VOLUME 71 | ISSUE 3 | JULY - SEPTEMBER 2020 ISSN 2241-4347

ACTA ORTHOPAEDICA ET TRAUMATOLOGICA HELLENICA

SPECIAL ISSUE
Hand Surgery and Microsurgery in Greece - Part 2

Official Journal of the
HELLENIC ASSOCIATION OF ORTHOPAEDIC SURGERY AND TRAUMATOLOGY
Athens Academy Award 2004

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HELLENIC ASSOCIATION
OF ORTHOPAEDIC SURGERY
AND TRAUMATOLOGY

Published by: ZITA MEDICAL MANAGEMENT S.A.
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INSTRUCTIONS TO AUTHORS

1. Scope

"Acta Orthopaedica Et Traumatologica" is the official journal of the Hellenic Association of Orthopaedic Surgery and Traumatology, first published in 1948. This revived edition of Acta Orthopaedica Et Traumatologica, published in English, aspires to promote scientific knowledge in Orthopaedics and Traumatology worldwide. It is a peer-reviewed Journal, aiming at raising the profile of current evidence-based Orthopaedic practice and at improving the scientific multidisciplinary dialogue. Acta Orthopaedic Et Traumatologica Hellenica presents clinically pertinent, original research and timely review articles. It is open to International authors and readers and offers a compact forum of communication to Orthopaedic Surgeons and related science specialists.

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The journal follows the guidelines of the International Committee of Medical Journal Editors (www.icmje.org). For all original articles a statement in the text of approval from the local ethics committee, a statement that research was performed according to the ethical standards as described by the Declaration of Helsinki and a statement that informed consent for participation in the study was obtained from all subjects, are required. In case of study with animals the following statement needs to be added in the text: "All applicable international, national, and/ or institutional guidelines for the care and use of animals were followed".

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10. Figures and Tables

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Figures need to be of high quality. Vector graphics, scanned line drawings and line drawings need to be in bitmap format and should have a minimum resolution of 1,200 dpi. Halftones (photographs, drawings or paintings) need to be in TIFF or JPEG format, up to 174 mm wide and up to 234 mm high and in minimum resolution of 300 dpi.

Patient anonymity should be ensured. All identifying data (name, identification numbers, initials) must be removed from text, images and tables. If it is mandatory for a patient's face to be included in the manuscript, the eyes should be sufficiently masked. If there is a possibility that a patient may be identified from a photograph or relevant legend and text, the patient's written consent should be submitted.

A figure caption and a table caption need to be added in the figure and table section respectively for each figure and table.

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All authors (surnames and initials of first name) should be listed when they are three or fewer. If authors are more than three, the first three authors should be listed, then 'et al.' needs to follow the name of the third author.

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or

Papaioannou NA, Triantafyllopoulos IK, Khaldi L, et al. Effect of calcitonin in early and late stages of experimentally induced osteoarthritis. A histomorphometric study. *Osteoarthritis Cartilage* 2007; 15(4): 386-95.

■ Book chapters:

Triantafyllopoulos IK, Papaioannou NA. The Effect of Pharmacological Agents on the Bone-Implant Interface. In: Karachalios Th. (ed). Bone-Implant Interface in Orthopaedic Surgery. Springer – Verlag, London 2014, pp 221-237.

■ Online document:

National Institute for Health and Care Excellence. Fractures (Complex): Assessment and Management. Available via www.nice.org.uk/guidance/ng37. Published Feb 2016. Updated Sept 2017. Accessed January 2014.

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LETTER FROM THE GUEST EDITOR

It gave me great pleasure to accept the invitation of the Editorial Board committee of the Acta Orthopaedica Hellenica journal to coordinate the edition of a volume on Hand Surgery and Microsurgery.

I would like to refer to some milestones that were major breakthroughs for the evolution of Hand Surgery and Microsurgery in Greece.

Everything started in the 1960s when the Head of the Orthopaedic Department, of the University of Athens, in the "KAT" Hospital, Professor G. Hartofilakidis recognised and ardently supported the need for the development of the specialty of Hand Surgery.

In 1967, the first reimplantation of an amputated upper limb proximal to the elbow joint was accomplished by A. Giannikas and P. Ballas, while in the 1970s the team of P.N. Soucacos performed the first reimplantation of an amputated finger with microsurgery techniques.

In the mid 1980s, the Hand Surgery and Microsurgery Department in "KAT" Hospital was organised and headed by N. Daoutis and afterwards by N. Gerostathopoulos. This Department played a significant role in the evolution of Hand Surgery and Microsurgery and gave a high-level training to young orthopaedics in Greece.

During the same period, in 1989, a systematic three-month workshop in Microsurgery in laboratory animals started taking place in the Laboratory for Research of the Musculoskeletal System "Th. Garofalidis" of the University of Athens in the "KAT" Hospital. Since then, more than one thousand surgeons of various specialties have been trained in this lab workshop.

Similar workshops have been organized by the Orthopaedic Department, University of Ioannina, while Microsurgery workshops in lab animals are also organized on a regular basis at the "Soucacos" Orthopaedic Center at "Attikon" Hospital.

Nowadays, we have achieved mastery in Hand Surgery techniques such as brachial plexus surgery, new techniques on peripheral nerve lesions, free flap transfers, toe transfers, arthroscopic techniques, arthroplasties, and gradual expansion of operations on the entire upper limb.

At the moment, surgical teams specialized in Hand Surgery and Microsurgery with rich clinical, educational and scientific experience work in both the public and private health system.

Last but not least, I would like to thank all the authors who have accepted my invitation and contributed to this volume by submitting manuscripts of high quality.

Sincerely,
Sarantis G. Spyridonos

Head of Hand Surgery-Upper Limb & Microsurgery Department
"KAT" Hospital

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ORIGINAL ARTICLE

Dupuytren's contracture: Long-term outcomes and complications after operative treatment with resection of the contracted palmar fascia.

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Department of Orthopaedic Surgery & Musculoskeletal Trauma, University of Thessaly, Greece

ABSTRACT

Dupuytren's disease is a condition that affects skin fascia of palm and fingers resulting in the formation of nodules and cords, and the sequential "Dupuytren's contracture". Fingers are pulled inward and towards the palm, interfering with hand function. Operative treatment of Dupuytren's contracture includes percutaneous division and partial or total excision of the affected palmar fascia. Partial fasciectomy remains the most effective type of treatment in advanced, late stages, although technically demanding. Complications are frequent with the most serious being a digital nerve and artery injury, haematoma formation and skin necrosis, infection, complex regional pain syndrome and recurrence of the disease.

KEY WORDS: Dupuytren's disease, nodules and cords, palmar fascia contracture, fasciectomy, open palm technique

Introduction

Dupuytren's disease represents a clinical entity, typically described as a contracture of the hand palmar fascia which compromises hand function and appearance, affecting more commonly middle-aged males 40 to 60-years-old. The disease was first described in the scientific literature by Guillaume Dupuytren, a French military surgeon [1, 2, 3].

Clinical presentation includes subcutaneous nodules and cords in the palm and fingers usually on the ulnar side of the hand. Cords cause MCP and PIP joint extension lag and stiffness. Functional impairment in everyday activities is associated to restricted range of motion. Moreover, diverse descriptions of patients' clinical experiences do exist, that can influence cosmesis and self-confidence (**figure 1**). Pain though not characteristic of the disease, can be present especially at the early onset of nodules [4, 5].

Antiepileptic drugs, alcohol intake, smoking and diabetes mellitus have been reported as predisposing factors and an autosomal dominant pattern of inheritance has been well described. Prevalence of the disease has geographic variations affecting northern Europeans (up to 30% in Norwegians over 60 years

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of age) while very rare in Africans and Asians [6, 7].

The earlier the onset of the disease, the more likely is thought to be the recurrence and progression [1].

The pathophysiology includes 3 phases: proliferative, involutional and residual. Proliferation of fibroblasts which are transformed into myofibroblast cells and produce abnormal connective tissue and collagen deposition in the palm and fingers, results to flexion contraction deformities via transformation of normal ligaments and bands in pathological cords [8].

Molecular basis has been well documented, with alterations in the disease process including deregulated signaling of FGF, WNT, cytokines, matrix metalloproteinase, and TGF-β, which through a pathological cascade involving vascular constriction and tissue hypoxia subsequently result in abnormal proliferation and differentiation of fibroblasts into myofibroblasts. These increased concentrations of myofibroblasts consequently lead to over-abundance and abnormal modification of ECM proteins, namely collagen type III [9].

There are several treatment options including non-invasive, minimally invasive and surgical interventions. The aim of this study is to present the results of partial fasciectomy. Complications and long-term outcome were studied in a large group of patients with Dupuytren's disease treated with resection of the contracted palmar fascia of the affected rays.

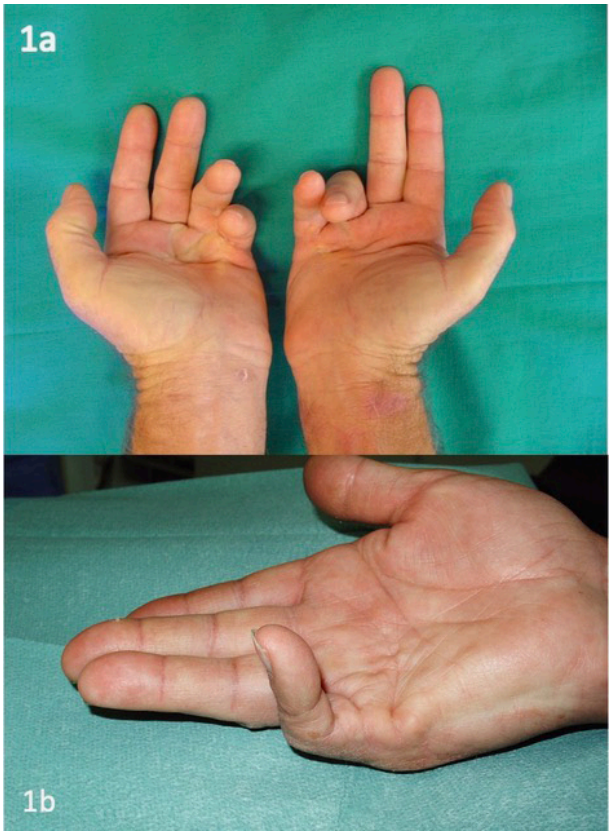

Figure 1: *Dupuytren disease affects usually middle-aged males and in almost 50% of cases, is bilateral. Nodules in palm and cords starting in palm and progressing to fingers are the characteristic findings, located more commonly at ulnar-sided rays of the hand (a). Subcutaneous fibrotic contractures cause extension lag in MCP and PIP joints (b).*

Material and methods

Between January 2000 and January 2018, 234 patients (190 men, 44 women), were treated operatively for Dupuytren's contracture, with excision of the contracted palmar fascia in the affected rays (partial fasciectomy). Indications for operative intervention and subsequent inclusion to the study were: the presence of cord and flexion contraction causing extension lag of more than 25° at the level of MCP joint and more than 30° at PIP joint of ring and little finger (for the index and middle finger the limit is 20°), positive Hueston test and objective functional impairment. In addition, patients' follow-up of at least 2 years was required for inclusion in the present study.

Mean age was 68 years (range 37-86 years). The dominant hand was affected in 146 patients (62,3%). The fourth ray (ring finger) was most often affected (149 patients, 63,6%) with the little finger following, while in 98 patients (41,88%) two or more finger rays were affected. Preoperative flexion contracture at the level of MCP and PIP joints was recorded, with mean values of 38° (range 32-48°) and 32° (range 15-90°) respectively.

Postoperative clinical outcome was evaluated in terms of possible minor and major complications and functional improvement using a standard rehabilitation and follow-up examination protocol. Cases of post-operative haematoma formation, superficial or deep infection, digital nerve and artery injury, wound healing impairment, recurrence, complex regional pain syndrome (CRPS) and cold intolerance were recorded and patients were observed until possible resolution of the condition or additional intervention.

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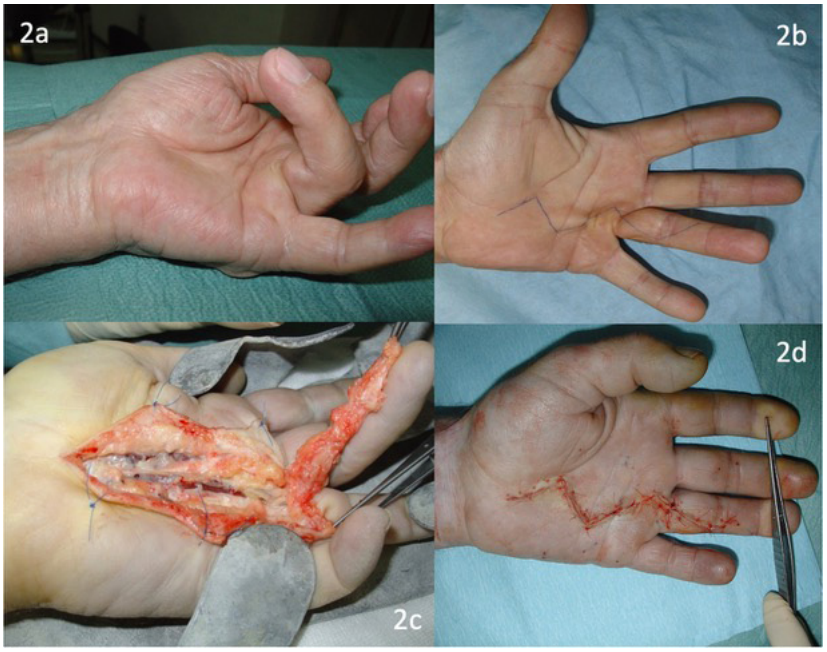

Figure 2: *extension lag of more than 25º at the level of MCP joint and more than 30º at PIP joint, are indications for operative treatment (a). Zigzag incisions are planned, taking into account viability of skin flaps (b). Diseased fascia is excised from proximally to distally. Neurovascular structures must be recognized and protected through-out the procedure (c). Surgical wounds are closed without tension and not hermetically, to avoid haematoma formation subcutaneously (d).*

The post-operative flexion contracture was objectively recorded in degrees at MCP and PIP joints immediately postoperatively and at the long-term follow-up. Functional results and post-operative patients' satisfaction were evaluated using the DASH score.

Operative technique

The procedure was performed with the patient lying in supine position with the hand over an arm support extension table. Axillary nerve block anesthesia was performed in all patients by anaesthesiologist experienced in regional anaesthesia techniques. A tourniquet was applied at the arm and magnifying surgical loupes were used in all cases. After preparing the operating field in an aseptic manner, zigzag incisions were designed in the palm and conducted avoiding passing vertically the palmar creases (**figure 2b**). Superficially dissection starts proximally in the palm and after recognizing neurovascular bundles, continues distally, creating full-thickness skin flaps. Diseased fascia is excised from proximally to distally. Extension to the affected fingers is performed by the Bruner type incisions (**figure 2c**). Vertical septa are resected, and capsular release is carried out via checkrein cut, if necessary. Protection of the neurovascular bundles in all stages of the procedure is mandatory, especially at the level of proximal phalange where the spiral cord can transpose the digital neurovascular bundle medially and superficially (**figure 3**). Meticulous haemostasis is performed after tourniquet release in order to restrict possible haematoma formation and subsequent overlying skin necrosis. Primary closure of the wound is carried out by suturing previously created skin flaps without tension or by the z-plasty technique (**figure 2d**). In cases that the skin was infiltrated by the disease, or skin defect has been created, wound is left to close by secondary healing process (McCash technique) or full thickness skin grafts are used. Finally, a boxer dressing is applied (**figure 4**).

