



Semi-quantitative electromyography as a predictor of nerve transfer outcome



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HIGHLIGHTS

- Neurophysiology has great potential for nerve transfer surgery planning.
- A rapid semi-quantitative interference pattern analysis technique helps to select donor nerves.
- Even 2 years since denervation should not prevent referral to a reconstructive neurosurgeon.

ABSTRACT

Objectives: Evaluate correlation between donor nerve semi-quantitative electromyography (sqEMG) and strength outcome in nerve transfer surgery.

Methods: Retrospective review of pre-operative donor nerve semi-quantitative neurophysiology and post-operative recipient muscle force after at least one-year follow-up. The semi-quantitative technique is the average motor unit number estimate associated with needle recorded interference patterns in the donor muscle (IP-AMUNE), which was correlated with hand-held manometry, standardized as a percent of the contralateral arm, using multivariable linear regression with backward selection.

Results: Twenty-eight nerve transfer cases were included. The correlation between the donor nerve IP-AMUNE and the recipient muscle strength was moderate to strong and highly significant ($r = 0.67$, $p < 0.001$). Medical Research Council (MRC) grading did not predict strength ($p > 0.54$).

Conclusions: IP-AMUNE is a good predictor of strength after nerve transfer surgery and should be considered in the evaluation and planning of patients undergoing nerve transfer to aid in donor nerve selection.

Significance: IP-AMUNE may significantly benefit those undergoing nerve transfer surgery for the restoration of movement.

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1. Introduction

Nerve transfer has become a key component of the reconstructive neurosurgical armamentarium (Brown et al., 2012, 2017) for

restoration of limb function, particularly in brachial plexus injury (BPI) and peripheral nerve injury (PNI). More recently, in concert with restorative neurology, the technique has begun to offer options for those with weakness of central nervous system (CNS) origin, especially cervical spinal cord injury (Brown, 2011; Bertelli and Ghizoni, 2014; Zyl et al., 2014).

Nerve transfer involves surgically redirecting healthy axons within a nerve branch or fascicle, which are under conscious control (the “donor” nerve), to a nerve that has either lost its axons or its connection to conscious control for any reason (the “recipient” nerve). The degree and character of voluntary control restored by the procedure should outweigh the partial or entire loss of the original donor nerve function. There are a number of nerve transfer pairings commonly utilized to restore function to the upper limb

Abbreviations: BPI, Brachial Plexus Injury; CNE, Concentric Needle Electrode; EIM, Electrical Impedance Myography; EMG, Electromyography; IP, Interference Pattern; IP-AMUNE, Interference pattern – average motor unit number estimate; LMN, Lower Motor Neuron; MRC, Medical Research Council; MU, Motor Unit; MUNE, Motor Unit Number Estimate; PNI, Peripheral Nerve Injury; qEMG, Quantitative Electromyography; QOL, Quality of Life; SCI, Spinal Cord Injury; SD, Standard Deviation; UMN, Upper Motor Neuron.

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(Wood and Murray, 2007); the most common being restoration of elbow flexion using ulnar or median fascicles to musculocutaneous branches to biceps and brachialis, and shoulder abduction using spinal accessory nerve fascicles to the suprascapular nerve or a branch to a triceps head to the axillary nerve. Nerve transfer case series have described success rates ranging from 50 to 80% (Shin et al., 2005; Liverneaux et al., 2006; Bengtson et al., 2008; Tung and Mackinnon, 2010).

Success has historically been defined as achieving Medical Research Council (MRC) grade 3 or more. Predictors of outcome have predominantly included denervation time and reinnervation distance, but several others have been identified (Midha, 2004) with increasing evidence suggesting success is dependent upon the number of axons reaching their targeted muscle fibers. Because of proximity to the injured nerve, axons of the donor nerve are frequently partially injured. Consequently, the pool of useful axons to donate, even in an MRC 4 muscle group, may be insufficient. This is an important point and comprises one of the main reasons for undertaking this study.

