Original Contribution

PHASES Score for the Management of Intracranial Aneurysm

A Cross-Sectional Population-Based Retrospective Study

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Background and Purpose—The aim of this study is to assess whether the PHASES score allows to (1) match decisions taken by multidisciplinary team whether to observe or intervene, (2) classify patients being diagnosed with a ruptured versus unruptured intracranial aneurysm (UIA), and (3) discriminate patients at low risk of rupture from the population of patients diagnosed with intracranial aneurysm.

Methods—Population-based prospective and consecutive data were collected between 2006 and 2014. Patients (n=841) were stratified into 4 groups: stable UIA; growing observed UIA; immediately treated UIA; and aneurysmal subarachnoid hemorrhage (aSAH). All patients initially observed were pooled in a follow-up UIA group; patients from growing observed UIA, immediately treated UIA, and aSAH were pooled in a high risk of rupture group. Results are expressed as median [quartile 1, quartile 3].

Results—PHASES scores of immediately treated UIA patients were significantly higher than follow-up UIA group (5 [3, 7] versus 2 [1, 4]). Patients diagnosed with UIA and PHASES score of >3 were more likely to be treated, and the score ≤3 was predictive for observation (areas under these curves=0.74). Odds of being diagnosed with an aSAH were associated with PHASES score of >3 (UIA, 4 [2, 6]; aSAH, 5 [4, 8]; areas under these curves=0.66). Scores of stable UIA patients were significantly lower than high risk of rupture group (2 [1, 4] versus 5 [4, 7]; stable UIA outcome prediction by PHASES score of ≤3: areas under these curves=0.76).

Conclusions—There is a progression of PHASES score between stable UIA, growing observed UIA, immediately treated UIA, and aSAH groups. PHASES score of ≤3 is associated with a low but not negligible likelihood of aneurysm rupture, and specificity of the classifier is low. (***Stroke*. 2017;48:00-00. DOI: 10.1161/STROKEAHA.117.017391.)**

Key Words: hypertension ■ intracranial aneurysm ■ probability ■ risk ■ subarachnoid hemorrhage

Between 2% and 4% of the population may potentially be diagnosed with an intracranial aneurysm (IA), and between 3 and 50 of 100 000 inhabitants per year suffer a subarachnoid hemorrhage because of aneurysm rupture (aSAH).[1,2] Thus, most patients with unruptured IAs (UIAs) may remain asymptomatic.

The rate of incidental diagnosis of UIA is increasing globally with the multiplication of imaging facilities.[3] Overall, the average risk of rupture of UIA is estimated between 0.3% and >15% per 5 years (0.4–0.6 for lesions smaller than 7 mm).[1] Preventive treatment of these aneurysms exposes patients to a risk of 1% mortality and ≈5% morbidity (<0.1% and <3%, respectively, for small lesions).[4–6] The balance between risks and benefits on different management options needs to be personalized. As recently summarized, no randomized control trials have been successfully conducted to date to address the issue on the management of UIA.[7] Only 80 patients had been recruited after nearly 3 years during the unique attempt.[8] A decision then can only be based on (1) a consensus-based scoring strategy for the management of UIA (Unruptured Intracranial Aneurysm Treatment Score[9]) or (2) a 5-year rupture rate estimation using the PHASES score (Table 1) model based on 8283 patients diagnosed with UIA and 29 166 patient years of follow-up.[10] Neither decision support tool has been validated on an independent large cohort.

The aim of this study is to assess whether the PHASES score is able to (1) provide decision support and matches decisions taken by expert multidisciplinary team whether to observe or intervene a diagnosed UIA, (2) classify ruptured versus unruptured aneurysm, and (3) discriminate patients at low risk of rupture from the population of patients diagnosed with UIA.

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Table 1. Predictors, Criteria, and Points Composing the PHASES Score to Estimate the 5-Year Aneurysm Rupture Rate[10]

PHASES Aneurysm Risk Score	
Criteria	Points
Population	
North American, European (other than Finnish)	0
Japanese	3
Finnish	5
Hypertension	
No	0
Yes	1
Age	
<70 y	0
≥70 y	1
Size of aneurysm	
<7.0 mm	0
7.0–9.9 mm	3
10.0–19.9 mm	6
≥20.0 mm	10
Earlier SAH from another aneurysm	
No	0
Yes	1
Site of aneurysm	
ICA	0
MCA	2
ACA/PcoA/posterior circulation	4

Posterior circulation includes the vertebral artery, basilar artery, cerebellar arteries, and posterior cerebral artery. ACA indicates anterior cerebral arteries (including the anterior cerebral artery, anterior communicating artery, and pericallosal artery); ICA, internal carotid artery; MCA, middle cerebral artery; PcoA, posterior communicating artery; and SAH, subarachnoid hemorrhage.

