SCIENTIFIC ARTICLE

Steroid Injection and Needle Aponeurotomy for Dupuytren Disease: Long-Term Follow-Up of a Randomized Controlled Trial

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Purpose To compare long-term outcomes and retreatment rates for patients with Dupuytren disease who underwent needle aponeurotomy (NA) combined with a series of triamcinolone acetonide injections or underwent NA alone as part of a prior randomized controlled trial.

Methods During this follow-up study, 44 of 47 participants in the original study were examined as needed between 6 and 53 months from their initial procedure. Those who had not been reassessed within 18 months of the original NA were asked to return for follow-up. The average total active extension deficit (TAED) of previously treated joints was compared between groups 7 to 12, 13 to 24, 25 to 36, and 37 to 48 months following treatment. Timing of retreatment (if performed) was recorded.

Results Forty-four participants returned for assessment an average of 4.8 times over 53 months. Mean TAED was significantly less in needle aponeurotomy triamcinolone injection patients at 6 months and between 13 and 24 months. Sixty-two percent of NA group patients and 30% of needle aponeurotomy triamcinolone injection patients returned for a second treatment on the same digit(s) (retreatment). This difference was not significant. Mean time to retreatment and mean TAED immediately prior to retreatment did not differ significantly between groups. Kaplan-Meier survival estimates demonstrated a significantly higher percentage of NA group patients expected to return for retreatment by 24 but not by 36 months. Younger age, more than one joint treated at the initial NA, and TAED severity throughout the follow-up period were associated with earlier retreatment.

Conclusions Serial triamcinolone injections combined with NA was associated with lower TAED for up to 24 months. A larger study would more accurately quantify the potential benefits of combining triamcinolone injections with NA for treatment of Dupuytren disease. *(J Hand Surg Am. 2014;39(10):1942–1947. Copyright © 2014 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Therapeutic III.

Key words Dupuytren disease, randomized controlled trial, needle aponeurotomy, triamcinolone acetonide, needle fasciotomy.

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Needle aponeurotomy (NA) is an effective, noninvasive surgical option for patients with Dupuytren disease. Its benefits include rapid recovery and low risk of complications, which include tendon rupture and or laceration, nerve injury, and infection.[1,2] However, with reported recurrence rates ranging from 33% to 100%,[3,4] potential methods to maintain correction of joint contractures require further investigation.

Injections of triamcinolone acetonide have been reported to resolve keloids and hypertrophic scars by 50%.[5] Triamcinolone also modifies disease progression when injected into Dupuytren nodules.[6] In a randomized trial that followed participants for 6 months, we combined a series of triamcinolone injections with NA (NATI group) and compared total active extension deficit (TAED) with that of patients undergoing NA alone.[7] Our data indicated significantly lower TAED in the NATI group at 6 months, warranting follow-up investigation into a potential role for adjuvant triamcinolone injections in patients undergoing NA.

The purpose of the present study was to compare long-term outcomes of the original study groups. Specifically, we aimed to compare TAED of joints treated during the original study measured between 7 and 12 months and during each subsequent 12-month period up to 48 months and to compare the time between the original NA and a second treatment on the same digit(s), if performed.

MATERIALS AND METHODS

Study procedures were approved by the institutional research ethics board. The original study included 47 participants who were randomized to either the NA group or the NATI group using an electronic random number generator. Inclusion criteria consisted of a diagnosis of Dupuytren disease and at least 1 joint contracture of 20° or more.

The detailed procedure used for NA has been published previously.[7] Briefly, under local anesthesia, multiple points along the cord were percutaneously divided using the bevel of a 16-gauge hypodermic needle. The procedure was terminated in all participants when the finger could be passively straightened to a TAED of 0°. Immediately after NA and at 6 weeks and at 3 months, participants in the NATI group received injections of 8 to 48 mg of triamcinolone acetonide (injectable suspension; Sandoz Canada Inc., Boucherville, Quebec) per digit, administered between points of release. Dosage calculations were based on disease severity and published guidelines.[6]

All participants were instructed to follow up as needed after the original study. Patients who had not returned within 18 months were asked to attend a follow-up assessment. The senior author (P.B.) performed all examinations. A goniometer was used to measure TAED of contractures treated during the original study. Participants were not blinded to previous study group assignment.

