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ORIGINAL PAPER

Evaluation of the role of unconjugated hyaluronic acid repetitive injection during the primary repair of flexor tendons in no man's land: a randomized control trial

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Abstract

Background Zone 2 flexor tendon injuries are prone to poor results following repair due to adhesions. Different repair methods and physiotherapy protocols have been devised to improve outcomes, with variable results. Hyaluronic acid (HA) is a polysaccharide produced by the innermost layer of the tendon sheath that facilitates gliding in zones where the sheath is continuous.

Methods Sixty-two flexor tendons that were repaired using a double-stranded core suture were divided between groups A ($n = 32$) and B ($n = 30$). In the former, non-cross-linked HA was repeatedly instilled at the repair site, with a total of three injections per digit. The repair outcomes were assessed using the Strickland criteria, the ratio of total active motion to total passive motion (TAM/TPM), and active range of motion (AROM) for individual joints.

Results A total of 31.1% of group A patients had excellent to good outcomes in contrast to 13.3% in group B. The mean difference in TAM was 105° in group A and 71° in group B (p value < 0.05). The mean TAM/TPM was 0.65 in group A and 0.56 in group B (p value = 0.06).

Conclusions HA significantly improves the results of flexor tendon repair in zone 2.

Level of Evidence: I.

Keywords Zone 2 · Hyaluronic acid · Flexor tendons · Adhesions · Primary repair

Introduction

Since Verdan and co-workers described the five zones of flexor tendon laceration in 1972, zone 2, the "no man's land" as it was called by Bunnell, has been associated with the worst outcomes following tendon repair. Zone 2 extends from the A1 pulley to the insertion of the flexor digitorum superficialis (FDS) at the middle of the middle phalanx. In this zone, the FDS and flexor digitorum profundus (FDP) tendons lie together within the tight flexor sheath [1] (Fig. 1).

In the fibrous tunnel, both tendons are invested by a common synovial sheath that possesses parietal and visceral layers. The visceral layer of the sheath is also responsible for the production of glycosaminoglycans, including hyaluronic acid (HA), which provides an interface between the tendon and the sheath that is essential for smooth tendon gliding [3].

Following tendon injury and primary suturing, the healing process initiates. The fibroblasts in the repair zone appear to be of both intrinsic and extrinsic origins. Adhesion formation presents as an extrinsic pattern where fibroblasts migrate from the vicinity of the repair to the repair site [4].

Oedema peaks in the first week and persists through later weeks, while adhesions start to form in the second week. Therefore, early postoperative changes have three stages: initial (days 0–3, increasing resistance with oedema development), delayed (days 4–7, higher but consistent resistance with continuing oedema), and late (after days 7–9, hardening of subcutaneous tissue with adhesion formation). The extent and strength of adhesions vary substantially during the course of tendon healing; the ability of adhesions to resist tension decreases, and tissue elasticity increases from the middle to late healing stages [5].

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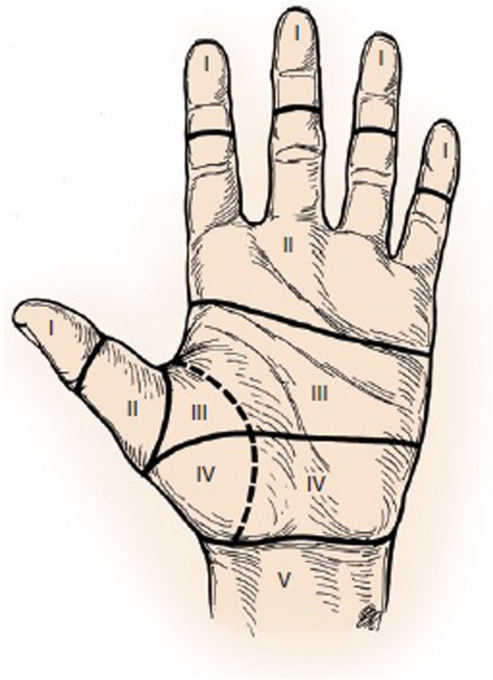

Fig. 1 Zones of flexor tendons [2]

Attempts to improve the strength of flexor tendon repair have focused on strategies to vary the material properties of the suture, the suture caliber, and the suture technique to co-apt the tendon ends accurately. A smooth tendon surface is important to restore low-friction gliding and aid tendon rehabilitation. Core suture configurations with the greatest tensile strength are those in which there are multiple sites of tendon-suture integration. However, two-strand suture methods are still practiced by many [6, 7] (Table 1).

