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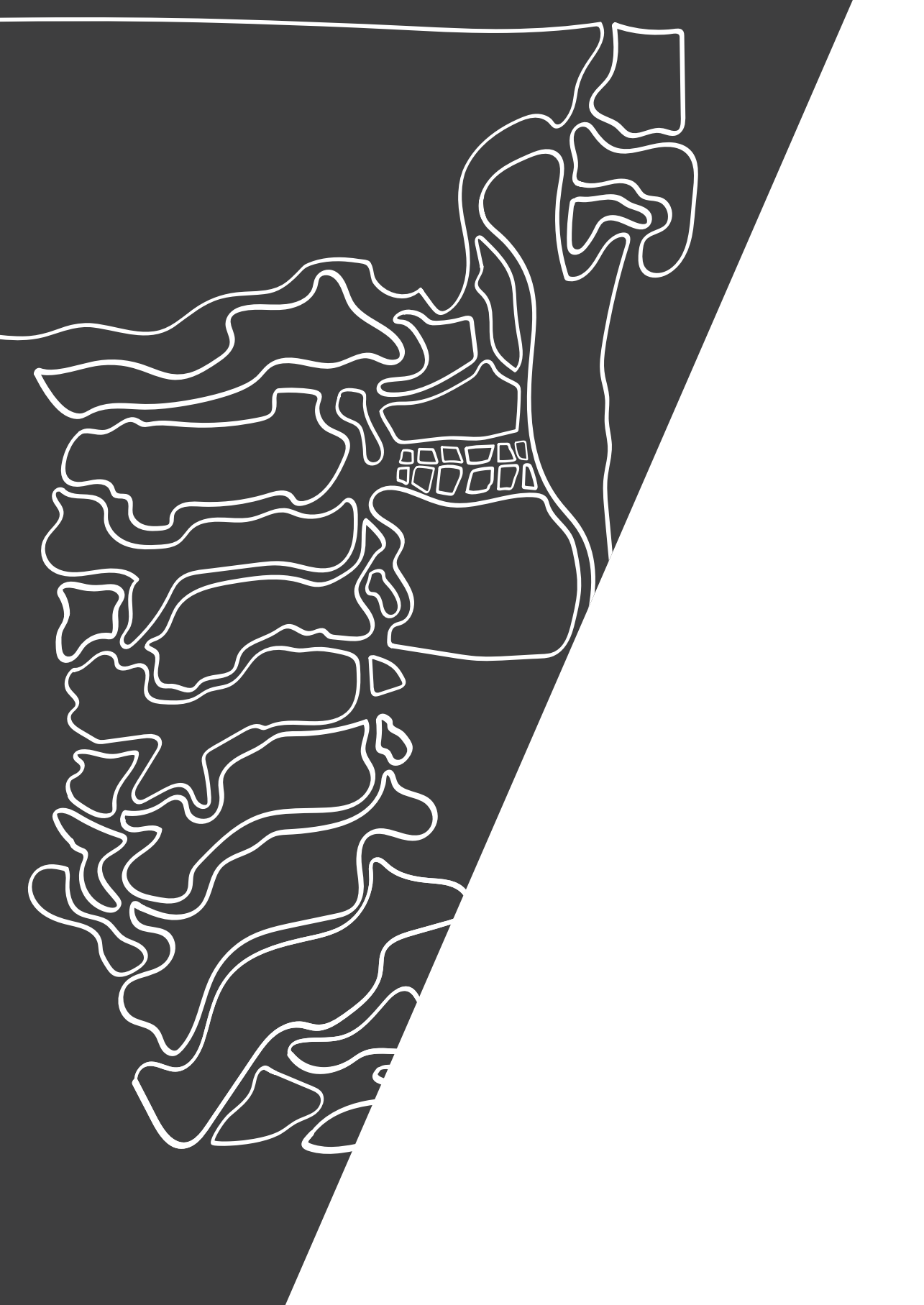
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CAROTID AND VERTEBRAL ARTERIAL DISSECTIONS AFTER MANUAL PHYSICAL THERAPY: A CASE CONTROL STUDY

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ABSTRACT

Introduction: An extra-cranial cervical arterial dissection (CeAD) can present like musculoskeletal neck pain or headache complaints. Therefore, it is important to identify these CeAD patients prior to treatment by manual physical therapists. The first aim of this study is to estimate the proportion of patients with CeAD that received a recent CSM. The second aim is to determine differences in patient demographics and clinical characteristics between patients with CeAD and controls receiving CSM in primary care.