The timing and details of retreatment, which was patient-driven, were recorded. Study participation ended once a patient received retreatment. The TAED on the day of retreatment was included in data analysis. No measurements of re-treated contractures were included as it would be impossible to attribute group differences to the use of triamcinolone injections after retreatment. Participants who did not return for examination after the original trial were excluded from the follow-up study.

Primary outcome measures included TAED in degrees and length of time between the original procedure and retreatment, if performed. The Fisher exact test was used to detect differences between groups for categorical data and independent *t* tests compared continuous data. Mean TAED was calculated for the time periods of 7 to 12 months, 13 to 24 months, 25 to 36 months, and 37 to 48 months. Measurements beyond 48 months were compared wherever possible. If a participant returned for follow-up more than once during the same 12-month period, only the most recent TAED was used to calculate the group mean for that period.

Kaplan-Meier survival analysis was used to estimate the percentage of participants undergoing retreatment as a function of time. Log rank tests were used to compare the percentage of patients in each group estimated to undergo retreatment within 24 months, 36 months, and 48 months. Treatment group, sex, baseline age (at the time of the original NA), number of digits and joints originally treated, and baseline TAED were considered in a stepwise proportional hazards regression. Follow-up TAED measurements prior to retreatment were included as a time-varying covariate to determine whether TAED throughout the follow-up period was associated with earlier retreatment.

RESULTS

Forty-four of 47 (94%) participants returned for reexamination an average of 4.8 times during the follow-up period, which ranged from 7 to 53 months after the original NA. Three participants in the original sample were lost to follow-up. Table 1 presents

TABLE 1. Baseline Characteristics of the Follow-Up Sample by Study Group

	NA Group (N = 21)	NATI Group (N = 23)	*P* Value
Men, N (%)	17 (81)	22 (96)	.2
Age, years (SD)	60 (10)	61 (8)	.6
Treated digits, N (SD)	1.2 (1)	1.6 (1)	.06
Treated joints, N (SD)	2 (1)	2.5 (1)	.3

baseline (time of enrollment in the original study) characteristics for the follow-up sample.

Table 2 presents a comparison between groups of TAED, mean length and range of follow-up, and the number of participants who returned for retreatment during each 12-month period up to 48 months and from 49 to 53 months. Mean TAED was significantly higher in NA patients than in NATI patients at 6 months and for the period between 13 and 24 months. Mean TAED between groups did not differ significantly during the 25- to 36-month and 37- to 48-month periods. An insufficient number of follow-up assessments were performed between 49 and 53 months to allow for statistical comparison. Figure 1 illustrates mean TAED for each group throughout follow-up beginning at baseline.

Thirteen NA patients and 7 NATI patients returned for retreatment within 53 months of the original NA. All second treatments were performed on one or more of the digits treated during the original study. No new contractures were treated at the same time as retreatment of originally treated digits. Table 3 displays the number of retreatments, mean time to retreatment, mean TAED prior to retreatment, and retreatment procedures performed for each group. Statistically significant differences were not detected when comparing groups based on the number of retreatments performed, mean time to retreatment, and TAED prior to retreatment.

Based on Kaplan-Meier survival estimates for each group, the percentage of NA patients expected to undergo retreatment was greater than that of the NATI group at 12, 24, and 36 months (Fig. 2). This difference was significant only at 24 months ($P = .05$). By approximately 48 months, the groups did not appear to differ. Based on the log rank test, the NA group tended to return for retreatment before the NATI group, but this was not significant ($P = .27$).