Two main protocols of rehabilitation are currently in practice in most centers: early passive mobilization and early active mobilization. The latter is becoming a gold standard in many centers due to its efficacy in minimizing adhesions at the expense of bulkier repair. Passive mobilization can be achieved with passive flexion exercises or the Kleinert splint. Active mobilization can be achieved through place and hold exercises or true active flexion of the affected digits. Although immobilization protocols set the perfect environment for tendon healing and strengthening of the repair, they have been condemned due to extensive adhesion formation and motion limitations [8].

Finding a balance between immobilization, which allows adequate tendon healing, and early motion, which prevents adhesion formation, is key to successful postoperative rehabilitation. Therefore, the goal is to perform a repair that will allow early rehabilitation by employing a construct with the greatest tensile strength while concurrently minimizing frictional resistance within the fibro-osseous tunnel. Increased bulk at the repair remains a problem after zone 2 tendon repair. A high-friction repair can offset the advantage gained in strength by increasing gliding resistance [9–11].

Strickland used the difference between the preoperative and postoperative total active motion (TAM) as the tool to judge the results (Table 2).

HA belongs to the glycosaminoglycan family and consists of repeated disaccharide units. It has strong hydrophilic properties, attracting water into the extracellular matrix. HA is secreted by the innermost layer of the fibrous flexor sheath to improve the gliding of flexor tendons. Tendon surface treatment using lubricants such as HA, phospholipids, or lubricin can reduce surface friction and adhesions. The effect of HA on flexor tendons has been investigated in animal models and clinical studies [14–18].

Previous experimental studies have shown that the application of HA between an injured tendon and its sheath promotes healing of the tendon and decreases the formation of adhesions. HA has a short half-life (within 4–7 days) when injected into human tissues. After injection, naturally occurring hyaluronidase will digest non-cross-linked HA, although HA might prevent adhesion formation between the tendon and surrounding tissue without affecting tendon healing. In vivo results have not been consistent, possibly because unmodified HA is rapidly metabolized [15, 19–25].

Table 1 Pros and cons of different core suture configurations [7]

	Double strand	Multi-strand
Advantages	• Easier • Less bulky • Applicable in difficult clinical situations	• Stronger, lower mechanical rupture rates, and less repair site gapping • Compatible with early active mobilization rehabilitation programs
Disadvantages	• Higher mechanical rupture rate • More repair site gapping • Incompatible with early active mobilization rehabilitation protocols	• More complex • Bulky repair • Inapplicable in difficult clinical situations • Example: Becker's technique

Table 2 Strickland assessment criteria of functional outcomes following flexor tendon repair [12, 13]

Grade	Difference in TAM
Excellent	85–100 (> 150°)
Good	70–84 (125–149°)
Fair	50–69 (90–124°)
Poor	0–49 (< 90°)

Different studies have adopted the repeated application of HA to preserve sufficiently effective levels. Meloni et al. examined the effect of periarticular injection of HA in patients suffering from supraspinatus tendinopathy. After the first injection, the injection was repeated once a week for 4 weeks. Özgenel reported the use a single dose of 0.3 ml of HA around the repair site before closing the wound. However, he criticized his work reporting that the single-dose application of HA around the sites of tendon repair could be a defect of the study because restoration of the circulation to the area would rapidly remove it. He argued that repeated application of the solution would increase the risk of infection and that this would not be considered a feasible clinical alternative. However, multiple injections of HA remained the logical next step in his investigation [26, 27].

Eight years later, Özgenel and Etöz conducted a randomized control in vivo study on 22 patients with injured tendons in zone 2 and divided the patients into two groups, one injected with HA and the other injected with saline. The injections were delivered through a 23 G catheter tip placed closest to the FDP tenorrhaphy site before closing the wound and fixed to the skin at the exit point by a suture to maintain the catheter tip adjacent to the tenorrhaphy site. The first dose was given at the time of tenorrhaphy, and two additional doses were given at 1-week intervals. A total of 0.4 ml of high molecular weight HA in high concentrations (15 mg/ml) was injected through the catheter each time. Özgenel and Etöz reported significant improvement observed in fingers treated with HA compared to placebo at 3 months and in the long term [28].

