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H. 知的財産権の出願・登録状況(予定を含む)

1. 特許取得

なし

2. 実用新案登録
なし

3. その他

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治療にもかかわらず関節破壊が進行する関節リウマチ患者の危険因子に関する研究

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研究要旨

関節リウマチ（RA）は関節破壊を必発し、身体機能低下に伴う社会的損失を生じてきた。関節破壊の進行を抑え、適切に治療するための目標を設定するために、RAに対する治療導入後1年間の関節破壊をX線で評価し、治療にもかかわらず関節破壊が進行するRA症例における新規血清学的マーカーの有用性を検討することを目的とし、RA患者249例を対象として検討した。新規血清学的マルチバイオマーカーMBDA scoreは、ベースライン値が高いと関節破壊は高度で、MBDA高値が持続すると治療にも関わらず関節破壊が進行した。一方、細胞内シャペロン蛋白である14-3-3η は、ベースライン値、及び、治療後の血清数値は、関節破壊の進行と相関した。以上より、MBDA scoreおよび14-3-3η は、治療にもかかわらず関節破壊が進行するRA症例の同定・予測、および関節予後改善に有用である可能性が示された。

A.研究目的

関節リウマチ（RA）は関節破壊を必発し、身体機能低下に伴う社会的損失を生じてきた。RAに対する治療の進歩により関節破壊制御が可能となったが、依然として約2割の症例で治療にもかかわらず関節破壊が進行するとされる。本研究では、斯様な症例を早期に見出し、適切に治療するための目標を設定するために、RAに対する治療導入後1年間の関節破壊をX線で評価し、治療にもかかわらず関節破壊が進行するRA症例における新規血清学的マルチバイオマーカーとしてMBDA score、細胞内シャペロン蛋白である14-3-3η の有用性を検討することを目的とした。

B.研究方法

当科にてRAに対する治療を導入して1年以上継続し、0週と54週の関節X線読影データおよび保存血清が存在するRA患者249例を対象とした。内訳は、TNF阻害薬149例(アダリムマブ49例、インフリキシマブ49例、エタネルセプト49例)、IL-6R阻害薬（トシリズマブ）50例、MTX 23例、トファシチニブ27例。関節破壊はSharp-van der Heijde score (SHS)の年間進行度で評価した。新規血清学的マルチバイオマーカーとしてMBDA score、細胞内シャペロン蛋白である14-3-3η に注目した。MBDA scoreはTNF阻害薬症例149例で0, 24, 52週の12バイオマーカーによるVectra DAアルゴリズム®を用い算出、14-3-3η は0, 52週においてELISAで測定し、各々SHSとの関係を検討した。

（倫理面への配慮）

臨床検体を使用する場合には、所属機関の倫理委員会、或は、IRBで承認を得た研究に限定し、患者からインフォームドコンセントを得た上で、倫理委員会の規約を遵守し、所属機関の現有設備を用いて行う。患者の個人情報が所属機関外に漏洩せぬよう、試料や解析データは万全の安全システムをもって厳重に管理し、人権擁護に努めると共に、患者は、経済的負担を始め如何なる不利益や危険性も被らない事を明確にする。

C.研究結果

(1) MBDA scoreの対象症例におけるRA患者背景は、年齢 58 歳、罹病期間 103 ヶ月、MTX 併用 86%、DAS28ESR 5.7、MBDA スコア 61、SHS 68。

(2) ベースラインにおいて MBDA score が高いと関節破壊は高度であった。

(3) 24 週において DAS28ESR>3.2 かつ低 MBDA score(≦29)であった症例のうち 88%がΔSHS≦0.5 を達成したのに対し、 DAS28ESR ≦ 3.2 かつ MBDA>29 であった症例では 68%であった。

(4) ベースライン、24 週、52 週の 3 visits のうち、低 MBDA score が 2 visits 以上の症例では、ΔSHS≦0.5 を達成しやすく(OR=14.3, p=0.002)、同様に高 MBDA score(>44)が 2 visits 以上の症例では、ΔSHS>3 となりやすかった(OR=15.3, p=0.002)。

