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Ventilation asymmetry, diaphragmatic mobility and exercise capacity in men with traumatic brachial plexus injury

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ABSTRACT

Objective: To investigate the repercussions of traumatic brachial plexus injury (TBPI) on diaphragmatic mobility and exercise capacity, compartmental volume changes, as well as volume contribution of each hemithorax and ventilation asymmetry during different respiratory maneuvers, and compare with healthy individuals. The velocity of shortening of the diaphragm, inspiratory, and expiratory muscles were also assessed.

Participants: The cross-sectional study was conducted with 40 male individuals (20 with TBPI who have not undergone nerve transfer surgery [mean age 30.1 ± 5.3] and 20 healthy paired by age and body mass index). Only patients with C8-T1 root avulsion were studied.

Main outcome: Compartmental and hemithoracic volumes, as well as asymmetry between the affected and unaffected sides were assessed using optoelectronic plethysmography. The 6 minute walking test was performed to evaluate exercise capacity, while diaphragm mobility was assessed during quiet breathing (QB) using an ultrasound device.

Results: TBPI patients with mean lesion time of 174 ± 45.24 days showed a decreased pulmonary function, respiratory muscle strength, exercise capacity, and diaphragm mobility (all $p < .001$) compared with healthy. The pulmonary ribcage compartment of the affected side was the main contributor to the reduction in volume during inspiratory capacity, vital capacity, and inspiratory load imposition (all $p < .05$). This compartment also exhibited a higher ventilation asymmetry with reduced shortening velocity of the inspiratory ribcage muscles.

Conclusion: Compared with healthy, TBPI patients who have not undergone nerve transfer surgery present low exercise capacity and diaphragmatic mobility, as well as reduced volume of the upper ribcage compartment on the affected side that leads to reduced shortening velocity and ventilation asymmetry.

Introduction

Half of the traumatic brachial plexus injuries (TBPI) are caused by stretch and/or contusions, with the majority due to motor vehicle accidents.[1] This kind of injury leads to motor and sensory lesions in the upper limbs that usually culminates with neuropathic pain, joint stiffness, and muscular weakness.[2–4]

As the trauma predominantly affects the upper limbs, most studies regarding the consequences of TBPI focus on motor recovery.[4–8] Conversely, the repercussions of TBPI on exercise capacity and diaphragm mobility in those patients who have not undergone nerve transfer surgery is still unknown. Also, there are no studies describing the pattern of compartmental volume changes, the contribution of each hemithorax to the chest wall volume (V_{CW}), and possible asymmetrical hemithoracic volume vari-

Conflict of interest: All named authors hereby declare that they have no conflicts of interest to disclose.

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ation at rest or during different respiratory maneuvers in these patients.

For this reason, we aimed to study the impact of TBPI on patients before nerve transfer surgery. The study evaluated only patients who had the phrenic nerve as a donor and C8-T1 root avulsion. Specifically, pulmonary function, respiratory muscle strength, exercise capacity, and diaphragmatic mobility were studied in TBPI patients and compared with matched healthy individuals. Additionally, 1) the pattern of compartmental volume changes, 2) the volume contribution of each hemithorax, and 3) hemithoracic ventilation asymmetry were evaluated. We using an optoelectronic plethysmography under four respiratory maneuvers: spontaneous quiet breathing [QB], inspiratory capacity [IC], vital capacity [VC], and inspiratory threshold load [ITL].

Furthermore, considering that the velocity of shortening of the respiratory muscles can be estimated from volumes displaced by the abdomen and ribcage compartments,[9,10] and alterations in respiratory muscle strength lead to a reduction in the velocity of muscle contraction;[11] the velocity of shortening of the diaphragm, inspiratory, and expiratory muscles were estimated. We hypothesized that all the above-mentioned parameters would be altered in TBPI patients compared with healthy individuals, and the reduction in the volume of the affected side would be the main determinant for the low compartmental volume changes, ventilation asymmetry, and exercise capacity.

Methods

Design

This is a cross-sectional study conducted following the Declaration of Helsinki and approved by the Ethics and Research Committee of the Federal University of Pernambuco (number 1.798.996). An informed consent form was signed by all individuals who agreed to participate in the study.

Participants, therapists, centres

A convenience sample of male patients with a confirmed diagnose of TBPI (by an experienced neurologist and using only electroneuromyography) with avulsion of the C8-T1 root followed in the outpatient peripheral nerve clinic of the Hospital da Restauração (Recife, Brazil) was studied. Patients were selected for the study from November 2016 to November 2018. Those with TBPI due to motorcycle accident in a period from three to nine months of the injury, aging between 20 and 50 years, and who were not in a rehabilitation program were included in the study. Patients who had undergone any kind of plexus surgery, with multiple costal fractures, pulmonary contusions, cognitive alterations, as well as those with cardiopulmonary or metabolic diseases associated, were excluded. Self-reported healthy individuals paired by age and body mass index with no previous cardiovascular or pulmonary diseases composed the control group. Those healthy who presented forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) <80% of predicted were excluded.

