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جامعة النهرين
تأسست عام ١٩٨٧

A COMPARATIVE STUDY BETWEEN CONSERVATIVE AND OPERATIVE TREATMENT OF DUPUYTREN DISEASE

A THESIS
Submitted to the department of surgery in
Al-Nahrain College of Medicine as partial Fulfillment of the requirements for graduation

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Table of Contents

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DEDICATION

To my beloved parents, who were there for me
With their support and encouragement,
I dedicate this work to all their loving tears and beautiful smiles.

To all my respectable teachers,
Who enlightened me with their knowledge and understanding

To all my fellow students, friends, and colleagues
For their unconditional Support and love.

To all patients out there, hoping this little work will do something to help them more in their sufferings.

ABSTRACT

BACKGROUND:

Dupuytren's disease (DD) is a common and progressive, fibroproliferative disorder of the palmar and digital fascia of the hand. Various treatments have been recommended for advanced disease or to retard progression of early disease and to prevent deterioration of the finger contracture and quality of life. Recent studies have tried to evaluate the clinical and cost-effectiveness of therapies for DD, but there is currently no systematic assessment and appraisal of the economic evaluations.

METHOD:

Complication and recurrence rate was evaluated for non-operative and operative treatment based on total of 11 Journal databases reviewed for DC in a structured literature review.

RESULTS:

Incidence of adverse events was numerically lower with non-operative management , and limiting the complication into only skin injury and pain due to injection. With corticosteroid was with the highest recurrence rate.

While the operative complication where higher ranging from neurapraxia (as the highest recorded compilation) , pain ,tendon injury , infection and skin injury .with percutaneous fasciotomy with highest recurrence rate .

KEYWORDS

Dupuytren's contracture ,Collagenase Clostridium histolyticum, , fasciectomy, Dermofasciectomy

TILT OF ABBREVIATIONS

(DD): Dupuytren disease
(DC): Dupuytren contracture
(CCH): collagenase Clostridium histolyticum
(MP) : metacarpophalangeal joints
(PIP): proximal interphalangeal
(MCP):metacarpophalangeal
(PNF): percutaneous needle fasciotomy

CHAPTER ONE:
INTRODUCTION AND AIMS

1.1 INTRODUCTION

Dupuytren's disease

Dupuytren's disease is a fibroproliferative disease that involves collagen deposition and ultimately affects hand mobility and grip strength.[1] The first reference to this pathology dates back to 1614, when Plater referred to a flexion contracture of the hand that he attributed to trauma to the flexor tendon.[2] [3]In France, Dupuytren described the anatomy of the disease as well as clinical history and presentation. He believed that trauma was the main causative factor of this pathology. The traditional treatment option for DC has involved surgical removal or disruption of fascial cord to allow release of the contracture. An alternative nonsurgical treatment for DC is collagenase Clostridium histolyticum (CCH), which is injected directly into the cord to weaken it by enzymatic degradation, allowing the treating physician to manipulate and break the cord

1.1 Epidemiology

Looking at the incidence of Dupuytren's disease (DD), white-northern Europeans have the highest rate whereas dark-skinned individuals have the lowest number of occurrences [4],[5]. Twin studies have shown that there is some evidence supporting the theory that this disease could be a familial disorder [6].

Scandinavians and people with Northern European ancestry were mainly responsible for the spread of this disease hence it is being called the "Viking disease" [7]. The theory of Nordic origin of the disease can be supported by the

high incidence rate among the people in Denmark as well as in the northern part of the UK [8].

Both age and sex, have an effect on the occurrence of Dupuytren's disease. The incidence is very low among teens and people in their twenties but the risk of having this condition increases each decade.

According to Mikkelsen et al. the onset of Dupuytren's contracture (DC) is indirectly proportional to the recurrence and progression of this disease. In other words the earlier the onset of the disease the more likely the recurrence and progression of Dupuytren's contracture in the future [9] ,[10].Men are up to 15 times more likely to suffer from this disease. DC however, is less sever in women and may even remain unnoticed. During the 8^{th} and 9^{th} decade of life the ratio between affected men and women is equal [11]. There is mixed evidence as to what the causes and consequences of Dupuytren' contracture may be.

1.2 Risk Factors

Non-modifiable

- People of Scandinavian or Northern European ancestry,[12] it has been called the "Viking disease",[13] though it is also widespread in some Mediterranean countries [14] Dupuytren's is unusual among ethnic groups such as Chinese and Africans.[15]
- Men rather than women; (men are more likely to develop the condition)
- People over the age of 50; the likelihood of getting Dupuytren's disease increases with age[16]
- People with a family history (60% to 70% of those afflicted have a genetic predisposition to Dupuytren's contracture)

Modifiable

- Smokers, especially those who smoke 25 cigarettes or more a day [17]
- Thinner people (i.e., those with a lower-than-average body mass index)
- Manual workers
- Alcoholics[18]

Other conditions

- People with a higher-than-average fasting blood glucose level
- People with previous hand injury[19]
- People with ledderhose disease (planter fibromatosis)[20]

- People with epilepsy (possibly due to anti-convulsive medication)[21]
- People with diabetes mellitus
- People with HIV [22]

In one study, those with stage 2 of the disease were found to have a slightly increased risk of mortality, especially from cancer.[23]

Table 1.1 : Risk factors

Author	Date	Study Design	incidence rate			Age group		heritability	Significant risk factors
Smith SP	2001	Cross-sectional study of 172 patients with shoulder pathology	total	M	F	M Mean 54.9 years	F Mean 54.9 years	7% of people with DD had first degree relative with DD.	Increased prevalence of DD in frozen shoulder patients
Finsen V	2002	Cross-sectional study 456 people in community	7.5%	11.9%	1.5 %	>50 years	>50 years	Higher prevalence in family members in same niche	
White HA	2003	Observational study of 197 inpatients.	6.6%			19–101 years	19–101 years	No mention	No mention
Ardic F	2003	Cross-sectional study of 78 type II diabetics	21.8%			46–70 years	46–70 years	No mention	Diabetes is risk factor for DD
Geohagan JM	2004	Cross-sectional study of 383,000 GP patients.	0.2%	0.15%	0.05 %	24–97 years	24–97 years	No mention	Diabetes is a strong risk factor for DD
Logan AJ	2005	Questionnaire survey of 1,100 climbers	19.5%			23–93 years	-	No mention	No mention

Burke FD	2007	Cross-sectional study of 97,537 miners	8.1%			25–99 years	-	No mention	Increased risk of DD in diabetics and increased age
Lucas G	2008	Cross-sectional study of 2,406 male civil servants.	-	8.8%	-	Mean age 50.7 years		20% had family history of DD	Manual work exposure appears to be associated with DD
Khan AA	2004	Review of National Morbidity Survey of 502,493 men	Incidence rate 34.3 per 100,000 men			40–84 years		No mention	No mention

1.3 Pathological anatomy

Dupuytren's disease primarily affects the longitudinal layer of the palmar fascia and usually spares the deeper fascial layers. The normally supple bands thicken to become deforming cords, resulting in contractures at the metacarpal phalangeal joint, the proximal interphalangeal joint, and, occasionally, the distal interphalangeal joint.[24] In the palm, the diseased cords are pretendinous cords or natatory cords. Within the digit, they are the spiral, central, and lateral cords (Fig. 1).

