



Surgical strategy in extensive proximal brachial plexus palsies

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Abstract

Purpose To describe and assess an overall surgical strategy addressing extensive proximal brachial plexus injuries (BPI).

Methods Forty-five consecutive patients' charts with C5–C6–C7 and C5–C6–C7–C8 BPI were reviewed. Primary procedures were nerve transfers to restore elbow function and grafts to restore shoulder function when a cervical root was available; when nerve surgery was not possible or had failed, tendon transfers were conducted at the elbow while addressing shoulder function with glenohumeral arthrodesis or humeral osteotomy. Tendon transfers were used to restore finger extension.

Results Forty-one patients underwent elbow flexion reanimation: thirty-eight had nerve transfers and eight received tendon transfers, including five cases secondary to nerve surgery failure; grade-3 strength or greater was reached in thirty-seven cases (90%). Twenty-nine patients had nerve transfers to restore elbow extension: twenty-five recovered grade-3 or grade-4 strength (86%). Forty-one patients underwent shoulder surgery: fourteen had nerve surgery and thirty-one received palliative procedures, including four cases secondary to nerve surgery failure; thirty patients recovered at least 60° of abduction and rotation (73%). Distal reconstruction was performed in thirty-seven patients, providing finger full extension in all cases but two (95%).

Conclusions A standardized strategy may be used in extensive proximal BPI, providing overall satisfactory outcomes.

Keywords Brachial plexus · Nerve transfer · Palsy · Shoulder fusion · Tendon transfer

The study was conducted at the Clinique du Mont Louis. Malo Le Hanneur and Thibault Lafosse equally contributed in the conception of this manuscript.

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Introduction

Numerous surgical techniques have been proposed regarding brachial plexus injuries (BPI). Depending on the extent and type of palsy, the delay from injury, the associated lesions and the mechanism of trauma, different combinations may be offered [1].

Since functional impairments are limited to shoulder function and elbow flexion in C5–C6 palsies, early primary nerve surgery may address all deficits at once. Bertelli and Ghizoni, for example, proposed a triple nerve transfer for avulsion cases where the spinal accessory nerve is transferred to the suprascapular nerve, the triceps long or lateral head motor branch to the axillary nerve, and ulnar nerve fascicles to the biceps motor branch [2].

In C5–C6–C7 palsies, however, which represent approximately 20–35% of patients with a brachial plexus stretch injury, deficiencies may variably affect elbow, wrist and finger extension; when the C8 root is involved, wrist flexion may be weakened as well [3]. Additionally, new therapeutic challenges arise, such as the inability to use a triceps motor branch to reinnervate the axillary nerve in cases of

triceps palsy, less ulnar nerve fascicles available to reanimate elbow flexion, or the restoration of wrist and finger extension with limited donor options [4]. Therefore, due to the complex and heterogeneous nature of these deficiencies and the subsequent limited panel of therapeutic options, a well-planned and staged strategy is mandatory to achieve satisfactory functional outcomes [5].

This retrospective study aims to describe and report on the results of a standardized surgical strategy for C5–C6–C7 and C5–C6–C7–C8 palsies that combines neurological and palliative procedures.

Materials and methods

Between January 2002 and December 2010, forty-five patients (forty-one males and four females) presented with a C5–C6–C7 brachial plexus injury (Table 1); in eighteen cases, clinical evidence of an additional C8 root injury was found (i.e., flexor carpi ulnaris weakness).

Surgical strategy

Nerve surgery was the primary step (Fig. 1). The average time between the injury and the nerve surgery was 8.2 months (range 2–60 months), including twelve delayed cases and six late cases (i.e., preoperative delay over 6 and 12 months, respectively). Contraindications were clinical evidence of spontaneous recovery, joint stiffness, and a preoperative delay over 12 months. For elbow function, a preoperative delay over 12 months was not considered as a contraindication, provided that fibrillations were detected on the electromyographic (EMG) study.

To reinnervate the biceps and the brachialis muscles, double nerve transfers were performed using ulnar and median fascicles, respectively (UBMB). Ulnar nerve fascicles to the flexor carpi ulnaris (FCU) were avoided in order to preserve it for secondary transfer. Subsequently, fascicles to the flexor digitorum profundus (FDP) or intrinsic muscles of the hand were selected. When intraoperative neurostimulation of the ulnar nerve fascicles was not satisfactory, the biceps was reinnervated by a second median nerve fascicle (MBMB), selecting fascicles to the flexor carpi radialis (FCR) muscle in order to preserve the flexor digitorum superficialis (FDS) muscle for secondary transfer. For elbow extension, three intercostal nerves (ICN, 3, 4 and 5) were transferred to the triceps long head motor branch (TLHMB).

