

Is poststroke complex regional pain syndrome the combination of shoulder pain and soft tissue injury of the wrist?

A prospective observational study: STROBE of ultrasonographic findings in complex regional pain syndrome

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Abstract

Patients with poststroke complex regional pain syndrome (CRPS) show different symptoms compared to other types of CRPS, as they usually complain of shoulder and wrist pain with the elbow relatively spared. It is thus also known by the term “shoulder-hand syndrome.”

The aim of this study is to present a possible pathophysiology of poststroke CRPS through ultrasonographic observation of the affected wrist before and after steroid injection at the extensor digitorum communis (EDC) tendon in patients suspected with poststroke CRPS.

Prospective evaluation and observation, the STROBE guideline checklist was used.

Twenty-three patients diagnosed as poststroke CRPS in accordance to clinical criteria were enrolled. They had a Three Phase Bone Scan (TPBS) done and the cross-sectional area (CSA) of EDC tendon was measured by using ultrasonography. They were then injected with steroid at the EDC tendon. The CSA of EDC tendon, visual analogue scale (VAS), and degree of swelling of the wrist were followed up 1 week after the injection.

TPBS was interpreted as normal for 4 patients, suspected CRPS for 10 patients, and CRPS for 9 patients. Ultrasonographic findings of the affected wrist included swelling of the EDC tendon. After the injection of steroid to the wrist, CSA and swelling of the affected wrist compared to that before the treatment was significantly decreased ($P < 0.001$). The VAS score declined significantly after the injection ($P < 0.001$).

Our results suggest that the pathophysiology of poststroke CRPS might be the combination of frozen shoulder or rotator cuff tear of shoulder and soft tissue injury of the wrist caused by the hemiplegic nature of patients with stroke.

Abbreviations: CRPS = complex regional pain syndrome, CSA = cross-sectional area, EDC = extensor digitorum communis, IASP = International Association for the Study of Pain, ROM = range of motion, TPBS = 3 phase bone scan, VAS = visual analogue scale.

Keywords: complex regional pain syndrome, rotator cuff, soft tissue injury, stroke

1. Introduction

Stroke is a common nontraumatic brain injury caused by rupture or occlusion of cerebrovascular structures. Such injuries result in sudden neurologic disabilities, such as motor and sensory deficit,

cognitive or language impairment, or even coma in severe cases.^[1,2] Complications after stroke vary among patients and can include neurological complications such as recurrent stroke and epileptic seizure, infections of the upper respiratory tract.

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Authorship: YWK and HSK had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. HSK and JSH designed the study protocol. YK and JMK managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. HSL provided statistical working.

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Sequelae of immobility may also result in the development of pressure ulcer and fall injuries, thromboembolism, pain of the shoulders, and psychological sequelae such as depression, emotionalism, anxiety, and confusion.^[3–6]

Pain of the affected upper extremity is one of the most common complications in patients with stroke.^[7,8] Adhesive capsulitis, rotator cuff injury, and complex regional pain syndrome (CRPS) are commonly found etiologies. Of these, immobilization with abnormal positioning may cause adhesive capsulitis and traction injury, and inappropriate passive physiotherapy may cause rotator cuff injuries.^[9,10] However, no definite hypothesis has yet been suggested to explain poststroke CRPS.

Patients with poststroke CRPS usually complain of shoulder and wrist pain with the elbow relatively spared. It is thus also known as by the term “shoulder-hand syndrome.”^[8,11–15] Based on such clinical characteristics, we hypothesized that the main pathophysiology of poststroke CRPS is a combination of shoulder and wrist injuries. This is based on the tendency that in the normal population, CRPS commonly occurs after soft tissue injuries. The aim of this study is to present a possible pathophysiology of poststroke CRPS through ultrasonographic observation of the affected wrist before and after steroid injection at the extensor digitorum communis (EDC) tendon in patients suspected with poststroke CRPS.