Outcome measures

Pulmonary function

Spirometry was performed to assess pulmonary function using a portable spirometer (Micro Medical, Microloop MK8, England). Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), peak expiratory flow (PEF), and the FEV1/FVC ratio were performed according to ATS/ERS recommendations.[12] The highest values obtained were compared with predicted ones for the Brazilian population.[13]

Respiratory muscle strength

A digital manovacuometer (MVD-300, Globalmed, Brazil) connected to a mouthpiece with a 2 mm hole was used to assess respiratory muscle strength according to ATS/ERS recommendations.[12] Three maximal inspiratory (MIP) and expiratory pressure maneuvers starting from residual volume and total lung capacity, respectively, were requested. The highest value obtained was compared with reference values for the Brazilian population[14] and included in statistical analysis.

Diaphragmatic mobility

An ultrasound device (Sonoace R3, Samsung Medison, South Korea) was used in M mode with the patient in dorsal decubitus with an inclination of 45°. A convex transducer (3.5 MHz) was placed perpendicular to the right chest wall, at the midaxillary line between the 9th and 10th right intercostal spaces (at the level of the zone of apposition). After positioning the patients, at least three deep inspirations from functional residual capacity up to total lung capacity were requested, and diaphragmatic excursions were captured by displaying sinusoidal curves. An average of the three major excursions with a difference of less than 10% was calculated and represented as diaphragmatic mobility (in millimeters).[15,16]

Exercise capacity

The six-minute walking test (6MWT) was used to evaluate exercise capacity. Subjects were asked to walk as far as possible along a corridor for six minutes, while standard phrases of encouragement were used every minute.[17] At the end of the test, the distance walked was recorded in meters and percentage of predicted values.[18]

Chest wall and compartmental volumes

V_{CW} and compartmental (pulmonary ribcage [V_{RCp}], abdominal ribcage [V_{RCa}], and abdominal [V_{AB}]) volumes were measured using optoelectronic plethysmography (BTS-Bioengineering, Milan, Italy). Eight infrared cameras (four in front and four behind the patient) captured the movement of 89 retro-reflexive markers positioned in the patients' thorax according to precise anatomical reference points.[19] The calibration of the apparatus was carried out before each data acquisition using a frequency of 60 frames•s^{-1}, while volumes were obtained following an experimental model according to the Gauss theorem.[20]

From optoelectronic plethysmography data, total and compartmental volume variation (ΔV_{CW}, ΔV_{RCp}, ΔV_{RCa}, and ΔV_{AB}) and the percentage of contribution of each compartment to V_{CW} (%RCp, %RCa, and %AB) were assessed. Shortening velocity index of the diaphragm, inspiratory, and expiratory muscles (V_{AB}/Ti, V_{RCp}/Ti, and V_{AB}/Te, respectively)[10,21] were calculated during QB and ITL.

For data analysis, the chest wall and its compartments were also partitioned into right and left hemithoraces (Fig. 1); and its volumes, as well as the percentage of volume contribution to each compartment, were assessed. Expansion asymmetry between hemithoraces was calculated as proposed by Lima et al.[22] Sides were defined as left and right in healthy individuals; while for TBPI patients, sides were defined as unaffected and affected by the traumatic injury.

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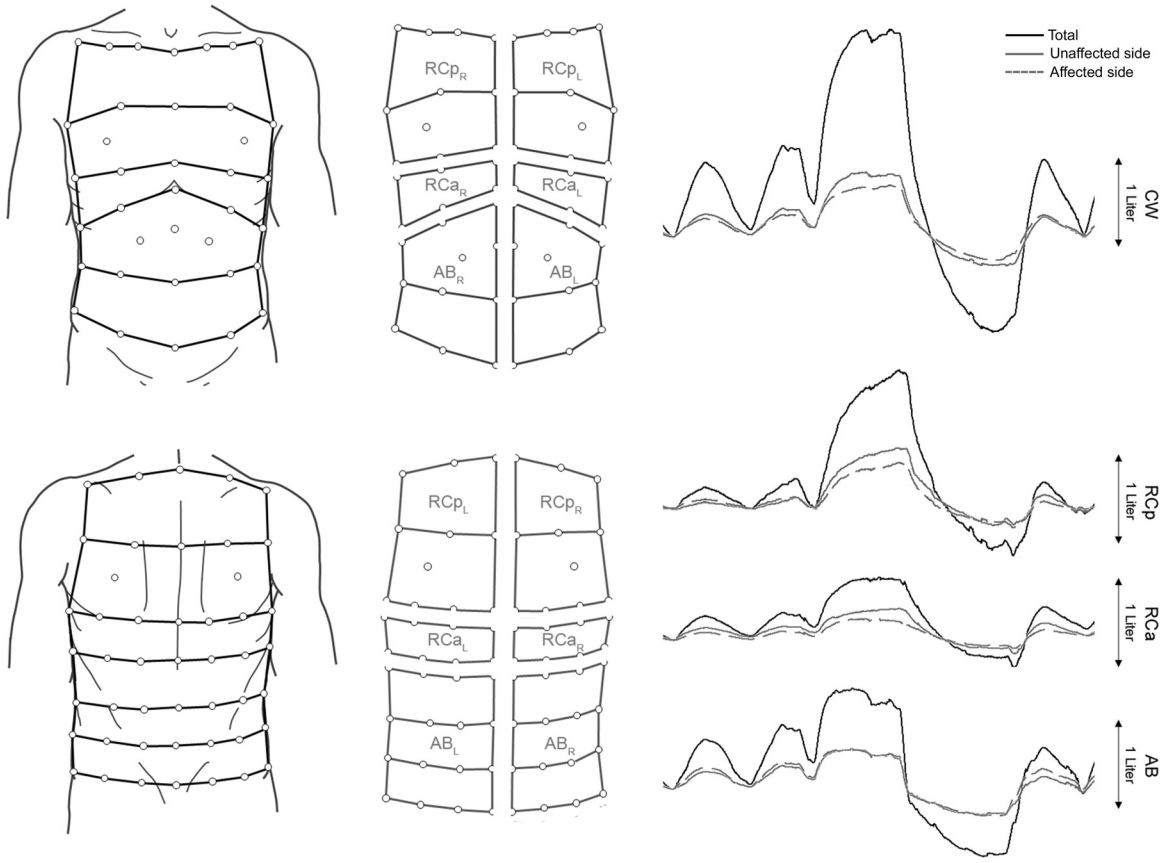

