J Shoulder Elbow Surg (2023) ■, 1–12

ELSEVIER

Journal of Shoulder and Elbow Surgery

www.elsevier.com/locate/ymse

Poor midterm clinical outcomes and a high percentage of unsatisfying results are reported after seizure-related shoulder injuries, especially after posterior proximal humerus fracture-dislocations

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Background: Treating seizure-related shoulder injuries is challenging, and an evidence-based consensus to guide clinicians is lacking. The aim of this prospective single-center observational clinical trial was to evaluate the clinical results of a cohort of patients undergoing treatment of seizure-related shoulder injuries, to categorize them according to the lesion's characteristics, with special focus on patients with proximal humerus fracture-dislocations (PHFDs), and to define groups at risk of obtaining unsatisfactory results. We hypothesized that patients with a PHFD, considered the worst-case scenario among these injuries, would report worse clinical results in terms of the quick Disabilities of the Arm, Shoulder, and Hand questionnaire (qDASH) as compared to the other patients.

Methods: Patients referred to a tertiary epilepsy center who have seizure-related shoulder injuries and with a minimum follow-up of 1 year were included. A quality-of-life assessment instrument (EQ-5D-5L), a district-specific patient-reported outcome measure (qDASH), and a pain assessment tool (visual analog scale [VAS]) were used for the clinical outcome evaluation. Subjective satisfaction and fear of new shoulder injuries was also documented. Categorization and subgroup analysis according to the presence and features of selected specific lesions were performed.

Institutional approval of the study protocol was obtained from the local ethics committee prior to data collection (Ethikkommission an der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn, ID 245/19).

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1058-2746/$ - see front matter
https://doi.org/10.1016/j.jse.2023.09.023

Results: A total of 111 patients were deemed eligible and 83 were available for follow-up (median age 38 years, 30% females), accounting for a total of 107 injured shoulders. After a median follow-up of 3.9 (1.6-8.2) years, overall moderate clinical results were reported. In addition, 34.1% of the patients reported a VAS score ≥35 mm, indicating moderate to severe pain, and 34.1% a qDASH score ≥40 points, indicating severe disability of an upper limb. These percentages rose to, respectively, 45.5% and 48.5% in the subgroup of patients with PHFDs and to 68.8% and 68.8% in patients experiencing posterior PHFD. Overall, 46.9% of the patients considered themselves unsatisfied with the treatment and 62.5% reported a persistent fear of a new shoulder injury.
Conclusions: Patients with seizure-related shoulder injuries reported only moderate clinical results at their midterm follow-up. Older age, male sex, and absence or discontinuation of antiepileptic drug (AED) treatment were identified as characterizing features of patients with posterior dislocation episodes. In patients with PHFD, a tendency to worse clinical results was observed, with posterior PHFD patients emerging as a definite subgroup at risk of reporting unsatisfying results after treatment.
Level of evidence: Level III; Retrospective Cohort Comparison; Prognosis Study

Keywords: Shoulder; seizure; epilepsy; dislocation; instability; fracture; function; quality of life

Seizures, specifically the tonic-clonic type, can cause various musculoskeletal injuries, which are a well-known but rather neglected complication of epilepsy. Among these injuries, shoulder injuries account for a major percentage and include acute or recurrent shoulder dislocations; fractures of the humerus, scapula, or clavicle; rotator cuff lesions; or a combination of these injuries.[25,71] A peculiarity of this specific subgroup of patients is that the occurrence of ''rare'' injuries, such as proximal humerus fracture-dislocations (PHFDs), posterior instability, and bilateral shoulder lesions, is much higher than that in nonepileptic patients.[12,31,58,59]

Depending on the type of injury, various treatment options have been described, ranging from conservative treatment over joint-preserving, arthroscopic, and open procedures, to joint replacement. When choosing the most appropriate treatment, the specific characteristics of the patient, the severity of the epilepsy, and the features of each shoulder injury must be taken into account; nevertheless, treating these injuries is challenging and frequently hampered by failures and complications. Most of the published reports detailing the treatment outcome after a seizure-related shoulder instability are case series reports that investigate the results of patients treated with a single, specific surgical technique, and only a limited number of studies exist that report the clinical results on cohorts of patients with epilepsy who are treated according to the specific characteristics of their injury and their underlying disease.[8,17,26,33,57,73,74] Even more scarce is the amount of available literature addressing the conservative treatment of seizure-related instability with seizure-related shoulder fractures.[15,31,35,40,60,73]

This scarcity of available outcome measures makes therapeutical decision making challenging, because an evidence-based consensus to guide treatment selection is lacking.[4,23,72,78] The aim of this study was to evaluate the clinical and functional results of a large cohort of patients undergoing treatment of seizure-related shoulder injuries and to categorize these results according to the lesion characteristics and the chosen treatment. We focused especially on PHFD, an injury consisting in the displacement of 1 or more of the 4 parts of the proximal humerus along with a simultaneous glenohumeral joint dislocation and considered ''rare'' outside the epileptic population but frequently encountered in this patient subgroup, which can dramatically reduce shoulder function and overall quality of life.[39,45] We hypothesized that patients with PHFD, considered the worst-case scenario among these injuries, would report worse clinical results in terms of the quick Disabilities of the Arm, Shoulder, and Hand questionnaire (qDASH) than other patients.