Regarding the shoulder, the indication depended on the injury type. When root lesions were determined as preganglionic during preoperative assessment (i.e., absent Tinel sign and avulsion evidence of C5, C6, and C7 roots), the supraclavicular brachial plexus was not explored surgically; otherwise, cervical exploration was performed and the

Table 1 Cohort details

Patients (no)	45
Age (years)	32 (16;60)
Sex ratio (M/F, no)	41/4
Etiologies	
RTA (motorbike/car/quad bike/bicycle, no)	40 (34/3/2/1)
Sports (judo/equestrianism, no)	2 (1/1)
Work related injury (no)	3
Associated injuries	
Ipsilateral UL fractures (shoulder-arm/elbow-forearm/wrist-hand, no)	20 (12/3/5)
Other fractures (spine/ribs/limbs, no)	6 (1/1/4)
Other injuries (head/thorax, no)	5 (3/2)
Strength at initial examination ($\leq 2/3/\geq 4$, no) ^a	
Elbow flexion	44/0/1
Elbow extension	33/6/6
Shoulder abduction	42/0/3
Shoulder external rotation	41/1/3
Wrist extension	36/2/7
Finger extension	33/1/11
Positive supraclavicular Tinel's sign (no)	20
MRI lesions	
Rootlet avulsions (C4/C5/C6/C7/C8, no)	45 (1/9/14/17/4)
PM (C5/C6/C7/C8, no)	23 (2/6/11/3)
Follow-up (months)	64 (28;136)

Data reported as mean (range), unless otherwise indicated

No number of patients and/or lesions (reported as absolute values), M male, F female, RTA road traffic accident, UL upper limb, FCU flexor carpi ulnaris, PM pseudomeningocele

^aMuscular strength was assessed according to the British Medical Research Council grading system

roots were assessed intraoperatively, based on their general appearance, firmness and response to electrostimulation. When a viable root was found, sural grafts were carried out, targeting the suprascapular nerve (SSN) and the axillary nerve (AN). In cases with no graftable root, nerve transfers involving ICN or the TLHMB were conducted when possible; in three cases, ICN was available to be transferred to the AN (two patients) or the SSN (one patient); in one case, the TLHMB was available to be transferred to the AN. In cases with no graftable root and without the TLHMB or ICN available for transfer, no transfer involving the spinal accessory nerve (SAN) was performed in order to preserve the trapezius function, and shoulder function was primarily addressed with palliative procedures.

Glenohumeral arthrodesis (GA) was performed in patients with flail shoulder, either primarily in avulsion injuries or late cases, or secondarily in cases of nerve surgery failure. In patients with a stable glenohumeral joint and a predominant lack of external rotation, an external derotation humeral osteotomy (HO) was performed.