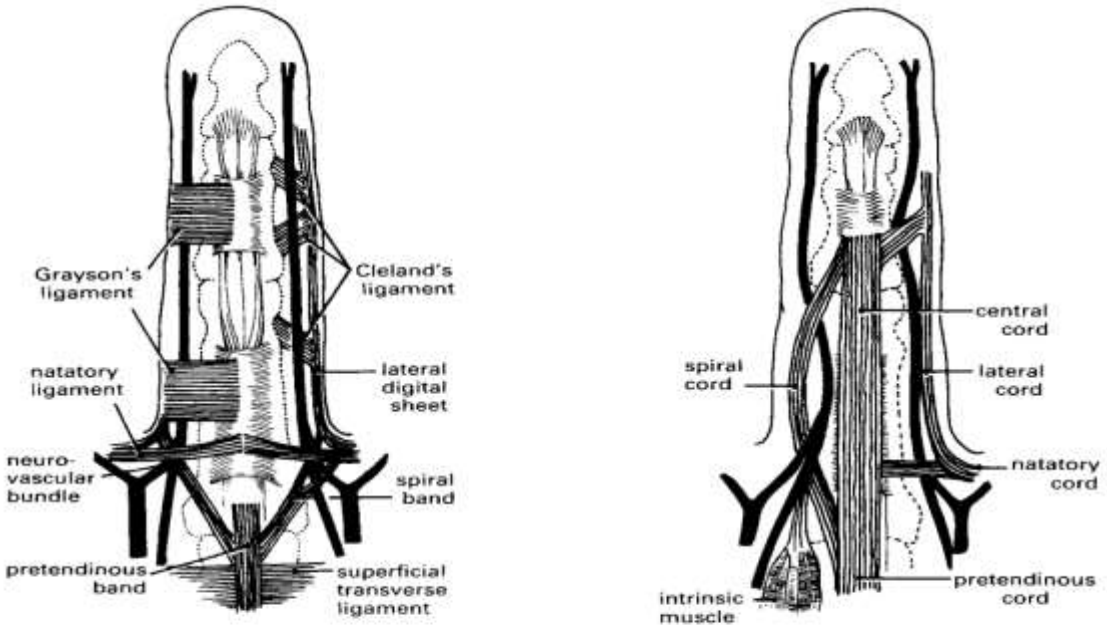

FIG. 1. The change in normal fascia bands to diseased cords of Dupuytren's disease. (*Left*) Normal fascia *bands* that may become involved in Dupuytren's disease. (*Right*) The deforming *cords* of Dupuytren's disease that result in joint contracture. (Reprinted with permission from McFarlane, R. M. The Finger. In R. M. McFarlane, D. A. McGrouther, and M. Flint (Eds.), *Dupuytren's Disease Biology and Treatment.* Edinburgh: Churchill Livingstone, 1990. Pp. 155–167.)

Dupuytren's disease causes thickening of the pretendinous band, which results in a pretendinous cord and subsequent metacarpal phalangeal joint flexion contracture. This joint flexion deformity is the result of the cord attachment to the skin in the distal palmar crease. The neurovascular bundles are not usually displaced by the formation of the pretendinous cord.[25]

The thickening and shortening of these ligaments converts the normal U-shaped web space fibers into a V-shape, resulting in limitation of abduction and progressing to adduction contractures of the fingers.The distal extension of the pretendinous band, the spiral band, lateral digital sheet, and Grayson's ligament thicken to form the spiral cord of Dupuytren's disease. The typical cord begins proximally as the pretendinous cord and passes dorsal to the neurovascular bundle just distal to the metacarpal phalangeal joint. Progressive thickening, shortening, and straightening of this cord produces a flexion contracture of the proximal interphalangeal joint. Because the neurovascular bundles normally run within the spiral fascial fibers, they are usually displaced proximally, superficial to the spiral cord, and toward the midline of the finger, thus becoming susceptible to injury during surgical release of the proximal interphalangeal joint contractures (Fig. 2).

The nerve displacement is progressive and occurs most often in patients with significant proximal interphalangeal joint contractures.[26] The diseased lateral digital sheet may thicken to form the lateral cord of Dupuytren's disease. It can

contribute to flexion contracture of the proximal interphalangeal joint and, occasionally, to distal interphalangeal joint contracture. This cord may also displace the neurovascular bundle toward the midline in the little finger.[27] A central cord, which has no fascial precursor but is usually an extension of the pretendinous cord, may form within the fibrofatty tissue located between the neurovascular bundles.The central cord is the most common cause of proximal interphalangeal joint contracture. However, it does not normally displace the neurovascular bundle.

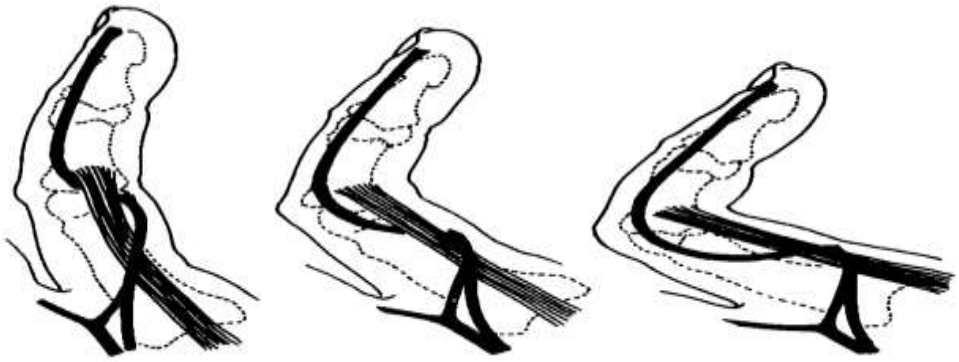

FIG. 2. With increasing flexion contracture of the proximal interphalangeal joint, the neurovascular bundle is displaced proximally, superficially, and toward the midline of the finger, thus becoming susceptible to injury during surgical release of contractures of this joint. (Reprinted with permission from McFarlane, R. M. The Finger. In R. M. McFarlane, D. A. McGrouther, and M. Flint (Eds.), *Dupuytren's Disease Biology and Treatment.* Edinburgh: Churchill Livingstone, 1990. Pp. 155–167.)

1.4 Clinical presentation

Dupuytren's contracture first presents as a thickening or nodule in the palm, which initially can be with or without pain. [28]Later in the disease process, there is painless increasing loss of range of motion of the affected fingers. The earliest sign of a contracture is a triangular "puckering" of the skin of the palm as it passes over the flexor tendon just before the flexor crease of the finger, at the (MCP) joint. Generally, the cords or contractures are painless, but, rarely, tenosynovitis can occur and produce pain. The most common finger to be affected is the ring finger; the thumb and index finger are much less often affected.[29] The disease begins in the palm and moves towards the fingers, with the (MCP) joints affected before the (PIP) joints.[30]

In Dupuytren's contracture, the palmar fascia within the hand becomes abnormally thick, which can cause the fingers to curl and can impair finger function. The main function of the palmar fascia is to increase grip strength; thus, over time,

Dupuytren's contracture decreases a person's ability to hold objects. People may report pain, aching and itching with the contractions. Normally, the palmar fascia consists of collagen type I, but in Dupuytren sufferers, the collagen changes to collagen type III, which is significantly thicker than collagen type I

The differential diagnosis of Dupuytren's disease should include hand abnormalities that cause nodules or *contractures*. These pseudoDupuytren's contracture conditions are caused by soft-tissue changes that can mimic early Dupuytren's disease and pathologic processes that could be mistaken for an established Dupuytren's contracture. These include intrinsic joint contractures, palmar ganglions, inclusion cysts, stenosing tenosynovitis, occupational hyperkeratosis, callous formation, soft-tissue giant cell tumors, epithelioid sarcomas, and changes secondary to rheumatoid arthritis.25 Dupuytren's disease in children or in teenagers must be differentiated from camptodactyly.5

1.5 stages of Dupuytren's contracture

Following Tubiana the degree by which the finger is bent is used to grade contracture into several stages. If more than one joint of a finger is bent, the angles of contracture are simply added together. Based on this total angle of contracture stages in the development of Morbus Dupuytren are usually classified as below

Table 1.4 DD Stages

stage	**Contracture**	Comment
0	0	healthy
N	0	feel nodules / cords
N/1	0-5 degrees	beginning contracture
1	6-45 deg.	
2	46-90 deg.	

3	91-135 deg.	
4	> 135 deg.	

1.6 Treatment

Treatment is indicated when the so-called table top test is positive. With this test, the person places their hand on a table. If the hand lies completely flat on the table, the test is considered negative. If the hand cannot be placed completely flat on the table, leaving a space between the table and a part of the hand as big as the diameter of a ballpoint pen, the test is considered positive and surgery or other treatment may be indicated. Additionally, finger joints may become fixed and rigid.

Treatment involves one or more different types of treatment with some hands needing repeated treatment.

Needle aponeurotomy is most effective for Stages I and II, covering 6–90 degrees of deformation of the finger. However, it is also used at other stages.

Collagenase injection is likewise most effective for Stages I and II. However, it is also used at other stages.

