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Brief report

Recognition, diagnosis and referral of patients with Dupuytren's disease: a review of current concepts for general practitioners in Europe

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Abstract

Background:
Dupuytren's disease (DD) is a fairly prevalent yet under-recognised disorder of the palmar fascia, resulting in fixed-flexion contractures of joints in the hand. Numerous population-based studies have been conducted in countries around the world, and published prevalence estimates vary widely. Nevertheless, most studies have shown that the prevalence of DD increases with age. Because the global population is aging, the prevalence of DD will also continue to increase.

Scope:
Patients with DD typically present to a variety of physicians, generalists and specialists alike. Thus, it is critical that providers have clear guidance on the early recognition of signs and symptoms, comprehensive evaluation of potential risk factors, differential diagnosis and when to refer a patient for treatment. Treatment options range from minimally invasive injections with collagenase to surgery.

Findings:
Results from a large-scale study of the surgical management of DD in Europe indicate that most DD diagnoses and referrals are made by general practitioners, but there is much inter-country variation. Different patient- and physician-based factors affect diagnosis rates and referral pathways. Different healthcare systems and regulations are also influential. A simple management algorithm is provided herein and explained.

Conclusion:
It is important for generalists to understand the natural history of DD and the potential benefits of early referral and treatment. General practitioners should diagnose and/or refer patients with DD to a specialist as early as possible to optimise disease management and treatment outcomes.

Background

Dupuytren's disease (DD) is a progressive, fibro-proliferative disorder that affects the palmar and digital fascia[1]. Across Europe, DD is relatively prevalent and, owing to its associated conditions and risk factors, patients will present to any of a number of physicians including – but not limited to – general, plastic and orthopaedic surgeons; rheumatologists; and general practitioners (GPs)[1]. Thus, it is critical that generalists and specialists alike have clear guidance on the early recognition of signs and symptoms, comprehensive evaluation of potential risk factors, differential diagnosis and when to refer a patient for treatment[2,3].

In this article, we provide a brief overview of the incidence and prevalence of DD, describe aspects of its pathophysiology and natural history and summarise some of the well-established and emerging treatment options for Dupuytren's contracture (DC). We also review recent findings from a large-scale study of the surgical management of DD in Europe. Using data from a survey of orthopaedic and plastic surgeons and a review of patient charts, the authors identified patterns of DD presentation and referral, factors contributing to the selection of a specific surgical procedure and resource utilisation, as well as surgical outcomes and complications. The findings afford us a better understanding of how DD has been managed in Europe and whether there are aspects to the process that might be improved to facilitate earlier identification and treatment of patients with DD.

Epidemiology

It is generally accepted that DD is most prevalent in people native to or descendents of ancestors from northern Europe. However, numerous population-based epidemiologic studies have been conducted in countries around the world. In a recent systematic review, Hindocha *et al.*[4] identified 49 evaluable studies of the prevalence and/or incidence of DD between 1951 and 2008. Nearly half of the studies ($n = 23$) were conducted in the United Kingdom, and the lowest (0.2%) and highest (56%) prevalence estimates were derived from its regions. Although published prevalence estimates vary widely, almost all studies have shown that the prevalence of DD increases with advancing age[4,5]. As the global population is aging, it is likely that the prevalence of DD is increasing and will continue to increase as well. The majority of included studies reported higher prevalence rates among men versus women[4]; one study calculated a male-to-female ratio of 5.9:1[6].

In the population-based Fourth National Morbidity Survey (1991–1992)[7], >500,000 men presenting to GPs over a 12 month period participated. The sample was representative of 1% of the male population in England and Wales, and the incidence of DD was estimated to be 34.3 per 100,000 men. In another study of patients referred to the Pulvertaft Hand Centre for surgery, the incidence of DD was estimated to be 32.5 per 100,000 in 1989–1990 and 33.0 per 100,000 population in 2000[8].

