Title: Measuring Hand Grip Strength in Rheumatoid Arthritis

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# Introduction

Rheumatoid arthritis (RA) is a systemic disease that results in synovial inflammation affecting joints, tendons and bursae [1]. It has a particular predilection for the hands – which can result in pain, deformity and functional limitation, often in a symmetrical pattern [2]. Measures of the severity of RA, such as the disease activity score with 28 joint count (DAS-28), are extremely useful in assessing and managing patients with RA as a whole, but there is some evidence to suggest that global measures of disease activity do not fully reflect the regional impact of RA on the hands [3]. It can be argued that assessment of hand function should be included as a separate entity in the global assessment of RA patients [3]. There are some objective assessment tools that focus specifically on the hands in RA – including measurements of grip strength, dexterity, and functional ability [4]. There is also some evidence to suggest that grip strength is one of the objectively measurable variables that correlates most strongly with hand disability [5].

In this review we aim to explore what is currently known about the assessment of hand grip strength; what it may indicate, how it is measured, some of the practical aspects and challenges associated with performing these tests, and how this information can be applied in a clinical setting. We will summarise the role that grip strength has in assessing patients with RA and will finish with some recommendations for how to use grip strength measurements in clinical practice, and what direction future research might take.

**Search Strategy**

Having defined the scope and parameters of this narrative review [6], **the PubMed database was searched** for English-language papers with the following keywords: rheumatoid arthritis, grip strength, hand grip, hand grip measurement and grip strength protocols. The reference lists of retrieved articles were also searched for additional sources. Searches were performed several times during the process of review and revision, between December 2014 and February 2017. The main body of the paper initially describes hand grip strength measurements (instruments, protocols and analysis) from a more general perspective, and additional searches were done for these sections not specifically limited to RA patients. Papers were not limited by publication date, but were considered on the basis of relevance. Except where specifically stated, papers were excluded which related to the application of grip strength testing for patients who did not have RA.

# What is Grip Strength?

Handgrip muscle strength describes the power or strength of the hand muscles used to grasp or grip [7]. There have been many ways of classifying hand grips. Broadly speaking there are two different types of grasp or grip:

1. Power grip: an object is held firmly by wrapping the fingers around it, pressing the object against the palm, and using the thumb to apply counter-pressure.
2. Precision grip: an object is held between the thumb and fingertip(s), without the use of the palm or rest of the hand [8].

Most studies of grip strength measure power grip [9, 10] as this is considered to be the most commonly used functional grip.

# How is it measured? – Instruments and Protocols

The measurement of grip strength requires a dynamometer - an instrument used to measure power or force; along with a method of quantifying and recording the values obtained. There are several different dynamometers available for the measurement of power grip strength. The Jamar Hydraulic Hand Dynamometer has been one of the most popular versions referenced in the medical literature [11]. Other models include the MIE digital grip analyser; the Lafayette Instrument hand dynamometer; and the Baseline Bulb Pneumatic Squeeze dynamometer.

The different instruments record the variable in different ways – for example, the Jamar and the Lafayette use an enclosed hydraulic system with output recorded in units of force, the MIE uses a strain gauge, and other models such as the Martin Vigorimeter make measurements using the squeezing of a rubber bulb and more accurately measure pressure rather than force. They are wholly reliant on accurate hand placement around the bulb, which limits the accuracy of these measures.

As with the measurement of any variable, it is important to consider the most appropriate instrument to use for a particular population. There have been various studies to compare the test-re-test reliability of the instruments with most concluding that individual instruments produce consistently reliable measurements over time, provided frequent calibration is maintained [12, 13]. Other factors such as cost and user preference may determine the device used [13]. Studies of the inter-instrument reliability have shown variable results [11, 12]. It must be assumed that the different available dynamometers cannot be used interchangeably unless the two have been specifically compared in head-to-head trials in the same population. By contrast, studies have found inter-observer reliability correlations are very high [14]. Roberts et al [9] include an overview of the different types of dynamometer with the advantages and limitations of each in the RA population.

There are a number of studies in the Occupational Therapy literature that use standardised assessments of hand function (including grip strength) in rheumatology. One study discusses the use of instruments that are standardised for the measurement of grip strength in RA; the two instruments listed that measure power grip strength are the Martin Vigorimeter and the Jamar Dynamometer [15]. There is limited data to suggest which dynamometer would be the best for measuring grip strength in an RA cohort [16]. Shiratori et al recommend the Jamar, as they report it is the most commonly used model [10]. Others have found that the Jamar may be relatively insensitive to small changes in strength in those with relatively weak grip [17] and also that it may be more difficult to handle for patients who are very frail [18]. It has been the experience of some research groups that the MIE strain gauge is a reliable and sensitive tool to use in the RA population instead [19].

