Validation of the unruptured intracranial aneurysm treatment score: comparison with real-world cerebrovascular practice

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OBJECTIVE The purpose of this study was to compare the unruptured intracranial aneurysm treatment score (UIATS) recommendations with the real-world experience in a quaternary academic medical center with a high volume of patients with unruptured intracranial aneurysms (UIAs).

METHODS All patients with UIAs evaluated during a 3-year period were included. All factors included in the UIATS were abstracted, and patients were scored using the UIATS. Patients were categorized in a contingency table assessing UIATS recommendation versus real-world treatment decision. The authors calculated the percentage of misclassification, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve.

RESULTS A total of 221 consecutive patients with UIAs met the inclusion criteria: 69 (31%) patients underwent treatment and 152 (69%) did not. Fifty-nine (27%) patients had a UIATS between –2 and 2, which does not offer a treatment recommendation, leaving 162 (73%) patients with a UIATS treatment recommendation. The UIATS was significantly associated with treatment ($p < 0.001$); however, the sensitivity, specificity, and percentage of misclassification were 49%, 80%, and 28%, respectively. Notably, 51% of patients for whom treatment would be recommended by the UIATS did not undergo treatment in the real-world cohort and 20% of patients for whom conservative management would be recommended by UIATS had intervention. The area under the ROC curve was 0.646.

CONCLUSIONS Compared with the authors' experience, the UIATS recommended overtreatment of UIAs. Although the UIATS could be used as a screening tool, individualized treatment recommendations based on consultation with a cerebrovascular specialist are necessary. Further validation with longitudinal data on rupture rates of UIAs is needed before widespread use.

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KEY WORDS stroke; unruptured intracranial aneurysm treatment score; UIATS; vascular disorders

UNRUPTURED intracranial aneurysms (UIAs) are seen in nearly 3% of the adult population, with a rising prevalence secondary to increased utilization of intracranial vascular imaging.^{9,25} Although thorough natural history studies are lacking, there is evidence that a small proportion of UIAs rupture, causing subarachnoid hemorrhage (SAH).^{6,13,14,18,19,21,26,27} Although previous reports are biased by aneurysm location, it has

been found that small UIAs especially have a low risk of rupture.⁶ Because of the higher prevalence of small aneurysms, a majority of aneurysmal cases of SAH are due to small aneurysms. Unfortunately, the specific factors associated with those small UIAs that proceed to rupture are not known.

The management of UIAs is subject to provider bias supported by data with varying levels of evidence; thus,

ABBREVIATIONS AUC = area under the curve; CC = correlation coefficient; CCI = Charlson Comorbidity Index; ROC = receiver operating characteristic; SAH = subarachnoid hemorrhage; UIA = unruptured intracranial aneurysm; UIATS = UIA treatment score.

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there is substantial variation in the management of UIAs among clinicians.^{3,5} The unruptured intracranial aneurysm treatment score (UIATS) was developed by 69 multidisciplinary specialists to guide clinical decision making in patients with UIAs.⁶ The score represents a consensus opinion regarding aneurysm management, rather than a scientific analysis of whether the aneurysm should be treated. The purpose of this investigation was to compare the UIATS with the real-world experience of a quaternary academic medical center with a high volume of patients with UIAs. We hypothesized that there would be a discrepancy when comparing the UIATS recommendation with the real-world experience of a quaternary academic high-volume center.

Methods

Patient Cohort

After obtaining IRB approval, we retrospectively queried a prospective database of all patients older than 18 years harboring a diagnosed UIA evaluated at the University of Utah Clinical Neurosciences Center from January 1, 2013, through December 31, 2015. A chart review was performed to abstract all 29 factors in the UIATS (Fig. 1). We also collected information about whether patients received treatment or were managed with observation. Patients who were missing any of the 29 variables from the UIATS were excluded from analysis. All treatment recommendations were made, and subsequent treatments performed, by one of 5 senior attending neurosurgeons with experience in treating complex cerebrovascular disorders, with a practice focused on cerebral aneurysms (W.T.C., R.H.S., J.D.M., P.T., and M.S.P.). The decision-making process is multifactorial, but it is not standardized. Patient involvement is crucial to the decision-making process, but no uniform set of factors is used among surgeons.