Methods

This is a prospective, comparative randomized clinical trial (RCT) in which 43 patients had primary repair of a flexor tendon injury, with a total of 62 repaired tendons. Patients were randomly distributed between groups A and B. The primary aim was to evaluate repetitive HA injection in the repair site intra-operatively and at weekly intervals after surgical repair with a total of three injections.

The study was conducted on patients with lacerated flexor tendons in zone 2 during the period from December 2015 to the present. Only patients who were operated on within 48 h of injury were included in the study. Patients younger than 12 years of age and older than 65 years were not included in the study. Patients with double-level tendon lacerations, associated fractures, and associated neurovascular bundle injuries were also excluded from the study.

Patients were then randomly assigned to groups by chronological order of their presentation; those with odd numbers, i.e., the 1st, 3rd, and 5th patients, were assigned to group A, while those with even numbers, i.e., the 2nd, 4th, and 6th patients, were assigned to group B.

1. Group A: Patients belonging to this group were injected with HA intra-operatively and at 1 and 2 weeks postoperatively.
2. Group B: Patients were managed conventionally without the use of HA.

Upon presentation, after control of bleeding and stabilization of the patient, a proper history was taken that focused on hand dominance, occupation, smoking, details of the traumatic event including the causative tool, timing, the position of the fingers at time of injury, medical comorbidities, and previous surgeries. An examination of the affected digit(s) was conducted next. The wound site and extent were noted, and sensation and vascularity in the affected digit(s) were assessed. Finally, active and passive range of motion was assessed and recorded in the metacarpophalangeal (MP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints, summing up to the total passive motion (TPM) and the total active motion (TAM). X-rays in the anteroposterior and lateral

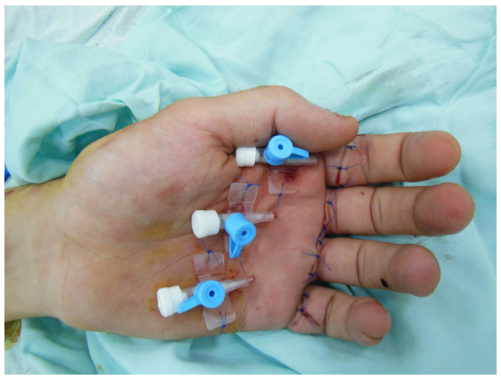

Fig. 2 Device for delivering hyaluronic acid

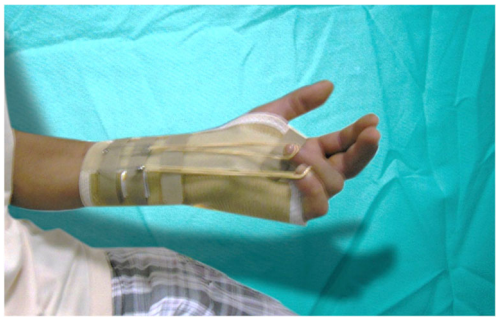

Fig. 3 Dynamic splint

positions and photographs documenting the functional deficits of the involved digits were taken.

Each patient was informed about the details of the operation, the expected outcome, possible complications, and role of physiotherapy. In group A, the patients were counseled about the injection of HA, including its potential pros and cons, stating clearly "this is a new therapy under clinical trial that could have promising results", and written informed consent was acquired.

In the operating theater, the wounds were cleansed, and tendons were retrieved through the wounds when applicable. Otherwise, wound extension was performed using Bruner incisions. A core suture using polypropylene 3/0 was placed in the modified Kessler configuration, followed by running epitenon graphing using polypropylene 5/0. Next, the fibrous pulley was approximated using 2–3 polypropylene 5/0 interrupted sutures.

In cases presenting with both superficialis and profundus tendon injuries, only the profundus tendon was repaired, and the injured superficialis tendon slip was excised to reduce bulk and adhesions and provide more room for the repaired profundus tendon to heal.

For group A patients, a 20–22 G cannula was inserted in the digital sheath through a skin puncture proximal to the wound before skin closure, so that its tip was just proximal to the repair site (Fig. 2). The cannulas were then maintained in position with polypropylene 3/0 sutures. After skin closure, 0.5 ml of non-cross-linked HA was delivered at the repair site. The hand was then immobilized in a dorsal blocking splint (DBS) with the MP joint in 80° of flexion and the IP joints in extension.