Hand surgery is effective at Stage I – Stage IV

- **Operative**

  new surgical techniques were introduced, such as fasciectomy and then dermofasciectomy. Most of the diseased tissue is removed with these procedures.

  In extreme cases, amputation of fingers may be needed for severe or recurrent cases or after surgical complications.[31]

Limited fasciectomy

Limited/selective fasciectomy removes the pathological tissue, and is a common approach
During the procedure, the person is under regional or general anesthesia.
A surgical tourniquet prevents blood flow to the limb.[32] The skin is often opened with a zig-zag incision but straight incisions with or without Z-plasty are also described and may reduce damage to neurovascular bundles.[33] All diseased cords and fascia are excised.[34] [35] [36] The excision has to be very precise to spare the neurovascular bundles.[37]Because not all the diseased tissue is visible macroscopically, complete excision is uncertain.
After surgery, the hand is wrapped in a light compressive bandage for one week. People start bending and extending their fingers as soon as the anesthesia has resolved. Hand therapy is often recommended.[38] Approximately 6 weeks after surgery people are able to completely use their hand

The average recurrence rate is 39% after a fasciectomy after a median interval of about 4 years.[39]

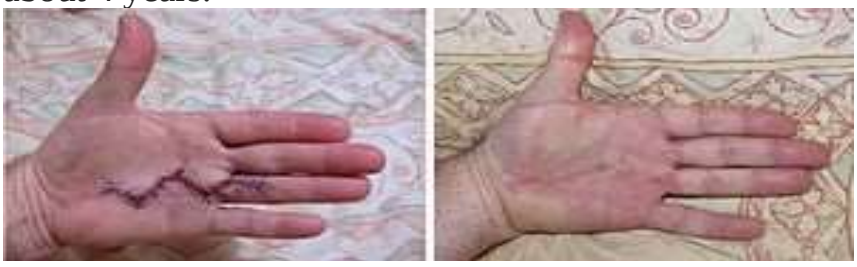

FIG3: limited fascietomy

Dermofasciectomy

Dermofasciectomy is a surgical procedure that is mainly used in recurrences and for people with a high chance of a recurrence of Dupuytren's contracture.[40] Similar to a limited fasciectomy, the dermofasciectomy removes diseased cords, fascia, and the overlying skin.[41] The skin is then closed with a skin graft, usually full-thickness,[42]consisting of the epidermis and the entire dermis. In most cases the graft is taken from the antecubital fossa (the crease of skin at the elbow joint) or the inner side of the upper arm.[43] [44] This place is chosen, because the skin color best matches the palm's skin color. The skin on the inner side of the upper arm is thin and has enough skin to supply a full-thickness graft. The donor site can be closed with a direct suture.[45]

The graft is sutured to the skin surrounding the wound. For one week the hand is protected with a dressing. The hand and arm are elevated with a sling. The dressing is then removed and careful mobilization can be started, gradually increasing in intensity.[46]After this procedure the recurrence of the disease can be low[47 48 49] but the re-operation and complication rate may be high.[50]

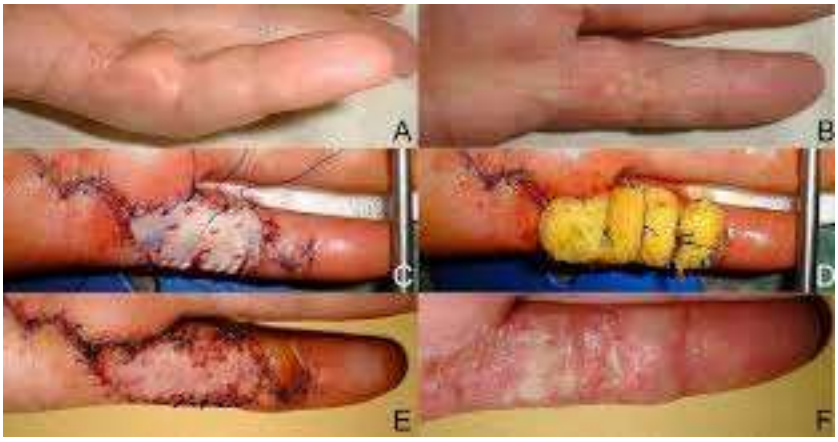

FIG4: Dermofasciectomy

Segmental fasciectomy with/without cell

Segmental fasciectomy involves excising part(s) of the contracted cord so that it disappears or no longer contracts the finger. It is less invasive than the limited fasciectomy, because not all the diseased tissue is excised and the skin incisions are smaller.[51]

The person is placed under regional anesthesia and a surgical tourniquet is used. The skin is opened with small curved incisions over the diseased tissue. If necessary, incisions are made in the fingers.[52] Pieces of cord and fascia of approximately one centimeter are excised. The cords are placed under maximum tension while they are cut. A scalpel is used to separate the tissues.[53] The surgeon keeps removing small parts until the finger can fully extend.[54 55] The person is encouraged to start moving his or her hand the day after surgery. They wear an extension splint for two to three weeks, except during physical therapy

Extensive percutaneous aponeurotomy and lipografting

A technique introduced in 2011 is extensive percutaneous aponeurotomy with lipografting.[56] This procedure also uses a needle to cut the cords. The difference with the percutaneous needle fasciotomy is that the cord is cut at many places. The cord is also separated from the skin to make place for the lipograft that is taken from the abdomen or ipsilateral flank.[57] This technique shortens the recovery time. The fat graft results in supple skin.[58]

Before the aponeurotomy, a liposuction is done to the abdomen and ipsilateral flank to collect the lipograft.[59] The treatment can be performed under regional or general anesthesia. The digits are placed under maximal extension tension using a firm lead hand retractor. The surgeon makes multiple palmar puncture wounds with small nicks. The tension on the cords is crucial, because tight constricting bands are most susceptible to be cut and torn by the small nicks, whereas the relatively loose neurovascular structures are spared. After the cord is completely cut and separated from the skin the lipograft is injected under the skin. A total of about 5 to 10 ml is injected per ray.[60]

After the treatment the person wears an extension splint for 5 to 7 days. Thereafter the person returns to normal activities and is advised to use a night splint for up to 20 weeks.[61]

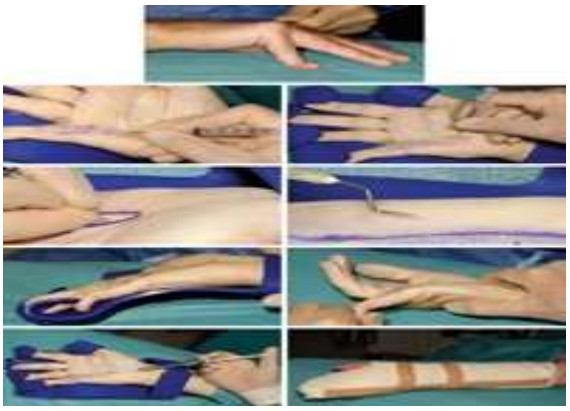

FIG5: percutaneous aponeurotomy

Percutaneous needle fasciotomy

Needle aponeurotomy is a minimally-invasive technique where the cords are weakened through the insertion and manipulation of a small needle. The cord is sectioned at as many levels as possible in the palm and fingers, depending on the location and extent of the disease, using a 25-gauge needle mounted on a 10 ml syringe.[62] Once weakened, the offending cords can be snapped by putting tension on the finger(s) and pulling the finger(s) straight. After the treatment a small dressing is applied for 24 hours, after which people are able to use their hands normally. No splints or physiotherapy are given.[63]

The advantage of needle aponeurotomy is the minimal intervention without incision (done in the office under local anesthesia) and the very rapid return to normal activities without need for rehabilitation, but the nodules may resume growing.[64] A study reported postoperative gain is greater at the MCP-joint level than at the level of the IP-joint and found a reoperation rate of 24%; complications are scarce.[65] Needle aponeurotomy may be performed on fingers that are severely

bent (stage IV), and not just in early stages. A 2003 study showed 85% recurrence rate after 5 years.[66]