Assuming the optimal measuring tool has been chosen, it is important to determine a standardised protocol for performing the test. There are a number of different protocols available, from various sources including the scientific literature, clinical practice guidelines, and clinical trials standard operating procedures. A number of papers have detailed problems found in clinical trials using measurements of hand grip strength – not least that the different studies use different equipment and different test protocols, which makes it difficult to compare results [9]. Many variables can affect the measurement of grip strength. The number of attempts a study participant is given to make the measurement can influence the final result. Some groups recommend using the best of three attempts [20] or the use of an average result [14] while others have found that one single attempt produces equally reliable results, and this method may be more popular amongst patients in whom grip strength testing causes pain [21]. Other factors, such as whether or not peak maximum strength is measured over a period of seconds or just the initial grip [22], and the positioning of the upper limb at the time the test is performed [23] can also have an impact. In patients with RA there have been limited attempts to define a standardised testing protocol [10]. The Mathiowetz protocol [24], which uses standardised positioning and verbal prompting, and records the best result of three attempts, is considered by some groups of hand therapists to be a good protocol that has worked well in RA research [19, 25].

A variety of additional patient-related factors can affect the results of grip strength testing; some of which are listed in Table 1. These variables may need to be given consideration when interpreting the results of grip strength tests. There has been little work so far to determine how these variables specifically affect patients with RA, although additional factors may influence results in this cohort, including pain, stiffness, fatigue and additional systemic features of disease, such as neuropathy and anaemia. Some, such as hand deformities [26], have been considered in the literature, and others have not.

Table 1 also lists specific factors that may influence the design of a grip strength testing protocol, including limb positioning, time of day, and which hand is used. The list includes factors that may affect both RA and non-RA patients and is probably not exhaustive.

# How are Grip Strength measurements analysed and interpreted?

Assuming data has been collected with the best instrument and using the optimal protocol, it is important to establish the best way of analysing and interpreting results to assess any statistical or clinical relevance. A number of trials have attempted to produce reference values for grip strength from healthy control groups for individual dynamometers [27]. In RA, hand function (grip strength) is less than in the general population [28]. Given that adults with RA are not the same as healthy control patients, data for RA patients may be better compared within an RA cohort than compared to values in a normal population. Normative values for grip strength in patients with RA have proved hard to determine [29]. Values for maximum grip strength in RA were approximately 25% that of a non-arthritic population [22]. It may be acceptable to compare RA patients with normal study participants but the data remains inconclusive. Much of the work on grip strength in RA has been done in the ‘pre-biologics’ era and advances in treatment with improvement of patient outcomes in RA may influence the comparison of future results with those already in the literature, including the pre-existing normative values [30].

There have been many approaches to determining statistical significance or minimal clinically important difference (MCID) in clinical trials of grip strength. One study, including both healthy women and those with non-specific regional pain [31] aimed to calculate how large a change in the value of a grip strength measurement must be recorded in order to ensure they were detecting a genuine change in results, and concluded that a change in grip strength must exceed 6kg in order for it to be considered a genuine result. For those with a much lower starting grip strength, such as patients with RA, a change of strength of >6kg may be harder to achieve than for healthy controls. Authors of clinical trials have looked at how the averaged grip strength results for different treatment arms vary over time and have used statistical tests to determine if the change in value is significant [32]. Sheehy et al [33] used normative data to calculate Z-scores (standard deviation from an age and gender matched average value) for grip strength for patients with RA, and confirmed that variations in Z-scores correlated with different disease activity states, and went back to near-normal when the disease was in remission. In the elderly, studies have divided grip strength into discrete categories (e.g. normal, intermediate and weak) [34].

From a clinical practice perspective, the use of a discrete cut-off value to define grip strength (or weakness) in RA patients has both advantages and disadvantages. It may be useful to apply it in a similar fashion to the measurement of DAS scores, with different values defining different states of disease activity, provided that such values allowed for additional factors that can affect measurements of strength (Table 1). It is likely to be some time before we have widely accepted and validated sets of normative data based on large cohorts of RA patients to use for either the creation of Z-scores or discrete data groups (and standardised data collection tools and protocols would need to be agreed before this would be possible) [35]. It may be possible to plot the change in grip strength values over time for an individual patient in the clinical setting, in order to review improvements or deterioration; the clinical utility of doing so has yet to be determined.

# Utility of measuring Hand Grip Strength in RA patients

There are two main settings in which grip strength data could be particularly useful. Firstly, in clinical trials, to compare outcomes for patients receiving different treatment strategies; and secondly, in clinical practice, as a marker of function and disability, which could then be used to help inform treatment plans.