Fig. 1. Representative figure of the placement of reflective markers on the ventral (left upper panel) and dorsal (left lower panel) aspects of the chest wall, as well as right (R) and left (L) compartmental subdivision (middle panels). The right panel shows the volume traces of the chest wall (CW), pulmonary ribcage (RCp), abdominal ribcage (RCa), and abdominal (AB) compartments. Black lines indicate total compartmental volume and grey lines indicate the hemithoracic volumes.

Table 1
Anthropometric, lung function, respiratory muscle strength, distance walked in the six-minute walking test, and diaphragmatic ultrasonography data of healthy subjects and traumatic brachial plexus injury patients included

	Healthy	TBPI	*ES*	p
Subjects (n)	20	20		-
Age (years)	28.20 ± 4.60	30.10 ± 5.30	0.38	0.246
Height (m)	1.75 ± 0.05	1.73 ± 0.05	1.2	0.101
Weight (kg)	74.95 ± 8.97	69.4 ± 13	0.49	0.125
BMI (kg/m^2)	24.5 ± 4.1	24.3 ± 4.0	0.04	0.993
FVC (L)	4.67 ± 0.66	3.61 ± 0.47	1.85	<0.001
FVC %pred	89 ± 8.2	75.6 ± 12.1	1.29	<0.001
FEV_1 (L)	3.82 ± 0.47	2.99 ± 0.45	1.80	<0.001
FEV_1 %pred	91.4 ± 2.5	75.25 ± 14.5	0.66	0.002
FEV_1/FVC	0.80 ± 0.07	0.84 ± 0.09	0.49	0.227
FEV_1/FVC %pred	94.9 ± 9.9	98.7 ± 10.3	0.37	0.243
PEF (L/s)	8.33 ± 0.92	5.94 ± 1.61	1.82	<0.001
PEF %pred	72.7 ± 8.3	53.1 ± 14.1	1.69	<0.001
MIP (cmH2O)	120 ± 22.42	86.5 ± 22.6	1.49	<0.001
MIP %pred	61 ± 11	44 ± 11	1.54	<0.001
MEP (cmH2O)	135.45 ± 26.46	99.8 ± 26.31	1.35	<0.001
MEP %pred	98.2 ± 18	68 ± 17.2	1.71	<0.001
Diaphragm Mobility (cm)	6.67 ± 0.94	5.72 ± 1.37	0.81	<0.001
Distance walked (m)	583.95 ± 64.38	390.4 ± 154.95	1.63	<0.001
Distance walked (%pred)	90.39 ± 10.60	67.69 ± 10.8	2.12	<0.001

Data shown as mean ± SD.
BMI = Body mass index; FVC = Forced vital capacity; FEV1 = Forced expiratory volume in the first second; PEF = Peak expiratory flow; MIP = Maximum inspiratory pressure; MEP = Maximum expiratory pressure; n: number; m = meters; cm = centimeters; L = Liters; %pred = percentage of predicted values; cmH_2O = centimeters of water.

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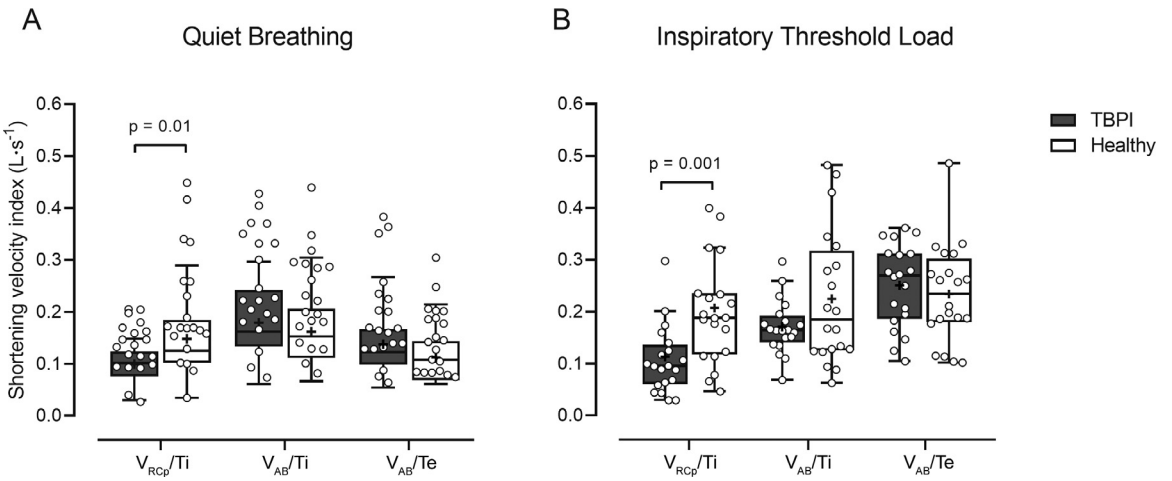

Fig. 2. Velocity of shortening velocity of the ribcage muscles (V_{RCp}/Ti), diaphragm (V_{AB}/Ti), and expiratory muscles (V_{AB}/Te) during quiet breathing (A) and inspiratory threshold load (B). Dots indicate individual values of both traumatic brachial plexus injury patients (TBPI) and healthy individuals.