Data Collection and UIATS Variables

Each of the 29 variables in the UIATS was abstracted from the patients' medical records. Demographic information included age (dichotomous by age < 65 years vs $\geq$ 65 years), sex, and race. Clinical information included whether the patient had experienced a previous SAH or had a history of hypertension, coagulopathies, epilepsy, and neurocognitive disorders. Aneurysm-specific information included multiplicity, presence of multilobulation, size in millimeters, location, thromboembolic events due to the aneurysm, mass effect, size ratio, aspect ratio, new aneurysm formation on imaging, contralateral steno-occlusive disease, and associated cranial nerve deficits. The high-complexity versus low-complexity variable was calculated by a neurosurgeon who was blinded to the treatment decision after reviewing the patient's medical record and neuroimaging findings. Additional comorbidity data included active tobacco use, active alcohol use, and illicit drug use. Family history information about cerebral aneurysms, previous aneurysmal SAH, multiple intracranial aneurysms, and other disorders associated with intracranial aneurysm development and/or rupture (polycystic kidney disease, hereditary hemorrhagic telangiectasia, arteriovenous malformations) was also collected. A Charlson

Comorbidity Index (CCI) score was calculated for each patient.⁴ The CCI was used to estimate the life expectancy of patients, with scores of 0–3 treated as > 10 years, those 4–8 as 5–10 years, and those $\geq$ 9 as < 5 years.^{1,2,17}

Statistical Analysis

All data analyses were carried out in a de-identified manner. Data were summarized using means and standard deviations for continuous variables and counts and frequencies for categorical variables. The demographic, clinical, and radiographic variables were compared among centers using the Student t-test for continuous variables and the chi-square test for categorical variables.

The validation analysis, performed by one person, was done by scoring each patient in the validation cohort using the UIATS. After scoring, patients were classified as UIATS recommends treatment (score $\geq$ 3; i.e., “Favors UIA repair” score was more than 3 points greater than “Favors UIA conservative management” score) or UIATS did not recommend treatment (score $\leq$ -3; i.e., “Favors UIA conservative management” score was more than 3 points greater than “Favors UIA repair” score), and no treatment recommendation (UIATS between -2 and 2; i.e., difference between “Favors UIA conservative management” score and “Favors UIA repair” score was $\leq$ 2 in either direction). Patients whose scores fell between -2 and 2 were excluded because the UIATS did not provide a recommendation. The remaining patients were categorized in a contingency table assessing UIATS recommendation versus the real-world treatment decision. We calculated the percentage of misclassification, sensitivity and specificity, and area under the receiver operating characteristic (ROC) curve for the UIATS in comparison with real-world experience. This comparison was analyzed using the chi-square test. We calculated the percentage of misclassification, sensitivity, specificity, positive predictive value, and negative predictive value. Before the study, validation was defined as a misclassification rate of < 25%.²⁰

A logistic regression model was developed for the UIATS risk categorization and its association with real-world treatment. Using this model, we calculated the area under the curve (AUC) for discrimination of the dichotomized UIATS. To determine which elements of the UIATS best predicted the real-world treatment decision, a correlation coefficient (CC) was calculated between each of the individual components of the UIATS and the real-world treatment decision for the entire cohort. Data were analyzed using Stata (version 12.1, StataCorp.).