(5) 14-3-3η の対象症例におけるRA患者の背景は年齢 60.0 歳、罹病期間 51 月、DAS28ESR 5.4、SHS 26.5。

(6) ベースラインにおいて 14-3-3η の中央値は 0.70 ng/ml、陽性例(＞0.19ng/ml)は 110 例 (74%)で、陰性例と比べ DAS28-ESR [5.6 vs. 4.8, p=0.01], CDAI [24.7 vs. 16.0, p=0.02], SDAI [26.8 vs. 18.8, p=0.02] いずれも高かった。

(7) 1 年後の 14-3-3η は中央値 0.37 ng/ml へ有意に低下 (p＜0.0001)、いずれの薬剤群でも低下した。陽性例は 97 例 (65%)に減少し、1 年後の 14-3-3η が陰性であると DAS28-ESR 活動性カテゴリーがより良好で (χ^2=11.0, p=0.018)、陽性であると関節破壊進行が顕著 (χ^2=3.7, p=0.05)であった。

D.考察

マルチバイオマーカーによる新規RA疾患活動性マーカーであるMBDAスコアは、関節リウマチの病態に関与し 0.2ml の血清から得られる 12 バイオマーカー濃度 (VCAM-1, EGF, VEGF-A, IL-6, TNF-RI, YKL-40, MMP-1, MMP-3, leptin, resistin, SAA, CRP)を基に、1 から 100 の整数値で算出される疾患活動性アルゴリズムとして開発された。MBDA スコアは、単に疾患活動性指標の代用マーカーとして有用であるのみならず、関節破壊の進行を従来の DAS28ESR 以上に良好に予測する因子である可能性が示唆された。

また 14-3-3η は本来細胞内シャペロン蛋白であるにも関わらず、血清中において検出可能であり、さらにRA 患者において疾患活動性、関節破壊とも関連し、特に関節破壊を制御するためには 14-3-3η の陰性化が治療目標となり得ることが示唆された。

以上の結果は、RA において新たな血清バイオマーカーの有用性が確立され臨床現場に適用されることにより、治療にもかかわらず関節破壊が進行する RA 症例を従来以上に効率的に減らすことに資する可能性が高いことを示していると考えられる。

E.結論

新規血清マーカーである MBDA score および 14-3-3η は、治療にもかかわらず関節破壊が進行する RA 症例の同定・予測、および関節予後改善に有用である可能性が示された。

F.健康危険情報

なし

G.研究発表

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H.知的財産権の出願・登録状況

(予定を含む)

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

Ⅲ. 研究成果の刊行に関する一覧

研究成果の刊行に関する一覧表

【H26.4.1～H27.3.31】

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Ⅳ. 研究成果の刊行物・別刷

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Clinical Study

Ischemic stroke after cervical spine injury: analysis of 11,005 patients using the Japanese Diagnosis Procedure Combination database

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Abstract

BACKGROUND CONTEXT: The incidence and relevant risk of ischemic stroke after cervical spine trauma remain unknown.

PURPOSE: To examine the incidence of ischemic stroke during hospitalization in patients with cervical spine injury, and analyze the impact of different types of cervical spine injuries on the occurrence of ischemic stroke.

STUDY DESIGN: Retrospective analysis of data abstracted from the Diagnosis Procedure Combination database, a nationally representative database in Japan.

PATIENT SAMPLE: We included all patients hospitalized for any of the following traumas: fracture of cervical spine (International Classification of Diseases, 10th Revision codes: S120, S121, S122, S127, S129); dislocation of cervical spine (S131, S133); and cervical spinal cord injury (SCI) (S141).

OUTCOME MEASURES: Outcome measures included all-cause in-hospital mortality and incidence of ischemic stroke (I63) during hospitalization.

METHODS: We analyzed the effects of age, sex, comorbidities, smoking status, spinal surgery, consciousness level at admission, and type of cervical spine injury on outcomes.

