Satisfaction and Functional Outcome of Surgical Treatment in Patients with Brachial Plexus Injury: A Decade of Retrospective Comparative Study

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Background: Brachial plexus injury (BPI) is a severe peripheral nerve injury resulting in physical disability. Few studies have investigated the postoperative functional status. We aimed to evaluate the satisfaction with surgical treatment in patients with BPI referred to the Panzdah-e Khordad Hospital, Tehran, Iran from 2011 to 2021.

ABSTRACT

Methods: In this descriptive-analytical retrospective comparative study, physical examination, along with BrAT, and DASH questionnaires were used to evaluate the patients' status. Then the collected data on the patients' functional status and movements were collected. To compare the mean of quantitative variables before and after the surgery, the dependent t-student was used.

Results: Generally, the patients stated that they still had considerable difficulty doing most of the items of the questionnaires. Nevertheless, there was a significant difference between the following variables before and after surgery; shoulder abduction goniometry (0-150) and force (M0:M5), shoulder external rotation goniometry (0-90) and force (M0:M5)), shoulder forward flexion goniometry (0-180) and force (M0:M5)), elbow flexion goniometry (0- 150), elbow extension force (M0:M5), and wrist and finger muscle force (M0:M5) (P<0.001).

Conclusion: Posterior approach in BPI surgery was associated with good outcomes in terms of shoulder external rotation and abduction. However, patients still suffered from difficulties in daily activities.

Keywords: Brachial nerve injury; Disability; Functional status; Nerve repair; Nerve transfer

Please cite this paper as:

Yavari M, Shahrokh Shahraki S, Mousavizadeh SM, Karimi Rouzbahani A, Mahmoudvand G, Sedghi Asl H. Satisfaction and Functional Outcome of Surgical Treatment in Patients with Brachial Plexus Injury: A Decade of Retrospective Comparative Study. World J Plast Surg. 2022;11(3):28-37. doi: 10.52547/wjps.11.3.28

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Received: 2022/08/09 **Accepted:** 2022/10/28 INTRODUCTION

Brachial plexus injury (BPI) is described as a drastic peripheral nerve injury that involves the upper extremities, leading to functional impairment and physical disability¹. BPI is caused by stretch or tearing of the C5 to T1 nerve roots due to penetrating injuries, motor vehicle accidents, falls, etc.^{2, 3}. The evaluation of BPI mainly depends



on a comprehensive physical examination, complemented by electrodiagnostic and imaging studies⁴. Denervation caused by injury can cause declined contractile strength and muscle atrophy⁵. As muscle atrophy will initiate immediately after the injury, early surgical management is considered the best predictor of a favorable outcome³.

Various surgical techniques are used to manage BPI, including nerve grafting, nerve transfers, muscle transfers, nerve repair, and neurolysis⁶. The main goal in BPI surgery is to stabilize the shoulder and recuperate abduction, and to achieve this, the accessory nerve can be transferred to the suprascapular nerve⁷. The nerve is mostly transferred through the anterior approach but it might be associated with some difficulties compared with the posterior approach ⁷. Only a limited number of studies have investigated the satisfaction of patients with surgical intervention and their quality of life⁸. The current data suggest that after treatment patients in their quality of life⁹.

We aimed to evaluate the satisfaction with surgical treatment in patients with BPI in Tehran, Iran from 2011 to 2021.

METHODS AND MATERIALS

Study design and participants

This was a descriptive-analytical retrospective comparative study conducted at the Panzdah-e Khordad Hospital, Tehran, Iran from 2011 to 2021. Patients with BPI who were eligible for surgery according to the Green's operative hand surgery book¹⁰, and underwent different approaches, including brachial plexus neurolysis, nerve repair, nerve transfer, muscle transfer, nerve graft, and free muscle transfer were included (Figures 1 and 2 illustrate the anatomy of brachial plexus).

We aimed to examine the patients' range of motion, functional status, and satisfaction with surgical treatment. Inclusion criteria were as follows; Patients with BPI who were candidates for surgical intervention, e.g. closed BPI with no improvement after 3 months of conservative treatment, brachial plexus avulsion within the first three weeks after the injury, plexus penetration damage within the first three weeks after the injury, iatrogenic damage to the plexus within the first three weeks, < 1 year-delay after the trauma for primary microsurgery such as nerve graft, neurolysis, nerve transfers, and close target neurotization, intact vessels of the arm and thoracoacromial vessels in physical examination and angiography imaging, and pliable skin if performing Free Functional Muscle Transfer, intact latissimus dorsi muscle in case of pedicle transfer of this muscle to the biceps, and absence of comorbidities and unfavorable conditions for surgery.