Post-operative rehabilitation protocol

A splint is applied for 24-48 hours post-operatively and the hand is kept elevated. Mobilization starts after 3-5 days postoperatively and physical therapy as soon as the wound healing has been completed. Night splints are used to reduce pain and preserve the achieved

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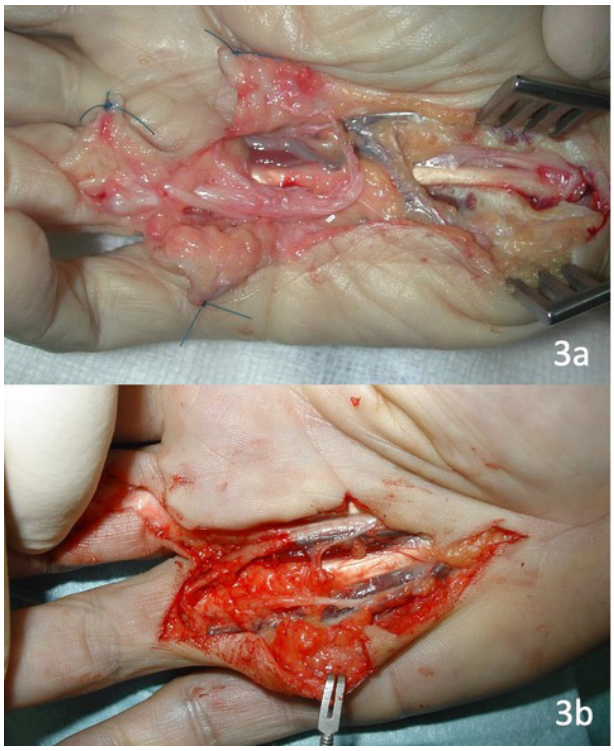

Figure 3: *spiral bands are transformed to fibrotic spiral cords that contracting, displace neurovascular bundle superficially and medially (even across the mid-line) at the region between mid-palm and the base of middle phalange (a). Under these circumstances, intra-operative, iatrogenic injury of digital nerve and artery (more commonly) is a possible complication, especially during secondary surgery after recurrence of Dupuytren disease (b).*

range of motion instead of 24h splinting. Post-operative follow-up was conducted on an outpatients' basis every week until complete wound healing, at 3 and 6 months and every year later on.

Results

Patients' post-operative follow-up period was ranged from 2 to 16 years, with a mean duration of 10 years. The average pre-operative extension deficit in the MCP and PIP joint was 38° and 32° respectively. Post-operative value at the final follow-up was 10° in both joints which represents an improvement of 28° (73,68%) and 22° (68,75%) respectively. Mean recorded DASH score value was 38 (range 32-46) pre-operatively and 5 (range 0-35) post-operatively, difference that is statistically significant.

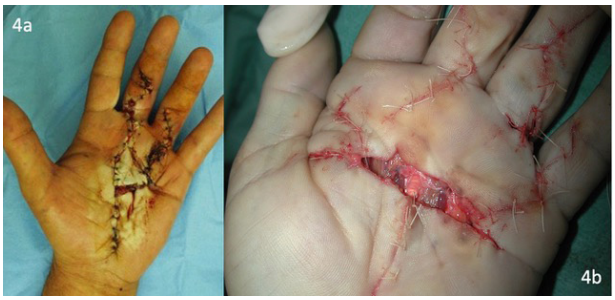

Figure 4: *closure of the wounds may not be uneventful. MCP and PIP joint contracture excision often creates skin defects and forceful approximation can violate blood supply of skin flaps (a). Therefore, wound can be left partially open to heal by secondary intention (as in McCash technique) (b).*

Complications occurred in 61 patients (26%) including 16 cases of recurrence, 15 cases with CRPS, 7 superficial infections, 5 injuries of digital nerves, 7 sensory neuroapraxias and 7 patients with cold intolerance. Digital nerve injury required immediate end-to-end repair, while sensory neuroapraxias resolved after a mean period of 6 months (range 4-8 months) without intervention. Cold intolerance was observed to subside at two years post-operatively and in one case amputation of the distal phalange was performed 2 weeks postoperatively due to delayed ischaemia in a patient with a history of atherosclerosis. Three patients were treated with arthrodesis as a salvage procedure for non-reducible flexion contracture at the indexed operation.

Discussion

Dupuytren's disease is a non-traumatic, progressive disease of the hand which involves fibrotic cords in the fascia of the palm and fingers, leading to formation of nodules, cords and contracture of the affected rays usually on the ulna side of the hand (**figure 1**). There is a higher reported incidence in men, white, hypertensive patients as well as older, diabetic individuals who have higher consumption of alcohol [10, 11].

An increased prevalence of Dupuytren's contracture has been found in working population using pneumatic tools, compared to other working groups [12]. In a recent meta-analysis, manual laborers using vibration tools appear a higher risk of developing Dd with a prevalence of 9.8% and 3-fold higher incidence

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compared with controls [13].

On the other hand, genetic linkage between Dupuytren's contracture and epilepsy is possible, taking into account a 40% prevalence in male chronic institutionalized epileptics over 40-years-old and geographic distribution of the disease, as well [14]. The rapidly progressing contractures, presenting in young persons indicate a strong 'Dupuytren's diathesis'. Such a defined diathesis can be recognized in cases of strong family history, early onset of the disease, and diffuse conditions with dermal involvement, as Dupuytren disease can be associated with similar lesions found in other body regions like Garrod's nodules or Peyronie and Ledderhose diseases [15].

Apart from the consecutive bad cosmesis, functional impairment related to the disease can be severe, with the most disabling self-reported limitations affecting activities such as body washing and grooming, putting on gloves, shaking hands, and performing fine hand movements in general. [16].

Several treatment options have been reported varying from non-operative to operative techniques.

Non-invasive treatment includes physiotherapy and splinting. More sophisticated techniques as extra-corporeal shockwave therapy, fractionated CO_2 laser, and radiotherapy have been proposed but the evidence is still weak and does not clearly support their practical use [17, 18, 19]. Furthermore, based on the molecular mechanism of the disease, a novel, non-invasive, molecular therapy has been proposed for investigation [20].

Minimally invasive treatment options include Clostridium histolyticum collagenase (CHC) injection (Xiapex®) and percutaneous needle fasciotomy (PNF). Both can be office-based procedures, offering fast recovery, low complication rates and significantly lower costs when compared with surgical intervention. However, both are associated with high recurrence rates, ranging from 30% to 80% over a 2 to 5-year follow-up [21, 22, 23].

On the other hand, partial or total fasciectomy and dermofasciectomy are surgical procedures that are usually applied in most advanced stages of the disease. They aim to excise nodules and cords of fibrotic tissue releasing the contractures of the affected rays. Palmar aponeurosis is completely excised in total fasciectomy. In more severe cases Hueston dermofasciectomy is used [24, 25].

Comparing minimally invasive and surgical treatment options, PNF has the lowest overall direct cost and CHC is much more cost-effective compared with fasciectomy. However, taking into account the recurrence rate of CHC, especially in cases of more severe PIP joint contractures and young age of initial intervention (predictive factors of possible re-intervention after collagenase injection), fasciectomy turns out to be still the more widely used treatment [26].

In our case series, partial fasciectomy was the treatment of choice. Excision of the affected and contracted palmar fascia showed to be an effective procedure in the treatment of Dupuytren's contracture. The results show significant reduction of extension lag in MCP and PIP joints with consequent improved patients' satisfaction rate (**figure 2**).

McFarlane in late 80's stated that "it is not necessary, nor wise, to operate upon a patient simply because the disease is present". The presence of a large cord interfering with hand function, however, would constitute a well-established operative indication. As a general rule, surgery is justified for contractures of 30° or more at the MCP joint due to the eventual risk of post-operative complications [27].

However, fasciectomy remains a technically demanding method, especially in cases where the contracted fascia is extended distal to MCP joints, requiring hand surgery and microsurgery expertise. Care must be paid in the following three steps of the surgical procedure: making of incisions, neurovascular bundles dissection and wound closure.

Skin incisions must be carefully planned in order to provide access to the subcutaneous fascia that must be excised, anticipating possible extension need without compromising skin blood supply. In case there are two or more affected rays and contractures distal to MCP joint, in the proximal phalanges, pre-operative planning of complex incisions and Z-plasty technique may be needed for giving the ability of skin elongation over the contracted area. Excision of the fascia too superficially can create avascular skin flaps that will be necrotized, delaying wound healing and increasing infection rates (**figure 2, 4**).

Neurovascular bundles must be carefully rec-

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ognized and protected throughout the procedure. Pathologic cords transpose the proximal digital neurovascular bundle medially and superficially and such distorted anatomy may put it in danger, especially in revision cases, requiring special surgical skills and familiarity with the specific anatomic area. Microsurgical skills are essential not only for the safe handling of these structures but also for the repair of possible intra-operative injuries of the digital artery and nerve. Arteries are more commonly injured and both structures are in greater danger during secondary surgery in case of Dupuytren's disease recurrence. In our case series, there were 5 patients (2,13%) with intra-operative digital nerve laceration treated with immediate end-to-end repair using microsurgical technique while no arterial injury was occurred (**figure 3**).

Wound closure without tension and meticulous intra-operative haemostasis to avoid hematoma formation, are prerequisites. Skin complications include necrosis subsequent to bad surgical technique or to haematoma formation, inadequate coverage and infection. Our results regarding wound healing complications include 7 cases of superficial infection (2,99%), but no recorded skin necrosis or deep soft tissues infection. To prevent or cope with these complications, suitably planned skin flaps can be re-ordered to facilitate skin elongation in a Z-plasty mode. Alternatively, full thickness skin grafts can be used. However, secondary wound healing is an option in cases that complete primary wound closure is impossible. As it has been described by McCash in the "open palm" technique, skin defects in the palm are very well healed by secondary intention (figure 4). Studies on this procedure give satisfactory results including less pain, better motion, and low complication rate regarding hematoma, skin necrosis, and infection [28, 29, 30, 31]. Malingue's procedure and Z-plasty are simple local flap techniques while other described flaps, like Cronin cross-finger flap or Ekerot dorsal intermetacarpal flap are considered as a second-line treatment, keeping in mind the implied donor site sequelae [32, 33, 34].

Le Gall and Dautel have proposed the 3-flap plasty for defects reaching up to 40% of the palmar surface of the proximal phalange in order to allow a tension-free skin closure. This type of coverage involves incisions delineating three local flaps: a radially based quadrangular palmar flap, a triangular proximally based laterodigital flap and a distally based triangular web space flap. This technique has been found reliable, making it possible to achieve skin closure in serious cases, without skin necrosis [35].

Our post-operative rehabilitation protocol includes beginning of physiotherapy as soon as possible in order to achieve early movement and return to the desired functional level. However, several studies have shown that an increase of range of motion is poorly correlated with patients' reported hand function improvement [36, 37].

Hand's appearance might be also important to patients with Dupuytren's disease, as suggested by the large improvement in the 'aesthetic' subscale that is greater when compared to finger goniometry improvement and function-related subscales. These findings are in line with analogous ones in patients with degenerative or inflammatory joint diseases or with injuries, who despite the clear loss of function, still have concerns about hand appearance [38].

Though complex regional pain syndrome (CRPS) complication of Dupuytren's disease operative treatment is considered relatively rare generally, patients unable to cope with early physical therapy were found to be prone to develop it. In our study there were 15 cases with post-operative CRPS treated with repeated week sessions of i.v. steroid and anaesthetic drug therapy via Bier's block. Cold intolerance was noticed in 7 patients (3%) and it is one of the most common complications of Dupuytren's disease operative treatment. As after any hand surgery, altered sensitivity to the cold can be present. It resolves gradually often over several winters but meanwhile it can be quite annoying, and gloves need to be used in a permanent basis during cold seasons.

Recurrence is another surgeon's great concern in terms of preferred treatment. Patients with recurrent disease often have larger extension deficit and worse self-assessed hand function and complication rates appear to be higher. On the other hand, treatment of recurrent Dupuytren's disease seems to be as effective as the initial treatment, in reducing contracture correction and improving patient reported hand func-

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tion [39]. Recurrence appears histologically the same after limited fasciectomy or collagenase injection [40]. In patients where recurrence is noted soon after fasciectomy, diathesis for further tissue production is very strong indeed. In such cases, great care must be taken to select the appropriate surgical procedure, which will achieve to arrest this process probably by involving dermofasciectomy or skin replacement [41]. In our study, there were 16 cases of recurrence observed at a minimum of 2 years follow-up (range 2-7 years). Only 2 of these patients accepted to be re-operated due to severe functional impairment (post-operative DASH score higher than 30).

Conclusion

Excision of the contracted palmar fascia is effective in the treatment of Dupuytren's contracture. Although it is technically demanding, it remains the most effective type of treatment in advanced stages. Complications, early and late, are frequent with the most serious being digital artery and nerve injury, infection, complex regional pain syndrome and recurrence of the disease. Early complications need immediate and appropriate treatment for a satisfactory outcome while recurrence may compromise the final long-term outcome.

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Athanaselis E.D., Papageorgiou F., Deligeorgis D., Dailiana Z.H., Malizos K., Varitimidis S.E. Dupuytren's contracture: Long-term outcomes and complications after operative treatment with resection of the contracted palmar fascia. *Acta Orthop Trauma Hell* 2020; 71(3): 107-115.

ORIGINAL ARTICLE VOLUME 71 | ISSUE 3 | JULY - SEPTEMBER 2020

The patient's approach in congenital hand differences

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ABSTRACT

The patients with congenital hand differences need a special approach which is often complicated, as it involves the delicate handling of psychological issues, the crucial decision-making process concerning the treatment and its timing, as well as the careful prognosis of the evolution of the congenital difference with growth. Depending on the type of the congenital difference of the child, referral for genetic counseling is important, as is the meticulous clinical examination and consultation for the exclusion of concomitant anomalies of internal organs and life-threatening medical conditions. The physician has also to take in consideration the child's adaptation to its disability and the alterations that any correction might cause at functionality's expense, as well as the important issue of every function's cortical representation that changes with age.

KEY WORDS: Congenital hand differences, timing for surgery, radial club hand, Fanconi anemia, cortical representation

Introduction

The recently introduced word "differences" was established in the literature as a substitute to the terms "malformations" and "anomalies", in order to avoid the subsequent verbal discrimination of children born with abnormal hands and the psychological effects such abnormalities can cause. The professional approach of a young patient and his or her family in those cases is often complicated, as it involves the delicate handling of psychological issues, the important decision-making process concerning the treatment and its timing, as well as the careful prognosis of the evolution of the congenital difference with growth. The physician has to also take in consideration the child's adaptation to its disability and the alterations that any correction might cause at functionality's expense, as well as the important issue of every function's cortical representation that changes with age.