Grip strength data has already been used as an outcome measure in RA clinical trials; to demonstrate benefits of various different treatments. Eberhardt et al [3] found that there was a significant improvement in grip strength over the first year of anti-TNF treatment in RA patients, in keeping with (although poorly correlating with) DAS-28 scores. Grip strength has been used as an outcome measure in trials of other treatments, including medications trials, targeted hand exercise programmes, and joint replacement surgery.

In a clinical setting in RA, grip strength has been shown to be important in the assessment of both disability and hand function [4]. Up to 81% of RA patients have evidence of hand disabilities [5] and even with biologic treatment hand pain and disability remain a problem [30]. Hand disability is important in RA patients, because hand function is so vital to activities of daily living. One study [36] looked at comparing measurements of grip strength in RA patients with various other measures of disease impact – including DAS-28, HAQ (Health Assessment Questionnaire) , VAS (visual analogue scales) , SOFI (Signals of Functional Impairment) and a modified Sharp Score. They found that there was a statistically significant negative correlation between grip strength and all the other variables; so that the more active the disease is, the worse the grip strength becomes. Other studies have also shown that assessments of function in RA, including grip strength, are able to demonstrate responsiveness to changes in disease activity state, as demonstrated by the ACR response criteria [37], and with variation in a patient’s active joint count [38]. In addition to disease activity, grip strength has also been shown to correlate significantly with joint damage and disability scores [5].

Not only are changes in measurements of grip strength correlated with changing disability, they can also be used to predict potential change. The Swedish TIRA project followed a cohort of early RA patients for 5 years. Grip force appeared to be an important predictor of HAQ scores in both a cross-sectional and longitudinal perspective [39]. Other work has shown grip strength measurements may be useful predictive tools for detecting the degree of disability and articular damage in patients with RA [40].

In order to promote the use of grip strength as an additional parameter to be measured in the rheumatology clinic, it is necessary to establish that it has clinical utility beyond the assessments that are already routinely carried out. There are several different arguments that may be used to show this. It is also necessary to give some thought to practical issues associated with the introduction of a new test into clinical practice.

There is evidence that specific assessments of hand function correlate only moderately with traditional measures of disease activity and disability. A study looking at the utility of hand function tests in a population with RA, found that assessments of hand function showed only weak to moderate correlations with DAS28 and HAQ. Thus they concluded that it would be optimal to assess hand function separately to global measures of disease activity [3].

Grip strength testing may be a surrogate marker for predicting accumulated radiographic damage in RA, another marker of disease progression. A systematic literature review has shown that there is a positive association between radiographic joint damage and the accumulation of disability in RA patients [41]. Aspects of radiographic damage (joint space narrowing, subluxation and erosions) are inversely related to grip strength as a marker of disability in RA [42]. In RA grip strength may have a better correlation with the Larssen radiographic score of joint damage than does the modified HAQ score [43].

There is increasing evidence that predictions of morbidity and mortality may be linked to measurements of grip strength. In one large prospective cohort study, which did not specifically recruit rheumatology patients [44] it was found that grip strength had an inverse association with all-cause mortality, cardiovascular and non-cardiovascular mortality, myocardial infarctions and stroke [45]. Long-term outcome in patients with RA and early inflammatory arthritides also appears to be correlated with measurement of grip strength. Hand involvement in early inflammatory arthritis has been shown to be a strong predictor of a poor long-term disease outcome [46] and poor grip strength at baseline confers a worse prognosis [47]. Other studies have shown that baseline variables in RA patients, including handgrip strength, can help predict long-term outcome [48]. In addition, data from the VERA project has demonstrated that in RA patients, reduced grip strength in the dominant hand is predictive of an increased economic burden associated with the condition [49]. It is clear that there would be significant clinical utility from routine accurate and sensitive measurements of grip strength in RA patients.

We suggest that measurements of grip strength can add further value to a patient’s clinical assessment in RA, acting as a marker of hand function, a surrogate marker of radiographic damage (and possibly resultant hand disability), and an indicator of longer-term outcomes.

Before incorporating a new investigation into the clinical environment it is necessary to consider practical issues, such as cost, timings, and feasibility. Initial prices would depend on the specific instrument purchased; as an example, the MIE strain gauge has a UK RRP of £1850 (personal communication from MIE-UK.com to authors, unreferenced, January 2017). One upcoming clinical trial has addressed the issue of training new assessors, which it anticipates will take 20-30 minutes per person [50]. Once both patient and clinician are trained to carry out the test, it would be anticipated that each repeat test would take less than thirty seconds to perform [10]. The frequency with which the test should be repeated in the context of an individual patient’s disease course has yet to be established.

Additionally, it is important to consider other clinical states that are known to be independently associated with reduced grip strength, such as frailty, cardiovascular disease and OA. Such conditions frequently overlap with RA and the impact of these additional conditions on the interpretation of grip strength results in RA patients is not yet known.