Basic anatomy of the hand and pathophysiology

In the hand, the palmar fascial complex (PFC) is comprised of the radial (thenar), ulnar (hypothenar) and central (palmar) aponeuroses; palmodigital fascia; and digital fascia (Figure 1)[9]. The central aponeurosis, a key

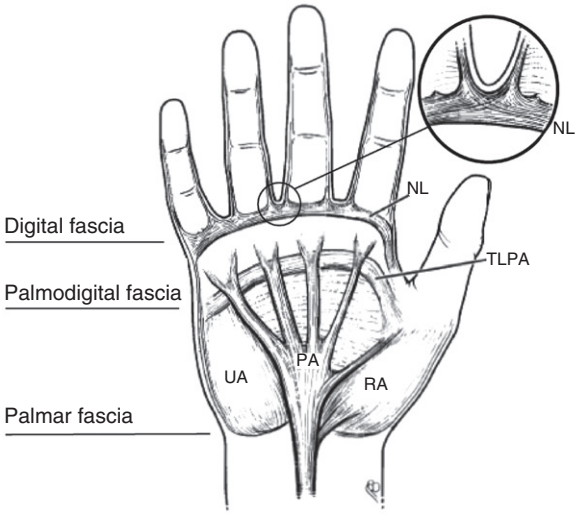

Figure 1. The palmar fascial complex. NL = natatory ligament; PA = palmar aponeurosis; RA = radial (thenar) aponeurosis; TLPA = transverse ligament of the palmar aponeurosis; UA = ulnar (hypothenar) aponeurosis. Adapted from Rayan[9], with permission.

component in DD, is a triangularly shaped fascial layer with fibres that are oriented longitudinally, transversely and vertically. The longitudinal fibres fan out into four pre-tendinous bands that bifurcate distally and extend on either side of the four long digits[9,10]. In addition, in the little finger, longitudinal fibres arise from the abductor muscle and blend with those of the pre-tendinous bands. The transverse fibres are primarily comprised of the distal natatory ligament and proximal transverse ligament of the palmar aponeurosis, both of which extend into the web space between the thumb and index finger. The superficial vertical fibres are abundant, small and strong, anchoring the palmar aponeurosis (the thickened central portion of the deep palmar fascia) to the skin. The deep vertical fibres form minute bands and septa that contain and protect flexor tendons and neurovascular bundles.

In DD, normal fascial bands and ligaments of the PFC become diseased nodules containing myofibroblasts and cords[9,10]. The appearance of a nodule is a hallmark sign for diagnosis. However, in atypical DD, a cord can develop without a palmar nodule, although this form of DD remains controversial (see below). Nodules are fixed to the underlying aponeurosis and adhere to the skin. As collagen is produced by myofibroblasts, the cord becomes thicker and shorter with time, and the affected metacarpophalangeal (MP) and/or proximal interphalangeal (PIP) joint contracts toward the palm[10] (Figure 2). Web-space contractures between any pair of adjacent fingers may also develop, causing adduction deformities. Involvement of the thumb and first web space is not uncommon among DD patients with affected digits on the ulnar side of the hand; however, only a small percentage of these patients have problems using the thumb for pinching and gripping

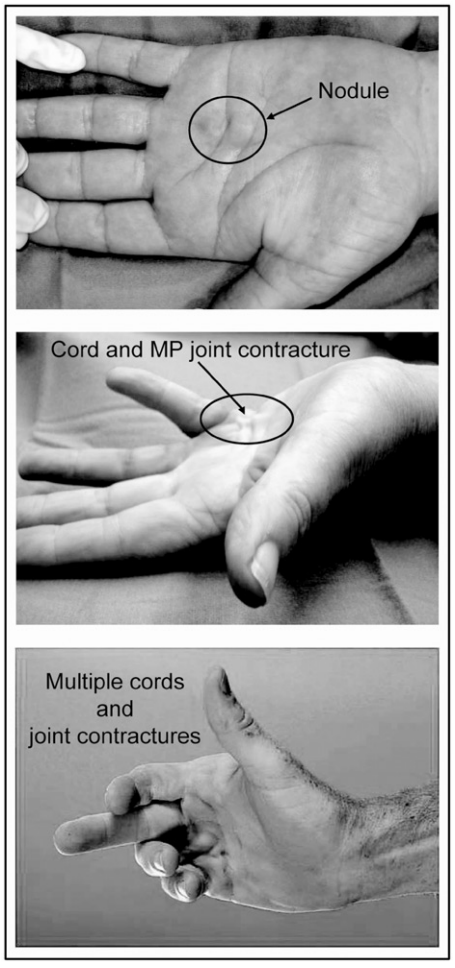

Figure 2. Stages of Dupuytren's disease. MP = metacarpophalangeal. Photographs courtesy of Paul Werker.

until closure of the first web space becomes severe[11,12]. In general, it can take months or years for DC to develop and become increasingly severe[1,13].