Postoperatively, patients were scheduled for a weekly follow-up for the next 4 weeks and then monthly afterwards. Throughout the visits, any complication was documented and managed accordingly.

- The first visit (day 7): Wound dressing was performed. The DBS was reapplied. Patients were instructed to passively flex their fingers manually on a daily basis as tutored by the surgeon. For group A patients, a second dose of 0.5 ml of non-cross-linked HA was instilled via the cannula before covering the wound.
- The second visit (day 14): The sutures were removed, the DBS was discarded, and the hand was placed in a dynamic splint (Fig. 3). Patients were instructed to extend the affected tendon against resistance 10 times per exercise, which should be repeated five times daily. In group A, the last injection of 0.5 ml of non-cross-linked HA was given via the cannula before removing it.
- The third visit (day 21): The dynamic splint was revised.
- The fourth visit (day 28): The dynamic splint was discarded, and the patient was referred to a physiotherapist after the TPM and TAM were measured again.
- During the next visits, patients were followed up to ensure that they were connected with the physiotherapist and that physiotherapy was going as scheduled. Dropouts from physiotherapy were excluded from the study.
- The last visit (6 months after the repair): The final TPM and TAM measurements as well as active range of motion (AROM) and passive range of motion (PROM) for individual joints were measured and documented.
- At the completion of follow-up, the following form in Table 3 should be fulfilled.

Demographic data and basic statistics regarding the mode of trauma were collected and analyzed in both groups. Complications were documented and compared between both groups as well. The efficacy of minimizing adhesions was compared between the two groups by calculating the TAM/TPM proportion, the difference between the pre- and postoperative AROM for the DIP and PIP joints separately, and the difference in TAM, which was then matched to the Strickland grading system.

The data are statistically described in terms of mean ± standard deviation (± SD), median and range, or frequency (number of cases) and percentage when appropriate. Comparison of numerical variables between the study groups was performed using Student's t test for independent samples. For comparing categorical data, a Chi square (X^2) test was performed. An exact test was used instead when the expected frequency was less than

5, and p values less than 0.05 were considered statistically significant. All statistical calculations were performed using the computer program SPSS version 15 for Microsoft Windows (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA).

Table 3 Final form

HA	3	0
Complications	Infection	None
TPM post	250	240
TAM post	190	170
Passive range PIP post	110	100
Active range PIP post	100	90
Passive range DIP post	50	50
Active range DIP post	40	20
TPM pre	270	240
TAM pre	60	140
Passive range PIP pre	120	100
Active range PIP pre	0	80
Passive range DIP pre	60	50
Active range DIP pre	0	0
Affected tendon(s)	FDP FDS	FDP
Affected finger	Middle	Index
Affected hand	Left	Left
Mode of trauma	Knife	Knife
Position of injury	Flexion	Extension
Physiotherapy	36	24
Age	26	17
Group	A	B
#	**1**	**2**

Results

The patients' ages ranged from 12 to 50 years with a mean age of 27.7 years. The mean age was higher in group A (31.0 years) than in group B (24.2 years). The study showed a striking male predominance, in which 86.0% of all patients were males.

The majority of injuries were sustained in the flexion position, which represented 64.5% of all injuries, 43.8% of group A injuries, and 86.7% of group B injuries. Regarding the culprit tool, the majority of injuries were caused by knives, which occurred in 54.8% of all injuries. The second most common culprit tool was glassware, which caused 16.1% of injuries. Other causative agents included electric saws, falling objects, metal strings, and sharp tools, in decreasing order of frequency.

Injuries were almost equally distributed between the right and left hands, with a slight left-hand predominance, which presented in 51.6% of all injuries. The most affected finger was the little finger, sustaining 29% of all injuries. Next, the ring finger sustained 25.8% of injuries, and lastly, the index and middle fingers had an equal incidence of 22.6%.

Four patients (6.5%) presented with isolated FDP tendon injury. They were divided evenly into each group, and the remaining patients with FDP injury presented with combined FDP and superficialis tendon injury.

By comparing the preoperative and postoperative TPM for both groups, the mean TPM decreased by 7.5% in group A, from 243.55 to 225.32° with a 5.4% drop, and a 14.6% drop was observed in group B. For individual joints, the DIP passive range of motion dropped by 5.45%, while that for the PIP decreased by 12.1% for all patients. The decrease in TPM was significantly higher in group B patients, in whom the joints lost 30° of their mean TPM, than in group A patients, who lost 16°.

