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POSSIBILITIES AND LIMITATIONS IN PERIPHERAL NERVE SURGERY

Abstract: *Introduction:* Autologous nerve graft is still the most common used technique for peripheral nerve repair, but usefulness of nerve repair has not been precisely defined in literature so far.

Methods. A meta-analysis included our results (690 nerve repairs) and literature data (72 papers, 1972–2014). Incidence of an useful sensorymotor recovery was defined according to BMRC scales and the influence on outcome for the following six factors was investigated: nerve type, repair level, length of nerve defect, preoperative interval, local condition, and patient, s age. On the basis of obtained results, we defined the situations when nerve repair is probably unuseful.

Results. An useful sensorymotor recovery was obtained in the range of 25% to 90%, depending on the nerve type and the repair level. Recovery potential is significantly greater for the radial, musculocutaneous, and femoral nerves, than for other nerves. Length of nerve defect, preoperative interval, local condition, and patient, s age influence treatment outcome significantly as well.

Conclusions. Excellent recovery grades are infrequent or absent. Usefulness of high-level peroneal and ulnar nerve repairs is questionable because of rare recovery of distal effectors and minor sensory functional importance.

Key words: *Nerve graft repair, Nerve injuries, Recovery of Function, Treatment outcome*

INTRODUCTION

Peripheral nerve injuries are relatively uncommon, but morbidity and invalidity after such injuries are still unacceptably high [1]. The knowledge about nerve injuries has been based mostly on the wartime experiences and to the lesser extent on the civilian clinical series [2]. During the war combats, nerve injuries account for about 10% of all injuries and for nearly 30% of all injuries to the extremities [2,3]. Autologous nerve graft is still the gold standard in peripheral nerve repair, but it is

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wellknown that this technique has several limitations and scientists are searching for new treatment possibilities [3,4].

METHODS

For this meta-analysis, I used our own results and literature data dealing with complete nerve injuries tretated by secondary nerve graft repair. Graft donors were the sural nerve, the superficial radial branch or the medial cutaneous antebrachial nerve. The most commonly used operative technique was grouped interfascicular suture (monofilament interrupted nylon, Ethilon 8–0).

Experience of the Belgrade Military Medical Academy includes 2,660 prospectively assessed missile-caused peripheral nerve injuries treated conservatively or surgically. For the purpose of the present analysis we excluded 222 injuries to the cutaneous nerves, brachial plexus and closely related nerves, 830 conservatively treated nerve injuries, and 918 surgically treated incomplete nerve injuries. So, we focused on 690 complete nerve lesions repaired with nerve graft. Nerve discontinuity was intraoperatively found in 465 (67.4%) and non-transmitting lesion in the remaining 225 patients (32.6%). The series was operated on by 6 neurosurgeons and include repairs of 85 median, 132 ulnar, 131 radial, 22 musculocutaneous, 15 femoral, 175 peroneal, and 130 tibial nerves. The minimal postoperative follow-up period was 7.2 years and the mean follow-up period was 8.8 years.

Literature data dealing with secondary graft repair are presented through the *British Medical Research Council* grading scales considering the recoveries better or equal to M3S2+ grades to be useful. Data collecting was not easy because of different injury mechanisms, different assessment protocols and different definitions of repair levels. We excluded the data from the World War II, the Korean War, and the Vietnam War, because operative technique was far below present standards. Finally, we collected data reported by 55 first authors in 72 papers during the 1972–2014 period.

Factors potentially influencing the outcome of nerve repair. We tested the influence on outcome for the following six factors: nerve type (recovery nerve potential), level of the repair, length of nerve defect, duration of preoperative interval, local state and co-morbidities, and patient' s age. Each factor was tested in a group of patients homogenized according to the remaining 5 factors. Level of repair was defined as *high*, *intermediate* or *low* but we united results for proximal repairs for better comparison with the literature data. The borderline between high and intermediate repairs went across the middle of the upper arm /tigh and the borderline between intermediate and low repairs went across the junction of the upper and middle thirds of the forearm / leg.

RESULTS AND DISCUSSION

Factors influencing the outcome of nerve repair

Nerve type (recovery nerve potential). Results were obtained in a homogenous group of patients: intermediate level of repair, nerve graft shorter than 4 cm, preoperative interval shorter than 3.5 months, patient's age ranging from 21 to 30 years, no combined nerve injuries, and favorable local condition in repair region. According to our results, *potential* for *sensory recovery* is similar for the median, ulnar and tibial nerves (useful sensory recovery was 66.6%, 64.3% and 63.9%, respectively; P>0.05). On the contrary, *potential for motor recovery* differs significantly, classifying nerves into groups with *excellent, moderate,* and *poor* potential (P<0.001). Excellent recovery potential exists for the radial nerve (useful motor recovery in 85.7% of cases), the musculocutaneous nerve (83%), and the femoral nerve (78.4%). The group with moderate recovery potential includes the median nerve (useful motor recovery in 53.6% of cases), the ulnar nerve (50.1%), and the tibial nerve (60.8%). Finally, the peroneal nerve is the only one with poor recovery potential (useful motor recovery in only 28% of cases) [5].

