



# Validation of clinical criteria for referral to head imaging in the neurologic emergency setting

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## Abstract

**Background** In recent decades, diagnostic imaging became an important generator of large increases in medical spending. Inappropriate head CT referrals also increase population irradiation and unnecessarily burden and frighten patients.

**Objective** To validate previously proposed clinical criteria for referral to head imaging (age > 55 years, focal neurological deficit, changed mental state, nausea or vomiting, coagulation disorder, cancer) in a setting of emergency neurological service.

**Methods** We retrospectively analyzed electronic records of 500 consecutive referrals to neurological emergency and 500 referrals to emergency head imaging. In patients with several referrals, only results of the first evaluation were further analyzed. We calculated relations between clinical predictors, referrals, and findings of head imaging.

**Results** Of 486 first referrals of consecutive patients, 216 (44%) were referred to the emergency, and 100 (21%) to non-emergency head imaging. Remaining 170 (35%) were not referred to head imaging. Clinical predictors of pathologic head imaging fulfilled 77%, 41%, and 43% of patients, respectively. Pathologic head imaging had 153 of 490 (31%) referred patients. Referral criteria fulfilled 146 (sensitivity 95%) of them. Intracranial pathology was found in 7 of 125 patients not fulfilling referral criteria (negative predictive value 94%): 3 reported transient neurological symptoms, 2 sudden headache, and 2 headache with nausea and vomiting.

**Conclusion** We confirmed utility of previously proposed clinical criteria for referral to head CT in emergency neurological setting. In addition, we found transient neurological symptoms, sudden severe headache, and headache with nausea or vomiting as additional independent indications for emergency head imaging.

**Keywords** Emergency · Head imaging · Neurological examination · Referral criteria · Retrospective analysis · Validation

## Introduction

In recent decades, diagnostic imaging became one of the main generators of large increases in medical spending worldwide. In the USA, between the years 2000 and 2006, the imaging spending increased for 17% annually (from 3.6 to 7.6 billion \$ per year) and was growing the fastest of all medical spending [1]. Majority of this increase (80%) was due to increased proportion of referrals, and only 20% due to larger patient burden [2]. The result is a low yield of diagnostic imaging, as revealed

by studies in populations of atraumatic patients in US emergency centers, reporting 0–15% rate of pathologic head CT [1].

Apart from increasing medical spending, inappropriate head CT referrals also increase irradiation of the population. It was estimated that about 50% of irradiation in the general population is due to medical diagnostics, particularly CTs [3]. However, even more importantly, inappropriate imaging referrals unnecessarily burden and frighten patients and lead to further excessive testing and treatment. All these resulted in decision of US Medicare and Medicaid to introduce referrals of patients with atraumatic headache to head CT as a new quality indicator [4]. More selective imaging of the head, imaging of the neck, and imaging of the lumbar spine are also three of “Top 5” goals of emergency medicine in Canadian “Choosing Wisely” initiative [5].

For rational use of head CT in clinical practice, valid guidelines are needed, and for their development, clinical predictors

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of pathologic head CT need to be known. In a previous study analyzing data from three Canadian emergency centers [6] from 15 candidate variables, authors identified six clinical predictors of pathologic head CT in atraumatic patients: (1) age, (2) focal deficit on neurological examination, (3) changed mental state, (4) nausea or vomiting, (5) coagulation disorder, and (6) cancer. This set was later validated in an US emergency center study [7]. Those authors also developed a 7-point scale: 1 point for patient's age of > 55 years, 2 points for deficit on neurological examination, and 1 point for each of remaining 4 clinical predictors. They found that  $\geq 2$  points on their scale had 98% sensitivity for pathologic head CT and a negative predictive value of 99.4%. This scale was to our knowledge not validated by other investigators. It is also not known whether the scale would be useful and valid in a setting of neurological emergency service, taking care of atraumatic patients. Both previous studies were performed in general emergency units served by emergency physicians.

The principal aim of the present study was therefore to validate a scale proposed by Bent et al. [7] in our emergency service evaluating atraumatic neurological patients. Using retrospective analysis of patients' electronic records, we primarily checked whether in the neurological emergency setting the modified score identifies all patients with relevant pathological head imaging findings. We calculated potential reduction in number of imaging studies achieved by using the score, analyzed clinical characteristics of patients missed by the score, and proposed additional criteria to round up all patients with pathologic head imaging.

