

On-line Appendix and Figure

Maximizing the Patient Population Utility Method

Utility is a measure of the importance of the state of health for a given individual. The population utility (U) is represented as the sum of the utilities for each state of health, including true-positives (TP), false-positives (FP), true-negatives (TN), and false-negatives (FN). The population utility is mathematically expressed as

$$U = (TP \times U_{TP}) + (FP \times U_{FP}) + (TN \times U_{TN}) + (FN \times U_{FN}).$$

The CBF or MTT threshold that maximizes the population utility is, therefore, the value that minimizes FP and FN to achieve a maximal NBNCR. The NBNCR can simply be defined as the number of patients with no DCI who receive treatment, in an effort to avoid missing treatment for a single patient with DCI.¹ A weighting coefficient (R) is used to incorporate the NBNCR and prevalence of disease to allow maximization of the average state of health for the population.²⁻⁵ The optimal threshold is the value for which the slope of the ROC curve is equal to the weighting coefficient.^{2,3} When the average net cost (NC) is greater than the net benefit (NB), the threshold that maximizes population utility favors specificity. On the other hand, when the NB is greater than NC, the threshold that maximizes population utility favors sensitivity.⁵

The point-estimation method uses these properties to determine the CBF or MTT threshold that maximizes population utility. In this formula, σ^2 represents the variance, $R = NC/NB \times 1-p/p$, μ_H = mean CBF or MTT of healthy subjects (no DCI), and μ_D = mean CBF or MTT of diseased subjects (DCI). The point estimation (T) is mathematically expressed as

$$T = \frac{2\sigma^2 \ln(R) - \mu_H^2 + \mu_D^2}{2(\mu_D - \mu_H)}.$$

Calculation of the weighting coefficient is based on a 40% prevalence of DCI. For this study, an NC/NB ratio of 0.5 was determined on the basis of the clinical goals in managing patients with SAH for DCI. This NC/NB ratio corresponds to a CBF threshold of 35.3 mL/100 g/min (90% sensitivity, 68% specificity) and an MTT threshold of 5.5 seconds (73% sensitivity, 79% specificity). In the subgroup analysis of vasospasm, the CBF threshold is 36.5 mL/100 g/min (95% sensitivity, 70% specificity) and the MTT threshold is 5.4 seconds (78% sensitivity, 70% specificity). From a clinical perspective, CBF and MTT thresholds with higher sensitivity are favorable to minimize false-negatives, with physicians managing patients with aneurysmal SAH treating more patients for DCI in the population to minimize the likelihood of not treating a patient with DCI and risking development of permanent neurologic deficit, infarction, and death.

Appendix References

1. DeNeef P, Kent DL. Using treatment-tradeoff preferences to select diagnostic strategies: linking the ROC curve to threshold analysis. *Med Decis Making* 1993;13:126-32
2. Vermont J, Bosson JL, Francois P, et al. Strategies for graphical threshold determination. *Comput Methods Programs Biomed* 1991;135:141-50
3. Robert C, Vermont J, Bosson JL. Formulas for threshold computations. *Comput Biomed Res* 1991;24:514-29
4. Somoza E, Mossman D. Comparing and optimizing diagnostic tests: an information-theoretical approach. *Med Decis Making* 1992;12:179-88
5. Jund J, Rabilloud M, Wallon M et al. Methods to estimate the optimal threshold for normally or log-normally distributed biologic tests. *Med Decis Making* 2005;25:406-15