Regeneration process is not the reason for differences in motor recovery potential. Probably, such differences are the consequence of characteristics of main muscle effectors, characteristics of nerve microanatomy, and topography of neurons in the spinal cord [4, 6].

We found 10 risk factors for the bad motor recovery potential in the literature: distal position of main effector, need for numerous regenerated fibers, need for strong muscle contraction, need for coordinated or precise contraction, lack of alternatives for the main movements, great proportion of intraneural connective tissue, great proportion of sensitive nerve fibers, great number of nerve fascicles in repair region, inadequate vascularization, and numerous and scattered neurons in spinal cord [4, 6, 7, 8, 9, 10]. In the group with excellent recovery motor potencial only 1–2 risk factors are present, 5–6 risk factors exist for the nerves with moderate recovery potential, and as much as 8 risk factors for the peroneal nerve.

Level of repair influences significantly repair outcome. Literature reports on *median nerve* repair mostly include wrist-level lesions and useful motor recovery exist in 67.1% (366/545) of distal and in 45.7% (58/127) of proximal repairs. We noted such recovery in 70% of distal and in 29.2% of proximal repairs. Useful sensory recovery of the median nerve is more frequent: 71.8% (438/610) of distal and 64.9% (63/97) of proximal repairs. We found such recovery in 75% and 56.9% of cases, respectively [11].

Recent reports on *ulnar nerve* repairs are more optimistic than previously and useful motor recovery occurs in 65.8% (364/553) of distal repairs and in 39.2% (51/130) of proximal repairs. We found useful motor recovery in 72.9% of distal and in 28.6% of proximal ulnar nerve repairs. As for the median nerve, an useful sensory recovery was more frequent than an useful motor recovery: 72.3% (418/578) for distal and 69.9% (79/113) for proximal repairs [12]. In our series, useful sensory recovery was noted in 79.2% of distal and in 60.7% of proximal ulnar nerve repairs [13].

After tibial nerve repair, useful motor recovery can be expected in 65.7% (136/207) of proximal and in 83.7% (36/43) of distal repairs. An useful sensory recovery was again more frequent in relation to an useful motor recovery: 84.3% (43/51) for distal repairs and 69.7% (203/295) for proximal repairs. Our results are slightly worse: for distal and proximal tibial nerve repairs the incidence of an useful motor recovery was 76% and 59% and incidence of an useful sensory recovery was 80% and 60.9%, respectively [14].

Reports on *femoral nerve* repair include small series or single cases. Literature data point to an useful motor recovery in 71.8% (51/71) of cases and we found such recovery in 80% of patients.

Excluding the brachial plexus neurotisation, literature reports on *musculocutaneous nerve* repair are uncommon. An useful motor recovery is possible in over 88.2% (97/110) according to the literature data and in 81.8% of cases, according to our results.

Useful recovery is almost the rule after *radial nerve* repairs because it has been obtained in 90% (63/70) of distal and in 72.4% of proximal repairs (276/381). Results were similar in our series: 92.8% and 85.5%, respectively [15].

The authors reported catastrophic results after *peroneal nerve* repair, but recent studies are more encouraging. Useful recovery can be expected in 55% of distal and in 35.1% of proximal repairs (in our series 53.8% and 25%, respectively) [16].

In general, our results are *worse to some extent* than the collected results and I offer several explanations for that: frequent co-morbidities in the repair region, the series includes almost exclusively the adults, direct sutures are excluded, and great proportion of patients requiring long grafts.

*Length of nerve defect***.** Defect was measured after resection of stumps or non-transmitting segment to the appearance of normal fascicular and vascular architecture. Critical length for significant worsening of results in our series was 4–10 cm, depending on the nerve injured [17]**.**: 4 cm for the peroneal nerve, 5 cm for the tibial, median and ulnar nerves, and 10 cm for the radial nerve (specificity 75.3–92.1% and sensitivity 68.3–76.2%). The calculated critical defects giving minimal chances for success were 9.4 cm for the peroneal nerve, 12.8 cm for the tibial, 14 cm for the ulnar nerve, and 15.1 cm for the median nerve.

