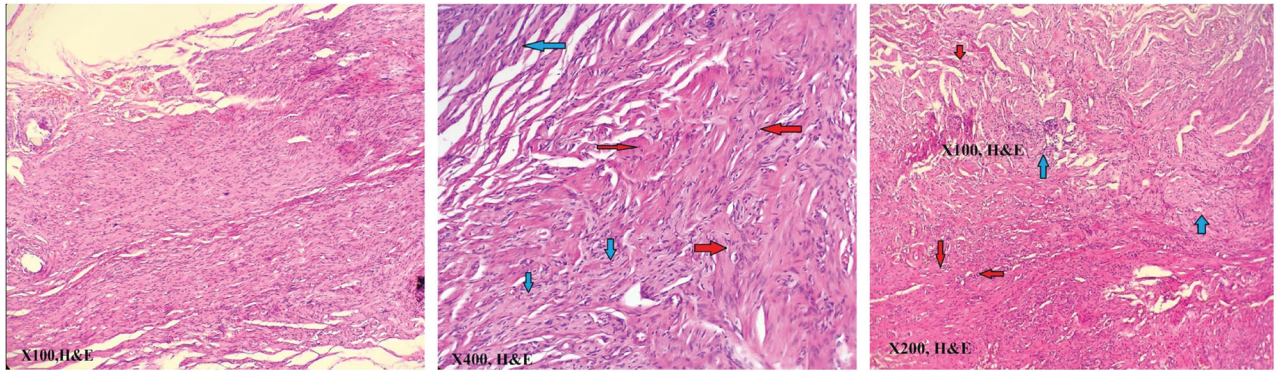

Figure 6. Microscopic assessment of the Nerve Graft, Flap-Forward and Flap-Reverse groups with the light microscope. The Nerve Graft group (left); the Flap-Forward group (middle); the Flap-Reverse group (right). Red arrow: Prominent collagen fibers in the regeneration zone; Blue arrow: Disorganized unregular nerve fibers.

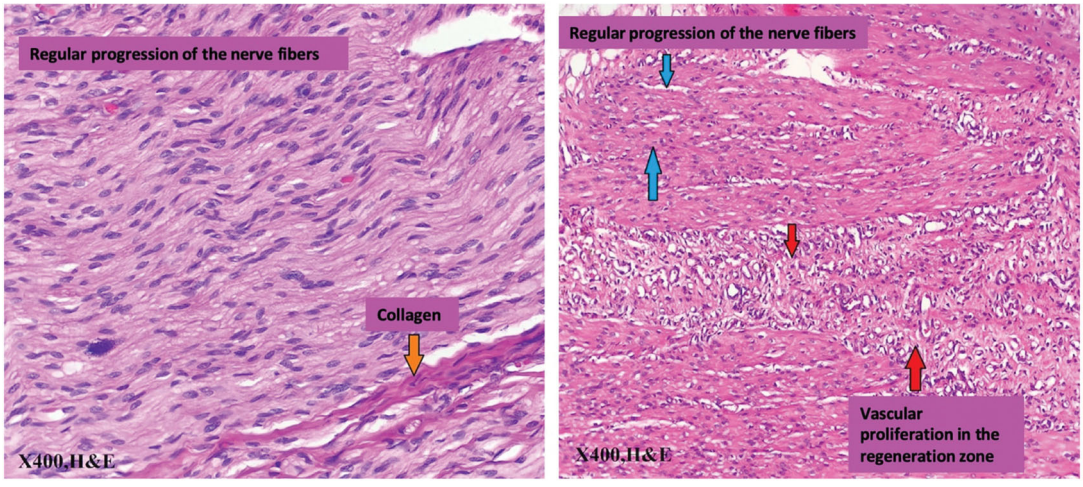

Figure 7. Microscopic assessment of the Graft-Forward and Graft-Reverse groups with the light microscope. The Graft-Forward (left); the Graft-Reverse group (right). Red arrow: Prominent collagen fibers in the regeneration zone; Blue arrow: Disorganized unregular nerve fibers.

