

Recent Surgical and Medical Advances in the Treatment of Dupuytren's Disease - A Systematic Review of the Literature

R. Mafi¹, S. Hindocha^{*2} and W. Khan³

¹The Hull York Medical School, Hertford Building, Hull, HU6 7RX, UK

²Department of Plastic Surgery, Whiston General Hospital, Liverpool, L355DR, UK

³University College London Institute of Orthopaedics and Musculoskeletal Sciences, Royal National Orthopaedic Hospital, Stanmore, Middlesex, HA7 4LP, UK

Abstract: Dupuytren's disease (DD) is a type of fibromatosis which progressively results in the shortening and thickening of the fibrous tissue of the palmar fascia. This condition which predominantly affects white-northern Europeans has been identified since 1614. DD can affect certain activities of daily living such as face washing, combing hair and putting hand in a glove. The origin of Dupuytren's contracture is still unknown, but there are a number of treatments that doctors have come across throughout the years. Historically surgery has been the mainstay treatment for DD but not the only one. The objective is to make a structured review of the most recent advances in treatment of DD including the surgical and medical interventions. We have looked at the most relevant published articles regarding the various treatment options for DD. This review has taken 55 articles into consideration which have met the inclusion criteria. The most recent treatments used 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. 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 to eradicate this disease.

Keywords: Dupuytren contracture, dupuytren disease, medical, surgical, treatment, advances.

BACKGROUND INFORMATION

The first doctor who came across this condition was Plater in 1614 [1]. In 1831 a French military surgeon called Guillaume Dupuytren became famous for describing and operating on palmar fibromatosis, which is now commonly known as Dupuytren's disease. The disease is described as a type of fibromatosis characterized by nodular and/or distributed aggregates of immature fibroblasts dispersed in a dense collagen [2]. The progressive and irreversible flexion contractures of the phalangeal joints of the hand are the nature of this disease. These flexions which predominantly affect the small and ring finger are due to the proliferation of myofibroblasts in the fascia of the hand. Myofibroblasts were the first responsible cause for contracture in this disease. It was first due to their ultrastructural identification in transmission electron-microscopic studies but later on scientists showed that the contracture was mainly due to the expression of Alpha-smooth muscle actin (SMA) in cells from tissue explants. Furthermore, it was shown that myofibroblasts can generate contractile force [3, 4].

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 [5, 6]. Twin studies have shown that there is some evidence supporting the theory that this disease could be a familial disorder [7]. It is still uncertain whether Dupuytren's disease is a monogenic or a polygenic condition as this condition has variable inheritance patterns and different levels of gene expression.

Scandinavians and people with Northern European ancestry were mainly responsible for the spread of this disease hence it is being called the "Viking disease" [8]. 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 [9].

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 [10, 11] Men are up to 15 times more likely to suffer from this disease. DC however, is less severe in women and may even remain unnoticed. During the 8th and 9th 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's contracture may be. Scientists

*Address correspondence to this author at the Department of Plastic Surgery, Whiston Hospital, Warrington Road, L35 5DR, UK; Tel: 01244366265; Fax: 01244366265; E-mail: hindocha2001@yahoo.com

agree on a well-established link between this disease and diabetes mellitus (DM). Patients who develop Dupuytren's disease and suffer from DM have more nodules and less contraction [12]. There is no reliable evidence for other diseases such as liver disease, TB, syphilis, high serum lipids and HIV+ to be associated with Dupuytren's contracture. There is a degree of controversy as to whether there is an association between epilepsy, smoking and alcohol intake and Dupuytren's disease. There are a considerable number of individuals suffering from this condition who have never smoked or drunk alcohol. Moreover, a direct link between work-related activities such as using vibrating machines and increasing risk of Dupuytren's disease has not been established [13,14]. One statistical finding that should not be underestimated is that 42% of people with severe DC died of cancer. It is evident that more investigation is needed to confirm what can be the cause of this disease and for the time being the patients should be told that the cause of this condition is unknown [15].

