Sex Differences in Recovery After Brachial Plexus Injuries: Anatomical and Physiological Basis and Clinical Study

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ABSTRACT

Introduction: Brachial plexus injuries (BPIs) are severe, disabling, and impose a high socioeconomic burden. Restoring elbow flexion is paramount to functional recovery. Anatomical and physiological characteristics of peripheral nerves in males and the peripheral effects of testosterone may contribute to better recovery in men than in women. **Materials and Methods:** Observational, retrospective case series. Thirty-nine patients with BPI who underwent musculocutaneous nerve neurotization were included. **Results:** In males, the mean BMRC score was 4; the functional reinnervation rate (BMRC ≥3) was 89%, and the surgical failure rate (BMRC <3) was 11%. In females, the mean BMRC score was 3.5; functional reinnervation was achieved in 67%, with a surgical failure rate of 33%, and there was a greater tendency to failure with increasing patient age. Differences in strength achieved by subgroup according to the BMRC scale were statistically significant (p = 0.05). **Conclusions:** Men show a greater capacity for motor recovery than women after musculocutaneous nerve neurotization. Additionally, the risk of surgical failure increases with age in females. These findings may be explained by sex-related differences in peripheral nerve anatomy and physiology and by testosterone-related mechanisms acting on the nervous system and muscle.

Keywords: Brachial plexus injuries; neurotization; nerve transfers; testosterone.
Level of Evidence: IV

Diferencias entre los sexos en la recuperación de las lesiones del plexo braquial. Bases anatómicas, fisiológicas y estudio clínico

RESUMEN

Introducción: Las lesiones del plexo braquial son graves, incapacitantes y generan un alto costo socioeconómico. Restaurar la flexión del codo resulta primordial para la recuperación. Las características anatomofisiológicas de los nervios de los varones y los efectos periféricos de la testosterona podrían jugar un papel en la mejor recuperación de los hombres sobre las mujeres. **Materiales y Métodos:** Estudio observacional, retrospectivo, tipo serie de casos. Se incluyó a 39 pacientes con lesiones del plexo braquial sometidos a neurotizaciones del nervio musculocutáneo. **Resultados:** En el sexo masculino, el puntaje promedio de la escala BMRC fue 4; la tasa de reinervación funcional (BMRC ≥3), del 89% y la tasa de falla quirúrgica (BMRC <3), del 11%. En el sexo femenino, el puntaje promedio de la escala del BMRC fue 3,5; se logró la reinervación funcional en el 67%, con una tasa de falla quirúrgica del 33%, hubo una mayor tendencia a la falla conforme aumentaba la edad de la paciente. Las diferencias de fuerza lograda por subgrupo según la escala del BMRC fueron estadísticamente significativas (p = 0,05). **Conclusiones:** Los hombres tienen una capacidad de recuperación motora mayor que las mujeres luego de las neurotizaciones del nervio musculocutáneo. Además, existe una mayor tendencia a la falla quirúrgica en el sexo femenino conforme aumenta la edad. Esto podría explicarse por las diferencias anatomofisiológicas del nervio periférico entre los sexos y por mecanismos ligados a la testosterona tanto sobre el sistema nervioso como en los músculos.

Palabras clave: Lesiones del plexo braquial; neurotizaciones; transferencias nerviosas; testosterona.
Nivel de Evidencia: IV

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INTRODUCTION

Brachial plexus injuries (BPI) are severe, highly disabling, and impose a substantial socioeconomic burden on the health system. Their incidence, although difficult to quantify precisely, has increased in recent years due to improved survival after severe motor vehicle accidents.[1] The mean patient age at the time of injury is 26.4 years, and 90.5% of cases occur in males.[2]

Restoring elbow flexion is a critical first step toward final function and recovery of the affected limb. Neurotization of the musculocutaneous nerve or its branches using different techniques has been established as the reference procedure to achieve this goal.

In this study, two neurotization strategies were used according to the pattern of BPI to be reconstructed: Oberlin type I (ulnar nerve fascicle to the biceps branch of the musculocutaneous nerve) for upper BPI (C5–C6) and transfer of the spinal accessory nerve (XI) to the musculocutaneous nerve with an autologous sural graft for total BPI.