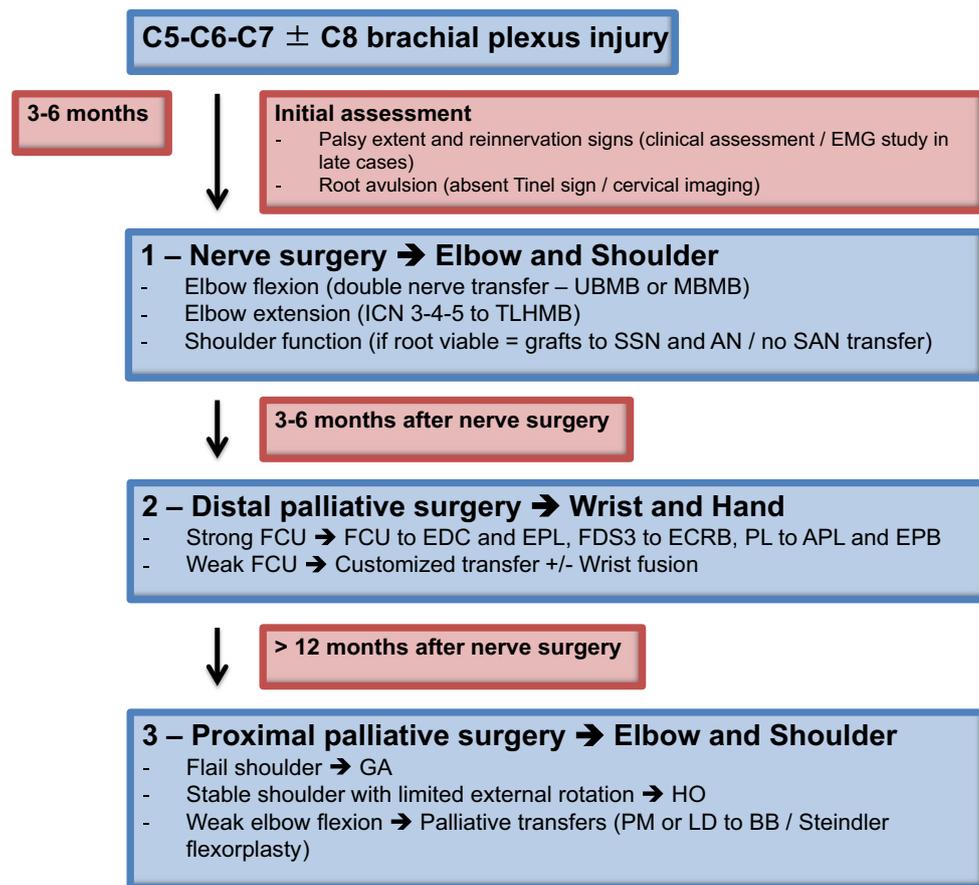


Fig. 1 Flowchart of the surgical strategy (C5–C6–C7±C8: cervical roots; *EMG* electromyography, *UBMB* ulnar fascicle to biceps motor branch and median fascicle to brachialis motor branch, *MBMB* median fascicles to biceps and brachialis motor branches, *ICN* intercostal nerves, *TLHMB* triceps long head motor branch, *SSN* suprascapular nerve, *AN* axillary nerve, *SAN* spinal accessory nerve, *FCU*

flexor carpi ulnaris, *EDC* extensor digitorum communis, *EPL* extensor pollicis longus, *FDS3* flexor digitorum superficialis of the third finger, *ECRB* extensor carpi radialis brevis, *PL* palmaris longus, *APL* abductor pollicis longus, *EPB* extensor pollicis brevis, *GA* glenohumeral arthrodesis, *HO* external derotation humeral osteotomy, *PM* pectoralis major muscle, *LD* latissimus dorsi muscle)

Regarding elbow flexion, tendon transfers were carried out in late cases with no electrical activity on the EMG or following nerve surgery failure. Pectoralis major (PM) or latissimus dorsi (LD) bipolar transfers to the biceps were our primary choices; the Steindler flexorplasty was reserved to cases with PM and LD palsies.

To restore wrist and finger extension, our primary choice was to transfer the FCU to the extensor digitorum communis (EDC) and extensor pollicis longus (EPL), the FDS of the third finger to the extensor carpi radialis brevis (ECRB), the palmaris longus (PL) to the extensor pollicis brevis (EPB) and abductor pollicis longus (APL). In patients with FCU palsy, customized transfers were conducted, most commonly involving the FDS. Wrist fusion was performed in patients with lack of donor muscles.

Data collection

Investigations were conducted according to the 1964 Declaration of Helsinki ethical standards and to the MR-003 reference methodology [6]; the study was registered in the CNIL database register (No. 2052222 v 0); and each patient was individually informed and consented before any data collection.

Review of all the charts yielded patient demographics, initial clinical and imaging findings, surgical strategy, and last postoperative physical examination findings, including active range of motion of all joints and elbow flexion–extension strengths based on the British Medical Research Council (BMRC) grading system. A qualitative scale was then established for each joint based on this information.

Regarding elbow flexion and extension, poor, fair and good results were, respectively, defined as grade-2 strength or less; grade-3 strength; grade-4 strength. In patients with grade-4 elbow flexion strength, the maximum weight the patient could lift at the wrist with the elbow flexed at 90° was noted; when grade-4 elbow extension strength was observed, the patient was asked to press on a scale with the wrist with the elbow flexed at 90°. Shoulder function grading depended on active abduction and rotational arc of motion (i.e., sum of internal rotation and external rotation, which were measured from neutral rotation); poor, fair and good results were, respectively, defined as abduction and/or rotation lesser than 45°; both abduction and rotation of 45° or greater; both abduction and rotation of 60° or greater. Regarding distal reconstruction, poor, fair and good results were, respectively, defined as incomplete extension of the metacarpophalangeal (MP) joints; passive full extension of the MP joints due to wrist flexion (tenodesis); active full extension of the (MP) joints with the wrist 20° extended.

Statistical analysis

To compare postoperative active range of motion after palliative or neurological procedures, the Shapiro–Wilk test was used on all data and excluded their normal distribution; Mann–Whitney *U* tests were subsequently used. Results were presented as mean (range), unless otherwise stated. The level of significance was defined as $P < .05$, for all tests.

Results

The average duration of follow-up after first surgery was 63.6 months (range 28–136 months).