Methods

Inclusion/Exclusion Criteria

All patients diagnosed with IA between September 1, 2006 and August 31, 2014 (1164 patients) were recruited prospectively and consecutively (Ethics approval Geneva CCER 07-056). Patients known to have a positive familial history for IA or subarachnoid hemorrhage (n=119), polycystic kidney disease (n=40) or who suffered symptoms of the aneurysm (cranial nerve compression, embolization from an aneurysm, or suffering sentinella headaches, n=26) were excluded. PHASES score was calculated for 841 patients. In cases diagnosed with multiple aneurysms, the lesion producing the highest score was used to calculate the PHASES score. Patients were classified into 4 groups: observed and stable UIA (S); observed and growing UIA (G); immediately treated UIA (T); and patients diagnosed in the context of an aSAH. For analysis purposes, S and G were pooled in a follow-up UIA group (F), and patients from G, T, and aSAH were classified as high risk of rupture (H).

Risk Stratification

The decision of the multidisciplinary team (at least 1 senior neurosurgeon and 1 senior endovascular neuroradiologist) to observe or treat patients with incidentally discovered aneurysms was taken on the basis of a systematic assessment of the patients, cerebrovascular architecture, and aneurysm morphology. Basic demographic information, such as sex, age, occupation status, habitus, risk factors, comorbidities, and medications, was recorded. Previous history of SAH, smoking, hypertension (blood pressure >140 mm Hg systolic), alcohol abuse (>15 drinks per week), and drug abuse were considered patient-related risk factors. Occlusions, stenosis, dominance, or fetal-type arteries upstream of the aneurysm and extreme open bifurcation angle were considered angioarchitecture risk factors. High size ratio (>3), high aspect ratio (>1.6), irregularity of the aneurysm dome, and presence of a thrombus or calcifications were considered as aneurysm dome risk factors. All aneurysms located in the posterior circulation, posterior communicating artery, anterior communicating artery, and pericallosal artery (per anterior cerebral artery) >4 mm in diameter were considered for treatment. All lesions with a size of <4 mm were considered for observation. Aneurysms of sizes between 4 and 7 mm in low-risk locations were either observed or treated according to the number and importance of risk factors. Patients in the F group were reviewed with cerebrovascular imaging at 6 months, 1 year, 2 years, 5 years, and every 5 years thereafter. Intervention was advised if any change in morphology, new symptoms, or significant change in risk factors were observed. The safety of the management was assessed >1177.6 aneurysm-years and exposed patients to 0.24% per year risk of unexpected aneurysm rupture, an annual lethal risk of 0.078% and 2.6±0.1% per year probability of aneurysm growth.[11]

The ability of the PHASES score to provide decision support on follow-up or immediate treatment of incidentally diagnosed UIA was assessed by comparing patients of groups F and T. The ability to classify ruptured from unruptured aneurysms was assessed by comparing group UIA with aSAH. The ability to discriminate patients at low risk to experience an aneurysm rupture was assessed by comparing group S with H.

Statistical Analysis

The performance of binary classification of the PHASES score was assessed both by odds ratio (OR) and areas under these curves (AUCs): forest plots display the odds that an outcome (T, H, aSAH) will occur given a particular PHASES score and control group (F, UIA. S); the higher the odds, the better the classification functions. response operating characteristic (ROC) curves are empirical curves in the sensitivity and specificity space[12]: higher AUCs signify better classification results. Statistical difference between ROC curves was tested with de Long method.[13] Confidence intervals (CIs) of sensitivity and specificity were computed with bootstrap resampling and the averaging methods.[14]

Means are reported with their corresponding SDs, medians with their interquartile range [quartile (Q)1, Q3]. OR and AUCs are reported with their 95% CIs.

Overall statistically significant difference between all patients groups was tested with a Kruskal–Wallis rank-sum test. Post hoc comparisons between 2 groups of patients were performed by a 1-sided pairwise Wilcoxon rank-sum test correcting for multiple testing. *P* values smaller than 0.05 were considered to indicate statistical significance.