THE DISEASE PROCESS

The known process of the disease is similar to wound healing which involves the proliferation of the fibroblasts and deposition of the collagen and myofibroblast contraction. This process works with the aid of a number of growth factors such as transforming growth factor Beta [16, 17]. Bands of fascial fibres, which are lining longitudinally in the subcutaneous tissue of the palm that anchor the skin of the palm grow thick fibrous cords which result in the contraction of the digits [18]. Scientists have found similarities between the presenting features of neoplastic process and Dupuytren's disease. They both include specific chromosomal defects and high rates of recurrence post surgery [16, 17, 19, 20].

Dupuytren's contracture can be related with other fibromatoses such as Peyronie disease, Ledderhose disease as well as fibromatosis of the dorsum of the proximal interphalangeal joints known as Garrod's nodules or knuckle pads. Investigations have shown that these diseases are identical from the histopathological perspective and patients who suffer from additional fibromatosis can develop new occurrences of the disease in different areas post operatively [21].

DD can be classified into 3 main stages: First stage is the early onset of the disease where small nodules and lumps appear under the digits of palmer crease. In stage two the condition becomes more extensive and involves the fascia and the digits. The final and third stage is the spread of the disease into the fingers and the creation of strong cords which result in the flexion of the fingers and loss of normal extension [15].

This disease remains mainly undetected until there is some flexion deformity of the digits. In the case of a certain diagnosis, there are two major criteria for referral and treatment of the patient. 1. If the contracture is becoming progressively worse on repeated examination and compared to previous history. 2. When there is a noticeable functional disability of the hand [15]. Dupuytren's disease can affect certain activities of daily living. Among the most significant is face washing in which the eye is being poked by the affected digit. Combing hair and putting the hand in a glove

are also ranked as the difficulties that a patient with such a disease will encounter [15]. Dupuytren's contracture develops in both hands regardless of hand dominance. The digits which are predominately affected are the ring finger and the small finger which are followed by the index, the middle finger and the thumb. The severity and the impact of the disease is different for every individual but DD presents more aggressively in the younger individuals when it occurs [15].

ASSESSMENT OF SUSPECTED DUPUYTREN'S DISEASE

The diagnosis of Dupuytren's disease is often made by the general practitioner. Even though there are a variety of different causes that lead to hand contracture these do not present with nodules in the palm. Once the patient is referred to a hand specialist Orthopedic or a plastic surgeon the assessment initiates with a thorough history taking that involves gathering the most relevant information such as: Age, gender, ethnicity, occupation, manual hobbies, hand dominance, family history of this condition, age of onset, symptoms, disease progression, previous treatment, medical history of DM and epilepsy, drug history as well as psychosocial history [15] With the help of a detailed history one can predict how the disease will affect the patient's occupation and by looking at the family history the post operative reoccurrence rate can be estimated.

The physical examination commences with the inspection of both hands in particular the affected hand. Great attention is given to the site of nodules, skin dimpling on the palm and digits, degree of skin involvement as well as signs of other types of fibromatoses in the hand. Furthermore, the patient might have previous scars in the palm in the case of disease recurrence [15].

One useful test that greatly aids staging Dupuytren's disease is the Hueston Table Top Test [22]. This is a simple test as the patient needs to put his/her hand prone on the table. If the hand does not go flat then one can say the Hueston Table Top Test is positive which indicates that the disease is in an active or moderate stage. The early stages of the disease are not easy to identify since Dupuytren's disease starts asymptotically. By the time the patient sees the doctor it is already in its moderate or severe stage.

MATERIAL AND METHOD

In this review, the relevant articles were searched primarily from the electronic data bases AMED, ASSIA (CSA Illumina), CINAHL (EBSCO), Conference Proceedings Citation Index: Science (ISI) on Web of Knowledge, EMBASE, Medline, PREMEDLINE In-Process & Non-Indexed Citations (OvidSP), PsycINFO (OvidSP), PubMed, Science Citation Index (ISI) on Web of Knowledge, Social Sciences Citation Index (ISI) on Web of Knowledge and Cochrane Library (Wiley) and ZETOC. The following key words were used for citing the appropriate articles: Dupuytren's disease _ Contracture _ assessment _ referral _ medical treatment _ surgical treatment _ non-surgical treatment _ radiotherapy.

The following inclusion criteria were used to select relevant studies: A) Any type of surgical treatment from the first to the most recent methods, B) All relevant medical and

non surgical treatments, C) Articles experimenting new methods of treatment on animals for human applications. Articles which were excluded: A) did not include treatment for Dupuytren's disease, B) Articles that were written in a language other than English. Out of 97 articles and studies that were viewed 55 were found relevant and suited the inclusion criteria. The relevant information from these articles is summarized in the result section.