Microscopic assessment with the electron microscope

SEM sections obtained from the nerve area were evaluated ultrastructurally. In the Nerve Graft group, the axons were more organized and brightly stained, indicating healthy morphology, and the number of myelinated axons was higher than in other groups. SEM micrographs of the Graft-Forward and Graft-Reverse groups showed that myelin and axon structures were quite regular and abundant blood vessels and nerve counts were higher than in the Flap-Forward and Flap-Reverse groups. In addition, lumen epithelial cells in the tuba uterina in the Flap-Forward and Flap-Reverse groups were observed to have a more organized and healthy morphology compared with those in the Graft-Forward and Graft-Reverse groups. The ultrastructural results for the tubular flaps groups and tubular graft groups show a similar morphology (Figures 8 and 9).

Discussion

Peripheral nerve repair has been performed for over the past two hundred years, and the first hypotheses for the regeneration of the peripheral nervous system date back to the fourteenth century [14].

Today, unknown aspects of peripheral nerve repair are still under investigation and there are persistent questions that have yet to be answered. The main task in the repair of the peripheral nerve is to bring the non-damaged epineurium and fascicules end-to-end without causing tension, otherwise the fascicles will fold over each other during coaptation and the expected regeneration cannot be achieved [15]. In the light of this information, peripheral nerve defects may occur, either by trimming to create a suitable ending or by injury.

Studies on nerve conduits began in 1880 with attempts to create nerve conduits using arteries, veins, muscles, cartilage, organic and non-organic materials (gelatin, metal, plastic) [6,16–18]. Williams et al. [18] presented a study on a silicon nerve conduit for a 1-cm sciatic nerve defect that was important in clarifying the mechanism of nerve regeneration in the nerve conduits. This study shed light on other nerve conduit studies that had been carried out.

Autogenous and synthetic materials can be used as nerve conduits in peripheral nerve surgery. All of the autogenous materials used as nerve conduits have been used as grafts until now. Autogenous materials in peripheral nerve repair surgery include the following: arteries, veins, muscles, tendons, amnion, mesothelium, pseudo synovial sheaths. All have been used as a grafts according to the literature [3]. In addition, non-absorbable synthetic materials such as silicon and collagen, gelatin, hyaluronic acid, polyglycolic acid, poly-L-Lactid Glycolic-Acid (PLGA), polyester, copolyester, and alginate-containing synthetic materials are also found in the literature as nerve conduits used in peripheral nerve repair [3,19]. The literature contains studies in which the various advantages and disadvantages of both autologous grafts and synthetic materials are discussed. In recent years, nerve