2. Patients and methods

2.1. Patients

This study was approved by the institutional review board (su-yon 2012-045), and all the patients wrote informed consent and performed in accordance with the principles set forth in the Declaration of Helsinki. Twenty-three participants who had shoulder and wrist pain suggesting CRPS were recruited from March 2014 to June 2015 (Fig. 1). A clinical assessment protocol, 3 phase bone scan (TPBS), and ultrasonography were used to evaluate and diagnose CRPS. Patients who fulfilled the CRPS protocol revised at International Association for the Study of Pain (IASP) in 2003 were diagnosed as poststroke CRPS, with exception with those who were not able to follow the diagnostic protocol because of aphasia or severe neglect. Such patients were clinically diagnosed with poststroke CRPS when even a very light touch or simple passive range of

motion (ROM) movement of the wrist joint provoked pain manifested by facial expressions of agony or yelling, suggesting allodynia.

The exclusion criteria were: brain lesions involving the thalamus, steroid injection within 1 month, history of sympathetic blockade, and refusal by the patient.

Considering the improvement of therapy if CRPS scores reduced by ≥ 2 , 5 patients have the 98% power of test, using the 5% level of significance. However, we collected more patients for parametric statistics.^[16]

2.2. Measures

Shoulder flexion, abduction, extension, and external rotation ROM were measured, and manual muscle test of the shoulder and degree of shoulder pain based on the visual analogue scale (VAS) was taken before injection. VAS was collected from only 10 patients who had aphasia, poor cooperation, and severe neglect. Shoulder subluxation was confirmed via physical examination and shoulder X-ray evaluation.

2.3. Three-phase bone scintigraphy

TPBS was performed after clinical diagnosis of poststroke CRPS. All TPBS was performed using 99mTechnetium labeled methylene diphosphonate (99mTc-MDP) and a dual-head γ camera (E.CAM.; Simens, Germany), (Millennium VG; GE, WI) equipped with a low-energy high resolution collimator. To avoid any reactive hyperemia from the injection, patients were injected at the dorsal vein of the foot. After the intravenous bolus injection of 740 MBq of 99mTc-MDP, dynamic perfusion images of both hands and arms were obtained in every 8 seconds for 128 seconds, which is phase I. Subsequently, 500,000 count blood pool images were obtained 3 to 5 minutes after injection, which is phase II. Finally, the delayed bone images of the whole body as well as regional views of both hands were taken 3 hours after injection, which is phase III. Pattern analysis was conducted by comparing degrees of radiotracer uptake in affected extremities with contralateral extremities. A specialist in nuclear medicines (KSJ) with 18 years of clinical experience in nuclear medicine blinded to the clinical information of the participants confirmed findings of TPBS. The TPBS diagnostic criteria for CRPS were as follows: concordance between phase I and II findings, in terms of increased or decreased uptake; and increased uptake in the affected extremity on phase III. Case with no definite increased uptake was considered as suspected CRPS (Fig. 2).

2.4. Ultrasonography and intervention

Ultrasonography was also performed after clinical diagnosis of poststroke CRPS. A board-certified physiatrist (KHS) with 7 years of musculoskeletal ultrasonographic experience performed ultrasonographic studies for the evaluation of wrist pain and swelling by utilizing 5 to 12 MHz (Voluson i; GE, WI) linear array transducer.

The patients were asked to sit with the forearm pronated and a shallow pillow was placed underneath the wrist during the sonographic examination. The cross-sectional area (CSA) of both EDC tendon sheaths were measured at the distal level of the ulnar styloid process and calculated directly by continuous tracing of the boundaries along the echogenic boundary (Fig. 3). The 1 mL of 40 mg triamcinolone was injected at the tendon sheath of EDC using sterile techniques.

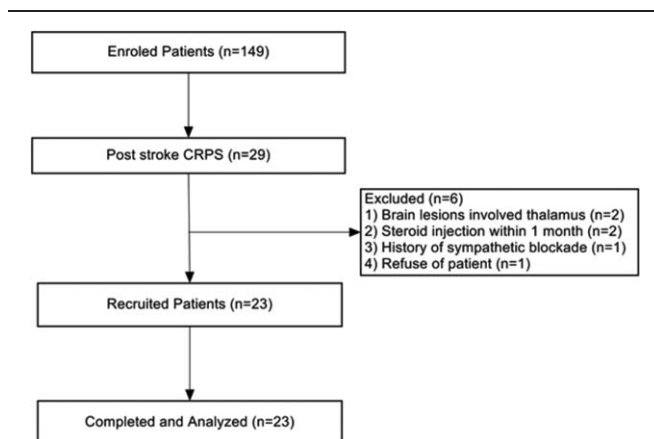


Figure 1. Flowchart describing study sample, complex regional pain syndrome (CRPS).