## Materials and methods

### Patients

We retrospectively analyzed the electronic records of the first consecutive patients referred to the neurological emergency service of the Division of Neurology, University Medical Center Ljubljana, Slovenia, in the year 2016. Two groups were studied: (1) the first 500 records of patients evaluated at the unit and (2) the first 500 records of evaluated patients referred to the emergency head imaging. At our institution, neuroradiologists review and report all neuroimaging studies. Due to the retrospective analysis of patients' electronic records with no direct patient involvement, the National Ethics Committee of Slovenia waived the necessity of obtaining patients' written informed consent.

### Data collection

The first author (PŽ) performed analysis of all electronic records. He collected data on gender, age, referral diagnosis, five predictive factors of pathologic head imaging

(i.e., abnormality on the neurological examination, nausea or vomiting, change in the mental state, coagulopathy, known malignant disease [6, 7]), sudden headache, head trauma, transient neurological symptoms, attending neurologist's name, referral to head imaging, findings on head imaging, and final diagnosis. Scores of 5 factors predictive of pathologic head imaging (abnormality on neurological examination scored 2 points, other 4 clinical predictors, and patient's age > 55 years scored 1 point) were calculated. In addition to non-contrast head CT, findings of other CT studies (e.g., contrast head CT, CTA of the head and neck vessels, and head CT perfusion), and MR studies were analyzed.

### Statistical analyses

In evaluated groups, median age, age ranges, and percentages of men, factors predictive of pathologic head imaging, patients with scores of  $\geq 2/7$ , patients reporting sudden headache, and patients with head trauma were calculated and compared using chi-square test, likelihood ratio test, or Kruskal-Wallis test as appropriate.

Some patients presented to the neurological emergency service more than once and had head imaging studies more than once during the study period. Only results of the first clinical and imaging evaluation were used for further statistical analysis (i.e., records from repetitive evaluations were excluded). In a group of patients evaluated at the emergency unit presenting with four common neurological syndromes (i.e., dizziness or vertigo, diplopia, transient loss of consciousness, and headache), we also calculated percentages of patients with scores of  $\geq 2/7$ , referrals to head imaging, and pathologic head imaging. The same percentages were also calculated for individual neurologists that evaluated at least 10 patients in the series.

In a group of patients referred to the emergency head imaging, we calculated percentage with pathologic head imaging (i.e., diagnostic yield). In a group with pathologic head imaging, we calculated percentage of patients with scores of  $\geq 2/7$  (i.e., sensitivity of criteria predicting pathologic head imaging) and frequencies of various pathologies. We also calculated specificity, the positive predictive value, and the negative predictive value of criteria. We also analyzed clinical findings in patients missed by predictive criteria.

To test association between several possible risk factors and pathological imaging outcome, we built univariate and multiple logistic regression models. Associations with  $p$  value < 0.05 were treated as statistically significant. All analyses were done by using statistical software IBM SPSS Statistics v. 24 (IBM Corporation, Armonk, New York, USA).

## Results

### Patients evaluated at the neurological emergency service

Table 1 shows demographic and clinical characteristics of several patient groups. In a group of the first 500 consecutive emergency neurologic evaluations, 486 different patients were examined; i.e., records of the 14 patients' second visits were excluded. Of these, 49% were men, and their median age (range) was 62 (19–94) years. From this group, 216 (44%) patients were referred to the emergency, and 100 (21%) to the non-emergency head imaging. Patients referred to the emergency head imaging were older than patients from the other two groups (i.e., referred to the non-emergency head imaging and not referred to head imaging;  $p < 0.001$ , Table 1). They more often had clinical predictors of pathologic head imaging, including abnormalities on neurological examination ( $p < 0.001$ ), change in mental state ( $p = 0.003$ ), coagulopathy ( $p = 0.031$ ), and malignant disease ( $p = 0.004$ ). No difference in nausea/vomiting was found between groups ( $p = 0.797$ ). Clinical score predicting pathological head imaging (i.e.,  $\geq 2$  points) fulfilled 280 (58%) patients. This percentage was almost twice higher in a group of patients referred to the emergency head imaging than in groups referred to the non-emergency head imaging and not referred to head imaging ( $p < 0.001$ , Fig. 1).

