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General

The Hoffmann parallax: a prospective study to determine the benefit of Hoffmann's sign

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Background

Degenerative cervical myelopathy (DCM) is the most common cause of age-related spinal cord dysfunction worldwide. Despite the widespread use of provocative physical exam maneuvers in the workup of DCM, the clinical significance of Hoffmann's sign is controversial.

Objective

The purpose of this study was to prospectively assess the diagnostic performance of Hoffmann's sign for DCM in a cohort of patients treated by a single spine surgeon.

Materials & Methods

Patients were divided into two groups based on the presence of a Hoffmann sign on physical examination. Advanced imaging studies were independently reviewed by four raters for confirmation of a diagnosis of cervical cord compression. Prevalence, sensitivity, specificity, likelihood, and relative risk ratios for the Hoffmann sign were calculated, with subsequent Chi-square and receiver operator characteristic (ROC) analysis to further characterize correlative findings.

Results

Fifty-two patients were included – of whom, thirty-four (58.6%) patients presented with a Hoffmann sign, and eleven (21.1%) patients demonstrated cord compression on imaging. The Hoffmann sign demonstrated a sensitivity of 20% and a specificity of 35.7% (LR = 0.32; 0.16—1.16). Chi-square analysis revealed that imaging findings positive for cord compression were proportionally greater for patients lacking a Hoffmann sign than those with a confirmed Hoffmann sign (p =0.032) ROC analysis demonstrated that a negative Hoffmann sign performed moderately well in predicting cord compression (AUC.721; p =0.031).

Conclusions

The Hoffmann sign is an unreliable marker for cervical cord compression, and the lack of a Hoffmann sign may be more predictive of cervical cord compression.

INTRODUCTION

Degenerative cervical myelopathy (DCM) is the most common cause of age-related spinal cord dysfunction in adults worldwide, with an estimated prevalence of 60.5 cases per 100,000 adults in North America.[1-3] Patients with cervical myelopathy may describe symptomatology consistent with upper and/or lower motor neuron lesions, and characteristic subjective findings elicited on history may include neck pain, sensory changes, loss of balance, weakness, and bowel/bladder dysfunction. Therefore, physical examination is invaluable in the workup of DCM, and provocative testing, prior to obtaining advanced radiographic imaging, remains a mainstay of good clinical practice.

The Hoffmann sign has been used to identify potential upper motor neuron disorders, specifically those affecting the corticospinal pathways, for over a century.[4-6] Advocates of its use believe that Hoffmann sign accurately denotes pyramidal-tract dysfunction, while its critics suggest that a positive Hoffmann sign indicates a non-specific "state of enhanced muscle tone," which may be caused by conditions unrelated to compression the spinal cord.[7] As evidence of the latter, the overall incidence of a positive Hoffmann sign in the general population is estimated to be 2-3%, with reportedly low sensitivity ranges of 8-59% and specificity ranges of 49-85%.[6,8-10]

Other physical exam findings thought to correlate with impedance of the corticospinal track and cord compression have been similarly evaluated. In asymptomatic, neurologically intact patients, the incidence of the inverted radial reflex (IRR) has been found to approach 26%.[7] Acharya et al. investigated the time to resolution of neurological physical examination signs after laminoplasty in patients with severe cervical spondolytic myelopathy.[11] Preoperatively, a positive Babinski sign was the most common sign (95%), followed by IRR (91%), Hoffmann (86%), and clonus (48%) signs. Resolution of these signs was most apparent in patients with a positive Babinski, clonus, and IRR – yet a positive Hoffmann sign persisted in 38% of patients postoperatively.

The utility of the Hoffmann sign in the evaluation of DCM alone or in combination with other provocative tests to screen for myelopathy remains questionable. Although previous studies have investigated the relationship between DCM and provocative tests such as the Hoffmann sign, and have reported variable measures of diagnostic accuracy, few have employed multiple tests in a prospective fashion. Therefore, the goal of this study was to prospectively assess the diagnostic performance of the Hoffmann sign, along with the IRR and Spurling sign, in patients with suspected cervical cord compression treated by a single spine surgeon over three years at a single institution.

MATERIALS & METHODS

ETHICAL CONSIDERATIONS

The study protocol was submitted to the Hughston Sports Medicine Institutional Review Board (IRB) and approval was obtained prior to study initiation (IRB #: HIRB2019-02). Verbal and written consent was obtained from all study participants prior to their inclusion in the study. All data was collected electronically on a private server and deidentified in order to maintain confidentiality of participants.

