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Rheumatoid Forefoot Reconstruction Following Minimally Invasive Surgery and Hoffmann-Clayton Procedure with Administration of Plasma Rich in Growth Factors - A 3-Year Follow-Up: A Retrospective Study

Reconstrucción del antepié reumatoide después de una cirugía mínimamente invasiva y un procedimiento de Hoffmann-Clayton con administración de plasma rico en factores de crecimiento - Seguimiento de 3 años: Estudio retrospectivo

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SUMMARY

From 80 % to 90 % of foot deformities in adults are due to rheumatoid arthritis. Despite various surgical approaches, early functional and cosmetic results have been the greatest concern among patients. Thus, optimal surgical choice in rheumatoid forefoot correction is of vital importance for better subjective and clinical results. Our work evaluates the results of minimally invasive surgery (MIS) and resection arthroplasty per Hoffmann-Clayton along with the administration of Plasma Rich in Growth Factors (PRGF) in rheumatoid-affected forefoot patients. This retrospective study included 28 patients (50 feet) aged around 45 ± 4.5 years. The examination was made for the following parameters: pain, insoles, ambulant, function of the foot, recurrence rate and revision surgery, and patient comfort. Though the function of the forefoot was quite challenging to

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assess, the ability to wear conventional shoes had been increased to 70 %. The patients could walk more distances with shoes rather than walking without shoes (P<0.01). Seventeen reoperations were carried out on 12 patients. The recurrence rate had been too minimal which was common for hallux valgus cases. The results of 3 years follow-up of patient-reported questionnaires demonstrated that a large number of patients (more than 80 %) were significantly satisfied. Especially, PRGF favours the treatment by minimizing the rehabilitation period, post-operative edema, pain, and better cosmesis.

Keywords: *Rheumatoid arthritis, human forefoot, minimally invasive surgical procedures, platelet-rich plasma*

RESUMEN

Del 80 % al 90 % de las deformidades de los pies en adultos se deben a la artritis reumatoide. A pesar de los diversos abordajes quirúrgicos, los resultados estéticos y funcionales tempranos han sido la mayor preocupación entre los pacientes. Por lo tanto, la elección quirúrgica óptima en la corrección del antepié reumatoide es de vital importancia para obtener mejores resultados subjetivos y clínicos. Nuestro trabajo evalúa los resultados de la cirugía mínimamente invasiva (CMI) y la artroplastia de resección según Hoffmann-Clayton junto con la administración de Plasma Rico en Factores de Crecimiento (PRGF) en pacientes reumatoides con afectación del antepié. Este estudio retrospectivo incluyó a 28 pacientes (50 pies) con una edad de 45 ± 4,5 años. Se realizaron exámenes de los siguientes parámetros: dolor, plantillas, deambulante, función del pie, tasa de recurrencia y cirugía de revisión, y comodidad del paciente. Aunque la función del antepié fue bastante difícil de evaluar, la capacidad para usar zapatos convencionales se incrementó al 70 %. Los pacientes podían caminar más distancias con zapatos que caminar sin zapatos (P < 0,01). Se realizaron diecisiete reintervenciones en 12 pacientes. La tasa de recurrencia fue mínima, lo que era común en los casos de hallux valgus. Los resultados de 3 años de seguimiento de los cuestionarios informados por los pacientes demostraron que un gran número de pacientes (más del 80 %) estaban significativamente satisfechos. Especialmente, PRGF favorece el tratamiento minimizando el período de rehabilitación, el edema posoperatorio, el dolor y una mejor estética.