# Summary and Implications:

Global measures of disease activity may not fully reflect the regional impact of RA on the hands. We believe that hand function should be included as a separate measurement in the assessment of RA. Grip strength is an objectively measureable variable that can be used as a surrogate marker of function/disability of the hand. In this review we have attempted to address various questions with regards to grip strength testing and RA. We have discussed the use of various instruments and measurement protocols, and consider research into grip strength to be a fertile field for future work.

Grip strength is already being used as an outcome measure in some clinical trials but, due to the lack of standardisation of test procedures and reporting of results, it has yet to become widely accepted and commonly used. In routine clinical practice, grip strength has been found to correlate with both objective and patient reported outcome measures (PROMS) including disease activity states [37, 38], joint damage and disability scores, and changes in function [5, 51], while global measures of disease activity correlate at best weak-moderately with assessments of hand function. Measuring grip strength as a separate variable would allow clinicians to gain a more complete understanding of the impact of RA on hand function[3]. We believe that many other potentially useful pieces of information can result from the measurement of grip strength including predicting disability [39], and articular damage [40] and the accumulation of radiographic damage [41], leading towards a more accurate prognosis for the disease in an individual [46, 47].

As yet there remains a lack of overall consensus as to which instrument is the best. There are a wide number of options available, and it appears that most can be considered generally reliable; although they cannot necessarily be used interchangeably [11, 12]. For RA there is still some uncertainty about which instrument is the most appropriate[16]. While both the Martin Virigometer and the Jamar Dynamometer have been reported as being standardised for the measurement of grip strength in rheumatology patients [15], it has been found that other instruments, such as the MIE strain gauge [19] or the electronic Grippit [17] are more sensitive and therefore more discriminative, and are lighter (so more manageable for patients who tend to have a weaker grip).

So far there has been a lack of uniformity in clinical trial protocols for measuring hand grip strength and no definition of optimal test protocols can be attempted with the available data from either normal cohorts or in RA. The Mathiowetz protocol [24] has been found to work well in RA research trials [19, 25] but there is no consensus as which protocol is the best for use in RA in the typical clinic setting. There has been research looking at specific variables that can influence the results of grip strength testing (Table 1). Some of these can be standardised for the purposes of grip strength testing, while others can either be considered non-modifiable (including age, gender and hand dominance) or likely to be a reflection of disease activity and/or accumulated damage (such as CRP, stiffness and fatigue). There is also significant heterogeneity in how results are analysed and reported, and the optimal methods to determine the clinical significance of these results are not yet clear. From the point of view of routine clinical practice, the most straightforward application is likely to be a comparison of how an individual patient’s results change over time, and the patient’s rating of perceived improvement. There will need to be further research to determine how we can define a clinically significant change – a cohort study looking at patients’ perceived levels of disease activity and functional ability and a comparison with their ranges of grip strength may provide a useful starting point.

One area of potential further research may be to investigate how grip strength in RA correlates with specific prognostic indicators and additional comorbidities. A possible relationship between grip strength and cardiovascular mortality rates in RA may be of particular interest owing to the high risk of cardiovascular disease in RA. The measurement of grip strength could prove to be a quick and cost-effective indicator of a wider health issue.

# Conclusion

For RA patients in clinical practice, we consider that currently the most appropriate tool for measuring hand grip strength is the MIE Digital Grip Analyser. An exact protocol has yet to be determined, but for RA patients it would be preferential to test in the seated position, using a single measurement. Other factors that will vary between appointments, such as time of day and medication, should be clearly documented. Measurements can be carried out by any practitioner at the time of clinical review. Initially results would be compared longitudinally over time for individual patients, to track changes in clinical state, where they may influence decisions to modify treatment regimens.

We understand that there are many outstanding questions regarding the measurement of grip strength data in practice, but still believe that its measurement may have a role to play in the clinical assessment of RA patients, and can provide useful clinical information not offered by the use of other standardised assessment instruments. This conclusion potentially leads to a series of discrete studies to attempt to validate our recommendations.

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| Patient-related factors that may influence the result of grip strength testing   * Age and gender [27] * Hand dominance [28, 52] * Nutritional status [53] * CRP [29] * Height [30] * Participation in regular exercise [30] |
| Variables that may influence the design of a hand grip strength testing protocol   * Measurement of peak strength over a period of time versus initial measurement [22] * Positioning of the upper limb [23, 54] * Number of attempts allowed (single versus best of three approach) [10, 14, 55, 56] * Use of the dominant versus non-dominant hand [10] * Number of digits used for the grip [31] * Time of day for testing [57, 58] |

Table 1. Factors that may influence the results of Hand Grip Strength testing.