Although the precise mechanism of histopathology is not fully understood, myofibroblast proliferation and collagen deposition are central features of the process. As the name infers, myofibroblasts have characteristics of smooth muscle cells and connective tissue. These specialised cells produce actin, which allows for contraction; they also produce fibronectin and an integrin that allow for these cells to attach to each other and to the extracellular stromal matrix[1,10].

There is no cure for DC, and recurrence or extension after treatment is common. Owing to the contracture of one or more fingers, patients may have difficulty performing activities of daily living and work-related tasks. Many are also embarrassed by the visible deformity[1,14]. These issues may have a substantial negative impact on a patient's quality of life.

Treatment options

Surgery

To date, surgery has been the conventional and most widely used treatment for DC[10,15]. In Europe, surgical procedures for DC involve either division (fasciotomy) or excision (fasciectomy) of the collagen cord in the affected finger(s). Dermofasciectomy is a procedure that involves the removal of affected skin and fascia, followed by skin grafting over the excised surface. Some surgeons use a skin graft as a 'firebreak', or barrier between potential sites of recurrence[16–19]. Overall, recurrence rates are typically higher after fasciectomy than after dermofasciectomy (reviewed by Crean *et al.*[20]).

There are no established standards for determining a recommendation for or against surgery to a patient with DD[13]; although, as a general rule, a specialist may recommend surgery if the MP or PIP contracture exceeds 40° or 20°, respectively[21,22]. While the British Society for Surgery of the Hand (BSSH) acknowledges the lack of supporting evidence, the society's guidance indicates surgery if MP contracture is >30° or if there is any degree of PIP contracture[23]. Others propose that, in lieu of fixed degrees of contracture, surgery is indicated when there is clear worsening of the deformity and functional disability[3]. Also, it is not uncommon to use a combined approach, where both measures of contracture and extent of disability are factors in the decision-making process. Nevertheless, despite the large variability in indications for intervention in DD, the common element across different guidance appears to be a recommendation for earlier intervention with PIP contractures.

Although surgery can improve outcomes, complications may occur, recurrence is common and patients typically require re-treatment. In a systematic review of the English literature from 1998 to 2008, Denkler[24] showed that surgical complication rates after fasciectomy ranged from 4 to 39%, including major injuries such as complex regional pain syndrome (6%) and nerve and artery injury (3% and 2%, respectively). Minor complications included delayed wound healing (23%) and flare reaction (10%). After recurrence, surgical re-treatment may be complex and results in higher complication rates, including higher rates of nerve injury, compared with primary procedures. In three studies that compared primary and secondary surgeries, digital nerve and artery injuries were ten times more common in the group undergoing surgery for recurrence[24].

Minimally invasive procedures

Alternatives to surgery are becoming increasingly popular among patients with DD because they are less invasive, have faster recovery times and result in

fewer complications. These characteristics are important to active individuals who rely on manual dexterity to perform their jobs and participate in leisure activities. Minimally invasive approaches are uniquely suited for elderly patients, and this segment of the global population continues to increase.

Percutaneous needle fasciotomy

During a percutaneous needle fasciotomy (PNF), a needle is used to make small cuts throughout the length of the cord while the finger is extended. Because the skin is not opened, it is considered a non-surgical approach to correct DC. The primary advantage of PNF is that the recovery period is short; thus, patients may return to their normal activities sooner than they can after fasciectomy[25]. In clinical trials, the short-term efficacy of PNF is comparable with that of fasciectomy, provided the contracture is not >90°. With time, recurrence rates after PNF are higher than those after fasciectomy (reviewed by Crean *et al.*[20]). In a study by van Rijssen *et al.*[25], total passive extension deficit was improved by 63% in PNF patients and 79% in limited fasciectomy (LF) patients ($p = 0.001$). However, the rate of major complications was 0% in the PNF group and 5% in the LF group. Furthermore, PNF patients perceived their hand function to be better than did LF patients ($p = 0.003$)[25]. After 5 years of follow-up, the recurrence rates among patients in the PNF and LF groups were 85% and 21%, respectively ($p < 0.001$)[25].