RESULTS: We identified 11,005 patients with cervical spine injury (8,031 men, 2,974 women; mean [standard deviation] age, 63.5 [18] years). According to the types of cervical spine injury, we stratified the patients into three groups: cervical fracture and/or dislocation without SCI (2,363 patients); cervical fracture and/or dislocation associated with SCI (1,283 patients); and cervical SCI without fracture and/or dislocation (7,359 patients). Overall, ischemic stroke occurred in 115 (1.0%) patients during hospitalization (median length of stay, 26 days). In-hospital death occurred in 456 (4.1%) patients. Multivariate analyses showed that ischemic stroke after cervical

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spine injury was significantly associated with age, diabetes, and consciousness level at admission. The highest in-hospital mortality was observed in patients with cervical fracture and/or dislocation associated with SCI (7.6%), followed by cervical SCI without fracture and/or dislocation (4.0%), and cervical fracture and/or dislocation without SCI (2.6%). Unlike mortality, risks of stroke did not vary significantly among the three groups.

CONCLUSIONS: This analysis revealed that ischemic stroke after cervical spine injury was not uncommon and was associated with increased mortality and morbidity. Occurrence of ischemic stroke was significantly associated with age, comorbidities such as diabetes, and consciousness level at admission, but not with the type of spine injury.

Keywords: Cervical spine; Trauma; Cerebral infarction; Risk; Spinal cord injury; Complication

Introduction

Stroke is a potentially life-threatening condition that can lead to prolonged hospital stay, significant disability, and long-term institutionalization. Strokes are classified as either ischemic or hemorrhagic. Ischemic stroke refers to stroke caused by thrombosis or embolism. It is more common than hemorrhagic stroke. Ischemic stroke is known to be associated with multiple risk factors, including advancing age, hypertension, history of stroke, and the presence of atrial fibrillation [1].

Ischemic strokes may occur after cervical spine injuries, such as fracture, dislocation, or spinal cord injury (SCI). Previous studies have demonstrated that cervical spine injury is a risk factor for blunt cerebrovascular injury [2–4]. In addition, recent prospective studies have suggested that SCI patients have an elevated risk of stroke in the years after the injury [5–7]. Although several lines of evidence indicate an increased risk of stroke after cervical spine injury, its pathologic mechanism remains largely unknown.

Despite the suggested link between stroke and cervical spine trauma, the available information on stroke after cervical spine injury is scarce and largely limited to anecdotal case reports or single-institution experiences with small number of patients. To our knowledge, no nationwide studies have examined the incidence of ischemic stroke after cervical spine injury. In addition, it remains to be clarified whether the stroke risk profiles vary substantially among different types of cervical spine injury.

In this analysis of nationwide inpatient administrative data, we examined the incidence of ischemic stroke during hospitalization in patients with cervical spine injury. We also analyzed the impact of different types of cervical spine injuries on the occurrence of ischemic stroke.

Methods

Data source

The Diagnosis Procedure Combination (DPC) database is a national administrative claims and discharge abstract database for acute care inpatients in Japan, the details of which have been described elsewhere [8–12].

We obtained inpatient data for a total of 39 months, comprising July 1 to December 31, 2007 to 2010, January 1 to December 31, 2011, and January 1 to March 31, 2012 (the DPC survey was conducted only between July and December, 2007–2010). In 2011, 980 hospitals participated and provided data for 6.3 million patients, representing approximately 50% of all inpatient admissions to acute care hospitals in Japan. The database includes the International Classification of Diseases 10th Revision (ICD-10) codes for primary and secondary diagnoses, comorbid conditions that existed at admission, and complications that occurred after admission. To optimize the accuracy of the recorded diagnoses, the physicians in charge are obliged to record the diagnoses with reference to medical charts. The institutional review board at The University of Tokyo approved the study design and waived informed consent because the data are anonymous.