In groups of patients with four common neurological presentations (Fig. 2), criteria for referral fulfilled 24% (headache) to 85% (diplopia and transient loss of consciousness) of patients. Urgent head imaging was performed in 33%

(dizziness and vertigo) to 54% (diplopia), and pathologic head imaging was found in 0% (diplopia) to 40% (transient loss of consciousness) of patients.

Seventeen neurologists examined at least 10 patients consecutively evaluated at the neurological emergency service. For individual neurologists, clinical criteria predictive of pathologic head imaging fulfilled 31–87% of patients (median 57%,  $p = 0.059$ ), emergency head imaging referral rate was 12–91% of patients (median 46%,  $p < 0.001$ ), and pathologic emergency head imaging findings were reported in 0–100% of referred patients (median 37%,  $p = 0.081$ , Fig. 3).

### Patients referred to the emergency head imaging

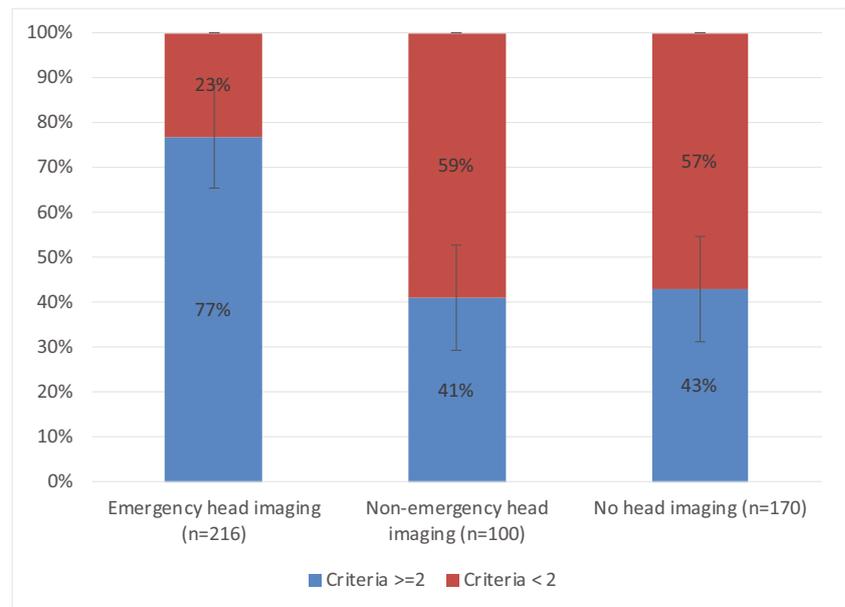
In a group of the first 500 consecutive referrals to the emergency head imaging, 490 different patients were included; i.e., records of the 10 patients' second head imaging studies were excluded. Of these, 51% were men, and their median (range) age was 68 (20–95) years (Table 1). Clinical criteria for referral to head imaging ( $\geq 2$  points) fulfilled 369 (75%) patients. Pathologic abnormalities on head imaging were found in 153 (31%) patients, most commonly ischemic lesions (60%), followed by hemorrhagic lesions (24%), and tumors (11%). Clinical criteria for referral to head imaging ( $\geq 2$  points) fulfilled 146 of 154 (sensitivity 95%) patients with pathologic head imaging. Clinical criteria were negative in 114 of 337 patients with negative head imaging (specificity 34%, diagnostic accuracy 65%). Pathologic head imaging was found in 146 of 369 patients with fulfilled clinical criteria ( $\geq 2$  points) for referral to head imaging (positive predictive value 40%). Pathologic head imaging was found in 7 of 121 patients that

**Table 1** Demographic and clinical features in the first 500 emergency neurological evaluations and 500 referrals to emergency head imaging