Parental responses to the child's hand abnormality

The birth of a child with a visible congenital difference influences its family in many ways. The parents usually go through phases of denial, anger and distress [1] in varying forms and intensity. These early responses reflect their sense of loss of an anticipated "perfect" baby. Additionally, a sense of lack of control and anxiety about future pregnancies is added to this loss. Another important matter is other people's opin-

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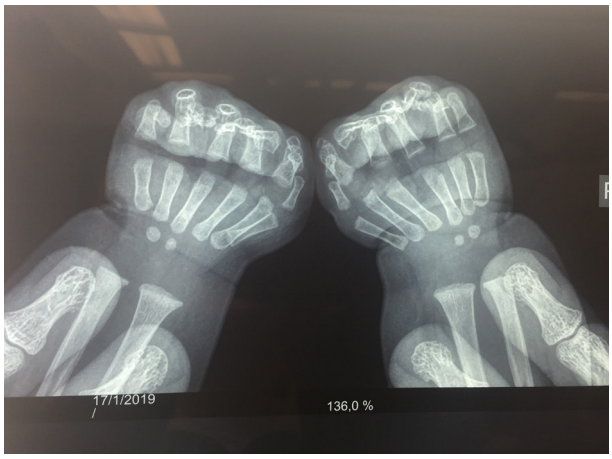

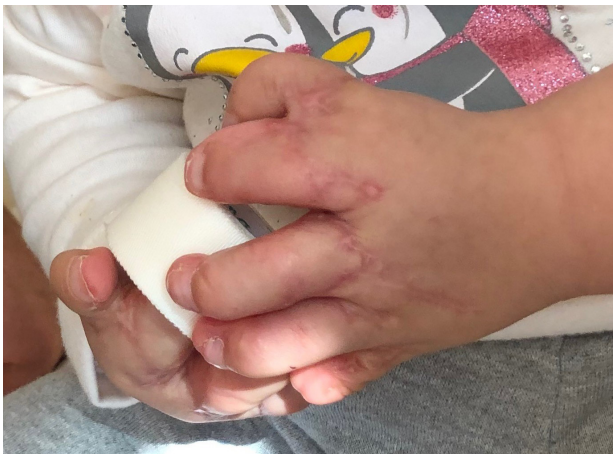

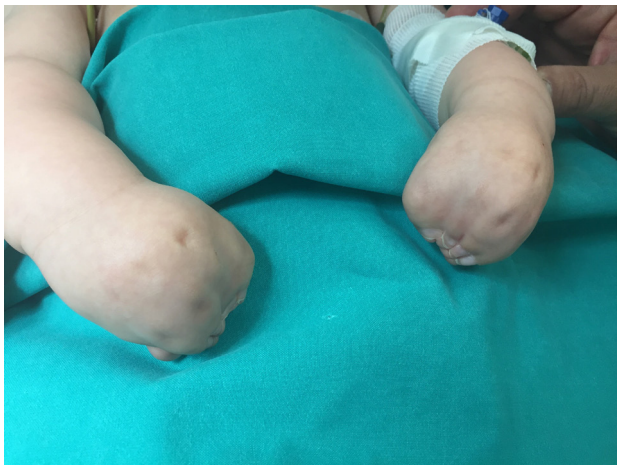

Picture 1: *Complex bilateral symbrachydactyly with polydactyly and early post-op results after four bilateral surgeries. The child's parents were informed from the beginning about the series of early surgical interventions needed and the results expected in terms of function and appearance.*

ions, including the response of family members to the child's malformation.

Although all parents feel enmeshed in the lives of their children and have a fundamental sense of responsibility for them, their course of adjustment to the difference of their baby's hand, varies [2]. Some are able to accept the situation and look for the best available treatment solutions, while others go through a long process of unresolved denial, grief and distress that emerges over the years. They usually feel a strong emotional sense of personal guilt and shame that leads to the tendency to hide the baby's hands. Furthermore, parents might encourage the child, as it grows, to keep the deformed hand covered, which has a devastating impact on the functionality of the whole upper extremity of the child due to lack of usage [8].

First consultation

During the first consultation, a thorough clinical examination must be conducted, followed by a detailed discussion with the parents. The best and most practical support that can be offered is a detailed and factual explanation of the incidence of these anomalies, their genetic heritage, the potential for growth, and the role of surgery in providing increased function and cosmetic improvement [3]. Depending on the type of the congenital difference of the child, the parents should be referred to genetic counseling and the young patient must be meticulously examined in order for concomitant anomalies of internal organs to be ruled out [9]. This is specifically important in cases of radial ray deficiency, which has been associated with almost every possible non-syndromic congenital abnormality as triphalangeal thumb, radio-ulnar synostosis, syndactyly, scoliosis, Sprengel deformity, club foot, congenital hip dislocation, ventricular septal defect, patent ductus anteriosus, lung abnormalities, cleft lip and palate, tracheoesophageal fistula, anal atresia, hydrocephalus, deafness, genitourinary anomalies and

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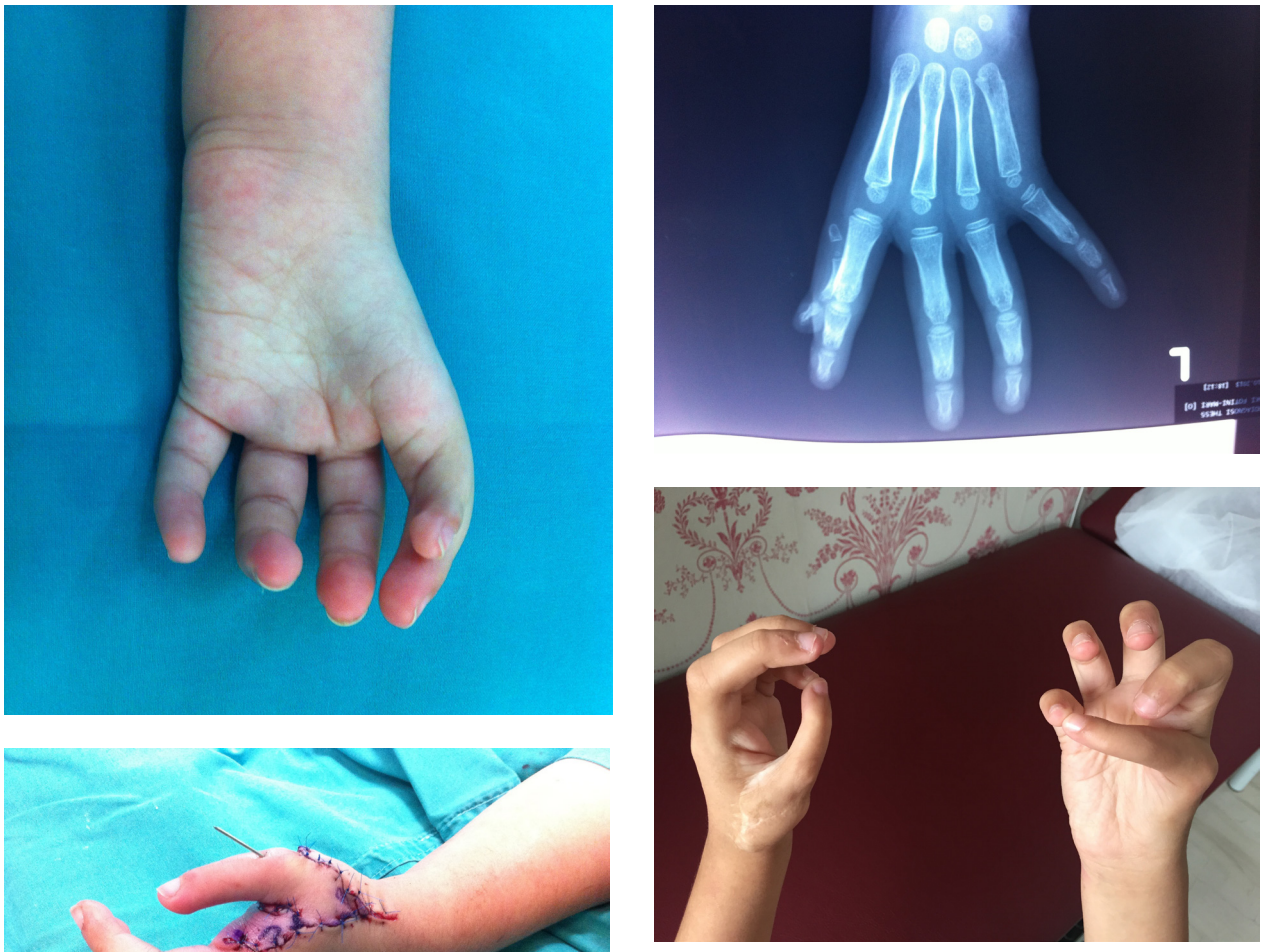

Picture 2: *A five-year old girl with thumb aplasia (Blauth V) of the left hand and right five fingered hand who underwent pollicization of the index finger (L). Because of late surgery she needed a prolonged period of physical therapy in order to incorporate the pollicized finger in her hand's function.*

other syndromes (TAR, Holt-Oram, VATER, Nager, Roberts and others). The most dangerous concomitant condition that needs attention is Fanconi anemia, which is an autosomal recessive disorder characterized by severe hypoplasia or aplasia of the bone marrow with anemia, thrombocytopenia and leukopenia. The pancytopenia usually develops progressively and appears between 5 and 10 years of age, with episodes of generalized purpura, bleeding and recurrent infections. Due to the fact that the prognosis is bad with survival only 2-5 years after the onset, and that bone marrow transplant is the only possible solution, the family and the attending pediatrician must both be alert, so that the child has frequent blood tests in order to achieve the earliest possible diagnosis. A hand surgeon's detailed information and counseling of a young patient's family about the danger of Fanconi anemia can actually save the child's life. In general indications for genetic counseling include: a known or suspected genetic disease in a patient or family, an individual who has a congenital malformation, unexplained mental retardation, advanced maternal age, abnormal prenatal screening tests, teratogen exposure and consanguinity. Genetic counseling should play a

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major role in the comprehensive medical management of a child with a hand malformation.

When discussing with the parents the treatment options, it is very important to define the goals of treatment and explain the specific methods that these goals can be achieved. Many children can clearly gain functional advantage from reconstructive surgery, but for some others the benefit is not always clear and the cost in terms of undergoing surgery and gaining secondary scars might be considerable. In cases that the anomaly's severity does not allow for reconstruction in a way that the hand would be more functional and cosmetically acceptable, the family should be informed about the cosmetic prostheses available, mainly for psychological reasons. The difficulty of balancing the needs of functional improvement with those of cosmesis should be emphasized and the fact that function is always prioritized over appearance should be made clear and be accepted. In case of different cultural priorities – for example cultures in which appearance is more important than function for the female hand – the parents should be given in detail the information that they need in order to make a decision themselves within that context. In addition, the optimal time for surgical intervention must be decided, bearing in mind all the developmental, social and psychological factors. The process of mutual understanding and shared decision-making involving the medical professional, the parents and the child, if appropriate, is absolutely necessary. The surgeon should respond to the needs, beliefs, and wishes of the parents, while also offering professional advice on the matter.

Timing for surgery

The three major goals of hand surgery are to enable the patient to orient his or her hand in space, to provide adequate and sensate skin cover, and to provide the patient a satisfactory power grasp with the ability to handle objects precisely [4]. A number of factors must be considered in organizing the timing of each procedure, including the psychosocial development of the child, the presence of other pathological conditions, the size of the structures to be operated on, and the normal growth and development of the hand [5]. Many congenital conditions as Apert syndrome, radial dysplasia and arthrogryposis require a complex planning of the reconstructions needed.

Historically, pediatricians have been reluctant to allow neonates to be subjected to surgery, due to their limited immune systems and the inherent risk of infection. Currently, urgent surgery is carried out in the first 5 weeks of life, while the child still has the passive immunity conferred by the mother, whereas less urgent procedures are delayed until the child is at least 5 months old, when active immunity has matured. Plans for surgical reconstruction should be designed to be completed by school age so that the child may adapt to and fully use the reconstructed limb instead of self-consciously trying to conceal it. [4]

Congenital differences treated in the immediate neonatal period

Simple procedures can be done conveniently in the neonatal period, such as ligating an extra digit attached by a skin tag or separating an acrosyndactyly connected by a minimal skin bridge. Severe constriction band syndrome that causes distal lymphedema and totally inhibits hand function should be treated by 10-12 weeks of age or ever earlier.

Congenital differences treated during the first year of life

The rationale for early surgery includes the avoidance of deformity and malfunction and the optimal use of infantile tissue plasticity. Syndactyly between border digits of the hand that have unequal length, syndactyly with bony bridges between terminal phalanges, acrosyndactyly with partial aplasia of the adjacent digit and club hand with partial or total radial aplasia are conditions that require early operation, possibly before the age of 6 months, to avoid a progressive bowing deformity. [4] Incongruent and irreversible joint changes may develop if certain conditions are not treated in a timely fashion, such as wedge-shaped triphalangeal thumb and congenital flexion contracture of the PIP joint. Early corrective surgery may occasionally be required for patients with camptodactyly, arthrogryposis and absent or deficient intrinsic musculature if no benefit has been obtained from splinting up to 6 months of age.

Early operation might be required not only because of the rapid growth that occurs in the first 2 years of life, but also because of functional consequences. Sur-

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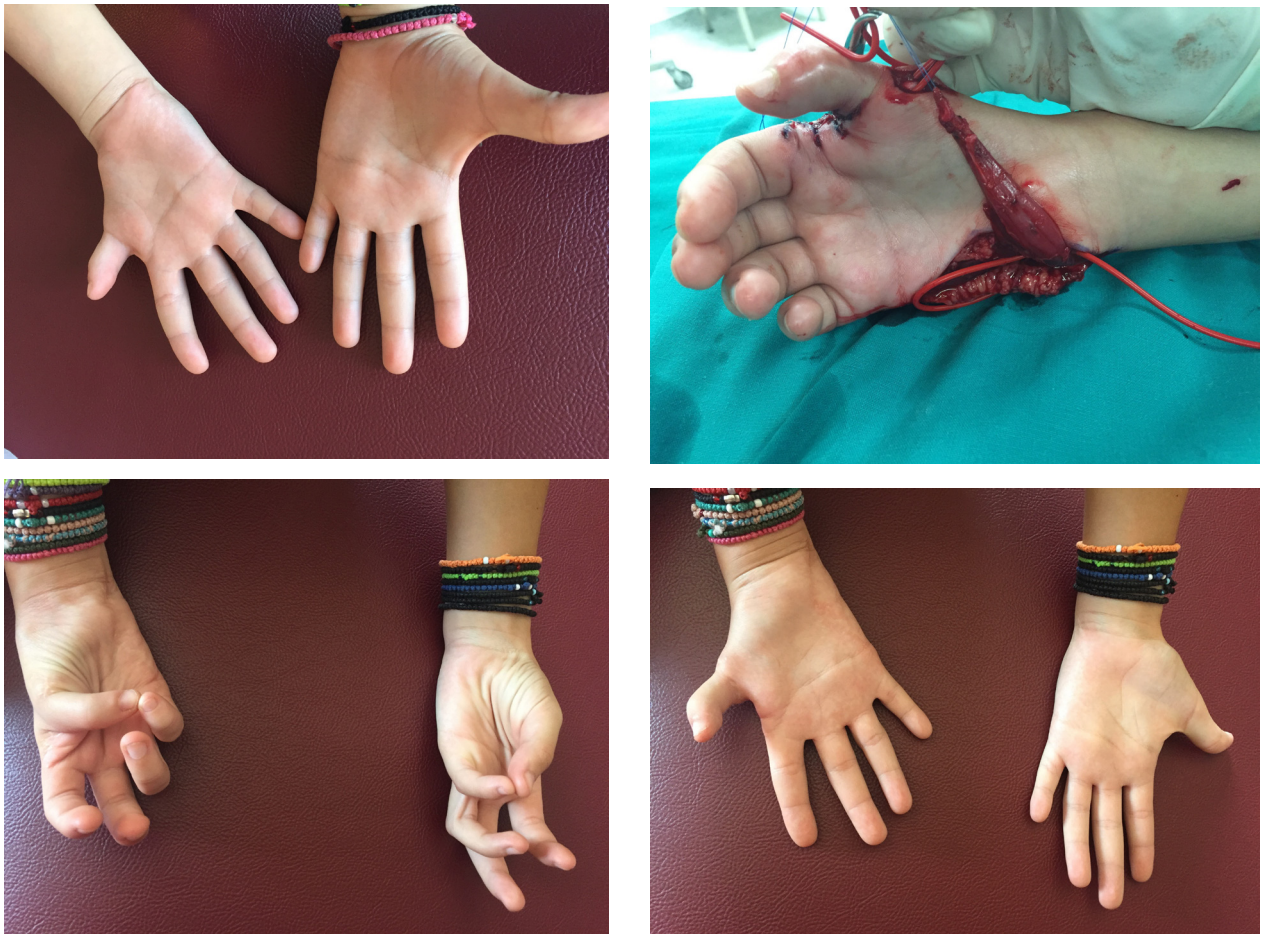

Picture 3: *A girl with Blauth II thumb hypoplasia that underwent Huber transfer with 1st web space Z-plasty at the age of 7 with excellent results.*

gery at a young age is considered mandatory in children with malformations in which hand function may be altered by surgery or in children at risk of developing certain grasping habits that would have to be altered by prolonged periods of physical therapy after corrective surgery, as in cases of cleft hand, proximal thumb duplication (Wassel IV) or pollicization of an index finger for aplasia or severe thumb hypoplasia. In all cases the physical ability of infant bones and soft tissues to adapt to changes produced by surgery in a key factor in deciding when to operate.

