

Research

Risk assessment of vascular complications following manual therapy and exercise for the cervical region: diagnostic accuracy of the International Federation of Orthopaedic Manipulative Physical Therapists framework (The Go4Safe project)

Rogier F de Best ^a, Michel W Coppieters ^{a,b}, Emiel van Trijffel ^c, Annette Compter ^d,
 Maarten Uyttenboogaart ^e, Joost C Bot ^f, Rene Castien ^a, Jan JM Pool ^g, Barbara Cagnie ^h,
 Gwendolyn GM Scholten-Peeters ^a

^a Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, Amsterdam, The Netherlands; ^b Menzies Health Institute Queensland, School of Health Sciences and Social Work, Griffith University, Brisbane and Gold Coast, Australia; ^c Ziekenhuisgroep Twente, ZGT Academy, Almelo, The Netherlands; ^d Department of Neuro-Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands; ^e Department of Neurology and Radiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; ^f Department of Radiology, Amsterdam University Medical Center, Amsterdam, The Netherlands; ^g Research Group Lifestyle and Health, HU University of Applied Sciences Utrecht, Utrecht, The Netherlands; ^h Department of Rehabilitation Sciences, Ghent University, Ghent, Belgium

KEY WORDS

Validity
 Cervical artery
 Physical therapy
 Complication
 Spinal manipulation



ABSTRACT

Question: What is the diagnostic accuracy of the International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT) framework to assess the risk of vascular complications in patients seeking physiotherapy care for neck pain and/or headache? **Design:** Cross-sectional diagnostic accuracy study. **Participants:** One hundred and fifty patients seeking physiotherapy for neck pain and/or headache in primary care. **Methods:** Nineteen physiotherapists performed the index test according to the IFOMPT framework. Patients were classified as having a high, intermediate or low risk of vascular complications, following manual therapy and/or exercise, derived from the estimated risk of the presence of vascular pathology. The reference test was a consensus medical decision reached by a vascular neurologist and an interventional neurologist, with input from a neuroradiologist. The neurologists had access to clinical data and magnetic resonance imaging of the cervical spine, including an angiogram of the cervical arteries. **Outcome measures:** Diagnostic accuracy measures were calculated for 'no contraindication' (ie, the low-risk category) and 'contraindication' (ie, the high-risk and intermediate-risk categories) for manual therapy and/or exercise. Sensitivity, specificity, predictive values, likelihood ratios and the area under the curve were calculated. **Results:** Manual therapy and/or exercise were contraindicated in 54.7% of the patients. The sensitivity of the IFOMPT framework was low (0.50, 95% CI 0.39 to 0.61) and its specificity was moderate (0.63, 95% CI 0.51 to 0.75). The positive and negative likelihood ratios were weak at 1.36 (95% CI 0.93 to 1.99) and 0.79 (95% CI 0.60 to 1.05), respectively. The area under the curve was poor (0.57, 95% CI 0.49 to 0.65). **Conclusion:** The IFOMPT framework has poor diagnostic accuracy when compared with a reference standard consisting of a consensus medical decision. [de Best RF, Coppieters MW, van Trijffel E, Compter A, Uyttenboogaart M, Bot JC, Castien R, Pool JMM, Cagnie B, Scholten-Peeters GGM (2023) Risk assessment of vascular complications following manual therapy and exercise for the cervical region: diagnostic accuracy of the International Federation of Orthopaedic Manipulative Physical Therapists framework (The Go4Safe project). *Journal of Physiotherapy* 69:260–266]

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Introduction

Atherosclerosis and cardioembolic sources are common causes of stroke.^{1,2} However, a cervical arterial dissection is the most frequent reason for stroke in young and middle-aged adults.³ Patients with cervical arterial dissection can present with musculoskeletal neck pain and/or headache as one of the first symptoms and sometimes the only symptom.^{4,5} For these complaints, patients often first visit primary care clinicians such as general practitioners and physiotherapists.

It is of the utmost importance that primary care clinicians can accurately distinguish between vascular and musculoskeletal neck pain and headache. However, vascular pathology is often missed in the screening and diagnostic processes.^{6,7} This leads to inadequate referral and treatment, and decreases the safety of primary care interventions. Adverse events due to missed or misdiagnosed vascular pathology rank high in malpractice claims.⁸

Cervical mobilisation, manipulation and exercise (MT/Ex) are frequently used and effective treatments for musculoskeletal neck

pain and headache^{9–11} and are recommended in clinical practice guidelines.¹² However, cervical manipulation has also been associated with vascular complications.¹³ Serious adverse events (eg, dissection of the vertebral or carotid artery) have been reported in the literature,^{14,15} but the reported incidence of vascular pathology following spinal manipulation is low (ranging from 0.4 to 5.0 per 100,000 patients).^{13,16} These serious adverse events may be the result of misdiagnosed or missed vascular pathologies,^{15,3} or the direct consequence of the intervention without pre-existing vascular pathology. The causality still remains debatable.¹⁷

To reduce diagnostic errors and the risk of serious adverse events following MT/Ex, the International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT) developed a clinical reasoning framework for the cervical spine (the IFOMPT framework) based on the best available evidence.¹⁸ The purpose of this framework is to make the best judgment on the risk of vascular complications following MT/Ex derived from the estimated risk of the presence of vascular pathology. The IFOMPT framework guides physiotherapists generating and testing hypotheses related to vascular complications following treatment. For this, an adequate patient interview with knowledge of signs, symptoms and risk factors for vascular pathology is required. However, the diagnostic accuracy of the IFOMPT framework remains unknown.¹⁹

Therefore, the research question for this cross-sectional diagnostic accuracy study was:

What is the diagnostic accuracy of the IFOMPT framework to assess the risk of vascular complications in patients seeking physiotherapy care for neck pain and/or headache?