	486 evaluated patients					490 patients referred to emergency imaging	
	All	Emergency imaging	Pathologic emergency imaging	Non-emergency imaging	No imaging	All	Pathologic emergency imaging
Number	486 (100%)	216 (44%)	78 (36%)	100 (21%)	170 (35%)	490 (100%)	153 (31%)
Men (%)	239 (49%)	116 (54%)	43 (55%)	50 (50%)	73 (43%)	250 (51%)	81 (53%)
Age (median, range) (years)	62, 19–94	68, 22–94	73, 25–94	51, 19–88	54, 19–94	68, 20–95	73, 25–94
Neurological abnormality	219 (45%)	135 (63%)	69 (88%)	32 (32%)	52 (31%)	296 (60%)	135 (88%)
Change in mental state	84 (17%)	46 (21%)	17 (22%)	6 (6%)	32 (19%)	106 (22%)	34 (22%)
Nausea or vomiting	45 (9%)	19 (9%)	6 (8%)	11 (11%)	15 (9%)	65 (13%)	15 (10%)
Coagulopathy	35 (7%)	23 (11%)	7 (9%)	4 (4%)	8 (5%)	45 (9%)	16 (10%)
Malignant disease	29 (6%)	21 (10%)	9 (12%)	5 (5%)	3 (2%)	43 (9%)	14 (9%)
> 55 years	284 (58%)	156 (72%)	67 (86%)	44 (44%)	84 (49%)	355 (72%)	130 (85%)
$\geq 2$ points	280 (58%)	166 (77%)	75 (96%)	41 (41%)	73 (43%)	369 (75%)	146 (95%)
Sudden headache	15 (3%)	15 (7%)	2 (3%)	0 (0%)	0 (0%)	42 (9%)	8 (5%)
Head trauma	9 (2%)	5 (2%)	2 (3%)	2 (2%)	2 (1%)	10 (2%)	3 (2%)

Repeated evaluations of the same patients were excluded from the analyses

**Fig. 1** Percentages of patients referred to the emergency head imaging, non-emergency outpatient head imaging, and not referred to head imaging that fulfilled clinical criteria for referral



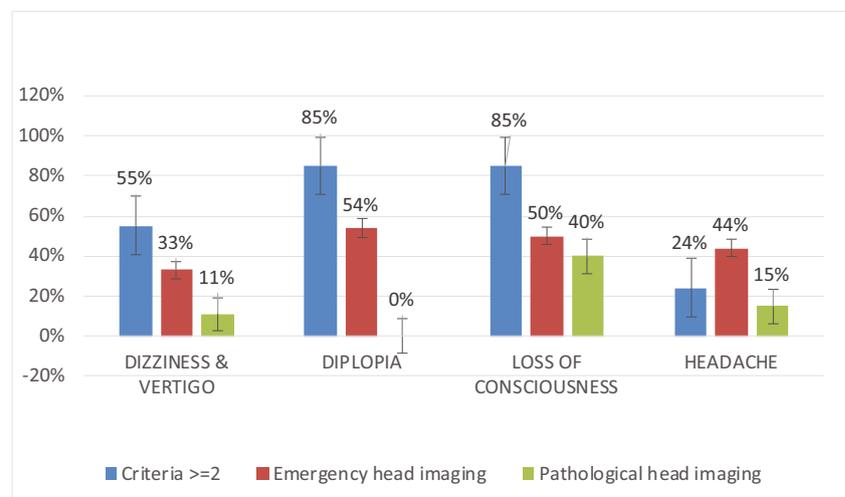
did not fulfill referral criteria ( $< 2$  points); i.e., negative predictive value of these criteria was 94%. Three of these patients were examined after transient neurological symptoms (epileptic seizure in 2 and recurrent TIA in 1), 2 reported headache of sudden onset, and in remaining 2, headache was accompanied by nausea and vomiting (Table 2). Pathologic head imaging was found in 8 of 42 (19%) patients with headache of sudden onset. Of 123 patients that did not fulfill previously proposed clinical criteria and would not need head imaging, 28 presented with sudden headache, 26 with transient neurological symptoms suggestive of TIA or seizure, and 7 with headache accompanied by nausea and vomiting. Expansion of referral criteria to include these 3 additional indications (Table 3) thus halved the reduction in the number of head imaging, finishing at 13% reduction (i.e., 62 of 490 patients).

When other predictors were controlled for in the regression model, significant predictors of abnormal head imaging findings were neurological abnormality (OR 8.2, 95% CI 4.5–14.9), age  $> 55$  years (OR 2.0, 95% CI 1.1–3.5), and change in mental state (OR 1.9, 95% CI 1.1–3.2). By contrast, patients with transient neurological symptoms had reduced odds for abnormal head imaging findings (OR 0.3; 95% CI 0.1–0.6; Table 3).

