Correlation of a Modified Disease Activity Score with the Validated Original Disease Activity Score in Patients with Juvenile Dermatomyositis

Running Head: Modified DAS for JDM

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Abstract

Objective: Juvenile dermatomyositis (JDM) is a rare disease in children that is treatable, but patients may suffer from long-term effects of the disease. Clinical trials are needed to find better treatments for affected patients. Among validated tools for evaluating disease activity clinically is the disease activity score (DAS), but it is not routinely collected in all clinics. We developed a modified DAS (DAS_{mod}) which can be scored using data routinely collected by our clinical staff, and has been used in previous studies. This study's objective was to determine if our DAS_{mod} correlates with the validated DAS in patients with JDM.

Methods: In this study, we used DAS_{mod} (scored 0-12) and DAS scores (scored 0-20) for patients with JDM in our clinic. We analysed the correlation between the DAS_{mod} and the validated DAS.

Results: For 51 patients seen in our JDM clinic, the median (IQR) DAS_{mod} score was 2.0 (0, 4.0) and the median (IQR) DAS score was 3.0 (0, 5.5). Scores on the two tools were highly positively correlated ($r = 0.94$, $p < 0.001$, 95% CI [0.89, 0.96]). The linear regression was significant ($R^2 = 0.88$, $F(1, 49) = 357.60$, $p < 0.001$) and in this dataset, the tools can be used interchangeably with the regression equation: DAS score = $-0.26 + 1.5*DAS_{mod}$.

Conclusion: If the regression equation from this dataset is successfully tested against future datasets, then further research collaborations between centres that collect different data related to disease activity in children with JDM will be facilitated.

INTRODUCTION

Juvenile dermatomyositis (JDM) is a rare disease, yet it is the most common inflammatory myopathy of childhood. In the United States, the incidence rate of JDM is 2.5 to 4.1 per million children per year (1).

There is a need for clinical trials investigating new intervention targets to determine more effective treatments and better disease outcomes for patients with JDM. Currently, patients typically receive high doses of corticosteroids and methotrexate as the first step of treatment after diagnosis. However, patients may need additional treatment if their symptoms do not resolve or if side effects from medication, especially corticosteroids, are intolerable (2). Despite routine courses of treatment, many patients continue to have chronic disease activity which results in long-term suffering from disease features. Therefore, there is a need for further study of more targeted interventions to enhance treatment effectiveness for these patients.

To evaluate the effectiveness of treatments in patients with JDM, there are different ways of measuring and documenting disease progression and activity, including the validated Disease Activity Score (DAS) (3). The DAS is part of the Pediatric Rheumatology International Trials Organisation (PRINTO) core set of disease activity measures for use in clinical trials, but not the core set of the International Myositis Assessment and Clinical Studies Group (IMACS) (4). It is a physician tool which evaluates and quantifies muscle and skin disease severity, including "vasculitis". In total, 19 items are scored to yield a total score range from 0-20, with higher scores indicating more severe disease activity. The DAS is therefore an important tool for measurement of disease activity in JDM. However, the DAS has items that must be scored contemporaneously; it cannot easily be scored retrospectively from clinically collected data. The

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DAS has not been routinely collected at many clinical centres, perhaps because it is not one of the core set measures used by the IMACS group.

Of note, the DAS, and likewise the DAS_{mod}, are only components of disease activity measurement, and are not meant to capture the whole construct (which, for example, is captured well by the core sets referenced above).

We developed a modified DAS (DAS_{mod}), based on the validated DAS but with slightly different parameters for use in clinical studies using previously collected (clinical database / clinical chart) data. The DAS_{mod} is based on data that have been routinely collected at our centre (5,6) and that are also included in the published optimal data set (7). Similar to the DAS, our DAS_{mod} tool also assesses muscle and skin disease activity. There are 7 items on the DAS_{mod} which yield a total score ranging from 0-12. All items on the DAS_{mod} are included in the JDM optimal dataset "to be completed at every clinic visit" data collection form (7). Determining the agreement between the DAS_{mod} and the DAS will allow for further research collaborations between centres that collect, or have collected, different data related to disease activity in children with JDM.