The main hypothesis was that men would have greater functional recovery potential after peripheral nerve injuries, including BPI, and would therefore obtain better results after nerve transfers for BPI. This was based on the following considerations:

- Male axons have up to 80% greater cross-sectional area and up to 55% more microtubules, which makes them more resistant to stretch injury.3
- After trauma, intracellular calcium rises rapidly in female axons, which reduces excitability; this response is less pronounced in males.[3]
- Testosterone appears to play a key role in two effector systems:[3-6]
  - In neurons: it promotes axonal growth and repair after peripheral nerve injury and protects neurons in the injured pathway from dendritic atrophy through interactions with androgen receptors in the central nervous system.4,5
  - In muscle: it delays degeneration after denervation and reduces the shift from type I to type II fibers.6 This is crucial in neurotization because it prolongs the time during which a denervated muscle remains amenable to reinnervation.

In published BPI neurotization series,[1,2,7,8] we did not find clear reports of sex-based differences in recovery. Given our sample size, extended follow-up, and a relatively higher proportion of women than in most series, we conducted this study to assess whether sex-related differences in recovery potential truly exist. Our findings may help set realistic goals and prognoses for postoperative recovery.

MATERIALS AND METHODS

The primary objective was to determine whether there were significant differences in recovery of bíceps strength between men and women operated on for BPI. The secondary objective was to identify other factors associated with biceps strength recovery after BPI surgery.

Study Design

We conducted an observational, retrospective case series of patients operated on between January 2009 and July 2022 at one public and one private institution in Córdoba. The surgical techniques were the Oberlin procedure and XI-to-musculocutaneous nerve transfer with a sural nerve graft. All surgeries were performed by the senior author (FJC).

Patient Selection

We included consecutive patients with traumatic BPI and loss of elbow flexion who underwent surgery during the study period. Exclusion criteria were follow-up shorter than 6 months, conditions that delayed or precluded proper surgical technique or rehabilitation (more than 1 year from injury), and irreparable complete BPI.

Selection of the Surgical Technique

Technique selection depended on the BPI pattern. For upper BPI (C5–C6 or C5–C7), the ulnar nerve was available as an intraplexal donor and the Oberlin procedure was chosen. For total BPI (C5–T1), intraplexal donors were not available and the spinal accessory nerve was used as an extraplexal donor.

Data Collection

From electronic medical records we extracted age, sex, date of birth, cause and type of injury, affected limb, time from injury to first specialist visit, type of surgery, time from injury to surgery, motor recovery after surgery, length of follow-up, and postoperative biceps strength according to the British Medical Research Council (BMRC) scale.[9]

Outcome Measurement

The primary outcome was improvement in biceps strength measured with the BMRC scale.[10] Several publications report excellent correlation between dynamometer-measured torque and electromyographic activity when compared with BMRC functional grades.[11] A BMRC score lower than 3 was considered surgical failure.

Statistical Analysis

Because variables were not normally distributed, nonparametric tests were used. For comparisons of numerical variables we applied the Wilcoxon rank-sum test, Fisher's exact test, and the exact Wilcoxon test. A p value lower than 0.05 was considered significant. Analyses were performed with RStudio Version 1.4.1106.

RESULTS

Thirty-nine patients were included: 33 men (84.6%) and 6 women (15.4%). Demographic characteristics are shown in Table 1.

Six of the 33 men did not meet inclusion criteria; no women were excluded. The statistical analysis included 27 men (81.8% of included patients) and 6 women (18.2%) (Figure 1).

The two groups were homogeneous with respect to age, time from BPI to surgery, and length of follow-up (Table 2).

Overall mean age was 25 years. The mean interval from injury to surgery was 211 days and mean follow-up was 1043 days. Fourteen patients (42%) underwent XI-to-musculocutaneous nerve transfer and 19 (58%) underwent the Oberlin procedure. The mean BMRC score was 4. Surgical failure occurred in 5 patients (15%).

When techniques were compared regardless of sex, the XI-to-musculocutaneous group had a mean BMRC score of 3.1 and a failure rate of 21%. In the Oberlin group, the mean BMRC score was 3.5 with a failure rate of 11% (Table 3).

Table 1. Demographic characteristics of the study patients.