Congenital differences treated after the first year of life

The repair of an uncomplicated syndactyly, mild Blauth type II hypoplasia, symbrachydactyly and polydactyly can be put off until the second or third year of life, nevertheless surgery should be completed before school age, especially when several operations are required. One should not rush to treat conditions such as trigger thumb and minor clinodactyly because they may never require surgical correction. Other conditions that may be due to an underlying congenital anomaly with a strong genetic basis (such as certain types of camptodactyly) [7] manifest themselves only in older children. Complicated tendon transfers should generally be delayed until the child is 5-6 years old and able to cooperate in rehabilitation. The surgical treatment of some congenital hand deformities may have to be delayed beyond the first year of life because of life-threatening associated anomalies which must be treated and stabilized first.

Congenital differences that should not be treated

In certain conditions, surgical treatment may ac-

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tually be contraindicated. Lack of elbow flexion in a child with radial club hand is a contraindication to centralization of the hand, since the procedure would hamper the child's ability to move the hand to the mouth and would interfere with tasks as toileting. No treatment is indicated in unilateral or minor synostosis, since attempts to restore active rotation in radio-ulnar synostosis have been unsuccessful in the past. [6] In severe cases, a rotational osteotomy is done through the synostosis, at about 5 years of age.

The case of an older, well-adjusted child on whom surgical correction has not yet been undertaken, for whatever reason, should receive serious consideration, even in the presence of significant deformity, before the hand surgeon agrees to an operation. Soft tissues in older children do not adapt well, and functional patterns have already been established. An older child or a teenager should be psychologically evaluated and it must be explained that he or she should not have high expectations of achieving a normal hand.[7] Unrealistic prognoses are cruel, but because so much can be done for a child with a malformed hand, sympathetic optimism is completely justified. [3]

Conclusions

Surgeons specializing in the care of children's hand anomalies have the opportunity to treat not only the hand but also the child and the family. Understanding the psychological and social issues is an essential part of the care and treatment of the young patient. Early diagnosis of concurrent medical conditions or life threatening situations is of paramount importance. Timing of surgical interventions is also crucial and should be carefully determined. Children with congenital hand differences are challenging patients to care for, but they are undoubtedly the most rewarding, repaying success with years of function.

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ORIGINAL ARTICLE VOLUME 71 | ISSUE 3 | JULY - SEPTEMBER 2020

The role of sensory re-education of the brain in functional restoration of the hand after median nerve re-attachment

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ABSTRACT

PURPOSE: The aim of this study is to prove the role of sensory re-education of patients after the restoration of complete, distal damage to the median nerve, through comparative tests between a group of retrained patients and a group of patients who did not participate into a similar re-education program.

PATIENTS - METHOD: In this study, a comparative evaluation of 63 patients (51 men and 12 women with a mean age of 38 years (20 -51)) with complete, distal median nerve transection and surgical restoration was performed among a group of patients who had sensory re-education and a group without re-education. Evaluation was done through re-education tests that began after successful reattachment and nerve regeneration. The clinical evaluation took place after 18 months, 3 years and 6 years.

RESULTS: From the statistical analysis, the conclusions obtained were that the individuals in the re-educationgroup displayed superiority in the sensoryrehabilitation and functional ability of the hand in a shorter time compared to the non-re-education group, in all the tests, especially in the test concerning the ability of recognition and location of the stimuli in the hand.

CONCLUSIONS: The damage to the median nerve leaves a significant sensory and functional disorder in the hand. Surgical restoration alone is not sufficient for the functional rehabilitation of the hand, which requires sensoryre-education in order to produce better results in a shorter time.

KEY WORDS: Median nerve, re-education, microsurgical technique

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Introduction

Besides the eyes, hands are man's most useful tool for identifying and communicating with the surroundings. These are the first tools of communication with the environment immediately after birth. A person senses the touch and vibrations and perceives the texture, shape and dimensions of the objects he or she touches using the hands, as a collective - sensitive sensory organ. Finally, through hands a person can feel the temperature of the body and the objects. The optical-motorcoordination, which is the synchronized movementof the hand and optical stimuli, leads to the execution of a multiple precision movements making the hand the ultimate tool of creativity and expression of man.

The median nerve plays an important role in the functionality of the hand as a sensory tool. It is the nerve that has the most involvement in the sensory path. The hand is the area of the body with the highest number of receptors per unit area than any other part of the body. Thus,itis the limb with the largest representation in the sensory area of the brain. There, each part of the limb is assigned to a specific part of the gyrus. (**fig.1a,b**)

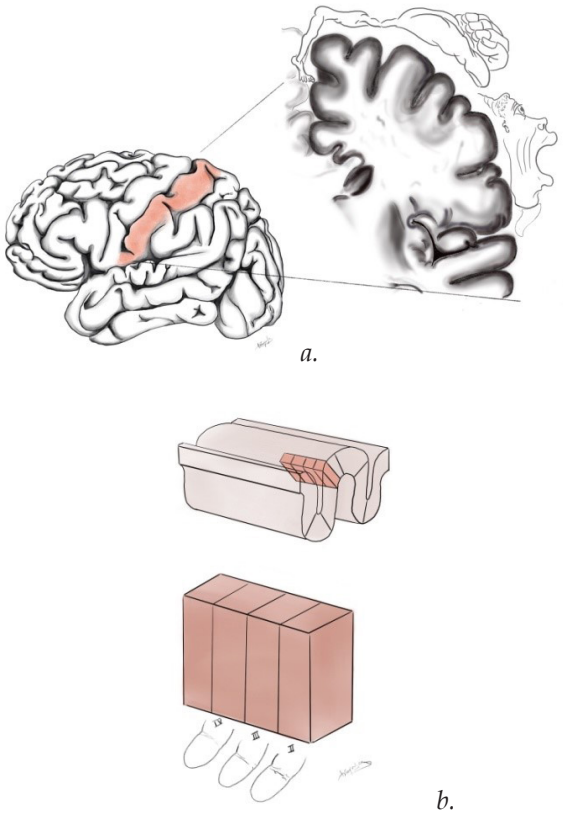

Figure 1. *a. Somatotopic representation of the brain. b. Representation of the final phalanx of the fingers in the sensory area of the brain.*

It is known that the representation of each part of the hand in the somatosensory cortex, in the posterior central gyrus, can vary depending on personal experiences and is related to brain plasticity. For example the representation of the index finger is greater in blind people due to the need for reading by the Braill method, or, the representation of the left hand is greater in the musicians, as it is the hand of skill concerning the musical instruments. (**fig.2**)

The median nerve allows people to "see" with their eyes closed. The amount of receptors in the hand, the abundance of nerve fibers and the size of the sensory field it occupies, the high perception of touch, and stereognosia combined with its large response to the brain, make scientists consider it as human's "third eye".

Neurological damage to the median nerve by disrupting its fibers and the sensory pathway to the brain leads to loss of perception of position and recognition of stimuli, a loss that indirectly affects the motor function of the hand, since the response is related to the receiving and processing of the stimuli. An important part in this is also the loss of kinesthesia, which is important for the functionality of the hand. Thus, people cannot perform tasks without seeing what they touch and how their hand performs them. It is similar to wearing a metal glove and the hand is unable to feel.

Non-neurological repair initially leads the area of the corresponding cortical representation to disorganization. Then, through the plasticity of the brain and the necessary use of the hand, adaptive reorganization occurs over time, with the establishment of new structural and functional nerve pathways in the cortex, with new synapses and a change in nerve networks. [1, 2, 4, 5, 16, 23, 24, 52] It is therefore obvious that immediate nerve repair with nerve suture is required.

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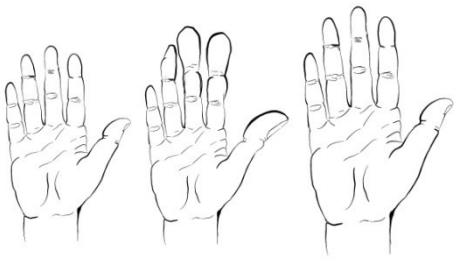

Figure 2. *Differences of hand's representation in the brain, in a blind person (middle) due to increased use of the fingertips that get their stimulation from the median nerve and in a musician (right), due to required increased virtuosity in comparison with the usual representation in a regular person (left).*

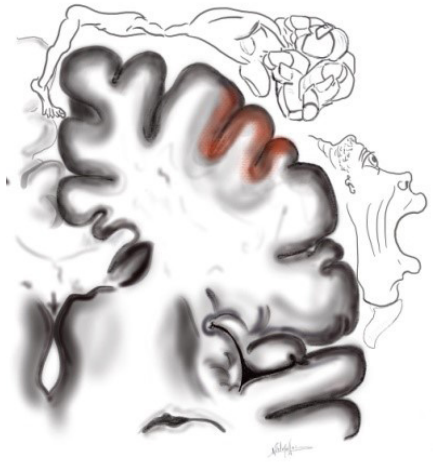

Figure 3. *Disturbance of somatosensory area of the hand after median nerve's transection.*

Successful nerve regeneration will lead to the restoration of the sensory pathway and there-information of the corresponding cortical area. However, after nerve restoration, the brain will have to re-learn to "read" the incoming information by hand such as learning a foreign language. [5, 25, 52]

In nerve reattachment the results are evaluated in the long term with multiple criteria, many of which are subjective, and with various parameters which perhaps are unknown in their entirety. Factors such as the time elapsed from transection to nerve reattachment, the incorrect orientation of nerve regeneration in target organs, the number of fibers regenerated, the age, any co-existing diseases, smoking, alcohol, etc. play an essential role in the process of nerve regeneration. [35, 53]

For this purpose, the idea of re-education[17,21,25,38,55] from the early stages of nerve rehabilitation has been proposed, which will provide more complete functional rehabilitation of the hand in a shorter time. Without re-education the brain has difficulty in re-defining the area that represents the reattached median nerve, unable to interpret the input data from the sensory receptors of the hand. As a result, nerve rehabilitation and nerve regeneration do not lead to full functioninghand rehabilitation, even after successful nerve reattachment and nerve regeneration. [18,28]. (**fig.3**)

Several studies [6,9,17,21,25,38,55] have investigated the benefits of sensoryre-education, using a control group and tests related to hand functionality such as the hand stimulus recognition and locating test, [16, 23, 24, 44, 46] the Moberg Pickup test, [41,45] and the static and moving two-point discriminationtest. [20, 22, 31, 37, 42, 43, 46, 49]

Patients and method

In the present study, a comparative evaluation was performed on 63 patients (51 men and 12 women; mean age 38 years (20 - 51)) with complete,distal transection of the median nerve and surgical restoration with or without sensoryre-education. All patients had low median nerve damage unilaterally and the wounds were neither neglected nor contaminated. **(Figure 4, 5)** Rehabilitation was performed soon after injury in all patients with microsurgery techniques. The study did not include children, as it has been observed that brain dynamics during childhood lead to excellent sensory, functional rehabilitation.[13] Patients with bilateral impairment were also not included, since the healthy hand was used in order to compare sensitivity with the damaged hand as well as cases of major complicated damages (spaghetti wrist).

In all patients included in the study, the surgical technique was found to be excellent and ideal for nerve rehabilitation. After surgical restoration of the limb, a plaster cast was placed on the wrist in few degrees of flexion for immobilization, which lasted

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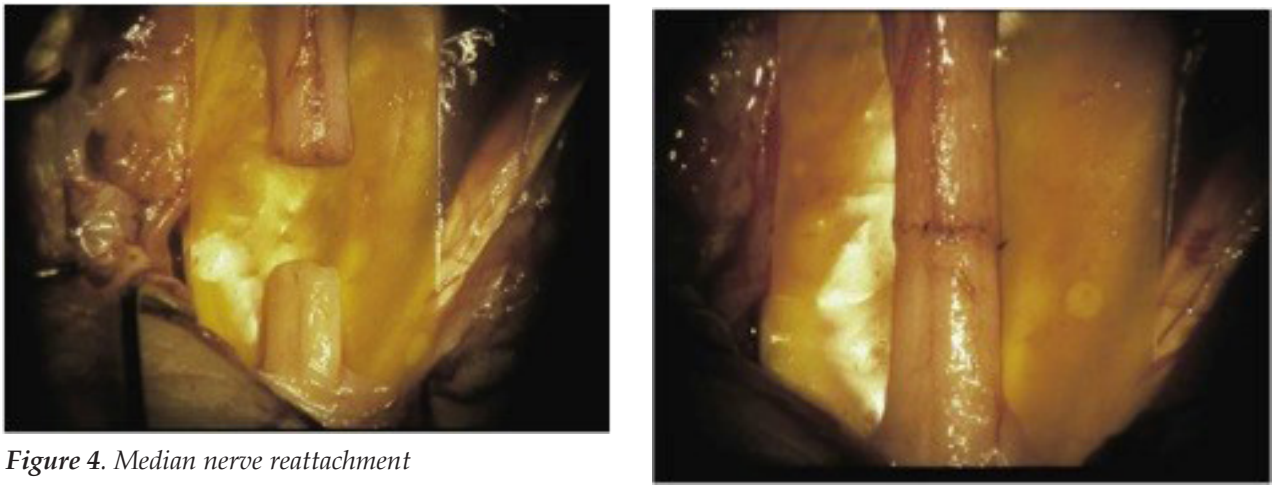

***Figure 4**. Median nerve reattachment*

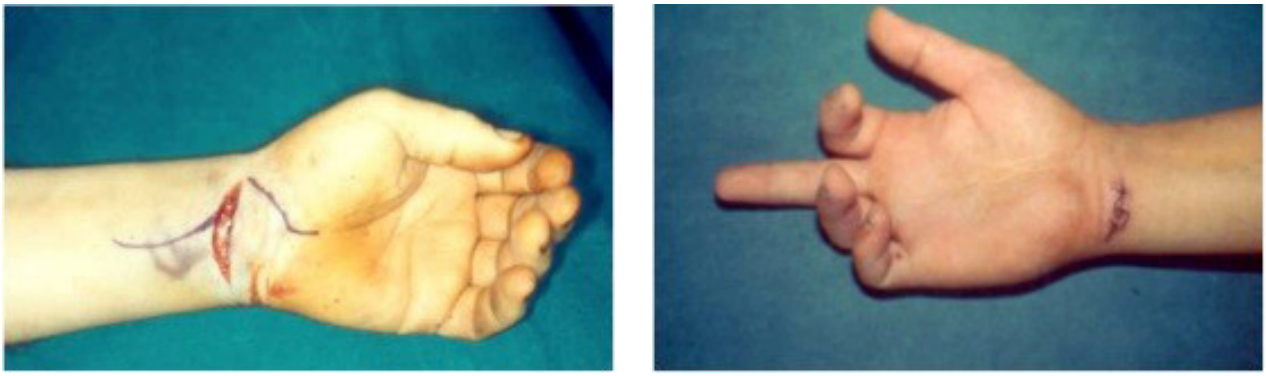

***Figure 5.** Restoration of collateral damages*

for 4 weeks. Patients with sutures of flexor tendons were following a mobilization protocol.