Methods

Design

This diagnostic accuracy study compared the outcome of the IFOMPT framework with a reference standard consisting of a consensus medical decision. Approximately two-thirds of the patients also participated in a study to determine the reliability of the IFOMPT framework in assessing the risk of vascular complications following MT/Ex; these findings have previously been reported.¹⁹

Participants

Patients with neck pain and/or headache were recruited between July 2017 and March 2019 from 12 primary care physiotherapy practices in the Netherlands. Patients were eligible if they consulted a physiotherapist for neck pain and/or headache, were aged ≥ 18 years and had sufficient knowledge of the Dutch language to complete a questionnaire. Patients with claustrophobia, internal pacemaker, metal implants in/or around the neck or face, or those who were unable to lie supine for 20 minutes were excluded, as they were ineligible to undergo part of the reference test.

Index test

The original IFOMPT framework was published in 2014¹⁸ and revised in 2023.²⁰ In this study, the index test was performed according to the original version of the IFOMPT framework,¹⁸ as the

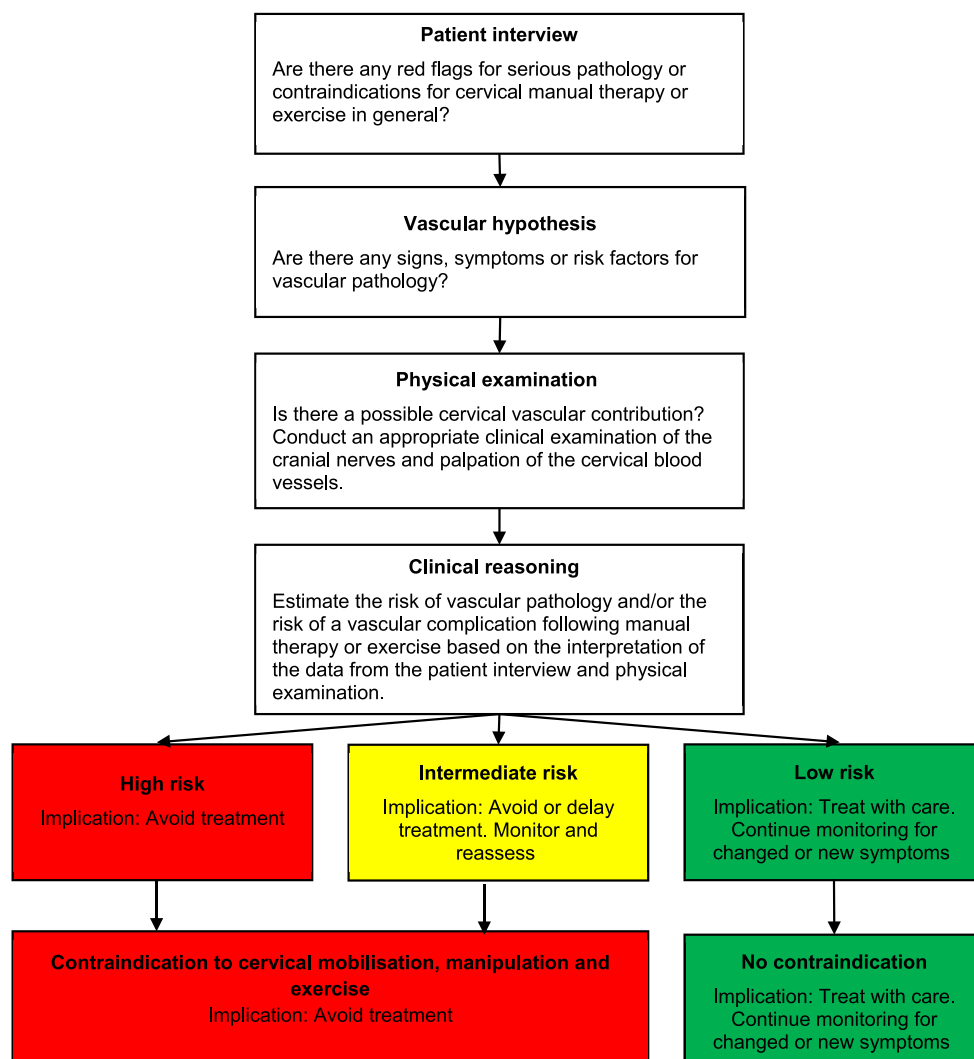


Figure 1. Flow of the IFOMPT framework.

study was already in progress when the revised framework was released. First, the physiotherapist screened for general red flags for serious pathology or contraindications for MT/Ex. Then, a structured clinical reasoning process was conducted, in which the patient interview was used to establish and test hypotheses regarding the origin of the neck pain and/or headache (ie, musculoskeletal or vascular pathology). To make a best judgment on the probability of either the presence of vascular pathology or contraindications for treatment, knowledge of risk factors for vascular pathology and an understanding of the measurement properties of diagnostic tests are essential.