Methods

This study was designed as a single-center prospective observational clinical with a minimum follow-up of 1 year. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement guidelines were followed for methods and result presentation.

Study population

All adult patients who were referred to a tertiary epilepsy center (University Hospital Bonn, Germany: approximately 2500 patients, 6000 consultations per year) for diagnosis and treatment of epilepsy were considered eligible candidates (June 2019-June 2022). Among these, patients with any kind of seizure-related shoulder injury with a minimum follow-up of 1 year were included. Exclusion criteria were the absence of seizure-related shoulder injuries and inability or unwillingness to participate in the clinical data collection.

Collection and classification of data

Documentation of trauma mechanism, lesion characteristics and performed treatment was recorded at the time of stationary

admittance or during outpatient consultations and shoulder injuries were classified depending on bony and soft tissue involvement and direction of glenohumeral instability, if present.

Both conservative and operative treatments were evaluated; the latter consisted of arthroscopic procedures, open stabilization or osteosynthesis procedures, and joint replacement procedures.

Seizure and epilepsy type were classified according to the International League Against Epilepsy (ILAE) definition of 2017. The ILAE classification is a 2-level classification, which in a first level addresses seizures types (classified into focal onset, generalized onset, and unknown onset) and in a second level epilepsy types, based on the diagnosis of epilepsy published in 2014.[19,20,63] Epilepsy types were grouped into 3 categories: focal, generalized, and unknown. Tonic-clinic seizures were classified as seizures with focal onset, generalized onset, or unknown onset, taking into account diagnostic findings and seizure semiology.

Patients with seizures but no evidence of epilepsy were classified as acute symptomatic seizures or first unprovoked seizures. Antiepileptic drug therapy at the time of injury and the response to medication were documented for all patients.

Collection and stratification of clinical outcome parameters

To evaluate the clinical outcome, a combination of a quality-of-life assessment instrument (EQ-5D-5L) with a district-specific patient-reported outcome measure (PROM) and a pain assessment tool were used (visual analog scale [VAS]).[64] Following local recommendations, the Disabilities of the Arm, Shoulder, and Hand questionnaire (DASH) was collected as district-specific score, in its short form (qDASH).[29,50] Fear of new shoulder injuries and subjective satisfaction regarding the treatment results in terms of pain and upper limb function were also documented as dichotomous variables.

Stratification of results was performed for the VAS and DASH scores, according to previous publications and to the DASH outcome measure user's manual.[6,32]

Statistical analysis

A power analysis indicated that a minimal total sample size of 50 patients was sufficient to evaluate a clinically relevant difference in terms of qDASH between patients with and without PHFD with a power >80% and significance level set at 5%. Using the minimal clinically important difference values recommended for the qDASH by Franchiglioni et al,[21] the sample size calculation was based on previously published studies on shoulder injuries presenting outcomes in terms of qDASH.[9,10,13,18,24,27,28,38,41,47,48,54,61,65,79]

Demographic data, as well as the aforementioned information on diagnosis and treatment of epilepsy and data regarding shoulder injuries, were entered into a spreadsheet for analysis. Statistical analysis was performed using R Statistical Software (version 4.0.0; R Foundation for Statistical Computing, Vienna, Austria) and GraphPad Prism v 6.0 software (GraphPad Software Inc., Boston, MA, USA). The Shapiro-Wilk normality test was used to evaluate the normal distribution of the sample. Continuous variables were expressed as the mean ± standard deviation (SD) or medians and first and third quartiles (Q1-Q3) as appropriate. The differences between 2 groups of patients for continuous variables were evaluated with unpaired Student *t* test or Mann-Whitney test; the differences among more than 2 groups of patients were evaluated with 1-way analysis of variance (ANOVA) or Kruskal-Wallis test, according to the characteristics of the data distribution. When significant interaction effects were found, Holm-Sidak or Dunn multiple comparison tests were applied as a post hoc test for multiple comparisons of groups. Categorical variables are expressed in number of cases and frequencies; their differences were tested using χ^2 or Fisher exact test. For all analyses, the significance level was set at a P value lower than .05.

This audit of data collected during clinical care was approved by the local medical ethics committee (Ethikkommission an der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn, no. ID 245/19).

Results

Demographic and historical data

A total of 111 patients were deemed eligible, and 83 were available for follow-up, accounting for a total of 107 injured shoulders (Supplementary Table S1). Reasons for dropping out included loss to follow-up (n = 18), unwillingness to participate (n = 8), and medical comorbidities requiring inpatient treatment in another hospital impairing follow-up investigation (n = 2). The average age at the time of injury was 39.9 ± 17.0 years, and a male predominance was recorded (69.9%). Focal epilepsy was the most frequently documented type, followed by unknown epilepsy type and genetic generalized epilepsy; approximately half of the patients (49.4%) were taking antiepileptic drugs (AEDs) when the shoulder injury occurred.