Patients

We included all patients who were admitted on an emergency basis for fracture of the cervical spine (ICD-10 codes: S120, S121, S122, S127, S129), dislocation of the cervical spine (S131, S133), and cervical SCI (S141). We excluded those who had severe head trauma such as cerebral contusion or intracranial hemorrhage from analysis. We further classified the patients into three groups according to the absence or presence of SCI and bone injury as follows: cervical fracture and/or dislocation without SCI; cervical fracture and/or dislocation associated with SCI; and cervical SCI without fracture and/or dislocation.

The variables abstracted from the DPC database were age, sex, comorbid conditions that existed at admission, smoking status, consciousness level at admission measured with the Japan Coma Scale [13], presence of vertebral artery injuries (VAIs), use of spinal surgery (including open reduction of dislocation), and the length of stay. In terms of comorbid conditions, we focused on those that were known to be associated with the occurrence of strokes: diabetes; heart disease (associated with angina pectoris, old myocardial infarction, heart failure); atrial fibrillation; and hemodialysis. Smoking status was classified into three groups: nonsmoker (Brinkman index=0); smoker (Brinkman

index>0); and unknown status. Patients' activities of daily living at discharge were evaluated by the Barthel Index.

Outcomes

Primary outcomes included cerebral infarction (ICD-10 code: I63) and death during hospitalization. We focused on ischemic stroke because hemorrhagic stroke can be indistinguishable from the sequelae of concurrent head trauma.

Statistical analysis

We used the *t* test, analysis of variance, or the Kruskal-Wallis test to compare continuous data as appropriate. The χ^2 test was used to compare categorical data. In the logistic regression analyses, ischemic stroke and in-hospital death were modeled as functions of age, sex, comorbid conditions, smoking status, spinal surgery, Japan Coma Scale at admission, and the type of cervical spine injury. The logistic regression models were fitted with a generalized estimating equation to adjust for the clustering of patients within hospitals [14]. The threshold for significance was $p<.05$.

Results

We identified 11,594 patients with cervical spine injury. Among them, 589 (5.1%) had concomitant severe head trauma and were excluded from the analysis. Of the remaining 11,005 patients, there were 8,031 men and 2,974 women with a mean age of 63.5 years. According to the types of cervical spine injuries, we stratified the patients into three groups: cervical fracture and/or dislocation without SCI (2,363 patients); cervical fracture and/or dislocation associated with SCI (1,283); and cervical SCI without fracture and/or dislocation (7,359). Table 1 shows the characteristics of the patients according to the types of cervical spine injuries.

Ischemic stroke occurred in 115 (1.0%) patients during hospitalization (median length of stay, 26 days). In-hospital death occurred in 456 (4.1%) patients. Regarding the location of stroke, posterior stroke involving the cerebellum or brain stem occurred in 17 patients (14.8%). Of the 115 patients who had ischemic stroke, 15 patients (13.0%) died. Patients' activities of daily living at discharge were evaluated by the Barthel Index in 12,281 patients (74.1%). Patients who had strokes had a significantly lower Barthel Index at discharge than those without strokes (mean, 51.9 in patients with stroke vs. 68.3 in patients without stroke; $p<.001$). Vertebral artery injuries were found in 50 patients (0.5%). Patients with VAIs had a significantly higher rate of strokes than those without (16.0% vs. 1.0%, $p<.001$). The in-hospital stroke rate increased with advancing age, diabetes, heart disease, and worse consciousness level at admission (Table 2). Multivariate analyses showed that ischemic stroke after cervical spine injury was significantly associated with age, comorbidity, and consciousness level at admission (Table 3). The types of cervical spine injuries had a substantial impact on the observed in-hospital mortality (Table 2). The highest in-hospital mortality was observed in patients with cervical fracture and/or dislocation associated with SCI (7.6%), followed by cervical SCI without fracture and/or dislocation (4.0%), and cervical fracture and/or dislocation without SCI (2.6%). In contrast, the risks of ischemic stroke were similar among the three subgroups after adjusting for confounding variables (Table 3).