Palabras clave: *Artritis reumatoide, antepié humano, procedimientos quirúrgicos mínimamente invasivos, plasma rico en plaquetas.*

INTRODUCTION

Rheumatoid arthritis (RA) is a prolonged autoimmune disorder causing pain and swelling of joints. For years, disease-modifying antirheumatic drugs (DMARDs) (1,2) have been improved but the inflammatory process continues to cause severe destruction and substantial forefoot deformities such as deterioration of tendons, and loss of function (3), inflammation of metatarsal bursae. Patients of such kind require orthopedic shoes for daily wear. Failure of anti-rheumatism drugs (4) paves way for various surgical methods to rectify the deformity and minimize pain (5,6). According to Larsen's classification, in the early stages of deformities, minimally invasive surgery (MIS) is encouraged to preserve the bones and joints and better cosmesis. Whereas in severe cases, Hoffmann-Clayton arthroplasty on the lesser rays is the choice of surgery. During the procedure, arthrodesis of the hallux is often performed (7,8). Other methods include Tillmann arthroplasty, a well-interpreted surgery by Karl Tillmann (9). The surgery is carried out via plantar access for lesser metatarsal head resection and dorsomedial approach for the Hueter-Mayo procedure of the great toe. However, the purpose of all methods is to minimize pain, increase ambulant, especially with conventional shoes and keep up the forefoot function (10).

Wound healing - is a composite biological process including haemostasis, inflammation, proliferation, and remodeling (10). Regeneration becomes more complex in the forefoot than in other soft tissue structures. Growth factors, a biologically active material play a vital role in managing cellular processes like chemotaxis, mitogenesis, cell differentiation, and metabolism. Platelets enhance growth factors distribution in the early phases of wound healing (11). In 1999, for the first time, Anitua proposed Plasma rich in growth factors (PRGF) technology (12). "PRGF" is associated with characteristics such as 100% autologous and biocompatibility formed with the help of a single process of centrifugation using calcium chloride and sodium citrate as activators and anticoagulants, respectively. PRGF includes moderated platelet concentration but no leukocytes to exclude the proinflammatory reactions of proteases and acid hydrolases in leukocytes (13,14).

Our work aims to evaluate 3 years of follow-up of RA patients with mild to severe forefoot deformities who underwent MIS and complete forefoot reconstruction per Hoffmann-Clayton with infiltration of PRGF, respectively.

MATERIALS AND METHODS

Our retrospective study included RA patients from City Clinical Hospital No. 13, Moscow, Russia before February 1, 2018. All patients were given informed consent.

Plasma Rich in Growth Factors (PRGF): Thirty-six mL of blood were collected from the veins of all patients. Collected blood was shifted to four vacutainer tubes, each containing blood anticoagulant of 5 mL in quantity. Followed by eight minutes of centrifugation at 460g allowing it to separate various blood phases according to the BTI standard. From each tube around 2 mL of rich plasma, fragments were drawn that were present directly on top of the buff coagulated plasma. This rich plasma was then shifted to a sterilized vacutainer tube followed by the addition of 10% calcium chloride (PRGF activator) in the ratio of 50 microliters per mL of PRGF to begin clotting and stimulate thrombocytes to deliver growth factors (Figure 1). Activated PRGF was allowed for four minutes at room temperature to form a consistent gelatinous layer and was used intraoperatively before the wound closure.

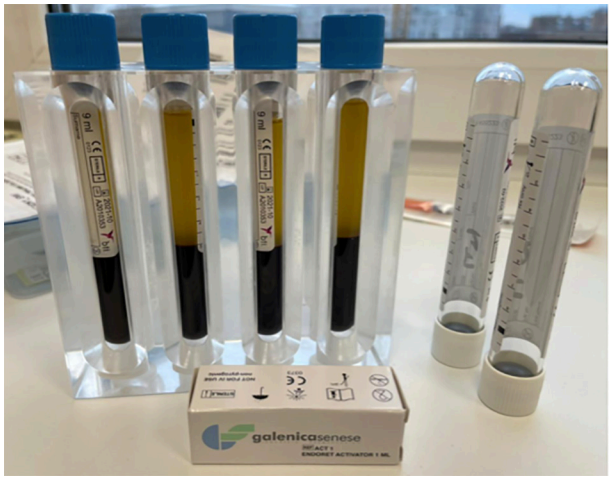

Figure 1. Preparation of PRGF and PRGF activator.