RESULT

According to the genetic analyses, Dupuytren's disease is an autosomal dominant disorder with a variable penetrance and gene expression [23]. Therefore, there is no cure for this disease and only very few treatment options are available for the individuals suffering from this condition. These treatment options are summarized in Tables 1 and 2. The most commonly used treatments are surgery, open or percutaneous needle aponeurotomy, collagenase clostridium histolyticum injections, corticosteroid injections and radiotherapy [24]

SURGICAL INTERVENTION

Surgery is the most commonly used treatment option which is recommended for functionally impaired patients with contractures more than 30° of the MP joint [25-27]. There is some degree of disagreement as to when surgery is recommended when PIP joints are affected. Certain authors would consider any degree of contracture of PIP joints as an indication for surgery. Others suggest 15° to 30° of PIP joint to take operation as an option [26,28]. In contrast to these professor McGrouther states that it is better to "rely on functional difficulty and the rate of progression when deciding on surgery, rather than choosing a set amount of joint contracture [29].

Open, limited fasciectomy is currently ranked as the most commonly used surgical treatment [30-34] It is interesting to note that between 2003 and 2008 fasciectomy was the main surgical method in treatment of Dupuytren's contracture in England [35]. In a limited fasciectomy the involved fascia is removed and in cases where the disease is not very extensive fasciotomy of the affected fascia is performed [15]. Even if surgery is the treatment of choice it does not mean that there are no complications associated with it. Among the most significant postoperative complications are haematoma, injuries to nerves, vascular injury, skin necrosis, oedema, reflex sympathetic dystrophy and amputation of the finger which is rare. The most common complication that patients encounter post operatively is joint stiffness and reduced flexion ability compared to their pre-operative state [29].

There are two types of fasciotomies, open and closed fasciotomies. Open fasciotomy is the classic fasciotomy where the surgeon uses a scalpel to section the cords [36]. The closed technique or percutaneous needle aponeurotomy involves a minimally invasive operation with a very low complication rate and good short-term results in mild or moderate contractures [37-41] In this technique a small needle is used to weaken and manipulate the cords. The targeted cords will eventually snap very easily after being weakened, by simply extending the fingers passively. The post operative results are predominantly satisfactory but extensive hand therapy such as using night splints and

regular physiotherapy exercises are required for better outcomes [42]. Despite its advantages studies have shown that percutaneous needle aponeurotomy has a high recurrence rate [42].

When treating a patient with Dupuytren's disease, surgery has the best outcome but not all individuals with digital contractures will benefit from it [29]. By way of illustration, open fasciotomy is not performed on elderly patients, those with co-morbidities or both. For these individuals closed fasciotomy or percutaneous needle fasciotomy can prove helpful even though the chance of developing this disease is very high.

Dermofasciectomy is the preferred procedure for the patients with advanced Dupuytren's disease or patients with high recurrence. In this technique the skin and the affected fascia are both removed and the wound is grafted [21]. A further surgical treatment for this condition is the Jacobsen flap, which was first described by Jacobsen and Nielsen. This is a modification of McCash's technique which was first performed in 1964 [43]. This modification allows the surgeon to expose the disease in both the palm and the fingers using only two linear incisions [44]. There are many advantages when choosing this type of surgery, for instance reducing the risk of developing haematoma as well as oedema. Furthermore, there is no need for skin grafting and causing additional scars on the donor site. The patient will be able to mobilize the hand immediately after the operation which reduces the risks of developing oedema. Due to the fact that the wound is left open, the patient has to wear a dynamic orthoplast splint for approximately 10 weeks in addition to physical therapy. The wound can easily become infected and thus needs to be checked and looked after very carefully particularly in patients who are suffering from diabetes mellitus and other metabolic disorders. Skin necrosis as well as progressive flexion deformity in the distal interphalangeal joint as a result of shrinking of the skin should also not be underestimated when considering this procedure [45]. Table 1 will summarize some popular surgical procedures and their outcomes towards treating DD.