Patients were then entering to an additional 4 weeksprogram of physiotherapy for the restoration of mobility of the stiff joints. In all patients the mobility of the joints and the functionality of the tendons were considered complete and satisfactory.

Postoperatively and after removal of the plaster cast, regeneration of the median nerve was evaluated with the Tinelpoint.Completionofnerveregenerationwasestimatedusinga 256 cpstuningfork (cyclespersecond)atthe 31/2fingertips, approximately 3.5 months (3-4M) inallpatientsincludedinthestudyafterepineuralsuture. **(Figure 6)** The use of the tuning fork as a criterion is based on the fact that once the nerve regeneration has reached the fingertips receptors the vibration will be perceived, even though roughly, diffusely perceptible through the stimulation of the respective receptors. A perceivable sense from the tuning fork means incomplete nerve regeneration. [47]

According to the monitoring protocol, patients were divided into two groups at this time. In group A 32 patients were selected who would undergo a sensory re-education program while in group B, 31 patients selected would not follow a re-education program. Patients were randomly divided. However, care was taken in order to have isometric division of men and women and also even distribution of age. At the same time, in group A, patients who were preferred were those being more cooperative and motivated by the outcome.

Sensory re-education of Group A patients was performed in two stages according to Dellon [18,28,55]. The first stage began when there was a

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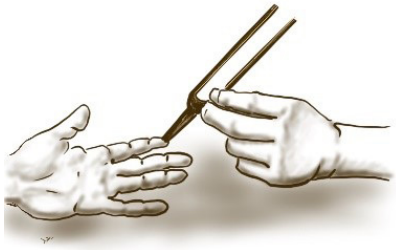

***Figure 6**. Use of tuning fork for the evaluation of the regeneration.*

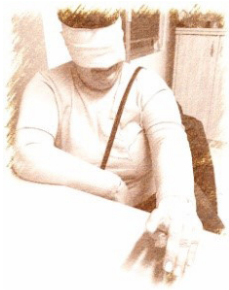

***Figure 7.** Recognition of objects through feeling, with the eyes closed.*

***Figure 8**.Moberg's pick-up test.*

renewal of innervation at the fingertips that get their stimulation by the median nerve. At this stage, patients were asked to recognize the shape, texture, material of different objects from their environment, both with their eyes open or closed [27] at various times. **(Figure 7)** This exercise leads to the stimulation of thebrainin order to identify stimuli received by different sensory receptors of the hand and the development of stereognosia. This stage also includes the stimulus recognition and locating test, using stimuli such as those coming from cotton, pressure from a spike or a blunt object, sting or application of warm-cold on the hand, modified byMarsh [44,46] for the separation and recognition of the senses. At this stage the tests seek to continually irritate the sensory area of the hand corresponding to the brain so that it is gradually reorganized, by re-sensing the area. [17,50]

The second, late stage took place when static and kinetic discrete sensation was perceived in the 3 1/2 Dellon18 fingers from the radius side, about 3.5 months after the start of the early phase. (3-4M). This phase includes: a) the Moberg's Pick-up test, (stereognosia) [41,45] b) two-point discrimination test [31,42,43,49] and recognition ability exercises and c)detectionofseveralstimuli on the hand (locognosia) [44,46].There were also exercises to identify objects through palpation, similar to each other, such as coins, keys and fruits. In addition, at this phase, group A patients were advised to carry various small items in their pockets (keys, screws, dice, fruits, coins) that they were asked to feel and recognize through their pockets without seeing them.

Stimulus recognition testing had a standard execution procedure. Itwasdone four times per day, lasted 10'-15'each time and was performed in a quiet environment keeping the patient's attention. After that, the examination and assessment of patients' progress was being performed weekly. Patients were initially monitored by physicians or physiotherapists and later by their family. Finally, the results were evaluated at 18 months (63 patients), 3 years (40 patients) or 6 years (18 patients) and included the evaluation of patient's test results of both groups.

a) The assessment of the efficiency of the use of the hand, when there is no visual-motor participation and the effectiveness of the re-education at this level was done with the Moberg's Pick-up test, which was performed with the patient sitting in an office in a quiet environment. Inside the office twelve different objects were placed in terms of size, shape,

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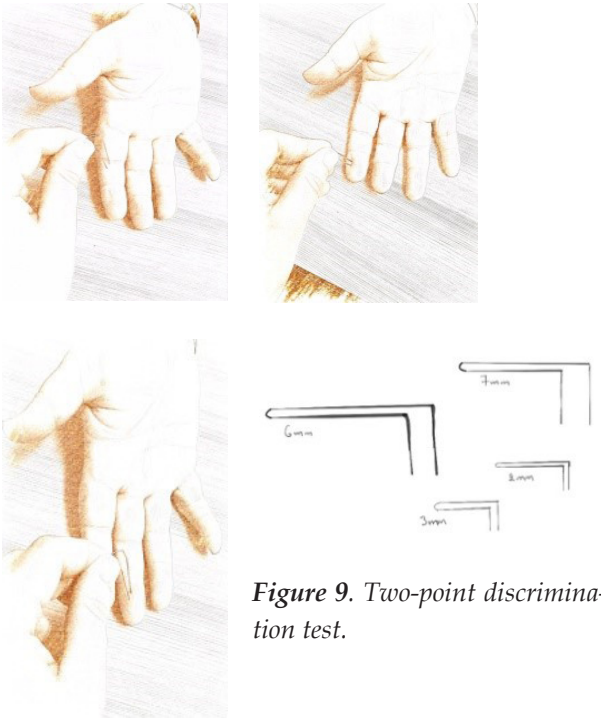

***Figure 9**. Two-point discrimination test.*

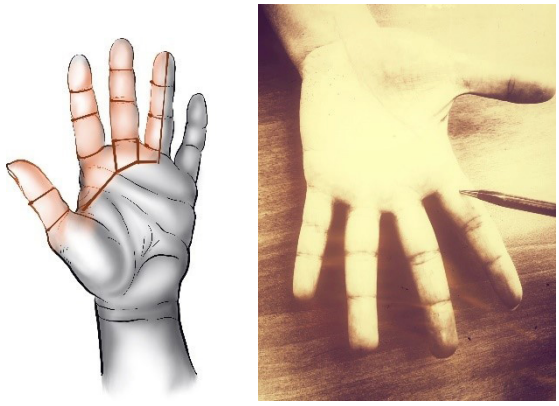

***Figure 10.**Hand stimulus recognition and locating ability test*

texture and construction material. The patient was asked, first with his eyes open, to place the objects one by one in a container next to him. Then, the exercise was repeated with the eyes closed. **(Figure 8)** The average of the time required to complete the placement of all items in the container in both cases was considered as the performance of the test. The grading was based on the performance in four categories: "Excellent", "Good", "Moderate", and "Poor".

(b) According to the two-point discrimination test, the examiner exerts pressure, initially static, along the fingers innervated by the median nerve, on the palm, with pairs of spikes placed 8mm-1mm apart. The purpose is to identify the shortest spike distance that can be seen by the patient as two rather than one touch. **(Figure 9)** The average score on the control fingers (3½ fingers in the radius side) was being noted as the score of performance with grading scale: "Excellent", "Good", "Moderate", "Poor". Then, he applies each pair of spikes moving along the longitudinal axis of the finger from proximal to distal.

The test is based on the fact that the human hand can normally identify two distinct points that are at least 1mm apart, with greater sensitivity at the tips of the fingers that are innervated by the median nerve. Irritation of the skin of the fingers with spikes less than 1mm apart is not recognized as two points. After brain disorganization, discrimination decreases.

c) The hand stimulus recognition and locating ability test was done using the modified Marsh's test, where the fingers that are innervated by the median nerve (thumb, index, middle, radius rim of ring finger) are divided into a total of 14 zones (4 zones for the three fingers and two for the thumb). The examiner randomly touches the zones in the hand of the patient who is asked to identify the touch and mark the corresponding zone in the hand profile with the eyes closed. **(Figure 10)** One point was awarded for each correct detection of a zone and another point was assigned for each exact locating of the position (Excellent: 28 points).

It is obvious that after the transection of the nerve the stimuli in the hand cannot be fully matched due to the disorganization of the cortical area. The re-education aims to reorganize the respective central area through a continuous stream of hand stimuli. [23,25,26,27,54] Performance-based grading was done in four categories: "Excellent", "Good", "Moderate", "Poor".

Evaluations were made each time by the same examiner using the above techniques. Statistical analysis was performed using simple analysis of variance (ANOVA) for baseline data and x^2 test for data recorded in the 4 categories: Poor / Moderate / Good

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TABLE 1 *The grading was based on the performance in four categories for each test*

	Marsh	S2PD	M2PD	MOBERG PICK UP TEST
Poor	0-7	>16mm	>8mm	>30''
Moderate	8-14	12-15mm	6-8mm	20-30''
Good	15-21	7-11mm	4-6mm	10-20''
Excellent	22-28	2-6mm	<4mm	<10''

TABLE 2 *Statistical analysis performed using simple analysis of variance (ANOVA)*

S2PD (a)	**18M-A**	**18M-B**	**36M-A**	**36M-B**	**72M-A**	**72M-B**
>16mm	**5**	**9**	2	4	0	1
12-15mm	**11**	**13**	6	9	3	3
7-11mm	**16**	**9**	12	7	5	5
2-6mm	**0**	**0**	0	0	1	0
Statistical analysis	ANOVA P=0,164 X^2 P=0,197		ANOVA P=0,239 X^2 P=0,275		ANOVA P=0,536 X^2 P=0,572	
M2PD (a)	**18M-A**	**18M-B**	**36M-A**	**36M-B**	**72M-A**	**72M-B**
>8mm	**0**	**3**	0	2	0	0
6-8mm	**5**	**8**	2	4	1	1
4-6mm	**14**	**11**	7	8	2	3
<4mm	**13**	**9**	11	6	6	5
Statistical analysis	ANOVA P=0,203 X^2 P=0,190		ANOVA P=0,170 X^2 P=0,240		ANOVA P=0,724 X^2 P=0,865	
Modified Marsh test(b,c)	**18M-A**	**18M-B**	36M-A	36M-B	72M-A	72M-B
0-7	0	1	0	0	0	0
8-14	3	7	1	2	0	0
15-21	9	16	5	13	1	3
22-28	20	7	14	5	8	6
Statistical analysis	ANOVA P=0,009 X^2 P=0,013		ANOVA P=0,034 X^2 P=0,017		ANOVA P=0,269 X^2 P=0,257	

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Moberg's pick up test (a,b)	**18M-A**	**18M-B**	36M-A	36M-B	72M-A	72M-B
>30sec	5	7	2	3	0	0
20-30sec	11	15	5	11	1	1
10-20sec	16	9	11	5	2	3
<10sec	0	0	2	1	6	5
Statistical analysis	ANOVA P=0,162 X^2 P=0,235		ANOVA P=0.147 X^2 P=0,169		ANOVA P=0.712 X^2 P=0,865	

TABLE 3 *Statistical analysis performed using x^2 test*

S2PD (a)	**18M-A**	**18M-B**	**36M-A**	**36M-B**	**72M-A**	**72M-B**
Poor – Moderate	16	22	8	13	3	4
Good - Excellent	16	9	12	7	6	5
Statistical analysis	X^2 P=0.089		X^2 P=0.113		X^2 P=0.628	
M2PD (a)	**18M-A**	**18M-B**	**36M-A**	**36M-B**	**72M-A**	**72M-B**
Poor – Moderate	5	11	2	6	1	1
Good - Excellent	27	20	18	14	8	8
Statistical analysis	X^2 P=0.070		X^2 P=0.114		X^2 P=1	
Modified Marsh test(b,c)	**18M-A**	**18M-B**	**36M-A**	**36M-B**	**72M-A**	**72M-B**
Poor – Moderate	3	8	1	2	0	0
Good - Excellent	29	23	19	18	9	9
Statistical analysis	X^2 P=0.086		X^2 P=0.548		X^2 P=1	
Moberg's pick up test (a,b)	**18M-A**	**18M-B**	**36M-A**	**36M-B**	**72M-A**	**72M-B**
Poor – Moderate	16	22	7	14	1	1
Good - Excellent	16	9	13	6	8	8
Statistical analysis	X^2 P=0.089		X^2 P=0.027		X^2 P=1	

Results A=group with sensory re-education / B=group B with no sensory re-education
S2PD=static 2point discrimination / M2PD=moving 2point discrimination
Results at 18, 36,72 months of the study
a= A lower value indicates a better performance
b= Mean values with eyes closed and open
c= A higher value indicates a better performance

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/ Excellent. The x^2 test was also used to compare the sum of the results readjusted for two categories of excellent - good versus moderate - poor. (**table.1**)

Results

The statistical analysis ANOVA & x^2, which was performed upon the collection of results regarding the ability to recognize and detect hand stimuli (Locognosia),suggested a statistically significant difference in patients of group A who received sensory re-education compared to patients of group B in the control period of 18 and 36 months.

ConcerningMoberg's Pick-up test using x^2 per group of Good-Excellent results versus Poor - Moderate results, statistical trend was shown for group A patients (who underwent sensory re-education) for 18 months and statistically significant difference in favor of group A for 36 months.

Also, for the M2PD using the x^2 test when grouping Good-Excellent results versus Poor-Moderate, statistical trend was shown in favor of group A for 18 months.

Finally, for the S2PD using the x^2 test when grouping the Good-Excellent results versus Poor-Moderate, a statistical trend was shown for group A for 18 months. (**Table. 2,3**)

Often, the execution of the surgeon's task ends with nerve suturing whereassensoryre-education is neglected. At the same time, more attention is paid to the protective sensation and the motor function of the limb, which, however, is incident to sensation because the hand that does not feel does not move normally. [9,17,29]

Sensation disorder can occur after damage in the sensory pathway at any level and not just after a peripheral nerve transection. The idea of sensoryre-education finds application in all cases where the loss of sensation will lead by the same mechanisms to disorganization of the area and functional redesign in order to compensate for the loss, such as damage to the sensory area of the CNS, [1,15,40, 48,49] transfer of flaps with vessels and nerves, [12, 36, 51] andlimb reattachments [6, 9, 30, 39].

The idea of sensoryre-education in cases of patients with sensory nerve transection is suggested by studies coming from the 1970s by various researchers. [18, 19, 31-38] In all the above studies, regardless the individual techniques applied, the contribution of the method to sensory restoration and functionality was recognized, reducing the minimum limit, that is the threshold of recognizing the stimuli of pressure, touch, perception, position, as well as the restoration of stereognosia. [3, 6, 7, 8, 10, 11, 14, 17]

The above, as well as other techniques, help patients with sensory dysfunction after neurological damage and restoration, to reinterpret the incoming feelings, redefining through the plasticity of the brain the perception of each stimulus separately. Practically, the patient learns again in more detail and in a short time.

Sensoryre-education as a method does not promote nerve regeneration, but promotes the perception and redefinition of incoming information from stimuli of peripheral hand receptors. The goal is the most complete sensory restoration possible.