Exclusion criteria were as follows; Birth paralysis of the brachial plexus, patient's non-consensual for surgery, age over 65 years, the presence of underlying diseases interfering the surgical process, and also presence of cut off sign, damaged anatomy of the site, and presence of severe scars if performing Free

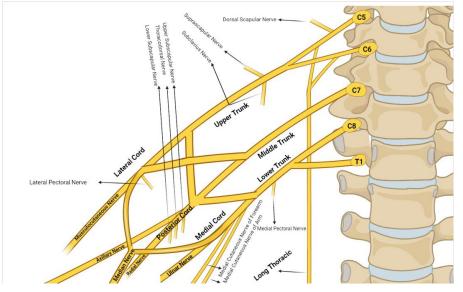


Figure 1: The anatomy of brachial plexus and its branches (Drawn by co-author Arian Karimi Rouzbahani)

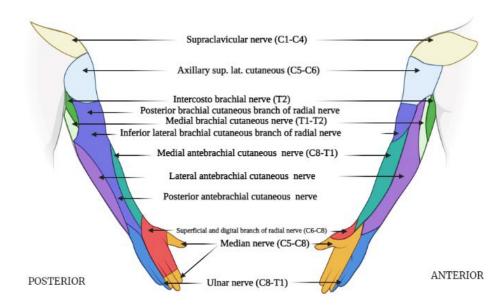


Figure 2: Posterior and anterior views of upper extremity dermatomes (Drawn by co-author Arian Karimi Rouzbahani)

Functional Muscle Transfer. Finally, a total number of 50 patients were included in this study.

Data collection

Close-target neurotization was used for patients with lower trunk injury or proximal ulnar injury. In this technique, nerve transfer is performed so that a direct coaptation is achieved at a more distal area closer to the target leading to a better recovery¹¹. In the Oberlin I procedure, fascicles of the ulnar nerve are transferred to the biceps nerve. However, in the Oberlin II procedure, $1 \le$ fascicles of the ulnar nerve are transferred to the biceps and a fascicle of the median nerve is transferred to the brachialis muscle motor branch¹². We also used gracilis free flaps obtained from the contralateral leg. Unipedicular latissimus dorsi transfer, and flexor carpi ulnaris transfer to extensor pollicis longus and extensor digitorum communis were applied. At least 3 months after surgery, the patients were asked about their severity of pain and were examined for shoulder, elbow, and finger movements. The demographic information was registered into a checklist. All the patients answered the questions of The Brachial Assessment Tool (BrAT) and the Disability of the Arm, Shoulder and Hand (DASH) questionnaires. The BrAT is a 31 item 4-respone Patient-Reported Outcome Measures that assesses activity limitation in patients with BPI 13. DASH is a 30-item; self-report questionnaire invented to evaluate physical function and symptoms in patients with musculoskeletal disorders of the upper extremity ¹⁴. Then the data on the patients' functional status, movements, and satisfaction with the procedure considering the interval between the accident and surgery and the duration of follow-up were collected and analyzed.

Data analysis

Qualitative indexes such as percentile, mean, and SD were used to describe the data. To compare the mean of quantitative variables before and after the surgery, the dependent t-student was used. The significance level was set at 0.05.

Ethical considerations

This study was conducted with the permission of the Research Ethics Committee of Shahid Beheshti University of Medical Sciences with the ethical code IR.SBMU.RETECH.REC.1400.472. Written informed consent was obtained from all participants. The principles of the Declaration of Helsinki were observed.

RESULTS

Fifty patients were included, from which 45 patients (90%) were male. The mean age was 25.54 ± 8.46 years. In 29 patients (58%) the type of injury was pan-brachial. The cause of injury was motor vehicle accidents in most of the patients (86%; n= 43).

Further demographic and clinical information is listed in Table 1.

Frequency distribution of the studied patients by their answers to the BrAT questionnaire is shown in Table 2. In terms of dressing and grooming items, arm and hand items, and no hand items, the total subscales showed that only 15%, 21.18%, and 34.33%, reported to do the activities easily. The results of the *t*-test showed that the subjects generally reported the ability of using hand in daily activities as very hard to do and could not do. The results of the *t*-test showed that the subjects generally reported the ability of using arm and hand in daily activities as very hard to do and could not do (Table 3).

Frequency distribution of the studied patients by their answers to the DASH questionnaire is shown in Table 4.