Participants in both groups treated initially for 2 or more joint contractures tended to return for retreatment

TABLE 2. TAED, Follow-Up Time, and Retreatment by Study Group

	NA Group	NATI Group	*P* Value
Baseline (N)	21	23	
TAED (SD)	77 (44)	101 (77)	.2
6 months (N)	21	23	
Mean follow-up (SD)	6	6	1.0
TAED (SD)	29 (20)	14 (17)	**.009**
6–12 months (N)	4*	7	
Mean follow-up (SD)	9.5 (3)	11 (2)	.2
TAED (SD)	34 (5)	16 (24)	.4
Retreatment	2	0	
13–24 months (N)	8	12	
Mean follow-up (SD)	19 (5)	18 (5)	0.8
TAED (SD)	70 (31)	27 (25)	**.003**
Retreatment	4	1	
25–36 months (N)	9	8	
Mean follow-up (SD)	32 (4)	30 (4)	.8
TAED (SD)	62 (21)	47 (56)	.45
Retreatment	2	3	
37–48 months (N)	7**	7	
Mean follow-up (SD)	42 (2)	42 (3)	.7
TAED (SD)	63 (33)	52 (75)	.75
Retreatment	4	3	
49–53 months (N)	4	2	
Mean follow-up (SD)	50 (2)	50 (0.3)	n/a
TAED (SD)	52 (26)	34 (33)	n/a
Retreatment	1	0	

Statistically significant *P* values (< .05) are in bold font. Retreatment refers to the number of patients undergoing a second procedure during that time period.
*TAED measurements unavailable for 2 participants.
**TAED measurements unavailable for one participant.

significantly sooner than those with only one affected joint ($P = .02$). Regardless of study group, younger participants (41–59 y) at the time of the original NA tended to return for retreatment significantly sooner than those in older age groups (60–65, 66+) ($P = .04$).

There was no significant difference in time to retreatment between patients who were treated initially for 1 affected digit and patients who were treated for 2 or more affected digits ($P = .5$). Baseline TAED did not have a significant effect on time to retreatment ($P = .14$).

In the stepwise proportional hazards regression analysis, sex could not be used for modeling due to the paucity of women in the sample. Only baseline age

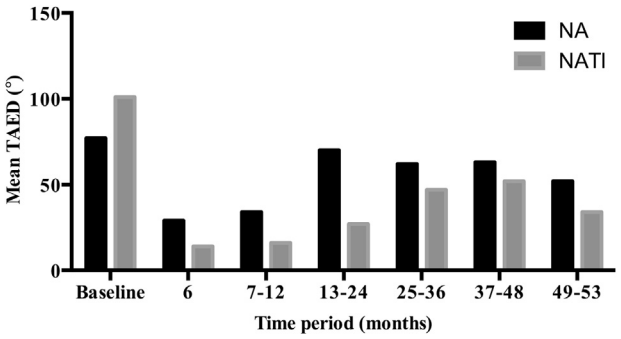

FIGURE 1: Mean TAED for each group throughout follow-up.

TABLE 3. Retreatment Rate, Mean Time to Retreatment, TAED Prior to Retreatment, and Type of Procedure Performed by Study Group

	NA Group (N = 21)	NATI Group (N = 23)	*P* Value
Number of retreatments (%)	13 (62)	7 (30)	.07
Months to retreatment (SD)	29 (14)	34 (9)	.37
TAED prior to retreatment (SD)	84 (21)	104 (56)	.3
Fasciectomy (%)	3 (23)	0 (0)	n/a
PNA (%)	10 (77)	7 (100)	n/a

