Rodrigues, J.N. and Zhang, Weiya and Scammell, Brigitte E. and Chakrabarti, I. and Russell, P.G. and Fulllilove, S. and Davidson, D. and Davis, T.R.C. (2016) Functional outcome and complications following surgery for Dupuytren's disease: a multi-centre cross-sectional study. Journal of Hand Surgery (European Volume) . ISSN 2043-6289

FUNCTIONAL OUTCOME AND COMPLICATIONS FOLLOWING SURGERY FOR DUPUYTREN'S DISEASE: A MULTI-CENTRE CROSS SECTIONAL STUDY

SUMMARY

Variables associated with recurrent Dupuytren's disease, or a 'diathesis', have been investigated, but those associated with functional outcome and complications are less well studied.

Outcomes 1 or 5 years after an aponeurotomy, fasciectomy or dermofasciectomy were assessed by patient interview and examination at five UK centres. Four hundred and thirty two procedures were studied.

The reoperation rate did not differ at 1 year (p=0.396, Chi-square test with Monte Carlo simulation), but was higher after aponeurotomy in the 5-year group (30%, versus 6% after fasciectomy and 0% after dermofasciectomy, p=0.003, Chi square test with Monte Carlo simulation).

Loss of function (DASH>15) did not differ between procedures at 5 years, even when reoperation and other variables were controlled. Diabetes, female gender and previous ipsilateral surgery were associated with poorer function in logistic regression analysis.

The variables associated with poor function after treatments differ from diathesis variables. Aponeurotomy had lower complication rates than fasciectomy and dermofasciectomy. This may counterbalance the former's higher recurrence rate and explain why aponeurotomy demonstrated similar long-term functional outcome compared to excisional surgery in this study.

Level of evidence: III

INTRODUCTION

The factors associated with a 'Dupuytren's diathesis', or tendency for disease recurrence or extension, have been studied (Abe et al., 2004, Dias et al., 2013, Hindocha et al., 2006, van Rijssen et al., 2012). However the objective outcomes studied, such as recurrence, provide an incomplete representation of the diverse disability and functional impairment experienced by patients with Dupuytren's disease (Rodrigues et al., 2014). Recurrence and extension are not the only causes of poor outcome after surgery for Dupuytren's disease. For example, complications causing loss of finger flexion may also have serious functional consequences. In addition failure to fully straighten a finger with treatment may not adversely affect outcome. This is outcome measures such as the Disabilities of the Arm, Shoulder and Hand (DASH) patient-reported outcome measure (PROM) and the Sollerman hand score correlate poorly with angular deformity (Degreef et al., 2009, Engstrand et al., 2009, Jerosch-Herold et al., 2011, Sinha et al., 2002, Zyluk and Jagielski, 2007). However, a new Dupuytren's disease-specific PROM, the Unité Rhumatologique des Affections de la Main (URAM) scale correlates with angular deformity (Beaudreuil et al., 2011).

A recent review has considered the reported rates of complications following treatment of Dupuytren's disease (Crean et al., 2011), but factors associated with poor functional outcome and complications of surgery have not been investigated. Such factors may not be captured by all outcome measures, for example the URAM does not evaluate pain and concentrates on assessing activities that require finger extension, rather than flexion (Beaudreuil et al., 2014).

This study assessed the functional outcomes and adverse outcomes of surgery for Dupuytren's disease and the factors associated with them, rather than those associated with recurrence or extension alone.

METHODS

Patient recruitment and data collection

This project was independently approved as service evaluation at each participating centre. Information governance and, when required, Caldicott Guardian approval were also obtained locally. Clinical coding departments at five UK NHS hand surgery centres (Derby, Livingston, Nottingham, Plymouth, Rotherham) identified patients who had undergone aponeurotomy, fasciectomy or dermofasciectomy either 1 year or 5 years earlier. Patients living within 20 miles of the centre were invited to attend a locally approved service evaluation. A single surgeon (JR) assessed all patients who could be assessed 1 or 5 years (+/- 2 months) after their surgery. A standardised history and examination was performed on all patients.

Data collected included patient demographics, known and suggested risk factors for the progression of Dupuytren's disease, complications of surgery, reoperation to the same digit since the index procedure, angular deformity and the DASH PROM.

If more than one digit on a hand had been treated with the same procedure (e.g. fasciectomy to the ring and little fingers in a single procedure), then only one digit was assessed. The digit selected in such cases was the digit with the worst total active extension deficit.

If different procedures were performed in one operation (e.g. fasciectomy to the ring finger and dermofasciectomy to the little finger), then both procedures were analysed as separate events for the study of objective outcomes, but the patient was not included in the analyses of functional outcome.

If both hands were treated with the same procedure in one operation (this only occurred with aponeurotomy) then only the treated digit on the dominant hand was assessed; this was included in the analyses of both the objective and functional outcomes. This avoided any patient being recruited to the same subgroup more than once (Sauerland et al., 2003).

We chose to assess three main types of variables: functional outcome, which was the focus of the study; objective outcomes, i.e. researcher-defined measures of the complications of treatment; and patient variables, i.e. non-surgical factors that might affect outcomes such as comorbidities. Thus, we would be able to compare the functional outcomes of different procedures, with objective outcomes (such as reoperation) and control for other variables such as comorbidities.