Traditional pre-surgical assessment relies heavily on MRC grading and imaging. MRC grading has been well documented as to its limitations (James, 2007; MacAvoy and Green, 2007; Bengtson et al., 2008) and although numerous modified MRC grading scales have been suggested, none are used widely except subdividing grade 4 into the subjective 4–, 4, and 4+ categories, which itself has been significantly criticized (Vanhoutte et al., 2012). Use of quantitative force measurements (Andres et al., 1987; Andres et al., 2012; Great Lakes ALS Study Group, 2003), has been limited due to time constraints and difficulty of application. Furthermore, imaging remains poor at estimating number or functionality of axons (Ohana et al., 2014). Thus, many surgeons turn to non-quantitative neurophysiology as a surrogate for how many functional motor axons are available to donate.

A single prior retrospective study (Schreiber et al., 2014) compared the binary variable of pre-operative “normal” or “abnormal” EMG interference pattern to post-operative MRC graded strength, finding a significant correlation. This study also addresses the correlation between pre-operative EMG and post-operative outcome but differs in two important ways: we use semi-quantitative EMG (sqEMG) analysis of donor nerve muscles and a post-operative quantitative outcome of recipient muscle force using a handheld manometer (instead of MRC or modified MRC).

2. Methods

This was an IRB-approved retrospective study of patients who suffered traumatic nerve damage and underwent nerve transfer at our institution between 2011 and 2015. From database and chart review, we obtained the documented pre-surgical sqEMG data associated with the donor nerve muscle and compared this to the recipient muscle's documented ability to generate force as measured by handheld manometry, as a percent of the unaffected contralateral side. Inclusion criteria required force measurements to be obtained at least one-year post-surgery. Secondary aims included assessment of the suitability of MRC as both a predictor and an outcome measure through comparison of: pre-operative donor muscle MRC with post-operative recipient muscle force as measured by manometry; pre-operative donor MRC with post-operative recipient muscle MRC; and pre-operative donor muscle sqEMG with post-operative recipient MRC.

The primary sqEMG technique is the average motor unit number estimate associated with needle recorded interference patterns (IP-AMUNE) (Mandeville et al., 2017) within the donor nerve muscle, using a concentric needle electrode (CNE) to sample multiple areas. This was performed at maximal effort and estimated by the examiner in real time, or later review of recordings.

Although subjective interference pattern (IP) analysis is performed routinely in neurophysiology labs, the categorical grading scale used (mild, moderate, severe) lacks the precision required for optimal decision making in nerve transfer surgery, especially within the grade of “severe”. This parallels issues with MRC grading, which lacks sensitivity, especially within MRC grade 4 that covers as much as 96% of a muscle's range of force (MacAvoy and Green, 2007; Bengtson et al., 2008). On the belief that IP-AMUNE should enhance accuracy and precision in predicting number of functioning donor axons, and hence force outcomes, compared to the traditional IP grading scale, IP-AMUNE has been used as standard care in joint clinics with the neurosurgeon in our center since 2011. Even though IP-AMUNE focuses only on the severe spectrum, this is the highly relevant range for surgical decision making—within this range, in our experience, there appears to be a threshold below which expectations for a good outcome drop precipitously; whether there is a sharp “cut-off” or a more gradual decline constitutes a significant part of the reason for this study. IP-AMUNE cannot be applied to IP's that have moderate severity or better due to difficulty in discerning overlapping units, unless research software is being utilized (Stashuk, 1999). Thus, the range is typically limited to between 0 and 6 MU's, with ≥ 7 MU's capturing the remainder of the severity spectrum (moderate severity and better). A normal IP might include roughly 17 focused motor units (Brownell and Bromberg, 2007); therefore, this technique of IP-AMUNE may only be applied when the motor axon cohort has been reduced to approximately 35% or less of normal.

The donor nerve sqEMG analysis was undertaken by a single experienced neurophysiologist, using one of two Viking on Nicolet® EDX Electrodiagnostic Systems in the same EMG lab. A sensitivity setting of 50 μ V per division or above and a sweep speed of 10 ms per division were used. To be accepted as individual motor units, no concrete criteria were used, but the MUs needed to be focused with short rise times (approximately less than 300–500 μ s) and size generally more than 20 μ V. Low frequency filters are typically set to 10 Hz and high frequency to 10 kHz. The duration of each contraction (time taken to identify MU's) was not set and lasted until confident identification of individual units was possible. Multiple contractions were made in each muscle studied (allowing time to recover as needed), manipulating the CNE each time to sample areas distributed within the same muscle (2–6 areas depending on muscle size), preferably at a distance greater than 0.5–1 cm axially from each other, if possible, and close to the midpoint of the muscle. All settings were occasionally adjusted, at the time of acquisition or later recording, for improved resolution as necessitated to optimize MU identification. For each muscle, the average motor unit count of the sampled areas was recorded.