In 57 patients (68.7%), the shoulder injury was caused solely by the muscular activation during the seizure, without any external acting force or fall—a distinctive dynamic of injury in patients with seizures significantly associated with the occurrence of shoulder instability (>75%, $P = .0116$).

The distribution of all reported injuries is illustrated in Figure 1. Bilateral injuries occurred in 24 patients (28.9%), 15 of which (62.5%) occurred simultaneously. In 10 cases, the PHFD was bilateral (4 bilateral anterior PHFDs, 3 of which occurred simultaneously, and 6 bilateral posterior PHFDs, with 5 occurring simultaneously). Detailed information on lesions and performed treatments for each patient is available in the supplementary materials (Supplementary Table S1).

Clinical results

Surgery was performed in 62 patients, whereas 21 were treated conservatively (74.7% vs. 25.3%); patients experiencing PHFD were treated surgically significantly more frequently than those without PHFD ($P = .0013$).

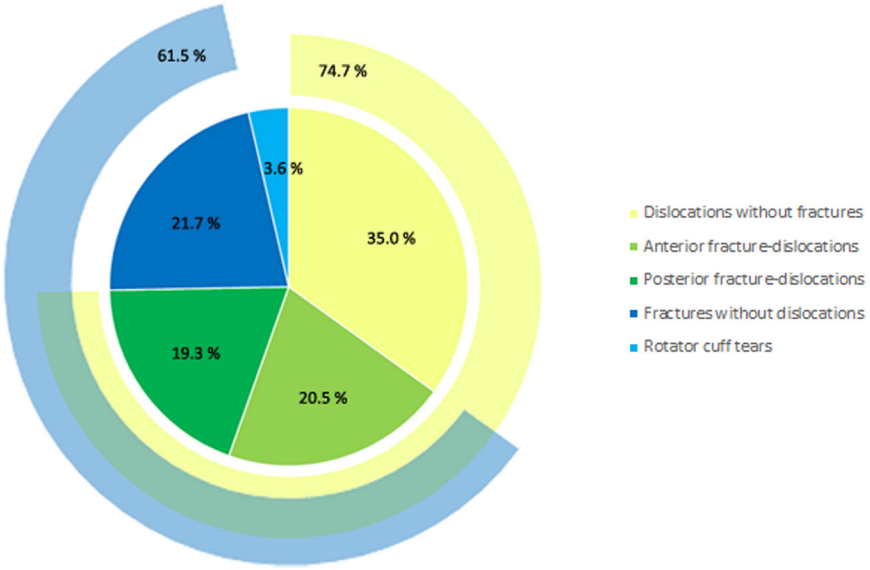

Figure 1 Graphic representation of the distribution of different shoulder lesions in the study cohort. The *blue* and *yellow* circular sectors surrounding the main pie chart represent the cumulative percentage of patients with fractures and dislocations.

After a median follow-up of 3.9 (1.6-8.2) years, overall moderate clinical results were reported in the collected scores (Table I). Notably, 34.1% of the patients reported a VAS score ≥35 mm, indicating moderate to severe pain,[6] and 34.1% a qDASH score ≥40 points, indicating a severe disability of an upper limb.[32] Only 24.7% of the patients scored <15 points in the qDASH, indicating "no relevant upper limb problems" (Fig. 2).

Overall, 46.9% of the patients considered themselves unsatisfied with the treatment because of persistent pain, compromised upper limb function, or as a consequence of complications. Of all evaluated patients, 62.5% persistently feared a new shoulder injury.

In the subgroup of patients with PHFD (n = 33; 39.8% of the entire cohort), the percentage of patients with VAS ≥35 mm and qDASH ≥40 points rose to 45.5% and 48.5%, respectively, with only 23.1% of patients scoring <15 points in the qDASH. As opposed to this, in the group without PHFD the percentage of patients with VAS ≥35 mm was 26.1%, and that with qDASH ≥40 was 28.9%, with 26.7% of patients scoring <15 points in the qDASH. The variations in the percentage of patients meeting the predefined cutoffs did not achieve statistical significance.

Subgroup analysis: presence and direction of PHFD

Within the subgroup of patients experiencing PHFD, significant differences related to their presence and direction emerged: patients experiencing anterior PHFD (n = 17; 20.5% of the entire cohort) were diagnosed with epilepsy significantly earlier and were significantly younger at the time point of shoulder injury than those experiencing posterior PHFD (n = 16; 19.3% of the entire cohort) and fractures without instability (epilepsy diagnosis: $P = .0185$ and $P = .0287$, respectively; shoulder injury: $P = .0105$ and $P = .0384$, respectively); patients experiencing posterior PHFD were diagnosed later and injured later than those experiencing glenohumeral instability without fractures ($P = .0029$ and $P = .0007$, respectively) (Tables II and III). As expected, patients with instability were younger than those with fractures ($P < .0001$). Furthermore, when examining the medical treatment for epilepsy at the time of shoulder injury, this appeared to be significantly less frequent in patients experiencing posterior PHFD (13%; $P = .0345$). No significant differences were found in VAS and qDASH scores and EQ-5D-5L index, fear of reinjury, and satisfaction related to presence and direction of PHFD. However, there was a significant difference in the fraction of patients reporting particularly unsatisfying results (such as VAS ≥35 mm and qDASH ≥40 points), both reported more frequently in patients experiencing posterior PHFD (68.8%). This frequency was double that of all other subgroups (always <30%, with the exception of the VAS ≥35 mm in patients with fractures without instability, reported in 35.3% of the cases).