Inspiratory threshold load

To explore possible alterations between affected and unaffected sides in the face of an inspiratory effort, the individuals were asked to breathe against an inspiratory threshold valve (PowerBreathe Classic IMT, Warwickshire-UK) with a constant load set at 30% of the highest MIP. This threshold was used because it is the minimum load that can effectively cause an increase in tidal volume and velocity of contraction of the inspiratory muscles).[23,24]

Study protocol

After anthropometric, pulmonary function and respiratory muscle strength data acquisition, the subjects included in the study underwent the ultrasound and exercise capacity assessments with an interval of 30 minutes in between. Right after, the subjects were positioned seated, feet supported, knees and hips at 90°, upright column, and arms supported with 45° abduction of their shoulders. Optoelectronic plethysmography acquisition was performed in the following order with an interval of five minutes between each moment: 1) Three minutes of QB, 2) three vital capacity (VC) maneuvers with 30 seconds of QB in between, and 3) three minutes breathing against the inspiratory threshold load.

Inspiratory capacity (IC) was calculated by analyzing the ascending portion of the VC curve (ie, the difference between maximal inspiratory and end-expiratory volumes). The highest VCW of three attempts generated during the VC maneuver was included in data analysis. Conversely, data analysis during QB and ITL were carried out during the whole three minutes of the protocol. All assessments were performed by a single trained, blinded assessor.

Data analysis

V_{CW} data derived from the IC maneuver of a previous study using optoelectronic plethysmography was used to guide a sample size calculation.[25] Thus, using the means and SD of the study (0.647 ± 0.467 L and 1.438 ± 0.704 L, affected and unaffected sides, respectively), an alpha error of .01 and statistical power of 99%, a total sample of 19 TBPI subjects was estimated for this study.

Data are shown as mean ± SD, otherwise stated. Shapiro-Wilk test was used to assess data normality. Comparisons between TBPI and healthy were studied using Mann-Whitney or unpaired t-test, while Wilcoxon or paired t-test was used to compare data derived from hemithoraces. Right and left CW and compartmental sides were compared for healthy individuals, while affected and unaffected sides were compared for TBPI patients. As low MIP values

Table 2
Chest wall and compartmental volume variation as well as its percentage of contribution during quiet breathing (QB), inspiratory capacity (IC), vital capacity (VC) and inspiratory threshold load (ITL) between healthy subjects and traumatic brachial plexus injury patients (TBPI)

	Healthy	TBPI	*ES*	p
Quiet Breathing				
ΔV_{CW} (L)	0.717 ± 0.267	0.664 ± 0.218	0.22	0.496
ΔV_{RCp} (L)	0.278 ± 0.133	0.190 ± 0.064	0.84	0.01
ΔV_{RCa} (L)	0.135 ± 0.058	0.136 ± 0.062	0.01	0.958
ΔV_{AB} (L)	0.306 ± 0.130	0. 340 ± 0.137	0.25	0.434
RCp (%)	38.1 ± 9.4	29.1 ± 7.7	1.04	0.002
RCa (%)	18.8 ± 5.3	20.3 ± 5.6	0.27	0.292
AB (%)	43.1 ± 11.7	50.6 ± 10.8	0.66	0.04
Inspiratory Capacity				
ΔV_{CW} (L)	2.604 ± 0.563	2.084 ± 0.414	1.05	0.002
ΔV_{RCp} (L)	1.263 ± 0.479	0.811 ± 0.293	1.14	0.001
ΔV_{RCa} (L)	0.592 ± 0.177	0.456 ± 0.118	0.90	0.007
ΔV_{AB} (L)*	0.748 ± 0.283	0.817 ± 0.351	0.06	0.693
RCp (%)	47.5 ± 11.8	38.6 ± 10.1	0.80	0.01
RCa (%)	22.6 ± 4.9	22.1 ± 4.6	0.10	0.75
AB (%)	29.9 ± 13.4	39.2 ± 11.9	0.73	0.02
Vital Capacity				
ΔV_{CW} (L)	3.774 ± 0.783	2.996 ± 0.758	1.01	0.002
ΔV_{RCp} (L)	1.637 ± 0.555	1.055 ± 0.409	1.19	0.001
ΔV_{RCa} (L)	0.754 ± 0.221	0.610 ± 0.177	0.72	0.02
ΔV_{AB} (L)	1.382 ± 0.328	1.329 ± 0.450	0.13	0.673
RCp (%)	42.6 ± 8.8	34.9 ± 8.1	0.90	0.007
RCa (%)	19.7 ± 3.4	20.5 ± 3.6	0.22	0.492
AB (%)	37.7 ± 9.5	44.5 ± 9.2	0.73	0.02
Inspiratory Load				
ΔV_{CW} (L)	1.290 ± 0.448	1.048 ± 0.427	0.55	0.08
ΔV_{RCp} (L) *	0.521 ± 0.231	0.335 ± 0.231	0.40	0.01
ΔV_{RCa} (L)	0.239 ± 0.118	0.205 ± 0.109	0.30	0.351
ΔV_{AB} (L) *	0.528 ± 0.210	0.508 ± 0.168	0.01	0.920
RCp (%)	39.3 ± 11.2	29.8 ± 10.8	0.85	0.01
RCa (%)	18.2 ± 5.2	19.1 ± 5.1	0.17	0.581
AB (%)	42.6 ± 13.7	51.1 ± 11.7	0.66	0.04