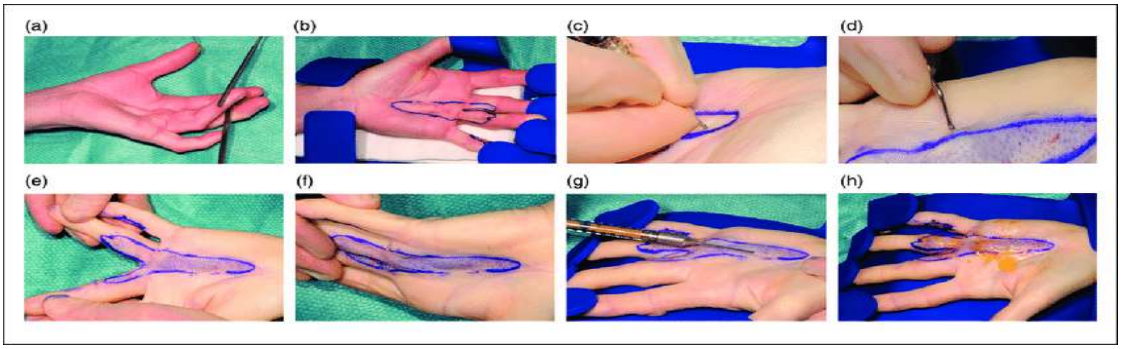

FIG 6: Percutaneous needle fasciotomy

- **Non-operative**

Massage Therapy

these studies are clinically translatable, prophylactic massage treatments may inhibit inflammatory processes and affect the development of fibrosis by mediating differential cytokine production. Consequently this may stabilize the progression of contractures and in some cases ameliorate the degree of deformity

Collagenase

Clostridial collagenase injections have been found to be more effective than placebo.[67] The cords are weakened through the injection of small amounts of the enzyme collagenase, which breaks peptide bonds in collagen.[68 69 70 71 72]

The treatment with collagenase is different for the MCP joint and the PIP joint. In a MCP joint contracture the needle must be placed at the point of maximum bowstringing of the palpable cord.[73]

The needle is placed vertically on the bowstring. The collagenase is distributed across three injection points.[74] For the PIP joint the needle must be placed not more than 4 mm distal to palmar digital crease at 2–3 mm depth.[75] The injection for PIP consists of one injection filled with 0.58 mg CCH 0.20 ml.[76] The needle must be placed horizontal to the cord and also uses a 3-point distribution.[77] After the injection the person's hand is wrapped in bulky gauze dressing and must be elevated for the rest of the day. After 24 hours the person returns for passive digital

extension to rupture the cord. Moderate pressure for 10–20 seconds ruptures the cord.[78]

After the treatment with collagenase the person should use a night splint and perform digital flexion/extension exercises several times per day for 4 months.[79]

Alternate therapies

Alternate therapies such as vitamin E treatment, have been studied, although without control groups. Most doctors do not value those treatments.[80] None of these treatments stops or cures the condition permanently.

Laser treatment (using red and infrared at low power) was informally discussed in 2013 at an International Dupuytren Society forum,[81] as of which time little or no formal evaluation of the techniques had been completed.

Only anecdotal evidence supports other compounds such as vitamin E

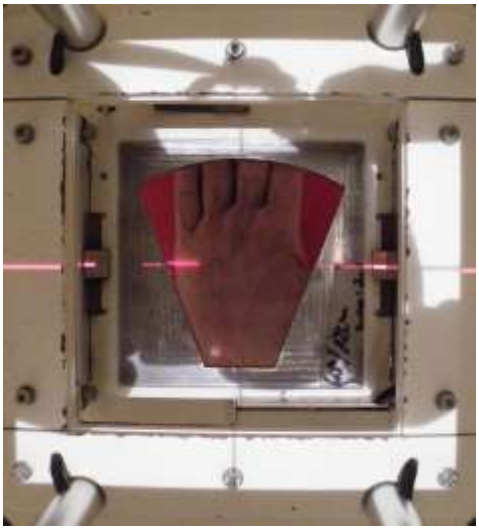

FIG 8: Radiation therapy

CHAPTER TWO:
REVIEW OF LITERATURE

Table :1.2 summarization for major surgery complications in DD

Author	Technique	Outcome	complication
Coert et al 2006	Partial fasciotomy	Patients (age<45) had higher recurrence compared to older patients Outcome of contracted PIP joints were significantly worse than other joints	Nerve lesions in 7.7° Higher risk of infection necrosis in recurrent surgery
Van Rijssn et al 2006	Percutaneous needle fasciotomy	No major complications	High recurrence rate
Lubahn 1999	dermofasciotomy	Very low recurrence rate Reduced risk of developing haematoma as well as oedema	Infections Flexion deformity in DIP joints
Beaudreuil et al 2011	Multi-needle aponeurotomy	High post-operative satisfaction Not painful safe and effective for advanced Dupuytren's disease	High Post operative complications compared to percutaneous needle fasciotont
Hovius et al 2011	Extensive percutnaous aponeurotomy	Shortens recovery time Adds to the deficient subcutaneous fat Leads to starless supple skin	No major complication

Table 2.2: Recent medical interventions for treating and reduction the DD

Author	Technique	Outcome	Complications
Gilpin et al. 2010	Injectable collagenase Clostridium histolyticum	Significantly greater range of 'notion Has a similar outcome to surgery	No major complication
Tomasek et al... 1999	Use of IFN-gamma for suppressing both the differentiation of the myofibmblast and the generation of contractile force	IFN-gamma can suppress both the differentiation of the myolibroblast and the generation of contractile force	No major complication
Ketchum et al... 2000	Triamcinolone acetonide injection into the nodule.	At the early stages. of DO reduces the need for surgery	50% recurrence rate
Knobloch et al. 2011	Extracorporeal shockwave therapy	Can be applicable to prevent the progression of DC as well as a form of treatment	No major complication
Tripoli el al... 2011	Administration of benzodiazepine, retrospective investigation	Compared to phenobarbital which induce DD carbamazepine induce risk of DD	No major complication
Christie (2012)	Heat, splinting, stretching	Improvement in Degrees of digital motion	Not reported

CHAPTER THREE:
PATIENTS AND METHODS

3.1 Design:

The study is system literature review

3.2 data collection:

A total of 11 Journal databases review of treatment outcomes and recurrence for DC found that different types of complications occurred in surgically managed patients compared with non-operative management

We used **keywords** Dupuytren's contracture, Collagenase Clostridium histolyticum, , fasciectomy, Dermofasciectomy , vitamin E , radiotherapy

3.3 Inclusion criteria

- Articles must be directly related to Dupuytren's disease
- Articles must be less than 20 years old
- Articles must be peer reviewed

3.4 Exclusion criteria:

- Articles that did not report outcome
- Articles didn't report rate of complications
- Articles not related to Dupuytren's disease

CHAPTER FOUR:
RESULTS

The incidence of adverse effects in conservatively-treated patients and equivalent fasciectomy complications are presented . These nonoperative-related AEs generally occurred at a lower incidence than equivalent fasciectomy complications. conservatively -treated patients experienced smaller incidences (%) of the following AEs vs. patients treated with fasciectomy (median % [range]): nerve injury (0% vs. 3.8% [0–50+]), neurapraxia (4.4% vs. 9.4% [0–51.3]), complex regional pain syndrome (0.1% vs. 4.5% [1.3–18.5]) and arterial injury (0% vs. 5.5% [0.8–16.5]). Incidence of tendon injury (0.3% vs. 0.1% [0–0.2]), skin injury (16.2% vs. 2.8% [0–25.9]) and haematoma (77.7% vs. 2.0% [0–25]) were numerically higher with conservatively treated vs. surgery, with the most frequent skin-related and haematoma-related AEs in conservatively -treated patients being skin lacerations (11.1%) and contusions (54.5%), respectively.

The ‘other’ category shows the remainder of the conservatively-related AEs that occurred at a frequency ≥2%, but did not have equivalent fasciectomy complications reported in the structured review . The most common of these ‘other’ AEs included edema peripheral, injection site pain, pain in extremity, injection site hemorrhage, tenderness, injection site swelling, pruritus and lymphadenopathy.

All of these ‘other’ treatment-related AEs were deemed by the clinical trial investigators to be possibly or probably related to the actual injection procedure. The majority of these non-operative AEs were considered to be mild or moderate in intensity and were transient, with most such AEs resolving within 7–10 days.