Subgroup analysis: presence and direction of instability

Significant age differences emerged in relation to the presence and direction of instability: patients affected by anterior and multidirectional shoulder instability were diagnosed with epilepsy earlier (anterior: $P = .0004$ and $P < .0001$; multidirectional: $P = .0157$ and $P = .008$) and injured earlier (anterior: $P = .0029$ and $P < .0001$; multidirectional: $P = .0188$ and $P = .0017$) than those experiencing posterior instability and those without instability.

Table I Patient demographics and clinical results

Group	Overall (n = 83)	PHFD (n = 33)	No PHFD (n = 50)	*P* value
Gender: n, F/M ratio	0.30/0.70	0.27/0.73	0.32/0.68	n.s.
Side: n, L/R/B ratio	0.28/0.43/0.29	0.33/0.36/0.31	0.23/0.49/0.28	n.s.
Age at epilepsy diagnosis, yr				n.s.
Median (IQR)	28.00 (17.00-47.50)	29.0 (19.0-45.0)	23.00 (17.00-45.50)	
Mean ± SD	32.35 ± 20.40	32.92 ± 17.32	30.88 ± 21.13	
Age at shoulder injury, yr				n.s.
Median (IQR)	38.0 (26.5-53)	40.0 (28.0-49.0)	35.0 (23.0-56.0)	
Mean ± SD	39.93 ± 17.02	40.27 ± 13.59	38.22 ± 18.34	
AED use during shoulder injury: n, Y/N ratio	0.49/0.50	0.39/0.61	0.53/0.47	n.s.
Follow-up, yr				n.s.
Median (IQR)	3.9 (1.6-8.2)	3.5 (1.3-6.8)	4.6 (1.9-9.3)	
Mean ± SD	6.13 ± 7.10	4.98 ± 4.60	7.13 ± 8.51	
Surgical treatment: n, Y/N ratio	0.75/0.25	0.94/0.06	0.62/.038	.001
EQ-5D-5L index				n.s.
Median (IQR)	0.82 (0.60-0.91)	0.82 (0.60-0.89)	0.83 (0.69-0.91)	
Mean ± SD	0.74 ± 0.23	0.73 ± 0.24	0.77 ± 0.21	
VAS score				n.s.
Median (IQR)	20.0 (0.0-50.0)	30.0 (5.0- 60.0)	12.5 (0.0-41.3)	
Mean ± SD	27.07 ± 27.93	31.97 ± 27.87	23.59 ± 26.96	
% VAS score ≥35 mm	34.1	45.5	26.1	n.s.
qDASH score				n.s.
Median (IQR)	31.82 (14.77-47.73)	36.36 (15.91-56.82)	27.27 (13.64-43.18)	
Mean ± SD	33.87 ± 23.72	38.84 ± 25.70	29.75 ± 20.87	
% qDASH ≥40 points	34.1	48.5	28.9	n.s.
Satisfaction with treatment results: n, Y/N ratio	0.53/0.47	0.51/0.49	0.56/0.44	n.s.
Fear of reinjury: n, Y/N ratio	0.63/0.37	0.60/0.40	0.67/0.33	n.s.

F/M, female/male; *L/R/B*, left/right/bilateral; *IQR*, interquartile range (first and third quartiles, Q1-Q3); *SD*, standard deviation; *AED*, antiepileptic drug; *Y/N*, yes/no; *VAS*, visual analog scale; *qDASH*, quick Disabilities of the Arm, Shoulder, and Hand questionnaire; *PHFD*, proximal humerus fracture-dislocation; *n.s.*, not significant.

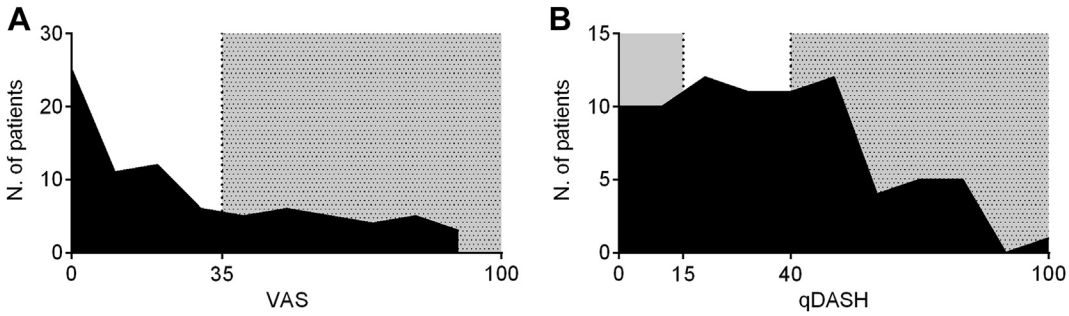

Figure 2 Graphic representation of results obtained in terms of visual analog scale (VAS) and quick Disabilities of the Arm, Shoulder, and Hand questionnaire (qDASH) scores in the study population. *Dashed lines* represent cutoff levels for pain and function according to previous guidelines.[6,32] The *dotted* area highlights scores indicating (**A**) moderate to severe pain and (**B**) severe disability of the upper limb.