Patient	Type of surgery	Age (years)	Sex	Time to surgery (days)	Follow-up (days)	BMRC Scale
1	SAN-TO-MCN TRANSFER	30	M	300	3476	3
2	SAN-TO-MCN TRANSFER	22	F	280	1572	4
3	SAN-TO-MCN TRANSFER	19	M	145	2621	4
4	SAN-TO-MCN TRANSFER	44	M	215	1700	3
5	SAN-TO-MCN TRANSFER	21	M	317	1880	5
6	SAN-TO-MCN TRANSFER	31	M	241	1981	3
7	SAN-TO-MCN TRANSFER	27	F	280	361	2
8	SAN-TO-MCN TRANSFER	38	M	143	850	4
9	SAN-TO-MCN TRANSFER	19	M	241	220	0
10	SAN-TO-MCN TRANSFER	43	M	158	740	4
11	SAN-TO-MCN TRANSFER	28	M	148	373	3
12	SAN-TO-MCN TRANSFER	23	M	311	1687	0
13	SAN-TO-MCN TRANSFER	19	M	167	616	4
14	SAN-TO-MCN TRANSFER	17	M	211	1435	4
15	Oberlin	23	M	538	1314	3
16	Oberlin	28	M	623	4296	3
17	Oberlin	23	M	338	1735	4
18	Oberlin	18	M	180	1043	5
19	Oberlin	49	M	305	169	3
20	Oberlin	25	F	101	435	4
21	Oberlin	33	M	204	988	4
22	Oberlin	50	F	260	1145	2
23	Oberlin	22	M	240	337	4
24	Oberlin	25	M	185	1411	3
25	Oberlin	24	F	234	945	5
26	Oberlin	33	M	287	1376	4
27	Oberlin	29	M	149	387	4
28	Oberlin	20	M	130	1686	4
29	Oberlin	28	M	195	848	4
30	Oberlin	25	F	200	322	3
31	Oberlin	38	M	130	1433	0
32	Oberlin	17	M	136	989	4
33	Oberlin	30	M	122	424	3
34	SAN-TO-MCN TRANSFER	25	M	321	0	-
35	SAN-TO-MCN TRANSFER	28	M	162	0	-
36	Oberlin	53	M	631	0	-
37	Oberlin	39	M	185	0	-
38	Oberlin	21	M	163	0	-
39	Oberlin	28	M	s/d	0	-

SAN-TO-MCN TRANSFER = spinal accessory nerve to musculocutaneous nerve transfer; F = female; M = male; BMRC = *British Medical Research Council*.