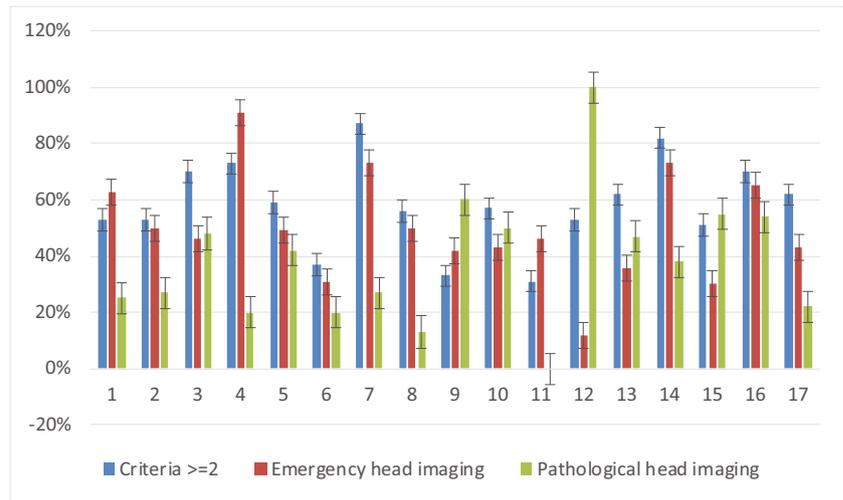
## Discussion

The present study confirmed utility of previously proposed clinical criteria for referral of non-traumatic patients to emergency head imaging [7, 8]. In addition, we demonstrated

**Fig. 2** Percentages of patients with four neurological complaints that fulfilled clinical predictive criteria for pathologic head imaging were referred to emergency imaging and had pathologic emergency head imaging



**Fig. 3** Percentages of patients evaluated by 17 neurologists that fulfilled clinical predictive criteria for pathologic head imaging, were referred to the emergency head imaging and had pathologic emergency head imaging findings



utility of these criteria also in a setting of neurological emergency service not seeing patients after head trauma. In our series, clinical criteria for referral [7, 8] fulfilled 95% of patients (sensitivity) with pathologic head imaging. These criteria are also in agreement with factors generally recognized to predict pathologic head imaging: (1) focal neurological abnormalities, (2) changed mental state point to a possible structural lesion in the nervous system, (3) nausea and vomiting to increased intracranial pressure possibly due to intracranial expansive process or infratentorial lesions, (4) coagulation disorders to intracranial bleeding, and (5) cancer to intracranial metastasis.

However, pathologic head imaging was found also in 7 of 121 patients that were scanned, but did not fulfill criteria for referral (negative predictive value 94%). These 7 patients were evaluated after transient neurological episode (epileptic seizure and recurrent TIA), headache of sudden onset, or headache accompanied by nausea and vomiting. Etiology of transient neurological deficits always needs to be established, which in the present series confirmed finding of brain tumors in both patients after epileptic seizure and severe carotid stenosis in a patient after recurrent TIA.

In all patients reporting sudden severe headache, subarachnoid hemorrhage (SAH) needs to be excluded, as confirmed by two of our patients. Likewise, after exclusion of migraine, nausea and vomiting accompanying the headache also needs to be taken seriously, as it may be due to raised intracranial pressure, possibly caused by structural lesion.

Based on our findings, we propose expansion of 6 predictive factors for pathologic head imaging by adding (1) sudden severe (i.e., thunderclap) headache [9], (2) transient neurological symptoms suggestive of TIA or seizure, and (3) after exclusion of migraine, a headache accompanied by nausea and vomiting (Table 4). Experienced neurologists would also regard all these three clinical presentations as sufficient for referral to head imaging on their own. With proposed expansion of referral criteria, all our neurological emergency service patients with pathological head imaging would have fulfilled referral criteria (i.e., sensitivity and negative predictive value 100%).