Data is shown as mean ± SD. Volume variation of the chest wall (ΔV_{CW}), pulmonary ribcage (ΔV_{RCp}), abdominal ribcage (ΔV_{RCa}), and abdomen (ΔV_{AB});
ES = Effect-size; L = Liters; % = percentage of contribution;
* non-parametric data distribution.

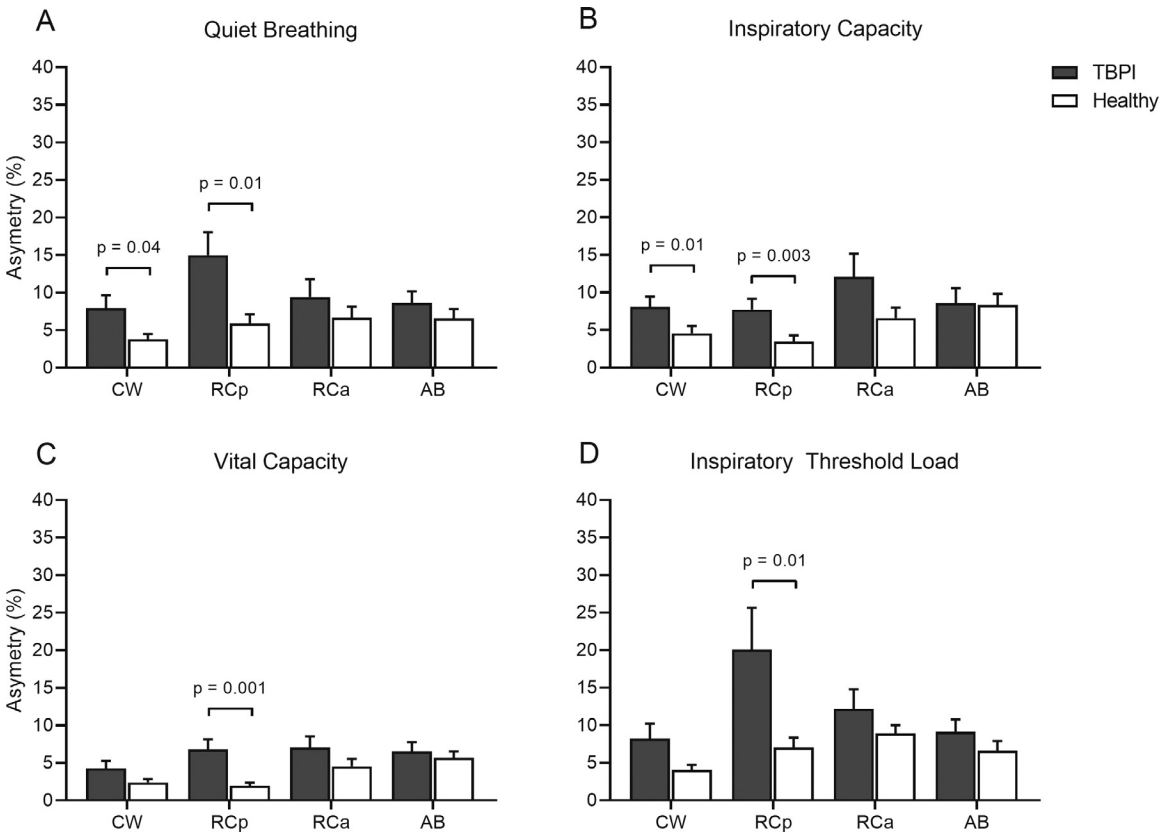

Fig. 3. Ventilation asymmetry of the chest wall (CW), pulmonary ribcage (RCp), abdominal ribcage (RCa), and abdominal (AB) compartments between healthy and traumatic brachial plexus injury patients (TBPI) during different respiratory maneuvers. %: percentage.

would interfere in the ITL load adjustment of the TBPI patients, the ANCOVA was used to analyze data regarding shortening velocity during ITL, with MIP as a covariate. Relationships between diaphragmatic mobility, functional capacity, and chest wall and compartmental volumes during QB, VC, IC, and ITL maneuvers were studied using Pearson's r or Spearman's *rho* correlations.

To avoid type II error, effect-sizes were calculated for parametric data using Cohen's d, and interpreted as small (<0.50), moderate (between 0.50 and 0.80), and large (>0.80).[26] For nonparametric data distribution, Cohen's r was calculated and interpreted as (<0.25), moderate (between 0.25 and 0.38), and large (>0.38).[27] For relationships, coefficients of correlation (r) and determination (r^2) were computed.