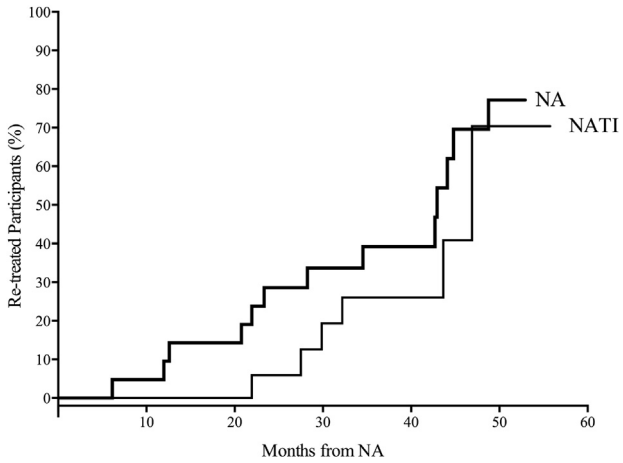

FIGURE 2: Kaplan-Meier survival curves displaying the percentage of patients in each group expected to return for retreatment plotted against months from initial NA.

TABLE 4. Multivariate Survival Summary of Factors Significantly Affecting Time to Retreatment

Variable	Hazard Ratio (95% Confidence Interval)	*P* Value
Baseline age	0.93 (0.89, 0.98)	**.009**
Number of treated joints at baseline	1.53 (1.13, 2.08)	**.006**
Number of TAED assessments since baseline	1.02 (1.01, 1.04)	**< .001**

Note: Statistically significant *P* values (< .05) are in bold font.

and number of joints initially treated were retained in the Cox proportional hazards model. Younger age and multiple affected joints treated at the time of the original NA were significantly associated with earlier retreatment ($P = .009$ and $P = .006$, respectively). When follow-up TAED measurements were included as a time-varying covariate, only younger baseline age and higher follow-up TAED measurements were significantly associated with earlier retreatment ($P = .003$ and $P < .001$, respectively). Hazard ratios, 95% confidence intervals, and *P* values are presented in Table 4. Treatment group, number of digits treated initially, and baseline TAED did not significantly affect time to retreatment.

DISCUSSION

In this study, a series of triamcinolone acetonide injections combined with NA was significantly associated with lower mean TAED than NA alone at 6 months and between 13 and 24 months. Based on Kaplan-Meier survival estimates, the percentage of NATI patients expected to undergo retreatment by 24 months was also significantly lower than that of NA patients. Benefit beyond 24 months remains unclear.

Participants in the NATI group received injections immediately after the original NA and at 6 weeks and 3 months.[7] Ketchum et al[6] found that 50% of patients who received a series of triamcinolone injections into Dupuytren nodules experienced disease reactivation 1 to 3 years after the last injection. Based on our comparisons of mean TAED and retreatment rates, triamcinolone injections appeared to provide benefit for a similar length of time. This is also supported by our data beyond 24 months, which showed that groups no longer differed significantly in terms of follow-up TAED or the percentage of participants expected to undergo retreatment. It is possible that any protective effects associated with triamcinolone injections were limited to approximately 18 months after the last injection, which was 6 months after the original NA. We summarized mean follow-up TAED

measurements into 12-month periods, which were then compared between groups. Although this method allows for statistical comparison in a limited sample, it lacks precision in that participants assessed during the same 12-month period were potentially measured months apart from each other. Consistent re-evaluation of every participant at predefined time points would have provided a more complete follow-up data set, allowing for more accurate group comparisons. Despite inconsistent follow-up assessments, we found that participants returned, on average, at similar time points after the initial NA (Table 2), indicating that groups were comparable in this respect.

An additional consideration in comparing our study groups is that the NATI group exhibited a higher mean TAED at both baseline and immediately prior to retreatment relative to the NA group. We also observed a higher number of affected digits at baseline in the NATI group. Although these differences did not reach statistical significance in any case, this may suggest that the NA group was composed of individuals who tended to seek treatment for less severe disease than those in the NATI group. Although not impossible, this type of bias was not anticipated with a randomized design and resulted from the randomization of 2 individuals, each with 6 severely contracted joints into the NATI group, increasing its mean baseline TAED. The same 2 participants also returned for retreatment with severe contractures, creating a similar discrepancy in TAED between groups immediately prior to retreatment. The use of larger study groups and a baseline functional evaluation would likely resolve this variability and better characterize study groups.