Results

A total of 221 consecutive patients with UIAs met the inclusion criteria: 69 of 221 (31%) patients were treated and 152 of 221 (69%) were not treated. Fifty-nine patients (27%) had a UIATS between -2 and 2, which does not offer a treatment recommendation, leaving 162 of 221 (73%) patients who had a UIATS treatment recommendation for inclusion. The scores of 117 patients indicated UIATS recommendations of no treatment, whereas the scores of 45 would recommend treatment. The mean patient age of the

		Patient		Aneurysm		Treatment		Favors Favors UIA conservative repair management	
Patient	Age (single)	< 40 years	4	☐					
		40-60 years	3						
		61-70 years	2						
		71-80 years	1						
		> 80 years	0						
	Risk factor incidence (multiple)	Previous SAH from a different aneurysm	4	☐					
		Familial intracranial aneurysms or SAH	3						
		Japanese, Finnish, Inuit ethnicity	2						
		Current cigarette smoking	3						
		Hypertension (systolic BP > 140 mm Hg)	2						
		Autosomal-polycystic kidney disease	2						
		Current drug abuse (cocaine, amphetamine)	2						
		Current alcohol abuse	1						
	Clinical Symptoms related to UIA (multiple)	Cranial nerve deficit	4	☐					
		Clinical or radiological mass effect	4						
		Thromboembolic events from the aneurysm	3						
		Epilepsy	1						
	Other (multiple)	Reduced quality of life due to fear of rupture	2	☐					
		Aneurysm multiplicity	1						
	Life expectancy due to chronic and/or malignant Diseases (single)	< 5 years	4	☐					
5 - 10 years		3							
> 10 years		1							
Comorbid disease (multiple)	Neurocognitive disorder	3	☐						
	Coagulopathies, thrombophilic diseases	2							
	Psychiatric disorder	2							
Aneurysm	Maximum diameter (single)	≤ 3.9 mm	0	☐					
		4.0-6.9 mm	1						
		7.0-12.9 mm	2						
		13.0-24.9 mm	3						
		≥ 25 mm	4						
	Morphology (multiple)	Irregularity or lobulation	3	☐					
		Size ratio > 3 or aspect ratio > 1.6	1						
	Location (single)	BasA bifurcation	5	☐					
		Vertebral/basilar artery	4						
		AcomA or PcomA	2						
Other (multiple)	Aneurysm growth on serial imaging	4	☐						
	Aneurysm de novo formation on serial imaging	3							
	Contralateral stenooclusive vessel disease	1							
Treatment	Age-related risk (single)	< 40 years	0	☐					
		41-60 years	1						
		61-70 years	3						
		71-80 years	4						
		> 80 years	5						
	Aneurysm size-related risk (single)	< 6.0 mm	0	☐					
		6.0-10.0 mm	1						
		10.1-20.0 mm	3						
		> 20 mm	5						
	Aneurysm complexity-related risk	High	3	☐					
Low		0							
Intervention-related risk	Constant*		☐	☐					
								☐	☐
								Favors	Favors
								UIA	UIA
								repair	conservative
								management	management

FIG. 1. The UIATS. To calculate a management recommendation for a UIA, the number of points corresponding to each patient-, aneurysm-, or treatment-related feature in both management columns of the scoring form ("In favor of UIA repair" and "In favor of UIA conservative management") are totaled. This will lead to 2 numerical values, one favoring aneurysm repair (surgical or endovascular) and the other favoring conservative management. Reproduced with permission from Etminan N, Brown RD Jr, Beseoglu K, Juvela S, Raymond J, Morita A, et al: The unruptured intracranial aneurysm treatment score: a multidisciplinary consensus. *Neurology* 85(10):881-889, 2015. <http://www.neurology.org/content/85/10/881.long>.