Objective outcome measurement

Reoperation (defined as further surgery for recurrence or extension of Dupuytren's disease in the same digit) was assessed by patient recall and confirmed via hospital records if unclear. The same single observer (JR) assessed passive extension deficit at the metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints for all cases. During all measurements, the other joints in the same finger being assessed were held in maximum passive flexion, to standardise the effect of dynamism (Rodrigues et al., 2014).

Functional outcome

Proportions of patients with poor functional outcome 1 and 5 years after the three different types of procedure (aponeurotomy, fasciectomy or dermofasciectomy) were compared.

Functional outcome was based on the DASH (DASH≥15 considered "poor", DASH<15 considered "good" (Kennedy et al., 2011)). As the operation groups were not matched, it was necessary to control for differences between the groups that might influence the comparison of functional outcome using logistic regression.

Adverse outcomes

The adverse outcomes assessed were:

- cold intolerance (described using an existing scale (Campbell and Kay, 1998))

- loss of flexion (defined as a fingertip pulp to distal palmar crease distance over 10mm on active flexion)
- infection (defined as patient recall of the need for at least one postoperative course of antibiotics that was not prescribed as prophylaxis)
- complex regional pain syndrome (CRPS) (defined using the modified International Association for the Study of Pain (IASP) criteria based on examination and patient recall (Harden et al., 2007))
- altered sensation (defined as failure to identify 2/3 tests of two point discrimination at 6 millimetres over the pulp of the operated digit in the territory of either digital nerve)

Sample size

A sample size with ten outcome events per predictor variable is often quoted for logistic regression analyses. As we used twelve predictor variables were used, this would require 120 poor functional outcomes (DASH>15) in our study. However, more recent examination of this rule has suggested that five to nine outcome events per predictor variable may be acceptable (Vittinghoff and McCulloch, 2007), in which case 60-108 poor functional outcomes would be needed. As the proportion of patients with poor functional outcome following Dupuytren's disease surgery is not well described, it was assumed that approximately 25% of treatments would result in poor functional outcomes. On this basis, a total target of 400 was required to achieve a target of 100 poor functional outcomes.

Statistical analysis

Analyses were performed using Prism 6.0 for Mac OS X (GraphPad® Software, 2012) and SPSS® Statistics version 21 (IBM® Software, 2012). DASH scores were dichotomised into those above 15 (symptomatic scores) and those below 15 (asymptomatic scores), based on guidance from the developer of the DASH (Kennedy et al., 2011).

The suitability of the data for logistic regression was verified prior to analysis. In particular, the data was examined for the absence of multicollinearity, which occurs when two or more of the independent variables studied correlate with each other very strongly. If present, this can affect regression (Pallant, 2010). To do this tolerance, the amount of variance that cannot be accounted for by other variables, was calculated for each variable. If it is low, then the variable may show collinearity with another variable, or multicollinearity with several variables (Pallant, 2010). In keeping with convention, an unacceptable level of tolerance was defined as <0.1. Binary logistic regression analysis was performed to identify and control for independent variables associated with impaired function defined as DASH>15 at 1 year after treatment (this is the threshold at which the developers of the DASH score consider that a score becomes symptomatic (Kennedy et al., 2011)) and with adverse outcomes. The operation type was entered with aponeurotomy as the constant with fasciectomy and dermofasciectomy compared to it.

The independent variables that were hypothesised to affect functional outcome were controlled in these comparisons with the aim of achieving a more accurate comparison of true functional outcome. The variables were: further ipsilateral Dupuytren's disease surgery since the index procedure (based on patient report, scar examination and clinical note verification when possible; termed "surgery since"), the length of follow up (1 year or 5 years) and eight others, some of which are part of the traditional Dupuytren's diathesis, and others are factors that might be expected to influence functional outcome:

- Self reported alcohol consumption >28 United Kingdom units per week (where 1 unit is 10 milligrams ethanol)
- Active smoker
- Self reported positive family history of Dupuytren's disease
- Surgery to the little finger

- The presence of knuckle pads on examination
- The index procedure was revision of previous surgery (defined as previous surgery to the same digit)
- Diabetes mellitus
- Gender

Some of these are part of the traditional Dupuytren's diathesis, whilst the others are factors that might be expected to influence functional outcome.

A similar approach was used to study adverse events. Proportions of patients with each adverse outcome were compared between the three treatments (aponeurotomy, fasciectomy and dermofasciectomy) with Chi square tests. Hierarchical binary logistic regression analyses were performed for each adverse outcome in a similar manner as for functional outcome. The independent variables selected for study were ones that might influence the risk of complications. In addition to further ipsilateral surgery for Dupuytren's disease, they were:

- Multiple digit surgery during index procedure
- Gender
- Diabetes mellitus
- Smoking status
- Index procedure was revision of previous surgery (defined as previous surgery to the same digit)

For adverse outcomes expected to change between 1 and 5 years postoperatively, the time point (1 year versus 5 years) was also studied. These were loss of flexion and cold intolerance (which might improve in the intervening period). For other adverse outcomes, the 1 year and 5 year assessments were studied together.

Loss of flexion was studied as an 'adverse outcome' that might result from hand surgery, even in Dupuytren's disease, where the goal of surgery tends to relate to finger extension.