The outcome was the risk of vascular complications following MT/Ex, derived from the estimated risk of the presence of vascular pathology, scored as 'high risk', 'intermediate risk' or 'low risk' (Figure 1). In addition, the physiotherapist documented which factors of the IFOMPT framework had contributed to this decision and whether they suspected a musculoskeletal or vascular origin of the symptoms. Furthermore, the physiotherapists scored the certainty of their decision on a numerical rating scale (0 to 10), ranging from 0 'completely uncertain' to 10 'completely certain'.

The index test was conducted by 19 experienced physiotherapists: 14 males and five females, with a median age of 39 years (IQR 31 to 47), median (IQR) physiotherapy experience of 18 years (IQR 9 to 22) and median manual therapy experience of 7 years (IQR 4 to 16). All had successfully completed an IFOMPT-recognised post-graduate program in manual therapy. All physiotherapists had also attended a 3-hour refresher training on how to apply the IFOMPT framework. The training was provided by two instructors of the Master of Science program in manual therapy of the SOMT University of Physiotherapy, Amersfoort, the Netherlands. The instructors had 6 years (RdB) and 14 years (JC) of teaching experience in manual therapy, and 10 years and 37 years of relevant clinical experience, respectively. The objectives of the training were to: refresh the risk factors and clinical manifestations of cervical arterial pathology; practise clinical reasoning focused on the estimation of the probability of vascular pathology or vascular complications following MT/Ex; and train diagnostic skills (ie, taking blood pressure measurements, examining the cranial nerves and palpating the carotid artery to assess asymmetry between left and right arteries, a pulsatile or an expandable mass).

Reference test

The reference test was a consensus medical decision reached by a vascular neurologist (AC) and an interventional neurologist (MU), with input from a neuroradiologist (JCB). For patients with neck pain or headache, no single test is available as a gold standard to determine the risk of an underlying vascular pathology or the risk of a vascular complication following MT/Ex to the cervical spine.²¹ As part of the reference test, all patients underwent magnetic resonance imaging examination of the cervical spine to assess degenerative spine disease (eg, herniated discs, degenerative disc disease, spinal stenosis) and a magnetic resonance angiogram (MRA) of the cervical arteries to identify possible vascular pathology (eg, dissection, aneurysm, fibro-muscular dysplasia, atherosclerosis and stenosis).^{22–24} The degree of stenosis was based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) formula and determined by the neuroradiologist.

Magnetic resonance was performed on a commercial scanner^a using a protocol consisting of sagittal T2-weighted fast relaxation fast spin echo to detect cervical degenerative disease, axial 3D time of flight spoiled gradient echo MRA for vessel lumen imaging, and a 3D black blood T1-weighted sequence (Cube, fast spin echo with variable flip angle) with fat-suppressed images for vessel wall imaging.

The neurologists based their decision on the patient's characteristics gathered via a questionnaire, the MRA and magnetic resonance report provided by the neuroradiologist. The questionnaire for the patient's characteristics was based on the literature,^{4,25–27} and discussed and amended in a focus group meeting of medical specialists (n = 3) and physiotherapists (n = 2). The questionnaire consisted of

clinical and history data, and information about risk factors for various types of vascular pathologies.^{4,22–24}

The neurologists evaluated the patient data, MRA and magnetic resonance report, and independently assigned a high risk, intermediate risk or low risk of vascular complications derived from the estimated risk of the presence of vascular pathology. In case of disagreement, a meeting was organised to reach consensus. Similar to the physiotherapists for the index test, the neurologists individually scored the degree of certainty of their risk classification for the reference test (numerical rating scale 0 to 10).

Blinding and timing

The patients, neurologists and neuroradiologist were blinded to the results of the index test. Patient data for the reference test were gathered after the index test was performed. The magnetic resonance examination was performed within 3 weeks of the index test. Patients received no treatment before the reference test was performed.

Data analysis

Sample size calculation

As the IFOMPT framework serves as a screening instrument, high sensitivity is required. It was determined that a 95% CI lower limit of 0.8 was needed for sensitivity. The anticipated prevalence (0.3) of a

Table 1
Participant characteristics.

Characteristics	Participants (n = 156)
Sex, n female (%)	94 (60)
Age (y), median (IQR)	49 (38 to 60)
Body mass index (kg/m^2), median (IQR)	25.5 (23.3 to 28.7)
Distribution of symptoms ^a , n (%)	
occipital headache	6 (4)
headache around ear and jaw	6 (4)
mid/upper cervical spine	36 (25)
lower cervical spine	24 (16)
mid/upper cervical spine and occipital headache	26 (18)
mid/upper cervical spine and ear/jaw headache	5 (3)
other (eg, lower cervical spine and arm pain)	43 (29)
Mean of previous week pain intensity (0 to 10), median (IQR)	
headache	5 (4 to 7)
neck pain	5 (3 to 7)
Cause ^b , n (%)	
trauma within 30 days	22 (14)
non trauma	134 (86)
Duration of symptoms ^c , n (%)	
< 6 weeks	21 (15)
6 to 12 weeks	19 (13)
> 12 weeks	102 (72)
Additional symptoms, n (%)	
dizziness ^d	61 (41)
reduced sensation in arms or legs ^d	63 (42)
reduced muscle force in arms or legs ^e	47 (32)
difficulty swallowing ^e	20 (13)
difficulty speaking ^d	20 (13)
diplopia ^e	23 (15)
fainting/risk of falling ^d	34 (23)
Other risk factors present, n (%)	
high blood pressure ^f	36 (23)
high cholesterol ^g	32 (21)
history of cardiovascular event ^g	7 (5)
history of cerebrovascular accident ^b	7 (5)
smoking ^b	22 (14)
alcohol use (> 1 unit a day) ^d	16 (11)
infection in the past 30 days ^g	11 (7)
migraine without aura ^b	10 (7)
cervical manipulation in history ^b	101 (66)

^a 10 missing values.

