

# Long-term follow-up of Dupuytren disease after injection of triamcinolone acetonide in Chinese patients in Taiwan

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## Abstract

Injection of triamcinolone acetonide is a non-operative treatment for early-stage Dupuytren disease in Caucasians, but its effectiveness in non-Caucasians is unclear. We report averaged 5-year follow-up results of 37 patients (49 affected hands) with early-stage Dupuytren disease for patients in Taiwan (non-Caucasian) who received a single dose of 5 mg triamcinolone acetonide injection into nodules monthly for 3 months. Using ultrasound, we recorded no progression of sizes of the modules following injection after 6 months. After an average 5-year follow-up, two patients with three hands (6%) experienced reactivation of the treated nodules. None required surgical intervention. Ultrasound examination showed that sizes of the treated Dupuytren nodules decreased significantly by 40% 6 months after injection and 56% at the final follow-up. We conclude that in these Chinese patients in Taiwan with early Dupuytren nodules, triamcinolone acetonide injection was effective in reducing the size of the Dupuytren nodules and maintaining long-term durable control of the nodular growth.

**Level of evidence:** III

## Keywords

Dupuytren's disease, triamcinolone acetonide, ultrasound, ethnicity

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## Introduction

Various non-operative treatments, including external beam radiation, vitamin E, local injection, ultrasound and physical therapy have been used for early-stage Dupuytren disease (Davis, 2015; Keilholz et al., 1996; Markham and Wood, 1980; Meek et al., 2002; Pentland and Anderson, 1985; Pittet et al., 1994; Rayan, 2008). Compared with surgical intervention, these non-operative treatments have lower incidences of morbidity and complications (Boyer and Gelberman, 1999). Intralesional injections with various pharmaceutical agents have been investigated in both preclinical and clinical studies (Rayan, 2008). Direct injection of corticosteroids into Dupuytren nodules has also been used, but with only modest success (Davis, 2015; Ketchum and Donahue, 2000; Pentland and Anderson, 1985).

Ketchum and Donahue (2000) proposed intralesional injections of triamcinolone acetonide as an antifibrotic agent for reducing and softening Dupuytren nodules. Their study showed short-term

success in suppressing the disease in Caucasian patients with Dupuytren nodules following intralesional triamcinolone acetonide injection, but the reactivation incidence approached 50%; complications related to injection, including dermal atrophy, skin depigmentation and tendon rupture, were reported.

We conducted a study to evaluate the suppression and reactivation rate of Dupuytren nodules after

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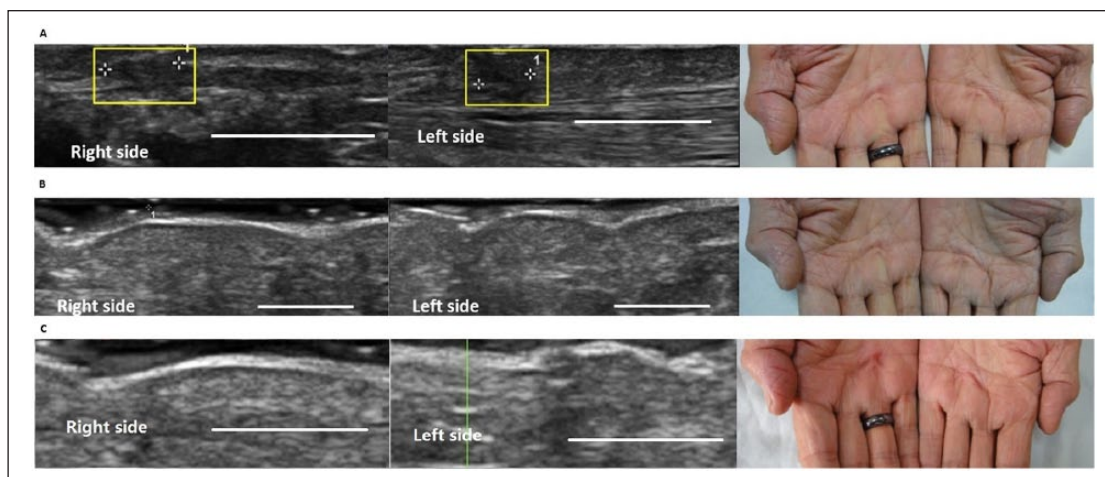
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**Figure 1.** Serial sonograms and photos of a 78-year-old man with bilateral involvement of Dupuytren disease. (A) Pre-injection visit: the size of nodule on the right hand = 3 mm; the size of nodule on the left hand = 4 mm. (B) Six-month post-injection visit: no detectable nodule on ultrasound examination was noted. (C) Last follow-up visit: no detectable nodule on ultrasound examination was noted. Bars on sonogram = 10 mm.

steroid injection in ethnic Chinese. The objectives of this study were to evaluate the efficacy of reducing the size of treated nodules using ultrasound measurement and to evaluate long-term control of treated nodule in Chinese patients with Dupuytren nodules.