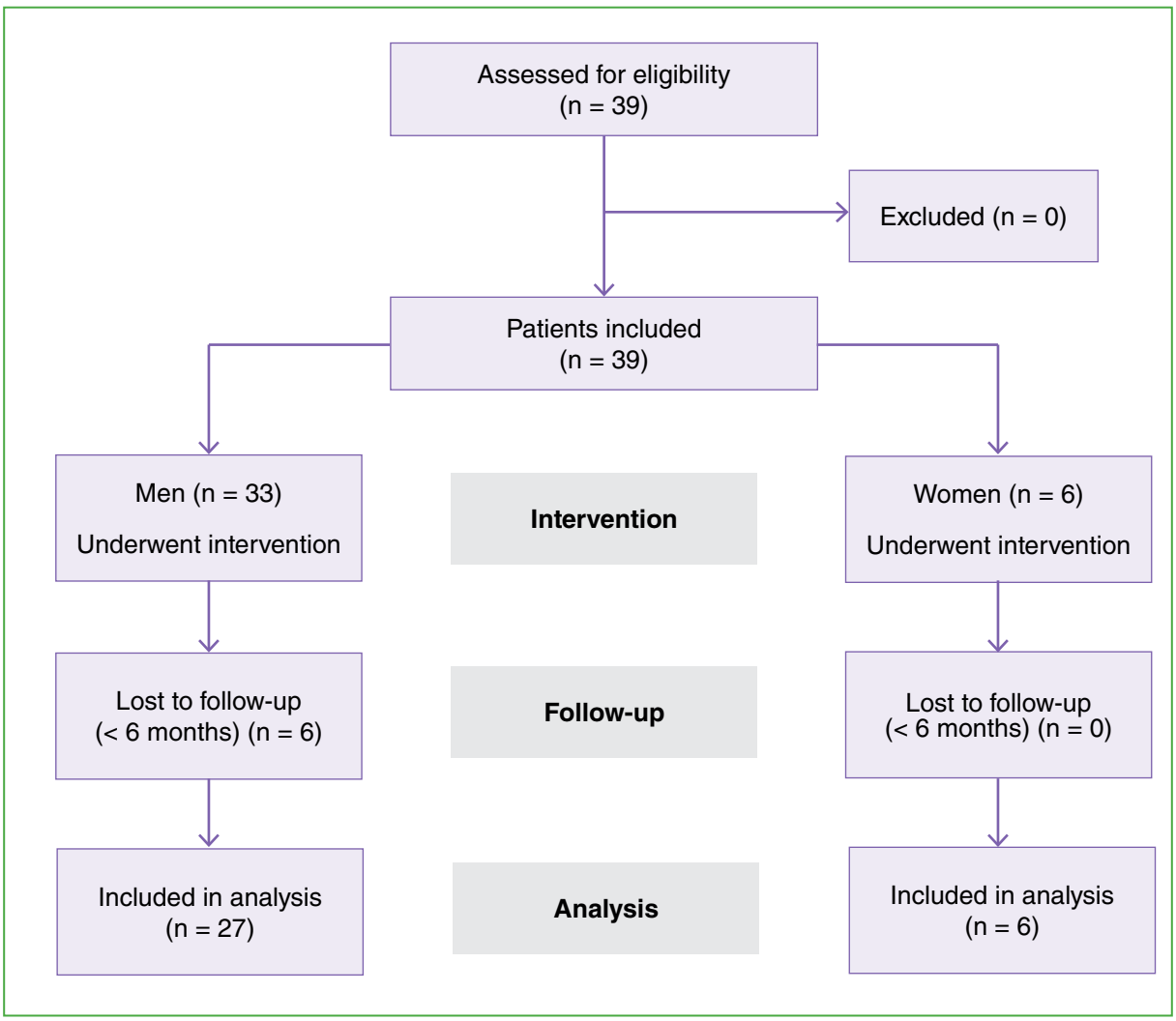

Figure 1. Flow diagram showing the distribution of the overall patient sample.

In women, mean age was 25 years (range 22–50), mean time from injury to surgery was 247 days, and mean follow-up was 690 days. Sixty-seven percent underwent the Oberlin procedure. The mean BMRC score was 3.5 and there were 2 failures (33%).

In men, mean age was 28 years (range 17–53), mean time from injury to surgery was 204 days, and mean follow-up was 1314 days. Fifty-six percent underwent the Oberlin procedure. The mean BMRC score was 4 with 3 failures (11%).

Within BMRC strength subgroups, 24 of 27 men (89%) and 4 of 6 women (66%) achieved M3 or greater. Overall surgical failure (BMRC ≤ 2) occurred in 5 of 33 patients (15%): 2 women (33% of women) and 3 men (11% of men) (Table 2; Figure 2). These subgroup differences on the BMRC scale were statistically significant ($p = 0.05$) (Table 2).

On multivariate analysis correlating age and sex with functional outcomes, age was not related to failure rate among men. In women there was a greater tendency toward failure with increasing age (Figure 3). The two failures in this group occurred in the two oldest women in the series.

Table 2. Overall sample results

Characteristic	Population (n= 33)*	Female sex (n= 6)*	Male sex (n= 27)*	p**
Age	25 (17-53) (IQR 22-31)	25 (22-50) (IQR 24-27)	28 (17-53) (IQR 21-32)	0.9
Time of evolution (days)	211 (149-280)	247 (209-275)	204 (149-294)	0.8
Time of evolution (months)	7.03 (4.97-9.33)	8.23 (6.95-9.17)	6.8 (4.95-9.78)	0.8
Surgery				
SAN-TO-MCN TRANSFER	14 (42%)	2 (33%)	12 (44%)	
Oberlin	19 (58%)	4 (67%)	15 (56%)	
Follow-up (days)	1043 (435-1686)	690 (380-1095)	1314 (678-1694)	0.2
Follow-up (months)	35 (15-56)	23 (13-37)	44 (23-56)	0.2
BMRC scale (categorical)				0.05
0	3 (9.1%)	0 (0%)	3 (11%)	
2	2 (6.1%)	2 (33%)	0 (0%)	
3	10 (30%)	1 (17%)	9 (33%)	
4	15 (45%)	2 (33%)	13 (48%)	
5	3 (9.1%)	1 (17%)	2 (7.4%)	
Average BMRC scale (numerical)	4 (3-4)	3.5 (2.25-4)	4 (3-4)	0.8
Surgical failure	5 (15%)	2 (33%)	3 (11%)	0.2

*Mean (range); IQR = interquartile range; n (%)
**Wilcoxon rank sum test, Fisher's exact test and Wilcoxon exact test.
SAN-TO-MCN TRANSFER = spinal accessory nerve to musculocutaneous nerve transfer; BMRC = *British Medical Research Council*.