EVIDENCE & METHODS

Context
Patients who sustain cervical spine trauma and spinal cord injury may be at elevated risk of ischemic stroke, with an attendant negative impact on physical function and survival. The incidence of stroke following cervical injury and risk factors for its development have not been previously characterized in large population-based studies.

Contribution
The authors relied on a national Japanese database to evaluate the incidence of ischemic stroke following cervical spine trauma and describe risk factors for its development. One percent of the population developed ischemic stroke following cervical spine trauma. Age, diabetes and level of consciousness at presentation were factors statistically associated with the diagnosis of ischemic stroke.

Implications
The authors' findings add to the spine trauma literature in terms of characterizing the incidence of ischemic stroke following cervical injury. As this information was derived from a national registry, it suffers from the possibility of confounding due to errors in coding as well as missing patient data. A further limitation rests in the fact that ischemic stroke could only be identified in patients who remained hospitalized and post-discharge development of this complication could not be assessed. The incidence of ischemic stroke in this setting, therefore, is almost certainly underestimated.
—The Editors

Discussion

Our study had three main findings. First, ischemic stroke was not uncommon after cervical spine injury, occurring in 1.0% of patients during hospitalization with a threefold increase in mortality (13%). Also, patients' activities of daily living at discharge as evaluated by the Barthel Index was significantly lower in those who had strokes than in those without strokes, indicating a considerable negative impact

Table 1
Characteristics of the study population

Characteristics	Overall (n=11,005)	Cervical fracture* (n=2,363)	Cervical fracture* with SCI (n=1,283)	Cervical SCI without fracture* (n=7,359)	p
Age (y), mean [SD]	63.5 [18.0]	62.9 [19.8]	63.3 [17.7]	63.8 [17.4]	.12
≤49	2,034 (18.5)	531 (22.5)	236 (18.4)	1,267 (17.2)	<.001
50–59	1,452 (13.2)	261 (11.0)	167 (13.0)	1,024 (13.9)	
60–69	2,736 (24.9)	486 (20.6)	331 (26.7)	1,907 (25.9)	
70–79	2,861 (25.9)	600 (25.4)	331 (25.8)	1,930 (26.3)	
80–89	1,727 (15.7)	416 (17.6)	186 (14.5)	1,125 (15.3)	
≥90	195 (1.8)	69 (2.9)	20 (1.6)	106 (1.4)	
Sex					
Female	2,974 (27.0)	847 (35.8)	302 (23.5)	1,825 (24.8)	<.001
Male	8,031 (73.0)	1,516 (64.2)	981 (76.5)	5,534 (75.2)	
Comorbid conditions					
Diabetes	1,722 (15.6)	306 (12.9)	140 (10.9)	1,276 (17.3)	<.001
Heart disease	572 (5.2)	122 (5.2)	54 (4.2)	396 (5.4)	.21
Atrial fibrillation	149 (1.4)	43 (1.8)	9 (0.7)	97 (1.3)	.018
Hemodialysis	333 (3.0)	62 (2.6)	54 (4.2)	217 (2.9)	.023
Smoking status					
Nonsmoker	5,422 (49.3)	1,199 (50.8)	663 (51.7)	3,560 (48.4)	.033
Smoker	2,281 (20.7)	450 (19.0)	263 (20.5)	1,568 (21.3)	
Unknown	3,302 (30.0)	714 (30.2)	357 (27.8)	2,231 (30.3)	
Spinal surgery	2,533 (23.0)	635 (26.9)	583 (45.4)	1,315 (17.9)	<.001
JCS at admission					
0 (alert)	9,118 (82.9)	2,012 (85.0)	969 (75.5)	6,137 (83.4)	<.001
1–3 (drowsy)	1,405 (12.8)	273 (11.6)	193 (15.0)	939 (12.8)	
10–30 (somnolence)	246 (2.2)	39 (1.7)	60 (4.7)	147 (2.0)	
100–300 (coma)	236 (2.1)	39 (1.7)	61 (4.8)	136 (1.8)	
Postoperative length of stay (d), median [IQR]	26 [11–51]	29 [14–54]	38 [18–63]	23 [9–46]	<.001