^b 4 missing values.

^c 14 missing values.

^d 6 missing values.

^e 7 missing values.

^f 2 missing values.

^g 3 missing values.

Table 2
Distribution of the test results (n = 150).

Index test	Reference test three categories			Reference test two categories	
	High risk	Intermediate risk	Low risk	Contraindication ^a	No contraindication ^b
High risk	9	10	10	41	25
Intermediate risk	3	19	15		
Low risk	3	38	43	41	43

For the two-category analysis, high risk and intermediate risk were merged into 'contraindication'.

^a Contraindication for manual therapy and exercise.

^b No contraindication for manual therapy and exercise.

high risk of vascular complications following MT/Ex was based on a pilot study in primary care physiotherapy practices. For a 95% CI lower limit of 0.8, a prevalence of 0.3 and allowing for 4% loss to follow-up, 156 patients were needed. The sample size was calculated using free software^b.

Statistical analysis

In cases of incomplete data from the questionnaire, the main investigator (RdB) approached the participants to obtain the missing items. Participants with missing risk classification on the index test or reference test were excluded from the analysis. The characteristics of the physiotherapists and patients were summarised using descriptive statistics. Data were checked for normality using visual inspection of a histogram and boxplot, and tested with the Shapiro–Wilk test.

Means and standard deviation were calculated when continuous data were normally distributed. When data were not normally distributed, the median and IQR were presented. For categorical data, absolute and relative frequencies were presented.

To determine diagnostic accuracy, the variable 'risk category' was dichotomised into 'contraindication for MT/Ex' and 'no contraindication for MT/Ex'. 'Intermediate risk' and 'high risk' were combined as 'contraindication for MT/Ex', as MT/Ex should be avoided or delayed (MT/Ex is contraindicated) for these categories, whereas there is no contraindication for MT/Ex and MT/Ex could be indicated in the 'low risk' category.

Two-by-two tables were constructed, in which the results of the index test were plotted against the results of the reference test to calculate prevalence, sensitivity, specificity, predictive values,

likelihood ratios and the area under the curve. For the interpretation of sensitivity and specificity values, sensitivity and specificity values were considered as follows: ≥ 0.80 as high, 0.60 to 0.79 as moderate and < 0.60 as low. A positive likelihood ratio (LR+) < 2 or negative likelihood ratio (LR-) > 0.5 were considered to be weak; LR+ from 2 to 5 and LR- from 0.5 to 0.2 were considered to be moderate; and LR+ > 10 and LR- < 0.1 were considered to be strong.^{28,29} An area under the curve > 0.9 was considered to be outstanding, 0.8 to 0.9 was considered excellent, 0.7 to 0.8 was considered acceptable and 0.5 to 0.6 was considered poor. An area under the curve of 0.5 suggested that the index test had no discriminatory ability.³⁰ All data were analysed using free software^c.

Results

Most patients were middle-aged women with prolonged symptoms of neck pain and/or headache (> 12 weeks). Around 40% reported additional symptoms such as reduced sensation, reduced muscle strength and dizziness (Table 1).

Based on the reference test, 10.0% of the patients were categorised as having a 'high risk'. The median certainty of this decision was NRS 7 (IQR 6 to 8) for one neurologist and 7 (IQR 7 to 8) for the other neurologist; 44.7% were categorised as 'intermediate risk' with a median certainty score of 7 (IQR 5 to 7) and 7 (IQR 7 to 7) for the two neurologists, and 45.3% as 'low risk' with a median certainty score of 7 (IQR 6 to 8) and 7 (IQR 7 to 7).

Based on the IFOMPT framework, 19.3% of the patients were classified as having a 'high risk' and the median certainty of their decision was NRS 8 (IQR 7 to 9); 24.7% were categorised as 'intermediate risk' with a median certainty score of 7 (IQR 6 to 8); and 56.0% were categorised as 'low risk' with a median certainty score of 8 (IQR 7 to 9) (Table 2). Consequently, the prevalence of 'contraindication for MT/Ex' was 44.0% for the index test and 54.7% for the reference test. The flow of the patients is presented in Figure 2.

The neurologists predominantly used the clinical information combined with the results of the MRA to make their decision. No decisions were based solely on physical tests or the MRA scan (Table 3). The physiotherapists used clinical information from the history taking as the most important source of information for decision-making (Table 4).

The sensitivity of the IFOMPT framework was low (0.50, 95% CI 0.39 to 0.61) and the specificity was moderate (0.63, 95% CI 0.51 to 0.75). The LR+ of 1.36 and LR- of 0.79 were weak. The area under the