As shown in Table 5, in 22 of 30 items, the subjects reported moderate to severe difficulty.

As shown in Table 6, there was a significant difference between the following variables before and after surgery; shoulder abduction goniometry (0-150) and force (M0:M5), shoulder external rotation (goniometry 0-90) and force (M0:M5), shoulder forward flexion (goniometry 0-180) and force (M0:M5), elbow flexion (goniometry 0- 150), elbow extension force (M0:M5), wrist and finger muscle force (M0:M5) (P<0.001).

Characteristic		Frequency (percentage)
Carlan	Male	45 (90)
Gender	Female	5 (10)
	< 20	15 (30)
	20-30	23 (46)
Age (yr)	31-40	9 (18)
	$41 \le$	3 (6)
	Left	26 (52)
Side of injury	Right	24 (48)
	< 20	9 (18)
	20-50	7 (14)
Interval between surgery and interview (months)	51-80	10 (20)
	81-100	18 (36)
	101 ≤	6 (12)
Internet between DDI on decomposition (as each a)	<10	45 (90)
Interval between BPI and surgery (months)	10 ≤	5 (10)
	0	27 (54)
	1	14 (28)
Number of fractures	2	3 (6)
Number of fractures	3	3 (6)
	4	1 (2)
	7	2 (4)
	1	28 (56)
Number of procedures needed	2	17 (34)
	3	5 (10)
	C5 and C6	14 (28)
Nerve roots affected	C5-C7	7 (14)
	Pan-brachial	29 (58)
	Motor vehicle accident	43 (86)
	Fall	2 (4)
Cause of injury	Gunshot	0 (0)
Cause of injuly	Penetrating trauma	4 (8)
	Rotational injuries	0 (0)
	Other causes	1 (2)
Incidence of coma state	No	37 (74)
	Yes	13 (26)

 Table 1: demographic and clinical characteristics of patients undergoing BPI surgery.

	Frequency (percentage)					
Activity	Cannot do	Very hard	A little hard	Easy to do		
	now	to do now	to do now	now		
Use both arms to put on a T-shirt	21 (42)	12 (24)	12 (24)	5 (10)		
Use both arms to put on a pair of trousers	17 (34)	11 (22)	15 (30)	7 (14)		
Use both hands to put on socks	19 (38)	9 (18)	10 (20)	12 (24)		
Use both hands to put toothpaste on a toothbrush	24 (48)	7 (14)	12 (24)	7 (14)		
Use both hands to do up belt buckle	19 (38)	8 (16)	13 (26)	10 (20)		
Tuck your shirt in using your affected hand	11 (22)	16 (32)	14 (28)	9 (18)		
Use both hands to do up shirt buttons	17 (34)	15 (30)	13 (26)	5 (10)		
Use both hands to do up tight trouser buttons e.g. jeans	19 (38)	12 (24)	14 (28)	5 (10)		
Subscale 1: Dressing and grooming items (total)	147 (36.75)	88 (22)	105 (26.25)	60 (15)		
Wash both hands at same time	5 (10)	15 (30)	13 (26)	17 (34)		
Use both hands to push a pram, lawnmower or shopping Trolley	10 (20)	14 (28)	13 (26)	13 (26)		
Use both hands to do up zip including putting ends together	6 (12)	20 (40)	15 (30)	9 (18)		
Use both hands to spread butter or jam on a piece of bread	9 (18)	17 (34)	9 (18)	15 (30)		
Use both hands to tie up a rubbish bag and put in the bin	17 (34)	10 (20)	15 (30)	8 (16)		
Use both hands to tie up shoe laces	21 (42)	6 (12)	14 (28)	9 (18)		
Use a knife and fork at the same time	24 (48)	12 (24)	8 (16)	6 (12)		
Carry an object only using your affected arm so your other arm/hand is free to do another task	23 (46)	4 (8)	9 (18)	14 (28)		
Pick up a small object with the fingers of your affected hand eg a tablet, coin or pen	22 (44)	4 (8)	6 (12)	18 (36)		
Hold a pot of food with 1 hand and stir it with the other	11 (22)	12 (24)	15 (30)	12 (24)		
Use both arms/hands to change the sheet on a bed	7 (14)	17 (34)	10 (20)	16 (32)		
Use both hands to wash your face	14 (28)	19 (38)	15 (30)	2 (4)		
Use both arms to peg clothes on the washing line	11 (22)	13 (26)	18 (36)	8 (16)		
Use both hands to type on a keyboard	25 (50)	3 (6)	6 (12)	16 (32)		
Turn on a light switch using only your affected arm	19 (38)	17 (34)	2 (4)	12 (24)		
Use your affected hand to wash your other armpit	29 (58)	11 (22)	8 (16)	2 (4)		
Use both arms to lift a box or bag onto a shelf at eye level	21 (42)	8 (16)	18 (36)	3 (6)		
Subscale 2: Arm and hand items (total)	274 (32.23)	202 (23.77)	194 (22.82)	180 (21.18)		
Maintain control of your affected arm so you don't need to wear a sling	3 (6)	2 (4)	7 (14)	38 (76)		
Hold an object between your affected upper arm and your chest wall, e.g. a book	10 (20)	10 (20)	19 (38)	11 (22)		
Hold an object draped over your affected forearm, e.g. an article of clothing	6 (12)	8 (16)	8 (16)	28 (56)		
Stabilize an object with your affected arm while you manipulate it with your other hand	8 (16)	13 (26)	26 (52)	3 (6)		
Lift your affected arm to put it through the sleeve of a shirt	10 (20)	10 (20)	18 (36)	12 (24)		
Roll over when sleeping without having to wake to move your affected arm	4 (8)	12 (24)	23 (46)	11 (22)		
•		55 (18.33)		103 (34.33)		