Table 4.1: comparing operative vs conservative outcome

Operative complication	Average %	Non-operative complication	Average %
Complex regional pain syndrome **Limited** **Dermofasciectomy** **Not specified**	 4.5 2.6	Complex regional pain syndrome	0.1
Pain **Limited**	 5.5	Pain	3.4
Haematoma **Limited** **Dermofasciectomy** **Total**	 2.0 1.2	Contusion Ecchymosis Haematoma Haemorrhage	54.5 17.9 5.2 0.1
Neurapraxia **Limited** **Dermofasciectomy** **Total** **Not specified**	 9.4 3	Paraesthesia Hypoaesthesia Hyperaesthesia Sensory disturbance Peripheral neuropathy	2.2 1.7 0.3 0.2 0.1
Nerve injury **Limited** **Dermofasciectomy** **Total**	 3.8 1.5	Nerve injury	0

Skin injury **Limited** **Dermofasciectomy** **Total**	2.8	Skin laceration Blister Skin discoloration Wound Skin disorder Skin hemorrhage Skin tightness Skin exfoliation Skin lesion Skin necrosis Wound dehiscence	11.1 2.3 0.8 0.6 0.3 0.3 0.3 0.2 0.2 0.1 0.1
Infection **Limited**	4.5	Infection	0
Tendon injury **Limited**	0.1	Tendon rupture	0.3
Other	NR	Edema peripheral Injection site pain Pain in extremity Injection site hemorrhage Tenderness injection site swelling	77.4 40.6 36.2 34.1 28.7 24.1

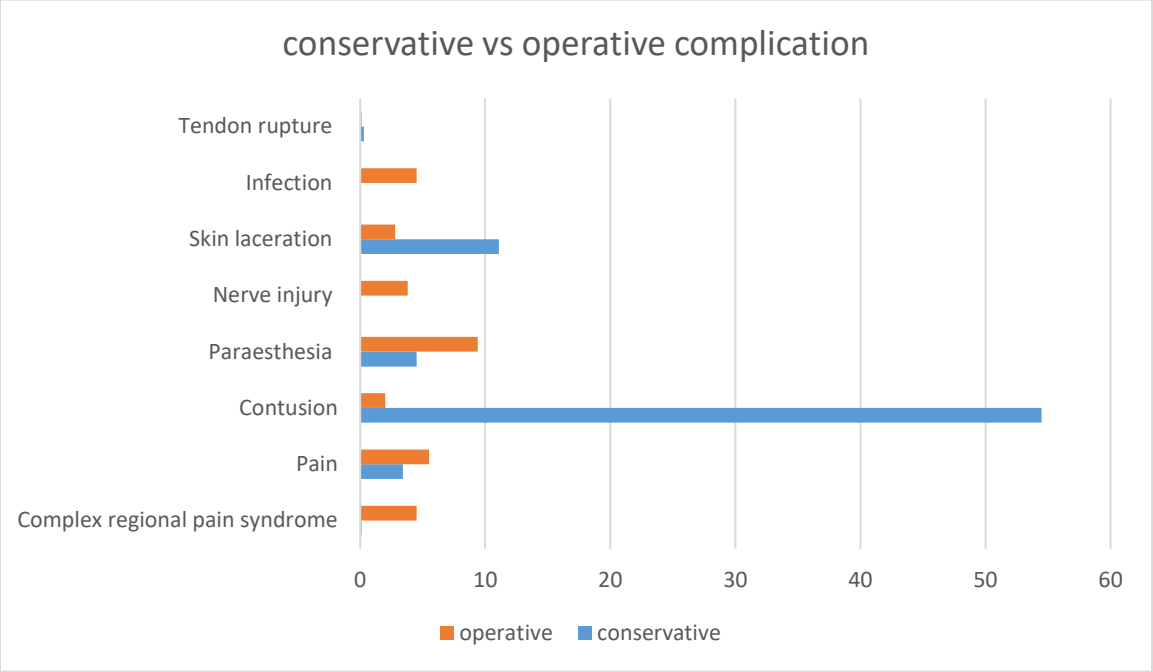

Figure 1: conservative vs operative complication

Table 4.2 : showing Recurrence rate

Procedure	Recurrence rate
fasciectomy	39%
percutaneous fasciotomy.	65%
collagenase injection	19.3%
dermofasciotomy	42%
steroid injection	40%

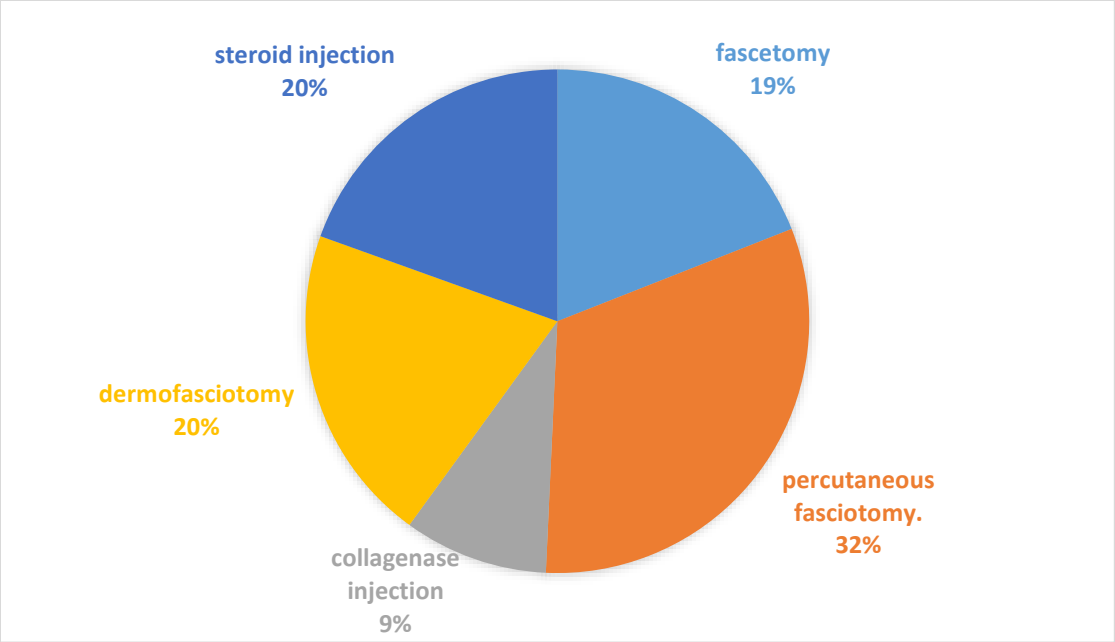

Figure 2 : Recurrence rates

Treatment	Cost
Fasciectomy	$2102.56
CCH injection	$1418.04
Steroid injection	$1,120
dermofasciectomy	$14,751

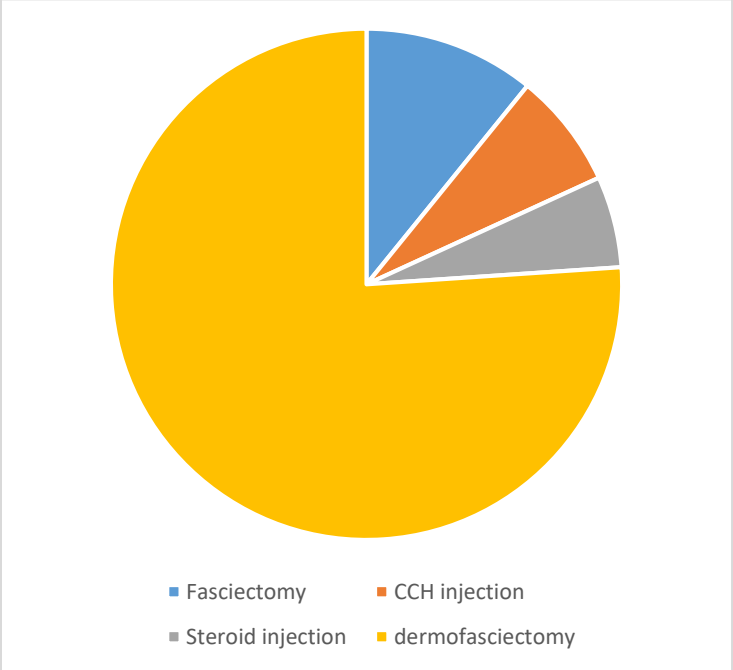

Figure 3 :Cost-effectiveness in the management

CHAPTER FIVE:
DISCUSSION AND CONCLUSIONS

4.1 DISSCUSION

Most AEs associated with non-operative management occurred at a lower incidence than complications reported for operatively treated patients.