To control for false discoveries (false positives), the p value threshold considered significant was adjusted using a described method (Benjamini and Hochberg, 1995). As the variables associated with poor functional outcome have not been studied widely, a false discovery rate (Q) of 20% was considered reasonable to minimise the risk of a type 2 error. The variables in the model were ordered by p value and ranked and the threshold for each variable calculated using the formula (i/m)*Q, where 'i' was the rank of the variable and 'm' was the total number of tests (13 in the analysis of functional outcome). If the p value obtained was smaller than 0.05 and also lower than its calculated threshold, then the result was considered significant.

RESULTS

Patients and procedures

We recruited and assessed 414 patients between September 2011 and June 2013 across all sites. They had undergone 433 procedures. One had undergone an amputation after the index procedure and was excluded from the analysis.

All remaining 432 procedures in 413 patients were included in analyses of reoperation and complications, as these were recorded at digit level (see Table 1). However, function is assessed at patient level; only the dominant hands were assessed for ten of the 413 patients, who had undergone aponeurotomy to both hands in a single procedure. A further nine patients had undergone different procedures to different digits and so were excluded from analyses of function. Thus, 404 patients were included in analyses of function (see Table 1).

Nine patients (2%) had two different procedures. This comprised seven patients in the 1-year postop group who had undergone fasciectomy to a digit and dermofasciectomy to a different digit of the same hand and one patient in the 5-year postop group. The other patient had undergone fasciectomy to one hand and aponeurotomy to the other hand in the same procedure.

The demographics of the 413 patients are shown in Table 2. There were reoperations following 11 aponeurotomies and 11 fasciectomies but none following dermofasciectomy. Following aponeurotomy there were 4/11 further aponeurotomies and 7/11 fasciectomies. Following fasciectomy, there was one aponeurotomy, 5/11 fasciectomies and 5/11 dermofasciectomies. These proportions were significantly different (p=0.041 (99% confidence intervals: 0.036, 0.046), Chi square test with Monte Carlo simulation (10 000 replicates)). It was not clear whether these choices were due to patient preference, surgeon preference or other reasons.

Objective outcomes

The percentage of procedures that had undergone reoperation was not different between the three procedures at 1 year (p=0.396, Chi square test using Monte Carlo method, see Table 3). However, the reoperation rate was significantly greater after aponeurotomy at 5 years (p=0.000, Chi square test, see Table 3). The reoperation rate after aponeurotomy was significantly higher at 5 years than at one year (6/20 versus 5/114, p=0.002, Fisher's Exact test). The reoperation rate did not change between 1 and 5 years for fasciectomy (3/126 versus 8/125). There were no reoperations following dermofasciectomy.

We assessed a sub-group of 'poor objective outcomes' (which we defined as patients who had undergone reoperation or had not undergone reoperation but had either MCP joint or PIP joint fixed flexion contractures >25^{o}) to account for patients who may have declined revision surgery or been considered unsuitable for further surgery. This group comprised those who had undergone reoperation and those who had considerable loss of extension but had not undergone further surgery. The proportion of 'poor objective outcomes' was significantly greater 1 year after more invasive procedures (see Table 3). However, there was no difference between procedures at 5 years.

Functional outcome

Overall 96/404 (24%) had poor functional outcomes. The proportion of patients with symptomatic DASH scores (DASH>15) was not significantly different between the three procedures either at 1 or 5 years (Table 4). However different proportions of these patients had undergone further surgery over the 1 or 5 years, with a significantly higher reoperation rate 5 years after aponeurotomy than after dermofasciectomy.

As the prerequisites were met in terms of tolerance of the variables studied, logistic regression analysis was performed. The omnibus test demonstrates whether the model built by the analysis performs well in terms of 'goodness of fit', i.e. whether the included variables do contribute to predicting poor functional outcome. Here, it was statistically significant ($p<0.001$), demonstrating that this was the case. The results of the logistic regression analysis are shown in Table 5. Controlling for confounding variables such as the effect of further surgery and length of follow up, the only other variables that showed significant associations with poor function were female gender, diabetes mellitus and previous ipsilateral surgery for Dupuytren's disease. The variables considered part of the classical Dupuytren's diathesis were not associated with a poor functional outcome.

Adverse outcomes

The rates of different adverse outcomes are shown in Table 6, grouped by procedure (and length of follow up where relevant). Complications that were hypothesised to improve over time (cold intolerance and loss of flexion) were more common at 1 than at 5 years. Infection and altered sensation were observed more frequently after more invasive procedures than after aponeurotomy. At 1 year cold intolerance and loss of flexion were more common after more invasive procedures. There was no difference between procedures at 5 years, although significantly more of the aponeurotomy group had undergone further surgery ($p=0.002$).

Tolerances for all variables studied in relation to complications were acceptable, and logistic regression analyses were performed for all complications except CRPS, as

this was found infrequently. Each of the models for cold intolerance, loss of flexion, altered sensation and infection was significant on omnibus testing, which confirms that each of the regression models performed well relative to the baseline data without the independent variables controlled. All statistically significant results from the analyses are shown in Table 7.