Radiotherapy

The rationale for the use of radiotherapy is that proliferating myofibroblasts are radiosensitive; thus, radiotherapy produces free radicals that impair the proliferative activity and reduces cell density[26]. Although there is little evidence for a corrective effect on contractures, some studies, including a recent 13 year analysis by Betz *et al.*[27], have reported that radiotherapy may slow progression of the disease. For most, however, radiotherapy is considered too dangerous for this chronic but relatively benign condition[28]. Moreover, based on information provided in two reviews[29,30], the BSSH does not recommend the use of radiotherapy owing to the lack of evidence regarding clinical efficacy[23].

Collagenase *Clostridium histolyticum*

Collagenase *Clostridium histolyticum* (CCH) is the first injectable option with European licensing since 2011 for the treatment of DC with a palpable cord. CCH is a minimally invasive, non-surgical therapy with proven efficacy in correcting DC, as shown in placebo-controlled clinical trials[31–33]. In the Collagenase Option for Reduction in Dupuytren's (CORD) I study, 64% of joints injected with CCH versus 7% of those injected with placebo showed a reduction in contracture to ≤5° 30 days after the last injection ($p < 0.001$)[33]. The change from baseline in range of motion (ROM) was significantly larger after CCH versus placebo (37° vs. 4°; $p < 0.001$). CORD II results were similar: 44% of joints injected with CCH versus 5% of those injected with placebo showed a reduction in contracture to ≤5° ($p < 0.001$); the change from baseline in ROM after CCH was 35° versus 8° with placebo ($p < 0.001$)[32]. In both trials, the most commonly reported adverse events were related to the injection or finger extension procedure, including localised bruising, pain and swelling. Most adverse events were mild to moderate in intensity and resolved without intervention. Serious adverse events included two tendon ruptures and one case of complex regional pain syndrome in CORD I and one flexion pulley rupture in CORD II[32,33].

Until recently, treatment options for DC have been mostly surgical, with some limited use of PNF. In the authors' clinical experience, patients are less likely to pursue a referral for treatment if it involves surgery, especially at early stages when the patient has few to no symptoms. The Internet provides a wealth of information for patients to make educated decisions about their treatment (in consultation with their physician). Online, patients can find, for example, research results demonstrating that early intervention leads to better outcomes. Much of the topically relevant medical literature has been 'translated' to lay language and posted on society pages and discussion forums.

Results from the European surgeon survey and patient chart review

Twelve European countries participated in this study, including Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, the Netherlands, Poland, Spain, Sweden and the UK. The study consisted of the following two parts: a surgeon survey and patient chart review[15,34]. For the survey, a random sample of orthopaedic and plastic surgeons ($N = 687$) with 3–30 years of experience were asked about DC procedures performed during the past 12 months. For the patient chart review, the surgeons used a standardised questionnaire to extract information from charts ($N = 3357$) of up to five consecutive patients they treated for DC in 2008. Further details regarding study methodology and findings have been published[15,34].

Diagnosis

Overall results for the 12 countries in the European patient chart review showed that 49% of patients were diagnosed

Table 1. Mean percentage of diagnosing and referring physicians by specialty and for major European countries.