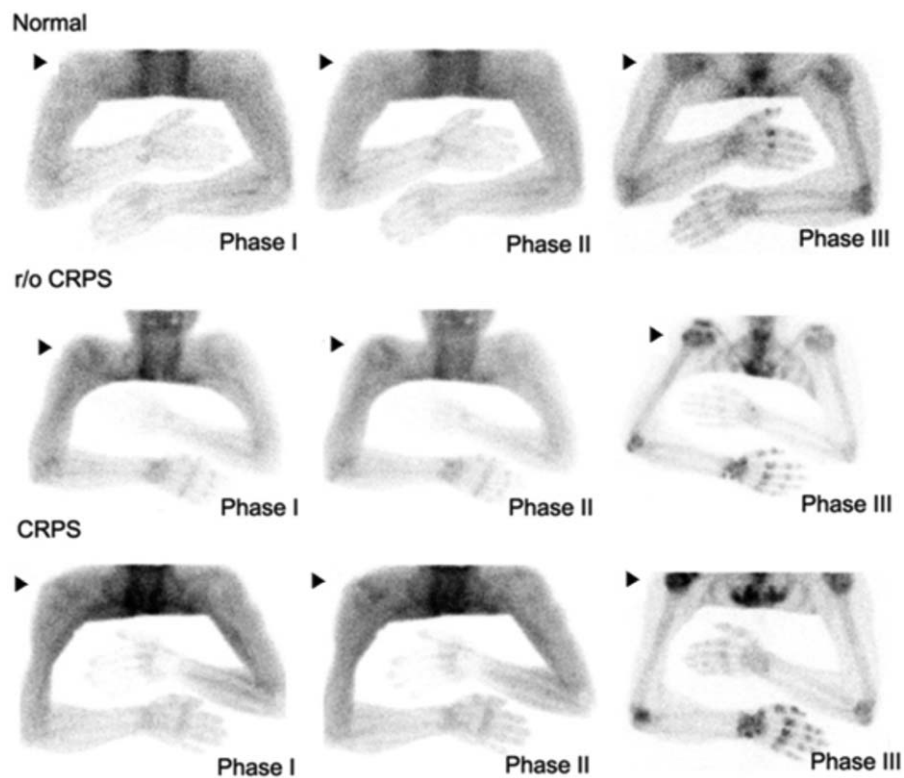


Figure 2. Three phase bone scan findings of the poststroke complex regional pain syndrome, which are interpreted as normal, rule out CRPS, and complex regional pain syndrome (CRPS). The arrow heads refer to affected side.

2.5. Follow-up study

One week after injection, the CSA of both EDC tendon sheaths, VAS, and the degree of swelling of the wrist were followed up (Fig. 4). The CSA of both EDC tendon sheaths were performed by another board-certified physiatrist (HJS) with 2 years of musculoskeletal ultrasonographic experience. The degrees of swelling of the wrists were identified by either the patient or their caregiver before and after injection, and are classified into 6 categories – 0: aggravated, 1: no interval change, 2: minimal decline, 3: moderate decline, 4: maximal decline, and 5: complete decline.

2.6. Statistical analysis

Wilcoxon signed rank tests were performed to measure the association of comparison of the CSA of the EDC tendon sheaths and VAS of pain before versus after injection. All values are mean ±SD. Mann–Whitney *U* test was also performed to determine

whether the swelling of the affected wrist had declined or not. The value is median (minimum, maximum). Interrater correlation coefficient was obtained by comparison of the CSA of sound EDC tendon measured by KHS and HJS respectively before and after injection. The correlation coefficient over 0.7 is considered as the good correlation, the correlation coefficient between 0.3 and 0.7 considered as the moderate correlation and the correlation under 0.3 considered as the poor correlation. Data were analyzed using SAS 9.2 software (SAS Institute, Cary, NC).