We used hand-held isometric manometry (*MicroFET2*, Hoggan Scientific LLC) to measure force required to overcome the muscle in standardized positions, usually in mid-position. Isolating the muscle was generally made easier by a lack of agonist muscle activity as a result of the trauma, and the patient was tested in the seated or lying position to aid in removing compensatory mechanisms, with the joint stabilized as much as possible. Standardized positions included: shoulder abducted 45 deg, measured just proximal to lateral epicondyle for shoulder abduction; elbow flexed 90 deg, measured just proximal to the proximal wrist crease for elbow flexion (the patients had no brachioradialis activity); elbow flexed 90 deg, measured at the level of the ulnar styloid process for elbow extension; elbow held at side and flexed 90 deg and in rotational mid-position, measured at the level of the ulnar styloid process for external rotation of the arm; flexed distal thumb joint, measured over thumb pad for anterior interosseous nerve reinnervation (flexor pollicis longus); and flexed proximal interphalangeal joint, measured over pad of digit 3 intermediate

phalange for flexor digitorum superficialis reinnervation (there was no deep finger flexor or intrinsic hand muscle activity). The average force obtained in the recipient muscle after 3 measurements was compared to the same muscle in the unaffected contralateral limb and the percent recorded as the outcome. If the contralateral limb was affected, published regression equations and tables for individual muscles were used that take account of age, sex, and laterality (*The National Isometric Muscle Strength NIMS* (last 1996; Andres et al., 2012). This technique was chosen as the generally agreed gold standard isokinetic dynamometry is limited by cost, time, manpower, and applicability in the clinic setting (James, 2007). We did not adjust for handedness when comparing to the unaffected limb; we speculated the unaffected contralateral limb likely attained a strength not reliant on handedness, but instead optimized for purpose.

Occasionally, multiple nerves are transferred to restore function of a single joint, such as supraspinatus and deltoid for shoulder abduction, or brachialis and biceps for elbow flexion. In this situation, force outcome was divided between the nerve transfers evenly (50% applied to each transfer). However, if a clear difference on EMG or clinical exam existed between the two recipient muscles, this was reflected accordingly. For instance, if one muscle had no activity on EMG or no palpable contraction clinically, the force was attributed 100% to the other muscle. If one muscle had only 1–2 units firing on EMG, and the other had more than 5, then force was ascribed 25:75. Anything less obvious than these specific scenarios was treated as though each muscle generated equal force.

2.1. Statistical analysis

Construction of a multiple regression model began with univariable analysis of potential predictors individually against the outcome (*Force*). Multiple regression with backward model selection and elimination at the 0.20 significance level was used, with the prespecified predictors and confounders forced into the model. Prespecified predictors included *time to surgery*, *re-innervation distance*, and *age*, reported to significantly impact outcomes in prior literature (Tung and Mackinnon, 2010; Sakellariou et al., 2014), as well as *diabetes*, known to impact nerve regeneration in general. Other variables analyzed included *smoking*, *alcohol*, *time since surgery*, *joint reanimated*, reported *complication*, and *gender*. The variable *complication* was only applicable to a single case and constituted abscess formation not directly impacting the nerve but requiring further surgical management and antibiotics. Results were tabulated and displayed including significance. Model diagnostics were run to assess for correctness of assumptions including: linearity, constant variance, and normality. There was a ceiling effect in *IP-AMUNE* (maximum value of seven) and a floor effect in *Force* (minimum value of zero), otherwise a normal distribution was observed. SPSS Version 24 was used for the analysis.

Sample size was calculated using the online Harvard sample size calculator (Hedwig). Review of the prior 6 months of clinic data suggested approximately a 0.1 standard deviation (SD) for force and a 2 MU SD for *IP-AMUNE*, with a 0.05 minimal detectable difference per Motor Unit. A two-sided 0.05 level of significance and power of 0.8 suggested a sample size of 11 nerve surgeries. A post hoc sample size calculation arrived at a 0.08 minimal detectable difference, *IP-AMUNE* SD 1.6, and force SD 0.19, recommending a sample size of 34 surgeries.