All statistical analysis was performed with the software package R,[15] plots and statistical analysis of ROC curves were performed with the R package pROC,[12] and forest plots of OR were generated with the R package metafor.[16]

Results

General

A total of 841 patients diagnosed with IA were included in the study and all PHASES scores calculated retrospectively (Figure 1). The cohort was composed of 598 patients (71%) diagnosed incidentally with UIA and 243 patients (29%) who suffered an aSAH secondary to the rupture of an IA. Patients with UIA were either observed or treated according to the decision of patients informed about the risks associated with

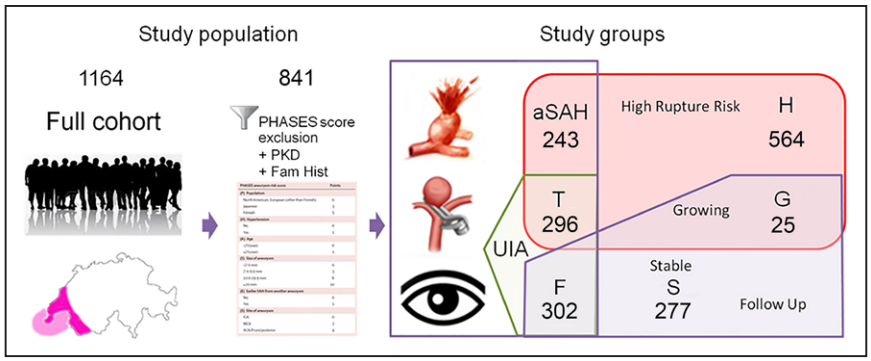

Figure 1. Study cohort and study groups. aSAH indicates aneurysmal subarachnoid hemorrhage; F, follow-up UIA group; G, growing observed UIA; H, high risk of rupture; PKD, polycystic kidney disease; S, observed and stable UIA; T, immediately treated UIA; and UIA, unruptured intracranial aneurysm.

both options and the position of a multidisciplinary team that reviewed each case. Most patients with UIA were initially observed (302 patients [36%] in the F group). Patients in group T were prophylactically secured (296 cases [35%]). After a mean follow-up time of 3.2 years and 1177.6 aneurysm-years, 25 patients (2.6±0.1%) were diagnosed with an aneurysm shape change and the aneurysm prophylactically treated (group G).

Basic characteristics of the cohort and subgroups are presented in Table 2. Overall, the cohort characteristics are similar to other previously reported recent cohorts. The male:female ratio is 1:3. One quarter of the patients have been diagnosed with multiple aneurysms. The average aneurysm size in the cohort is 6.6 mm. Most aneurysms are <7 mm, and 22.5% are between 7 and 12 mm. Aneurysms >13 mm in maximal diameter make up <10% of the lesions. The most frequent sites of aneurysms are the anterior communicating artery and anterior cerebral artery, followed by the middle cerebral artery bifurcation and the internal carotid artery. The relative prevalence of aneurysms located in the posterior communicating artery segment of the internal carotid artery seems to be less frequent in the current cohort than our earlier observations and other

Table 2. Baseline Characteristics of the Full Cohort and Groups

Baseline Characteristics	Full Cohort	UIA	F	S	G	T	aSAH	H
n	841	598	302	277	25	296	243	564
Age (mean [SD])	55 [14]	56 [14]	56 [16]	56 [16]	50 [14]	55 [12]	54 [13]	55 [13]
Gender ratio (% of female)	73.0	75.0	75.0	74.4	88.0	74.3	70.0	73.0
Ratio of multiple aneurysms (%)	26	28	28	28	24	27	21	24
Max aneurysm diameter, mm (mean [SD])	6.6 [6.5]	5.9 [4.3]	3.9 [1.8]	3.8 [1.7]	5.3 [2.5]	8.0 [5.0]	8.2 [10]	7.9 [7.5]
Size of aneurysm (no. of patients [%])								
2–6.9 mm	68.5	73.7	93.7	94.9	80.0	53.4	56.7	56.0
7–12 mm	22.5	20.4	5.6	4.7	16.0	35.5	28.2	31.5
13–24 mm	7.4	4.8	0.7	0.4	4.0	9.1	13.9	10.9
>24 mm	1.1	1.0	0.0	0.0	0.0	2.0	1.3	1.6
Location of aneurysm (no. of patients [%])								
Internal carotid artery	20	24	41	43	28	7	10	9
Anterior communicating or anterior cerebral artery	33	33	19	18	20	47	35	40
Middle cerebral artery	28	30	31	30	44	29	22	26
Posterior communicating artery	10	7	2	3	0	11	18	13
Vertebrobasilar system	9	7	7	7	8	7	15	10
Medical history								
Hypertension (%)	46	46	48	46	66	44	34	45
Hypertension therapy (%)	37	39	44	43	52	34	19	33
Behavioral history								
Alcohol (>150 g/wk; %)	6	4	4	4	0	5.5	7.5	6
Current smoker (%)	32	33	31	30	36	35	31	33
Former smoker (%)	16	16	17	17	16	14	17	15