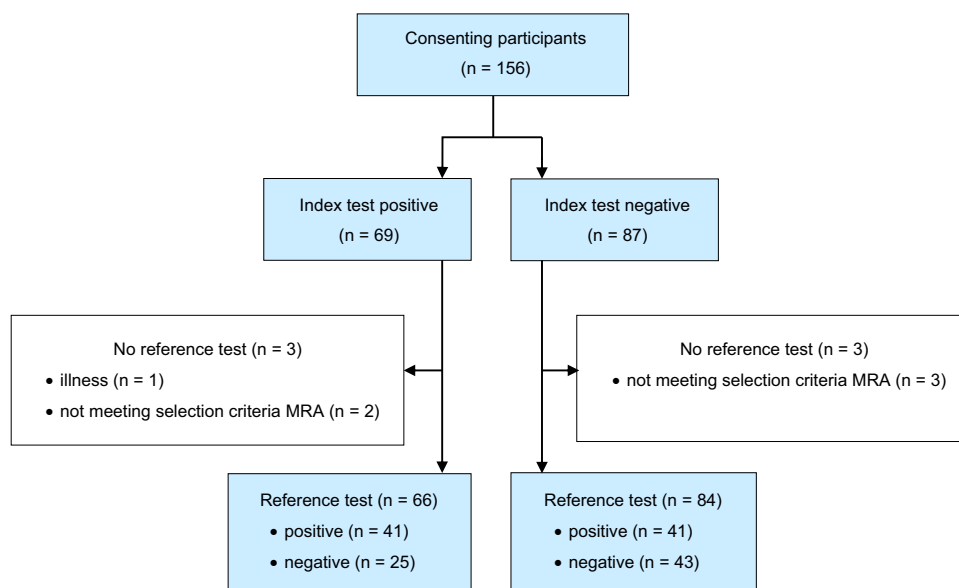


Figure 2. Flow of participants through the study.

Table 3
Contributing factors for risk category assessment by expert panel.

Potential underlying pathology (n)	Risk category (n)	Contributing factors (n)
Vascular (dissection) (71)	High (10)	Clinical information only (3) Clinical information and MRA (7)
	Intermediate (61)	MRA only (0) Clinical information only (37) Clinical information and MRA (24)
	High (4)	MRA only (0) Clinical information only (0) Clinical information and MRA (4)
	Intermediate (4)	MRA only (0) Clinical information only (2) Clinical information and MRA (2)
Vascular (non-dissection) (8)	High (1)	MRA only (0) Clinical information only (0) Clinical information and MRA (1)
	Intermediate (2)	MRA only (0) Clinical information only (0) Clinical information and MRA (2)
Other (eg, osteoarthritis, stenosis, rheumatoid arthritis) (3)	High (1)	MRA only (0) Clinical information only (0) Clinical information and MRA (1)
	Intermediate (2)	MRA only (0) Clinical information only (0) Clinical information and MRA (2)

The numbers in parentheses indicate the number of people.
MRA = magnetic resonance angiography.

curve was poor (0.57, 95% CI 0.49 to 0.65) (Table 5). The receiver operating characteristic curve is presented in Figure 3.

Discussion

The diagnostic accuracy of the IFOMPT framework compared with a consensus medical decision was low. As the IFOMPT framework aims to detect patients who are at risk of vascular complications following MT/Ex, derived from the estimated risk of the presence of vascular pathology, a high sensitivity is required.³¹ In this study, a sensitivity of 0.50 (95% CI 0.39 to 0.61) was found. In other words, there is a 50% chance of correctly identifying patients with a high risk of vascular complications from and contraindications for MT/Ex. The specificity of 0.63 (95% CI 0.51 to 0.75) was moderate, but the lower bound was low. Moreover, a 0.37 false positive rate reflects a fairly frequent incorrect assumption that MT/Ex is contraindicated and may lead to unnecessary referrals to medical specialists and expensive medical work-up. Moreover, due to a high pre-test probability of 54.7% (prevalence), the IFOMPT framework adds on 7.3% to the post-test probability (62% positive predictive value).

Table 4
Contributing factors for risk category assessment by physiotherapists.

Potential underlying pathology (n)	Risk category (n)	Contributing factors (n)
Vascular (dissection) (13)	High (6)	History taking only (4) History taking and physical examination (2)
	Intermediate (7)	History taking only (5) History taking and physical examination (2)
	High (23)	History taking only (18) History taking and physical examination (5)
	Intermediate (30)	History taking only (26) History taking and physical examination (4)
Vascular (non-dissection) (53)	High (0)	History taking only (0) History taking and physical examination (0)
	Intermediate (0)	History taking only (0) History taking and physical examination (0)
Other (eg, osteoarthritis, stenosis, rheumatoid arthritis) (0)	High (0)	History taking only (0) History taking and physical examination (0)
	Intermediate (0)	History taking only (0) History taking and physical examination (0)

The numbers in parentheses indicate the number of people.

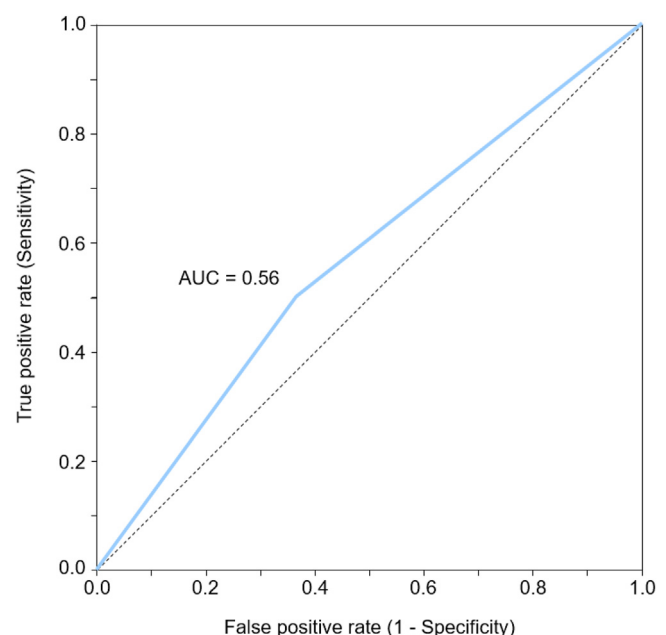
Table 5
Diagnostic accuracy estimates.