Effects sizes were calculated using the G*Power software (version 3.1.9.2, Kiel, Germany), while inferential data analyzes were performed using the Statistical Package for Social Sciences software, version 22 (SPSS; IBM Corp.). All analyses were performed assuming a p value < .05 (two-tailed).

Results

Flow of participants, therapists, and centers through the study

Twenty male patients with TBPI, only C8-T1 root avulsion (mean age 30.10 ± 5.30, mean lesion time 174 ± 45.24 days) and twenty healthy subjects (mean age 28.2 ± 4.6) were included. It is worth mentioning that it took two years of follow-up at the peripheral nerves outpatient clinic to capture the entire sample of patients, concomitantly, for the pairing, healthy individuals were also selected. All patients complained of pain in the arm of the affected side; however, no additional discomfort was reported during the assessments.

For spirometric and respiratory muscle strength data between groups, only FEV_1/FVC (in liters and percentage of predicted values) was not significant. Exercise capacity and diaphragm mobility were found to be low in TBPI patients (all p < .001) (Table 1) when compared with matched-paired healthy. Diaphragmatic mobility was correlated significantly with $FVC_{(L)}$ in TBPI patients (r = 0.490, r^2 = 0.240, p = .02).

A post hoc analysis considering the calculated effect size for volumes of ICCW (Cohen's d=1.05) showed a statistical power (1-β) of 0.95 for this study.

Chest wall volumes and velocity of shortening TBPI and healthy

The ΔV_{RCp} was significantly lower in TBPI patients during QB and ITL maneuvers but with no changes in ΔV_{CW} when compared with healthy individuals. Conversely, ΔV_{CW} was significantly lower during both the VC and IC maneuvers, mainly due to reduced ΔV_{RCp} and ΔV_{RCa} (Table 2).

Independently of the maneuver requested, the %AB was always increased, probably compensating the significant decreases in %RCp (Table 2). The magnitude of the reduction in %RCp was higher during QB (Cohen's d=1.04), while the increase in %AB was higher during both IC (Cohen's d=0.73) and VC (Cohen's d=0.73) maneuvers.

Regarding the velocity of shortening, V_{RCp}/Ti was found to be significantly reduced during both QB (Cohen's d=0.85, p = .01) and ITL maneuvers (Cohen's d=0.87, p = .001) when compared with healthy subjects (Fig. 2).

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Table 3
Right-left* chest wall and compartmental volume variation as well as its percentage of contribution during quiet breathing (QB), inspiratory capacity (IC), vital capacity (VC) and inspiratory threshold load (ITL) between healthy subjects and traumatic brachial plexus injury patients (TBPI)

	Healthy			TBPI		
	Right	Left	*ES*	Affected	Unaffected	*ES*
Quiet Breathing						
ΔV_{CW} (L)	0.355 ± 0.130	0.364 ± 0.139	0.06	0.326 ± 0.110	0.339 ± 0.121	0.11
ΔV_{RCp} (L)	0.140 ± 0.066	0.140 ± 0.069	0.00	0.091 ± 0.037	0.098 ± 0.035	0.19
ΔV_{RCa} (L)	0.066 ± 0.029	0.070 ± 0.031	0.13	0.066 ± 0.029	0.069 ± 0.033	0.09
ΔV_{AB} (L)	0.151 ± 0.068	0.156 ± 0.063	0.07	0.169 ± 0.064	0.171 ± 0.079	0.02
RCp (%)	50.71 ± 4.22	49.29 ± 4.22	0.23	47.32 ± 9.51	52.68 ± 9.51	0.56
RCa (%)	48.80 ± 4.56	51.20 ± 4.56	0.32	49.68 ± 7.16	50.32 ± 7.16	0.08
AB (%)	48.81 ± 3.90	51.19 ± 3.90	0.30	50.68 ± 5.54	49.32 ± 5.54	0.24
Inspiratory Capacity						
ΔV_{CW} (L)	1.316 ± 0.265	1.286 ± 0.309	0.10	0.997 ± 0.213	1.086 ± 0.243	0.38
ΔV_{RCp} (L)	0.642 ± 0.238	0.620 ± 0.246	0.09	0.385 ± 0.140†	0.425 ± 0.161	0.26
ΔV_{RCa} (L)	0.301 ± 0.086	0.289 ± 0.096	0.13	0.208 ± 0.069†	0.247 ± 0.069	0.56
ΔV_{AB} (L)	0.372 ± 0.122	0.375 ± 0.167	0.02	0.403 ± 0.152	0.415 ± 0.207	0.06
RCp (%)	51.12 ± 2.31	48.88 ± 2.31	0.56	47.85 ± 4.44†	52.15 ± 4.44	0.96
RCa (%)	51.51 ± 4.34	48.49 ± 4.34	0.59	45.55 ± 8.06†	54.45 ± 8.06	1.11
AB (%)	50.07 ± 10.13	49.93 ± 10.13	0.01	50.40 ± 6.23	49.60 ± 6.23	0.12
Vital Capacity						
ΔV_{CW} (L)	1.926 ± 0.387	1.878 ± 0.383	0.12	1.498 ± 0.377	1.564 ± 0.427	0.16
ΔV_{RCp} (L)	0.817 ± 0.276	0.799 ± 0.277	0.06	0.507 ± 0.195†	0.549 ± 0.220	0.20
ΔV_{RCa} (L)	0.379 ± 0.109	0.365 ± 0.117	0.12	0.288 ± 0.087†	0.321 ± 0.099	0.35
ΔV_{AB} (L)	0.684 ± 0.166	0.700 ± 0.174	0.09	0.672 ± 0.211	0.670 ± 0.248	0.01
RCp (%)	50.59 ± 1.21	49.41 ± 1.21	0.54	48.39 ± 4.27	51.61 ± 4.27	0.75
RCa (%)	51.34 ± 2.95	48.66 ± 2.95	0.60	47.38 ± 4.11†	52.62 ± 4.11	1.27
AB (%)	49.48 ± 3.44	50.52 ± 3.44	0.30	50.53 ± 4.30	49.47 ± 4.30	0.24
Inspiratory Load						
ΔV_{CW} (L)	0.649 ± 0.228	0.640 ± 0.224	0.03	0.509 ± 0.217	0.540 ± 0.224	0.14
ΔV_{RCp} (L)	0.267 ± 0.121	0.253 ± 0.114	0.11	0.154 ± 0.119† ‡	0.181 ± 0.119	0.22
ΔV_{RCa} (L)	0.123 ± 0.062	0.117 ± 0.057	0.10	0.098 ± 0.052	0.106 ± 0.061	0.14
ΔV_{AB} (L)	0.259 ± 0.112	0.270 ± 0.104	0.10	0.257 ± 0.085	0.253 ± 0.093	0.04
RCp (%)	50.72 ± 5.18	49.28 ± 5.18	0.27	43.22 ± 11.57† ‡	56.78 ± 11.57	1.17
RCa (%)	48.78 ± 4.27	51.23 ± 4.27	0.47	48.49 ± 8.39	51.51 ± 8.39	0.35
AB (%)	50.20 ± 2.53	49.80 ± 2.53	0.15	50.98 ± 5.87	49.02 ± 5.87	0.33