DISCUSSION

Objective outcomes

This study confirms that aponeurotomy has a higher reoperation than fasciectomy or dermofasciectomy. The cross-sectional design of our study means that patients' immediate preoperative condition and postoperative outcome are not known, which limits the interpretation of our data in Table 3. In particular, it is possible that the patients in this study who underwent more invasive procedures had presented with more severe preoperative disease and not achieved full correction at surgery. This might explain why more of them had 'poor objective outcomes' at 1 year here. However, reliable rates of initial correction have been demonstrated, including for aponeurotomy (Pess et al., 2012).

Reoperation may be an important clinical and economic endpoint to study, but is a complex variable. In order to undergo further treatment, a patient would have to have recurrent or extended disease that is amenable to further surgery, be offered surgery by a clinician and consent to the further treatment. Some of our study group described progressive recurrence but had not sought further intervention. This pattern has been previously reported, with 'reoperation rates' lower than 'treatment failure' rates (van Rijssen et al., 2012). As a result, reoperation is not an accurate or valid surrogate for recurrence. In this study, the proportions of patients undergoing reoperation within 5 years of treatment were higher after aponeurotomy, as might be expected, but were still lower than reported by others (Foucher et al., 2003; van Rijssen et al., 2012). One randomised controlled trial reported a reoperation rate within 5 years of 33/52 (63%) for aponeurotomy and 4/41 (9%) for fasciectomy (van Rijssen et al., 2012). Whereas their reoperation rate for aponeurotomy was two times greater than that in our study, their reoperation rate after fasciectomy was similar to ours (6%)

Abe and colleagues investigated the factors associated with reoperation at a mean follow-up of 5 years in a small Japanese population (Abe et al., 2004). They found that the factors in the classical diathesis had prognostic value. However, the applicability of their findings to other populations is not clear. Additionally, the length of follow-up ranged from 3 to 12 years. As Dupuytren's disease is a slowly progressive condition, patients 3 years following Dupuytren's disease surgery are not comparable to those 12 years after treatment.

Hindocha (2006) studied the factors associated with recurrence of palpable disease in the operated field (Hindocha et al., 2006). They identified that male gender and young age of onset were associated with recurrence of palpable disease. Whilst this is a common definition of recurrence (Becker and Davis, 2010), it is not clinically relevant. The reappearance of palpable disease alone does not require treatment, as supported by comparing the proportion of patients who have poor objective outcome to those who have undergone reoperation (Table 3 here). In addition reappearance of palpable disease does not necessarily impair function.

van Rijssen et al. (2012) studied factors associated with recurrence defined as a progressive angular deformity. They concluded that the scoring system proposed by Abe et al (2004) did not predict recurrence. As further treatment might become advisable with deterioration in angular deformity, this may be a more clinically applicable and reliable endpoint than those used in either of the earlier studies by Abe et al. and Hindocha et al. However, it does not describe the patient's hand function or health-related quality of life, which is probably also influenced by factors such as complications.

Most recently, Dias (2013) investigated factors associated with contracture recurrence in a randomised controlled trial of firebreak dermofasciectomy versus z-plasty closure of fasciectomy wounds (Dias et al., 2013). They found that shorter disease duration, worse preoperative function and longer operation time were associated with recurrence, though the degree of progression that constituted

recurrence was not formally defined. These factors could not be studied with the cross sectional study design used here.

Others have investigated the factors associated with poor outcome in the absence of recurrence of disease (Misra et al., 2007), highlighting that 'poor outcome' in Dupuytren's disease is not entirely due to recurrence.

Recurrence has been the focus of much research in Dupuytren's disease (Becker and Davis, 2010). Whilst treating recurrent disease may be challenging, doing so following an aponeurotomy may be more straightforward than after more invasive surgery (van Rijssen and Werker, 2012), and so not all recurrences may have the same implications regarding future treatment. Furthermore, recurrence alone cannot be used as a surrogate for functional outcome, as the correlation between angular deformity and loss of function is weak (Engstrand et al., 2009, Jerosch-Herold et al., 2011, Zyluk and Jagielski, 2007).

The choice of recurrence as the primary endpoint for studying treatment in Dupuytren's disease is challenged by the data presented here, which demonstrates the different rates of complications after different treatments. As many of these complications are not associated with recurrence, they will not be captured if recurrence is used as the sole outcome measure. Consequently, recurrence may be a surgeon-centred outcome, but is less likely to be patient-centred and it may be of limited value in cost utility analyses.

Functional outcome

After controlling for some independent variables that might differ between the groups (Table 5), functional outcome was not significantly different between these three procedures. This finding requires confirmation in a study with a larger number of patients treated with dermofasciectomy and aponeurotomy with 5-year follow-up. This is as complications that limit function, such as loss of flexion, cold intolerance and altered sensation may be more frequent following more invasive procedures, which typically had higher complication rates in this study.

The variables associated with poorer outcome in this study differ from those identified as contributing to the Dupuytren's diathesis in other studies (Abe et al., 2004, Hindocha et al., 2006, Hueston, 1963). This suggests that those patients whose hand function is worse following surgery may not always be the patients who experience recurrence.