Max aneurysm diameter was measured on initial imaging. aSAH indicates aneurysmal subarachnoid hemorrhage; F, follow-up UIA group; G, growing observed UIA; H, high risk of rupture; S, observed and stable UIA; T, immediately treated UIA; and UIA, unruptured intracranial aneurysm.

previous reports.[17–20] Almost half of the patients (46%) suffer arterial blood hypertension, but only 37% benefit from a treatment adequately controlling blood pressure. One third of the patients are active smokers, and one sixth are former smokers. Less than 10% of the patients abuse alcohol and drink >15 glasses of alcohol per week.

Comparing the different groups, it can be observed that the average age, sex ratio, and prevalence of multiple aneurysms are similar. The mean aneurysm dome size is smallest in the S group (3.8 mm) and increasing from group G, T, to the aSAH group where it is the largest (5.3, 8.0, and 8.2 mm, respectively).

Treatment Versus Observation

Aneurysms located in the anterior cerebral artery and posterior circulation, including posterior communicating artery aneurysms, are more likely to be initially treated (OR, 5.2; 95% confidence interval [CI], 3.6–7.6; $P<0.0001$). In contrast, patients with aneurysms located at the internal carotid artery are more prone to be observed and remain stable (OR, 10.5; 95% CI, 6.3–17.5; $P<0.0001$).

The distribution of PHASES scores in the full cohort peaks at the score of 4 and is skewed toward lower values. A quarter of the cohort diagnosed with an IA has a PHASES score of <3, a third of the cohort a score <4, and half a score <5.

Most patients (first to third quartile) of the F group have scores between 1 and 4 in contrast to patients of the T group having scores between 3 and 7. Patients diagnosed with aSAH have score between 4 and 8 (Figure 2).

The median PHASES score of each group is statistically significantly different ($P<0.001$, Kruskal–Wallis rank-sum test) and increases in correlation to an increased estimated risk of aneurysm rupture (Figure 2; Table 3).

The ability to use the PHASES score to decide whether to observe or treat patients incidentally diagnosed with UIA was assessed comparing F with T. UIA patients with PHASES score of <3 are more likely to be observed. In contrast, patients with scores >4 are much more likely to be considered for intervention. Finally, patients with scores at 3 or 4 seem to be at equipoise. Classifying UIA cases in F or T using PHASES scores with a threshold between 3 and 4 allocated 74.2% cases correctly (Figure 3A; Table I in the online-only Data Supplement).

Incidental Versus aSAH

Comparing the odds being diagnosed incidentally or after aSAH for each PHASES score shows a sudden transition from high likelihood of incidental finding below a score of 4 to high likelihood of aSAH above a score of 3. The sensitivity and specificity to discriminate UIA from aSAH patients using a PHASES score threshold of 4 is 46% and 84%, respectively. The AUC of the ROC is 0.66 and the 95% CI 0.62 to 0.70 (Figure 3B; Table I in the online-only Data Supplement).

Low Risk Versus High Risk

The ability to discriminate low-risk cases was assessed by comparing S and H groups of patients. The patients with PHASES score of <3 are more likely to be classified as S, and those >3 are more likely to be H, whereas patients with score at 3 seem to be equally likely S or H. The AUC of a classifier using PHASES score of >3 as a threshold between low- and high-risk patients is 0.76 (95% CI, 0.73–0.79), and the sensitivity and specificity identifying patients of the H group is 75% and 64%, respectively (Figure 3C; Table I in the online-only Data Supplement).

The PHASES score used as a classifier with a threshold set >3 matches better with expert multidisciplinary team decisions and better distinguishes low- from high-risk lesions than discriminates between unruptured aneurysm and aSAH patients (AUC: 0.74, 0.76, 0.66, respectively; $P<0.01$; Figure 3D).