## Materials and methods

### *Patient inclusion*

This was a single institution prospective study, which included patients with diagnosis of early-stage Dupuytren disease treated between 2009 and 2013. Those included were in stable medical condition and with at least one non-treated Dupuytren nodule without digital flexion contracture. Patients with a minimal cord, which was palpable and less than 10 mm in length, and nearby the nodule without presentation of a flexion contracture were also included. Exclusion criteria included patients whose Dupuytren nodules had been treated surgically or non-surgically; all patients with digital flexion contractures, recent cerebrovascular accidents, bleeding disorders, anticoagulation medication in previous 7 days, allergy to triamcinolone acetonide or steroid-related medication; or patients with chronic neurologic, muscular or neuromuscular disorder affecting upper extremities. This study was approved by the institutional review board of the authors' hospital.

### *Method of injection and assessments during follow-up*

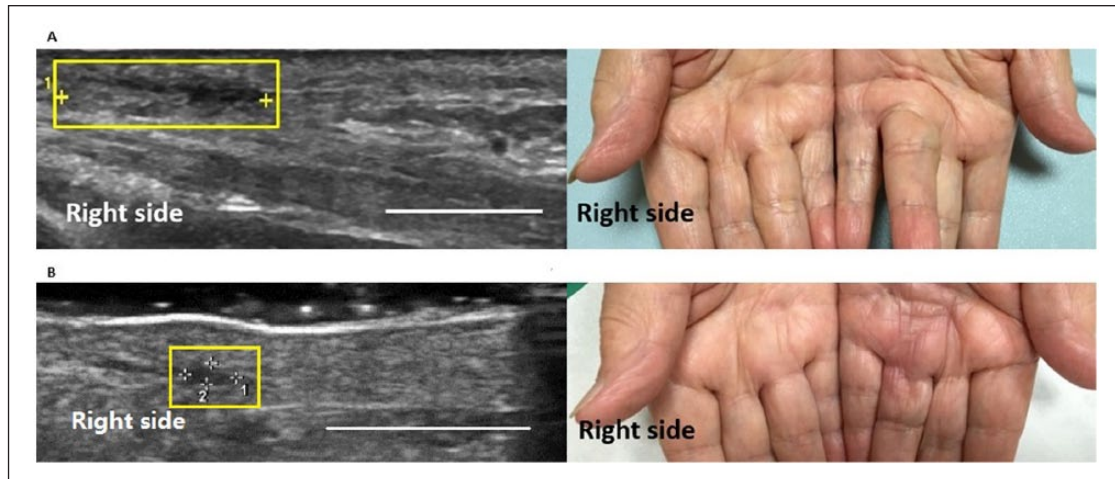
Triamcinolone acetonide (Yung Shin, Shincort suspension for injection 10 mg/ml 5 ml, Taichung,

Taiwan) was directly injected into nodules in a single dose of 5 mg once a month for 3 months. This method is modified from the method of Ketchum and Donahue (2000). For multiple nodules in a single affected hand, each nodule was injected separately with the same dosage of triamcinolone acetonide described above. Injection was performed by a single experienced hand surgeon specialist (Tang, 2009; Tang and Giddins, 2016).

All the patients were followed with clinical visits and ultrasound examinations. Quantitative measurement of nodule reduction was determined via ultrasound by a single radiologist. The maximal diameters of the nodules were measured in the sonogram before injection, at the 6-month post-injection follow-up visit, and then annually (Figures 1 and 2). We took photographs of the nodules during each visit for qualitative measurement. We judged whether or not the nodule reactivated from serial ultrasound examinations. Reactivation was defined as no increase in size of Dupuytren nodule at 6-month follow-up, but increasing at subsequent follow-up evaluation as compared with that before injection.

### *Statistical analysis*

The change of diameter of Dupuytren nodule at each time was reported using means with standard deviations. The paired Wilcoxon signed ranks test was used to compare the extent of reduction of the treated nodules between 6-month post-injection and at the last follow-up visit. A level of significance was set at a  $p$  value less than 0.05.



**Figure 2.** Serial sonograms and photos for 78-year-old woman with bilateral involvement of Dupuytren disease with different stages. (A) Pre-injection visit: the size of nodule on the right hand = 13 mm. There is a flexion contracture on the left ring finger. (B) Last follow-up visit: the size of nodule on the right hand = 4 mm. She received open fasciotomy for the left ring finger. Bars on sonogram = 10 mm.

## Results

This study initially included 48 patients who meet the inclusion criteria from 2009 to 2013. All patients had early-stage Dupuytren disease. In the average 5-year follow-up period, 11 patients were lost to follow-up. Two patients had passed away, two patients could not complete ultrasound due to poor physical condition following cerebral vascular accidents, three patients could not be contacted and four patients did not return for follow-up since they felt they had gotten complete resolution of the nodules.