Data is shown as mean ± SD. Volume variation of the chest wall (ΔV_{CW}), pulmonary ribcage (ΔV_{RCp}), abdominal ribcage (ΔV_{RCa}), and abdomen (ΔV_{AB});
ES = Effect-size; L = Liters; % = percentage of contribution;
* Healthy (right-left) and TBPI (Affected-Unaffected);
† $p < .05$ when compared with unaffected side;
‡ non-parametric data distribution.

Hemithoraces analyzes

During QB, neither the volumes nor the percentage of contribution of both hemithoraces differed significantly in healthy and TBPI patients. On the other hand, both the ΔV_{RCp} and ΔV_{RCa} on the affected side of TBPI patients were significantly lower compared with the unaffected side during IC ($p = .03$, Cohen's d=0.51; $p = .03$, Cohen's d=0.52, respectively) and VC maneuvers ($p = .04$, Cohen's $r = 0.54$; $p = .01$, Cohen's d=0.61, respectively). As shown in Table 3, these differences accounted for a significant reduction of about 4.3% in volume of the affected RCp ($p = .04$, Cohen's d=0.74) and 8.9% of the affected RCa ($p = .01$, Cohen's d=1.10) during IC maneuver; as well as 3.2% in the RCp ($p = .04$, Cohen's d=0.75) and 5.2% of the RCa ($p = .01$, Cohen's d=1.27) during VC.

During ITL, only the ΔV_{RCp} on the affected side was significantly lower ($p = .01$, Cohen's $r = 0.47$), and a difference of 13.56% in the percentage of contribution between sides was observed ($p = .006$, Cohen's $r = 1.17$). Despite these reductions, no significant changes were observed in ΔV_{CW}.

Ventilation asymmetry

As shown in Figure 3, TBPI patients presented a significantly higher expansion asymmetry of the RCp during all conditions studied when compared with healthy subjects. Chest wall asymmetry showed to be significantly higher in TBPI patients only during QB ($p = .04$, Cohen's $r = 0.71$) and IC ($p = .01$, Cohen's $r = 0.66$) maneuvers. No correlations were found regarding asymmetry data.

Discussion

The main findings of the present study were that compared with matched healthy subjects, patients with TBPI due to traumatic lesion and who have not undergone nerve transfer repair present lower diaphragmatic mobility and exercise capacity, as well as decreased volume variation of the upper ribcage compartments during different respiratory maneuvers. In TBPI, the affected side was the main contributor to the reduction in volume, and expansion asymmetry of the RCp compartment was present in all maneuvers performed. Additionally, the velocity of shortening of the inspiratory ribcage muscles was lower in TBPI patients during quiet spontaneous breathing and inspiratory load imposition compared with healthy.