Classifications based on PHASES score were compared with classifications based on location and size of aneurysms only according to the current guidelines. Aneurysms located in the internal carotid artery and middle cerebral artery smaller than 7 mm and aneurysms located in other locations smaller than 4 mm were classified as low risk. All remaining aneurysms were considered high risk. The AUC (95% CI)

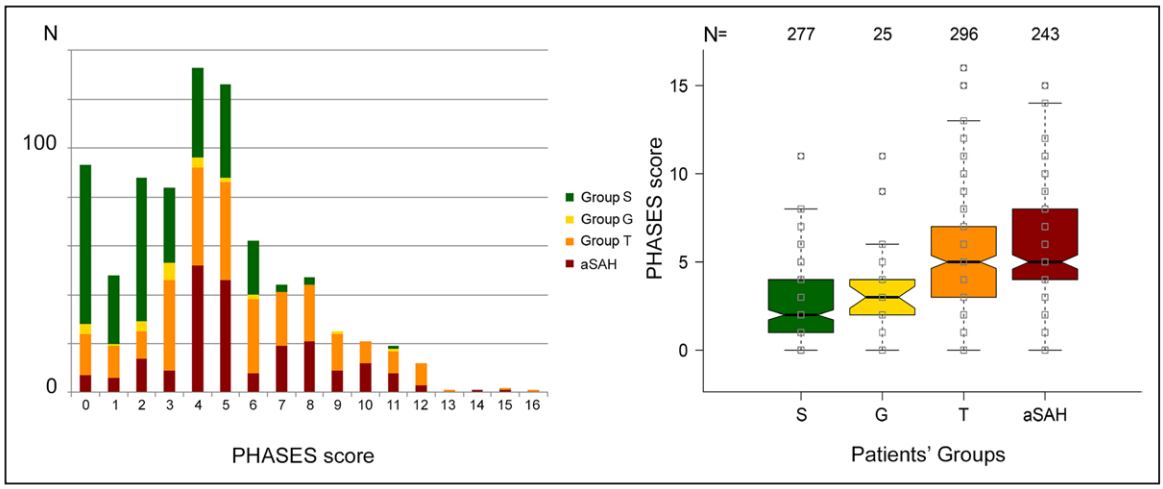

Figure 2. Cumulative histogram showing the distribution of PHASES score in the full cohort. **A**, The number of cases corresponding to each group S (green), G (yellow), T (orange), and aSAH (red) is encoded in color (left). **B**, Notched box plot representing the distribution of PHASES scores in each group. aSAH indicates aneurysmal subarachnoid hemorrhage; G, growing observed UIA; S, observed and stable UIA; T, immediately treated UIA; and UIA, unruptured intracranial aneurysm.

Table 3. Mean and SD as well as Median First and Third Quartile Values of the PHASES Score Distributions' for Each Study Group

					n	Mean	SE Mean	Median	Q1	Q2	*P* Value
Full cohort					841	4.46	0.10	4	2	6	<0.001
				S	277	2.68	0.13	2	1	4	N.S.
			F		302	2.74	0.13	2	1	4	Ref
				G	25	3.44	0.53	3	2	4	N.S.
		UIA			598	3.99	0.12	4	2	6	<0.001
				T	296	5.28	0.18	5	3	7	<0.001
	H				564	5.34	0.13	5	4	7	<0.001
				aSAH	243	5.61	0.18	5	4	8	<0.001

Statistical significance is calculated compared with the F group defined as reference group. Attention of the reader is raised on the mean given as an indicative value. The distribution of PHASES scores is not Gaussian and highly skewed. aSAH indicates aneurysmal subarachnoid hemorrhage; F, follow-up UIA group; G, growing observed UIA; H, high risk of rupture; N.S., not significant; Q, quartile; S, observed and stable UIA; T, immediately treated UIA; and UIA, unruptured intracranial aneurysm.

sensitivity and specificity of the location and size-based classifier was 0.79 (0.76–0.82), 74% and 85% on the prediction of UIA to be followed up or initially treated, 0.63 (0.6–0.67), 72% and 56% to discriminate UIA from aSAH patients and 0.79 (0.77–0.82), 71% and 87.4% to discriminate S from H patients. The differences are not statistically significant.

Discussion

When excluding patients known to have a positive familial history, polycystic kidney disease, aneurysm-related symptoms including sentinella headaches, a classifier based on PHASES score and a threshold set between 3 and 4 is able to (1) provide some decision support and matches decisions taken by multidisciplinary team whether to observe or intervene with 84% sensitivity and 51% specificity; (2) classify unruptured versus ruptured aneurysm with 88% sensitivity and 33% specificity; and (3) discriminate patients at low risk of rupture from the population of patients with IAs with 85% sensitivity and 52% specificity.