Thus, after damage and surgical restoration of the median nerve, the method is suggested as necessary for the restoration with the best possible final outcome. [9,10,18,30,31-39]

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REVIEW

Carpal Tunnel Syndrome: Complications and Legal Implications

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ABSTRACT

Purpose. Carpal tunnel surgery, although very frequent, may be complicated by median nerve injury, representing a significant source of litigation in hand surgery. There is no available data regarding negligence claims in carpal tunnel surgery in Greece. The aim of this study was to identify the number of claims related to carpal tunnel surgery in Greece and to estimate the corresponding financial burden to the National Health System.
Material and Methods. All legal claims of negligence for hand and upper extremity surgery that went to a trial, attributed to all surgical specialties, in Greece for a 20-year period were reviewed. Data was further analysed to identify claims related to carpal tunnel release.
Results. One successful claim related to carpal tunnel surgery was identified. The case involved a 36-year-old patient who underwent open carpal tunnel release and suffered from intraoperative injury of the median nerve. After further procedures, the patient was disclosed incapable to work. Subsequently a claim was set, which reached to a trial. An indemnity payment of €20.000 was set.
Conclusion. This is the first report of negligence claim about carpal tunnel surgery that went to trial in Greece. Carpal tunnel release is a common procedure, seldomly accompanied with devastating complications, representing a frequent cause for litigation in hand surgery. Legal claims related to carpal tunnel surgery can be a considerable financial burden for surgeons and health systems. Understanding the factors that lead to successful legal proceedings will help surgeons improve their practice to prevent injury and subsequent litigations.

KEY WORDS: Carpal tunnel syndrome; complications; negligence; iatrogenic; litigation; claim.

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Introduction

Carpal tunnel syndrome (CTS) is a disabling condition commonly presenting to orthopaedic, plastic, neuro- and hand surgeons. It is the most frequent compressive neuropathy of the upper extremity and has been defined as a symptomatic compression neuropathy of the median nerve at the level of the wrist, by the American Academy of Orthopaedic Surgeons (AAOS). Surgical release of the carpal tunnel is the gold standard for the management of CTS. It is a commonly performed hand procedure, with more than 500.000 releases being performed in the United States each year [1-3].

Either an open or an endoscopic approach can be applied for carpal tunnel release. However, neither approach is without risk of complications. Nerve, arterial or tendon injury, incomplete transverse carpal ligament release and incomplete symptom resolution, infection, scar hypersensitivity, and complex regional pain are associated complications. Although rare, they can be devastating and life-altering for the patient. Injury of the median nerve can be sustained during carpal tunnel release with an incidence of approximately 0.1% in both endoscopic and open approach [4]. Median nerve injury has been described as the most common cause for claim in carpal tunnel surgery and has been associated with highest probability for successful litigations [1,2,5].

There have been previous studies on medical litigations related to carpal tunnel surgery, mainly in the United Kingdom and the United States [1-3,6]. However, there is no available literature on medical malpractice in carpal tunnel surgery and in hand surgery generally in Greece.

The purpose of this study is to seek the available data about medical malpractice for carpal tunnel surgery in Greece and compare them with the international malpractice data, and to evaluate the burden of successful litigations in Greece.

Material and Methods

We requested data on all legal claims of negligence for hand and upper extremity surgery that went to a trial, attributed to all surgical specialties, from the archives of the Council of State, in Greece, within the period 2000-2019. We further analysed data to identify the number of claims related to carpal tunnel surgery that went to court, the decision and the total payment, in case of a successful claim.

Our study has been approved by our institutional research ethics board. All data was anonymised, as indicated by the General Data Protection Regulation (GDPR).

Results

Among the malpractice claims that went to a trial in the period 2000-2019, 12 were related to hand and wrist surgery and only one case was related to carpal tunnel release within this period. The claim was successful, and a compensation was set for the plaintiff.

Summary of Case

A 36-year-old female cleaner presented to the orthopaedic outpatient department of a general hospital in Greece complaining of pain and unpleasant tingling in her right hand. She was examined by an orthopaedic surgeon and diagnosed with Carpal Tunnel Syndrome (CTS). Subsequently, release of transverse carpal ligament was performed, under local anaesthesia, by the aforementioned orthopaedic surgeon. Two years postoperatively, the patient visited the same doctor, because of persisting pain and discomfort in her right hand. After clinical examination a diagnosis of De Quervain's syndrome was made and the patient had another operation, performed again by the same surgeon. According to the operative report, release of the sheath of the abductor pollicis longus (APL) and the extensor pollicis brevis (EPB) was performed intraoperatively. However, the patient had no improvement of her symptoms, even after the second operation and for this reason she visited a hand surgeon. An electromyography was performed then, revealing injury of the median nerve and of a sensory branch of the radial nerve. Therefore, she underwent two further operations, but there

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was no improvement of her symptoms. The patient was registered incapable for work.

A claim was set against the orthopaedic surgeon who performed the carpal tunnel release and the first dorsal compartment (APL, EPB) release, four years after the carpal tunnel release surgery. As the patient claimed, the orthopaedic surgeon did not perform any electromyography tests preoperatively and the diagnosis was based only on clinical examination, while intraoperatively he provoked injury to the median nerve and the sensory branch of the radial nerve of her right hand, and finally, postoperatively he gave her no clear explanation about the complications she experienced, nor did he refer her to a more specialised surgeon for their management. As a result, the patient has been registered incapable to work.

The case reached to a conclusion after the testimony of an expert witness. The amount of €20.000 was set as a compensation for the patient. The case closed 12 years after the claim was set.

Discussion

Carpal tunnel syndrome is a common compressive neuropathy. Approximately 4-5% of people suffer from CTS worldwide. It is more prevalent in population aged between 40 and 60 years and most often affects females with rates up to 9.2%, while for men the respective rates are up to 6% [7-9].

A thorough clinical examination is important to be performed before setting the diagnosis of CTS. Phalen's and Tinel's provocative tests can also be used for diagnosis. Nerve Conduction Studies (NCS) have been considered the gold standard for the diagnosis of CTS, since they are objective tests that determine the conduction of the median nerve. The evidence shows that a combination of clinical and electrophysiological studies can better confirm the diagnosis and provide treatment orientation for the physician [7,8].

Carpal tunnel release remains the gold standard for the treatment of carpal tunnel syndrome. More than 500.000 carpal tunnel releases through open, mini-open or endoscopic approach are performed in the United States each year, while the rate of the release in the United Kingdom is 43-74 per 100.000. Patients generally report high satisfaction with the results and prospective studies have shown that approximately 70-90% of patients have good to excellent long-term results following surgical management of CTS [2,8]. However, complications can arise even during operations that are often perceived as routine operations, such as carpal tunnel release. Infection, hematoma, scar hypersensitivity, injury to neighbour tendons and vessels, pillar pain, complex regional pain syndrome and damage to the median nerve have been described after carpal tunnel release [4,7,10]. While these complications are rare, they can be devastating and can affect the quality of life of the patient. Major nerve injuries, during carpal tunnel release procedures, are reported in 0.13% of endoscopic cases and in 0.10% of open cases [4].

Injury of the median nerve during carpal tunnel release has been described as the most common cause for claim in carpal tunnel surgery and additionally as the commonest reason for successful litigations [1,2]. Khan and Giddins analysed 160 claims related to negligence in hand and wrist surgery in the United Kingdom; treatment of wrist fractures and carpal tunnel syndrome were the commonest causes for a claim, 48% and 22% respectively, with median nerve laceration intraoperatively being the commonest cause for litigation (78%) [3]. Atrey et al reviewed legal claims of orthopaedic negligence in the United Kingdom from 2000 to 2006. In a total of 69 hand and wrist surgery claims, 39 claims involved laceration of the median nerve during carpal tunnel release [11]. In a study of 42 cases of carpal tunnel surgery that went to a trial, by Gill et al, the most common reason for litigations was nerve injury (39.1%), followed by persistent pain and numbness (32.6%) and regional sympathetic dystrophy (19.6%). Additionally, 33.3% of these claims ended in decision in favour of the plaintiff, while the remaining claims ended in favour of the physician. Furthermore, in the same study it was reported that there was no signifi-

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cant difference between the amounts of money set as compensations after a trial and for the amounts settled in an out-of-court arrangement [6].

Successful litigations about carpal tunnel release can be a considerable financial burden for the health systems. Krauss et al determined that 33% of litigations for upper extremity nerve injury resulted in an indemnity payment, with a payment rate higher than the average rate within all medical specialties, and with the carpal tunnel release being the most common reason for litigation (41% of claims), with an average indemnity $177.912 per case [5]. In a 2016 study of 60 successful claims about carpal tunnel surgery over a 10-year period in the United Kingdom, it was estimated that the total cost to the NHS was £3.9 million and the mean cost of settlement approximately £65.440 [1].

Iatrogenic injury of the median nerve during carpal tunnel release is a known risk of the procedure and should be always included in informed consent discussions. Additional discussion of the risks of the operation contributes to the development of a trusting relationship between the patient and the surgeon, since patient's trust is mainly based on the impression of clinical competence that emerges in discussions with physicians and surgeons [9]. Sub-standard quality of care has also been described an important factor for initiating a medical claim, as well as the lack of explanation or an apology by the treating physician, when an error had occurred [5,12]. The case presented in the current study filled a claim based on several of the aforementioned reasons: poor preoperative diagnostic approach, poor quality of care resulting to injury of the median nerve and the sensory branch of the radial nerve, absence of an explanation about the complications postoperatively, and failure of referral to a specialised surgeon.

The present civil system in Greece provides compensation for cases of medical negligence. According to the Greek Civil Code's concept of tort, whoever harms another person illegally and culpably is obliged to compensate him (article 914, Civil Code). The conditions of liability for compensation based on the tort law are: i) the unlawful act or omission, ii) the fault, iii) the damage and ix) the causal link. The indemnity payment that was decided in the present case was €20.000. It is much lower than the average payments that were described in previous studies by Awjani and Ganesh [1,2]. Since this has been the only malpractice claim for carpal tunnel surgery that has reached the court in Greece, there has been no available case law regarding compensation for similar cases and this may explain why a low compensation payment was set.

This is the first report of medical negligence claims about carpal tunnel surgery that went to a trial in Greece. There has been only one successful claim over a 19-year period. Considering that there is an increasing tendency for medical negligence litigations worldwide, including Greece, hand surgeons need to protect themselves by maintaining good standard of care, keeping their patients well informed and building good relationship with them. Carpal tunnel release is a very common procedure which may be accompanied with devastating complications for the patient, financial burden for the health trust and emotional and reputational damage for the physician. A better understanding of the factors that lead to successful legal proceedings will help surgeons to improve their practice to minimize legal implications and litigation.

Conflict of interest

The authors declared no conflicts of interest.

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Vasdeki D, Chryssanthakis C, Varitimidis S, Dailiana ZH. Carpal Tunnel Syndrome: Complications and Legal Implications. *Acta Orthop Trauma Hell* 2020; 71(3): 133-137.

REVIEW

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Is there any role for the selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs) in the postoperative flexor tendon adhesion formation? A literature review

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ABSTRACT

Tendon injuries are considered the second most frequent lesions of the hand (29%), whereas fractures are first (42%). Despite the progress in the surgical techniques and postoperative rehabilitation protocols for preventing adhesions, still several pharmacological agents are being studied in order to inhibit the excessive inflammatory response and the production of growth factors that follow tendon injuries and repair.

A large number of studies has targeted the inflammatory cascade, and in particular COX enzyme isoforms in an effort to inhibit adhesion formation and promote tendon healing and although results have been promising regarding adhesion formation, non-steroidal anti-inflammatory drugs (NSAIDs) have repeatedly shown concomitant losses in the strength of repair, a concerning outcome for tissues that experience high loads such as the flexor tendons.

In conclusion, selective and non-selective NSAIDs seem to have a significant effect in limiting adhesion formation. Nonetheless, the questions that arise about their role on tendon healing, and their potential detrimental effect, are primarily to be addressed by larger animal studies that will provide a better viewpoint for statistical implementation and will check the safety of these drugs for side effects and the danger of tendon re-rupture.

KEY WORDS: Flexor tendons, adhesion, NSAID, COX-2

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Introduction

Tendon injuries are considered the second most frequent lesions of the hand (29%), whereas fractures are first (42%) [1]. According to the study by de Jong et al. the incidence of traumatic injuries of tendons reached 33.2 patients per 100,000 people with an average age at injury of 35.9 years [2,3]. More specifically, regarding flexor tendons in the hand, the most frequently involved anatomical location was the flexor zone II (19.1%) [2]. Up to 30-40% of these injuries result in postsurgical adhesion formation between the tendon and the surrounding tissues leading to poor functional results [4] and a significant burden for both the individual and society because they usually involve young blue and white collar workforce [5].

Despite the progress in the surgical techniques and postoperative rehabilitation protocols for preventing adhesions, still several pharmacological agents are being studied in order to inhibit the excessive inflammatory response and the production of growth factors that follow tendon injuries, including corticosteroids, NSAIDs, antimetabolites, hyaluronic acid, antibodies for TGF-b1, nanoparticles and novel gene therapy models [5-17]

In particular, the NSAIDs, as a specific and distinct group of drugs prescribed on a daily basis for a large number of orthopaedic pathologies, have been studied extensively since the early 1980s in vitro and in vivo experimental studies with inconclusive results on flexor tendon adhesion formation after repair.

General considerations on NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drugs worldwide. They are mainly prescribed for chronic orthopaedic conditions such as osteoarthritis or other soft tissue injuries.

NSAIDs competitively inhibit cyclooxygenase (COX), an enzyme essential for the metabolism of arachidonic acid to prostaglandins [8]. COX, as an enzyme, metabolizes arachidonic acid by acting sequentially as a dioxygenase and peroxidase leading to the formation of prostaglandin G (PGG2) initially and prostaglandin H (PGH2) thereafter [18].

Historically, NSAIDs came from the discovery of some plants and their extracts that were occasionally used to relieve pain or as antipyretics. In the mid 19th century salicylates were discovered as new active ingredients, which allowed the synthesis of salicylic acid, known as aspirin (Aspirin). Subsequently, progress during the 19th and 20th century led to the development of the first NSAIDs, most of which were organic acids, and compounds of completely different composition [19]. After World War II, there was a period until 1970, when the role of prostaglandins had not yet been fully understood. During this period the development of new NSAIDs was mainly based on the empirical study of the analgesic, antipyretic and anti-inflammatory properties of these molecules in laboratory animal models. In the early 1980s, studies started focusing on the ability of drugs to inhibit prostaglandin synthesis and production, while after the discovery of the Cycloxygenase (COX) isoforms in the 1990s, studies focused on a purely molecular level [20].

The development of the first compound of this large class of NSAIDs was phenylbutazone in 1946 by JR Geigy in Basel, Switzerland, while indomethacin was discovered by Merck & Co, USA, in the 1960s. At the same time, ibuprofen was discovered by Boots in the UK and because of its safe side effects profile, it became the first non-prescribed NSAID after aspirin. The discovery of ibuprofen was followed by the development of a large number of medicinal products with different biological and chemical properties [21].

Since the late 1980s, the isoform of the COX-2 enzyme has been recognized, launching the search for new safer NSAIDs [22]. This way, COX-2 selective NSAIDs could inhibit the isoform involved in the inflammatory response without inhibiting COX-1 enzyme, which is essential for the production of the "protective" or "house-keeping" prostaglandins in various organs. The main goal was to produce pharmacological compounds that would maintain their analgesic and anti-inflammatory action while reducing at the same time the side effects of the older non-selective NSAIDs. Today NSAIDs can be categorized by their selectivity in

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inhibiting the two isoforms of COX enzyme. By determining the drug concentration needed to inhibit COX-1 and COX-2 by 50% (IC50) and calculating the COX-1/COX-2 IC50 ratio, selectivity of each drug can be compared. (table) [23, 24]

The first COX-2 selective inhibitors were approved by the United States FDA in 1999 for clinical use and released in more than 80 countries worldwide. In the mid 2000s, second generation COX-2 inhibitors such as valdecoxib, parecoxib and etoricoxib were approved for clinical use, presenting fewer side effects regarding the cardiovascular system [23].