Surgical Procedure

Minimally Invasive Surgery (MIS) includes tenotomies of flexors and extensors, phalangeal osteotomies (Akin, Hohmann), and metatarsal (MT) osteotomies (Subcapital osteotomies of 2-3-4 MT, Wilson) (Figure 1(A)).

Figure 1(A). Clinical picture MIS (A) before surgery, (B) immediately after surgery

Hoffmann-Clayton Surgery: it is metatarsal (MT) head resection through transverse-plantar surgical access where the plantar approach is more common, which uses fish-mouth incision to excise hyperkeratotic skin and inflamed bursae. The plantar incision distally matches the MT head cascade. Whereas the proximal approach is done to remove the maximum amount of plantar calluses and also the hypertrophied soft tissues to increase the flap size. Hoffmann-Clayton recommends the removal of the proximal phalangeal base based on the requirements of alignment and adjustments. Once the resection is complete, alignment is secured with the temporary Kirschner wire fixation (Figure 1(B)) (15). The reconstructed MT heads are covered by a short extensor tendon and dorsal capsular flap. To carry out the manipulation in the first metatarsophalangeal (MTP) joint, a separate dorsomedial approach is used, followed by arthrodesis with one screw fixation, and in cases of flexion contractures temporary K-wire is added. During the procedure, the sesamoids are excised in almost all cases.

Figure 1(B). Pre- and postoperative anterior-posterior radiological picture of patient B.

Figure 1(b) (left picture) presents a radiograph before surgery illustrating a case of severe HV and MTP joint destruction of lesser toes. Figure 1(b) (right picture) presents a radiograph after Hoffmann-Clayton and arthrodesis of 1st MTPJ. In this case, the sesamoids are preserved, and the MT heads of lesser toes are resected according to the forefoot parabola.

Figure 2. Clinical picture (left picture) before surgery, (midle picture) immediately after surgery, (right picture) after 6 months.

To achieve better outcomes with strong correction and satisfactory mobility, the surgical resection is supposed to maintain 6-8 mm elastic distraction among the reconstructed MT heads and the proximal phalanges. This must be achieved without damaging the quality of correction and suture fixation.

Patients

Based on inclusion norms, 46 patients were eligible from the hospital database. Among them, details of 42 patients were recorded from a computer database, 4 patients from film records, and 8 patients dropped out of the study due to the absence of data. The remaining 38 patients were contacted based on the information presented in the administrative office. Among 38 patients, 3 patients had passed away. Patient-based surveys in the form of questionnaires were posted to the remaining 35 participants. Five did not show interest in participating in the study and 2 were untraceable as shifted from their registered address. Finally, 28 patients who collectively underwent 50 forefoot surgeries accepted the invitation and sent back the completed questionnaire.

Of a total of 28 patients, among them 24 were female and 4 were male. The mean age during the surgical intervention was 45 ± 4.5 years. From the database, 40 cases were bilateral surgery, 7 cases were only left foot and 3 cases were only right foot. The minimum follow-up duration after the surgery was 3 years, an average of 3 ± 0.5 years.

Table 1

Patient allocation

Patient allocation	First visit	Follow up visit
Hospital based (n = 46) √ Computer based (n= 42) √ Film Archieve (n = 4)	28	28
On DMARDs	28	28
CVD	14	14
Nephropathy	14	14

Questionnaire

The survey was a self-made questionnaire with specific outcome parameters.

- Pain: no pain, pain under strain and at rest.
- Insoles: Everyday use of conventional shoes with or without alterations.

- Ambulant: the distance covered by wearing shoes and without shoes from 0-100 meters.
- Foot function: a 2-legged tiptoe stand, a plantar 1-legged stand, and a 1-legged tiptoe stand for 5 seconds each.
- Recurrence: HV, hammertoes, and plantar callosities.
- Patient comfort: 4-point Likert scale.
- Revision surgery: Yes/No.

The self-made questionnaire was made in the interest of specific parameters to understand the difference in the patient's daily life, social and emotional life before and after surgery, and most importantly to understand the outcomes of surgery with respect to specific foot functions. Scales such as SF-36-HAQ, and QOL-RA had limitations in achieving these parameters.