Several variables were associated with poor function. Patients undergoing revision treatment may not achieve as good hand function as those undergoing primary surgery due to an accumulation of iatrogenic insult to the hand or perhaps due to disease severity. Women reported worse hand function than men, though it is not clear why. It may be intrinsic to the DASH itself, as similar patterns have been reported with the QuickDASH in carpal tunnel release (Jenkins et al., 2012). Diabetics might be expected to have greater risk of complications, such as infection and poor healing, and so worse rehabilitation. Alternatively, their higher DASH scores may reflect a higher prevalence of comorbid upper limb conditions, such as cheirarthropathy, trigger fingers and carpal tunnel syndrome (Larkin et al., 2014, Pandey et al., 2013). Although at least two Dupuytren's-specific measures (Beaudreuil et al., 2011, Mohan et al., 2014) exist, the DASH is the most commonly employed measure to assess the outcome after Dupuytren's disease surgery (Ball et al., 2013). Therefore, the data presented here are important to consider when interpreting the findings of studies regarding functional outcome in Dupuytren's disease.

When the independent variables studied were controlled for, there was no difference in the odds of having poor hand function 5 years after aponeurotomy compared to fasciectomy or dermofasciectomy. This may reflect a greater risk of recurrence after aponeurotomy being offset by the less invasive nature of the procedure resulting in less frequent or less severe complications. However, given the limitations of this study, a randomised controlled trial with hand function as the primary endpoint is

388 required to confirm this and to facilitate comparison of the relative cost effectiveness
389 of different treatments for Dupuytren's disease.
390
391 **Limitations**
392 The most important limitation to this study relates to its cross-sectional design. As a
393 result, the preoperative and immediate postoperative states of patients are not
394 known and may not have been matched between the three different treatments.
395 Steps were taken to improve the reliability of the data presented. Firstly, centres that
396 contributed had different treatment preferences, with some favouring aponeurotomy
397 and others fasciectomy. Secondly, our use of logistic regression analyses
398 compensated for differences between groups. Despite this, our comparison between
399 procedure types is not as robust as one based on the results of a prospective
400 comparative study. Nevertheless, our findings for the factors associated with poor
401 functional outcome are important in their own right, but require verification with a
402 prospective, preferably randomised, study.
403 Some of our variables were self-reported and may not have been accurate. For
404 example, smoking status may have changed since the patient underwent surgery,
405 there may have been recall bias and social desirability responses may have
406 influenced the data with patients denying or underestimating factors such as
407 excessive alcohol intake or smoking. Studying such variables prospectively would
408 be more reliable.
409 Some sub groups within our study were relatively small and our findings need to be
410 validated in larger size studies or even with registry-level data. However, our rates of
411 complications are largely comparable to those previously reported (Crean et al.,
412 2011).
413 There are other limitations to our data that might explain why some findings differ
414 from those of other studies. There may have been selection bias in our study as we
415 recruited retrospectively. There may also be differences in the preoperative states of

the digits treated in different studies, or in patient or surgeon attitudes. The latter may either relate to different cultural norms in different countries or perhaps related to involvement in a trial compared to routine clinical practice. However, given the paucity of literature that focuses primarily on functional outcome in Dupuytren's disease, rather than recurrence, we believe that our study is important and should influence the design of future research studies.

References

Abe Y, Rokkaku T, Ofuchi S, Tokunaga S, Takahashi K, Moriya H. An objective method to evaluate the risk of recurrence and extension of Dupuytren's disease. J Hand Surg Brit Eur. 2004, 29: 427-30.

Ball C, Pratt AL, Nanchahal J. Optimal functional outcome measures for assessing treatment for Dupuytren's disease: a systematic review and recommendations for future practice. BMC Musculoskelet Disord. 2013, 14: 131.

Beaudreuil J, Allard A, Zerkak D et al. Unite Rhumatologique des Affections de la Main (URAM) scale: development and validation of a tool to assess Dupuytren's disease-specific disability. Arthrit Care Res. 2011, 63: 1448-55.

Beaudreuil J, Orcel P, Bardin T et al. Re: Rodrigues JN, Zhang W, Scammell BE, Davis TRC. What patients want from the treatment of Dupuytren's disease - is the Unite Rhumatologique des Affections de la Main (URAM) scale relevant? J Hand Surg Brit Eur. 2014, 39: 673-5.

Becker GW, Davis TR. The outcome of surgical treatments for primary Dupuytren's disease--a systematic review. J Hand Surg Brit Eur. 2010, 35: 623-6.

Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. J R Stat Soc Series B Stat Methodol. 1995, 57: 289-300.

Campbell DA, Kay SP. What is cold intolerance? J Hand Surg Brit Eur. 1998, 23: 3-5.