NSAIDs in Orthopaedic Surgery and Trauma

NSAIDs are largely prescribed for the symptomatic treatment of musculoskeletal injuries and postoperative pain, and despite their indisputable contribution to the management of symptoms of bone and ligament injuries, clinical experience has raised questions and concerns regarding the adverse effects of these drugs particularly on fracture healing and the restoration of bone biomechanical properties [24].

NSAIDs side effects on fracture healing have been extensively studied over the last four decades [25, 26]. These studies have shown that all selective and non-selective NSAIDs can influence and impair the process of fracture healing, reducing the mechanical stability of the fracture callus as well [27].

A number of studies have shown that traditional non selective NSAIDs such as aspirin, indomethacin and ibuprofen inhibit fracture healing in various animal experimental models [25,33, 35, 29, 30, 28, 26, 31, 32, 27, 34].

With the advent of selective COX-2 NSAIDs, with their aforementioned advantages over traditional NSAIDs, research focused on the effect of COX-2 inhibitors on fracture healing. The first studies comparing non selective and selective NSAIDs argued that COX-2 inhibitors did not have the same deleterious effect on fracture healing as traditional NSAIDs such as indomethacin [36, 37, 38, 39].

Most of the animal studies to date show the inhibitory effect of these drugs on fracture healing [40, 41, 42]. According to Singh et al. administration of etoricoxib on rabbits has led to a smaller callus formation with various histological differences [43]. In addition, studies on femoral fractures in rats have shown that celecoxib and rofecoxib have the same inhibitory effect as the rest of the COX-2 inhibitors [44]. Several other studies have led to the same conclusions regarding the inhibitory effect of NSAIDs on fracture healing. On the other hand, a much smaller number of studies have led to different results. Karachalios et al., Gerstenfeld et al and Brown et al. have shown that selective NSAIDs did not affect fracture healing in terms of radiological imaging and biomechanical stability [38, 37, 28, 43].

Studies on humans are fewer in number and more controversial. They mainly investigate long bone fracture healing and spinal fusions [46, 47, 48, 49, 50].

All these results have raised concerns about the clinical consequences of NSAIDs on fracture callus formation and healing and although the conclusions are mainly based on experimental models with specific limitations, the current data document the following points [39]:

- Most NSAIDs studied have the potential to inhibit bone formation
- NSAIDs tend to have their greatest effect during the early phase of bone healing.
- NSAIDs have a dose-dependent effect on bone healing
- NSADs have duration-dependent and reversible effects on bone healing
- NSAID use before bone injury or fracture does not affect bone healing

NSAIDs on flexor tendon adhesion formation. What's the supporting evidence?

The proper function of the hand after tendon injury requires on one part the immediate tendon surgical repair [51 52, 53, 54] and, on the other part, to maintain the ability to slide freely within their sheath [55]. The inflammatory response and scarring, following injury and suture of the flexor tendons, promote healing, but at the same time prevent them from sliding into their sheath [56, 57].

Tendon healing occurs in three overlapping phas-

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es. In the initial, inflammatory phase, erythrocytes and inflammatory cells, particularly neutrophils, enter the site of injury. In the first twenty-four hours, monocytes and macrophages predominate and phagocytosis of necrotic materials occurs. Vasoactive and chemotactic factors are released with increased vascular permeability, initiation of angiogenesis, stimulation of tenocyte proliferation, and recruitment of more inflammatory cells [58]. Tenocytes gradually migrate to the wound, and type-III collagen synthesis is initiated [59]

After a few days, the proliferative phase begins. Synthesis of type-III collagen peaks during this stage and lasts for a few weeks. Water content and glycosaminoglycan concentrations remain high during this stage [59, 60].

The remodeling phase begins after approximately four to six weeks characterized by decreased cellularity and collagen formation and glycosaminoglycan synthesis. Repair tissue changes from cellular to fibrous. Tenocyte metabolism remains high and tenocytes and collagen fibers (higher proportion of type I collagen) become aligned in the direction of stress [61].

Tendon healing can occur intrinsically, by proliferation of epitenon and endotenon tenocytes, or extrinsically by invasion of cells from the surrounding tissues, particularly sheath and synovium according to the studies by Gelberman et al [62]. As already shown, intrinsic healing results in better biomechanics and fewer complications. In particular, a normal gliding mechanism within the tendon sheath is preserved. In extrinsic healing, scar tissue results in adhesion formation, which disrupts tendon gliding [60]. Therefore, while the formation of scar tissue provides the necessary physical continuity between the sutured ends of the tendon, it restricts, at the same time, the range of motion of the fingers [63]. The problem is particularly evident when the injury involves the anatomical flexor tendon zone II, which not by chance, was considered by surgeons as "no man's land" because of the poor postoperative results.

As aforementioned, despite the progress in the surgical techniques and postoperative rehabilitation protocols for preventing adhesions, still several pharmacological agents are being studied in order to inhibit the excessive inflammatory response and the production of growth factors that follow tendon injuries.

In particular, the NSAIDs, as a specific and distinct group of drugs prescribed on a daily basis for a large number of orthopaedic pathologies, have been studied in vitro, in vivo on animal tendon models and occasionally in human clinical trials (Table 1). According to the main hypothesis of these studies, the net effect of treatment with NSAIDs is to decrease the metabolites and by-products of arachidonic acid metabolism and, consequently, their effect on local tissues. By reducing these pro-inflammatory agents, endogenous local damage may be decreased after trauma. The consequence could be a decrease in peritendinous adhesions [64].

Most of these studies, apart from the anti-adhesion effect of the NSAIDs, also take under consideration the decrease of the breaking strength or load to failure of the tendons under investigation, as a possible adverse side effect of these drugs.

Since the early 1980s, experimental studies on animal models demonstrated the anti-adhesion effect of indomethacin and ibuprofen. Kulick et al. demonstrated the anti-adhesion effect of ibuprofen after oral administration in 21 primates with concomitant reduction of the breaking strength of the repaired tendons after 4 and 6 weeks [9]. Szabo et al. investigated on the indomethacin effect on adhesion formation after zone II flexor tendon repair in rabbits. They concluded that the animals treated with indomethacin had a greater tendon excursion and angular rotation of the joint than the control animals, implying a suppression of peritendinous adhesions. Results were controversial regarding the tensile strength of the repaired tendons, concluding that the action of indomethacin in suppressing adhesions is not a general suppression of collagen synthesis [65].

On the other hand, Vogel et al. found that systemic indomethacin increased tensile strength and collagen cross-linking in rat tail tendons [66], while Carlstedt et al. demonstrated that indomethacin accelerates recovery of tensile strength after repair of transected rabbit plantaris longus tendons through

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increased cross-linking of collagen [66, 67].

During the same period of time in vitro studies with non-selective NSAIDs on human tendon fibroblasts showed that NSAID medication may have potentially negative effects during the proliferative phase since it is associated with decreased DNA synthesis, but beneficial effect in the maturation and remodeling phase since it stimulates protein synthesis [68].

Furthermore, in another in vitro study, Tsai et al. showed that non-selective NSAIDs can inhibit cell migration, such as neutrophils during the early inflammatory phase of tendon healing. The authors postulated that ibuprofen inhibited tendon cell migration associated with downregulation of paxillin expression, not related to the expression of focal adhesion kinase [69].

In the first study of its kind to be performed in humans, Rouhani et al. investigated on the effect of ibuprofen in a double-blind clinical trial on 35 patients after complete flexor tendon laceration and tenorraphy in zone II. The intervention group received a high dosage of ibuprofen (2400mg/day) and according to their findings, the administration of high-dose ibuprofen with anti-inflammatory effects had a statistically significant effect on range of motion improvement after operation and flexor tendon repair. No adverse reactions to the medication and no re-ruptures were observed [70].

All these results on the traditional non-selective NSAIDs have been insufficient to warrant recommendation of NSAIDs for the adhesion formation inhibition on flexor tendons after repair.

With the advent of the selective COX-2 NSAIDs during the late 1990s and early 2000s there have been several comparative in vivo animal studies between non-selective and COX-2 selective NSAIDs with inconsistent results. According to Dimmen et al. parexocib, when administered short-term, caused a significant reduction in functional stiffness and thus better biomechanical behavior compared to indomethacin and placebo groups, but tensile strength was also reduced marking the negative effects of both NSAIDs in the tendon healing process. Thus, the authors suggested that short-term COX inhibition can delay tendon healing but administered in the later phase of healing might be beneficial [71].

Forslund et al. in their in vivo study in rats showed that both indomethacin and celecoxib treated groups presented reduced cross-sectional areas compared to the control group, without affecting the failure loads. In fact, tensile strength seemed to increase for both treated groups in different time-points. This data would suggest that COX inhibitors could be beneficial in clinical situations where swelling of the healing tendon would represent a problem, like in zone II flexor tendons after repair [72].

In another comparative in vivo study between selective and non-selective NSAIDs, Tan et al. comparing the anti-adhesion effects of rofecoxib and ibuprofen on a rabbit model found no differences between them at 6 weeks, based on histology, but significantly better results were found for ibuprofen treated rabbits at 12 weeks, based on ROM results. No load to failure was measured by the authors [73].

Furthermore, Virchenko et al. showed that parecoxib impairs early tendon repair but improves later remodeling of the tendon. In particular administration of parecoxib in the first five days did not affect the size of the early callus, but the force at failure was decreased, indicating normal proliferation and a disturbance of differentiation and matrix production, similar to bone repair. On the other hand, avoiding administration of the COX-2 inhibitor for the first five days resulted in decreased cross-sectional area and higher maximum strength, maybe because parecoxib inhibited the negative effects of inflammation during the remodeling phase of tendon [74].

One of the latest studies on COX-2 inhibitors and tendon healing was conducted by Blomgran et al. in 44 rats after Achilles tendon transection. Cross-sectional area, peak force and stiffness were reduced by parecoxib. Looking at all cell subpopulations at two time points separately, no significant effect of parecoxib could be seen, and the pattern of cell composition appeared quite similar between the parecoxib and control groups at each time point, but different between day 3 and day 10 [75].

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These in vivo studies on animals are in accordance with the concept that NSAID treatment has an inhibitory effect on migration and proliferation of tenocytes during the tendon healing process. Tsai et al. investigated the effects of a COX-2 inhibitor like celecoxib, on cell migration, proliferation and collagen expression in isolated tendon cells in vitro. It turned out that celecoxib inhibited tendon cell migration, and furthermore, this effect was dose-dependent. On the other hand, celecoxib did not interfere with the expression of type I and III collagen. The results of this study suggest that decreased tendon cell migration and proliferation might compromise and impair the early inflammatory phase of tendon healing after repair [76].

Celecoxib, in particular, as a COX-2 inhibitor can reduce inflammation as well as neovascularization and thus provide inhibition of intra-abdominal adhesions. [77]. In that direction, Li et al. conducted an in vitro and in vivo study on a chicken experimental model. They tested the release of celecoxib from a bi-layer biomimetic tendon sheath in order to prevent flexor tendon adhesion. The data confirmed that the celecoxib-loaded outer PELA layer can prevent adhesion and associated inflammation. Thus, a celecoxib-loaded anti-adhesive tendon sheath can continuously act as a bi-layer biomimetic tendon sheath releasing celecoxib from the outer layer to prevent tendon adhesion [78].

During the last decade, some new gene therapy models have been used. More specifically, Zhou et al. developed a local sustained gene delivery system to regulate the expression of COX enzymes as an effective therapeutic strategy for tendon adhesions and tested it on chickens. The engineered miRNA plasmid/nanoparticles embedded in hyaluronic acid hydrogel were synthesized to downregulate the expression of cyclooxygenases in the tendon tissue during the early stage of tendon healing with inflammatory response. After six weeks, the treated group presented smaller scores in the adhesion grading and increase of the tensile strength of the repaired tendons [79].

Finally, instead of focusing exclusively on the inhibition of the COX enzyme that catalyzes the conversion of Arachidonic acid to Prostaglandins, there has been an effort to directly inhibit the deleterious effects of the inflammatory response on tendons and specifically the Prostaglandin E2 (PGE2) effects via the deletion and/or the antagonism of the prostanoid receptors (EP1-4). Prostaglandin E2 has been implicated as an inflammatory mediator in tendon injuries and tendinopathy and through one of the downstream receptors EP1 - EP4, all of which belong to the superfamily of G-protein coupled receptors [80]. Various authors have suggested a potential therapeutic role for selective EP4 receptor antagonists with controversial results [81].

Studies conducted by Geary et al. on a murine model showed that flexor tendon repairs treated with a systemic EP4 antagonist exhibited impaired early ROM and increased gliding resistance while the biomechanical properties of the repair were no different between antagonist treated mice and control group [80].

On the other hand, Ackerman et al. suggested that deletion of EP4 receptor in mice reduces scar tissue formation and adhesions during the early stages of tendon healing (14 days post-surgery) while tendon gliding is impaired during the later stages of healing (28 days post-surgery) due to an up-regulation of EP4 by an alternative cell population, possibly myofibroblasts, reactivating inflammation and promoting scar mediated tendon healing [82].

Discussion

A large number of studies have targeted the inflammatory cascade in an effort to improve flexor tendon healing after repair over the last forty years. Common among these studies has been the use of selective and non-selective NSAIDs while more recently, new studies have focused on COX isoforms, Prostaglandins and Prostanoid receptors (EP1-4).

All data up to date suggests that while inflammation is required for repair, including recruitment of new cells that synthetize granulation tissue and collagen, an excessive inflammatory response contributes to adhesion formation between the tendon and surrounding structures [80]. Main hypothesis of most of these studies, is that attenuation of the

inflammatory response through the use of NSAIDs and COX inhibition, can decrease adhesion formation after tendon repair, but compromising the strength of the repair at the same time.

In vivo experimental studies

In vivo studies on animal experimental models try to elucidate these two main issues by measuring a) adhesion formation on one hand and b) tensile strength of the repair on the other.

In regard to adhesion formation most of these experimental models focus mainly on the biomechanical testing and the histological analysis of the specimens' tendons with the help of various grading systems. In addition, a smaller number of studies use the macroscopic evaluation of adhesion formation. Tensile strength of the repair, on the other hand, is usually evaluated by measuring the load to failure under traction in various post-operative time points.

In vitro experimental studies

In vitro experimental studies mainly focus on DNA and protein synthesis (collagen types I and III in particular). More specifically, these studies investigate on tenocyte, macrophage, and neutrophil proliferation and migration during the different phases of tendon healing.

In accordance with the data from most of the studies aforementioned:

- Selective and non-selective NSAIDs seem to have a significant effect in limiting adhesion formation after tendon repair.

Early experimental studies on traditional non-selective NSAIDs showed the anti-adhesion effect of indomethacin and ibuprofen [9, 65], while some showed no differences between indomethacin and control groups [67]. Later studies on COX-2 selective NSAIDs like parecoxib, celecoxib and rofecoxib suggested the effect of these drugs in limiting tendon adhesion formation under certain conditions and different post-operative time points [32, 74, 72, 73]. Finally, the study of NSAIDs on human flexor tendons showed that ibuprofen was effective in improving the range of motion of the involved fingers after injury and repair [70].

In vitro investigations on cell populations such as tenocytes, macrophages, fibroblasts and myofibroblasts etc, could not directly provide answers on adhesion formation, but most likely on the biomechanics and the possible side effects of NSAIDs on tendon healing. Finally, studies on deletion of EP4 prostanoid receptor resulted in contradictory time-dependent results regarding the biomechanical behavior of tendons [82], while flexor tendon repairs treated with a systemic EP4 antagonist exhibited impaired early ROM and increased gliding resistance while the biomechanical properties of the repair were no different between antagonist treated mice and control group [80].

- Selective and non-selective NSAIDs impair tendon healing after repair.