Elbow flexion

Elbow flexion reanimation was conducted in forty-one patients (Figs. 2, 3). Thirty-eight patients received double nerve transfers, including thirty-four UBMB and four MBMB. Good (twenty-eight patients) and fair (one patient) results were observed in twenty-nine patients (76%); patients with grade-4 strength resisted to a mean loading of 6.2 kg (range 2–11 kg). Poor results were observed in nine patients after nerve surgery; five underwent secondary tendon transfers (i.e., four bipolar PM transfers and one Steindler flexorplasty), allowing for grade-3 strength in all cases; no palliative options were suitable for the others (i.e., two patients refused to undergo additional surgery, two patients presented secondary stiffness due to prolonged lack of passive mobilization). Palliative surgery was performed primarily in three late cases without electrical reinnervation signs (i.e., two bipolar PM transfers and one Steindler flexorplasty); grade-3 strength was obtained in all cases. At last follow-up, good and fair results were thus observed in thirty-seven patients (90%). Conservative treatment was conducted in four patients; two presented with elbow stiffness due to concomitant fractures, and one recovered spontaneously; the last patient presented with a five-years-old injury, previously operated on at another institution (i.e., sural grafts from C5

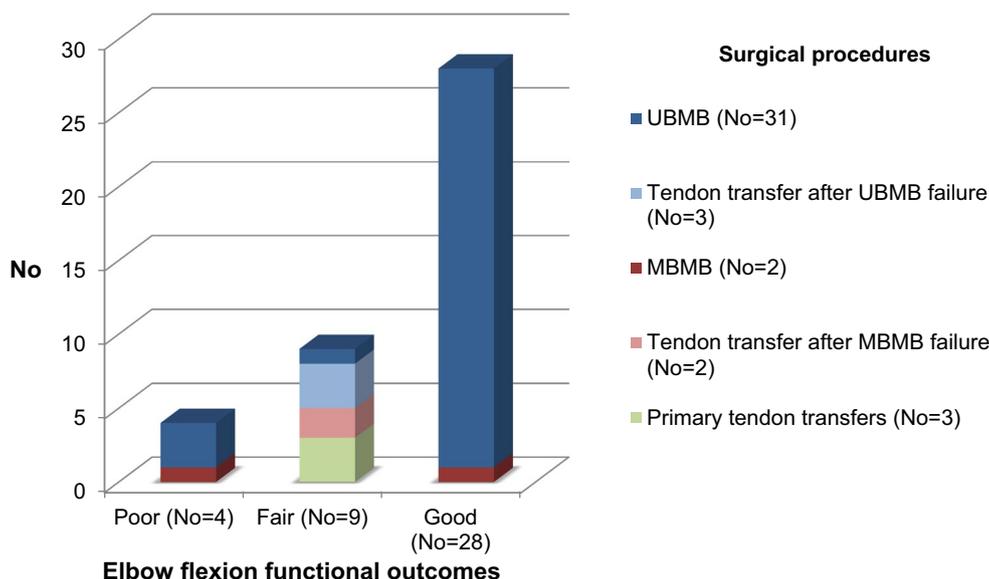
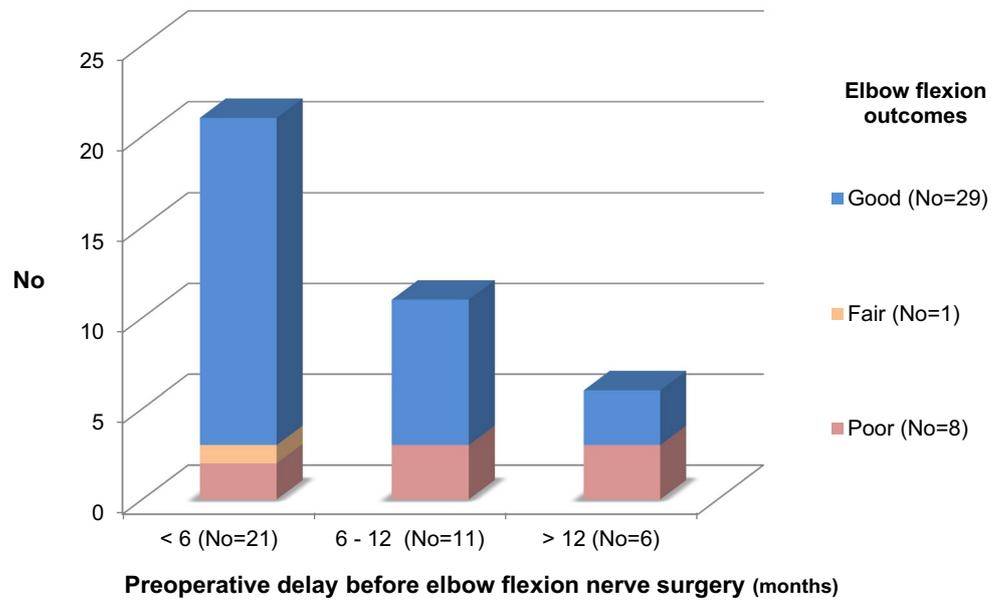


Fig. 2 Bar graph illustrating the outcomes of the different surgeries performed to restore elbow flexion (No number of patients, UBMB ulnar fascicle to biceps motor branch and median fascicle to brachialis motor branch, MBMB median fascicles to biceps and brachialis motor branches)

Fig. 3 Bar graph showing the repartition of elbow flexion outcomes according to the delay between the initial injury and the nerve surgery (*No* number of patients)



root to musculocutaneous nerve), with grade-2 strength noted at last follow-up but no palliative option available.