Crean SM, Gerber RA, Le Graverand MP, Boyd DM, Cappelleri JC. The efficacy and safety of fasciectomy and fasciotomy for Dupuytren's contracture in European

444 patients: a structured review of published studies. J Hand Surg Brit Eur. 2011, 36:
445 396-407.
446 Degreef I, Vererfve PB, De Smet L. Effect of severity of Dupuytren contracture on
447 disability. Scand J Plast Recons. 2009, 43: 41-2.
448 Dias JJ, Singh HP, Ullah A, Bhowal B, Thompson JR. Patterns of recontracture after
449 surgical correction of Dupuytren disease. J Hand Surg Am. 2013, 38: 1987-93.
450 Engstrand C, Boren L, Liedberg GM. Evaluation of activity limitation and digital
451 extension in Dupuytren's contracture three months after fasciectomy and hand
452 therapy interventions. Journal of Hand Ther. 2009, 22: 21-6.
453 Foucher G, Medina J, Navarro R. Percutaneous needle aponeurotomy:
454 complications and results. J Hand Surg Brit Eur. 2003, 28: 427-31.
455 Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria
456 for complex regional pain syndrome. Pain Med. 2007, 8: 326-31.
457 Hindocha S, Stanley JK, Watson S, Bayat A. Dupuytren's diathesis revisited:
458 Evaluation of prognostic indicators for risk of disease recurrence. J Hand Surg Am.
459 2006, 31: 1626-34.
460 Hueston JT. The Dupuytren's diathesis. In: Hueston JT (Ed.) *Dupuytren's*
461 *contracture*. Edinburgh, E & S Livingstone, 1963: 51-63.
462 Jenkins PJ, Duckworth AD, Watts AC, McEachan JE. The outcome of carpal tunnel
463 decompression in patients with diabetes mellitus. J Bone Joint Surg Br. 2012, 94:
464 811-4.
465 Jerosch-Herold C, Shepstone L, Chojnowski A, Larson D. Severity of contracture and
466 self-reported disability in patients with Dupuytren's contracture referred for surgery. J
467 Hand Ther. 2011, 24: 6-10.
468 Kennedy C, Beaton D, Solway S, McConnell, Bombardier C. *The DASH and*
469 *QuickDASH Outcome Measure User's Manual*, Third ed. Toronto, Institute for Work
470 and Health, 2011.

Larkin ME, Barnie A, Braffett BH et al. Musculoskeletal complications in type 1 diabetes. Diabetes Care. 2014, 37: 1863-9.

Misra A, Jain A, Ghazanfar R, Johnston T, Nanchahal J. Predicting the outcome of surgery for the proximal interphalangeal joint in Dupuytren's disease. J Hand Surg Am. 2007, 32: 240-5.

Mohan A, Vadher J, Ismail H, Warwick D. The Southampton Dupuytren's Scoring Scheme. J Plast Surg Hand Surg. 2014, 48: 28-33.

Packham T. Clinical commentary in response to: Severity of contracture and self-reported disability in patients with Dupuytren's contracture referred for surgery. J Hand Ther. 2011, 24: 12-4.

Pallant J. Part 4: Statistical techniques to explore relationships between variables: Logistic Regression. *SPSS Survival Guide*, 4th ed. Maidenhead, Open University Press, 2010.

Pandey A, Usman K, Reddy H, Gutch M, Jain N, Qidwai S. Prevalence of hand disorders in type 2 diabetes mellitus and its correlation with microvascular complications. Ann Med Health Sci Res. 2013, 3: 349-54.

Pess GM, Pess RM, Pess RA. Results of needle aponeurotomy for Dupuytren contracture in over 1,000 fingers. J Hand Surg Am. 2012, 37: 651-6.

Rodrigues JN, Zhang W, Scammell BE, Davis TR. Dynamism in Dupuytren's contractures. J Hand Surg Brit Eur. 2014.

Rodrigues JN, Zhang W, Scammell BE, Davis TR. What patients want from the treatment of Dupuytren's disease -- is the Unite Rhumatologique des Affections de la Main (URAM) scale relevant? J Hand Surg Brit Eur. 2014.

Sauerland S, Lefering R, Bayer-Sandow T, Bruser P, Neugebauer EA. Fingers, hands or patients? The concept of independent observations. J Hand Surg Brit Eur. 2003, 28: 102-5.

Sinha R, Cresswell TR, Mason R, Chakrabarti I. Functional benefit of Dupuytren's surgery. J Hand Surg Brit Eur. 2002, 27: 378-81.

van Rijssen AL, ter Linden H, Werker PMN. Five-year results of a randomized clinical trial on treatment in Dupuytren's disease: percutaneous needle fasciotomy versus limited fasciectomy. Plas Reconstr Surg. 2012, 129: 469-77.

van Rijssen AL, Werker PM. Percutaneous needle fasciotomy for recurrent Dupuytren disease. J Hand Surg Am. 2012, 37: 1820-3.

Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol. 2007, 165: 710-8.

Zyluk A, Jagielski W. The effect of the severity of the Dupuytren's contracture on the function of the hand before and after surgery. J Hand Surg Brit Eur. 2007, 32: 326-9.