Table 2: Frequency distribution of patients by their answers to the BrAT questionnaire

Variable	Mean	SD	<i>t</i> -test	Degrees of freedom	P-value
The use of hand in daily activities (Dressing and grooming)	2.20	0.97	- 5.893	49	< 0.001
The use of arm and hand in daily activities	2.30	0.92	- 5.40	49	< 0.001
No hand items	2.87	0.71	- 1.135	49	0.262

	Frequency (percentage)							
Activity	No difficulty	Mild difficulty	Moderate difficulty	Severe difficulty	Unable			
Open a tight or new jar	25 (50)	4 (8)	1 (2)	0 (0)	20 (40)			
Turn a key	23 (46)	6 (12)	0 (0)	1 (2)	20 (40)			
Write	19 (38)	7 (14)	2 (4)	3 (6)	23 (46)			
Prepare a meal	4 (8)	10 (20)	12 (24)	4 (8)	20 (40			
Push open a heavy door	4 (8)	7 (14)	13 (26)	11 (22)	15 (30			
Place an object on a shelf above your head	2 (4)	1 (2)	10 (20)	4 (8)	33 (66			
Do heavy household chores (e.g., wash walls, wash floors)	3 (6)	2 (4)	13 (26)	15 (30)	17 (34			
Garden or do yard work	1 (2)	9 (18)	14 (28)	13 (26)	13 (26			
, Make a bed	3 (6)	15 (30)	18 (36)	5 (10)	9 (18)			
Carry a shopping bag or briefcase	3 (6)	14 (28)	14 (28)	1 (2)	18 (36			
Carry a heavy object (over 10 lbs).	4 (8)	12 (24)	8 (16)	6 (12)	20 (40)			
Change a lightbulb overhead	0 (0)	0 (0)	7 (14)	7 (14)	36 (72			
Wash or blow dry your hair	0 (0)	1 (2)	8 (16)	10 (20)	31 (62			
Wash your back	2 (4)	3 (6)	2 (4)	12 (24)	31 (62			
Put on pullover sweater	2 (4)	4 (8)	23 (46)	5 (10)	16 (32			
Use a knife to cut food	15 (30)	14 (28)	0 (0)	0 (0)	21 (42			
Recreational activities which require little effort (e.g., cardplaying,								
knitting, etc)	15 (30)	13 (26)	1 (2)	3 (6)	18 (36			
Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g golf, hammering, tennis,	4 (8)	9 (18)	14 (28)	2 (4)	21 (42			
etc) Recreational activities in which you move your arm freely (e.g., playing freesby, badminton, etc)	5 (10)	3 (6)	20 (40)	7 (14)	15 (30			
Manage transportation needs (getting from one place to another)	31 (62)	12 (24)	5 (10)	1 (2)	1 (2)			
Sexual activities	25 (50)	11 (22)	4 (8)	9 (18)	1 (2)			
During the past week, to what extend has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups? (circle number)	3 (6)	11 (22)	22 (44)	13 (26)	1 (2)			
During the past week, were you limited in your work or other regular daily activities because of your arm, shoulder or hand problem? (circle number)	0 (0)	18 (36)	18 (36)	13 (26)	1 (2)			
Arm, Shoulder or hand pain	18 (36)	23 (46)	9 (18)	0 (0)	0 (0)			
Arm, Shoulder or hand pain when you performed any specific activity	13 (26)	17 (34)	17 (34)	3 (6)	0 (0)			
Tingling (pins and needles) in your arm, shoulder or hand	17 (34)	14 (28)	16 (32)	3 (6)	0 (0)			
Weakness in your arm, shoulder or hand	3 (6)	5 (10)	31 (62)	10 (20)	1 (2)			
Stiffness in your arm, shoulder or hand	4 (8)	14 (28)	27 (54)	4 (8)	1 (2)			
During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand?	14 (28)	22 (44)	10 (20)	4 (8)	0 (0)			
I feel less capable, less confident or less useful because of my arm, shoulder or hand problem	4 (8)	19 (38)	8 (16)	10 (20)	9 (18)			