	Country					
	France ($n=456$)	Germany ($n=450$)	Netherlands ($n=176$)	Spain ($n=251$)	UK ($n=251$)	Overall ($N=3357$)
Diagnosing physician, %						
General practitioner	66	46	72	41	76	49
Treating surgeon	17	21	18	27	8	22
Other surgical specialty						
Orthopaedic surgeon	3	12	6	19	10	13
Hand surgeon	0.2	8	0.6	0.9	1	3
Plastic surgeon	0.4	0.7	2	0.7	0.2	0.6
Rheumatologist	8	0.4	2	3	0.9	5
Referring physician, %						
General practitioner	65	47	71	41	82	55
Treating surgeon	23	24	22	36	11	26
Orthopaedic surgeon	1	17	5	18	4	11
Rheumatologist	8	1	2	3	1	5
Internist	1	4	0	0.1	0.7	2

by a GP[15]. For all countries except Italy and Hungary, GPs represented the largest percentage of diagnosing physicians, with values ranging from 37 (Poland) to 80% (Denmark)[15]. Among the five major countries, GP referrals were highest for the UK (76%) and the Netherlands (72%) and lowest in Spain (41%; Table 1). Overall, 22% of patients were diagnosed by the treating surgeon[15]. Percentages for other countries were comparable, with the exception of the UK, where only 8% of diagnoses were made by the treating surgeon. About 17% of all patients were diagnosed by other surgical specialists; most of these were made by orthopaedic (13%) versus plastic (0.6%) surgeons[15]. These rates were highest in Spain (19%) and lowest in France (3%). Five percent of diagnoses were made by rheumatologists; rates were highest in France (8%) and lowest in Germany (0.4%; Table 1).

Referral

Overall, 55% of patients were referred to the responding surgeon by a GP[15]. For all countries except Italy, GPs represented the largest percentage of referring physicians, with values ranging from 37 (Hungary) to 86% (Denmark). Among the five major countries, GP referrals were highest for the UK (82%) and the Netherlands (71%) and lowest in Spain (41%; Table 1). About 26% of patients presented directly to the responding surgeon; they were not referred[15]. Rates were comparable in France (23%), Germany (24%) and the Netherlands (22%); rates were higher in Spain (36%) and notably lower in the UK (11%). Overall, 11% of patients were referred by another orthopaedic surgeon[15]; however, inter-country variability was high. Likewise, rheumatologists and internists accounted for only small percentages of referrals, and there were inter-country differences in rates (Table 1).

Study implications

Overall, results from the patient chart review show the main pathway as being diagnosed by a GP (49%), referred by the GP (55%) to a hand surgeon (56%) and managed post-operatively by a physiotherapist/occupational therapist (38%) or the treating surgeon (survey respondent; 40%)[15] (Figure 3). In the UK, the main pathway is being diagnosed by the GP (76%), being referred by the GP (82%) to a hand specialist (49%) and managed post-operatively by a physiotherapist (59%) or the treating surgeon (25%). In the Netherlands, the main pathway is being diagnosed by the GP (72%), being referred by the GP (71%) to a hand specialist (65%) and managed post-operatively by the same treating surgeon (59%). Only 28% of patients in the Netherlands see a physiotherapist after surgery.

Although the data from this study appear promising from a Europe-wide referral perspective, what remains to be determined is the number of individuals with early stage or undiagnosed DD who do not present to a GP or a specialist and the reasons why. It is critically important for GPs to understand the disease process and to realise the potential benefits of early referral and treatment. GPs should never wait until there is evidence of severe contracture or the patient manifests functional deficits. This applies to patients with first-time contractures and for those with recurrence and/or extension of disease.

It is clear that many patient- and physician-based factors may affect the rates and patterns of referral of DD patients in different countries. Different healthcare systems and country-specific regulations will also impact referrals. For example, referral rates by GPs might be influenced by the ability of hospital specialties to make direct referrals to other specialists without the GPs as gatekeepers, which is possible in some but not other