SCI, spinal cord injury; SD, standard deviation; JCS, Japan Coma Scale; IQR, interquartile range.
* Fracture and/or dislocation of the cervical spine. All data are shown as n (%), unless otherwise indicated.

of strokes on patients' clinical outcomes. Second, ischemic stroke increased with advancing age, comorbidity such as diabetes, and worse consciousness level at admission. Finally, we stratified the patients into three groups according to the types of cervical spine injuries: cervical fracture and/or dislocation without SCI; cervical fracture and/or dislocation associated with SCI; and cervical SCI without fracture and/or dislocation. The risks of ischemic stroke did not vary significantly among the three groups.

Strengths and weaknesses of the study

With the study population of 11,005 patients, the present analysis is the largest study to investigate stroke after cervical spine trauma. Use of a large administrative database enabled us to perform a nationwide investigation and comparison of the risks between subgroups.

There are several limitations to our study. First, a degree of misclassification or underreporting of outcomes is possible as with other studies using administrative data. Although we were unable to verify the data for each patient, we presume that the level of miscoding is low because the DPC data are coded by physicians and subject to an audit. Second, the DPC database provides only information during hospitalization. Therefore, we were unable to identify strokes that occurred after discharge. Longer follow-up of trauma patients might provide us with additional information of clinical importance. Third, several important factors that might provide further valuable information were not examined. We did not include obesity and hypertension in our analysis because of missing data or possible underreporting. Also, we were unable to obtain data regarding the timing of strokes from the DPC database. Finally, we were unable to compare stroke risks between different fracture types because the DPC database does not contain detailed information on the fracture pattern of each patient.

Pathomechanism of strokes

The precise pathomechanism of strokes after cervical spine injury is largely unknown. Previous research in this field has focused primarily on cerebrovascular injury associated with blunt cervical trauma. It is widely accepted that trauma can cause blunt cerebrovascular injury, especially VAI, in patients with cervical spine fracture or subluxation [15–18]. Vertebral artery injury was reported to be associated with more severely injured patients (ie, higher injury severity score, lower Glasgow Coma Scale) [19]. Several injury patterns, including fracture through the foramen transversarium, facet fracture dislocation, or vertebral subluxation, are considered to be especially high-risk patterns. Age and sex were not predictive of VAI [19]. Many efforts have been made to identify subgroups of high-risk patients based primarily on the type and severity of injury.

Table 2
Occurrence of stroke and mortality during hospitalization

	Stroke, n (%)	p	In-hospital mortality, n (%)	p
Overall	115 (1.0)		456 (4.1)	
Age (y)				
≤49	6 (0.3)	<.001	26 (1.3)	<.001
50–59	8 (0.6)		24 (1.97)	
60–69	27 (1.0)		68 (2.5)	
70–79	44 (1.5)		140 (4.9)	
80–89	23 (1.3)		170 (9.8)	
≥90	7 (3.6)		28 (14.4)	
Sex				
Female	29 (1.0)	.746	94 (3.2)	.002
Male	86 (1.1)		362 (4.5)	
Comorbid conditions				
Diabetes (+)	29 (1.7)	.005	79 (4.6)	.314
Diabetes (−)	86 (0.9)		377 (4.1)	
Heart disease (+)	13 (2.3)	.003	34 (5.9)	.026
Heart disease (−)	102 (1.0)		422 (4.0)	
Atrial fibrillation (+)	1 (0.7)	.651	6 (4.0)	.943
Atrial fibrillation (−)	114 (1.1)		450 (4.1)	
Hemodialysis (+)	7 (2.1)	.054	141 (42.3)	<.001
Hemodialysis (−)	108 (1.0)		315 (3.0)	
Smoking status				
Nonsmoker	58 (1.1)	.913	207 (3.8)	<.001
Smoker	22 (1.0)		74 (3.2)	
Unknown	35 (1.1)		175 (5.3)	
Spinal surgery				
(+)	26 (1.0)	.917	75 (3.0)	.001
(−)	89 (1.1)		381 (4.5)	
JCS at admission				
0 (alert)	73 (0.8)	<.001	235 (2.6)	<.001
1–3 (drowsy)	29 (2.1)		85 (6.0)	
10–30 (somnolence)	7 (2.8)		23 (9.3)	
100–300 (coma)	7 (2.5)		113 (47.9)	
Type of injury				
Cervical fracture* with SCI	17 (1.3)	.576	97 (7.6)	<.001
Cervical SCI without fracture*	754 (1.0)		297 (4.0)	
Cervical fracture*	24 (1.0)		62 (2.6)	