Group A patients had a better active range of motion in all individual joints and hence the TAM (Table 4) (Fig. 4). The net gain in TAM was significantly higher in group A, with an average of 105°, than in group B, with an average of 71° (p value = 0.000). Additionally, the average TAM/TPM proportion was almost significantly higher in group A (0.653) than in group B (0.565) patients (p value = 0.065) (Table 5).

The mean difference at the DIP joint between passive and active motion was 13.75° for group A patients in comparison to 20° for group B patients. Similarly, the difference at the PIP joint was 35.63° for group A and 48° for group B patients (Table 6).

The most frequently occurring complication was surgical site infection, accounting for a total of 10 out of

Table 4 Results according to Strickland criteria

	Total (%)	A (%)	B (%)
Excellent	4 (6.5)	3 (9.3)	1 (3.3)
Good	10 (16.1)	7 (21.8)	3 (10)
Fair	28 (45.2)	16 (50)	12 (40)
Poor	10 (16.1)	1 (3.1)	9 (30)
Failed	10 (16.1)	5 (15.6)	5 (16.7)
Total	62 (100)	32 (100)	30 (100)

62 patients, 6 of whom were trivial and resolved with conservative measures, while the remaining 4 ended in wound dehiscence and ultimately repair failure. Most infections were observed in group A patients; the ratio of infected patients in group A:B was 7:3. However, repair failure that was not related to infection occurred in 6 patients, with a higher incidence in group B patients (group A:B ratio = 1:2) (Table 7).

Discussion

The *concept* of this study was based on the fact that despite the evolution and advances made in flexor tendon in for the past decades, the results have been unsatisfactory to most patients with injuries in zone 2. This outcome is primarily due to adhesions between the tendon and its surrounding tissues within the narrow fibro-osseous tunnel. Consequently, hand surgeons started modifying techniques and physiotherapy protocols to minimize adhesions and hence improve tendon gliding within the pulley system.

To incorporate active motion protocols, a minimum of 4-strand core suturing plus epitenon running sutures should be incorporated. However, the fewer the number of strands, the less bulky the repair is, and hence, the less gliding resistance there is. Thus, we adopted the modified Kessler double-strand grasping suture for the core suture with epi-tenorrhaphy for the repair and early passive motion for rehabilitation. For the same reasons, we preferred not to repair but rather to excise the superficialis tendon in cases where both the profundus and superficialis tendons were injured to give more room for the repaired profundus to heal [29].

Many aspects of adhesion formation have been studied to develop algorithms for the prevention of these unwanted sequelae. Animal studies involving the administration of HA at the repair site were conducted with promising results. In January 2012, Özgenel and Etöz suggested through their placebo-controlled clinical study that repetitive injections of non-cross-linked HA can improve clinical outcomes, presumably due to the effect on decreasing adhesions in primary tendon repairs.

In designing the current study, we were bound by several facts, the first of which was that adhesions develop by day 7 postoperatively and peak at day 14, as reported by Cao et al. in 2008. This phenomenon obliged us to focus injection therapy during the first 3 weeks postoperatively. Another important fact was that non-cross-linked HA is eliminated from the body after 5–7 days, and thus, injections had to be repeated on a weekly basis [30].

The choice of non-cross-linked HA for injection in the repair site was based mainly on socioeconomic and physical factors, being less expensive than cross-linked products, and less viscous, which is believed to be more appropriate to the narrow space within the sheath. In addition, non-cross-linked products are less antigenic, reducing the risk of allergic reactions among patients. Most importantly, animal studies conducted earlier used only non-cross-linked products.