Table 1: Sample sizes studied

	1 YEAR FOLLOW UP		5 YEAR FOLLOW UP	
	Numbers of procedures having an objective analysis	Numbers of patients having a functional analysis	Numbers of procedures having an objective analysis	Numbers of patients having a functional analysis
Total	270	245	162	159
Aponeurotomy	114	104	20	19
Fasciectomy	126	118	125	124
Dermofasciectomy	30	23	17	16

Table 2: Patient demographics

Demographic	
Age (years)	Mean 66, Range 33-89
Men : Women	318 : 95 (77% men)
Right hand dominance	371/413 (90%)
Diabetic	61/413 (15%)
Smoker	60/413 (15%)
Self reported weekly alcohol intake (UK units/week)	Mean 14.7
(1 UK unit = 10 milligrams ethanol)	
Previous ipsilateral surgery prior to index operation	103/413 (25%)
Index operation was revision of previously treated digit	85/413 (21%)
Self reported positive family history of Dupuytren's disease	180/413 (44%)
Knuckle pads present	122/413 (30%)
Right hand treated	212/413 (51%)
Digit studied	248 little (60%)
	129 ring (31%)

25 middle (6%)

9 index (2%)

2 thumb (0.5%)

Table 3: Objective outcomes

Outcome		Aponeurotomy	Fasciectomy	Dermofasciectomy	Chi square test
Numbers of reoperations at:	1 year	5/114 (4.4%)	3/126 (2.4%)	0/30 (0%)	p=0.396 (0.384, 0.409)*
	5 years	6/20 (30.0%)	9/126 (7.1%)	0/17 (0%)	p=0.003 (0.002, 0.005)*
Objective outcome poor (Reoperation or no reoperation but either MCPJ or PIPJ>25^{o} fixed flexion contracture)	1 year	25/114 (21.9%)	48/126 (38.1%)	14/30 (46.7%)	p=0.006
	5 years	8/20 (40.0%)	61/125 (48.8%)	10/17 (58.8%)	p=0.521

* Due to small numbers in groups, Monte Carlo significances are presented, with 99% confidence intervals in brackets, based on 10 000 sampled tables

Table 4: Functional outcomes

Outcome	Time point	Aponeurotomy	Fasciectomy	Dermofasciectomy	Statistical significance between procedures
DASH summary score (mean (95%CIs))	1 year	9.5 (6.8, 12.2)	10.7 (7.6, 13.8)	14.3 (6.2, 22.5)	p=0.421*
	5 years	9.1 (4.7, 13.5)	10.9 (8.3, 13.5)	15.1 (5.5, 24.8)	p=0.448*
Proportion of patients reporting DASH>15	1 year	19/104 (18.3%)	26/118 (22.0%)	7/23 (30.4%)	p=0.416†
	5 years	5/19 (26.3%)	34/124 (27.4%)	5/16 (31.3%)	p=0.952 (0.947, 0.958)†

*One way ANOVA

†Chi square test, with Monte Carlo simulation when group frequencies include 5 or fewer (99% confidence intervals in brackets, 10 000 replicates)

Table 5: Logistic regression of function

Independent variable		Adjusted Odds Ratio (OR)	95% confidence intervals of adjusted OR	Rank by p value (i) †	(i/m)*Q p value threshold †	Significance of association (p value)
Gender						
	Women	**3.88**	**2.15-6.99**	**1**	**0.015**	**<0.001**
	Men	1				
Previous ipsilateral Dupuytren's surgery						
	Yes	**2.13**	**1.18-3.85**	**2**	**0.031**	**0.012**
	No	1				
Diabetic						
	Yes	**2.07**	**1.10-3.91**	**3**	**0.046**	**0.025**
	No	1				
Smoker						
	Yes	1.67	0.83-3.37	4	0.062	0.149
	No	1				
Little finger surgery						
	No	1.34	0.79-2.27	5	0.077	0.268
	Yes	1				
Length of follow up						
	5 years	1.34	0.79-2.27	6	0.092	0.284
	1 year	1				
Knuckle pads						
	Present	1.31	0.76-2.28	7	0.108	0.334
	Absent	1				
Further surgery since material operation						
	Yes	1.60	0.58-4.43	8	0.123	0.364

	No	1				
Age at surgery						
	Under 50 years	1.53	0.56-4.16	9	0.138	0.409
	50 years or over	1				
Procedure was fasciectomy						
	Fasciectomy	1.25	0.68-2.28	10	0.154	0.479
	Aponeurotomy	1				
Procedure was dermofasciectomy						
	Dermofasciectomy	1.21	0.45-3.27	11	0.169	0.702
	Aponeurotomy	1				
Family history of Dupuytren's disease						
	Yes	1.05	0.64-1.74	12	0.184	0.842
	No	1				
Weekly alcohol intake						
	≤ 28 units	1.01	0.49-2.08	13		0.981
	>28 units	1				

† - These columns form part of the false discovery rate adjustment to the p value threshold. The variables are ordered by their p value, and ranked (their rank is labelled as 'i'). The total number of tests ('m') is 13. The false discovery rate that has been tolerated in the analysis ('Q') is 20%. The adjusted p value threshold to protect against false discovery for each variable is (i/m)*Q.