JCS, Japan Coma Scale; SCI, spinal cord injury.
* Fracture and/or dislocation of the cervical spine.

Table 3
Adjusted risks of stroke and in-hospital death

	Stroke		In-hospital death	
	OR (95% CI)	p	OR (95% CI)	p
Age (y)				
≤49	Reference		Reference	
50–59	1.77 (0.61–5.18)	.30	1.24 (0.69–2.24)	.47
60–69	3.07 (1.23–7.69)	.016	2.36 (1.48–3.76)	<.001
70–79	4.53 (1.90–10.8)	.001	4.73 (3.05–7.32)	<.001
80–89	3.94 (1.56–9.93)	.004	12.6 (8.20–19.4)	<.001
≥90	10.1 (3.25–31.2)	<.001	22.4 (12.9–38.9)	<.001
Sex				
Female	0.80 (0.52–1.22)	.30	0.53 (0.41–0.69)	<.001
Male	Reference		Reference	
Comorbid conditions*				
Diabetes	1.65 (1.07–2.53)	.023	1.27 (0.95–1.69)	.11
Heart disease	1.76 (0.98–3.16)	.061	0.85 (0.55–1.32)	.48
Atrial fibrillation	0.43 (0.061–3.06)	.40	0.72 (0.26–2.00)	.53
Hemodialysis	1.42 (0.59–3.40)	.43	18.7 (13.6–25.7)	<.001
Smoking status				
Nonsmoker	Reference			
Smoker	0.94 (0.55–1.62)	.82	0.93 (0.66–1.30)	.67
Unknown	1.03 (0.67–1.57)	.90	1.40 (1.10–1.77)	.006
Use of spinal surgery	0.90 (0.58–1.42)	.66	0.58 (0.43–0.80)	.001
JCS at admission				
0 (alert)	Reference		Reference	
1–3 (drowsy)	2.39 (1.56–3.66)	<.001	2.09 (1.59–2.76)	<.001
10–30 (somnolence)	3.47 (1.55–7.75)	.002	3.40 (1.98–5.86)	<.001
100–300 (coma)	2.90 (1.09–7.70)	.033	28.5 (19.5–41.5)	<.001
Type of injury				
Cervical fracture† with SCI	Reference		Reference	
Cervical SCI without fracture†	0.80 (0.47–1.36)	.413	0.57 (0.42–0.78)	<.001
Cervical fracture†	0.87 (0.45–1.67)	.679	0.37 (0.25–0.54)	<.001

OR, odds ratio; CI, confidence interval; JCS, Japan Coma Scale; SCI, spinal cord injury.
* Patients without the corresponding comorbid condition were designated as reference.
† Fracture and/or dislocation of the cervical spine.

In contrast to the prevailing view, our data suggest that the type and severity of cervical spine injury are not the sole or predominant determinants of ischemic stroke after cervical spine trauma. We found that ischemic stroke after cervical spine injury was significantly associated with advancing age and comorbidities, similar to the case for nontrauma stroke patients. Our findings indicate that strokes after cervical spine trauma share a common pathologic mechanism, at least in part, with nontrauma strokes. Stroke after cervical spine injury may be multifactorial, and patients' characteristics such as age and preexisting comorbidities such as diabetes may play substantial roles in its occurrence.