The PHASES Score

The PHASES score was developed as a practical risk score to predict a patient's 5-year risk of aneurysm rupture rate on the basis of a set of routinely assessed patient and aneurysm

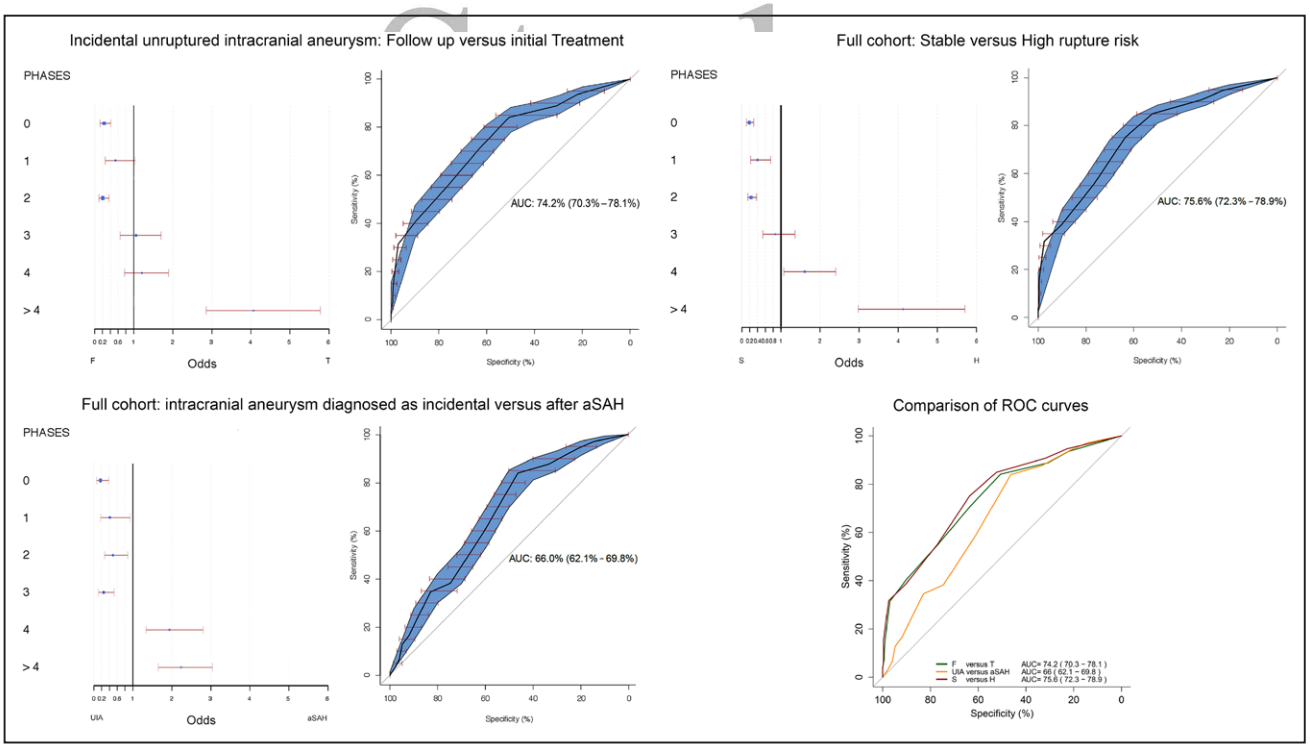

Figure 3. Forest plots and ROC curves corresponding to the assessment of PHASES score to predict multidisciplinary team decisions (**A**), status of aneurysm at diagnosis (**B**), discrimination of S patients from H (**C**). **D**, All ROC curves together. We observed no statistical difference between the AUCs of comparisons F vs T and S vs H (*P* value=0.59), but AUCs of both comparisons were significantly different from comparison UIA vs aSAH (*P*<0.01). aSAH indicates aneurysmal subarachnoid hemorrhage; AUC, areas under these curves; F, follow-up UIA group; G, growing observed UIA; H, high risk of rupture; ROC, response operating characteristic; S, observed and stable UIA; T, immediately treated UIA; and UIA, unruptured intracranial aneurysm.

characteristics and published online in late 2013.[10] Although the score has been developed by pooling the data of the 6 largest longitudinal studies measuring the rate of aneurysm rupture, the model has only been validated internally. Formal external validation is currently impossible because all data available worldwide have been used to develop the score. Generating a new data set will require a considerable effort and at least half a decade. We are currently not aware of such an effort having been initiated. In consequence, the aim of our study was to assess retrospectively a classifier based on PHASES score. We used prospectively and consecutively collected information in a population-based cohort recruited between September 1, 2006 and August 31, 2014.