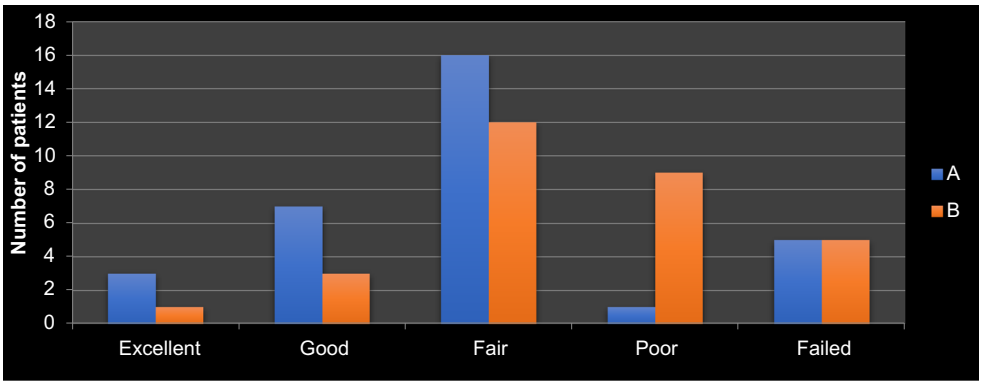

Fig. 4 Bar chart showing the functional outcome distribution between groups

Table 5 Independent sample tests of postoperative results

		t test for equality of means						
		t	df	*p* value	Mean difference	Std. error difference	95% confidence interval of the difference	
							Upper	Lower
Active range DIP post	Equal variances assumed	2.514	60	0.015	9.750	3.878	1.993	17.507
	Equal variances not assumed	2.509	58.967	0.015	9.750	3.886	1.973	17.527
Passive range DIP post	Equal variances assumed	1.035	60	0.305	3.500	3.381	− 3.263	10.263
	Equal variances not assumed	1.020	47.218	0.313	3.500	3.433	− 3.405	10.405
Active range PIP post	Equal variances assumed	1.836	60	0.071	14.583	7.943	− 1.305	30.472
	Equal variances not assumed	1.841	59.978	0.071	14.583	7.921	− 1.262	30.428
Passive range PIP post	Equal variances assumed	0.478	60	0.634	2.208	4.621	− 7.034	11.451
	Equal variances not assumed	0.469	43.856	0.641	2.208	4.705	− 7.274	11.691
TAM post	Equal variances assumed	2.112	60	0.039	23.750	11.244	1.259	46.241
	Equal variances not assumed	2.116	59.983	0.039	23.750	11.226	1.295	46.205
TPM post	Equal variances assumed	1.417	60	0.162	9.667	6.823	− 3.981	23.314
	Equal variances not assumed	1.389	42.159	0.172	9.667	6.958	− 4.373	23.706
TAM/TPM post	Equal variances assumed	1.877	60	0.065	0.08738	0.04656	− 0.00575	0.18051
	Equal variances not assumed	1.890	58.560	0.064	0.08738	0.04622	− 0.00513	0.17989
TPM diff	Equal variances assumed	2.562	48	0.018	13.429	5.242	2.890	23.969
	Equal variances not assumed	2.499	32.869	0.018	13.429	5.375	2.493	24.366
TAM diff	Equal variances assumed	5.005	48	0.000	34.135	6.819	20.423	47.846
	Equal variances not assumed	4.933	40.359	0.000	34.135	6.920	20.152	48.117

Table 6 Postoperative data

Group		Physiotherapy	Active range DIP post	Passive range DIP post	Active range PIP post	Passive range PIP post	TAM post	TPM post	TAM/ TPM post	TPM diff	TAM diff
A	Mean	12.67	28.75	42.50	61.25	96.88	148.75	230.00	0.6526	− 16.15	105.38
	N	32	32	32	32	32	32	32	32	32	32
	SD	14.262	14.756	9.837	32.503	12.297	45.277	17.227	0.20170	11.688	19.438
	Minimum	0	0	20	0	80	60	200	0.22	− 40	60
	Maximum	36	40	60	100	120	190	270	0.82	0	130
	Median	4.00	30.00	40.00	70.00	95.00	165.00	230.00	0.7446	− 10.00	110.00
B	Mean	19.73	19.00	39.00	46.67	94.67	125.00	220.33	0.5652	− 29.58	71.25
	N	30	30	30	30	30	30	30	30	30	30
	SD	12.089	15.779	16.210	29.866	22.854	43.112	34.264	0.16112	23.816	28.294
	Minimum	0	0	20	0	30	60	145	0.26	− 75	25
	Maximum	36	50	70	90	120	200	270	0.74	0	130
	Median	24.00	20.00	40.00	60.00	100.00	140.00	230.00	0.6000	− 30.00	80.00
Total	Mean	16.20	24.03	40.81	54.19	95.81	137.26	225.32	0.6103	− 22.60	89.00
	N	62	62	62	62	62	62	62	62	62	62
	SD	13.583	15.911	13.312	31.858	18.066	45.482	27.068	0.18696	19.542	29.416
	Minimum	0	0	20	0	30	60	145	0.22	− 75	25
	Maximum	36	50	70	100	120	200	270	0.82	0	130
	Median	15.00	30.00	40.00	60.00	100.00	150.00	230.00	0.6957	− 20.00	90.00