Both the pulmonary function and respiratory muscle strength values were reduced in TPBI patients. Although some patients may present normal values before surgical procedures,[5,28] the restrictive pattern observed in this study was probably the result of neuromuscular injury by trauma, uncooperativeness of the patients and/or muscular adaptations due to the antalgic posture adopted after the accident. Moreover, since a reduction of 14% in diaphragm

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mobility was found to be correlated with FVC, the alteration in the contractile force of the inspiratory muscles may have triggered muscle imbalance and thus contributed to the decreased pulmonary function and respiratory muscle strength.[5,29,30]

Diaphragm mobility depends directly on the strength of the inspiratory muscles and impacts on respiratory mechanics.[31] Evidence shows that diaphragm mobility is impaired before nerve transfer repair, while exercise performance is reduced in TBPI patients with altered minute ventilation.[5] Although exercise capacity is associated with diaphragmatic dysfunction in patients with isolated unilateral diaphragm paresis[32] and weakness,[33] no correlations were observed between these parameters in our cohort. This may have occurred because TPBI patients may experience deconditioning rather than ventilatory limitation, which is most likely related to restricted daily activity and exercise after the accident.[5,34]

The reduced volume of the affected side was the main contributor to the differences in volume observed in the upper ribcage compartments during ITL, IC, and VC. This was likely the result of muscle damage caused by the trauma since greater action of the accessory inspiratory muscles[35,36] is required to perform these maneuvers. Moreover, the avulsion of the C8-T1 roots may have affected the activity of the latissimus dorsi (C6-C8 roots), and both the pectoralis major (C5-T1 roots) and minor (C8-T1 roots). As these muscles are progressively recruited during inspiratory load imposition,[37,38] their impairment may have contributed to the observed difference in volume and ventilation asymmetry. Another important contributing factor could be a decrease in the compliance of the upper ribcage on the side of the injury. We believe that these alterations, together with decreased ribcage mobility,[11] also led to the reduction in velocity of shortening of the inspiratory ribcage muscles. It is worth noting that, although diaphragmatic mobility was lower in TBPI patients, the abdominal compartment contributed most to chest wall volume, indicating a compensation of the diaphragm to cope with the reduced action of the inspiratory ribcage muscles. As the altered diaphragm mobility had no effects on volume distribution between the affected and unaffected abdominal sides, it can be hypothesized that its reduced mobility was probably a consequence of the trauma and/or decondition; and would explain why no associations were observed with exercise capacity in our cohort. In this sense, the upper ribcage compartments were the primary site of volume impairment in our TBPI patients.

According to De Troyer et al.,[39] the volume changes of the affected and unaffected sides become asymmetrical during voluntary breathing when muscle action in uncoordinated. In this sense, it can be speculated that all the above-mentioned alterations led to an imbalance between the mechanical properties of the chest wall, inducing incoordination of the ribcage muscles during inspiration that altered the motion of the affected side and induced an asymmetrical ribcage expansion.[25,40] Also, as the electromyographic activity of the affected side decreases during progressive voluntary increases in tidal volume,[41] the exacerbation of the RCp asymmetry during ITL was probably the result of an increased muscle loading on the unaffected side. Another possible explanation for this disharmonious motion is related to the influence of the diaphragm in the upper ribcage. Since contraction of this muscle usually results in expansion of the lower ribcage (the portion of the ribcage apposed to the diaphragm),[9,42–44] any altered displacement may contribute to asymmetry of the upper ribcage compartments.

This study is not free of limitations. The major limitation is that diaphragm mobility was assessed in all subjects on the right side. However, we found no differences when comparing diaphragmatic mobility between TBPI patients with a left side injury and those with a right side injury ($p = .939$, data not shown). Apart from being the first study that assessed exercise capacity using the 6MWT in TBPI patients, the level of dyspnea, respiratory rate, blood pressure, heart rate, SpO_2, as well as respiratory and metabolic requirements were not evaluated during the test. Furthermore, some parameters could provide valuable information regarding the function of the respiratory system in these patients, such as the electromyographic activity of respiratory muscles, absolute lung volumes, chest wall compliance, gastric and esophageal pressures. Non-volitional tests (ie, twitch Pmouth or twitch Pdi) and electroneuromyography of the diaphragm could be useful in assessing muscle function and concomitant phrenic nerve involvement, respectively.

In conclusion, TBPI patients, specifically with C8-T1 root avulsion, who have not undergone nerve transfer surgery present restrictive pulmonary function, and reduced respiratory muscle strength and diaphragmatic mobility, as well as exercise intolerance compared to matched healthy individuals. The ventilation asymmetry observed and the reduced velocity of shortening of the inspiratory ribcage muscles were probably the result of the lesion on the structures of the affected side and alteration in respiratory mechanics. Further longitudinal studies are needed to identify the underlying mechanisms and observe if these alterations remain after surgery.

Clinical Implications

The main clinical implications of is that 174 days after the trauma, TBPI patients who had not been treated with nerve transfer surgery present a decrease in inspiratory muscle strength, exercise capacity, diaphragmatic mobility, as well as a reduced volume variation and ventilation asymmetry of the upper ribcage compartment. This suggests a need respiratory assessment and potentially for respiratory exercises or of incentive spirometry which may decrease the level of ventilation asymmetry.[22,45–47] This issue needs further investigation.

Authors Statement

Helen Fuzari: Conceptualization, data curation, formal analysis, investigation, methodology, project management, software, supervision, visualization, validation, initial and final writing. Armèle Dornelas: Conceptualization, financing acquisition, methodology, project management, resources, software, supervision, visualization, initial and final writing. Antônio Sarmento: Data curation, formal analysis, methodology, software, validation and final writing. Jacqueline Barcelar: Data curation, formal analysis, methodology, validation and final writing. Silvya Bernardino: Acquisition of funding, research, resources, validation and final writing. Fernando Henrique: Conceptualization, financing acquisition, research, resources, validation and final writing. Daniela Araújo: Conceptualization, financing acquisition, methodology, project management, resources, supervision, visualization, initial and final writing.

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