Elbow extension

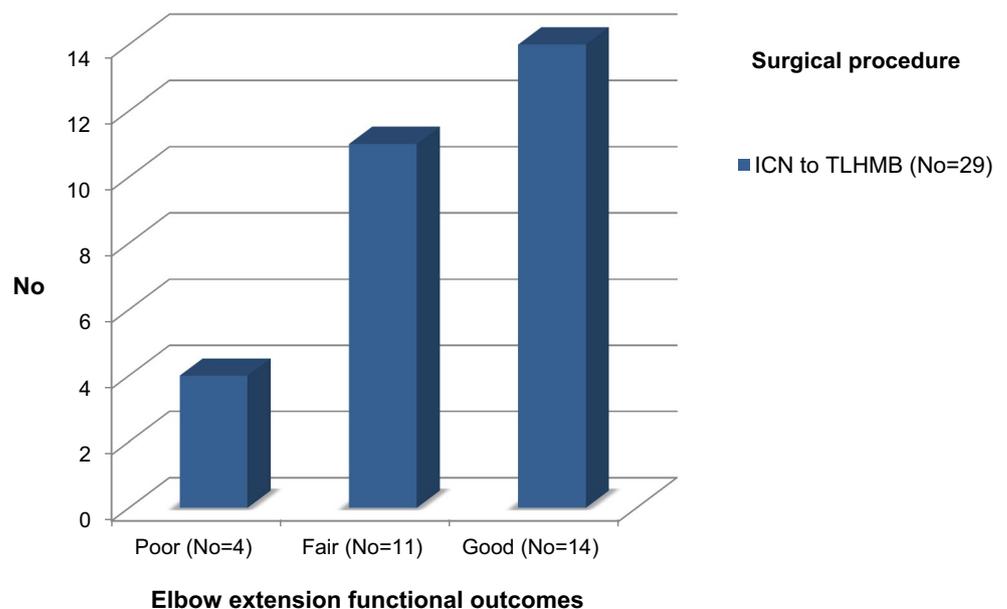
ICN was transferred to the TLHMB in twenty-nine patients (Figs. 4, 5). Good (fourteen patients) and fair (eleven patients) results were observed in twenty-five patients (86%); a mean pressing load of 3.4 kg (range 2–6 kg) was recorded in patients with grade-4 strength. Poor results were observed in four patients (grade-2 strength or less); however, improvement was considered satisfactory and no further palliative treatment was conducted. Conservative treatment

was adopted in sixteen patients, including five without initial triceps palsy and seven spontaneous recoveries. In four cases, nerve surgery was not an option because of delay (one patient), concomitant fractures with subsequent elbow stiffness (two patients), and concomitant proximal humeral open fracture with inclusion of the triceps motor branches into scar fibrosis (one patient); likewise, functional results were acceptable and no palliative treatment was carried out.

Shoulder

Forty-one patients required surgical attention. Nerve surgery was performed in fourteen patients, resulting in six

Fig. 4 Bar graph illustrating the elbow extension outcomes (*No* number of patients, *ICN* intercostal nerves, *TLHMB* triceps long head motor branch)



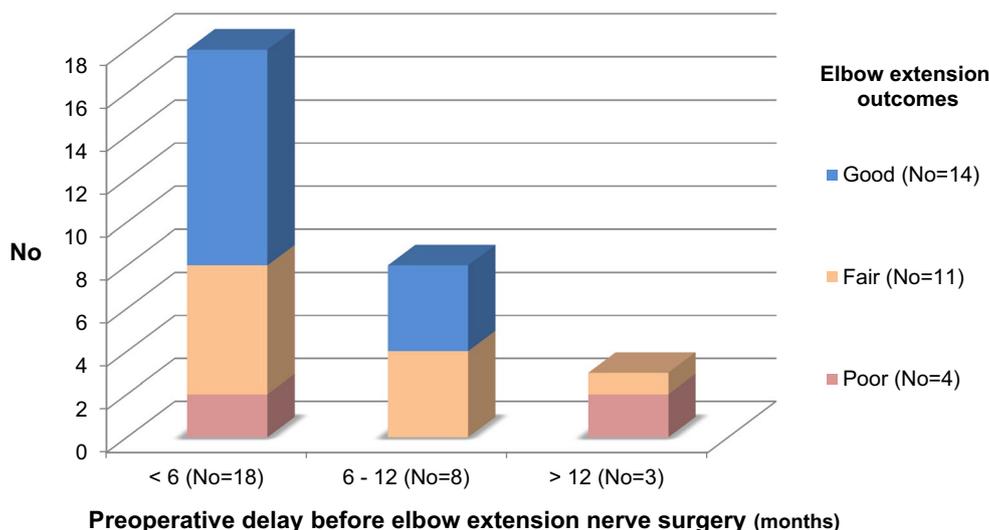


Fig. 5 Bar graphs showing the repartition of elbow extension outcomes according to the delay between the initial injury and the nerve surgery (No number of patients)