MEDICAL INTERVENTIONS

Since Dupuytren's contracture became known to scientists and medical professionals numerous ways of treating this disease have been investigated and different alternatives to surgery have been found. The most effective non surgical treatment which has also recently got approved by Food and Drug Administration (FDA) is injectable collagenase clostridium histolyticum which is known as Xiaflex. Collagenase clostridium histolyticum is an enzyme that dissolves collagen and thus it is injected directly into the cord. One day post Xiaflex injection the enzyme has had adequate time to dissolve certain part of the collagen and this makes it easier for the doctor to straighten the finger manually. Often more than one injection is necessary to give the finger its previous healthy condition back. If more than one digit is affected then several injections spread over months are required. On the grounds that injecting collagenase clostridium histolyticum is a very new treatment its long-term safety and recurrence rate requires further assessment [46].

Tomasek *et al.*, have investigated the effect of INF-gamma on myofibroblast and came to the conclusion that INF-gamma is able to suppress the differentiation of myofibroblasts and thus the contractile force is being reduced as well. Therefore, it has the potential to be used as a non surgical treatment for this condition [2]. According to Trojian *et al.*, using steroid injections into the Dupuytren nodule in the early stages of the disease can prevent its progression and the need of fasciectomy. Further research and investigation is needed to confirm this hypothesis.

Another non invasive tool that can be used for treatment of Dupuytren's disease is shock wave therapy. Knobloch *et al.*, have primarily done a randomized-controlled trial in Peyronie's disease using focused extracorporeal shock waves which reduced the pain and dramatically improved the erectile function and the quality of life. As Peyronie's disease resembles Dupuytren's to a large extent the same method was used in a randomized-controlled trail on individuals with Dupuytren's contracture. The hypothesis is that focused extracorporeal shock wave therapy can be use as a non-invasive tool to decrease the force of contracture and reduce the fibromatosis of the palm [47]. It is commonly alleged that antiepileptic drugs such as Phenobarbital are risk factors for developing Dupuytren's disease [48]. Tripoli *et al.*, studied a group of patients on Phenobarbital and some who were on benzodiazepine and managed to find out that the administration of benzodiazepine reduces the risk of recurrence of this condition [48]. Studies have also shown that radiotherapy can play an important role on preventing the progression of the disease when applied in the early-stages of Dupuytren's contracture [49]. The most recent

medical interventions for DD are demonstrated in Table 2.

DISCUSSION

The first ever treatment of Dupuytren's contracture was surgery which was performed by Guillaume Dupuytren and for many years doctors followed his way of dealing with the disease. Today, there are numerous ways of dealing with this condition and doctors can choose the most suitable method of treatment for their patients. Each technique has its own advantages and disadvantages. Certain surgical procedures have a very low recurrence rate such as dermofasciectomy [50] or Jacobsen flap [55] with a high risk of post-operative complication rates when compared to percutaneous needle aponeurotomy which has a low complication rate but a high rate of disease recurrence. There is a similar picture when looking at the non-surgical treatments, by way of illustration Injectable collagenase *Clostridium histolyticum* is an effective and immediate medical treatment but it is an expensive injection to get hold of, thus in certain countries where the insurance does not cover the costs patients might not be able to afford this treatment. Having mentioned that, recent statistics show that 3-5% of the UK population is suffering from Dupuytren's disease and the National Health Service has to provide the most cost-effective treatments for the patients [35]. At the moment Fasciectomy and fasciotomy are the main treatments for Dupuytren's contracture in the UK. The estimated costs for treatment of DD in year 2010-2011 were £41,576,141. In this year the costs per patient ranged from £2,736 for a day-case Fasciectomy to £9,210 for a day-case Revision Digital [35].