A significant difference in gender distribution was documented, with distinct male dominance in patients experiencing posterior instability, which was not observed in patients with anterior instability (83.3% vs. 46.7%, $P = .0115$). Significant differences were also detected in patients receiving medical treatment for epilepsy, which was less frequent in patients experiencing posterior instability (20.83%, >50% in all other subgroups, $P = .0061$). These results define a specific subgroup of patients (older males without AED treatment), which appears to be more prone to posterior instability episodes.

Results of operative stabilization for shoulder instability without associated proximal humerus fracture treatment were moderate (average VAS score: 21.50 ± 26.42 mm, median: 10.0 [0.0-30.0] mm; average qDASH score: 27.58 ± 21.94 points, median: 20.45 [11.36-38.64]) and

Table II Presence and direction of PHFD

Group	Anterior PHFD (n = 17)	Posterior PHFD (n = 16)	Glenohumeral instability, no fractures (n = 29)	Fracture without instability (n = 17)	*P* value
Gender: n, F/M ratio	0.41/0.59	0.13/0.88	0.34/0.66	0.28/0.72	n.s.
Side: n, L/R/B ratio	0.29/0.47/0.24	0.38/0.25/0.38	0.28/0.38/0.34	0.17/0.67/0.17	n.s.
Age at epilepsy diagnosis, yr					.003-.029*
Median (IQR)	20.0 (16.0-33)	44.5 (31.0-56.0)	18.0 (11.5-31.0)	46.0 (23-62.25.0)	
Mean ± SD	23.24 ± 13.01	43.22 ± 15.5	23.45 ± 17.06	43.56 ± 21.8	
Age at shoulder injury, yr					<.001-.038*
Median (IQR)	28.0 (25.0-38.0)	46.5 (40.88-56. 0)	27.0 (18.5-37.0)	56.0 (36.0-61.63)	
Mean ± SD	33.35 ± 12.67	47.63 ± 10.52	30 ± 14.6	51.47 ± 16.06	
AED use during shoulder injury: n, Y/N ratio	0.65/0.33	0.13/0.88	0.55/0.45	0.50/0.50	.035
Mechanism of injury—muscular activation during the seizure without any external acting force or fall: n, 0/1 ratio	0.71/0.29	0.75/0.25	0.86/0.14	0.35/0.65	.005
Follow-up, yr					n.s.
Median (IQR)	6.5 (2.4-8.2)	1.5 (1.1-3.5)	5.9 (1.6-11.4)	3.4 (1.9-6.5)	
Mean ± SD	6.29 ± 4.03	3.59 ± 4.88	8.15 ± 9.67	5.50 ± 6.11	
Surgical treatment: n, Y/N ratio	1/0	0.88/0.12	0.55/0.45	0.77/0.23	.002
EQ-5D-5L index					n.s.
Median (IQR)	0.84 (0.65-0.90)	0.70 (0.49-0.89)	0.83 (0.64-1.00)	0.78 (0.70-0.91)	
Mean ± SD	0.77 ± 0.23	0.69 ± 0.25	0.76 ± 0.24	0.77 ± 0.14	
VAS score					n.s.
Median (IQR)	15.0 (0.0-35.0)	40.0 (11.3-63.8)	10.0 (0.0-30.0)	20.0 (0.0-53.5)	
Mean ± SD	23.53 ± 26.21	40.94 ± 27.52	21.14 ± 25.96	27.76 ± 28.91	
% VAS score ≥35 mm	23.5	68.8	20.7	35.3	.010
qDASH score					n.s.
Median (IQR)	31.82 (14.77-46.59)	51.14 (24.43-67.05)	31.82 (7.955-42.61)	25 (15.91-47.73)	
Mean ± SD	31.82 ± 25.05	46.31 ± 24.98	28.98 ± 21.93	31.02 ± 19.6	
% qDASH ≥40 points	29.4	68.8	28.6	29.4	.042
Satisfaction with treatment results: n, Y/N ratio	0.59/0.41	0.44/0.56	0.50/0.50	0.65/0.35	n.s.
Fear of reinjury: n, Y/N ratio	0.67/0.33	0.53/0.47	0.78/0.12	0.50/0.50	n.s.

PHFD, proximal humerus fracture-dislocations; *F/M*, female/male; *L/R/B*, left/right/bilateral; *IQR*, interquartile range (first and third quartiles, Q1-Q3); *SD*, standard deviation; *AED*, antiepileptic drugs; *Y/N*, yes/no; *VAS*, visual analog scale; *qDASH*, quick Disabilities of the Arm, Shoulder, and Hand questionnaire; *n.s.*, not significant.