Table 4: Frequency distribution of patients by their answers to DASH questionnaire

Activity	Mean	SD	t-test	Degrees of freedom	P-value	Interpretation of level of difficul
Open a tight or new jar	2.72	1.92	- 4721	49	< 0.001	Moderate
Turn a key	2.78	1.9	- 4.544	49	< 0.001	Moderate
Write	2.92	1.82	- 4.204	49	< 0.001	Moderate
Prepare a meal	3.52	1.40	- 2.419	49	0.019	Moderate
Push open a heavy door	3.52	1.28	- 2.648	49	0.011	Moderate
Place an object on a shelf above your head	4.30	1.11	1.90	49	0.062	No
Do heavy household chores (e.g., wash walls, wash floors)	3.82	1.14	- 1.119	49	0.269	Mild
Garden or do yard work	3.56	1.13	- 2.759	49	0.006	Mild
Make a bed	3.04	1.18	- 5.766	49	< 0.001	Moderate
Carry a shopping bag or briefcase	3.34	1.38	- 3.384	49	0.001	Moderate
Carry a heavy object (over 10 lbs).	3.52	1.43	- 2.370	49	0.022	Moderate
Change a lightbulb overhead	4.58	0.73	5.611	49	< 0.001	No
Wash or blow dry your hair	4.42	0.84	3.56	49	0.001	No
Wash your back	4.34	1.08	2.23	49	0.031	No
Put on pullover sweater	3.58	1.14	- 2.6	49	0.012	Moderate
Use a knife to cut food	2.96	1.8	- 4.1	49	< 0.001	Moderate
Recreational activities which require little effort (e.g., cardplaying, knitting, etc)	2.92	1.74	- 4.4	49	< 0.001	Moderate
Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g golf, hammering, tennis, etc)	3.54	1.40	- 2.32	49	0.025	Moderate
Recreational activities in which you move your arm freely (e.g., playing freesby, badminton, etc)	3.48	1.27	- 2.91	49	0.005	Moderate
Manage transportation needs (getting from one place to another)	1.58	0.91	- 18.897	49	< 0.001	Severe
Sexual activities	2.01	1.23	- 11.508	49	< 0.001	Severe
During the past week, to what extend has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups? (circle number)	2.96	0.90		49	< 0.001	Moderate
During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem? (circle number)	2.94	0.84		49	< 0.001	Moderate
Arm, Shoulder or hand pain	1.82	0.73		49	< 0.001	Severe
Arm, Shoulder or hand pain when you performed any specific activity	2.2	0.90	- 14.087	49	< 0.001	Moderate
Tingling (pins and needles) in your arm, shoulder or hand	2.10	0.95	- 14.098	49	< 0.001	Moderate
Weakness in your arm, shoulder or hand	3.02	0.8	- 8.715	49	< 0.001	Mild
Stiffness in your arm, shoulder or hand	2.68	0.82	- 11.394	49	< 0.001	Moderate
During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand?	2.08	0.90	- 15.087	49	< 0.001	Moderate
I feel less capable, less confident or less useful because of my arm, shoulder or hand problem	3.02	1.29	- 5.390	49	< 0.001	Mild

Table 5: the results of the t-test to evaluate the ability to use upper limb based on the DASH questionnaire.