The purpose of this study was therefore to determine: 1) Is there a high correlation between the DAS_{mod} and the validated DAS in children with JDM? 2) Can the DAS_{mod} score be converted to the validated DAS score using a mathematical transformation?

METHODS

Patients

This cross-sectional study was approved by The Hospital for Sick Children (SickKids) Research Ethics Board (REB#1000056886) with a waiver for written informed consent. Included in this

study were consecutive patients seen in the JDM subspecialty clinic at SickKids between December 1, 2016 and March 1, 2018. Data from a single visit for each patient were used in which the DAS_{mod} and DAS were both scored. Data were collected in a similar way, for both tools, for the purposes of this study (see below).

Measures

The DAS_{mod} score was based on the medical record data and calculated independently (and blindly) from the validated DAS score (which was scored by a clinician at the time of a visit – see Table 1). DAS_{mod} data are collected from the physician / practitioner clinic note in combination with the global manual muscle testing score (gMMT), which is completed by a physiotherapist. The skin parameters were scored based on whether there was an indication of abnormality in the clinic note. For erythema, if the note indicated beyond discrete gottron's or heliotrope, it was considered to be widespread. Vasculitis was scored based on whether there was an indication of abnormal periungual nailfold capillary changes. The gMMT, historically measured at our centre since 1991, is calculated based on a Kendall score (0-10) for each of seven standardised motor movements (neck flexion, right shoulder abduction, left shoulder abduction, right hip flexion, left hip flexion, right hip abduction, and left hip abduction), yielding a total score of 0-70 (6). Many centres (including ours) now use the MMT8 (8) to measure muscle strength. In a separate analysis, we calculated the DAS_{mod} using the MMT8 instead of the gMMT and compared this version of the DAS_{mod} to the DAS.

Statistical Analysis

To determine if there is a high correlation between the DAS_{mod} and the validated DAS, Pearson's correlation coefficient was used. Linear regression analysis was then used to determine if the DAS_{mod} score can be converted to the validated DAS score. Standard regression diagnostics were

used to determine model fit. We conducted all analyses using R v3.4.3 (R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Data from 51 patients (31 female and 20 male) who were seen in the JDM subspecialty clinic at SickKids and had both the DAS and DAS_{mod} from the same visit were included in the analysis. According to the EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIMs) (9), 45 out of 51 patients had a probability of IIM of 80% or higher. Of these patients, 44 had a diagnosis of JDM and one had a diagnosis of anti-SRP Necrotising Myositis. Of the remaining six patients, one had a diagnosis of anti-HMGR necrotising myositis, four were hypomyopathic, and one had overlap myositis.

The median (IQR) DAS_{mod} score was 2.0 (0, 4.0) [mean (SD) = 2.8 (3.0)] and the median (IQR) validated DAS score was 3.0 (0, 5.5) [mean (SD) = 3.9 (4.7)]. The individual item scores are listed in Table 2. There was a highly positive correlation between the DAS_{mod} and the DAS ($r = 0.94$, $p < 0.001$, 95% CI [0.89, 0.96]) (Figure 1). This significant correlation also held true when the MMT8 was used in the DAS_{mod} score instead of the gMMT ($r = 0.94$, $p < 0.001$, 95% CI [0.89, 0.97]). Plotting the residuals against the DAS_{mod} score showed homoscedasticity (i.e., that the error term is normally distributed), suggesting that the assumptions of a linear model have been met (data not shown). The linear regression was significant ($R^2 = 0.88$, $F(1, 49) = 357.60$, $p < 0.001$) and the regression equation is: DAS score = $-0.26 + 1.5 * DAS_{mod}$.

There was also a highly positive correlation between the muscle domain on the DAS_{mod} and the muscle domain on the DAS ($r = 0.86$, $p < 0.001$, 95% CI [0.76, 0.92]) and between the skin

domain on the DAS_{mod} and the skin domain on the DAS ($r = 0.92$, $p < 0.001$, 95% CI [0.86, 0.95]).