Table 2 Nerve surgery at the shoulder

Techniques	No	Results (good/fair/ poor, no)
Grafts	9	5/1/3
C5 root to SSN and AN	8	5/1/2
C7 root to SSN and AN	1	0/0/1
Transfers ^a	5	1/2/2
SAN to SSN	2	1/0/1
LHTMB to AN	1	0/0/1
ICN 3, 4, 5 to AN	2	1/1/0
ICN 1 to SSN	1	0/1/0
No nerve surgery	31	–
Spontaneous recovery	6	–
Delay	9	–
No graftable root (PA)	6	–
No graftable root (IA)	10	–

No number of patients, SSN suprascapular nerve, AN axillary nerve, SAN spinal accessory nerve, LHTMB long head of the triceps motor branch, ICN intercostal nerves, PA preoperative assessment, IA intraoperative assessment

^aSome transfers were not performed at our institution (i.e., SAN to SSN). One patient benefited from 2 transfers, namely SAN to SSN (at other institution) and ICN 3, 4, 5 to AN (at our institution)

good results (43%) and three fair results (Table 2). Among the five patients with poor outcomes, secondary GA and HO were performed in one and three cases, respectively; one patient refused to undergo GA. In twenty-seven cases, palliative treatment was completed primarily; twenty-four patients underwent GA, with twenty-three good results

(85%) and one fair result; three patients underwent HO, providing a fair result in all cases. At last follow-up, good results were observed in thirty patients (73%); fair results were observed in ten patients; and one patient presented poor results, with only 40° of active abduction (Fig. 6). In patients with good results, ranges of motions following palliative treatment were inferior than after nerve surgery (Table 3). Conservative treatment was adopted in four patients who spontaneously recovered a satisfactory shoulder function.

Hand

Palliative surgery for wrist and finger extension was conducted in thirty-seven patients. Nineteen patients underwent FCU-based transfer, which provided good results in seventeen patients. Failure was observed in two cases; in both cases, tenodesis of the EPL and EDC tendons to the posterior aspect of the radius was performed as a revision, which provided one fair and one poor result. The remaining eighteen patients had FCU palsy, seven of whom underwent tendon transfers only and eleven required wrist fusion. Of these eleven, eight patients underwent associated transfers for finger extension while three did not (Table 4); good results were observed in all cases. At final evaluation, thirty-five patients presented with good results (95%). Conservative treatment was adopted in eight patients who did not suffer from finger and wrist extension palsy (four patients) or spontaneously recovered both functions (four patients).

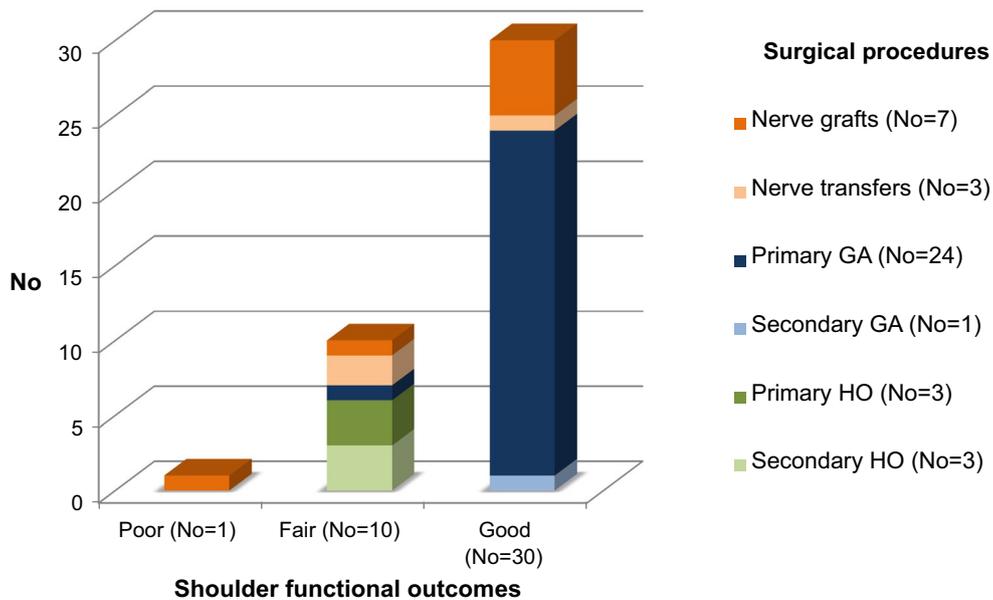


Fig. 6 Bar graph representing the functional results of the different surgeries performed to restore shoulder function (No number of patients, GA glenohumeral arthrodesis, HO external derotation humeral osteotomy)