3. Results

Twenty-eight nerve transfers were included. Table 1 breaks down the nerve transfer pairings, revealing the most common surgery as being restoration of elbow flexion through re-innervation

Table 1
Nerve transfer pairings.

Donor	Recipient	Frequency	Percent
ECRB	FDS	1	4
ECRB	Teres min	1	4
ECRB	AIN	1	4
Median	Biceps	4	14
Median	Brachialis	1	4
Median	Deltoid	1	4
SAN	Supraspinatus	3	11
SAN	Infraspinatus	3	11
SAN	Rectus fem ^a	1	4
Teres minor	Triceps	2	7
Triceps	Deltoid	3	11
Ulnar	Brachialis	5	18
Ulnar	Biceps	2	7
Total		28	100

ECRB: extensor carpi radialis brevis; SAN: Spinal Accessory Nerve; Rectus fem^a refers to a muscle and nerve transfer to restore elbow flexion.

of the biceps or brachialis, using fascicles of the ulnar or median nerves. Continuous and categorical variables are displayed in Tables 2 and 3 respectively. Table 2 is highlighted to demonstrate the greater sensitivity achieved through use of *IP-AMUNE* as a predictor variable, and *Force* as an outcome variable, compared to MRC for either predictor or outcome. We have also highlighted the *time to surgery* range; one patient undergoing surgery at 20 months. Fig. 1 shows the correlation between *IP-AMUNE* and *Force* without accounting for other variables. The correlation is moderate to strong ($r = 0.67$, $r^2 = 0.45$), showing a clear progression in force outcome as the pre-operative *IP-AMUNE* increases.

Fig. 2 compares the distributions of force outcome delineated by joint reanimated. We can see that in this cohort, shoulder abduction had an excellent outcome. Elbow flexion had the greatest variance, with some excellent outcomes. Consistent with the patients' proximal lesions and prior findings that distance to target muscle is an important prognostic factor (Tung and Mackinnon, 2010), restoration of hand function showed the least improvement.

Table 4 displays the results of the final multivariable linear regression model for predicting *Force* outcome after nerve surgery. This model includes the variables: *IP-AMUNE*; *Time to Surgery*; *Age*; *Diabetes*; *re-innervation Distance*; current *Smoking* status; and *Complications*. The only significant predictive variables were *IP-AMUNE* ($p < 0.001$) and current *Smoking* status ($p < 0.005$).

This final model predicts an 8.3% increase in *Force* for each MU increase in *IP-AMUNE* found pre-operatively, with a 95% confidence interval of between 4.09% and 12.52%. It also suggests that if the patient is a current smoker, the expected force outcome is worse by approximately 26.9%, albeit it with a wide confidence interval (−44.6% to −9.2%).

Further analysis included correlating secondary independent and dependent variables against the primary *IP-AMUNE* and *Force* variables; these included the Donor and Recipient modified MRC grades. Table 5 displays these results, both for univariable and multivariable regression analysis, none of which were significant.

4. Discussion

Pre-operative donor muscle *IP-AMUNE* predicted recipient muscle force at least one year after nerve transfer surgery ($p < 0.001$; $r = 0.67$). Although a small sample size and not a prospective study, this result suggests a more quantitative approach to neurophysiology has the potential to contribute significantly more to nerve transfer planning than the traditional more subjective grading of interference patterns or MRC grading. *IP-AMUNE* does not add sig-

Table 2
Continuous variables.

Variable	Min	Max	Mean	SE	SD	Variance
IP-AMUNE donor	3	7	5.32	0.29	1.56	2.43
MRC donor	3	5	4.7	0.15	0.79	0.63
Force	0	66	25	3.58	18.9	359
MRC recipient	0	5	4.0	0.21	1.13	1.29
Time to last exam	12	48	23.8	1.74	9.2	84.8
Time to surgery	4	20	8.8	0.9	4.58	21
Distance	3	18	5.9	0.72	3.8	14.5
Age	16	71	37	3.72	18.99	360.5
BMI	19.7	42.4	26.8	1.09	5.58	31.1

IP-AMUNE: interference pattern – average motor unit number estimate. MRC: Medical Research Council. Force: Percent force of contralateral arm. Distance: re-innervation distance. BMI: Body Mass Index.