Method: CeAD cases were identified and analyzed from three departments in the University Medical Centre Groningen. A case-control design was used to compare CeAD risk factors based on the IFOMPT framework between CeAD patients with patients receiving cervical manipulations in primary care. Cases and controls were individually matched and Pearson Chi Square and Fishers Exact were used to analyze differences.

Results: Sixty-nine CeAD patients were included in which a CeAD was diagnosed 70 times. The proportion of patients with CeAD that received a CSM prior to hospitalization was low (two) No relevant significant differences were found between patients with CeAD (cases) and neck pain or headache patients without a CeAD receiving a CSM in clinical practice (controls). Most spontaneous CeAD's occurred during summer.

Discussion: These results confirm the difficulty manual physical therapists experience in identifying the sporadic patients with a CeAD in clinical practice. Based on our results, manual physical therapists are advised to use the IFOMPT framework to enhance the clinical reasoning process instead of as a screening tool.

INTRODUCTION

An extra-cranial cervical arterial dissection (CeAD) is a tear in the interior wall of an internal carotid or vertebral artery and is considered to be an important cause of ischemic stroke in young and middle-aged adults.(Debette, 2014) The incidence of carotid CeAD and vertebral CeAD is respectively estimated around 2.6-3.0/100.000 and 1.0/100.000 individuals per year, with a mean age of 45 years.(Blum and Yaghi, 2015; Debette et al., 2009)

One of the early clinical symptoms of CeAD is neck pain or headache.(Debette et al., 2009) The presentation of those dissection-related symptoms are almost similar to the presentation of neck pain or headache symptoms from a musculoskeletal origin. (Debette et al., 2009; Hutting et al., 2018; Thomas, 2016) Generally, in patients with neck pain and headache consulting a manual physical therapist, these complaints have a musculoskeletal origin. For those patients, cervical manipulations (CSM) could be effective to relieve pain and regain function.(Bier et al., 2018; Blanpied et al., 2017; Gross et al., 2015) On the other hand, a CSM could be considered as a minor trauma. Therefore, it might be a potential trigger for a pre-existing CeAD in patients with neck pain from a vascular origin.(Debette et al., 2009; Thomas, 2016) Thus, CSM might induce a CeAD or aggravating a pre-existing dissection in a susceptible patient.(Eriksen et al., 2011) Suggested stroke rates following CSM range from 1/50,000 to 1/6,000,000 CSM.(Assendelft et al., 1996; Magarey et al., 2004; Nielsen et al., 2017) However, these rates seem debatable since conclusive evidence is missing for a causation between CSM and stroke on one hand and an underreporting of cases on the other hand.(Chaibi and Russell, 2019; Church et al., 2016; Hutting et al., 2018; Kranenburg et al., 2017) Notwithstanding, the rarity of CeAD makes solid epidemiological research challenging.

It is essential for manual therapists to know and recognize potential risk factors for CeAD, because of CeAD and its association with CSM. Also, clinical signs and symptoms which might not be of musculoskeletal origin, could be related to a pre-existing CeAD. To assist the manual therapists in this pre-manipulative process, the International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT) has developed an international framework.(Rushton et al., 2014) This framework provides guidance for manual physical therapists to construct a patient-centered pre-manipulative risk/benefit analysis, which might reduce the risk of major adverse neurovascular events following CSM. The framework was originally produced as a guidance document and therefore has an informative character. It comprises contraindications, risk factors, precautions, differential diagnoses and specific

tests for a physical assessment. Despite its intended purpose, in clinical practice the framework is regularly used as a screening tool for making clinical decisions. However, risk factors other than those defined in the IFOMPT framework have been described.(Baumgartner et al., 2005; Dabbouseh and Ardelt, 2011; Lee et al., 2006) For example, a seasonal variability of CeAD incidence has been suggested. (Grau et al., 1999; Kloss et al., 2012; Schievink et al., 1998; Thomas et al., 2017) The increase of CeAD seems to be higher in autumn and might be explained by the hypothesis that there is an increase in infections and coughing in autumn.(Kloss et al., 2012; Thomas et al., 2017) Therefore, the IFOMPT framework might be inconclusive.(Hutting et al., 2018) Furthermore, the exact validity and reliability of this framework as a screening tool is currently unknown.