TABLE 1. Demographic information for UIATS recommending treatment versus no treatment

Variable	UIATS Recommendation		
	No Treatment	Treatment	No Recommendation
No. of patients	117	45	59
Mean age in yrs ($\pm$ SD)	69.9 $\pm$ 12.32	50.8 $\pm$ 14	56.6 $\pm$ 13.9
Female	81 (69)	34 (76)	43 (73)
Risk factor incidence			
Previous SAH from different aneurysm	0	0	1 (1.7)
Family history of aneurysmal SAH	1 (0.85)	3 (6.6)	8 (13.5)
Japanese, Finnish, Inuit ethnicity	1 (0.85)	1 (2.2)	0
Caucasian	88 (75)	35 (77)	45 (76)
Current cigarette smoker	3 (2.5)	19 (42)	7 (12)
Hypertension	69 (59)	23 (51)	34 (58)
Alcohol use	25 (21)	17 (38)	13 (22)
Illicit drug use	0	6 (13.3)	0
Clinical symptoms related to UIA			
Cranial nerve deficit	3 (2.5)	9 (20)	3 (5)
Clinical or radiological mass effect	6 (5)	8 (18)	7 (12)
Thromboembolic events from aneurysm	22 (19)	12 (27)	16 (27)
Epilepsy	8 (6.8)	2 (4.4)	6 (10)
Other			
Reduced quality of life due to fear of rupture	5 (4.3)	5 (11)	2 (3.4)
Aneurysm multiplicity	10 (8.5)	13 (29)	12 (20)
Comorbid disease			
Neurocognitive disorder	15 (12.8)	2 (4.4)	1 (1.7)
Coagulopathies/thrombophilic disease	5 (4.2)	0	5 (8.4)
Morphology			
Mean aneurysm diameter in mm ($\pm$ SD)	5.4 $\pm$ 3.9	5.4 $\pm$ 2.62	7.05 $\pm$ 7.48
Multilobulated aneurysm	14 (12)	20 (44)	16 (27)
Size ratio >3 or aspect ratio >1.6	16 (14)	8 (18)	12 (20)
Aneurysm <7 mm	27 (23)	14 (31)	22 (37)
Location			
Basilar bifurcation or vertebral/basilar artery	1 (0.85)	8 (18)	2 (3.3)
Anterior or posterior communicating artery	27 (23)	16 (36)	16 (27)
Other			
Aneurysm growth on serial imaging	5 (4.3)	0	4 (6.8)
De novo formation on serial imaging	0	8 (18)	2 (3.4)
Contralateral steno-occlusive disease	0	1 (2.2)	2 (3.4)
High aneurysm complexity	1 (1)	2 (4.4)	3 (5.1)
No. of UIAs treated in our real-world scenario	23 (19.6)	22 (49)	24 (41)

Values are presented as the number of patients (%) unless indicated otherwise.

group for which treatment was not recommended was 70 years, and that of the group for which treatment was recommended was 51 years. The majority of patients in both groups were female (Table 1).

The UIATS recommendation was significantly associated with the actual treatment of UIAs ($p < 0.001$); the sensitivity of the UIATS was 49%, specificity was 80%, and percentage of misclassification was 28% (Table 2). Notably, 51% of patients in whom the UIATS would recommend treatment were untreated in our cohort and 20%

of patients for whom the UIATS would recommend conservative management had intervention. No patient in the conservatively managed group experienced a subsequent SAH due to aneurysm rupture during the follow-up period of up to 4 years. The AUC was suboptimal at 0.646 (Fig. 2).

The correlation between the individual elements of the UIATS and real-world decision to recommend treatment was significant for older age ($CC = 0.161$, $p = 0.016$), patient fear of rupture ($CC = 0.170$, $p = 0.012$), multilobulated aneurysm ($CC = 0.216$, $p < 0.001$), larger aneurysm size

TABLE 2. Contingency table of UIATS compared with real-world treatment decisions

	UIATS $\leq -3^*$	UIATS $\geq 3^\dagger$	UIATS -2 to $2^\ddagger$
Untreated UIA	94 (80)	23 (51)	35 (59)
Treated UIA	23 (20)	22 (49)	24 (41)

Values are presented as the number of patients (%). The sensitivity of the UIATS was 49%, specificity was 80%, and percent misclassification was 28%.