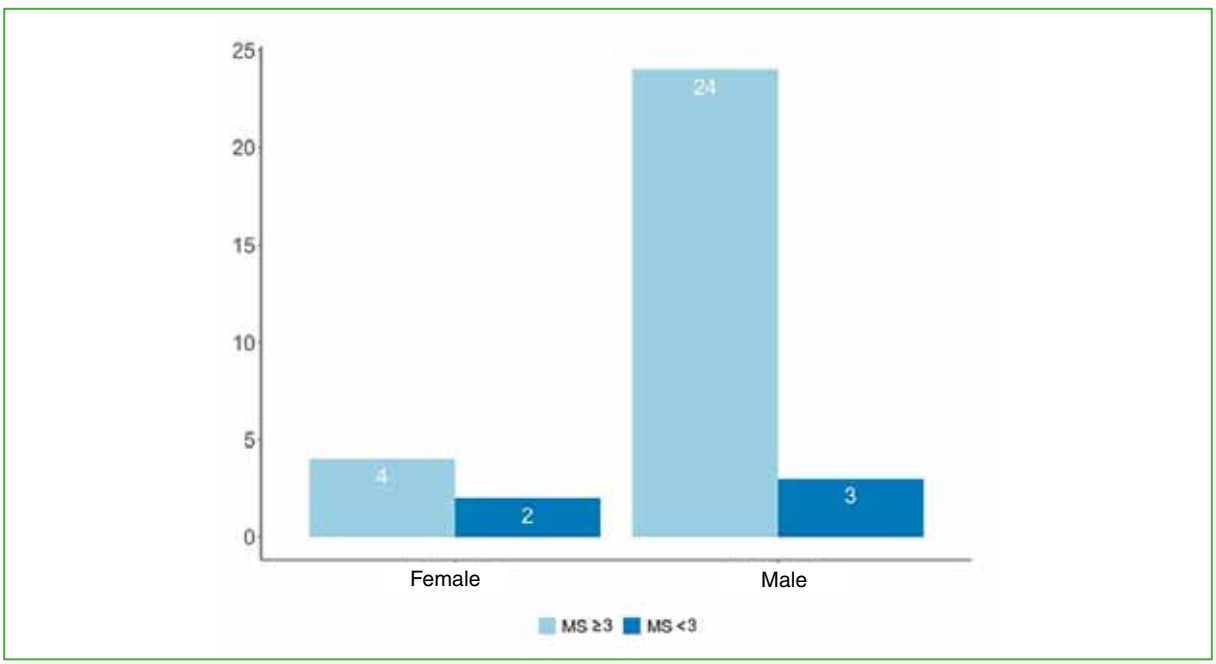

Figure 2. Distribution of surgical outcomes by sex.