Gilpin et al. 2010 vs Coert et al 2006 (e.g. CCH [%] vs. fasciectomy [median %]: arterial injury 0% vs. 5.5%; nerve injury 0% vs. 3.8%).
These AEs were generally reported due to the actual CCH injection procedure, as well as the pharmacodynamic properties, which have a demonstrated inability to digest type IV collagen in these structures. Skin injury (16.2% vs. 2.8%) and hematoma (77.7% vs. 2.0%) were higher with CCH.

However, in this comparison, the presence of wounds and swelling is generally accepted as a normal consequence of surgery and thus is not typically reported as a complication in surgical studies. Tendon injury is a serious but uncommon risk with both CCH and fasciectomy. Although the incidence of tendon injury was numerically higher with conservative management compared with fasciectomy, the 95% confidence intervals (CI) overlapped: CCH 0.3% [95% CI 0.00–0.59] vs. fasciectomy 0.1% [95% CI 0.03– 017]). However, because fasciectomy incidence rates were calculated from surgical studies that differed in design from each other and from the conservative management clinical trials, more research is required to determine whether the relatively small absolute difference between conservative management and fasciectomy in incidence of tendon injury has meaningful clinical or statistical significance.

Denkler, 2010 a published study of patients with primary and recurrent DC who underwent fasciectomy, scar hypertrophy (one study, 1/10 [10%] patients), scar contracture (one study, 3/32 [9%]), incisional scar pain (one study, 4/23 [17%]), joint stiffness (two studies, 55/356 [15%]) and cold intolerance (one study, 3/15 [20%]) have been reported .None of the complications, however, occurred at a clinically significant incidence in the CCH clinical trials. Although the variability in incidence for some of the CCH AEs and equivalent fasciectomy complications appeared to be small, these differences could still be factored into the process of

clinical decision-making when choosing a therapy that suits the needs of an individual patient with DC. Overall, CCH appeared to have a generally better safety profile than fasciectomy; this may have important clinical relevance because published efficacy outcomes in CCH clinical trials **(Gilpin et al., 2010; Hurst et al., 2009; Witthaut et al., 2013)** appeared similar to effectiveness with fasciectomy reported in the structured review **(Crean et al., 2011)**. For example, in all primary joints, CCH treatment has been shown to result in a change of contracture angle of 79.3% at 30 days after the last injection **(Hurst et al., 2009; Witthaut et al., 2011)**, whereas the reported mean improvement with fasciectomy was 76% **(Crean et al., 2011).**

In addition, the average recurrence rate across fasciectomy studies was ~39% at a median time of 4 years; however, only 14% of these studies included time-to-event data in their recurrence rates. In a recent study, 65% of CCH treated DC joints exhibited a durable correction for 3 years after treatment, with only 7% requiring surgical or medical intervention during the 3-year follow-up period **(Peimer et al., 2012a; Peimer et al., 2012b).**

Van Rijssn et al 2006 The rate of major complications in the LF group was 5% versus 0% in the PNF group. Patient satisfaction was almost equal but direct hand function after treatment was considered better in the PNF group, as was the degree of discomfort that patients experienced. This was underscored by the Disabilities of the Arm, Shoulder, and Hand scores in the PNF group, which were significantly lower than those in the LF group at all time points measured.

Knobloch et al. 2011: In early stage Dupuytren's contracture, radiotherapy has been suggested to limit disease progression. A cohort study of 135 patients with 208 hands involved received orthovoltage radiotherapy with a total dose of 30Gray separated by a six to eight week interval . After a follow-up of 13 years' nodules and cords remained stable in 59%, improved in 10% and progressed in 31%.

Tomasek et al... 1999: gamma-Interferon, a cytokine produced by T-helper lymphocytes, has been shown to decrease fibroblast replication, alpha-smooth-muscle actin (the actin isoform characterizing myofibroblasts) expression, and collagen production. have shown in this study the possibility that intralesional injections of gamma-interferon exert a beneficial effect on the evolution of hypertrophic scars and Dupuytren's disease. In the 14 selected patients, gamma-interferon decreased the symptoms and the size of the lesions of both diseases.

Ketchum et al... 2000 After an average of 3.2 injections per nodule 97% of the hands showed regression of disease as exhibited by a softening or flattening of the nodule(s). Although some patients had complete resolution of the nodules, most experienced definite but incomplete resolution of the nodules in the range of 60% to 80%. Although a few patients did not experience recurrence or reactivation of the disease in the injected nodules or development of new nodules, 50% of patients did experience reactivation of disease in the nodules.

In the matter of clinical experience, observed skin lacerations likely relate to post-anesthesia manipulations to break the cord by passive finger extension. Use of local anaesthesia prevents potential pain or discomfort related to the finger extension procedure. The various degrees of adherence of the Dupuytren's cord to the overlying skin may leave certain areas of skin frail because of the underlying condition. Therefore, manipulations may lead to skin tears in the anesthetized area. These lacerations typically heal in a short time without any additional medical intervention. All surgeries, of course, require intentional skin incision, so 'skin injury' and/or haematoma would be the rule, not the exceptional complication.

Limitations

These analyses have limitations, Due to the heterogeneity of the source studies, from different countries the cost of the treatment are not accurately reliable .

Moreover, follow-up times in the fasciectomy publications varied by the individual cases included, or by the study designs, which makes interpretation of the complication rates difficult across these studies. In addition, since this was not a head-to-head clinical trial, variability between the subjects should be expected due to a lack of consistent predefined inclusion and exclusion criteria across studies.

Although these findings are subject to the above limitations, the numerically lower incidence of most AEs with non-operative therapy (vs. operative) may become a useful factor in clinical decisions made by healthcare providers considering which treatment to choose for a patient's DC. We believe that these results have relevance for discussing with patients each treatment's risk–benefit characteristics and in considering the differences in the safety profiles to help decide which treatment option is the most suitable for each particular patient

4.2 CONCLUSIONS

Dupuytren's Disease is a type of fibromatoses characterized by nodular and distributed aggregates of immature fibroblasts dispersed in a dense collagen with no known origin.

The new advances in the treatment of this disease are the modified and improved versions of the previous treatments with lower complication rates. Among the most recent are Multi-needle aponeurotomy, Extensive percutaneous aponeurotomy and lipografting, injecting collagenase Clostridium histolyticum, INF-gamma and shockwave therapy as well as Radiotherapy. Each of these treatments has certain advantages and drawbacks and cannot be used for every patient, and depending on the stage of the disease the treatment might alter. In order to prevent this condition spending more time and money in the topic is required to reach better and more consistent treatments and ultimately eradicate this disease.

References

[1] Lurati AR. Dupuytren's contracture: work-related disorder? Workplace Health Saf 2017;65:96-99.

[2] Shaw RB, Chong AKS, Zhang A, Hentz V, Chang J. Dupuytren's disease: history, diagnosis, and treatment. Plast Reconstr Surg 2007;120:44e-54e.

[3] Elliot D. Pre-1900 literature on Dupuytren's disease. Hand Clin 1999;15:175

[4] Gudmundsson KG, Arngrimsson R, Sigfusson N, Bjornsson A, Jonsson T. Epidemiology of Dupuytren's disease clinical serological and social assessment. The Reykjavik Study. J Clin Epidemiol. 2000; 53(3):291–6.