Table 3
Categorical variables.

Variable	Category	# of nerves (28)	Percent (%)
Joint reanimated	Shoulder Abduction	7	25.0
	Ext Rotation	4	14.3
	Elbow Flexion	13	46.4
	Elbow Extension	2	7.1
	Hand	2	7.1
Alcohol	Significant	6	21.4
	Not significant	22	78.6
Gender	Male	25	89.3
	Female	3	10.7
Diabetes	Yes	3	10.7
	No	25	89.3
Smoking	Yes	5	17.9
	No	23	82.1

MRC, Medical Research Council grade.

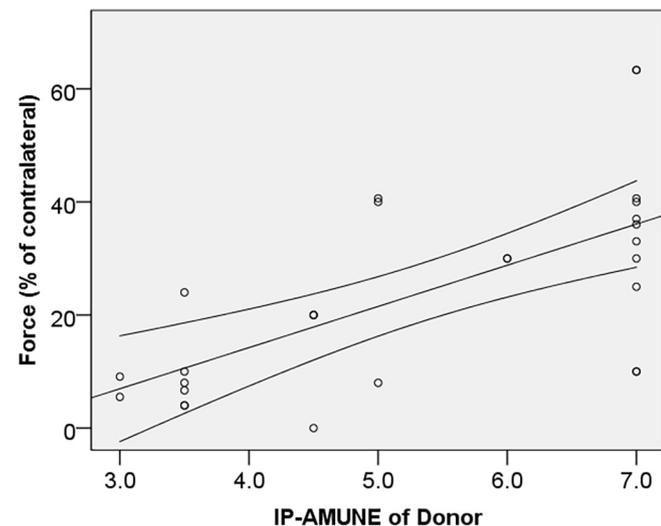


Fig. 1. Correlation of pre-operative IP-AMUNE to post-operative Force. A significant correlation can be seen ($r = 0.67$, $r^2 = 0.45$). IP-AMUNE: interference pattern – average motor unit number estimate. Force: percent force of contralateral limb.

nificantly to study time but may require reviewing IP recordings until proficiency is established in identifying individual motor units. It also has excellent potential to be automated using signal decomposition techniques.

None of the other variables were reliable predictors of force except for smoking, which adversely affected the outcome ($p < 0.005$). Although previously identified as significant predictors in literature, we found that time from injury to surgery, distance of nerve growth to target, and age were not clearly predictive in our study, likely due to small sample size. Additionally, no other

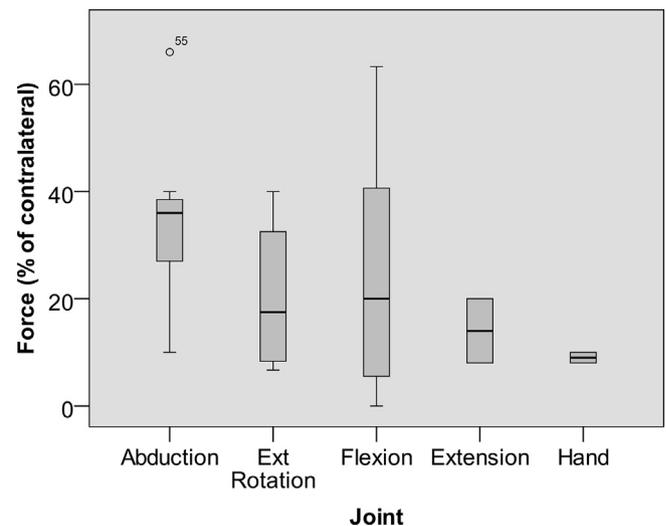


Fig. 2. Distribution of force outcomes by joint reanimated. “Abduction” = shoulder abduction; “Ext Rotation” = shoulder external rotation; “Flexion” = elbow flexion; “Extension” = elbow extension; “Hand” = finger flexion. Force: percent of contralateral limb.

potential confounder significantly contributed to predicting force outcome; including alcohol, gender, diabetes, and BMI.