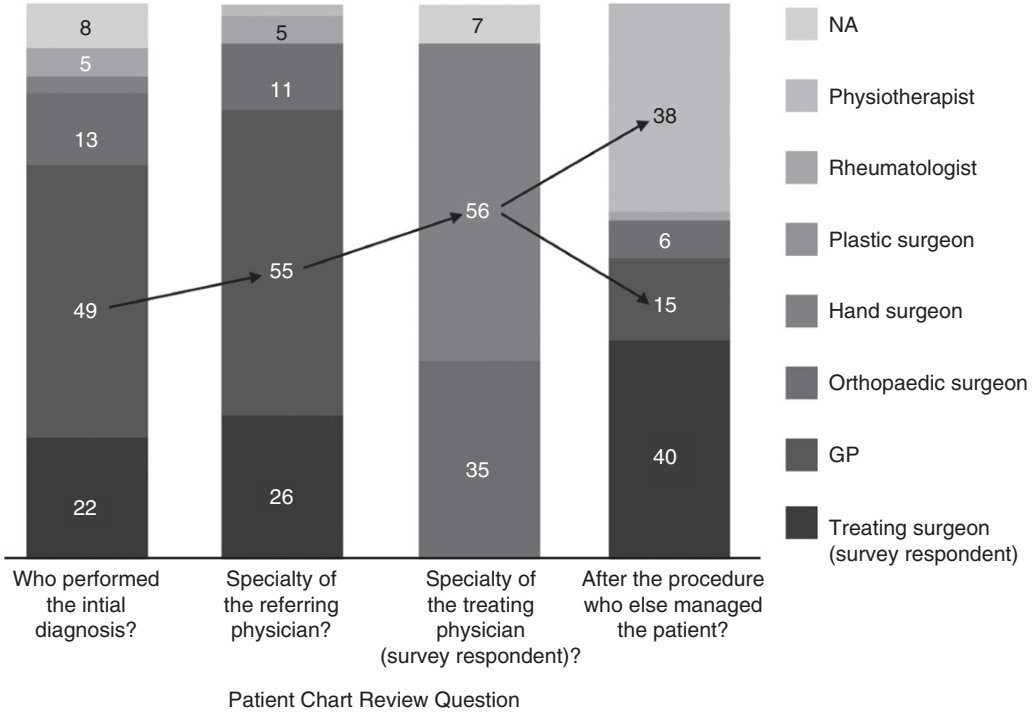

Figure 3. Overall referral pattern from European patient's chart review. GP = general practitioner; NA = not available.

European countries. Regional demographics likely play a part as well. For example, northern European countries have a higher prevalence of DD, and more people are aware of the disease and likely to have family members or friends with DD. Thus, patients may already know where to go for treatment.

Recognising Dupuytren's disease in your practice

Some patients will not present to their physician's office until the physical deformity associated with DD is obvious and/or hand function is compromised. However, the majority will ask their physicians for reassurance that the 'lump' they have in their hand is not a malignancy. Nevertheless, diagnosing DD in the early stages may be difficult, as other conditions manifest physical features that are quite similar to those in DD. In these cases, a careful differential diagnosis is critical (Table 2). Some have suggested that there is an 'atypical' form of DD – aptly named, as it is thought that some demographic (e.g. age, gender, ethnicity and family history of DD) and clinical characteristics (unilateral disease, palmar affection only and no recurrence) differ from typical DD[35,36]. Consideration of these characteristics may also be an important part of the differential.

Table 2. Dupuytren's disease: differential diagnosis.

Dupuytren's distinguishing signs	
Nodule	Firm, soft-tissue mass affixed to the skin and deeper fascia, well defined, localised; occurs on palm or digits; usually disappears in later stages of disease
Differentiate from:	
Callus	A thickened area of skin resulting from persistent friction or pressure
Inclusion cyst	Fluid-filled mass; usually occurs after an injury, oftentimes years later
Ganglion	Most common type of mass, most often found around the wrist, but also found at the base of the fingers, attached to a tendon sheath; likely due to variation in normal joint or tendon sheath function; small pouch contains clear fluid slightly thicker than synovial fluid
Epithelioid sarcoma	Rare, malignant soft tissue tumour occurring on the palm as an indurated, enlarging lump that may ulcerate in later stages; affects adolescents and young adults
Giant cell tumour	Slow-growing, mostly painless, soft tissue mass; typically presents among patients 30–50 years of age, peaks at 40–50 years; rare in those >60 years; male:female ratio: 2:3; easy to remove; highly recurrent
Cord	Aponeurotic; normal palmar/digital bands are precursors of cords
Differentiate from:	
Arthrogenic	Post-trauma or infection, degenerative
Neurogenic	Ulnar nerve palsy (e.g. 'claw hand')
Osseous	M. Kirner, after fracture
Tendinogenic	Trigger finger, after tendon repair, infection, camptodactyly
Dermogenic	Skin contracture after a burn, skin laceration or skin loss