Regarding the types of cervical spine injuries, we classified the patients into three groups according to the absence or presence of SCI and bone injury: cervical fracture and/or dislocation without SCI; cervical fracture and/or dislocation associated with SCI; and cervical SCI without fracture and/or dislocation. Among these subgroups, the highest in-hospital mortality was observed in patients with cervical fracture and/or dislocation associated with SCI, followed by cervical SCI without fracture and/or dislocation, and cervical fracture and/or dislocation without SCI. In contrast, and rather to our surprise, the risks of stroke did not vary significantly among the subgroups of cervical spine injury after adjusting for confounding variables. Patients with cervical spine injury may have similar risks of stroke, regardless of the presence of fracture and/or dislocation or SCI.

Conclusions

The present study has demonstrated that ischemic stroke is not a rare complication, as previously thought in patients with cervical spine injury. The occurrence of stroke was associated with age, diabetes, and consciousness level at

admission. The risks for stroke did not vary significantly with the type of cervical spine injury. Physicians should be aware of the possible occurrence of stroke that could further complicate the clinical course of patients. We believe that the findings of our study provide a basis for future research in this field.

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ORIGINAL ARTICLE

Usefulness of QuickDASH in patients with cervical laminoplasty

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Abstract
Purpose Clumsiness and numbness of the upper extremity is one of the most common complaints of patients with cervical myelopathy. However, most previous evaluations after cervical laminoplasty have only been based on physicians' points of view. We used Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) self-report questionnaire, which was designed to measure physical function and symptoms in people with upper-limb disorders to evaluate functional outcomes after laminoplasty.
Methods Ninety-four patients who underwent laminoplasty for cervical myelopathy and replied to the questionnaire were included in this study. The average age was 62 years, and mean follow-up period was 61 months. The Japanese Orthopedic Association (JOA) score, Neck Disability Index (NDI), Short-Form Health Questionnaire of 36 questions (physical component score, PCS), upper-extremity pain (Numerical Rating Scale), and QuickDASH (0–100, 0 being least severe) were used to evaluate surgical outcomes. Satisfaction with treatment was also investigated, and internal consistency and criterion-related validity were evaluated. The QuickDASH cutoff value for patient satisfaction was determined by receiver operating characteristic curve (ROC) analysis.
Results The mean total JOA scores were 10 before and 13 after surgery, and average postoperative QuickDASH score was 30. Cronbach α of the QuickDASH was 0.94. QuickDASH was significantly correlated with JOA score for upper-extremity motor and sensation, NDI, PCS, and pain. Cutoff value of the QuickDASH was 34.0 by ROC analysis. Significantly better QuickDASH scores were found for patients who were satisfied with treatment than for those who were not, whereas JOA score for upper-extremity motor function did not show a significant difference.
Discussion QuickDASH had significant correlations with disease-specific JOA scores and other generic outcome measures. Moreover, QuickDASH significantly reflected patients' satisfaction with treatment, whereas the JOA score for upper-extremity motor function did not.
Conclusion QuickDASH was useful in evaluating upper-extremity functional outcomes after cervical laminoplasty.

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Introduction

Patients with cervical compressive myelopathy usually have loss of dexterity and nonspecific weakness, numbness, and paresthesia of the upper extremities, as well as gait disturbances and urinary dysfunction [1]. These symptoms have an insidious course and gradually deteriorate. In cases of severe compression or progressive course, operative decompression is the accepted treatment for cervical myelopathy [2]. Cervical laminoplasty is a well-established procedure for the disease, and several studies on cervical laminoplasty report favorable results even after 10 years or more [3, 4]. However, most previous evaluations were determined from assessment methods based on physicians' points of view, such as the Japanese Orthopedic Association (JOA) score.

Dysfunction in the upper extremity is one of the main disabilities that could affect patients' activity of daily