Statistical Analysis

With the help of the statistics package SPSS version 23.0 (IBM Corp., Armonk, NY) statistical analysis was performed. Descriptive statistics values are indicated by the standard deviation (SD), frequencies, and percentages for nominal data. The Wilcoxon test helped in evaluating dissimilarities between the distance covered by wearing shoes and without shoes. The Kendall rank was utilized to evaluate the relation between pain, recurrence, and satisfaction. Based on accepted standards, statistical significance was accepted to a 2-tailed P value of 0.05.

RESULTS

Based on our study, at a mean follow-up of 3 years 9 patients (35%) had no pain or only mild pain. The walking ability of patients had been improved to more than 100 meters by wearing shoes ($p<0.001$) after surgery (Figure 3). 56.7% of patients were able to wear conventional shoes (Figure 4). 12 patients underwent revision surgery due to recurrence of deformities in the great toe and lesser toes (Table 2).

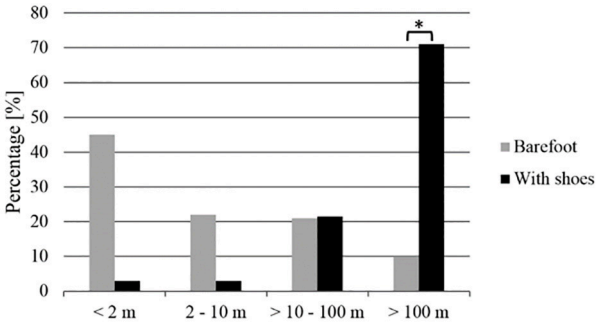

Figure 3. The graph illustrates the ability of patients to walk with or without shoes to a distance of up to and more than 100 meters (*P<0.001).

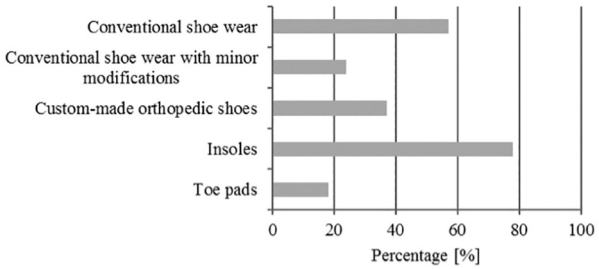

Figure 4. The graph describes the use of shoe wear and other orthoses. In total, values reach more than 100 %, because a few patients need different orthoses based on the condition of the foot-operated on.

Table 2

List of revision surgery in 12 patients (n=17 feet)

Great toe (D1)	Great toe (D1)	Lesser toes (D2-D5)	Lesser toes (D2-D5)
Re-Hueter-Mayo	3	< 4 toes	5
Arthrodesis	4	All 4 toes	5
Total (n)	7	Total (n)	10

The forefoot function of the patients is demonstrated as a percentage via the 2-legged tiptoe stand, the 1-legged stand, and the most advanced form, the 1-legged tiptoe stand (Figure 5). If patients were able to perform these stands, they were asked to specify whether it was possible to hold the position for 1 to 5 seconds or longer. Deformity relapses of the forefoot are demonstrated with bar graphs (Figure 6). No

significant differences are identified. However, the fewest deformity relapses were documented for hammertoes and plantar swelling. Most mild and severe deformity cases were seen for the hallux valgus (hallux valgus angle 20 to 40 degrees and more than 40 degrees, respectively).

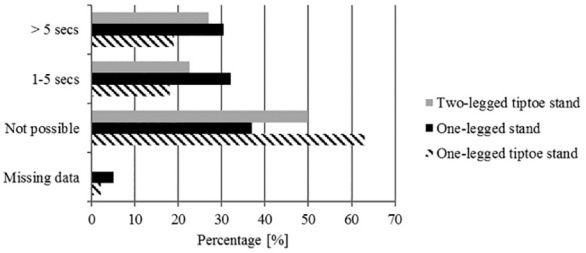

Figure 5. Demonstration of forefoot function in percentage. Patients were requested to notify whether they were able to do these stands, if so, could they hold it for 1 to 5 seconds or longer.