Examination and diagnosis

The diagnosis of DD relies almost exclusively on the presence of clinical signs and symptoms, and a thorough assessment of the patient includes a detailed patient history and complete physical examination. Because DD is associated with a number of demographic, clinical and social risk factors[4,22,37], the medical history should contain details about patient age and gender, ethnicity and ancestry, family history of DD, history of previous trauma, presence of diabetes or epilepsy, alcohol consumption, cigarette smoking and extent of manual labour activities. In the European chart review study, more than half of all patients reported functional limitations in both work (57%) and leisure (56%) activities, including difficulty grasping objects (44%), shaking hands (43%) and grooming (39%)[15].

Recently, the Unité Rhematologique des Affections de la Main (URAM) scale[38] was validated as the first patient-reported measure of hand function in patients with DD. The URAM is a nine-item questionnaire that assesses particular hand functions on a scale from 0 (no difficulty) to 5 (impossible), with a total score ranging from 0 (best) to 45 (worst). It is short and simple enough to be used by busy clinicians during their daily practice.

The physical examination should include visual inspection of the hands. According to Rayan[35], "the nodule and cord are the quintessential pathologic findings in Dupuytren's disease". In general, DD typically begins as a thickening of the fascia under the skin, sometimes combined with puckering or dimpling; 'pitting' is a reliable sign for the diagnosis of early DD[35]. The presence of firm nodules affixed to the skin and palmar fascia is also typical. A cord or cords may already be present, as well as contractures causing flexion deformity of the MP and/or PIP joints. The table-top test is a reliable indicator to decide upon referral of DD[2,3]; however, GPs should feel comfortable referring a patient before contracture is evident (e.g. painful nodules) or when there is uncertainty about the diagnosis.

Typically, the disease is bilateral, but time of onset and phase differ. If unilateral, the right hand is affected slightly more frequently than is the left hand[39]. The most commonly affected finger is the ring finger, followed by the little finger and then the middle finger. It is critical to look for ectopic lesions on the dorsum of the PIP joints, soles of the feet and penis. This part of the examination is important, as DD belongs to the group of fibromatoses that includes Garrod's knuckle pads (dorsal fibromatosis of PIP joint), Ledderhose disease (plantar fibromatosis) and Peyronie's disease (penile fibromatosis)[40–42] (Figure 4). The presence of these ectopic lesions as well as a family history of DD and early age of onset are risk factors for Dupuytren's diathesis, a hereditary predisposition to an aggressive form of DD in terms of severity of contractures and frequency of recurrences[43].

If there is no contracture and/or no significant loss of hand function, no treatment is necessary. Some surgeons recommend radiotherapy at this stage, yet evidence of its effectiveness is lacking (see above). Nevertheless, some research has shown that earlier surgical[44,45] and non-surgical (e.g. CCH)[46] intervention improves functional outcomes. Peimer *et al.*[46] have shown that patients with joint contractures $\leq 30^{\circ}$ (early stage) have a better final joint angle after CCH than do patients with joint contractures $>30^{\circ}$ (advanced stage). Clearly, determining the best time for corrective therapy will require more research and will likely depend on a number of individual patient- and disease-related characteristics. Still, in the authors' experience, a large number of patients with DD are being referred later than they would like.

Follow-up

After referral, one author (P.M.N.W.) reschedules patients with early stage DD after 6 months and, if they are stable, the follow-up period is extended to 12 months. If the disease has progressed, the patient is counselled again. Younger patients may need more frequent follow-up visits, as the disease is typically more progressive. In the small subset of patients with diathesis – a severe and aggressive form of DD characterised by an earlier age of onset, more bilateral involvement, more fingers affected, faster progression and more problems with recurrence – immediate referral to specialised centres is critical to optimise outcomes. As alluded to above, referral to a specialist – be it a hand surgeon, plastic surgeon or orthopaedic surgeon – will depend on the country of interest and its healthcare system. For example, in France, GPs frequently refer DD patients to rheumatologists. In the Netherlands, GPs refer patients to plastic surgeons; although, in rural areas, where there are few plastic surgeons, they will refer patients to general surgeons. GPs in the Netherlands do not refer to rheumatologists.