The first aim of this study is to estimate the proportion of patients with CeAD that received a recent CSM. The second aim is to determine differences in patient demographics and clinical characteristics between patients with CeAD and controls receiving CSM in primary care.

METHODS

PARTICIPANTS

Participants were recruited for 1] the dissection group: patients who were hospitalized and had a diagnosed cervical dissection; and 2] the control group: patients who were treated with CSM and did not report any major adverse event afterwards. The dissection group comprised patients who were hospitalized with the indication of cervical dissection and were collected at the University Medical Centre Groningen (UMCG). Controls were recruited in three private practices spread over The Netherlands. All patients receiving a cervical spinal manipulation as a part of their usual treatment were eligible to participate.

MATCHING

To minimize confounding, cases were matched for gender and age (Mansournia et al., 2018), using a range of 5 years for age.

PROTOCOL

DISSECTION GROUP

All medical records from the departments of Neurology, Neurosurgery and the Emergency Room from the UMCG concerning the years 2014, 2015 and 2016 were identified and analyzed. Cases of ischemic or hemorrhagic stroke were used for data collection. Identified cases were retrieved from the hospital information system

and searched for patient demographics, clinical characteristics and (pre-)existing risk factors for CeAD. To increase the quality of the screening, all selected medical records were independently screened by two reviewers.(Waffenschmidt et al., 2019) All records were analyzed by the first reviewer (RK) and all were also independently screened by a second reviewer (ILS, TC or SK) If no agreement could be obtained, a specialized stroke neurologist (GJL) made the final decision. Cases were included if a patient was diagnosed with a dissection of the vertebral artery (VAD, ICD10-S15.1 / I72.6) or the internal carotid artery (ICAD, ICD10-S15.0 / I72.0). Patient files in which an intracranial dissection, basilar artery dissections and cases of subarachnoid hemorrhage were diagnosed were excluded. Furthermore, cases in which a CeAD originated during an invasive procedure were considered a complication of that procedure and were excluded.

CONTROL GROUP

Patients receiving CSM as a part of their treatment as planned who did not experience any major adverse events afterwards were potential participants. Patients were excluded if they had previously experienced a CeAD.

OUTCOME MEASURES

The number of patients hospitalized with a CeAD and the season in which their CeAD occurred was inventoried. Furthermore, patient characteristics (gender and age), the CeAD risk factors as described in the IFOMPT framework section 3.2 were inventoried.(Rushton et al., 2014) These factors were supplemented with: 1] alcohol abuse; 2] cocaine abuse; 3] familiar cardiovascular history; 4] oral anticonception; and 5] vascular trauma.(Biller et al., 2014; Dabbouseh and Ardelt, 2011) If a variable was not present in the patient file, it was scored as "Absent/ Unknown". For the control group, the same patient demographics, risk factors and precautions for CeAD as in the dissection group were collected.

ETHICS

This study was registered in the UMCG Research Register (RR201500994) and the medical ethical committee of the UMCG approved a waiver (METc 2015/465) for this study.

DATA ANALYSIS

All analyses were performed using IBM SPSS statistics 23. Descriptive statistics were used to characterize the data sampled from each of the groups. All data was presented in frequencies and percentages unless otherwise noted. For the

comparison of risk factors between the two groups a Pearson Chi Square or a Fishers Exact was used on the corresponding contingency tables. When the observed or the expected count was <10 the Fishers Exact was used. Significance was set at level $\alpha < 0.05$. Hypertension was not tested for difference during the case-control comparison. Since blood pressure was measured after the CeAD event, instead of before, an unobtrusive comparison was unfortunately not possible.