The area under the ROC curve was suboptimal at 0.646.

* UIATS recommendation of no treatment.

† UIATS recommendation of treatment.

‡ No UIATS recommendation.

(CC = 0.196, $p = 0.003$), and size ratio > 3 or aspect ratio > 1.6 (CC = 0.258, $p < 0.001$).

Discussion

The management of UIAs is a controversial topic in the cerebrovascular literature. There is a large body of work with conflicting recommendations, and careful review of the literature regarding risk factors and modeling based on patient characteristics can be difficult in part because of the varying degrees of evidence.¹¹ A considerable effort has been put forth to guide clinical management and decision making by the creation of the UIATS,⁶ but this scoring system has not been broadly adopted. Our effort to compare this instrument with the experience of a single, high-volume, quaternary, academic medical center demonstrates several differences.

The UIATS was proposed by a multidisciplinary consensus group to aid management and decision making for

patients with UIAs.⁶ On its conception and in the initial report, the authors offered internal and external groups of patients for validation using a Delphi consensus. They also selected 30 UIA cases to analyze agreement with the UIATS based on a 5-point Likert scale. The authors found a high level of agreement of the 30 cases with the UIATS and high interrater agreement among the specialist group that devised the score and thus concluded that the UIATS captured excellent consensus of UIA management and endorsed its use for managing individual patients with UIAs.⁶

The UIATS differs from the PHASES score, which is a model based on prospectively collected data from 6 cohort studies on risk of UIA rupture that provides risks of rupture for the initial 5 years after aneurysm detection using 6 easily retrievable baseline characteristics (patient geographic location and age, aneurysm size and location, hypertension, and previous SAH from a different aneurysm).¹⁰ A criticism of the PHASES score, which has limited its use and generalizability, was that some groups of patients, specifically those with familial aneurysms or young smokers, were underrepresented;⁶ an additional criticism comes from the lack of long-term follow-up (> 5 years) and the exclusion of the risk of intervention or treatment, which the UIATS includes. Thus, the UIATS was designed to address these shortcomings and “harmonize” the variability seen among clinicians managing UIAs.

The factors used in the UIATS include many that have not been studied in previous observational or cohort studies (young age or long life expectancy, coexisting modifiable and unmodifiable risk factors, comorbidities, aneurysm characteristics, and clinical symptoms related to the UIA).^{7,15,16,18,22,24} The instrument was created using the Delphi method to reach consensus, which is accepted as a

FIG. 2. The ROC demonstrating an AUC of 0.646, indicating a low level of accuracy of the UIATS in comparison with real-world treatment decisions. Figure is available in color online only.

scientifically sound methodology and has been used to develop treatment scores on similarly complex subjects.^{8,12,28} The authors of the UIATS suggest the use of the UIATS as a complement to evidence, but our results indicate that there are discrepancies between the UIATS and the reality of a large cerebrovascular practice. There may be additional factors or persuading information that is left out of the UIATS. Ultimately, consultation with a specialist is necessary for any UIA.

Using a prospectively populated database, we found a low sensitivity of 49%, specificity of 80%, and percentage of misclassification of 28% when we compared the UIATS with the real-world decision of whether to treat a UIA. Low sensitivity is not desirable for a screening tool of this nature. In fact, if the UIATS had been used to make treatment decisions, rather than further diagnostic decisions in this cohort of patients, this low sensitivity would result in a poor performance when matched against the experience of 5 cerebrovascular neurosurgeons and would result in overtreatment in comparison. Nearly 51% of patients in our cohort for whom treatment would be recommended by the UIATS were untreated, thus suggesting that the UIATS would have recommended overtreatment in our cohort. Notably, no patient in the cohort of conservatively managed patients had a subsequent SAH from aneurysm rupture during a follow-up period of up to 4 years. This finding and interpretation should be taken carefully, however, given that this is the reflection of a single academic center. In addition, 20% of patients in our cohort for whom conservative management would be recommended by UIATS underwent intervention. This 2-sided mismatch indicates that there may be additional factors that influence decisions about treatment that are not reflected in the UIATS. Moreover, the overall performance of the model, despite being statistically significant, was quite low, with an AUC of 0.646, indicating discordance in the comparison between the UIATS and our experience.