Table 3 Active ranges of motion at last follow-up

Joints and motions ^a	Nerve surgery	Palliative surgery	P values
Elbow flexion (no)	29 133 (90;150)	8 99 (80;120)	< .001
Elbow extension (no)	25 − 6 (− 30;0)	–	–
Shoulder (no)	6	24	
Abduction	100 (70;120)	74 (60;90)	.003
External rotation	20 (10;40)	− 11 (− 30; 0)	< .001
Internal rotation	95 (90–100)	84 (70;90)	.002
Wrist (no) ^b		35	
Flexion	–	32 (10;60)	–
Extension	–	65 (30;80)	–
Metacarpophalangeal joints (no)		35	
Flexion	–	92 (70–100)	–
Extension	–	4 (0–20)	–

All data are reported in degrees as mean (standard deviation; range)

No number of patients

^aElbow values are based on good and fair results, whereas shoulder, wrist and metacarpophalangeal values are based on good results only. Metacarpophalangeal measurements were taken on the index finger with the wrist stabilized 20° extended by the examiner, when not fused

^bFused wrists were excluded from this analysis

Complications

Twenty-six postoperative complications were outlined during follow-up; their details and management are displayed in Table 5.

Discussion

In this retrospective study, a systematic approach to C5–C6–C7 and C5–C6–C7–C8 palsies was described, with nerve surgeries targeting primarily elbow flexion and

Table 4 Palliative surgery at the wrist and the hand

Techniques	No
FCU transfers	
FCU to EDC and EPL/FDS3 to ECRB/PL to APL EPB	15
FCU to EDC and rerouted EPL/FDS3 to ECRB	2
FCU to EDC and rerouted EPL/PT to ECRB	1
FCU to ECRB	1
Other transfers	7
FDS4 to EDC and EPL/FDS3 to ECRB/PL to APL EPB	1
FDS4 to EDC and rerouted EPL/FDS3 to ECRB	4
FDS3 to EDC and rerouted EPL	1
PT to ECRB	1
Wrist fusions	11
Simple fusion	3
Associated to transfer—FDS3 to EDC and rerouted EPL	8

No number of patients, *FCU* flexor carpi ulnaris, *EDC* extensor digitorum communis, *EPL* extensor pollicis longus, *FDS3 and 4* flexor digitorum superficialis of the 3rd and 4th fingers, *ECRB* extensor carpi radialis brevis, *PL* palmaris longus, *APL* abductor pollicis longus, *EPB* extensor pollicis brevis, *PT* pronator teres

extension, whereas proximal and distal reconstructions were mostly achieved through palliative procedures; applied in forty-five consecutive patients, satisfactory functional outcomes were observed in the majority of cases.

Elbow

As previously emphasized, elbow flexion outcomes following nerve surgery are less satisfactory in patients with an additional C7 and C8 root involvement [7]. Therefore, we performed a double transfer in all cases in order to maximize recovery chances [8]. In addition, since the FCU was to be transferred secondarily, fascicles to the FDP or intrinsic

hand muscles were selected as donors; Bertelli and Ghizoni demonstrated that hand strength is most commonly preserved after such transfers [9]. When no response to stimulation is observed in these fascicles, a second median fascicle may be used since they are the last to be impaired in extended palsies [10].

Regarding elbow extension, Goubier and Teboul reported effective triceps activity in eight cases out of ten using ICN transfers in their initial study [11]. Except the three failures depicted by Flores, similar outcomes are presented in the literature and in our series [11–13]; hence, we would recommend this procedure in such indications. Indeed, we consider that intraplexal alternatives (i.e., thoracodorsal and medial pectoral nerves) should be preserved in the event of nerve surgery failure, since bipolar PM and LD transfers are reliable palliative solutions [14]. Furthermore, extraplexal donors (i.e., phrenic nerve, hypoglossal nerve) appear to be more invasive options and should be avoided [15].

In our experience, UBMB and ICN to TLHMB transfers are reliable procedures for elbow flexion and extension reanimation, respectively. Therefore, we consider that cervical roots, when available, should be used to reanimate shoulder function.

Shoulder

Most authors agree on using viable roots to perform grafts targeting the upper trunk and/or its branches, but avulsion lesions remain controversial [5, 16–19]. In our previous experience, we observed disappointing results with the sole use of the SAN to SSN transfer to restore shoulder abduction. Furthermore, the lack of external rotation may not be addressed as well, as outlined by Baltzer et al. [18]. To enhance the chance of recovery of shoulder function, some authors recommend to add the reinnervation of the