* The detailed results of Dunn multiple comparisons test are reported in Table III.

were burdened by a high rate of instability recurrency (48%) and persistent fear of new injuries (71%). The results of conservative treatment of shoulder instability were slightly inferior, although without any statistically significant differences from the operatively treated patients (average VAS score: 27.67 ± 29.27 mm, median: 20.0 [5.0-30.0]; average qDASH score: 32.47 ± 21.88, median: 35.23 [15.34-43.75], fear of reinjury in 72% of the cases).

No significant differences in terms of VAS and qDASH scores and EQ-5L-5D index, fear of reinjury, and satisfaction emerged on comparing patients with different directions of instability. However, when grouping for direction of instability without fractures, no significant differences in the fraction of patients reporting very bad results (VAS ≥35 mm and qDASH >40) emerged; this is in contrast to what emerged in the subgroup analysis on PHFD, supporting the hypothesis that the entity of a posterior PHFD itself and not only posterior instability negatively affects the outcomes.

A significant difference was found in the rate of patients reporting treatment failures, recurrences, and complications: specifically, patients without instability experienced these adverse events at a significantly lower frequency (21.4%) than those with anterior instability, posterior

Table III Results of Dunn multiple comparison test applied as a post hoc test for multiple comparisons between groups based on the presence and direction of PHFD, to test for the difference between the age at epilepsy diagnosis and the age at shoulder injury

	Age at epilepsy diagnosis, yr		Age at shoulder injury, yr	
	Mean rank difference	Adjusted *P* value	Mean rank difference	Adjusted *P* value
Anterior PHFD vs. posterior PHFD	−23.65	.019	−22.07	.038
Anterior PHFD vs. GH instability, no fractures	1.308	*n.s.*	5.785	*n.s.*
Anterior PHFD vs. fracture without instability	−22.21	.029	−24.6	.011
Posterior PHFD vs. GH instability, no fractures	24.96	.003	27.86	.001
Posterior PHFD vs. fracture without instability	1.445	*n.s.*	−2.531	*n.s.*
GH instability, no fractures vs. fracture without instability	−23.51	.005	−30.39	<.001

PHFD, proximal humerus fracture-dislocations; *GH*, glenohumeral; *n.s.*, not significant.

instability, and multidirectional instability (46.2%, 53.3%, and 100.0%, respectively; $P = .0346$).

Subgroup analysis: bilateral injuries

No significant differences in patients' demographics, follow-up time, and mechanism of injury were found between patients experiencing bilateral and unilateral injuries. However, patients with bilateral injuries had a significant lower qDASH score at final follow-up (25.40 ± 4.86 vs. 37.23 ± 3.045, $P = .0422$), which was not associated with significant differences in the EQ-5D-5L index, VAS score, satisfaction, and fear of reinjury.

Subgroup analysis: treatment

Neither demographic nor clinical differences emerged between conservatively and surgically treated patients; however, when analyzing subgroups treated for different pathologies, significant differences distinguished the fraction of patients receiving operative treatment for posterior dislocations (including PHFD) and multidirectional instability, which reported unsatisfactory results after operative treatment (such as VAS ≥35 mm), with more than double the frequency of that of patients receiving operative treatment for anterior instability (58.8%, 59.0%, and 19.2% respectively, $P = .0492$). A similar trend was observed comparing the fraction of patients with qDASH >40 after operative treatment of operative posterior and anterior instability (64.7% vs. 30.8%), although not reaching statistical significance.

Discussion

This study shows that epileptic patients with seizure-related shoulder injuries are an extremely challenging group to achieve successful treatment. Only moderate results were obtained at midterm follow-up, regardless of the specific lesion characteristics and the type of treatment performed. However, subgroup analysis allowed to identify patients with posterior PHFD as a definite subgroup, with higher risk of particularly unsatisfying results after treatment. Furthermore, older age, male sex, and absence or discontinuation of AED treatment were identified as characterizing features of patients with posterior dislocation episodes, including PHFD. Considering the particularly negative results documented within this subgroup, care is advised when planning AED discontinuation on older (>35 years) male epilepsy patients.

The results reported in this cohort are substantially inferior to those reported in high-quality trials not restricted to patients with seizures using similar outcome metrics.[9,10,13,18,24,27,28,34,38,41,43,44,46-48,54,61,65,77,79] In particular, 34.1% of the evaluated patients reported a VAS score ≥35 mm, which indicates moderate to severe pain, and scored more than 40 points in the qDASH score, which indicates a severe disability of an upper limb[6,32]; furthermore, more than 45% of the patients were unsatisfied with their results, with almost two-thirds of them fearing the possibility of new injuries. It was not possible to identify a specific lesion or treatment type associated with significantly superior or inferior clinical results, suggesting that the underlying neurologic pathology itself is a critical aspect negatively influencing the results, regardless of the orthopedic treatment. This warrants special care and appropriate counseling when treating patients with seizures who have shoulder injuries.[78]

In the subgroup of patients with PHFD, considered the most severe injury in the study population, the percentages of patients with VAS score ≥35 mm and qDASH ≥40 points rose to 45.5% and 48.5%, respectively. Nevertheless, because of the high proportion of unfavorable results throughout the study population, it was not possible to confirm the hypothesis that patients with PHFD have a significantly higher qDASH than the other.