STUDY PARTICIPANTS

We utilized a prospective observational study design with data collection from March 2019 to March 2022. Patients referred to a single spine surgeon (DWP) for neck or arm pain or discomfort over a three-year period were deemed to be a high-risk population for DCM and were eligible for inclusion in this study. Patients with previously diagnosed cervical cord compression and a history of cervical spine surgery, brain lesions, prior history of trauma, and myasthenic syndromes were excluded. Physical examination and provocative testing maneuvers, including testing for the Hoffmann sign, IRR, and Spurling sign, were performed by the senior author (DWP). Magnetic resonance imaging (MRI) studies were reviewed by four raters including the senior author, two fellowship-trained musculoskeletal radiologists blinded to the patient's demographic and physical exam data, and an orthopaedic surgery residency trainee. In cases in which an MRI was unobtainable, the patient underwent evaluation using post-myelogram computed tomography (CTM) tests. For these studies, only cord compression was identified due to known limitations of this test. We collected demographic and physical exam data via chart review, and imaging results were identified as either MRI positive (MRI^+) or MRI negative (MRI^-) for diagnosis of cervical cord compression. We used the same nomenclature in evaluation of the CTMs and included this information collectively.

MEASUREMENTS

Patient age was collected as continuous data, and sex/gender, physical exam, and MRI findings were compiled as dichotomous categorical data. Cervical cord compression was confirmed by each individual rater – specifically capturing the loss of the normal oval appearance of the spinal cord on axial MRI or CTM imaging or deformation of the spinal cord with or without enhancement on T2-weighted and Short-Tau Inversion Recovery (STIR) MRI. Of note, cervical spinal stenosis was defined as absolute (with sagittal-plane MRI measurement of less than 10 millimeters) or relative (with sagittal-plane MRI measurement of 10-13 millimeters).[12] Four blinded MRI raters assessed for cervical cord compression (MRI^+) or no cervical cord compression (MRI^-). The overall inter-rater reliability was 0.72, which was considered substantial.[13] Conditional analysis revealed stronger agreement amongst raters for MRI^- reads in comparison to MRI^+ reads for cervical cord compression (0.922 versus 0.747), and therefore, we set the consensus criteria at 75% agreement (3 of 4 raters).

OUTCOME OF INTEREST

The primary outcome measures of this study were a positive or negative Hoffmann sign and a confirmatory diagnosis of cervical myelopathy, by MRI or CTM studies.

STATISTICAL METHODS

Parametric continuous data was assessed using Student's t-test and parametric categorical data was assessed with Pearson's Chi-Square test. We assessed the likelihood of a type II error with a posthoc power analysis. Fleiss' kappa statistic was utilized to determine inter-rater reliability for MRI findings. Likelihood (LR) and relative risk (RR) ratios are reported with respect to a positive physical exam finding. Receiver operator characteristic (ROC) analysis assessed the performance of the Hoffmann sign for the diagnosis of cervical cord compression based on at least 75% agreement among raters. Data analysis was conducted using SPSS® Version 27.0 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp). We considered results to be significant at $p<.05$.

RESULTS

There were 58 patients included within our analysis – of whom, 52 underwent MRI or CTM and had images available for review by all four raters. 29 patients (55.8%) demonstrated a positive Hoffmann sign while 23 patients (44.2%)

Table 1. Hoffmann Negative versus Hoffmann Positive Patient Characteristics.

		Negative (A)			Positive (B)			Sig.
		Mean	N	%	Mean	N	%	
Age		55.2±16.6	24	41.4%	54.9±13.5	34	58.6%	.931
Male: Female		1:3	24	10.3%	1:6	34	8.6%	.325
Chief Complaint	Gait Instability		1	1.7%		4	6.9%	.011*
	Weakness		2	3.4%		2	3.4%	
	Perineum		0	0.0%		0	0.0%	
	Extremity Numbness		13_B	22.4%		5	8.6%	
	Axial Pain		8	13.8%		23_A	39.7%	
IRR	Negative		5	8.6%		6	10.3%	.760
	Positive		19	32.8%		28	48.3%	
Spurling sign	Negative		20	34.5%		30	51.7%	.594
	Positive		4	6.9%		4	6.9%	

The Pearson Chi square statistic is considered significant at $p<.05$. For each significant pair, the significant value appears as a subscript [(A) or (B)] with respect to each column. Tests are adjusted for all pairwise comparisons using the Bonferroni correction. * denotes significance.

lacked a Hoffmann sign. There was no difference in the average age of patients with a negative Hoffmann sign versus those with a positive Hoffmann sign (55.2±16.6 versus 54.9±13.5, respectively; p=0.933). Hoffmann negative patients were significantly more likely to complain of extremity numbness in comparison to Hoffmann positive patients, and Hoffmann positive patients were more likely to complain of axial pain when compared to Hoffmann negative patients (p=0.011). We found no correlation between a Hoffmann sign and either an IRR or Spurling sign. These results, as well as the reported chief complaints and physical exam findings for both groups, are summarized in Table 1.