[5] Sladicka MS, Benfanti P, Raab M, Becton J. Dupuytren's contracture in the black population: a case report and review of the literature. J Hand Surg Am. 1996;21(5):898–9

[6] Burge P. Genetics of Dupuytren's disease. Hand Clin. 1999;15(1):63–71

[7] Hart MG, Hooper G. Clinical associations of Dupuytren's disease. Postgrad Med J. 2005;81(957):425–8

[8] Elliot D. The early history of contracture of the palmar fascia Part 1 The origin of the disease the curse of the MacCrimmons the hand of benediction Cline's contracture. J Hand Surg Br. 1988;13(3):246–53

[9] Wilbrand S, Ekbom A, Gerdin B. The sex ratio and rate of reoperation for Dupuytren's contracture in men and women. J Hand Surg Br. 1999; 24(4):456–9

[10] Ross DC. Epidemiology of Dupuytren's disease. Hand Clin. 1999;15(1):53–62

[11] Yi IS, Johnson G, Moneim MS. Etiology of Dupuytren's disease. Hand Clin. 1999;15(1):43–51.

12 "Your Orthopaedic Connection: Dupuytren's Contracture". Archived from the original on 2007-03-13.

[13] Hart, M. G.; Hooper, G. (2005). "Clinical associations of Dupuytren's disease". Postgraduate Medical Journal. 81 (957): 425–8

14 "Age and geographic distribution of Dupuytren's disease (Dupuuytren's contracture)". Dupuytren-online.info. 2012-11-21. Archived from the original on 2013-03-16. Retrieved 2013-02-27.

[15] Gudmundsson, Kristján G.; ArngríMsson, Reynir; Sigfússon, Nikulás; Björnsson, Árni; Jónsson, Thorbjörn (2000). "Epidemiology of Dupuytren's disease". Journal of Clinical Epidemiology. 53 (3): 291–6. doi:10.1016/s0895-4356(99)00145-6. PMID 10760640.

[16] Lanting, Rosanne; Van Den Heuvel, Edwin R.; Westerink, Bram; Werker, Paul M. N. (2013). "Prevalence of Dupuytren Disease in the Netherlands". Plastic and Reconstructive Surgery. 132 (2): 394–403.

[17] Gudmundsson, Kristján G.; ArngríMsson, Reynir; Sigfússon, Nikulás; Björnsson, Árni; Jónsson, Thorbjörn (2000). "Epidemiology of Dupuytren's disease". Journal of Clinical Epidemiology. 53 (3): 291–6. doi:10.1016/s0895-4356(99)00145-6. PMID 10760640

[18] Burge, Peter; Hoy, Greg; Regan, Padraic; Milne, Ruairidh (1997). "Smoking, Alcohol and the Risk of Dupuytren's Contracture". The Journal of Bone and Joint Surgery. 79 (2): 206–10. doi:10.1302/0301-620x.79b2.6990. PMID 9119843

[19] Lanting, Rosanne; Van Den Heuvel, Edwin R.; Westerink, Bram; Werker, Paul M. N. (2013). "Prevalence of Dupuytren Disease in the Netherlands". Plastic and Reconstructive Surgery. 132 (2): 394–403.

[20] Gudmundsson, Kristján G.; ArngríMsson, Reynir; Sigfússon, Nikulás; Jónsson, Thorbjörn (2002). "Increased total mortality and cancer mortality in men with Dupuytren's disease". Journal of Clinical Epidemiology. 55 (1): 5–10.

[21] Etiology of Dupuytren's Disease" Archived 2016-10-12 at the Wayback Machine Living Textbook of Hand Surgery.

[22] Hart, M. G.; Hooper, G. (2005). "Clinical associations of Dupuytren's disease". Postgraduate Medical Journal. 81 (957): 425–8.

[23] Gudmundsson, Kristján G.; ArngríMsson, Reynir; Sigfússon, Nikulás; Jónsson, Thorbjörn (2002). "Increased total mortality and cancer mortality in men with Dupuytren's disease". Journal of Clinical Epidemiology. 55 (1): 5–10.

[24] Strickland, J. W., and Leibovic, S. J. Anatomy and pathogenesis of the digital cords and nodules. Hand Clin. 7: 645, 1991

[25] Rayan, G. M. Palmar fascial complex anatomy and pathology in Dupuytren’s disease. Hand Clin. 15: 73, 1999.

[26]Umlas, M. E., Bischoff, R. J., and Gelberman, R. H. Predictors of neurovascular displacement in hands with Dupuytren’s contracture. J. Hand Surg. (Br.) 19: 664, 1994

[27] McFarlane, R. M. The Finger. In R. M. McFarlane, D. A. McGrouther, and M. Flint (Eds.), Dupuytren's Disease Biology and Treatment. Edinburgh: Churchill Livingstone, 1990. Pp. 155–167.

[28] "Dupuytren's contracture – Symptoms". National Health Service (England). 2017-10-19. Archived from the original on 2016-04-08. Page last reviewed: 29/05/2015

[29] Lanting, Rosanne; Van Den Heuvel, Edwin R.; Westerink, Bram; Werker, Paul M. N. (2013). "Prevalence of Dupuytren Disease in the Netherlands". Plastic and Reconstructive Surgery. 132 (2): 394–403

[30] Nunn, Adam C.; Schreuder, Fred B. (2014). "Dupuytren's Contracture: Emerging Insight into a Viking Disease". Hand Surgery. 19 (3): 481–90

[31] Townley, W A; Baker, R; Sheppard, N; Grobbelaar, A. O. (2006). "Dupuytren's contracture unfolded". BMJ. 332 (7538): 397–400

[33] Robbins, T. H. (1981). "Dupuytren's contracture: The deferred Z-plasty". Annals of the Royal College of Surgeons of England. 63 (5): 357–8.

[34] Skoff, H. D. (2004). "The surgical treatment of Dupuytren's contracture: A synthesis of techniques". Plastic and Reconstructive Surgery. 113 (2): 540–4.

[35] Khashan, Morsi; Smitham, P. J.; Khan, W. S.; Goddard, N. J. (2011). "Dupuytren's Disease: Review of the Current Literature". The Open Orthopaedics Journal. 5: 283–8.

[36] Van Rijssen, Annet L.; Gerbrandy, Feike S.J.; Linden, Hein Ter; Klip, Helen; Werker, Paul M.N. (2006). "A Comparison of the Direct Outcomes of Percutaneous Needle Fasciotomy and Limited Fasciectomy for Dupuytren's Disease: A 6-Week Follow-Up Study". The Journal of Hand Surgery. 31 (5): 717–25.

[37] Van Rijssen, Annet L.; Gerbrandy, Feike S.J.; Linden, Hein Ter; Klip, Helen; Werker, Paul M.N. (2006). "A Comparison of the Direct Outcomes of Percutaneous Needle Fasciotomy and Limited Fasciectomy for Dupuytren's Disease: A 6-Week Follow-Up Study". The Journal of Hand Surgery. 31 (5): 717–25.

[38] Van Rijssen, Annet L.; Gerbrandy, Feike S.J.; Linden, Hein Ter; Klip, Helen; Werker, Paul M.N. (2006). "A Comparison of the Direct Outcomes of Percutaneous Needle Fasciotomy and Limited Fasciectomy for Dupuytren's Disease: A 6-Week Follow-Up Study". The Journal of Hand Surgery. 31 (5): 717–25.

[39] Crean, S. M.; Gerber, R. A.; Le Graverand, M. P. H.; Boyd, D. M.; Cappelleri, J. C. (2011). "The efficacy and safety of fasciectomy and fasciotomy for Dupuytren's contracture in European patients: A structured review of published studies". Journal of Hand Surgery. 36 (5): 396–407.

[40] Khashan, Morsi; Smitham, P. J.; Khan, W. S.; Goddard, N. J. (2011). "Dupuytren's Disease: Review of the Current Literature". The Open Orthopaedics Journal. 5: 283–8.

[41] Armstrong, J. R.; Hurren, J. S.; Logan, A. M. (2000). "Dermofasciectomy in the management of Dupuytren's disease". The Journal of Bone and Joint Surgery. British Volume. 82 (1): 90–4

[42] Armstrong, J. R.; Hurren, J. S.; Logan, A. M. (2000). "Dermofasciectomy in the management of Dupuytren's disease". The Journal of Bone and Joint Surgery. British Volume. 82 (1): 90–4

[43] Armstrong, J. R.; Hurren, J. S.; Logan, A. M. (2000). "Dermofasciectomy in the management of Dupuytren's disease". The Journal of Bone and Joint Surgery. British Volume. 82 (1): 90–4

[44] Ullah, A. S.; Dias, J. J.; Bhowal, B. (2009). "Does a 'firebreak' full-thickness skin graft prevent recurrence after surgery for Dupuytren's contracture?: a prospective, randomised trial". Journal of Bone and Joint Surgery. British Volume. 91-B (3): 374–8.