Patients with epilepsy may have a vast spectrum of different shoulder injuries, including fractures, acute and recurrent instability, as well as combinations of bony and

soft tissue lesions. In these patients, a high frequency of ''rare'' shoulder injuries, such as bilateral shoulder lesions and posterior instability, is to be expected compared to the literature data from patient cohorts without epilepsy or seizures.[7,8,14,22,30,31,35,55,56,62,66]

Bone fractures and soft tissue musculoskeletal injuries are a frequent, but rather neglected, complication of epileptic seizures.[5,37,51,70] The increased risk of sustaining a fracture compared with that of the general population ranges between 1.91 and 2.45[3,51,75,76] and is especially pronounced in patients with tonic-clonic seizures.[51,67] The cause for such injuries can be either the uncontrolled powerful muscular contraction occurring during tonic-clonic seizures or an unprotected fall in patients with tonic, atonic, tonic-clonic, or myoclonic seizures.[1,36,76] The use of AEDs may also influence the risk of sustaining shoulder lesions by reducing bone mineral density[11,49,53,68] or increasing the risk of uncontrollable falling due to side effects such as sedation and gait insecurity.[52,67,69]

The complexity of shoulder injuries in patients with epilepsy, together with the comorbidities (eg, osteoporosis, depression, gait insecurity) and the underlying neurologic disease (eg, mental retardation, ataxia, paralysis), makes successful treatment challenging. Treatment choice depends on the patient's characteristics, on the course of the neurologic disease, and on the specific features of the shoulder injury. Many treatment options have been described, including conservative therapy, open and arthroscopic bony and soft tissue procedures, and joint replacement.[12,58]

Publications reporting results after seizure-related shoulder injury treatment are scarce, especially those dealing with complex and rare injuries such as PHFD, with only a few case series and some individual case reports available on the treatment of PHFD, including seizure-related injuries.[40] Open reduction procedures, associated with internal fixation of fractures, were the most frequently performed procedures in our cohort, which is similar to findings of previous reports with slightly different inclusion criteria.[31,73]

Dimon et al[15] described the treatment of 6 post-convulsive posterior PHFD, highlighting the diagnostic pitfalls while showing satisfactory results in 3 patients, and mentioning the risk of recurrent instability due to recurrent seizures. Within a cases series of 26 patients who sustained complex posterior PHFD, Robinson et al[60] described 11 seizure-related lesions. Overall, the clinical results 2 years after surgery were satisfying, with a median Constant-Murley score of 83.5 points and a median DASH score of 17.5 points; however, no separate analysis was presented of the outcomes of seizure-related lesions.[60] Königshausen et al[35] retrospectively evaluated in-hospital records of 17 bilateral proximal humerus fractures (none of them related to seizures), revealing a high complication and reoperation rate (59% and 78% of the patients, respectively). Our study showed particularly poor results in patients with seizure-related PHFD, identifying this subgroup as particularly difficult to treat with satisfactory results. The authors advise therefore to treat such complex cases in centers that have both specialized shoulder surgeons and a neurology service with expertise in epilepsy diagnostics and treatment.

Shoulder instability in epilepsy patients has been addressed somewhat more frequently; nevertheless, most published reports on outcomes after seizure-related shoulder instability treatment are case series investigating the results of surgical treatments; the need for surgical treatment after seizure-induced shoulder instability is rarely quantified, and no reports on conservative treatment for this patient subgroup have been identified in our literature review. The frequency of indication for surgical treatment reported by Langenbruch et al[40] was slightly inferior to that encountered in our subgroup of patients affected by shoulder instability without associated fractures (53% vs. 62%).

Recurrent instability appeared to be a serious problem in our subgroup of patients receiving stabilization procedures after seizure-related shoulder instability (48%), similar to what was documented in previous reports. Bühler and Gerber investigated 26 consecutive epilepsy patients with 34 unstable shoulders; good final results were reported in 23 cases, with a high recurrence rate after the first surgical intervention (29.4%-47% in patients with anterior and 12% in patients with posterior instability) and a high reoperation rate (23.5%).[8]

Thangarajah et al[73] published one of the currently largest available consecutive series of surgical data describing treatment of seizure-related recurrent shoulder instability (33 patients with 49 unstable shoulders, mean age at index dislocation: 20 years); out of 31 patients (36 shoulders) undergoing surgery, recurrent instability was found in 69%, approximating the percentage reported in our report (61.9%). A particularly high recurrence rate was documented for patients undergoing soft tissue repair alone (71%) as opposed to bone block procedures (28%).[73] Persistent postoperative seizures, affecting 82% of the patients, was considered the main reason for surgical failure. Both studies report higher recurrence rates for procedures addressing anterior shoulder instability (61% and 47%, respectively).[8,73]