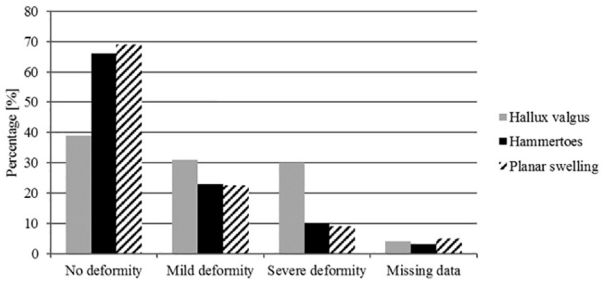

Figure 6. Demonstration of forefoot deformity relapses. Hammertoes and plantar swelling remain the fewest, whereas HV deformity relapse contributes to the highest.

According to clinical and radiological observations, infiltration of PRGF favors surgical treatment by minimizing the rehabilitation period, post-operative edema, pain, and better cosmesis. It has been reported that 24, 48 and 72 hours of PRGF relevantly enhances HGF proliferation and viability.

Table 3

Summary of 28 Patients' responses to the questionnaire (total 50 feet)

Category	Subcategory	No. of patients	%
Pain	No pain	9	35
	Under strain	11	40
	Rest pain	6	23
Orthoses	Conventional shoes	16	56.7
	Modified conventional shoes	7	25
	Custom-made orthopedic shoes	10	36.7
	Insoles	22	78.3
	Toe pads	5	18.3
Walking ability	Unable to walk unshod for >10 m	17	68
	Able to walk >100 m by wearing shoes (P<0.001)	20	70
Foot function (>5 sec)	2-legged tiptoe stand	7	26.7
	1-legged stand	8	30.5
	1-legged tiptoe stand	5	18.4
Recurrence	Hammertoes	3	10.3
	Plantar swelling	2	8.4
	HV- Mild to moderate	9	31.25
	HV – Severe	8	30.2
Satisfaction (Likert scale)	Very satisfied	7	25
	Satisfied	16	59
	Not satisfied	2	6
	Dissatisfied	3	10
Reoperation		12	43.3

DISCUSSION

Three years of follow-up of forefoot reconstructions according to Hoffmann-Clayton and minimally invasive surgery with the administration of plasma rich in growth factors is a much-needed study. Though joint preserving surgery with improved anti-rheumatism medications serves to be successful these days, the joint sacrificing surgery of II to V toes remains to be the gold standard method in cases of severely damaged forefoot in rheumatoid patients (16,17). Hoffmann-Clayton's technique commonly uses a plantar approach. The plantar access shows better results even after 20 years postoperatively. Revision surgery in these cases was mainly due to relapses for HV, hammertoes, and/or plantar callosities. Whereas only minor problems in the lesser toes like bone smoothing, and resections had to be re-evaluated just like Hoffmann-Clayton himself.

Based on observation, a slight osteotomy with soft tissue correction should be opted for early HV cases, whereas primary fusion of hallux should be chosen for severe cases where the HV angle is equal to or more than 40 degrees to avoid recurrence (15,18).

For the early stages of rheumatoid forefoot deformities, several modifications in techniques were developed to preserve the articular range of motion and to achieve better anatomic correction. Such alterations were well described by a French foot surgeon, Piclet-Legre´ including selective tenotomy of the flexor tendons (19). This selective tenotomy sustains the grasping function of the toes. In the year 2015, a paper published by Frey et al. (20) reported their results from a series of 57 feet presenting an isolated second toe PIPJ deformity without metatarsalgia or DIP deformity treated with a selective FDB tenotomy, plantar PIPJ release, and P1 osteotomy. In 42% of cases, extensor tenotomy was the choice. Subjective results demonstrated a total satisfaction rate of 89.5%, among them 98% for cosmetic results, and 81% for pain relief. Only 12% of toes were rigid, that is, stiffness in PIPJ with the absence of passive flexion. Eighty-six percent of the lesser rays had retained active plantar flexion compared to 74% of the lesser rays who were semi-rigid or rigid before the surgery. A revision was reported only in 2 cases (3.5%) in which PIPJ fusion was carried out (20).