Table 5 Postoperative complications and management

Complications (No)	Management
Shoulder (7)	
Nerve surgery failures (5)	GA or HO
GA non-union (2)	Autogenous iliac bone graft
Elbow (16)	
Elbow flexion nerve surgery failures (9)	Palliative transfers
Elbow extension nerve surgery failures (4)	Conservative treatment
FPL and FDP2 palsy due to median fascicles harvesting (1)	Tenodesis—FPL and FDP2 to FDP4
Co-contraction TB—BB (1)	TB BōTox injection
Wrist (3)	
Transfer failure (2)	Tenodesis—EPL and EDC to radius
Non-union (1)	Autogenous iliac bone graft

No number of complications, *GA* glenohumeral arthrodesis, *HO* humeral osteotomy, *FCU* flexor carpi ulnaris, *AIN* anterior interosseous nerve, *FPL* flexor pollicis longus, *FDP 2 and 4* flexor digitorum profundus of the 2nd and 4th fingers, *TB* triceps brachii; biceps brachii, *BōTox* botulinum toxin, *EPL* extensor pollicis longus, *EDC* extensor digitorum communis

axillary nerve [20]. In patients with grade-3 elbow extension strength, we consider that the TLHMB should not be transferred to the AN due to unpredictable outcomes [21]; however, if triceps function is sufficient, ICN might be used for shoulder function [22, 23]. In patients with grade-2 elbow extension strength or less, since the ICN are used to restore elbow extension, more invasive harvests would be needed, such as the phrenic nerve or a branch of the long thoracic nerve [19, 24].

Another approach would be to avoid this transfer (i.e., SAN to SSN transfer) in patients with greater than C5–C6 level injuries in order to perform primarily palliative surgeries in optimal conditions, including GA and tendon transfers [16, 18, 25]. With an average abduction around 70°, our results are consistent with the existing literature [26, 27] and thus moderately superior than what may be expected from tendon transfers [25, 28]. Nonetheless, Elhassan et al. recently described new possibilities of transfers involving the lower trapezius muscle, which provided promising outcomes regarding shoulder external rotation [25, 29].

Distal reconstruction

For the past decade, nerve transfers have been emphasized as a viable alternative to tendon transfers to reanimate hand and wrist functions. In brachial plexus palsy, Bertelli et al. [10] have experienced good results by transferring the pronator quadratus branch to the nerve to the ECRB to reanimate wrist extension; however, they recommended addressing finger extension secondarily with FCU transfer, due to the lack of nerve donors. In our experience, tendon transfers allow for a fast functional recovery without preventing delayed spontaneous reinnervation, providing consistent outcomes with finger and wrist extension independent from one another. In cases with lack of donors, radiocarpal arthrodesis remains a reliable solution [30].

General considerations

As previously outlined in the literature, nerve surgeries should be performed within the first 6 months to ensure optimal results (Figs. 3, 5) [1]. However, due to very encouraging results that we obtained for elbow function in early cases, we extended our indications to delayed and late cases, provided that fibrillations remained present on the preoperative EMG study. Regarding elbow flexion, we had six patients that met these criteria, and four of them recovered satisfactory function. Regarding elbow extension, three patients met these criteria; one patient recovered grade-3 elbow extension strength whereas the two remaining patients had grade-2 strength at final follow-up. In contrast, due to much more unpredictable outcomes in early cases, we did not perform any nerve surgery for shoulder function in late cases.

Distal reanimation was the next step, in order to enable early involvement of the hand in daily living activities, while proximal nerve surgeries progressively recovered [16]. Nonetheless, we routinely waited for an interval between nerve transfers for restoration of elbow flexion and distal tendon transfers, in order to acknowledge any postoperatively deficit and subsequently identify available donors. Proximal reconstruction was conducted last, at least 1 year after nerve surgery; however, when GA was performed primarily, such a delay was not observed since no recovery was expected.

Conclusion

While considering their clinical heterogeneity, C5–C6–C7 and C5–C6–C7–C8 palsies may be managed through a standardized association of neurological and palliative procedures, allowing for satisfactory functional outcomes. If elbow function may be addressed with nerve transfers in most cases, shoulder and hand functions mainly depend on palliative procedures; early nerve surgery should thus be performed accordingly, by preserving the SAN proximally and preserving ulnar fascicles to the FCU when selecting a motor branch for elbow flexion reanimation.

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Authors' contribution MLH contributed to conception, writing and editing. TL involved in conception, writing and editing. ACB helped with corrections, writing and editing. ZB contributed to corrections, writing and editing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards All investigations were conducted in accordance with the 1964 Declaration of Helsinki ethical standards and the MR-003 reference methodology*; the study was registered in the National Commission for the Computer Science and Liberties (Commission Nationale de l'Informatique et des Libertés—CNIL) database register (No. 2052222 v 0); and each patient was individually informed and gave his/her consent before any data collection and analysis.* Journal Officiel de la République Française n°0189 du 14 août 2016. Texte N°77. [legifrance.gouv.fr. https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000033028290&dateTexte=&categorieLie n=id](https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000033028290&dateTexte=&categorieLie n=id). Access date: 01/01/2018.

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