Table 6: Complications

Complication	Time point	Aponeurotomy (total n=134)	Fasciectomy (total n=251)	Dermofasciectomy (total n=47)	Significance between procedures (Chi square tests)
Reoperation	1 year	5/114 (4.4%)	3/126 (2.4%)	0/30 (0%)	0.396 (0.384, 0.409)*
	5 years	6/20 (30.0%)	8/125 (6.4%)	0/17 (0%)	**0.003 (0.002, 0.005)***
Cold intolerance	1 year	11/114 (9.6%)	39/126 (31.0%)	19/30 (63.3%)	**<0.001**
	5 years	1/20 (5.0%)	20/126 (15.9%)	5/17 (29.4%)	0.140 (0.131, 0.148)*
Flexion loss>10mm	1 year	20/114 (17.5%)	42/126 (33.3%)	13/30 (43.3%)	**0.002**
	5 years	3/20 (15.0%)	30/125 (24.0%)	3/17 (17.6%)	0.706 (0.694, 0.718)*
Altered sensation†		6/134 (4.5%)	38/251 (15.1%)	9/47 (19.1%)	**0.003**
Infection		2/134 (1.5%)	22/251 (8.8%)	7/47 (14.9%)	**0.004 (0.002, 0.005)***
CRPS		1/134 (0.7%)	5/251 (2.0%)	0/47 (0%)	0.411 (0.399, 0.424)*

Statistically significant results are emboldened

* Due to small numbers in some groups, Monte Carlo significances are presented, with 99% confidence intervals in brackets, based on 10 000 sampled tables

† Defined as absent 2 point discrimination at 6 millimetres in either radial or ulnar digital nerve territories over the pulp of the distal phalanx

Table 7: Significant independent variables in logistic regression analyses of adverse outcomes

Adverse outcome	Independent variable	Adjusted Odds Ratio (OR)	95% confidence intervals of adjusted OR	Rank by p value (i) †	(i/m)*Q p value threshold †	Significance of association (p value)
Cold intolerance						
	Dermofasciectomy	**14.77**	**5.78-37.74**	**1**	**0.02**	**<0.001**
	Aponeurotomy	1				
	Fasciectomy	**4.00**	**1.97-8.12**	**2**	**0.04**	**<0.001**
	Aponeurotomy	1				
	Dermofasciectomy	**3.69**	**1.75-7.80**	**3**	**0.06**	**0.001**
	Fasciectomy	1				
	1-year follow up	**2.68**	**1.54-4.67**	**4**	**0.08**	**0.001**
	5-year follow up	1				
	Smoker	**2.66**	**1.44-4.94**	**5**	**0.1**	**0.002**
	Non-smoker	1				
Loss of flexion>10mm						
	Dermofasciectomy	**5.34**	**2.16-13.21**	**1**	**0.02**	**<0.001**
	Aponeurotomy	1				
	Fasciectomy	**3.66**	**1.86-7.17**	**2**	**0.04**	**<0.001**
	Aponeurotomy	1				
Altered sensation						

	Fasciectomy	**3.09**	**1.21-7.85**	**1**	**0.02**	**0.018**
	Aponeurotomy	1				
	Dermofasciectomy	**3.91**	**1.19-12.80**	**2**	**0.04**	**0.024**
	Aponeurotomy	1				
	Female	**2.11**	**1.10-4.03**	**3**	**0.06**	**0.024**
	Male	1				
Infection						
	Dermofasciectomy	**7.59**	**1.42-43.42**	**1**	**0.02**	**0.018**
	Aponeurotomy	1				
	Fasciectomy	**6.07**	**1.33-27.60**	**2**	**0.04**	**0.020**
	Aponeurotomy	1				
	Revision procedure	**2.36**	**1.03-5.38**	**3**	**0.06**	**0.041**
	Primary procedure	1				

† - These columns form part of the false discovery rate adjustment to the p value threshold. The variables are ordered by their p value, and ranked (their rank is labelled as 'i'). The total number of tests in each regression model ('m') is 10. The false discovery rate that has been tolerated in the analysis ('Q') is 20%. The adjusted p value threshold to protect against false discovery for each variable is (i/m)*Q.

FUNCTIONAL OUTCOME AND COMPLICATIONS FOLLOWING SURGERY FOR DUPUYTREN'S DISEASE: A MULTI-CENTRE CROSS SECTIONAL STUDY

Authors: JN Rodrigues[1], W Zhang[2], BE Scammell[2], I Chakrabarti[3]*, PG Russell[4]*, S Fullilove[5]*, D Davidson[6]*, TRC Davis[2]

Affiliations: [1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Nuffield Orthopaedic Centre, Windmill Road, Oxford, OX3 7HE

[2]Division of Rheumatology, Orthopaedics and Dermatology, University of Nottingham & Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Derby Road, Nottingham, UK

[3]Rotherham General Hospital, Moorgate Road, Rotherham, UK

[4]Pulvertaft Hand Centre, Royal Derby Hospital, Uttoxeter New Road, Derby, UK

[5]Derriford Hospital, Derriford Road, Plymouth, UK

[6]St John's Hospital at Howden, Howden Road South, Livingston, UK

*These authors contributed equally to this work

Corresponding author: JN Rodrigues, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Nuffield Orthopaedic Centre, Windmill Road, Oxford, OX3 7HE

07929296069, j.n.rodrigues@doctors.org.uk

Keywords: Dupuytren's contracture; Dupuytren's disease; Patient reported outcome measures; late outcome; complications; function

Acknowledgements: JNR received educational support from a Scholarship from the National Institute for Health and Care Excellence (NICE) during this project.

Conflicts of interests: none

Funding statement: This work was supported by a BSSH Research Fellowship, Nottingham Hospitals Charity and Nottingham Orthopaedic Walk.

Ethical approval: This study was a service evaluation project studying treatment outcome in Dupuytren's disease. In keeping with UK National Research Ethics

Service guidance, it is exempt from ethical approval. Approval as service evaluation was prospectively obtained.