Coming to the point of wound healing and PRGF, normally an accumulation of platelets happens first and then the release of growth factors takes place. According to articles published, the final concentration of platelets of PRGF is an excellent concentration of platelets (21,22). Fibroblast generation was highly influenced by pH changes mainly due to the high concentration of platelets which was proposed by Liu et al. (23) that the diminished growth was dependent on pH.

The main surgical goal is to put the patients in conventional shoes. The follow-up shows that the need for customized orthopedic shoes after surgery was restricted to 36.7% of patients and this was made possible especially after resection arthroplasty, whereas, between 45% to 91% of patients needed special shoes (24).

Pain management is an important factor in any postoperative period. Improved postoperative pain management is also reported in several other techniques (18,25-29). Reports from our study state that the percentage of patients not experiencing pain was 35% whereas under strain was 40 % (Table 3). It could explain the reason behind the depreciation of walking distances without shoes in many patients resulting in prolonged pain relief than usual. It is noted that other groups with identical surgical manipulations have reported a better percentage of pain-free participants mainly because of better distribution of plantar pressure and reconstruction, but results of long-term follow-up are unavailable.

Re-establishing forefoot function is the most challenging factor in any forefoot arthroplasty. And this becomes no exemption in serious techniques like Hoffmann-Clayton. The one-legged stand was possible only by a few participants, whereas the one-legged tiptoe stand was even challenging for healthy or unoperated patients (Figure 5). One of the reasons identified by Hoffmann-Clayton (9) can be progressive stiffness in the joint. Other methods such as modified metatarsal shortening offset osteotomies can improve clinical scores but have some limitations, especially in the range of motion.

Limitations in the Study

Retrospective study: self-made questionnaire emphasized key issues of reconstruction surgery of the forefoot. As other established questionnaires like Foot and Ankle Disability Index or the Foot Function Index do not cover forefoot deformities, shoe wear, or the gripping or standing function of the toes.

Treatment regimens: Specific treatment regimens of rheumatoid patients were not gathered. This plays a vital role as antirheumatic medications are well developed and reduce the incidence of severity in forefoot disorders compared to 20 years ago.

Patient selection: There were difficulties in patient selection as it mainly depended on the number of patients who returned a questionnaire. A definitive dropout analysis could not be carried out. Various attempts to increase the number of participants did not work out due to dementia, aging, lack of interest, etc.

Clinical follow-up: deficit of clinical follow-up examinations was an issue. Nevertheless, the responses by most participants even after a long postoperative period provide relevant comprehension for surgeons opting for similar type of surgery in their practice.

CONCLUSION

3-year research illustrates compelling prolonged outcomes after the surgery. We could derive that pain experienced during rest was reduced in most patients (>70%) and above 60% of patients could use conventional shoes. Moreover, they had relevantly improved walking distances by wearing shoes than barefoot. Assessing forefoot function was difficult, especially in severe rheumatoid cases, but Hoffmann-Clayton manipulation continued to yield prolonged satisfying results, especially with the administration of PRGF for basic standing functions. PRGF strongly stimulates cell viability and growth. Overall, above 80% of patients were well pleased with the outcome. Thus, we could derive that minimally invasive surgery for mild RA cases and Hoffmann-Clayton for severe RA cases especially with infiltration of PRGF gives better results. PRGF favours the treatment by minimizing the rehabilitation period, post-operative edema, pain, and better cosmesis.

All patients were given written informed consent. No animal experiments were done.

Author Contributions. All authors have contributed to manuscript writing and hold full responsibility for the content mentioned.

Conflicts of Interest. No conflicts were declared.

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