3. Results

A total of 23 patients met the inclusion criteria. The mean age was 64.4 years and among the 23 patients, 12 were female (Table 1). Fifteen patients were right sided hemiplegic and the others were left sided hemiplegic. Radiologic evaluation (CT, MRI) revealed infarctions in 11 and hemorrhage in 12. Fifteen patients suffered

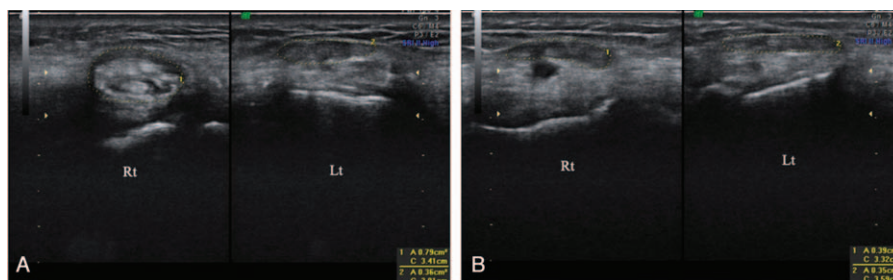


Figure 3. Ultrasonographic findings of the affected wrist of the poststroke complex regional pain syndrome, right of 66 year-old male patient with stroke. Swelling of the extensor digitorum communis tendon (cross-sectional area=0.79 cm²) is noted before injection, which is decreased 1 week after steroid injection (cross-sectional area=0.39 cm²). (A) Ultrasonography before injection, (B) ultrasonography 1 week after injection.

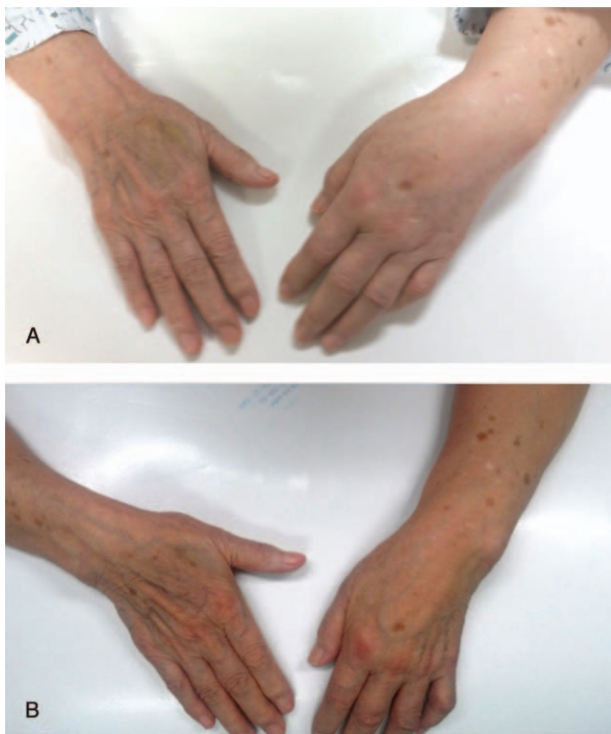


Figure 4. Ultrasonographic findings of the affected wrist of the poststroke complex regional pain syndrome, left of 76-year-old female patient with stroke. After injection, swelling at the dorsum of wrist and joints of hand declined, showing clearer crease of hand. Also, vein contour at the dorsum of hand is noted after the injection. (A) Before injection, (B) after injection.

from shoulder subluxation of the affected side and all patients complained of shoulder pain or frowned during passive abduction of the affected shoulder. The mean time from disease onset to TPBS examination was 90 days, ranging from 28 to 536 days. The official readings of the TPBS were normal in 4, probable CRPS in 10, and definite CRPS in 9. Only 3 patients showed spasticity at the elbow of the affected side. Preinjection VAS score was checked in only 10 patients, since the others were not able to answer properly due to aphasia or severe neglect.

All of the 23 patients underwent ultrasonographic evaluation, revealing swelling of EDC tendon of the affected wrist. After wrist injection, there was a significant decrease of CSA and swelling of the affected wrist compared with those before the treatment (Table 2), while the CSA of the sound wrist had no significant change even after the alteration of the observer (Table 2). The interrater correlation coefficient was 0.526, a moderate correlation. After steroid injection, swelling of the affected wrist and the VAS score declined significantly (Tables 3 and 4). No complaints and side effects were reported during and after the intervention in all patients.