Duration of preoperative interval. Primary nerve repair is rarely possible after war-related nerve injuries and it failed in all of our 11 patients operated on in the begining of the series. The main reasons are contused nerve edges, wound contamination, and massive soft tissue destruction. Preoperative interval was shorter than 4 months in about 60.9% of our patients (range 1–23 months, 4.4±3.6 months in average). The nerve should be operated on 4–6 weeks after injury if we were aware of the nerve section since the initial surgical treatment or 3–5 months after injury if the patient was monitored for signs of early regeneration [18]. Delayed repairs are usually the consequence of delayed referrals or prolonged treatment of associated injuries. Indication for an urgent repair was a neurological worsening or pain, caused by pseudoaneurysm, painful foreign particles or progressive nerve adhesions.

Critical interval for significant worsening of results is in the range of 3 to 6 months: 3 months for the peroneal nerve, 4.5 months for the tibial and ulnar nerves, 5 months for the median nerve, and 6 months for the radial nerve (specificity 70.3–84.6% and sensitivity 67–79.2%). Calculated intervals giving minimal chances for success were: 9.4 months for the peroneal nerve, 10.7 months for the tibial, 11.3 months for the ulnar nerve, and 13.4 months for the median nerve.

The local condition in repair region (bone fracture, main artery lesion, soft tissue defect) is an index of the severity of trauma. It was defined intraoperatively as *favorable, uncertain* or *unfavorable.* An useful motor recovery was significantly more frequent among patients with favorable local condition compared to patients with unfavorable local condition (73.3% and 26.6%, P<0.001). Individually, bone fracture, main artery lesion and soft tissue defect did not change the outcome significantly (P>0.05). Only if at least two local damages existed, significant inverse influence on the outcome was noted and an useful motor recovery was obtained in 61.2% and 25.7% of cases (P<0.001).

*Patient᾽s age***.** According to the most authors, repair results are better in children because of several reasons: shorter distance for regenerating axons, shorter latent period in the beginning of the reinnervation, faster and more intensive increase of muscle substance, and stability of the neuromuscular junction after denervation. Critical age for a good outcome was defined in the literature in the range of 10 to 54 years [19, 20, 21, 22].

Surgical complications

The only *intraoperative complication* we had was iatrogenic vascular injury in 6 patients with extensive scarring (lesion of the brachial vein, popliteal vein or axillary artery, all of them settled by simple lateral suture. *Postoperative complications requiring nerve re-suture* existed in 8 patients. Furthermore, we had 8 postoperative complications needing nerve resuture: postoperative hematoma in repair region (n=3), rupture of the suture line because of re-fracture (n=2), and purulent local infection (n=3). Finally, there were 15 postoperative complications not requiring nerve re-suture: partial necrosis of the existing skin flap (n=5), postoperative hematoma in repair region (n=3), and wound disruption without purulent secretion (n=7).

Limitations of nerve graft repair

Maybe the rates of useful sensorimotor recovery are acceptable, but the quality of recovery is still unsatisfying, because of several dark sides of nerve repair outcomes [23–27]:

Excellent recovery grade (M 5) is infrequent or absent, even after distal repairs. Usually, maximal grades achieved are M3 for high-level and M 4 for intermediate-level repairs corresponding to only 1/3 and 2/3 of maximal muscle strength, respectively. *Average point-scores* after nerve repairs are in the range of 0.9 ± 1.0 to 3.6 ± 1.1 for proximal repairs, and in the range of 2.8 ± 1.4 to 4.2 ± 0.7 for distal repairs. This is far from maximal scores and d*istal muscles* seldom, if ever, recovered after high-level repairs because they underwent irreversible denervation fibrosis.

Tendon transfer or other corrective procedures were frequently required, particularly after proximal median and ulnar nerve repairs and less frequently after radial nerve repairs. Corrective procedures are rarely needed after peroneal nerve repairs as well, in spite of poor repair outcome, because simple foot-drop brace is usually sufficient to enable relatively normal walk [28]. Finally, we found that patients are *less satisfied with recovery*, than we expect on the basis of obtained clinical outcome. This is the case particularly after war-related injuries, because of psychological reasons, unrealistic expectations and expectations of additional financial support or other compensations.

CONCLUSIONS AND FINAL REMARKS

1. Usefulness of *distal nerve repairs* is out of question. High-level lesions of the *radial, femoral, and musculocutaneous* nerves should be repaired as well, because of good chances for an useful motor recovery, as well as high-level lesions of the *median and tibial* nerves, because of chances for sensory recovery sufficient to prevent trophic ulcers.

2. However, usefulness of very high *peroneal and ulnar* nerve repairs in adults is questionable because useful recovery of distal effectors seldom occurs and sensory recovery is of minor functional importance. In such cases, maybe more useful are some *nerve transfer* or *end-to-side neurorrhaphy* techniques.

3. Scentists are searching for *nerve graft alternatives*. Many agents have been recognized as regeneration stimulators or neuroprotectors and many nerve conduits have been investigated. Of these techniques, we only used denatured *muscle graft* in a small series of radial nerve repairs. The initial results were at least comparable to nerve graft, but unfortunately long-term results were worse.

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