DISCUSSION

Using the data collected from our sample of JDM patients attending the subspecialty clinic at our centre, there was a very strong positive correlation between the DAS_{mod} and the DAS. We also found that a linear equation can accurately convert between scores, with the DAS_{mod} explaining 88% of the variance in DAS scores. Since muscle disease activity was measured by the attending physician/clinical trainee/advanced practice therapist on the DAS and by a physiotherapist for the DAS_{mod}, small discrepancies in scores could be a result of differences between clinician assessments.

Our study conclusions should be interpreted in the light of several possible limitations. First, both DAS_{mod} and validated DAS scores were not symmetrically distributed, but rather, skewed to low disease activity, meaning more patients were close to or in remission. However, the full range of scores across both tools were represented. Second, data from only one clinical centre were used. Nonetheless, our centre sees patients from a large geographical area and includes a diverse population. Third, the development of the DAS_{mod} occurred at a specialized tertiary care centre in a clinic with routine physiotherapy support, and therefore, gMMT scores, and more recently MMT8 scores, were readily available. In other centres with fewer resources available, use of the DAS_{mod} may be impractical due to the unavailability of a physiotherapy assessment. However, the MMT8 is suggested to be done at follow-up visits by recent guidelines (10). Fourth, we did not include longitudinal data in this study, so sensitivity of the correlation to

change over time could not be determined. Finally, no additional validation set was used in this study, so our results must be considered preliminary and should be corroborated.

Our analysis suggests that the two tools are roughly equivalent in the nature of the information that they add to the assessment of patients. For observational studies, in which the DAS is not routinely collected, the DAS_{mod} can be used as a surrogate. For ongoing studies, in which the DAS can be collected, it is the preferred tool as it has been validated and widely published on.

In conclusion, this study showed that the validated DAS and the DAS_{mod} score can be used interchangeably with the use of a regression equation in this cohort of patients. A validation cohort would help to confirm our findings.

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FIGURE LEGEND

Figure 1. Scatterplot of DAS score and DAS_{mod} score. DAS = disease activity score; DASmod = modified disease activity score.

Table 1: Modified DAS (DAS_{mod}) Scoring. gMMT = global manual muscle testing score.

	Scored Item	Options		Scores
Muscle DAS (0-7)	Muscle Strength	No muscle weakness (gMMT 68-70)	(MMT8 78-80)	0
		Minimal muscle weakness (gMMT 63-67)	(MMT8 72-77)	1
		Moderate muscle weakness (gMMT 56-62)	(MMT8 64-71)	2
		Severe muscle weakness (gMMT 0-55)	(MMT8 0-63)	3
	Functional Status	No limitation on activity		0
		Activities limited at the extra-curricular level		1
		Activities limited at the school/work level		2
		Activities limited at the self-care level		3
	Arthritis	Absent		0
		Present		1
Skin DAS (0-5)	Erythema	No erythema		0
		Local erythema (joints and face)		1
		Widespread erythema		2
	Heliotrope rash	Absent		0
		Present		1
	Gottron's Papules	Absent		0
		Present		1

	Vasculitis	Absent	0
		Present (nailfold abnormality)	1
Total Score (0-12)			

Table 2. Study sample demographics and individual item scores for the DAS_{mod} and DAS

	Median (IQR)	**Number of Patients with Non-Zero Score**
Age	12.8 (7.5, 15.6)	NA
gMMT	70 (65, 70)	NA
MMT8	80 (75.8, 80)	NA
DAS elements		
Functional status	0 (0, 0.5)	13
Neck flexor weakness	0 (0, 0)	10
Difficulty clearing scapula	0 (0, 0)	8
Upper proximal muscle weakness	0 (0, 0)	9
Lower proximal muscle weakness	0 (0, 0)	11
Gower's sign	0 (0, 0)	7
Abnormal gait	0 (0, 0)	3
Difficulty swallowing	0 (0, 0)	2
Nasal speech	0 (0, 0)	3
DAS weakness subtotal	0 (0, 1)	16
Skin involvement	0 (0, 2)	25
Skin involvement distribution	0 (0, 1)	24
Eyelid erythema	0 (0, 1)	15
Eyelid vessel dilation	0 (0, 0)	8
Eyelid thrombosis	0 (0, 0)	2
Nailfold erythema	0 (0, 1)	14
Nail bed telangiesctasia	0 (0, 1)	17
Palate dilation	0 (0, 0)	4
Other	0 (0, 0)	0
Gottron's papules	0 (0, 1)	18
DAS skin subtotal	1 (0, 5)	26
Total DAS score	3 (0, 5.5)	30
DAS_{mod} elements		