Variable		Mean	SD	<i>t</i> -test	P-value	
Shoulder abduction	Before	5	5.35	12.52	-0.001	
goniometry (0-150)	After	40.90	20.84	12.52	< 0.001	
Shoulder abduction force	Before	2.72	1.78	10.219	< 0.001	
(M0:M5)	After	5.30	0.65	10.219	<0.001	
Shoulder external rotation	Before	0	0	9.08	< 0.001	
(goniometry 0-90)	After	6.50	5.08	9.08	<0.001	
Shoulder external rotation	Before	1	0	9.49	< 0.001	
force (M0:M5)	After	3.64	1.97	9.49	<0.001	
Shoulder forward flexion	Before	5.10	6.19	11.20	< 0.001	
(goniometry 0-180)	After	34.02	19.02	11.20	<0.001	
Shoulder forward flexion	Before	94.1	1.52	13.315	< 0.001	
force (M0:M5)	After	5.24	0.69	15.515	<0.001	
Elbow flexion (goniometry	Before	15.30	17.57	2 272	2.273	0.027
0-150)	After	25.30	25.62	2.273	0.027	
Eller Aming (MOME)	Before	3.48	1.94	0.107	0.945	
Elbow flexion (M0:M5)	After	3.56	2.01	0.197	0.845	
Elbow extension lag	Before	3	4.04			
(guniometry 0-90)	After	2.20	3.37	- 1.273	0.209	
Elbow extension force	Before	1.68	1.50	3.81	<0.001	
(M0:M5)	After	2.86	2.17	3.81	< 0.001	
Wrist and finger muscle	Before	2.76	2.36	3.50	0.001	
force (M0:M5)	After	3.86	2.37	5.50	0.001	

Table 6: The results of the dependent T-test to compare the studied variables before and after surgery

DISCUSSION

Physicians generally tend to notice the objective findings of the patients instead of subjective parameters. However, patients may have normal neurological function but suffer from unbearable pain. Hence, to investigate the success of a surgical procedure, including BPI surgery, the subjective symptoms should also be taken into consideration¹⁵. There are a limited number of studies regarding functional outcomes in patients with BPI.

In the present study, men and young adults had the highest frequency, which is consistent with the literature^{1, 16}. As reported in the previous studies, the cause of injury was motor vehicle accidents in the majority of patients¹⁷⁻¹⁹. In this study, the type of injury was pan-brachial in 58% of the patients, which is in agreement with incidence of 53-57% reported previously^{18, 19}. In 90% of the patients, the interval between BPI and surgery was \leq 10 months. A similar work reported an interval of 6.6 months. Overall, the 6-month-window is a vital period for a patient with BPI to be managed by surgery, hence, referral of patients must be improved^{15, 20}. In this study, generally, the patients stated that they still had difficulty doing most of the items of the questionnaires. Nevertheless, physical examination revealed that BPI surgery improved many items of the range of motion in the upper extremity. For most of participants in this study BPI surgery had been performed thorough posterior approach. Previous studies have proposed this approach as an effective method in the repair of the upper BPI7, 21. In this study, posterior approach was associated with good outcomes in terms of shoulder external rotation and abduction. As mentioned before, gracilis free flaps were also used in this study. This procedure has been associated with good range of motion and DASH score²². Some studies have evaluated objective and subjective findings of the patients with BPI following surgical intervention. Aras et al. in a study of 27 patients reported that those who were operated for BPI benefited more from the point of pain than muscle strength¹⁵. Kretschmer et al. in a study of 99 patients showed that 87% were satisfied with the outcomes and 83% would undergo the surgery again. However, despite a high satisfaction rate, patients were still significantly disabled, and

50% of the previous workers could not return to work¹⁷. Similarly, Estrella et al. reported a high degree of disability and low quality of life among patients with traumatic BPI²³. Generally, extreme BPI results in loss of upper extremity function and has poor prognosis and motor function is commonly not completely restored²⁴. Therefore, it is important to provide patients with adequate information about this problem preoperatively to provide an accurate expectation and prevent frustration¹⁵.

The main limitation with this study was that patients did not complete the questionnaires before surgery. The strength of this study was evaluation of patients' status by both physical examination and subjective questionnaires.

CONCLUSION

Posterior approach in BPI surgery was associated with good outcomes in terms of shoulder external rotation and abduction. However, patients still suffered from difficulties in daily activities to some extent. It is important that physicians provide comprehensive preoperative education to create realistic expectations.

ACKNOWLEDGMENT

This article is taken from disease registry, titled " Design the organization for Brachial plexus damages patients, records in 15th Khordad Hospital, Tehran, Iran " and code number IR.SBMU.RETECH. REC.1398.496 from Ethic Committee, supported by Deputy of Research and Technology in Shahid Beheshti University of Medical Sciences (http:// dregistry.sbmu.ac.ir).

CONFLICT OF INTEREST

The authors of this study declare that they have no conflict of interest.

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