Table 7 Complications—Crosstab

			Group		Total
			Group A	Group B	
Complications	Contracture	Count	2	2	4
		% within group	6.3%	6.7%	6.5%
	Mechanical rupture	Count	2	4	6
		% within group	6.3%	13.3%	9.7%
	Infection	Count	4	2	6
		% within group	12.5%	6.7%	9.7%
	Infection/failed	Count	3	1	4
		% within group	9.4%	3.3%	6.5%
	Joint stiffness	Count	6	3	9
		% within group	18.8%	10%	14.5%
	None	Count	15	18	34
		% within group	46.9%	60.0%	54.8%
Total		Count	32	30	62
		% within group	100.0%	100.0%	100.0%

However, this study design had two major setbacks; the first was that it necessitated repeated injections due to having a short tissue half-life. In addition, supposedly, the device installed to deliver subsequent HA injections may cause a higher infection rate, just as any foreign body might. Knowing that, we still believed that this was a better alternative than repeated punctures at the repair site, which carries the risk of weakening the repair by faulty injection and inaccurate injection outside the fibro-osseous tunnel. The second setback was the complexity of the postoperative care and the 2-week delay before commencing physiotherapy.

To measure the success rate of HA, we had to assess both the global return of function by measuring the difference in pre- and postoperative TAM and the actual effect on minimizing adhesion formation by measuring the TAM/TPM ratio. Strickland used the former to describe the results of tendon repair, while Groth, in his pyramid of progressive force exercises in 2004, used the discrepancy between AROM and PROM to evaluate adhesion status and efficacy of treatment. We also measured the AROM at each individual joint to better describe our results [12, 31].

Our study showed that global return of motion was significantly higher in group A than in group B, with a TAM difference of 105 for group A in contrast to 71 for group B. The p values for the comparison of AROM at different joints and the TAM were all < 0.05. These results show that the HA injections generally improved the functional outcome. They also showed that group A had fewer adhesions as manifested by the TAM/TPM ratio (0.65 for group A versus 0.56 for group B), approaching statistical significance (p value = 0.065), yet a larger sample is needed to verify this result.

On the other hand, group A had a strikingly higher infection rate, with a total of 7 out of 32 cases, 3 of which actually ended in a failure. Group B had doubled the rate of mechanical rupture due to factors other than infection. However, the total number of failures was equal among both groups. Although none of these outcomes are statistically significant, they must be taken into consideration.

Our study was not, however, without limitations. First, we had a higher infection rate, which is probably related to the device used to deliver HA at the repair site, and a better alternative still needs to be devised. Second, a larger sample size is needed to determine the true effect on minimizing adhesions and the associated complications. Third, many of our patients were of lower socioeconomic standards, and adherence to hand therapy protocols has been questioned, which may have caused our results to be less optimal than those of other studies. Fourth, a true test for HA is when it is used with a multi-strand repair of both tendons in this zone, which was not analyzed in our study.

Although, theoretically, cross-linked HA preparations may provide the solution to obviate repeated injections, animal studies supporting their use are still lacking.

Cross-linked HA injections can be implemented in future preclinical and clinical trials to test their effectiveness.

In conclusion, repeated injections of HA at the repair site successfully improved the functional outcomes, but they were associated with a higher infection rate. Overall repair failures remained equal among both groups. For this reason, we find that instilling HA at the repair site is a very useful adjunct when dealing with zone 2 flexor tendon injuries.

Compliance with ethical standards

Conflict interest Omar Mohamed Nouh, Ahmed Safwat Salem, Youssif Ahmed Khachaba, Tarek Seif Eldin Ashour, and Khaled Makeen ElRefaei declare that they have no conflict of interest.

Ethical committee approval Plastic surgery department, Cairo University, ethical committee approval was obtained prior to the study.

Informed consent Informed consent was obtained from all patients enrolled in the study. The study included four minors in whom informed consent was acquired from their legal guardians. The consent included details of the preoperative measures, the operative procedure, and the postoperative treatment, including the physiotherapy program and potential complications. Patients or their legal guardians (in four cases) approved enrolment in the study and publication.

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