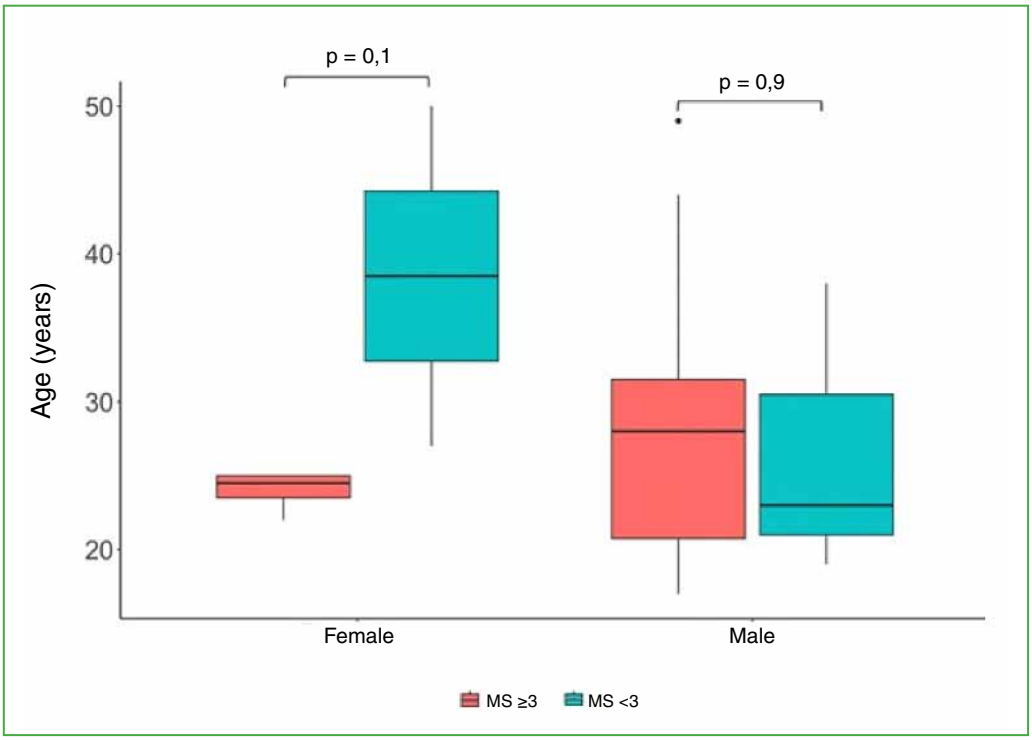

Figure 3. Relationship between functional outcome by sex and age.

Table 3. Functional outcomes and failures according to the technique used.

	SAN-TO-MCN TRANSFER (14)	Oberlin (19)	p
BMRC, mean ± SD	3.1 ± 1	3.5 ± 1	0.4
Failure, n (%)	3 (21)	2(11)	0.4

SAN-TO-MCN TRANSFER = spinal accessory nerve to musculocutaneous nerve transfer; BMRC = *British Medical Research Council*; SD = standard deviation.

DISCUSSION

Our literature search found no relevant reports addressing sex-based differences in postoperative biceps strength after neurotization. Even published meta-analyses do not mention such differences.[8-10] This likely reflects the predominance of BPI in men, which leaves most case series with too few women for meaningful comparison.

Overall, strength outcomes were better with the Oberlin procedure than with XI-to-musculocutaneous transfer, and failure rates were lower with the former. This can be explained by procedural features. In Oberlin type I, the nerve impulse crosses a single neurorrhaphy and travels a shorter distance to the target muscle. In XI-to-musculocutaneous transfer, the distance is longer and the impulse crosses two neurorrhaphies. This is critical because between 6 and 12 months after injury, the motor end plate undergoes progressive degeneration and loss of function. Axonal regeneration advances about 1 mm per day and requires roughly 30 days to cross each neurorrhaphy.[12] To date, there are no direct comparative studies of recovery between these two techniques. Our results align with expectations for the reasons noted.

In our series, men achieved significantly higher BMRC strength subgrades than women after musculocutaneous nerve neurotization ($p = 0.05$).

The mean BMRC score was also higher in men than in women (4 vs 3.5; $p = 0.8$), and functional reinnervation defined as BMRC ≥ 3 was achieved in 89% of men versus 67% of women ($p = 0.2$).

These differences may be attributable to sex-related anatomical and physiological characteristics of peripheral nerves and to the protective and regenerative effects of testosterone after nerve injury. The hormone may also slow muscle degeneration after surgery. Further research into these mechanisms would help clarify these findings.

We also observed an age-related trend toward surgical failure in women, which is important when counseling patients about prognosis and recovery. This may relate to progressive declines in endogenous estrogens and androgens with age and to physiologic loss of muscle mass associated with postmenopausal changes. This trend was not observed in men.

A strength of this study is the proportion of women, nearly 20%, which is higher than the approximately 10% reported in many series. Limitations include a mean interval from injury to surgery greater than 6 months, which reflects delays to specialist evaluation in the public health setting, and the use of two different surgical techniques according to BPI type, each with distinct technical features and reinnervation timelines.

CONCLUSIONS

Men had better functional outcomes and a lower failure rate than women after musculocutaneous nerve neurotization for BPI. There was also a greater tendency toward surgical failure in women as age increased. These findings may be explained by sex-related anatomical and physiological differences in peripheral nerves and by testosterone-linked mechanisms acting on both the nervous system and muscle. Larger series and deeper investigation of these mechanisms are needed to support these observations.

Conflicts of interest: The authors declare no conflicts of interest.

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