Getting away from the financial side of medicine, it is

Table 1. Summarizes the Major Surgical Procedures for Treating DD

Surgical Interventions			
Author	Technique	Outcome	Complications
Coert <i>et al.</i> , 2006 [30]	Partial fasciectomy on 261 patients and 7.3 years of follow up.	<ul style="list-style-type: none"> • Patients (age<45) had higher recurrence compared to older patients • Outcome of contracted PIP joints were significantly worse than other joints 	<ul style="list-style-type: none"> • Nerve lesions in 7.7% • Higher risk of infection and necrosis in recurrent surgery.
Lubahn 1999 [50]	Dermofasciectomy	<ul style="list-style-type: none"> • Very low recurrence rate • Reduced risk of developing haematoma as well as oedema. 	<ul style="list-style-type: none"> • Flexion deformity in DIP joints • Infections • necrosis
van Rijssen <i>et al.</i> , 2006 [38]	percutaneous needle fasciotomy, a 6-week follow-up study, 166 rays.	<ul style="list-style-type: none"> • No major complications • High patient satisfactory • Good short term results 	<ul style="list-style-type: none"> • High recurrence rate
Tripoli <i>et al.</i> ,2008 [45]	Jacobsen flap, review of 98 cases A modification of McCash technique	<ul style="list-style-type: none"> • significant correction of the contracture • Good alternative to dermofasciectomy or amputation. 	<ul style="list-style-type: none"> • High Post operative complications compared to percutaneous needle fasciotomy
Beaudreuil <i>et al.</i> , 2011 [51]	Multi-needle aponeurotomy on 30 patients, follow up after 1 and 6 months	<ul style="list-style-type: none"> • High post operative satisfaction • Not painful • safe and effective for advanced Dupuytren's disease 	<ul style="list-style-type: none"> • No major complication
Hovius <i>et al.</i> , 2011 [52]	Extensive percutaneous aponeurotomy and lipografting on 99 patients	<ul style="list-style-type: none"> • Shortens recovery time • Adds to the deficient subcutaneous fat • Leads to scarless supple skin 	<ul style="list-style-type: none"> • Digital nerve injury • Postoperative wound infection • Complex regional pain syndrome

Table 2. Demonstrates Recent Medical Interventions for Treating and Reducing the Recurrence of DD

Medical Interventions			
Author	Technique	Outcome	Complications
Gilpin <i>et al.</i> , 2010 [46]	Injectable collagenase Clostridium histolyticum (xiaflex) on 45 cords compared to 21 cords on placebo with maximum of 3 injections	<ul style="list-style-type: none"> Significantly greater range of motion Has a similar outcome to surgery 	<ul style="list-style-type: none"> No major complication
Tomasek <i>et al.</i> , 1999 [2]	Use of IFN-gamma for suppressing both the differentiation of the myofibroblast and the generation of contractile force	<ul style="list-style-type: none"> IFN-gamma can suppress both the differentiation of the myofibroblast and the generation of contractile force 	<ul style="list-style-type: none"> No major complication
Ketchum <i>et al.</i> , 2000 [53]	triamcinolone acetonide injection into the nodule on 75 hands and 4 years follow up.	<ul style="list-style-type: none"> At the early stages of DD reduces the need for surgery 	<ul style="list-style-type: none"> 50% recurrence rate
Knobloch <i>et al.</i> , 2011 [47]	Extracorporeal shockwave therapy	<ul style="list-style-type: none"> Can be applicable to prevent the progression of DC as well as a form of treatment 	<ul style="list-style-type: none"> No major complication
Tripoli <i>et al.</i> , 2011 [48]	Administration of benzodiazepine, retrospective investigation	<ul style="list-style-type: none"> Compared to Phenobarbital which induced DD, carbamazepine reduced risk of DD disease 	<ul style="list-style-type: none"> No major complication
Keilholz <i>et al.</i> , 1997 [49,54]	Radiotherapy in the early stage of Dupuytren's disease. 2 radiotherapy courses with daily fractionation of 5 x 3 Gy separated by a 6 weeks interval on 142 hands.	<ul style="list-style-type: none"> Reduction of symptomatic cords and nodules achieved in 75% of cases 77% of patients experienced no progression in long term follow up 	<ul style="list-style-type: none"> No major complications

essential to find the main cause of Dupuytren's contracture in order to prevent the spread of this disease. One way could be to invest more time in the genetic links of this condition and to explore the similarities between people suffering from this disease. It would also be beneficial to find out the cause of death of these patients as they might die from similar conditions. One study has shown that 42% of the patients with severe DD died of cancer; therefore it is worth considering whether people having DC are more likely to develop neoplastic conditions.

Using screening programs would help to identify individuals with high risk of developing DD and take immediate measures to prevent them from developing this condition. However the risk of recurrence might still be the same, unless the origin of this disease becomes known to us.

CONCLUSION

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.

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CONFLICT OF INTEREST

None declared.

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