A recent publication by the Multicenter Orthopaedic Outcomes Network (MOON) Shoulder Group highlighted 25 patients with a history of seizures from 1298 shoulder stabilization patients. Some of the pathologic hallmarks that might pose a threat to good surgical results were reported, such as more frequent prior dislocations and more extensive preoperative bone loss, leading to more frequent open stabilization procedures.[2] This tendency toward an extremely high rate of recurrent instability has encouraged treatment with bone block procedures, which may improve the outcome after surgical intervention.[23,72]

Erşen et al[17] compared the clinical and functional results of 9 patients (11 shoulders) with epileptic seizures causing

anterior shoulder instability who were treated with a Latarjet procedure against those of 53 patients undergoing the same treatment without any underlying neurologic disorders. Although the rate of postoperative recurrent instability was significantly higher in the patients with epilepsy, the functional scores were not significantly different between the groups of patients with epileptic seizures and patients without seizures. The concern about recurrence is also presented by Thon et al[74] and Raiss et al,[57] who report a 33% and 43% rate of recurrent instability, respectively, due to a postoperative seizure. In particular, Thon et al warned that having a seizure in the postoperative period increases the risk of recurrent instability by almost 40 times. More recently Dzidzishvili et al[16] compared 19 epileptic with 21 nonepileptic patients receiving an arthroscopic Latarjet procedure, documenting similar results and no seizure-related postoperative glenohumeral instability; on the other hand, a larger prospective cohort presented by Makaram et al[42] identified epilepsy as a risk factor for poorer results even after open Latarjet procedures.

On the other hand, Kather et al[33] described a multicenter series of 73 patients treated with an open Latarjet procedure after anterior instability following tramadol-induced seizures. Here, an excellent satisfaction rate was reported, as well as a low rate of seizure relapse after tramadol discontinuation (9%). These findings, which differ markedly from those reported in epilepsy patients, confirm that applying the appropriate therapy minimizes the risk of recurrent seizures while also improving surgical results. Nevertheless, comparing this special subgroup of seizure patients with epilepsy patients must be interpreted with care.

Raiss et al[57] and Thangarajah et al[73] also presented data on the long-term consequences of seizure-related shoulder instability in terms of osteoarthritic changes of the glenohumeral joint. These were observed in 57% of the shoulders analyzed by Raiss et al after a mean follow-up time of 8.3 years, and in 45% of those analyzed by Thangarajah et al after a mean follow-up time of 12 years. In the latter publication,[73] arthroplasty or arthrodesis were reportedly required as additional surgery in 10 cases.

In summary, multidisciplinary treatment of patients with shoulder injuries is absolutely necessary for minimizing the risk of recurrent seizures in the recovery phase. Antiepileptic drug therapy should be reconsidered and adapted, if necessary. Even mild side effects of the AED therapy should be tolerated to allow for best recovery, at least in the postoperative phase. In patients with pharmacoresistant epilepsy, the therapeutic concept of shoulder injuries should include the potential risk of recurring seizures. An extension of the indication to bone block procedures for this particular subgroup of patients is considered advisable to reduce the recurrence rate after instability treatment.

This study has a number of limitations. First, the investigated cohort is heterogeneous and includes patients with different lesion characteristics undergoing different treatments; this makes on one hand grouping extremely difficult, but on the other, it enabled us to obtain a broad overview of the clinical results obtained in patients with different seizure-related shoulder injuries. The results obtained suggest a shift in the focus of the clinician treating these patients from technical details to more generalized aspects afflicting many patients with epilepsy. Second, no comparison with a matched cohort of nonepileptic patients was performed; instead, categorization according to presence and features of selected specific lesions (such as PHFD) was possible thanks to the large number of included patients, permitting within-group comparisons. This allowed for the first time to define specific subgroups of patients at risk of obtaining unsatisfactory results. It should however be noted that having the power analysis only been performed for the primary study goal, secondary study results should be considered as preliminary and requiring further verification with a dedicated sample size calculation.

Conclusion

Patients with seizure-related shoulder injuries reported only moderate clinical results at their midterm follow-up; these results are substantially inferior to those reported in high-quality trials not restricted to patients with seizures and do not appear to be significantly affected by the specific lesion characteristics and by the type of performed treatment, suggesting that the underlying neurologic pathology itself is a critical aspect negatively influencing the results. Older age, male sex, and absence or discontinuation of AED treatment were identified as characterizing features of patients with posterior dislocation episodes, which suggests care when planning AED discontinuation on older male epilepsy patients. In patients with PHFD, a tendency to worse clinical results was observed, with posterior PHFD patients emerging as a definite subgroup at risk of reporting unsatisfying results after treatment.

Acknowledgment

The authors thank Karen Wörmann for proofreading the manuscript.

Disclaimers:

Funding: No funding was disclosed by the authors.
Conflicts of interest: Pietro Simone Randelli is a consultant for Arthrex, DePuy, Microport, and Medacta;

these activities were not related to the current study. Rainer Surges has received fees as speaker or consultant from Bial, Desitin, Eisai, LivaNova, Novartis, and UCB Pharma; these activities were not related to the current study. The other authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jse.2023.09.023.

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