The information presented in this section is summarised schematically in Figure 4. More detailed management algorithms have also been published[2,3]. It is hoped that the information provided above will assist GPs in recognising DD, monitoring disease progression and referring the patient to a specialist when the need for treatment becomes evident.

Conclusion

In Europe, DD is fairly prevalent and is associated with significant functional disability and negative effects on quality of life among patients. Although surgical approaches may improve outcomes, recurrence is

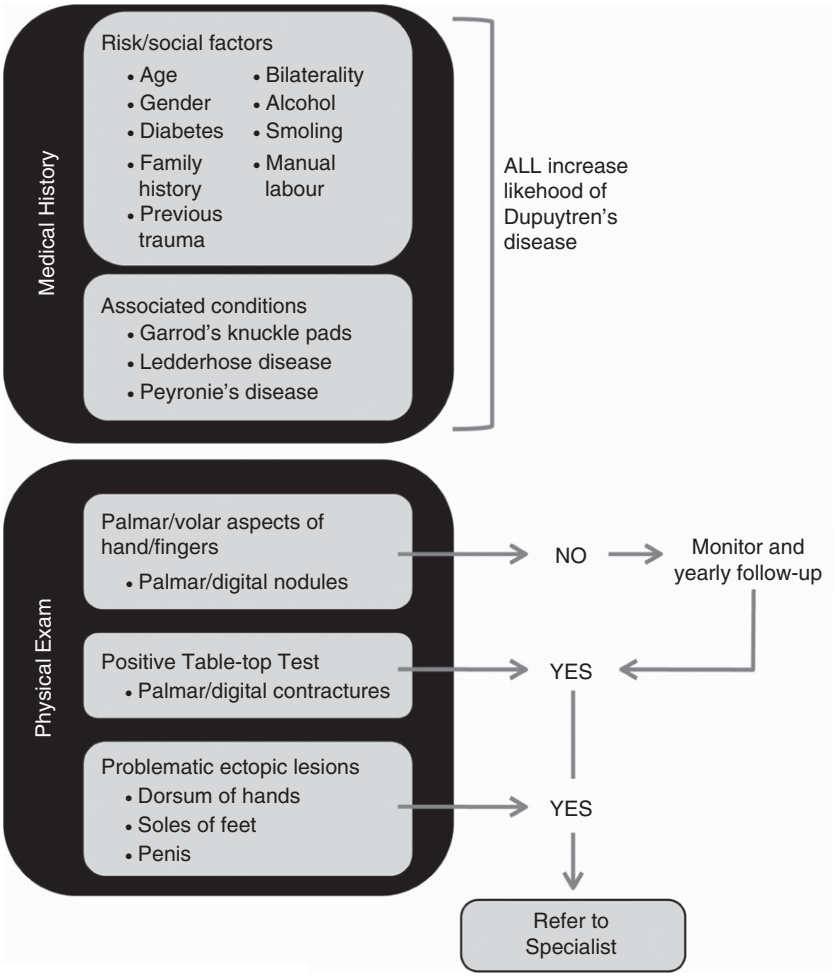

Figure 4. Differential diagnosis of Dupuytren's disease for general practitioners.

common and often requires a patient to undergo a second, third or multiple surgeries. Surgical re-treatment may be complex and result in higher complication rates versus primary procedures. Recent research shows that earlier intervention produces better outcomes. Thus, it is important for GPs and other generalists to understand the natural history of DD and the potential benefits of early referral and treatment. GPs should diagnose and/or refer DD patients to a specialist as early as possible in an effort to optimise disease management and treatment outcomes.

Transparency

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Declaration of financial/other relationships
D.v.D. and P.F. have disclosed that they have no significant relationships with or financial interests in any commercial companies related to this study or article. P.M.N.W. serves as a consultant for Pfizer. R.A.G. and P.P.S. are employed by and own stock in Pfizer Inc. and Pfizer Ltd, respectively.

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