4. Discussion

Claude Bernard first mentioned a condition associated with pain and the sympathetic nervous system in 1851, and is considered to be the first published description of CRPS. After Claude Bernard, various nomenclatures have been used to describe what is now known as CRPS.^[17] Lack of official consensus of CRPS had led to unorganized diagnosis and treatment in clinical setting. Finally in 1994, an internationally accepted diagnostic criteria of CRPS was determined under the consensus of the IASP.^[18] According to the

Table 1

Demographics and clinical characteristics of study population (n=23).

Patient	Age	Gender	3 Phase bone scan finding	CSA of EDC, Cm ²				VAS		Decline of swelling*
				Preinjection		Postinjection		Preinjection	Postinjection	
1	66	F	r/o CRPS	0.24	0.62	0.27	0.41	Aphasia		3
2	72	M	CRPS	0.29	0.45	0.29	0.39	Severe neglect		3
3	62	M	r/o CRPS	0.22	0.52	0.35	0.49	6	3	2
4	66	M	Normal	0.36	0.79	0.35	0.39	7	2	3
5	67	M	Normal	0.30	0.45	0.32	0.30	8	0	2
6	70	F	Normal	0.44	0.65	0.45	0.43	8	3	3
7	58	M	r/o CRPS	0.23	0.44	0.26	0.32	Aphasia		3
8	61	F	r/o CRPS	0.25	0.26	0.24	0.25	Aphasia		3
9	65	F	CRPS	0.21	0.43	0.28	0.30	Severe neglect		3
10	76	F	CRPS	0.27	0.47	0.25	0.27	8	5	2
11	48	F	r/o CRPS	0.21	0.34	0.19	0.20	7	3	3
12	79	M	r/o CRPS	0.29	0.49	0.27	0.31	Aphasia		2
13	53	F	CRPS	0.47	0.71	0.34	0.39	Aphasia		2
14	55	M	CRPS	0.22	0.35	0.18	0.27	5	1	4
15	68	M	CRPS	0.28	0.42	0.33	0.43	10	5	2
16	74	F	r/o CRPS	0.38	0.41	0.32	0.29	Aphasia		3
17	62	M	CRPS	0.23	0.43	0.22	0.31	Aphasia		3
18	76	M	r/o CRPS	0.24	0.34	0.24	0.28	Poor cognition		2
19	50	F	CRPS	0.31	0.68	0.30	0.46	Aphasia		3
20	72	M	Normal	0.24	0.41	0.28	0.32	6	2	2
21	61	F	CRPS	0.25	0.60	0.23	0.38	5	1	3
22	63	F	r/o CRPS	0.24	0.42	0.20	0.24	Aphasia		3
23	58	F	r/o CRPS	0.28	0.59	0.24	0.23	Aphasia		3

CRPS=complex regional pain syndrome, CSA=cross-sectional area, EDC=extensor digitorum communis, VAS=visual analogue scale.

* 0: aggravation, 1: no interval change, 2: minimal decline, 3: moderate decline, 4: maximal decline, and 5: complete decline.

Table 2
Comparison of the crossed-sectional area of the sound and affected wrist (n=23).

Side	Variables	Mean ± SD, cm ²	P
Sound	Before	0.28 ± 0.07	0.499
	After	0.27 ± 0.06	
Affected	Before	0.49 ± 0.13	
	After	0.33 ± 0.08	

SD=standard deviation.

IASP criteria, CRPS is diagnosed when at least 1 sign or symptom is reported in at least 3 of the following categories: sensory (hyperesthesia, allodynia), vasomotor (temperature asymmetry, skin color changes, skin color symmetry), sudomotor/edema (edema, sweating changes, sweating asymmetry), or motor/trophic (decreased ROM, motor dysfunction, trophic changes). Advent of the IASP criteria has led CRPS studies to be more objective than before.^[18] Still, the IASP criteria are quite subjective and often do not match the clinical diagnosis of poststroke CRPS. As a supportive tool for the precise diagnosis of poststroke CRPS, TPBS has been widely used.^[19,20]