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Muscle strength	0 (0, 1)	19
Functional status	0 (0, 0)	12
Arthritis	0 (0, 0)	1
DAS_{mod} muscle subtotal	0 (0, 2)	20
Erythema	1 (0, 1)	26
Heliotrope rash	0 (0, 1)	14
Gottron's papules	0 (0, 1)	20
Vasculitis	0 (0, 1)	23
DAS_{mod} skin subtotal	1 (0, 3)	31
Total DAS_{mod} score	2 (0, 4)	36

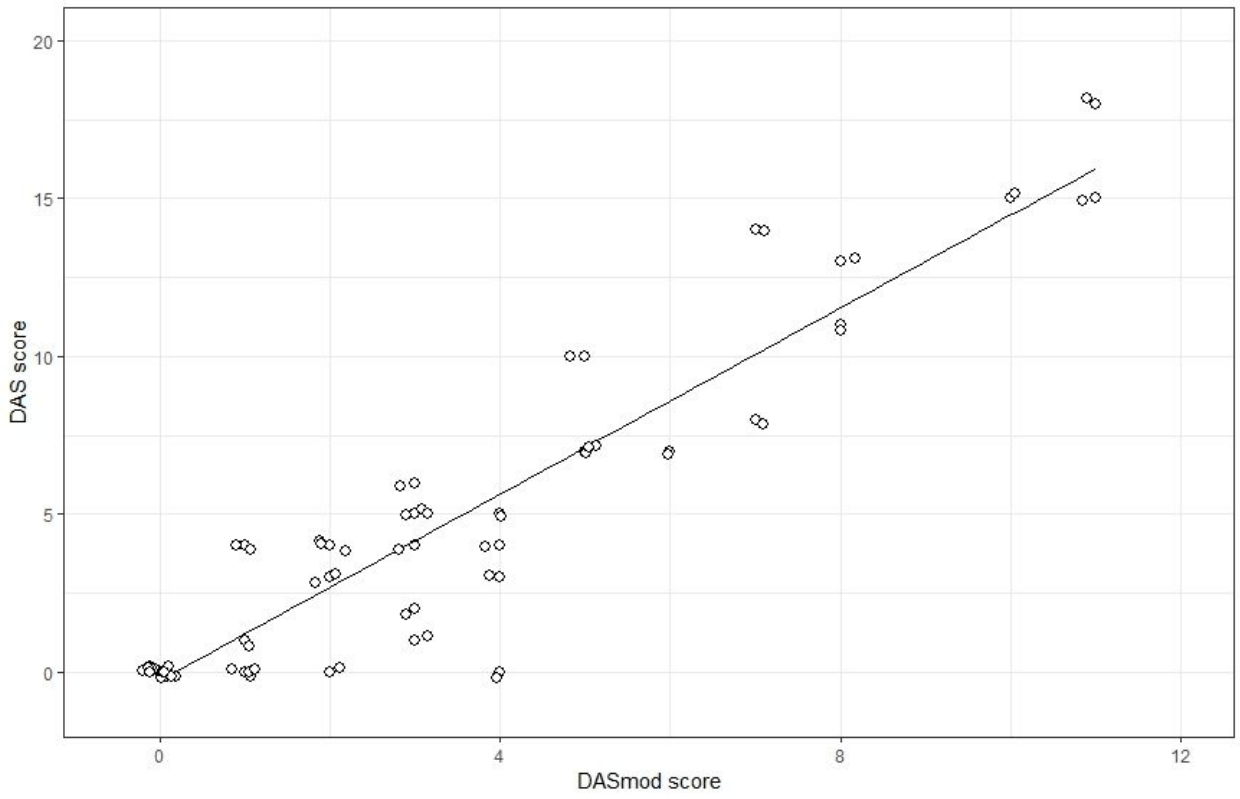

Figure 1. Scatterplot of DAS score and DAS_{mod} score. DAS = disease activity score; DASmod = modified disease activity score.