RESULTS

PARTICIPANTS

Of the 1,687 identified patients hospitalized with a stroke, a dissection was diagnosed 70 times (4.1%) in 69 patients. In 31 patients the dissection originated in the vertebral artery (44%) and in 39 the dissection originated in the internal carotid artery (56%). Furthermore, in four cases of VAD and one case of ICAD the arteries were bilaterally affected. The mean (sd) age at onset was 54 (15) years and 46 (66%) of 70 patients were male. Of the CeAD, 13 cases occurred during spring, 23 cases in the summer, 17 cases in the autumn and 13 cases in the winter. Two patients (3%) described recent CSM in the medical record. Unfortunately, no details were described if the CSM was considered the cause of the CeAD, regarding the CSM provider, the used technique, the time between the applied CSM and hospitalization. The ages of the CSM cases at onset were 22 and 48 and the male/female ratio was distributed evenly. The early clinical characteristics of the CSM cases were cervical pain (50%), headache (50%), ptosis (50%) and an asymmetry of the mouth/ tongue (100%). The late clinical characteristics were CVA (100%), Wallenberg syndrome (50%), diplopia (100%), dizziness (100%), nystagmus (50%), numbness (100%), nausea (50%) and ataxia (100%).

In the control group 168 patients who received a CSM in a private practice were included. They had a mean age of 47.7 years (SD18) and 110 were females (65.5%).

MATCHING

Of the dissection patients, 66 could be matched 1:1 to a control. The hindering parameter for the remaining three males were their high ages (85, 87 and 90 years). There were no patients who received cervical manipulations within their age range. Therefore, these cases were excluded from the comparison of the two groups.

COMPARISON

Two risk factors 'neck or head trauma' and 'long term steroid use' as described in the IFOMPT framework (Rushton et al., 2014, sec. 3.2) were found to be significantly

different between the cases and the controls. However, the significance was due to a larger presence in the control group.

Table 1. The presence of CeAD risk factors in hospitalized CeAD patients and controls (n=66 in each group), accompanied by results of the Chi Square or Fishers Exact.

		Case	Control	P-value
# Anticoagulation disorder	No	100%	95%	.244
	Yes	0%	5%	
# Cardiovascular history	No	67%	80%	.114
	Yes	33%	20%	
# Diabetes Mellitus	No	89%	97%	.164
	Yes	11%	3%	
# Hypercholesteremia/ hyperlipidemia	No	79%	80%	1.000
	Yes	21%	20%	
# Migraine	No	91%	95%	.492
	Yes	9%	5%	
# Neck or Head trauma	No	97%	80%	.002 *
	Yes	3%	20%	
# Hyperhomocystenia	No	100%	100%	NC
	Yes	0%	0%	
# Long term steroid use	No	100%	91%	.028 *
	Yes	0%	9%	
# Postpartum (lactation period)	No	100%	98%	.394
	Yes	0%	2%	
# Recent cervical manipulation	No	97%	94%	.274
	Yes	3%	6%	
# Recent infection	No	100%	94%	.119
	Yes	0%	6%	
# Smoking	No	74%	80%	.534
	Yes	26%	20%	
Alcohol abuses	No	97%	97%	1.000
	Yes	3%	3%	
Cocaine use	No	100%	98%	1.000
	Yes	0%	2%	
Familiar Cardiovascular history	No	77%	70%	.431
	Yes	23%	30%	

Table 1. Continued

		Case	Control	P-value
Oral contraception	No	97%	93%	.381
	Yes	3%	7%	
Vascular trauma	No	100%	98%	1.000
	Yes	0%	2%	

NC = Not computed; # = IFOMPT framework risk factor (§3.2); * = $P \leq 0.05$

DISCUSSION

The proportion of patients with CeAD that received a CSM prior to hospitalization was low (two out of 69) in our sample. Furthermore, all IFOMPT risk factors were absent in the majority of our sample (Table 1). (Rushton et al., 2014, sec. 3.2) The comparison between the cases of the hospitalized patients with CeAD and the patients receiving CSM in primary care did not confirm relevant risk factors in patients receiving CSM. Although 'neck and head trauma' resulted in a significant difference between the two cases and the controls, this was due to the larger presence in the controls. The latter might well be explained by the phenomenon that people experience neck pain or headache after their neck or head trauma and seek help from a manual physical therapist to relieve their pain or to improve their cervical function. Other risk factors also demonstrated no significant differences between the cases and the controls. (Table 1)