We calculated a prevalence of 21.1% (11 patients) for cord compression, a sensitivity of 20%, and a specificity of 35.7% for a positive Hoffmann sign in this cohort (LR = 0.32; 0.16—1.16). Chi-square analysis revealed MRI^+ findings were proportionally greater in Hoffmann negative patients (p=0.032). Moreover, the RR of a positive Hoffmann sign was 0.19 (CI: 0.05 to 0.85, p=0.029), suggesting that a positive Hoffmann sign is associated with a significantly decreased risk of cord compression. These results are summarized in Table 2.

Posthoc power analysis demonstrated the sample size was adequate to assess for differences in age about the mean (power = 0.833, p=0.05). The results of receiver operator characteristic (ROC) analysis shown in Figure 1 demonstrates that a *negative* Hoffmann sign performed moderately well in predicting cord compression (AUC=.721, p=0.031). The addition of the IRR and/or the Spurling sign in combination with the Hoffmann sign negatively impacted the ROC. When considering age as a factor, a cut-off of 70 years appeared to maximize the performance of a negative Hoffmann as a positive predictor. However, the AUC-difference above and below age 70 did not reach statistical significance (p=0.350).

DISCUSSION

In this study, we prospectively evaluated the diagnostic performance of the Hoffmann sign as a screening tool for cervical cord compression in patients referred to a spine surgeon prior to advanced imaging. Although patients with a Hoffmann sign initially presented with a chief complaint suggestive of myelopathy, our results indicate that the Hoffmann sign was not prognostic for cervical cord compression. In fact, our study exhibited the opposite – a positive Hoffmann sign may be predictive of the *absence* of cervical cord compression in an age-dependent fashion.

Patients with a Hoffmann sign appeared to present with an IRR and a negative Spurling sign, but neither of these associations were statistically significant. A majority of patients (86%) lacked specific indicators of myelopathy–weakness, clumsiness, or gait instability. Of the nine patients (14%) with these specific myelopathic symptoms, six had a positive Hoffmann sign. Surprisingly, only two of the nine were found to have cord compression on MRI; these two patients also demonstrated a positive Hoffmann sign.

We report a similar prevalence of the Hoffmann sign in our patient population but calculated a sensitivity of 20% and specificity of 37.5% for the Hoffmann sign – considerably lower values than those previously reported in the literature.[9,14,15] These lower values may be attributable to the relatively small sample size and inherent selection bias as this cohort were all patients referred to a single spine surgeon. On the other hand, these low values also support our finding that a negative Hoffmann sign was more indicative of cord compression in this study.

Our results suggest that a negative Hoffmann sign in patients with extremity numbness conveys a five-fold relative risk increase of cord compression. The impact of age on the utility of provocative examination maneuvers and MRI evaluation for cervical spinal cord compression has been reported by Cook et al. – who determined that multiple positive provocative physical exam maneuvers, including Hoff-

Table 2. Likelihood ratio (LR) of cord compression on MRI.

		MRI$^-$ (n=41) [A]	MRI$^+$ (n=11) [B]	Sig. (LR)
Sex	Male	4	5_A	*.005** *(3.98; 1.55-10.24)*
	Female	37_B	6	
Chief Complaint	Extremity Numbness	9	8_A	*.014** *(4.55; 1.39-14.87)*
	Radicular or Axial Pain	26_B	3	
Hoffmann sign	Negative	15	8_A	*.032** *(0.32; 0.16 – 1.16)*
	Positive	26_B	3	
IRR	Negative	8	3	*. 921* *(0.90; 0.61-1.34)*
	Positive	33	8	
Spurling sign	Negative	37	9	*.394* *(1.86; 0.39-8.88)*
	Positive	4	2	