Therefore, 37 patients (49 affected hands) completed the follow-up. Their average age was 72 years (ranged 49 to 84). There were 28 men and nine women. The length of follow-up was from 36 to 84 months, with an average of 5 years. The follow-up data from all 49 affected hands of these 37 patients were used in the statistical analysis reported below.

### *Changes in sizes of Dupuytren nodule*

From the ultrasound measurement, the average size of the nodules was 9 mm before the injection, 5 mm at 6-month follow-up and 3 mm at the final follow-up. The average size reduction of treated nodules at 6-month follow-up was 40% (SD 19%), and the average size reduction at the final follow-up was 56% (SD 27%). The size reduction of the nodule from pre-injection to 6-month post-injection and to the final follow-up visit were statistically significant ( $p < 0.05$  for both comparisons). We observed decreases in the sizes of the nodules by ultrasound and no progression in the cord with photograph during annual follow-up in some hands. Three hands (in two patients)

(6%) had reactivation of the treated nodules; they received three additional intralesional steroid injections with a dose of 5 mg at monthly intervals, and no further size progression of the treated nodule was noted after the additional injection for 3 months.

### *Complications*

We identified no complications. No patients had atrophy or depigmentation of skin or rupture of flexor tendons. Tenderness was reported by all patients over the injection site for the first 48 hours. Transient erythema over the injection site was present in six patients and resolved in 72 hours. Most patients were satisfied with reduction of the nodules and they expressed high willingness to receive intralesional injection if their Dupuytren nodule should enlarge.

## Discussion

Our study demonstrated that intralesional injection of triamcinolone acetonide into the nodule of Dupuytren disease is safe and effective treatment in reducing Dupuytren nodule size in a non-Caucasian population. Ultrasound evaluation can monitor the progress and confirm the responses of treated Dupuytren nodule. From literature review, collagenase can dissolve the fibrous cords in the nodules (French et al., 1987; Scherman et al., 2016; Starkweather et al., 1996; Warwick et al., 2016; Watt et al., 2010, Zhao et al., 2016), and the nodules can be inhibited by steroid (Ketchum and Donahue, 2000). In our study, we included patients with minimal cord (less than 10 mm without contracture); while the

nodules were reduced, the minimal cord was not altered and did not progress to contracture. Our result supports that the nodules can be reduced, but the nearby faint cord is not favourably or adversely affected by the steroid injection.

We noted several differences compared with the study by Ketchum and Donahue (2000). The average age of the patients (72 years) in our study was older than that in the study by Ketchum and Donahue (55 years). The male–female ratio of our study (28 men and nine women) was higher than that of the study by Ketchum and Donahue (38 men and 25 women). The dosage of triamcinolone acetonide in our study (5 mg for 3-monthly injections) was lower than that used in the study by Ketchum and Donahue (80 to 120 mg per injection with an average of 3.2 total injections). Nevertheless, the patients included in our study had medical comorbidities, and the trend of incidence for the male–female ratio was similar to an epidemiology study in ethnic Chinese population by Yeh et al. (2015). We considered that the patients in our study represented typical patients with Dupuytren disease among ethnic Chinese. We acknowledged that multiple other variables might contribute to this difference.

One strength of our study was measuring the response of the treated Dupuytren nodules using ultrasound. Ultrasound evaluation is convenient and provides objective findings for differential diagnosis of pathologies involving the palmar surface of the hand and measurement of Dupuytren nodules. To avoid intraobserver variability, a single radiologist performed all ultrasound examinations and measurements. Ultrasound is also useful as a guide for repeated injection if the nodule enlarged or recurred during follow-up. We determined the response of Dupuytren nodule following injection by clinical examination and ultrasound evaluation rather than by published scores or classification used for advanced stage Dupuytren disease (Akhavani et al., 2015; Rodrigues et al., 2016).

Limitations of our study include that 11 patients (15 affected hands) were lost to follow-up. The size of the Dupuytren nodule measured and recorded was the maximal diameter of the nodule rather than its volume. However, since two-dimensional measurement is commonly used clinically and response evaluation for solid tumours also uses maximal diameter of tumour lesion in an axial plane (Eisenhauer et al., 2009), we considered our quantitative measurement to be acceptable and reliable. Another limitation was that this was a prospective study of a cohort of patients with early Dupuytren nodules. While a prospective study with a control group would further elucidate effectiveness of steroids injection, it requires a

larger sample size and accrual time, which will be difficult for this relatively uncommon condition in our non-Caucasian population.

We conclude that intralesional steroid injections for early-stage Dupuytren disease not only reduced the size of nodules, but also arrested progression for long-term control. In addition, the reactivation incidence was low in our study. Given its promising results in ethnic Chinese, routine use of intralesional steroid injection in ethnic Chinese or East Asians should be considered as an excellent non-surgical treatment option.

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**Ethical approval** The study protocol and written informed consent forms were approved by the Institutional Ethics Committee/Institutional Review Board of Taipei Veterans General Hospital, Taiwan.

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