Statistic	Estimate	95% CI
Prevalence	0.55	
Sensitivity	0.50	0.39 to 0.61
Specificity	0.63	0.51 to 0.75
Positive predictive value	0.62	0.49 to 0.79
Negative predictive value	0.51	0.40 to 0.62
Positive likelihood ratio	1.36	0.93 to 1.99
Negative likelihood ratio	0.79	0.60 to 1.05
Area under the curve	0.57	0.49 to 0.65

There are no studies that have assessed the diagnostic accuracy of the risk assessment for vascular complications in patients with neck pain and/or headache prior to MT/Ex. However, there are studies that have assessed the diagnostic accuracy of clinical testing for upper cervical instability,³² cervical spine myelopathy³³ or pre-manipulative vertebralbasilar insufficiency.³⁴ However, these tests were performed in isolation or as an add-on test to filter false-negative test results on history taking, and had high risk of bias.

The IFOMPT framework was published in 2014¹⁸ and revised in 2023.²⁰ The revised framework distinguishes characteristics between dissection and non-dissection events, it has updated the diagnostic accuracy of provocative positional testing and upper cervical instability testing,^{32,34} and a risk-benefit analysis is advised as an outcome, instead of estimating three categories (high, medium and low risk). As data collection had started by July 2017, the current study used the first version of the IFOMPT framework,¹⁸ but modified some aspects, which were also reflected in the revised framework.²⁰ For example, the physiotherapists were aware of the difference between the characteristics of dissection and non-dissection events, and information on the lack of diagnostic accuracy of provocative positional testing and upper cervical instability testing was provided.^{32,34} In both versions of the framework, clinical reasoning is encouraged and physiotherapists need to combine patient interview items and clinical tests to verify or falsify the vascular hypothesis.

When taking the above into consideration, the three risk categories 'high risk', 'intermediate risk' and 'low risk' were dichotomised into 'contraindication for MT/Ex' and 'no contraindication for MT/Ex' for the analyses. This is also in line with the revised IFOMPT framework,²⁰ in which a risk-benefit analysis is advised, instead of estimating the three categories. As there are no fundamental differences between the framework as used in this study and the revised framework,²⁰ it is unlikely that the diagnostic accuracy would have

**Figure 3.** Receiver operating characteristic curve.

been substantially better if the revised IFOMPT framework had been assessed.

Our study reported a prevalence of 0.55 ('contraindication' category), which is higher than the reported incidence of vascular pathology related to manual therapy in the literature.^{13,16,35} This suggests that selection bias was present, and that patients 'at risk of vascular pathology' were predominantly included. Patients with more severe complaints may have been more willing to participate, as participation meant receiving a magnetic resonance examination free of charge, which is not part of standard care and could contribute to a better diagnosis and safer treatment. Unfortunately, we did not register all eligible consecutive patients, so selection bias could not be ruled out. It is, however, important to remember that the high prevalence reflects the percentage of patients 'at risk of vascular complications following MT/Ex' derived from the estimated risk of the presence of vascular pathology and not all patients with a contraindication for MT/Ex actually have vascular pathology or will experience a vascular complication after MT/Ex. The actual prevalence of vascular pathology is much lower.³⁶ Furthermore, by combining the 'intermediate risk' and 'high risk' categories for analyses as 'contraindication for MT/Ex', the prevalence increased from 0.10 to 0.55.

This study found that the IFOMPT framework has poor diagnostic accuracy when compared with a reference standard (medical consensus decision). The IFOMPT framework assists physiotherapists in considering whether a patient has an increased risk of a vascular complication following MT/Ex based on potential underlying vascular pathology. However, the results of this study show that the IFOMPT framework is unable to guide physiotherapists adequately in making an accurate risk estimation to identify patients with an increased risk of a vascular complication following MT/Ex.

A previous study into the reliability and agreement of the IFOMPT framework among physiotherapists showed a moderate reliability and an acceptable agreement (when contraindication versus no contraindication for treatment was considered).¹⁹ Although these results came from related studies, the reliability and diagnostic accuracy of the IFOMPT framework were both unfavourable. More research and a different clinical approach is needed to correctly identify patients at risk of vascular complications after MT/Ex to improve the safety of MT/Ex applied to the cervical spine.

What was already known on this topic: Patients with cervical arterial dissection can present with musculoskeletal neck pain and/or headache as one of the first symptoms and sometimes the only symptom. Physiotherapists must be able to distinguish between vascular and musculoskeletal neck pain and headache. To assist with this, the International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT) developed a clinical reasoning framework for the cervical spine.

What this study adds: The IFOMPT framework has poor diagnostic accuracy. The sensitivity was low and the specificity was moderate. The positive and negative likelihood ratios were weak. The area under the curve was poor.

Footnotes: ^a 3T Discovery mr750, General Electric, Boston, USA.

^b R-Studio, V.2021.09.0, R Core Team, Vienna, Austria.

^c R software, V.4.1.1, CRAN.R-project, Vienna, Austria.

Ethics approval: The Medical Ethics Review Committee of the Amsterdam University Medical Centre approved the study (METC-2017.086). All participants provided written informed consent prior to commencing the study.