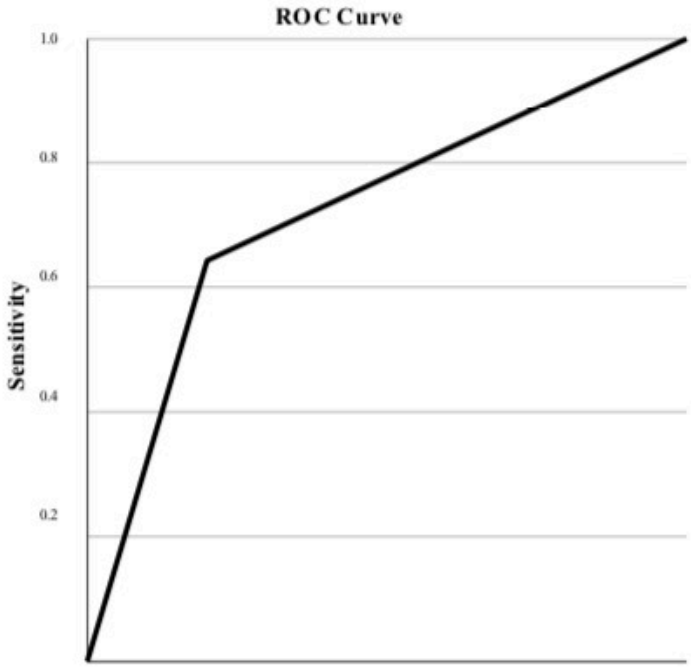
Results are based on two-sided tests. The Pearson Chi square statistic is considered significant at *p<.05.* For each significant pair, the significant value appears as a subscript [(A) or (B)] with respect to each column. Tests are adjusted for all pairwise comparisons using the Bonferroni correction. * denotes significance.

Hoffmann sign Sensitivity: 20%

Hoffmann sign Specificity: 35.7%

Relative Risk (Positive Hoffmann Sign, MRI$^+$): 0.19 (CI: 0.05 to 0.85, *p*=.029)

Fleiss' Kappa statistic for interobserver reliability = 0.72 (CI: 0.519 to 0.779, *p<.001*)



Area Under the Curve (AUC)	Std. Error	Asymptotic Significance	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.721	.087	.031	.551	.892

Test Result Variable(s): Hoffmann negative. Positive Actual State: MRI$^+$. The test result variable(s): Hoffmann has at least one tie between the positive actual state group and the negative actual state group. Under the nonparametric assumption, null hypothesis: true area = 0.5. Significance set at *p<.05.*

Figure 1. Receiver Operating Curve (ROC) depicting the diagnostic performance of a negative Hoffmann sign to accurately predict the presence of cord compression. (n=52, 11 MRI$^+$ patients; 41 MRI$^-$ patients).

mann and Babinski signs, in patients over 45 years of age improved the overall diagnostic performance in patients with DCM.[16] Although our results suggested an age cut-off of less than 70 years improved the performance of the (negative) Hoffmann sign, no statistical difference in test performance was found when comparing cohorts of those above and below the age cut-off.

We report a 21.1% prevalence of cord compression in this cohort; this is similar to the prevalence of cord compression in asymptomatic individuals due to age-related degeneration alone. While a decreased incidence of the Hoffmann sign in older patients has been reported previously, there is also an increased likelihood of comorbidities and polypharmacy in elderly patients that can confound the neurological exam. In evaluating the 12 patients over 70 years of age in this study, we found an average of eight active medications. Ten patients were taking one or more diuretic(s), six were receiving either thyroid or estrogen hormone replacement, and three were prescribed daily prednisone. Remarkably, only two patients were diabetic – which may alter electro-physiological reflex response – however, neither individual was diagnosed with cervical cord compression, and one had a positive Hoffmann sign.

LIMITATIONS

There are limitations to the present study. This is a prospective study conducted at a single institution and a single spine surgeon, and therefore, a larger longitudinal study is necessary to confirm the results of this study. The 2-3% reported rate of an incidentally positive Hoffmann sign in the general population is another confounding variable that may have impacted our results. Similarly, the reported increased incidence of degenerative asymptomatic cervical cord compression may have impacted our results. The gold standard for comparison – the MRI – was less reliable than anticipated amongst raters, and often did not clearly demonstrate cervical cord compression in patients with specific myelopathy symptoms. This may be a result of the MRI power (1.5T) or the reliability of raters.

CONCLUSION

Our prospective study evaluating the diagnostic performance of the Hoffmann sign established a comparatively lower baseline sensitivity and specificity versus previous reports. Additionally, we found that a negative Hoffmann sign was the only adequate predictor of cord compression in this cohort among the three provocative maneuvers that were evaluated individually, and in combination. Although our results suggest a paradigm shift when utilizing the Hoffmann sign, we caution against using a negative Hoffmann sign as a positive predictor of cord compression until these results can be reliably reproduced. Appropriate clinical judgement should be exercised in the diagnosis and treatment of patients with suspected cervical spinal cord myelopathy.

CONTRIBUTIONS

Authorship was determined using the ICMJE and CrediT criteria. EHG and SKV were responsible for data collection and analysis, drafting of the manuscript, and subsequent manuscript editing. RMS and CK interpreted all images and assisted with data collection. MAK and DWP developed the study idea, provided administrative support, and edited the manuscript.

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DISCLOSURE

The authors report no conflicting interests related to this work.

CONFERENCE PRESENTATION

This study was accepted as a poster presentation for the Global Spine Congress 2023 international meeting in Prague, CZ.

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