One of the major concerns regarding the use of NSAIDs after tendon injuries is the possible negative effect on the tensile strength of the repair. The proven inhibitory effect of these drugs on fracture healing has led to serious debates about the safety of NSAIDs after flexor tendon repairs. Most of the in vivo experimental studies aforementioned take under consideration the breaking strength of the tendons by measuring the load to failure under traction in various post-operative time points. Although results have been controversial until now, the majority of studies suggest that selective and non-selective NSAIDs can impair tendon healing. Traditional NSAIDs such as ibuprofen and COX-2 inhibitors, such as parecoxib and rofecoxib can have negative or even detrimental effects on the tensile strength of the tendon [9, 32, 73, 74]. In contrast, some studies showed that COX-inhibitors do not affect tendon healing adversely, or that can even have a beneficial effect, suggesting that NSAIDs would not have the same drawbacks for tendon repair as they might have for bone healing [67, 72]. Furthermore, NSAID treatment with ibuprofen after flexor tendon injury and repair in humans did not increase the re-rupture rate suggesting that COX-inhibitors do not affect the tendon's biomechanics and tensile strength [70].

In culture, NSAID treatment was shown to decrease DNA synthesis and, increase, at the same time, protein synthesis in human tendon fibro-

blasts which suggests a negative effect on tendon cell proliferation in the early phase of tendon healing but a positive effect on collagen deposition [68]. Similarly, various in vitro studies showed that NSAIDs can inhibit proliferation and migration of tendon cells, but increase collagen synthesis [69, 76, 83].

- Selective and non-selective NSAIDs have a dose-dependent and time-dependent effect of tendon healing after repair.

Inflammation, regeneration and remodeling occur during tendon healing and the cells and molecular processes involved at each distinct phase will respond differently to NSAID treatment and inhibition of COX enzyme isoforms. Thus, NSAIDs impact tendon healing in different ways depending upon the dosage, the initiation and duration of treatment [84]. Virchenko et al. showed that early administration of parecoxib for the first five days after injury led to decreased maximum strength of the tendon. When parecoxib was given after the first five days post-injury there was a decrease in cross-sectional area but a substantial increase in maximum strength [74]. Further studies showed that NSAID treatment has an inhibitory effect on migration and proliferation of tendon cells in culture, coinciding with the early inflammatory phase, but does not affect the collagen expression of the regeneration and remodeling phase of tendon healing [69, 75, 76]

Finally, most of the studies where different dosages of NSAIDs were used, present controversial and inconsistent results. Some of them suggest that NSAIDs have a dose-dependent effect on tendons and adhesion formation in particular [72, 76] while others present no differences or inversely proportional results when compared.

- COX-2 Selective NSAIDs have a more significant effect compared to non-selective NSAIDs in inhibiting adhesion formation after tendon repair.

With the advent of COX-2 selective NSAIDs there has been a number of studies comparing the effect of COX-2 inhibitors with the traditional NSAIDs such as ibuprofen and indomethacin. Some of them suggested that COX-2 selective NSAIDs like parecoxib had a more significant effect compared to non-selective NSAIDs in inhibiting adhesion formation through the measurement of functional stiffness [32], while others found no difference between selective and non-selective NSAIDs [72]. In another comparative in vivo study between selective and non-selective NSAIDs, Tan et al. comparing the anti-adhesion effects of rofecoxib and ibuprofen on a rabbit model found no differences between them at 6 weeks, based on histology, but significantly better results were found for ibuprofen treated rabbits at 12 weeks, based on ROM results [73]. In all cases, COX-2 inhibitors seemed to impair tendon healing and mechanical strength the same way traditional NSAIDs did. In conclusion, comparative studies on the effect of selective and non-selective NSAIDs to date seem inconclusive.

Experimental studies have certain limitations that must be taken under consideration. First of all, the differences between the species in terms of anatomy, structure and physiological functions as well as metabolism of drugs should be taken into account. In particular, small mammals and rodents exhibit higher metabolic rates leading to different concentrations of nutrients and drugs and different rates of excretion [85]. Therefore, results of experimental in vivo and in vitro studies cannot be directly extrapolated and applied to the human clinical setting.

Furthermore, all of the aforementioned studies use different ways of administration, dosages and post-operative time-points on different animals. This large number of variables makes result interpretation difficult.

Literature on the effects of NSAIDs on tendon healing and adhesion formation seems inconsistent. A large number of studies has targeted the inflammatory cascade, and in particular COX enzyme in an effort to inhibit adhesion formation and promote tendon healing. NSAIDs have been tested for the last forty years and although results have been promising regarding adhesion formation, COX-inhibitors have repeatedly shown concomitant losses in the strength of repair, a concerning outcome for tissues that experience high loads such as the flexor tendons. While inflammatory

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response is essential for repair, excessive inflammation contributes to adhesion formation between tendon and surrounding tissue. These discrepancies are probably due to timing issues, as it has been shown that NSAIDs have a detrimental effect in the early inflammatory phase, but a slight positive effect during remodeling [74, 75]

In conclusion, selective and non-selective NSAIDs seem to have a significant effect in limiting adhesion formation. Nonetheless, the questions that arise about the role of NSAIDs on tendon healing, and their potential detrimental effect, are primarily to be addressed by larger animal studies that will provide a better viewpoint for statistical implementation and will check the safety of these drugs for side effects and the danger of tendon re-rupture.

Conflict of Interest Disclosure:

The authors declare that there is no conflict of interest

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TECHNICAL NOTE ARTICLE

Extensor Indicis Proprius to Extensor Pollicis Longus Tendon Transfer under Local Anesthesia. Surgical Technique

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ABSTRACT

Rupture of the extensor pollicis longus (EPL) tendon at the wrist has been described after fracture of the distal radius at Lister's tubercle, in synovitis, tenosynovitis, or rheumatoid arthritis. The most common procedure for the treatment of irreparable ruptures of the extensor pollicis longus (EPL) tendon is the extensor indicis proprius (EIP) transfer. The main challenge of this technique is the correct tension setting of the transfer. The wide-awake technique allows patients to be awake during the operation and to retain full motor control of the hand. It provides the surgeon the ability to make clinical observations, adjust the tendon transfer tension according to active hand movement in order to make sure the transfer has the right tension before the skin closure. Hereby we present a technique for an EIP to EPL transfer for patients with irreparable rupture of the EPL tendon with the use of local anesthetic and tourniquet. This technique provides the surgeon the ability to assess properly the tension of the transfer by asking the patient to extend and flex his thumb during the operation.

KEY WORDS: Wide-awake; Local anesthesia; Extensor pollicis longus; Extensor indicis proprius transfer.

Introduction

Rupture of the extensor pollicis longus (EPL) tendon is a rare clinical finding [1,2]. It has been described after fracture of the distal radius at Lister's tubercle, in synovitis, tenosynovitis, or rheumatoid arthritis [3]. Especially, nondisplaced fractures of the distal radius have been a well-established risk factor of EPL rupture with an incidence of 0.2-5% [4]. Steroid treatment and misplaced external fixator pins, amongst others, have also been reported as various causes of EPL spontaneous rupture [5,6]. Furthermore some researchers report cases of spontaneous EPL tendon rupture caused by repeated movement of the wrist joint in association with occupational work activity, without a history of severe trauma, rheumatoid arthritis, or tenosynovitis [2,7].

The most common procedure for the treatment of chronic ruptures of the extensor pollicis longus (EPL) tendon is the extensor indicis proprius (EIP) transfer [8]. In order for this transfer to be successful, proper tensioning is an important aspect of the operation[9]. One way to assess the tensioning of the transferred tendon is to perform the operation while the patient is awake [10,11].

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The wide-awake technique allows patients to be awake during the operation and to retain full motor control of the hand. It also provides the surgeon the ability to adjust the tendon transfer tension and check the integrity of the suture weave with active movement before the skin closure [10]. Hereby we present an alternation of the wide awake technique described by Bezuhly M et al. and Lalonde DH in which we use local anesthesia for pain free operation and tourniquet for haemostasis.

Surgical Technique

Operation takes place under sterile environment in an operating room dedicated to minimal invasions. The patient lies supine on the operating table and a tourniquet is applied above elbow. The local anesthetic consists of a blend of 18 mL of 1% lidocaine and 2 mL of 8.4% bicarbonate in order to bring the pH up from 4.7 to 7.4 [12]. Also in order to reduce the injection pain, a 27-gauge needle is used and the anesthetic mixture is divided in two 10ml syringes. Local anesthetic is slowly injected below the dermis, with the needle oriented 90^0 to the skin. An area of, at least, 2cm beyond the three incision sites must be injected [13]. Then a 220 mmHg pressure is applied to the tourniquet after the limb has been exsanguinated with a sterile bandage.

First, a longitudinal incision is made over the dorsal side of the first metacarpal, approximately 2 cm proximal of the metacarpophalangeal joint, in line with the anatomical course of EPL. The distal part of the EPL is identified and the tendon is marked with a needle (**Fig.1a)**. Then a second 1.5-cm-long transverse incision is made over the dorsal side of the metacarpophalangeal joint of the index finger in order to expose the EIP, which is located on the ulnar side of the extensor digitorum (**Fig.1b)** Finally, a 1.5-cm-long longitudinal incision is made ulnar to Lister's tubercle. After dissecting the soft tissue, the EIP is recognized into the 4^{th} extensor compartment and marked with a vessel loop. Usually, it is the only tendon with muscle belly at this zone. (**Fig.1c)**. The EIP tendon is transected just proximal to the sagittal band of the extensor hood and retrieved at the level of the the wrist joint through the proximal incision. Afterwards, EIP tendon is transferred, subcutaneously, to the level of the first incision in order to follow the EPL path. The EIP is then weaved end to side to distal stump of EPL with wrist fully flexed. The two tendon ends are pulled by 2 different mosquito clamps to maintain the thumb in full passive extension, as in the regional anesthesia technique. Two temporary 3.0 nylon sutures are placed between the tendons and the tourniquet is released. The mean time of tourniquet application is 20-25 min. The patient is asked to actively extend his or her thumb and actively flex it till it reaches the fifth finger in order to test the tension of the transfer. If the tension is correct, a standard Pulvertaft weave technique with 3 passes is used to complete the EIP to EPL transfer. The same action is once more asked to be performed after finishing the weave and before closing the skin. The patient is able to fully

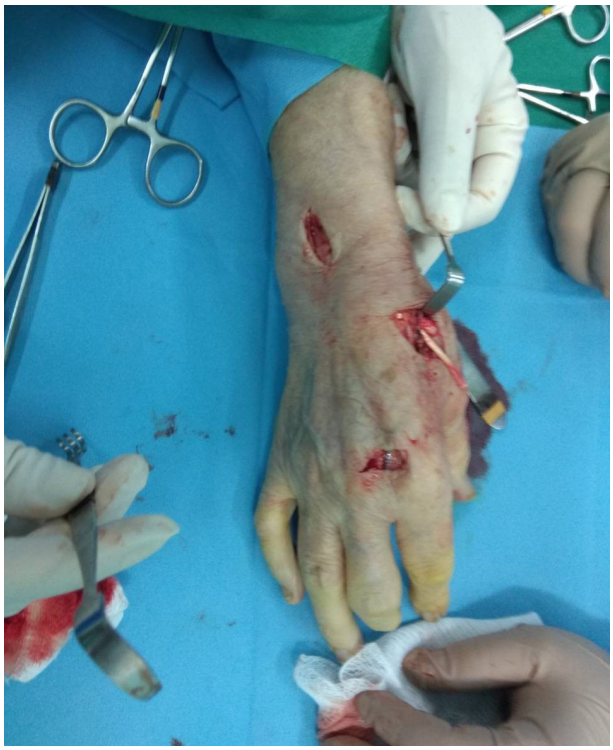

Fig1. *a. Longitudinal incision at the ulnar border of first metacarpal, proximal to MCP joint*
b. Transverse incision over the second metacarpal head
c. Longitudinal incision ulnar to Liester's tubercle, proximal to extensor retinaculum.
The local anesthetic is injected only around the area of the three skin incisions. After the transfer of EIP in the EPL stump, tourniquet is released

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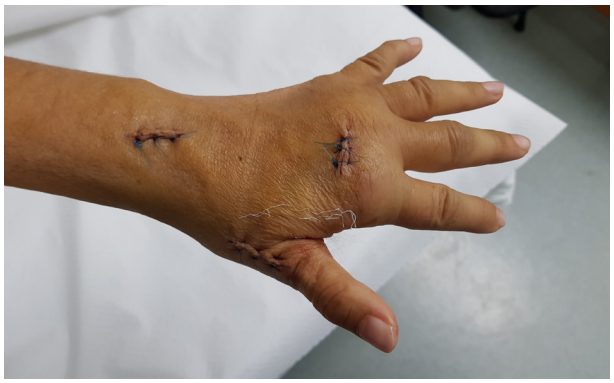

Fig 2. *A 64 yrs old male suffered EPL rupture after distal radial fracture. Two weeks post operatively patient is able to keep his thumb in extended position*

Fig 3. *48 yrs old man with EPL rupture during manual work. 14 months post operatively extending his thumb. The course of EIP tendon under the skin can be visualized.*

recognize the newly acquired movement of his/her thumb.

After thorough hemostasis and cleaning, skin is closed with 4.0 nylon sutures. The hand is immobilized in a thumb spica plaster splint, with wrist extended to 30^0 and thumb in 10^0 of extension.

Patient is discharged from hospital the same day, immediately after completion of the operation. Removal of the stiches takes place 12-14 days after the operation and the splint is preserved for 5 weeks. After cast removal, gradual movement in combination with sessions of physiotherapy commences, usually for 30 days.

Discussion

Tendon transfer consists a well-established treatment for chronic ruptures of the EPL as it provides satisfactory outcomes while it is a relatively simple technique [9]. The tendon that is preferred for this transfer is the EIP as it has an appropriate direction and excursion compared with the EPL while the tendon transfers using the EIP have demonstrated excellent outcomes in the past [10,14-16].

This procedure has historically been performed with good results using general and regional anesthesia. However, wide awake local anesthesia no tourniquet (WALANT) technique described by Lalonde DH [10,11] avoids the risks to the patient associated with these methods of anesthesia, is more time efficient and shows significantly better results, especially in the early stages [17]. Nevertheless, there is a rather serious complication of the use of epinephrine for hemostasis and that is the white thumb, which is associated with significant risk of vascular compromise of the digit. This situation can be treated with injection of 1 mg of phentolamine in 5 to 10 mL of saline wherever epinephrine has been injected, to reverse vasoconstriction, usually within 1 hour [11,18]. However, in Greece, phentolamine it is not available for use and thus the use of epinephrine for hemostasis could become dangerous since there is no antidote available in case of a white thumb complication occurrence.

The technique described above is an alteration and it differs at the method of hemostasis by using tourniquet instead of epinephrine. By lifting tourniquet pressure before completing the tendon weave patients' discomfort is minimized. The main advantage is the ability of the surgeon to assess properly the tension of the transfer by asking the patient to extend and flex his thumb during the operation In both of these techniques the surgeon is able to assess the range of motion of the affected thumb by asking the patient to extend it after placing a temporary positioning suture to the transferred tendon. That way he can observe its motion and even compare it to the contralateral thumb. All these can be done before the skin is closed and the surgeon can be even more certain about the transferred tendon and its tension. Second, the patients learn immediately how to use their thumb which results in faster re-learning after the cast removal.

Conclusion

The wide awake local anesthesia no tourniquet (WALANT) approach in treatment of irreparable

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EPL ruptures is a well-established method with better early results in terms of functional and subjective outcomes. The presented alternative surgical technique by using tourniquet control for a short period of time is a safe and equally efficient method.

Conflict of Interest Disclosure:
The authors declare that there is no conflict of interest

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