Using multivariable regression analysis of a larger cohort of 424 patients that included the 221 patients described in this report, Guan et al.¹¹ found that the presence of multiple aneurysms (OR 2.093), larger aneurysm size (OR 1.176), lower CCI (OR 1.536), and younger age (OR 2.913) were associated with the decision to pursue treatment. All of these factors are included, to some degree, in the UIATS, but the performance of the UIATS score on this testing cohort was suboptimal.

For this cohort, we calculated a CC between the individual elements of the UIATS and the real-world decision to recommend treatment. We found that there was significant correlation for older age, patient fear of rupture, multilobulated aneurysm, larger aneurysm size, and size ratio > 3 or aspect ratio > 1.6. This indicates that these variables may play a large role in the practitioner's decision to treat an aneurysm, and could be included, and weighted more heavily, in a potential treatment algorithm or scheme.

We theorize that the discrepancy between the UIATS recommendation and the actual treatment that patients received is likely multifactorial. The correlation between treatment and UIATS yielded older age, greater patient fear of rupture, multilobulated aneurysm, larger aneurysm size, and size ratio > 3 or aspect ratio > 1.6 as factors that

were significant based on our single-center cohort of patients. It could be that the practice pattern at our center differs from those involved in the creation of the UIATS, but it is unlikely that this alone accounts for the discrepancy. Factors that are considered when evaluating UIAs include size, irregularity of the aneurysm (geometry), family history, growth over time, and patient anxiety, as well as other comorbidities. Although the UIATS attempts to address anxiety and patient fear, the "human factor" clearly plays a role and is based on patient anxiety surrounding the lesion and its effect on quality of life,²³ as well as the interaction with the surgeon in the context of current treatment recommendations. This set of factors is difficult to quantify/qualify, but at our center it plays a large role in deciding whether to treat or observe over time. Because of the degree of discrepancy, the suggestion based on the current study is that consultation with a cerebrovascular specialist is necessary in all cases of UIAs.

Limitations

This single-center validation study was conducted on a retrospective cohort from a prospectively collected database, which may limit the accuracy and availability of the medical record. This study demonstrated a poor comparison between the UIATS and real-world treatment decisions, but the data presented represent only a single-center practice with 5 experienced cerebrovascular neurosurgeons. As with any evaluation of treatment decisions, patient and physician interpretations of the available information play a large role and may be subject to bias. Thus, treatment decisions may be biased by individual providers since no uniform treatment algorithm is used; however, the UIATS is based on consensus opinion, not a scientific analysis and thus is also a subjective measure. Further validation or study of the UIATS at multiple sites may be beneficial. Ultimately, prospective tracking and use of the UIATS is necessary prior to widespread use and implementation. We advise that clinical evaluation and multidisciplinary decision making should be paramount when making all diagnostic and treatment decisions.

Conclusions

This single-center comparison of the UIATS with a real-world experience found that UIATS generally recommended overtreatment of UIAs. Although the UIATS could be used as a screening tool, a further prospective validation of the UIATS is needed prior to widespread use.

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Disclosures

Dr. Taussky reports that he is a consultant for Medtronic.

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Conception and design: Park. Acquisition of data: Ravindra, Gooldy, Scoville, Guan. Analysis and interpretation of data: Park, Ravindra, de Havenon. Drafting the article: Ravindra. Critically revising the article: all authors. Reviewed submitted version of manuscript: Park, Ravindra, de Havenon. Approved the final version of the manuscript on behalf of all authors: Park. Study supervision: Park, Couldwell.

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