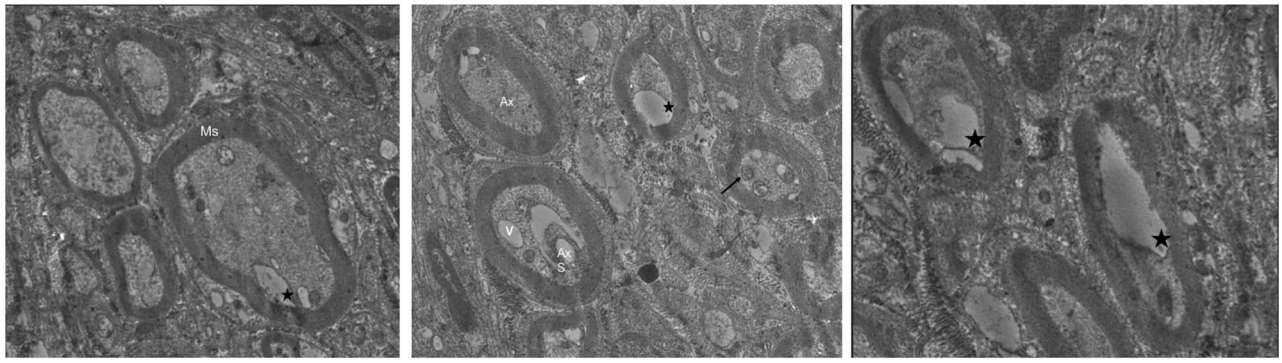

Figure 8. Microscopic assessment of the Nerve Graft, Flap-Forward and Flap-Reverse groups with the electron microscope. The Nerve Graft group (left); the Flap-Forward group (middle); the Flap-Reverse group (right). Ms, Myeline sheath; V, vacuole; Star, Axon- myelin dehiscence; Arrow, Mitochondria; Axs; Axonal shrinkage.

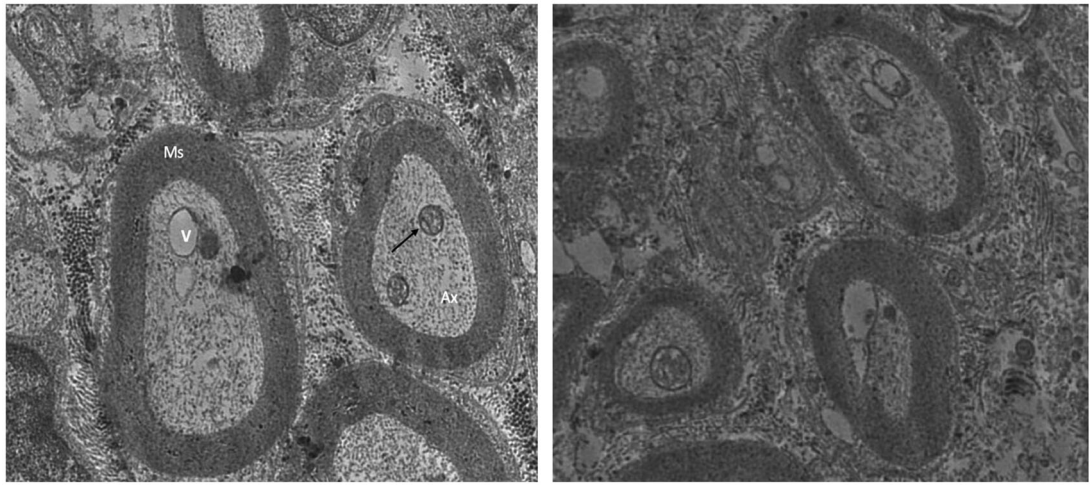

Figure 9. Microscopic assessment of the Graft-Forward and Graft-Reverse group with the electron microscope. The Graft-Forward group (left); the Graft-Reverse group (right). Ms, Myeline sheath; V, vacuole; Star, Axon- myelin dehiscence; Arrow, Mitochondria; Axs; Axonal shrinkage.

conduits have been used in clinical practice and a significant functional improvement has been claimed in peripheral nerve injuries [4,5,14,19–21]. Additionally, in nerve defects below 3 cm, it is possible to find studies in which functional recovery is reported using autologous vein grafts as a nerve conduit and chitosan/PGA nerve guides [3].

In 1993, Ozcan et al. placed a human amniotic membrane as a graft in the area supplied from the inferior epigastric artery of the rats. They then used this as a nerve conduit after the development of neovascularization [22].

In the literature, neural conduits in the form of a vascularized pedicle flaps have not been used in any human or animal study using their own tissues. We believe that our study is a unique model in this respect.

The clinical use of the tuba uterina as a nerve conduit may not seem possible at the present, due to its being a part of the female anatomy. However, with the development of tissue and cell engineering in the future, this may offer guidance for new models.