Competing interests: Nil.

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Correspondence: Gwendolyn GM Scholten-Peeters, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, The Netherlands. Email: g.g.m.scholten-peeters@vu.nl

References

1. Ekker MS, Boot EM, Singhal AB, Tan KS, Debette S, Tuladhar AM, et al. Epidemiology, aetiology, and management of ischaemic stroke in young adults. *Lancet Neurol.* 2018;17:790–801. [https://doi.org/10.1016/S1474-4422\(18\)30233-3](https://doi.org/10.1016/S1474-4422(18)30233-3)
2. Knight-Greenfield A, Nario JJQ, Gupta A. Causes of Acute Stroke. *Radiol Clin North Am.* 2019;57:1093–1108. <https://doi.org/10.1016/j.rcl.2019.07.007>
3. Biller J, Sacco RL, Albuquerque FC, Demaerschalk BM, Fayad P, Long PH, et al. Cervical arterial dissections and association with cervical manipulative therapy: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2014;45:3155–3174. <https://doi.org/10.1161/STR.0000000000000016>
4. Debette S, Compter A, Labeyrie M, Uyttenboogaart M, Metso TM, Majersik JJ, et al. Epidemiology, pathophysiology, diagnosis, and management of intracranial artery dissection. *Lancet Neurol.* 2015;14:640–654. [https://doi.org/10.1016/S1474-4422\(15\)00009-5](https://doi.org/10.1016/S1474-4422(15)00009-5)
5. Debette S. Pathophysiology and risk factors of cervical artery dissection. *Curr Opin Neurol.* 2014;27:20–28. <https://doi.org/10.1097/WCO.0000000000000056>
6. Singh H, Schiff GD, Graber ML, Onakpoya I, Thompson MJ. The global burden of diagnostic errors in primary care. *BMJ Qual Saf.* 2017;26:484–494. <https://doi.org/10.1136/bmjqs-2016-005401>
7. Clark BW, Derakhshan A, Desai SV. Diagnostic errors and the bedside clinical examination. *Med Clin North Am.* 2018;102:453–464. <https://doi.org/10.1016/j.mcna.2017.12.007>
8. Quinn GR, Ranum D, Song E, Linets M, Keohane C, Riah H, et al. Missed diagnosis of cardiovascular disease in outpatient general medicine: insights from malpractice claims data. *Jt Comm J Qual Patient Saf.* 2017;43:508–516. <https://doi.org/10.1016/j.jcjq.2017.05.001>
9. Hidalgo B, Hall T, Bossert J, Dugeny A, Cagnie B, Pitance L. The efficacy of manual therapy and exercise for treating non-specific neck pain: a systematic review. *J Back Musculoskelet Rehabil.* 2017;30:1149–1169. <https://doi.org/10.3233/BMR-169615>
10. Gross A, Langevin P, Burnie SJ, Bédard-Brochu MS, Empey B, Dugas E, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database Syst Rev.* 2015;9:CD004249. <https://doi.org/10.1002/14651858.CD004249.pub4>
11. Cumplido-Trasmonte C, Fernández-González P, Alguacil-Diego IM, Molina-Rueda F. Manual therapy in adults with tension-type headache: a systematic review. *Neurología.* 2021;36:537–547. <https://doi.org/10.1016/j.nrleng.2017.12.005>
12. Blanpied PR, Gross AR, Elliott JM, Devaney LL, Clewley D, Walton DM, et al. Clinical practice guidelines linked to the international classification of functioning, disability and health from the orthopaedic section of the American physical therapy association. *J Orthop Sports Phys Ther.* 2017;47:A1–A83. <https://doi.org/10.2519/jospt.2017.0302>
13. Cassidy JD, Boyle E, Côté P, Hogg-Johnson S, Bondy SJ, Haldeman S. Risk of carotid stroke after chiropractic care: a population-based case-crossover study. *J Stroke Cerebrovasc Dis.* 2017;26:842–850. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.10.031>
14. Kranenburg HA, Schmitt MA, Puenteadura EJ, Luijckx GJ, van der Schans CP. Adverse events associated with the use of cervical spine manipulation or mobilization and patient characteristics: A systematic review. *Musculoskelet Sci Pract.* 2017;28:32–38. <https://doi.org/10.1016/j.msksp.2017.01.008>
15. Hutting N, Kerry R, Coppieters MW, Scholten-Peeters GGM. Considerations to improve the safety of cervical spine manual therapy. *Musculoskelet Sci Pract.* 2018;33:41–45. <https://doi.org/10.1016/j.msksp.2017.11.003>
16. Nielsen SM, Tarp S, Christensen R, Bliddal H, Klokke L, Henriksen M. The risk associated with spinal manipulation: an overview of reviews. *Syst Rev.* 2017;6:64. <https://doi.org/10.1186/s13643-017-0458-y>
17. Murphy DR, Schneider MJ, Perle SM, Bise CG, Timko M, Haas M. Does case misclassification threaten the validity of studies investigating the relationship between neck manipulation and vertebral artery dissection stroke? No. *Chiropr Man Therap.* 2016;24:1–6. <https://doi.org/10.1186/s12998-016-0124-9>
18. Rushton A, Rivett D, Carlesso L, Flynn T, Hing W, Kerry R. International framework for examination of the cervical region for potential of Cervical Arterial Dysfunction prior to Orthopaedic Manual Therapy intervention. *Man Ther.* 2014;19:222–228. <https://doi.org/10.1016/j.math.2013.11.005>
19. de Best RF, Coppieters MW, van Trijffel E, Compter A, Uyttenboogaart M, Bot JC, et al. Interexaminer Agreement and Reliability of an Internationally Endorsed Screening Framework for Cervical Vascular Risks Following Manual Therapy and Exercise: The Go4Safe Project. *Phys Ther.* 2021;101. <https://doi.org/10.1093/ptj/pzab166>