When comparing the distribution of PHASES scores between groups of patients theoretically exposed to increasing risk of rupture, the mean and median PHASES score increases from a mean value of 2.68 and a median of 2 in the safest group (group of patients diagnosed with incidental aneurysms and observed over time with stable lesion [group S]) to 5.61 and 5, respectively, in the group of patients diagnosed with IAs subsequent to the bleeding of the lesion.

Risk Prediction and Treatment Implications

The odds of patients being diagnosed with a ruptured aneurysm or being treated after incidental discovery are low if the PHASES score is <4 or 3, respectively. In contrast, the odds are high if >4. Patients diagnosed with incidental aneurysms with a score of 3 or 4 are at an equipoise on performing a preventive treatment or observing. When dichotomizing the whole cohort according to the stability of lesion considering group S as patients with the lowest risk of rupture and all the other patients exposed to a higher risk, patients with PHASES score of <3 are more likely to be at low risk and patients with scores >3 more likely to be at high risk. Patients with a score of 3 are at equipoise.

The distribution of scores on the different patient groups are significantly different but overlap extensively. The ability to discriminate stable aneurysms from high-risk lesions is limited. Classifying patients with scores from 0 to 3 correctly identified 75% of patients considered at high risk. Concomitantly, 64% of the patients diagnosed in the S group had a score between 0 and 3. This strategy exposes patients to some risk of unexpected aneurysms ruptures during observation (16% of aSAH patients classified with a PHASES score of <4). Considering the ability of the score to identify patients who were diagnosed with ruptured aneurysms, a classifier using PHASES score of 0 to 2 was sensitive, and 12% of aSAH patients were incorrectly classified. When using this more conservative approach, 85% of H patients had score >2, but only 52% of S patients had PHASES score of <3. When assessing patients with unruptured aneurysms, PHASES score of <3 correctly classified only 51% of patients who were selected for observation by the multidisciplinary team consensus. This second strategy exposes patients to overtreatment and associated morbidity, mortality, and costs. The ability to correctly (specificity) identify F or S patients reaches 77% if the threshold is set at PHASES score between 4 and 5, but then the sensitivity identifying patients at risk declines to 59% (aSAH) and 55% (H). Considering a standard treatment risk and according to the Youden index used to identify the optimal threshold, patients with PHASES score of <4 (score between 0 and 3) should be considered for observation.

Classifiers based on the PHASES score and based on the current guidelines using only location and size of aneurysms were compared. Performances of both classifiers were similar on the ability classifying cases according to a multidisciplinary team decision to treat or not, identify patients at low risk of rupture and identify patient who suffered an aSAH. Although including a significant number of patients, this study is neither designed nor sufficiently powered to assess the superiority of one of the above-mentioned classifiers.

PHASES score was developed with the aim of predicting a rate of rupture to be balanced against mortality and morbidity associated with intervention. Because no new information was yet available on personalized intervention risk assessment,[18] this important variable was missing from our analysis. It is up to the physician in charge of the intervention to decide whether the risk associated with the intervention is standard, significantly smaller, or higher. The threshold could be adapted accordingly to be >4 if intervention risk is considered low, and <3 if the risks are considered high.

Implications and Limitations of the Present Study

The strength of the study resides in the prospective collection of information on consecutive cases recruited from a defined recruitment area. It can reasonably be considered as a population-based cross-sectional study of patients diagnosed with IAs. The consecutive nature of the patient recruitment reduces bias associated with case selection. All cases are screened and consented to. The rate of patients refusing to be recruited in the registry is <2% (n=23). No imputation was used, but 323 patients were excluded either because of positive familial history, polycystic kidney disease, symptomatic aneurysms where the PHASES score is not adequate or because of missing information (n=136, 14%). The latter may introduce some distortions.

Limitations Because of Model Design and Outcome Assessment

The risk associated with rupture and decisions to treat patients are based on knowledge obtained from longitudinal cohorts where most patients at risk have been excluded. Those studies face a similar issue as did the Center for Naval Analyses during the second World War that recommended armor be added to areas that showed the most damage done to aircrafts that had returned from mission. In 1943, Wald[21] proposed to reinforce the returning aircraft where unscathed, making the assumption that those were the areas that, if hit, would cause the plane to be lost. Perhaps a similar strategy to that proposed by Wald[21] should be applied to the field of IAs. The difficulty in our case is that we cannot identify hits on a plane but only distinguish characteristics much fuzzier to categorize and suffering much weaker causal links to the outcome. To better control for bias, we decided to always compare and report basic characteristics of our cohort and subgroups with previous works.[17–20] No conclusion could be drawn yet, but we hope that with the progress toward the Big Data era, more detailed information on a massive number of individuals will allow a precise identification of

factors associated with the disease and quantification of their respective weights.[22] Our proposed strategy to overcome those biases and nevertheless generate better evidence in the future is to combine longitudinal and cross-sectional approaches. The outcome measurement should then be failures in management, measured as treatment-induced mortality and morbidity or natural history-induced mortality and morbidity and the aim being an overall reduction of failures.