This expansion of referral criteria (Table 3) would, however, also increase the number of patients with indication for emergency head imaging and would halve the reduction in

**Table 2** Demographic data, clinical features, and head imaging findings in 7 patients not fulfilling diagnostic criteria for referral to head imaging

Number	Gender	Age (years)	Symptoms	Imaging findings
1	Man	45	Epileptic seizure	Intracranial meningioma
2	Man	80	Epileptic seizure	Intracranial glioma
3	Woman	73	Recurrent TIA	Stenotic carotid vessels on CTA
4	Man	40	Sudden headache, nausea and vomiting	SAH on CT
5	Woman	55	Sudden headache	SAH on CT
6	Woman	39	Headache, nausea and vomiting	Intracranial hypertension
7	Woman	48	Headache, nausea and vomiting	SAH on CT

**Table 3** Association of demographic and clinical features with abnormal head imaging findings in a series of 490 consecutive patients referred to the emergency head imaging

	Pathological head imaging		Univariate logistic regression		Multiple logistic regression	
	No ( <i>n</i> = 337)	Yes ( <i>n</i> = 153)	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Male gender	169 (50%)	81 (53%)	1.1 (0.8; 1.6)	0.567	1.2 (0.8; 1.9)	0.344
Age > 55 years	225 (67%)	130 (85%)	2.8 (1.7; 4.6)	< 0.001	2.0 (1.1; 3.5)	0.020
Neurological abnormality	161 (48%)	135 (88%)	8.2 (4.8; 14)	< 0.001	8.2 (4.5; 14.9)	< 0.001
Change in mental state	72 (21%)	34 (22%)	1.1 (0.7; 1.7)	0.831	1.9 (1.1; 3.2)	0.030
Nausea or vomiting	50 (15%)	15 (10%)	0.6 (0.3; 1.2)	0.131	0.9 (0.5; 1.9)	0.871
Cancer	29 (9%)	14 (9%)	1.1 (0.5; 2.1)	0.843	1.5 (0.7; 3.1)	0.339
Coagulation disorder	29 (9%)	16 (10%)	1.2 (0.7; 2.4)	0.511	1.1 (0.6; 2.4)	0.713
≥ 2 points	223 (66%)	146 (95%)	10.7 (4.8; 23.5)	< 0.001		
Sudden headache	34 (10%)	8 (5%)	0.5 (0.2; 1.1)	0.08	1.5 (0.5; 4.0)	0.436
Transient neurological symptoms	61 (19%)	7 (5%)	0.2 (0.1; 0.5)	< 0.001	0.3 (0.1; 0.6)	0.003
Head trauma	7 (2%)	3 (2%)	0.9 (0.2; 3.7)	0.933	3.0 (0.6; 15.4)	0.177

All significant *p* values are printed in italic. *OR* odds ratio

the number of head imaging, finishing at 13% reduction (i.e., 62 of 490 patients).

However, imaging could be safely omitted in many of patients fulfilling the referral criteria due to (1) recent imaging studies performed for the same complaint, (2) already explained neurological complaints, and (3) imaging study not expected to affect further management. Referrals to head imaging could be further reduced by more selective application of imaging in patients with abnormal neurologic findings, such as paralytic diplopia in a patient older than 50 years with preserved pupillary responses, which is unlikely due to

structural abnormality and is most often caused by nerve ischemia [10]. This is supported by normal head imaging in all 12 our patients with diplopia (Fig. 2). Another similar clinical presentation is dizziness or vertigo. Of 56 patients with these complaints, head imaging was performed in 77% and was abnormal in only 10% (Fig. 2). Referrals to head imaging (preferably MR) can be safely reduced to patients with acute vestibular syndrome and “red flags” pointing to central nervous system pathology [11]. Patients presenting after epileptic seizures should also be carefully differentiated from syncope patients, as the latter do not need head imaging, but some of them would profit from cardiology evaluation. Furthermore, young patients with typical primarily generalized seizure also do not need head imaging [12, 13]. Among patients with headache accompanied by nausea and vomiting, migraine patients do not need head imaging [14]. Similar to previous studies [15], we also found pathologic head imaging in only 19% of patients with headache of sudden onset. Utilization of head imaging could be reduced for about 36% by applying one of 3 models including predictive factors associated with SAH [16] also in this patient population. These factors are age ≥ 40 years, onset with exertion, witnessed loss of consciousness, arrival by ambulance, neck pain or stiffness, vomiting, diastolic blood ≥ 100 mmHg or systolic blood ≥ 160 mmHg [16]. More restrictive referrals seem also reasonable in other headaches, although well-established poor correlation between headache description and frequency of pathologic head imaging [17] makes this task more difficult.