20. Rushton A, Carlesso LC, Flynn T, Hing WA, Rubinstein SM, Vogel S, et al. Position Statement: International Framework for Examination of the Cervical Region for potential of vascular pathologies of the neck prior to Musculoskeletal Intervention: International IFOMPT Cervical Framework. *J Orthop Sports Phys Ther.* 2023;13:7–22. <https://doi.org/10.2519/jospt.2022.11147>
21. Handels RLH, Wolfs CAG, Aalten P, Bossuyt PMM, Joore MA, Leentjens AFG, et al. Optimizing the use of expert panel reference diagnoses in diagnostic studies of multidimensional syndromes. *BMC Neurol.* 2014;14:190.
22. Debrey SM, Yu H, Lynch JK, Lovblad K-O, Wright VL, Janket S-JD, et al. Diagnostic accuracy of magnetic resonance angiography for internal carotid artery disease: A systematic review and meta-analysis. *Stroke.* 2008;39:2237–2248. <https://doi.org/10.1161/STROKEAHA.107.509877>
23. Coppenrath EM, Lummel N, Linn J, Lenz O, Habs M, Nikolaou K, et al. Time-of-flight angiography: A viable alternative to contrast-enhanced MR angiography and fat-suppressed T1w images for the diagnosis of cervical artery dissection? *Eur Radiol.* 2013;23:2784–2792. <https://doi.org/10.1007/s00330-013-2891-1>
24. Schwarz F, Strobl FF, Cyran CC, Helck AD, Hartmann AD, Schindler A, et al. Reproducibility and differentiation of cervical arteriopathies using in vivo high-resolution black-blood MRI at 3 T. *Neuroradiology.* 2016;58:569–576. <https://doi.org/10.1007/s00234-016-1665-2>
25. Debette S, Metso T, Pezzini A, Abboud S, Metso A, Leys D, et al. Association of vascular risk factors with cervical artery dissection and ischemic stroke in young adults. *Circulation.* 2011;123:1537–1544. <https://doi.org/10.1161/CIRCULATIONAHA.110.000125>
26. Persu A, Giavarini A, Touz E, Januszewicz A, Sapoval M, Azizi M, et al. European consensus on the diagnosis and management of fibromuscular dysplasia. *J Hypertens.* 2014;32:1367–1378. <https://doi.org/10.1097/HJH.0000000000000213>
27. Touzé E, Oppenheim C, Trystram D, Nokam G, Pasquini M, Alamowitch S, et al. Fibromuscular dysplasia of cervical and intracranial arteries. *Int J Stroke.* 2010;5:296–305. <https://doi.org/10.1111/j.1747-4949.2010.00445.x>
28. Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. *JAMA.* 1994;271:703–707. <https://doi.org/10.1001/jama.271.9.703>
29. Sleijser-Koehorst MLS, Coppieters MW, Epping R, Rooker S, Verhagen AP, Scholten-Peeters GGM. Diagnostic accuracy of patient interview items and clinical tests for cervical radiculopathy. *Physiotherapy (United Kingdom).* 2021;111:74–82. <https://doi.org/10.1016/j.physio.2020.07.007>
30. Mandrekar JN. Receiver Operating Characteristic Curve in Diagnostic Test Assessment. Vol 5; 2010.
31. Leeflang MMG. Systematic reviews and meta-analyses of diagnostic test accuracy. *Clin Microbiol Infect.* 2014;20:105–113. <https://doi.org/10.1111/1469-0691.12474>
32. Hutting N, Scholten-Peeters GGM, Vijverman V, Keesenberg MDM, Verhagen AP. Diagnostic Accuracy of Upper Cervical Spine Instability Tests: A Systematic Review. *Phys Ther.* 2013;93:1686–1695. <https://doi.org/10.2522/ptj.20130186>
33. Cook CE, Wilhelm M, Cook AE, Petrosino C, Isaacs R. Clinical tests for screening and diagnosis of cervical spine myelopathy: A systematic review. *J Manipulative Physiol Ther.* 2011;34:539–546. <https://doi.org/10.1016/j.jmpt.2011.08.008>
34. Hutting N, Verhagen AP, Vijverman V, Keesenberg MDM, Dixon G, Scholten-Peeters GGM. Diagnostic accuracy of premanipulative vertebrobasilar insufficiency tests: A systematic review. *Man Ther.* 2013;18:177–182. <https://doi.org/10.1016/j.math.2012.09.009>
35. Cassidy JD, Boyle E, Côté P, He Y, Hogg-Johnson S, Silver FL, et al. Risk of Vertebrobasilar Stroke and Chiropractic Care. *Spine.* 2008;33:S176–S183. <https://doi.org/10.1097/BRS.0b013e3181644600>
36. Blum CA, Yaghi S. Cervical Artery Dissection: A Review of the Epidemiology, Pathophysiology, Treatment, and Outcome. *Arch Neurosci.* 2015;2. <https://doi.org/10.5812/archneurosci.26670>