Poststroke CRPS has several different traits compared to conventional CRPS. First, one of the most distinctive clinical characteristics of poststroke CRPS is that shoulder and wrist pain occurs simultaneously with the elbow joint relatively spared. For this reason, poststroke CRPS is also known as the “shoulder-hand syndrome.”^[8,11–15] From an anatomical point of view, the shoulder and wrist consists of an unstable ball-and-socket joint supported by many muscles. On the other hand, the elbow is a stable hinge joint that is sufficiently stabilized by bony structure.^[21–23] To be specific, the possibility of double primary lesions of unstable shoulder and wrist rises in hemiplegia patients with decreased muscle tone. According to the study of Ward, approximately 75% of hemiplegia patients suffer shoulder pain within 1 year of disability onset.^[24,25] In this study, wrists of poststroke CRPS patients diagnosed with the IASP criteria were evaluated via ultrasonography, revealing EDC swelling in all patients. Involvement of the EDC may be explained by the fact that since the EDC tendon is the biggest tendon among the wrist extensors, it can easily be injured or detected.^[26] After steroid injection, pain and swelling of the affected wrist decreased significantly.

Second, the TPBS of poststroke CRPS showed distinctive results compared to conventional CRPS. After tracer injection, TPBS shows tracer uptake at 3 different time points. Phases 1 and 2 are presented right after tracer injection, showing the perfusion and blood pooling in the limb, respectively, while phase 3, which is obtained 2 to 3 hours after injection, represents the latent image after washout of the tracer. When bone turnover is increased in conditions such as osteomyelitis, remnant tracer is noted in the phase 3 image.^[27] In case of hemiplegia, decreased muscle tone of the affected side causes insufficient blood circulation, which will result in an increased blood pooling compared to the unaffected

Table 3
Decline of swelling of the affected wrist (n=23).

Side	Mean (95% CI)	P
Affected	2.696 (2.454, 2.937)*	<0.001

CI=confidence interval.

*Decline of swelling of the affected wrist; 0: aggravation, 1: no interval change, 2: minimal decline, 3: moderate decline, 4: maximal decline, and 5: complete decline.

Table 4
Visual analogue scale (VAS) score of the affected wrist (n=10).

Side	Median (min, max)	P
Affected	Before	<0.001
	After	

side in phase 2. Increased uptake of tracer in phase 3 can take place when blood pooling is increased due to inflammation in muscles such as EDC. In this study, all patients underwent TPBS study, where there were normal findings in 4 patients, suspected CRPS in 10 patients, and definite CRPS in 9 patients. Furthermore, the uptake of tracer is noted mainly in the affected wrist during the phase 3, but not in the affected painful shoulder in poststroke CRPS patients. If the affected shoulder and wrist share the same pathophysiology, the TPBS must show the same findings in each joint.

Our results and TPBS findings suggest that poststroke CRPS may be the result of the double primary lesion in each site: adhesive capsulitis or rotator cuff injury of the shoulder and soft tissue injury around the wrist. Degenerative changes before stroke, traction injury caused by muscle weakness, and passive ROM exercise-induced injury after stroke are expected to be the cause of such injury.^[28] There are also some limitations. First, the small sample size limits the interpretation of the results and limits generalization to other populations. Second, absence of a control group in this study confines logical value and statistical power. Furthermore, due to the moderate correlation of interrater reliability of ultrasonographic finding (ICC=0.526), observer bias is likely to influence the results. Inaccuracy of understanding patient expression due to aphasia and neglect can lead to underestimation of the severity of pain in stroke patients, ultimately limiting proper diagnosis, evaluation, and treatment of poststroke CRPS. Further studies with larger sample size and control group are necessary to better understand the pathophysiology of poststroke CRPS and net clinical effect of steroid injection in such patients. There are several strengths in our study, including the originality of the study by utilizing ultrasonography and statistically significant proof of the therapeutic effectiveness of steroid injection in poststroke CRPS. In conclusion, in this study of stroke patients presenting shoulder and wrist pain, TPBS and the conventional diagnostic tool for CRPS showed diverse results while ultrasonography showed EDC swelling. Steroid injection at EDC significantly improved the clinical outcome of these patients. Our results suggest that the pathophysiology of poststroke CRPS might be a combination of adhesive capsulitis or rotator cuff tear of the shoulder with soft tissue injury of the wrist caused by the hemiplegic nature of patients with stroke.

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