We also found no significant correlation between any combination of secondary predictor and outcome variables. This included correlations between: donor MRC and force; donor MRC and recipient MRC; and IP-AMUNE and recipient MRC. These findings emphasize the need for appropriate outcome measures in clinical research. MRC grading is not an adequate surrogate for re-innervation or force and we should be cautious when using MRC grading to select potential donor nerves

Comparing our cohort to prior studies, the results are comparable. The largest subsection involved reanimation of elbow flexion whereby 10 of 13 patients (77%) achieved MRC grade 4 or greater. This is similar to historical outcomes from previously published series (Oberlin et al., 1994, 2009; Leechavengvongs et al., 1998; Sungpet et al., 2000; Mackinnon et al., 2005; Tung and Mackinnon, 2010). Similarly, the second largest subsection involved shoulder abduction reanimation, which resulted in 7 of 7 (100%) patients achieving MRC grade 4 or greater. Prior studies have also reported excellent outcomes (Leechavengvongs et al., 2003; Bertelli and Ghizoni, 2004; Bertelli et al., 2007; Garg et al., 2011; Lee et al., 2012). However, regarding time until surgery, our study included a case with an excellent result after a 20-month delay; the commonly held assumption that there may be little point performing surgery after one year or 18 months should be challenged.

Table 4
Coefficients for final regression model.

Variable	Unstandardized Coefficients		Standardized Coefficients			95.0% CI for B	
	B	Std. Error	Beta	t	Sig.	Lower	Upper
Constant	−18.7	11.34		−1.65	0.119	−42.73	5.34
IP-AMUNE	8.3	1.99	0.69	4.18	0.001	4.089	12.51
Time to Surgery	0.49	0.89	0.10	0.55	0.590	−1.39	2.37
Age	−0.075	0.21	−0.065	−0.35	0.728	−0.53	0.38
Diabetes	−28	22.3	−0.36	−1.26	0.226	−75.2	19.9
Distance	−0.2	1.18	−0.027	−0.17	0.870	−2.7	2.3
Smoking	− 26.9	8.35	−0.5	−3.22	0.005	− 44.6	− 9.2
Complication	5.9	19.76	0.09	0.3	0.767	−35.9	47.8

Dependent Variable: Force (percent of contralateral limb); IP-AMUNE: interference pattern – average motor unit number estimate of the Donor muscle; Distance: re-innervation distance.

Table 5
Secondary variable regression analyses.

Independent vs Dependent Variable	Regression model	Significance
IP-AMUNE vs MRC Recipient	Univariable	0.141
	Multivariable	0.421
MRC Donor vs Force	Univariable	0.712
	Multivariable	0.542
MRC Donor vs MRC Recipient	Univariable	0.733
	Multivariable	0.469

MRC: Medical Research Council; IP-AMUNE: interference pattern – average motor unit number estimate.

There are several limitations beyond the small sample size. Ascribing force to an individual muscle is difficult if more than one muscle acts across the joint, although our approach described earlier should help mitigate against this. Aggregating by the joint reanimated rather than the nerve pairing is not ideal but sample size was too small to allow further stratification. The interval between surgery and the final post-operative evaluation may need to be significantly more than 12 months to capture the full extent of reinnervation. Finally, this study only involved a single transfer associated with UMN weakness. Although studied extensively in the past (Shahani, 2014), more precise quantification of the proportion of weakness attributed to UMN versus LMN weakness is an area of neurophysiologic interest that needs developing.

Future endeavors should be aimed at establishing prospective nerve transfer surgery repositories. At our institution, we currently obtain pre-operative donor and recipient nerve histopathological axon counts. Nerve transfer surgery represents a unique opportunity not only to revisit classic quantitative neurophysiology techniques and imagine new bespoke techniques but also to evaluate other biomarkers such as Electrical Impedance Myography (Rutkove, 2009), ultrasound, and MR neurography, taking advantage of the potential for direct histopathologic validation.

5. Conclusion

The semi-quantitative EMG technique of IP-AMUNE appears to be a promising predictor of outcomes in nerve transfer surgery and may aid in donor nerve selection when evaluating patients pre-operatively. This, and other quantitative neurophysiological techniques, should be evaluated further in larger prospective studies and validated with histopathology where possible.

Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

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