Disease Progression as a Surrogate of Aneurysm Rupture

It has been suggested that aneurysm growth could be a surrogate measurement of the risk of aneurysm rupture. The probability of aneurysm growth is higher in groups of patients with increasing PHASES scores. Nevertheless, the hazard ratio for aneurysm growth in patients scored with PHASES score of 2 to 3 was marginally larger (1.07; 95% CI, 0.49–2.32) than patients with PHASES scores of 0 to 1.[23] The ability to initially discriminate aneurysms that will remain stable or will grow using the PHASES score in the follow-up cohort is limited. The number of events observed in our cohort was too small to draw any conclusion, but the presence or absence of hypertension seems to have a significant impact.[11] Nevertheless, one could suggest to add aneurysm growth or any marker of aneurysm disease progression (vessel wall enhancement[24]) as an additional factor to the PHASES score to increase the discrimination power between low- and high-risk patients diagnosed with incidental UIA.

Limitations Because of Variable Measurement Lack of Precision

The assessment of the factors is subject to imprecisions and controversies. The size of aneurysm is generally assumed to be the maximum diameter, but the method used to measure the maximum diameter and the imaging modality to obtain the data significantly affects the measurement.[25] To improve the precision of the prediction and the clinical pertinence and usability, the assessment of the criteria needs to be improved and refined.

To be able to balance the risks associated with the natural history with the risks associated with an intervention, the development of a similar score on interventions is required. Following a pragmatic approach collecting information from experts, an International Research Group proposed a new tool to assist in the management of UIA: the Unruptured Intracranial Treatment Score. The management model captured an excellent consensus on UIA management among highly informed individuals from diverse backgrounds. A comparable work to the present one and assessing Unruptured Intracranial Treatment Score has been initiated and will hopefully be extended to multiple collaborating centers.

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Disclosures

None.

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PHASES Score for the Management of Intracranial Aneurysm: A Cross-Sectional Population-Based Retrospective Study

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SUPPLEMENTAL MATERIAL

F *versus* T		
PHASES score	OR	95% CI
0	0.24	[0.13 - 0.40]
1	0.53	[0.24 - 0.94]
2	0.20	[0.08 - 0.32]
3	1.05	[0.68 - 1.80]
4	1.20	[0.70 - 1.78]
> 4	4.06	[3.13 - 6.35]

F *versus* T classifier (detection of F)			AUC	95% CI
			0.74	[0.70 - 0.78]
PHASES	sensitivity	specifity	PPV	NPV
0-2	0.51	0.84	0.77	0.63
0-3	0.63	0.71	0.69	0.65
0-4	0.77	0.55	0.64	0.70

UIA *versus* aSAH		
PHASES score	OR	95% CI
0	0.20	[0.09 - 0.43]
1	0.37	[0.16 - 0.89]
2	0.48	[0.27 - 0.88]
3	0.30	[0.15 - 0.61]
4	2.00	[1.35 - 2.95]
> 4	2.23	[1.63 - 3.07]

UIA *versus* aSAH (detection of UIA)			AUC	95% CI
			0.66	[0.62 - 0.70]
PHASES	sensitivity	specifity	PPV	NPV
0-2	0.33	0.88	0.87	0
0-3	0.46	0.84	0.88	0.39
0-4	0.61	0.59	0.79	0.38
0-5	0.75	0.38	0.75	0.38

S *versus* H		
PHASES score	OR	95% CI
0	0.19	[0.12 - 0.31]
1	0.37	[0.20 - 0.67]
2	0.23	[0.14 - 0.37]
3	0.94	[0.59 - 1.50]
4	1.53	[1.02 - 2.31]
> 4	4.27	[3.09 - 5.91]

S *versus* H (detection of S)			AUC	95% CI
			0.76	[0.73 - 0.79]
PHASES	sensitivity	specifity	PPV	NPV
0-1	0.32	0.91	0.63	0.73
0-2	0.52	0.85	0.63	0.78
0-3	0.64	0.75	0.56	0.81
0-4	0.77	0.55	0.46	0.83