[45] Armstrong, J. R.; Hurren, J. S.; Logan, A. M. (2000). "Dermofasciectomy in the management of Dupuytren's disease". The Journal of Bone and Joint Surgery. British Volume. 82 (1): 90–4.

[46] Armstrong, J. R.; Hurren, J. S.; Logan, A. M. (2000). "Dermofasciectomy in the management of Dupuytren's disease". The Journal of Bone and Joint Surgery. British Volume. 82 (1): 90–4.

[47] Khashan, Morsi; Smitham, P. J.; Khan, W. S.; Goddard, N. J. (2011). "Dupuytren's Disease: Review of the Current Literature". The Open Orthopaedics Journal. 5: 283–8.

[48] Armstrong, J. R.; Hurren, J. S.; Logan, A. M. (2000). "Dermofasciectomy in the management of Dupuytren's disease". The Journal of Bone and Joint Surgery. British Volume. 82 (1): 90–4.

[49] Ullah, A. S.; Dias, J. J.; Bhowal, B. (2009). "Does a 'firebreak' full-thickness skin graft prevent recurrence after surgery for Dupuytren's contracture?: a prospective, randomised trial". Journal of Bone and Joint Surgery. British Volume. 91-B (3): 374–8.

[50] Bainbridge, Christopher; Dahlin, Lars B.; Szczypa, Piotr P.; Cappelleri, Joseph C.; Guérin, Daniel; Gerber, Robert A. (2012). "Current trends in the surgical management of Dupuytren's disease in Europe: An analysis of patient charts". European Orthopaedics and Traumatology. 3 (1): 31–41.

[51] Moermans, J (1991). "Segmental aponeurectomy in Dupuytren's disease". The Journal of Hand Surgery: Journal of the British Society for Surgery of the Hand. 16 (3): 243–54

[52] Moermans, J (1991). "Segmental aponeurectomy in Dupuytren's disease". The Journal of Hand Surgery: Journal of the British Society for Surgery of the Hand. 16 (3): 243–54

[53] Moermans, J (1991). "Segmental aponeurectomy in Dupuytren's disease". The Journal of Hand Surgery: Journal of the British Society for Surgery of the Hand. 16 (3): 243–54

[54] Moermans, J (1991). "Segmental aponeurectomy in Dupuytren's disease". The Journal of Hand Surgery: Journal of the British Society for Surgery of the Hand. 16 (3): 243–54

[55] Degreef, Ilse; Tejpar, Sabine; De Smet, Luc (2011). "Improved postoperative outcome of segmental fasciectomy in Dupuytren disease by insertion of an absorbable cellulose implant". Journal of Plastic Surgery and Hand Surgery. 45 (3): 157–64.

[56] Hovius, Steven E. R.; Kan, Hester J.; Smit, Xander; Selles, Ruud W.; Cardoso, Eufimiano; Khouri, Roger K. (2011). "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease". Plastic and Reconstructive Surgery. 128 (1): 221–8.

[57] Hovius, Steven E. R.; Kan, Hester J.; Smit, Xander; Selles, Ruud W.; Cardoso, Eufimiano; Khouri, Roger K. (2011). "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease". Plastic and Reconstructive Surgery. 128 (1): 221–8.

[58] Hovius, Steven E. R.; Kan, Hester J.; Smit, Xander; Selles, Ruud W.; Cardoso, Eufimiano; Khouri, Roger K. (2011). "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease". Plastic and Reconstructive Surgery. 128 (1): 221–8.

[59] Hovius, Steven E. R.; Kan, Hester J.; Smit, Xander; Selles, Ruud W.; Cardoso, Eufimiano; Khouri, Roger K. (2011). "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease". Plastic and Reconstructive Surgery. 128 (1): 221–8.

[60] Hovius, Steven E. R.; Kan, Hester J.; Smit, Xander; Selles, Ruud W.; Cardoso, Eufimiano; Khouri, Roger K. (2011). "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease". Plastic and Reconstructive Surgery. 128 (1): 221–8.

[61] Hovius, Steven E. R.; Kan, Hester J.; Smit, Xander; Selles, Ruud W.; Cardoso, Eufimiano; Khouri, Roger K. (2011). "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease". Plastic and Reconstructive Surgery. 128 (1): 221–8.

[62] Van Rijssen, Annet L.; Werker, Paul M.N. (2012). "Percutaneous Needle Fasciotomy for Recurrent Dupuytren Disease". The Journal of Hand Surgery. 37(9): 1820–3

[63] Van Rijssen, Annet L.; Werker, Paul M.N. (2012). "Percutaneous Needle Fasciotomy for Recurrent Dupuytren Disease". The Journal of Hand Surgery. 37(9): 1820–3

[64] Lellouche, Henri (2008). "Maladie de Dupuytren : La chirurgie n'est plus obligatoire" [Dupuytren's contracture: surgery is no longer necessary]. La Presse Médicale (in French). 37 (12): 1779–81.

[65] Foucher, G (2003). "Percutaneous needle aponeurotomy: Complications and results". The Journal of Hand Surgery: Journal of the British Society for Surgery of the Hand. 28 (5): 427–31

[66] Van Rijssen, Annet L.; Ter Linden, Hein; Werker, Paul M. N. (2012). "Five-Year Results of a Randomized Clinical Trial on Treatment in Dupuytren's Disease". Plastic and Reconstructive Surgery. 129 (2): 469–77.

[67] Brazzelli, M; Cruickshank, M; Tassie, E; McNamee, P; Robertson, C; Elders, A; Fraser, C; Hernandez, R; Lawrie, D; Ramsay, C (October 2015). "Collagenase clostridium histolyticum for the treatment of Dupuytren's contracture: systematic review and economic evaluation". Health Technology Assessment. 19 (90): 1–202.

[68] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[69] Badalamente, Marie A.; Hurst, Lawrence C. (2007). "Efficacy and Safety of Injectable Mixed Collagenase Subtypes in the Treatment of Dupuytren's Contracture". The Journal of Hand Surgery. 32 (6): 767–74.

[70] Badalamente, Marie A.; Hurst, Lawrence C. (2000). "Enzyme injection as nonsurgical treatment of Dupuytren's disease". The Journal of Hand Surgery. 25 (4): 629–36.

[71] Badalamente, Marie A.; Hurst, Lawrence C.; Hentz, Vincent R. (2002). "Collagen as a clinical target: Nonoperative treatment of Dupuytren's disease". The Journal of Hand Surgery. 27 (5): 788–98.

[72] Hurst, Lawrence C.; Badalamente, Marie A.; Hentz, Vincent R.; Hotchkiss, Robert N.; Kaplan, F. Thomas D.; Meals, Roy A.; Smith, Theodore M.; Rodzvilla, John (2009). "Injectable Collagenase Clostridium Histolyticum for Dupuytren's Contracture". New England Journal of Medicine. 361 (10): 968–79.

[73] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[74] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[75] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[76] Hurst, Lawrence C.; Badalamente, Marie A.; Hentz, Vincent R.; Hotchkiss, Robert N.; Kaplan, F. Thomas D.; Meals, Roy A.; Smith, Theodore M.; Rodzvilla, John (2009). "Injectable Collagenase Clostridium Histolyticum for Dupuytren's Contracture". New England Journal of Medicine. 361 (10): 968–79.

[77] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[78] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[79] Bayat, Ardeshir; Thomas (2010). "The emerging role of Clostridium histolyticum collagenase in the treatment of Dupuytren disease". Therapeutics and Clinical Risk Management. 6: 557–72.

[80] Proposed Natural Treatments for Dupuytren's Contracture, EBSCO Complementary and Alternative Medicine Review Board, 2 February 2011Archived 23 July 2011 at the Wayback Machine.Accessed 21 March 2011.

[81] Cold Laser Treatment Archived 2013-11-09 at the Wayback Machine at International Dupuytren Society online forum. Accessed: 28 August 2012