We did not assign a cutoff TAED to categorize patients as experiencing recurrence or not, as the need for retreatment was patient-driven. The importance of standardized definitions for disease recurrence has been repeatedly recognized in the literature as a barrier to achieving meaningful comparisons between published studies.[3,8] Numerous definitions for recurrence in terms of extension deficit increase and the need for retreatment have been described.[2,3,9,10] A number of qualitative definitions have also been reviewed.[3] The use of patient-directed retreatment as an outcome in this study, despite representing a true clinical situation, cannot account for the motivational factors of patients and may have confounded comparisons of retreatment rates between groups. As a result, retreatment rates presented here may differ from existing published recurrence rates that were based on defined criteria.

The rate of retreatment in the NA group (62%) was only slightly higher than that reported by Van Rijssen et al[3] after 5 years (58%). The retreatment rate in the NA group was also higher than reports of long-term recurrence rates by Foucher et al[11] after a mean of 3 years (58%), Badois et al[12] after 5 years (50%), and Pess et al[8] after a mean of 3 years (48%). The retreatment rate in NATI patients (30%) was substantially lower than recurrence rates for NA alone in these reports. The provision of retreatment in this study likely depended upon flexion of previously treated joint(s) and additional factors not included in our analysis. We expected that patients not experiencing functional difficulties were less likely to return for follow-up. Therefore, participants with more severe contractures and/or more functional deficit may have returned more frequently for re-examination than participants with less severe contractures and/or fewer functional issues. This may have skewed the data by providing a more complete depiction of more severe cases. To avoid the impact of several data points for more severe cases, we included only one follow-up TAED measurement per participant, per time period.

The inclusion of functional assessments and patient-reported outcomes in the original trial and the follow-up study would have enabled a more comprehensive evaluation of the decision to undergo the initial NA, re-treatment, and factors affecting which type of second treatment a patient chooses.

A Kaplan-Meier survival estimate revealed a significantly lower percentage of NATI group patients than NA group patients undergoing retreatment by 24 months, with the percentages nearly equalizing by 48 months. This suggests a short-term benefit; however, the multivariate survival analysis indicated that younger baseline age and the involvement of multiple joints, but not treatment group, were significantly associated with earlier retreatment. This supports previous findings that older age at the time of initial NA predicts a delay to recurrence,[3] which is also consistent with Hindocha et al,[13] who reported that patients younger than 50 years at disease onset experience an increased risk of recurrence.

Because the multivariate survival analysis compared groups for the follow-up period from 7 to 53 months, failure to detect an overall effect of treatment group on time to retreatment is not unexpected. It is possible that the effects of triamcinolone injections were significant only over a shorter time period. This possibility is supported by our TAED data and Kaplan-Meier survival estimates, which suggest that any benefit associated with triamcinolone injections was short-lived and most likely undetectable after 53 months.

Limitations of this study include the use of a participant-driven outcome, the use of unblinded data collection, and by a decrease in statistical power at longer follow-up points. The original randomized study was designed to provide 81% power at an alpha of .05, requiring recruitment of 44 participants (22 per group). In the follow-up study, the number of participants per group decreased over time, as retreatments were performed. Implications of decreased statistical power include difficulty interpreting and generalizing results. Although the number of NA group patients returning for retreatment was nearly double that of NATI patients, this difference was not statistically significant, which may have been attributable to a shrinking sample size. The decreasing sample size may have also contributed to a failure to detect a significant effect of study group on time to retreatment.

The use of serial triamcinolone acetonide injections should be examined in an adequately sized randomized population to accurately characterize the long-term outcomes of this potentially beneficial adjunct to NA for patients with Dupuytren disease.

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