From another point of view, this procedure may be used unilaterally or bilaterally in women as autologous in major and significant nerve defects such as brachial plexus, spinal nerve or femoral nerve injuries. In addition, if the challenges of immunosuppression drugs in transplantation surgery are resolved in the future, it may also be possible to use the procedure in male patients. The unilateral harvesting of tuba uterina will not cause serious harm to reproductivity, and they can be harvested from menopausal women and women who are not considering further pregnancy. Furthermore, in a woman with severe nerve damage, the harvesting of one tuba uterina while protecting the other may cause no loss in terms of health, and its effects may be ignored. In addition, the tuba uterina can be easily harvested as a flap in humans by means of laparoscopic surgery.

Obviously, all of these are ideas for the future. However, there is an important advantage in using a paired organ section that has a tubular-shaped in research for nerve regeneration which is a subject that involves many unknowns. We think that this procedure can become an important model and a milestone for future studies.

The history of transplantation goes back to the late 19th and early twentieth century. In 1902, Ullmann performed first the transplantation in a dog [23]. Afterwards, many replantation attempts were performed by different scientists, but they were not successful due to the poor understanding of the immune system and to technical limitations. The first successful kidney transplant was performed by Murray in 1954 [24]. Today, solid organ transplantation such as kidney and liver transplants are performed in many centers all over the world. Moreover, in Turkey and Sweden some pregnancies have been achieved thanks to uterine transplants by Ozkan [25] and Brännström [26] respectively.

As has been the case throughout the history of transplantation, we believe that new ideas, innovations and successes will be achieved through the development of previous knowledge and models with new models and ideas for nerve regeneration.

Thus, we think that the tuba uterina tubular flap will become a new research area as a new model for nerve regeneration.

On the other hand, unilateral ureter and intestinal segments might also be used for this purpose in future studies due to their tubular structures. In this respect, we think that this study will be a model for future research.

Bioengineering and nanotechnological advances will allow biodegradable nanomaterials to be used as new nerve conduits. However, thanks to tissue, cell and genetic engineering, it will be possible to add supporting cells containing stem cells to the conduit, or to produce various lumen structures that can increase nerve regeneration. Our study investigated whether the motile cilia structures, their directions and secreted molecules for the survival of spermium and ovarium secreted from the lumen epithelium in the rat tuba uterina will contribute to the nerve regeneration. However, during a three-month of follow-up, it was observed upon macroscopic assessment that eight of the 20 rats in the flap groups (Flap-Forward and Flap-Reverse groups) had serious cystic formations. The reason for these cysts was thought to be the inability of the epithelium secretions to drain to the outside properly. While planning the study we had hoped that using as few stitches as possible would prevent the formation of these cysts.

However, since the EMG assessment was performed prior to euthanasia, it was not known which rat had cystic formations and all rats were included in the assessment. No animals were excluded. Thus, all the results (with or without cystic formation) were taken into consideration in order to prevent bias between the groups in statistical analyses.

We believe that the cystic formations in this study occurred due to the secretory functions of the lumen epithelium in tuba uterina tubular flap, which yielded less successful results than the graft groups. However, with technological developments, we think that the ciliated structures of the tuba uterina lumen epithelium may be a new model for synthetic materials. Groups using various biodegradable materials and groups formed by destroying the lumen epithelium by passing alcohol or creating controlled ischemia could have been added to the study. However, this study focused on comparing flap groups with graft groups and the direction of the ciliated epithelium. Therefore, the number of groups was not increased. From this perspective, the total number of groups can be considered as a limitation of this study.

Conclusion

It was observed that the transfer of the tuba uterina tubular conduit as a graft was statistically better in its effect on nerve regeneration than flap transfer, but the study also indicated that the direction of the ciliated structures had no significant effect. We believe that as this model improves with future clinical and experimental studies, it will shed light on new models, ideas and innovations about nerve conduits by creating a new research area.

Ethical approval

Not required

Disclosure statement

The manuscript was not sponsored by an outside organization. We (all of the authors) have agreed to allow full access to the primary data and to allow the journal to review the data if requested. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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