In two patient files out of 69 for patients with CeAD a CSM was described in the patient history. However, in both cases the CSM was described as any other usual risk factor and an expected causal relation between the CSM and the CeAD was not mentioned at all. Consequently, this suggests that none of the CeAD's was caused by a CSM. It might be that those two patients sought help for neck pain due to an underlying CeAD. The typical stuttering start of the CeAD with vague symptoms could be an explanation for these treatments. However, it might be more likely that those 2 patients sought help for an autonomous episode of musculoskeletal neck pain which occurred before the start of the CeAD. In contrast to the low estimated incidence of CeAD, the incidence of neck pain in The Netherlands is estimated at 16%. (Kim et al., 2018) Additionally, neck pain is seldom caused by serious pathology. (Blanpied et al., 2017)

In our samples, there seem to be no relevant differences between the cases and the controls. Therefore, our data seems to suggest that the risk factors for CeAD

as described in section 3.2 of the IFOMPT statement might not be suitable for use as a CeAD screening instrument. (Rushton et al., 2014) The intention of the IFOMPT framework was to enhance the clinical reasoning process and has an informative character. However, in clinical practice it is also regularly interpreted as a screening tool or seen as guideline to assist during a medico-legal case.(Thomas et al., 2019) The IFOMPT framework was not developed with that intention since the evidence at the time was limited and inadequate. Currently, evidence is still limited and will probably remain challenging since the clinical signs of spontaneous CeAD are only present in fewer than one-third of the patients.(Chaibi and Russell, 2019; Thanvi et al., 2005; Thomas, 2016)

In our sample most of the patients with CeAD were hospitalized during the summer. This seems to contrast with other literature discussing seasonality.(Grau et al., 1999; Kloss et al., 2012; Schievink et al., 1998; Thomas et al., 2017) Seasonality might be seen as an external or environmental factor leading to CeAD.(Baumgartner et al., 2005, pp. 44–53) Several theories have been proposed to explain the seasonality of CeAD occurrence, including weather related changes in blood pressure, coagulation parameters, diet and infections. (Baumgartner et al., 2005, pp. 44–53) The hypothesis that the presence of (upper-respiratory) infections is higher during the cold seasons and minor traumata like sneezing and coughing would be the triggering factor could not be confirmed by a large cohort study including 960 patients with CeAD.(Kloss et al., 2012)

LIMITATIONS

Our sample of patients hospitalized with CeAD were included from a comprehensive stroke center. The patients referred to these specialized centers are usually younger or have more complicated or serious symptoms. Therefore, selection bias might have played a role in the data collection. Furthermore, since the cases were retrospectively analyzed, it is uncertain whether all relevant information has been obtained and subsequently recorded in the patient file. Some risk factors like genetic factors or CSM are rare and might not have been checked or tested. Additionally, the low number (n=2) of patients with a CeAD and a CSM described in their file made it unfeasible to use these as a separate group for comparison.

STRENGTHS

Our sample comprised a substantial number (n=70) of CeAD patients from which a complete patient file was analyzed independently by two researchers. To improve the quality, the first researcher analyzed all patient files. Three other researchers

each also analyzed one third of the patient files. These four researchers were all manual physical therapists with advanced training and were all familiar with the IFOMPT framework.(Rushton et al., 2014) A specialized stroke neurologist (GJL) was consulted in three cases to obtain consensus.

FUTURE RESEARCH

A case-control study using a larger sample and three groups: 1] patients with CeAD; 2] patients with CeAD who experiences a recent CSM; and 3] a control group of patients without a CeAD experiencing a CSM might bring other relevant factors to the table. If international groups of cases were to be combined, the larger sample and intercultural differences would strengthen the study.

CONCLUSIONS

Few (n=2) cases of patients with CeAD who experienced a CSM were identified amongst 69 patients with a CeAD. Furthermore, no relevant significant differences were found between patients with CeAD and neck pain or headache patients without a CeAD receiving a CSM in clinical practice. These results confirm the difficulty manual physical therapists experience in identifying the sporadic patients with a CeAD in clinical practice. Based on our results, manual physical therapists are advised to use the IFOMPT framework to enhance the clinical reasoning process instead of as a screening tool.

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