At this point, we would suggest to carefully consider our suggested criteria (Table 4) in all patients before referral to head imaging. Although developed in the emergency neurology setting, our criteria could be, in our opinion, also helpful

**Table 4** Clinical criteria for head imaging in neurological emergency setting

Clinical finding	Comment
<b>Major criteria</b>	
Focal neurological deficit	Robust findings
Sudden severe headache	Maximum severity < 4 min
Transient neurological symptoms	Suggesting TIA or seizure
Headache accompanied by nausea or vomiting	After exclusion of migraine
<b>Minor criteria</b>	
Age > 55 years	
Changed mental state	
Nausea or vomiting	Not explained otherwise, migraine excluded
Coagulation disorder	
Cancer	

One major or at least 2 minor criteria are needed for referral to emergency head imaging

in other settings. We believe that applying all these criteria would importantly increase diagnostic yield of head imaging. As from our present data, precise quantification of this gain is not possible, and further prospectively designed studies would be needed.

Compared with previous studies reporting frequency of pathologic emergency head imaging of only 10% [7] and 14% [8], sensitivity of 31% we observed was much higher (Table 1). This difference is most probably due to different settings (i.e., general vs. neurological emergency service) and particularly due to different physician profiles (i.e., emergency physicians vs. neurologists). This speaks in favor of employing neurologists for managing neurological patients also in the emergency setting.

As reported previously [7, 8], the most common findings on head imaging in our study were ischemic lesions, followed by hemorrhagic lesions, and tumors. In addition to non-contrast head CT, results of head and neck vessel CTA and perfusion CT and rarely head MR were also included into our analyses, which may also affect diagnostic yield.

Nevertheless, as reported previously [4], we also observed large and significant variability in proportions of patients referred to emergency head imaging by our 17 evaluated neurologists (range 12–91%,  $p < 0.001$ ; Fig. 3). As a consequence, proportions of patients with pathologic head imaging findings also varied widely (range 0–100%,  $p = 0.081$ ). Probably even more interesting is a large variability in percentages of patients that fulfilled clinical criteria predictive of pathologic head imaging (median 57%, range 31–87%,  $p = 0.081$ ). Consecutive neurological emergency patients were evaluated; therefore, the samples evaluated by individual neurologists are supposed to be random. This finding therefore demonstrates large variability in thresholds for “abnormal neurologic findings” used by individual neurologists. More bedside discussions and education seem therefore reasonable, in order to better standardize interpretation of neurological findings.

One of the main findings of the present study is also low percentage of patients fulfilling referral criteria in a group of patients referred to the non-emergency head imaging. In this group, the actual percentage of these patients was only a half of percentage in a group of patients referred to the emergency head imaging and was even slightly lower than percentage in the group not referred to head imaging. Although we do not have imaging results for these patients, the same referral criteria should apply also for them. This would reduce the number of scanned patients for another 59 patients.

There are several limitations of our study. The main is that we do not have head imaging findings for all evaluated patients, but only for those that had emergency imaging performed. Therefore, it is possible that few non-scanned patients might have pathologic imaging of the head. Nevertheless, we believe that the proportion of such patients is probably not

much different than expected in the general population of older subjects [18], as previously established for patients with chronic headaches [14]. Limitation is also the retrospective design of the study, which is, however, essential to establish clinical patterns prevalent in daily routine clinical work. Further prospective studies would be needed to fully validate our recommendations.

We confirmed utility of previously proposed clinical criteria for referral to head imaging (age > 55 years, focal deficit on neurological examination, changed mental state, nausea or vomiting, coagulation disorder, and cancer) [7, 8] also in a setting of emergency neurological service. However, we recommend adding sudden severe (i.e., thunderclap) headache and transient neurological symptoms suggesting TIA or seizure and (after exclusion of migraine) headache accompanied by nausea or vomiting, as independent indications for emergency head imaging (Table 4).

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** The study was approved by the relevant research ethics committee that waived the necessity of obtaining written informed consent from patients.

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