On-line Table 1: Imaging characteristics of the study population and subgroup

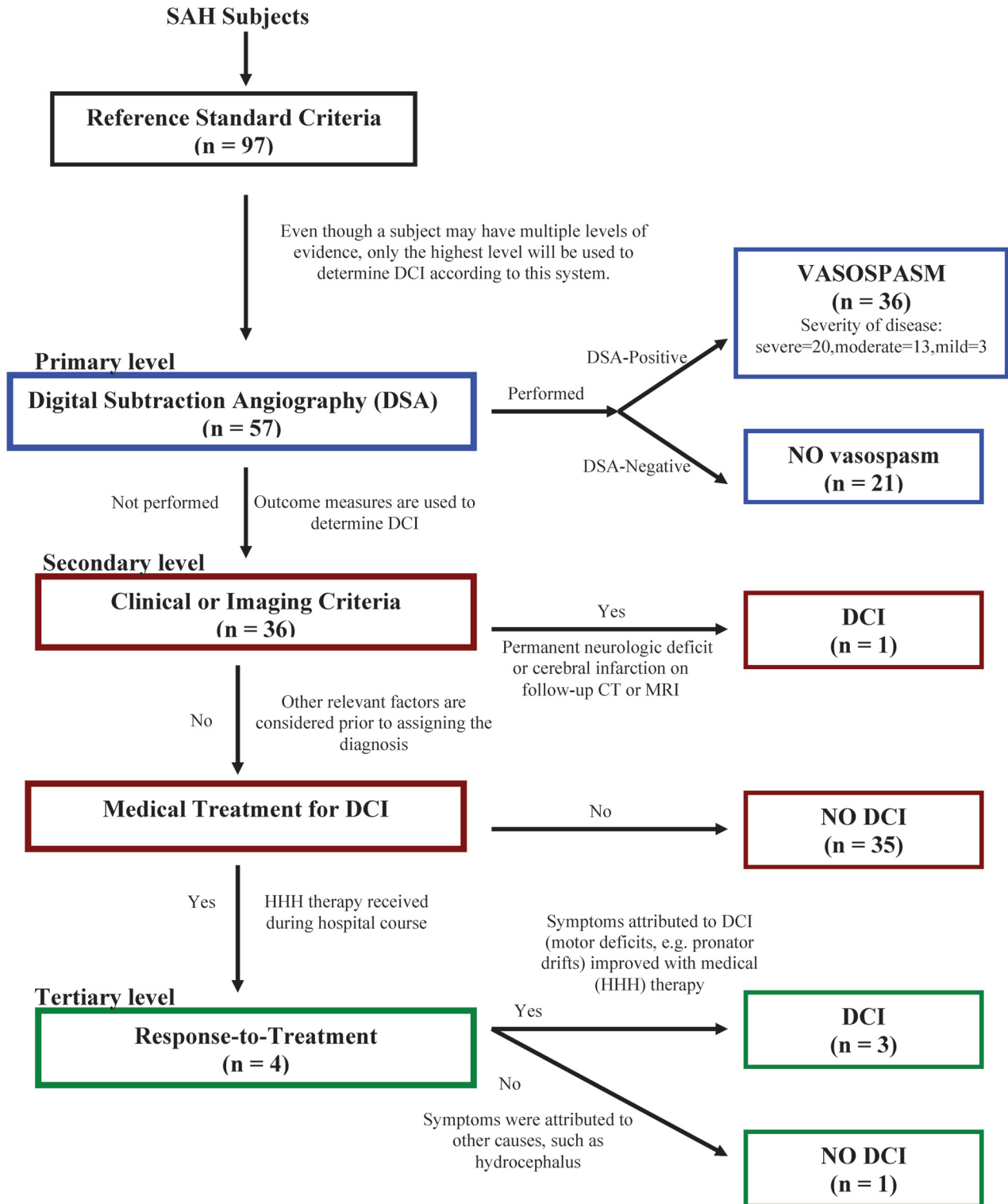
	Study Population (n = 97)			Subgroup ^a (n = 57)		
	All (n = 97)	DCI (n = 40)	No DCI (n = 57)	All (n = 57)	Vasospasm (n = 36)	No Vasospasm (n = 21)
Day of CTP (median)	7	7	7	7	7	7
Qualitative CTP deficit (%) (No.)	49 (48/97)	95 (38/40)	18 (10/57)	70 (40/57)	97 (35/36)	24 (5/21)
Timeframe between clinical deterioration CTP in days (median)	0	0	0	0	0	0
DSA (%) (No.)	59 (57/97)	90 (36/40)	37 (21/57)	100 (57/57)	100 (36/36)	100 (21/21)
Day of DSA (median)	8	8	10	8	8	10
Timeframe between CTP and DSA in days (median)	1	1	3	1	1	3

^a DSA as the reference standard.

On-line Table 2: Quantitative analysis of CTP parameters for the study population and subgroup

CTP Parameters	Study Population (n = 97)			Subgroup ^a (n = 57)		
	DCI (n = 40)	No DCI (n = 57)	P Value	Vasospasm (n = 36)	No Vasospasm (n = 21)	P Value
CBF (mL/100 g/min)	22.98	41.30	<.0001	22.67	43.76	<.0001
95% CI	(19.73-26.22)	(38.30-44.29)		(19.15-26.20)	(37.22-50.31)	
CBV mL/100 g	1.76	2.04	.0304	1.70	2.12	.0070
95% CI	(1.55-1.97)	(1.90-2.17)		(1.50-1.90)	(1.89-2.35)	
MTT (sec)	7.86	4.54	<.0001	7.70	4.55	<.0001
95% CI	(6.74-8.98)	(4.27-4.82)		(6.70-8.70)	(4.07-5.03)	

^a DSA as reference standard.



VASOSPASM
(n = 36)
Severity of disease:
severe=20, moderate=13, mild=3

NO vasospasm
(n = 21)

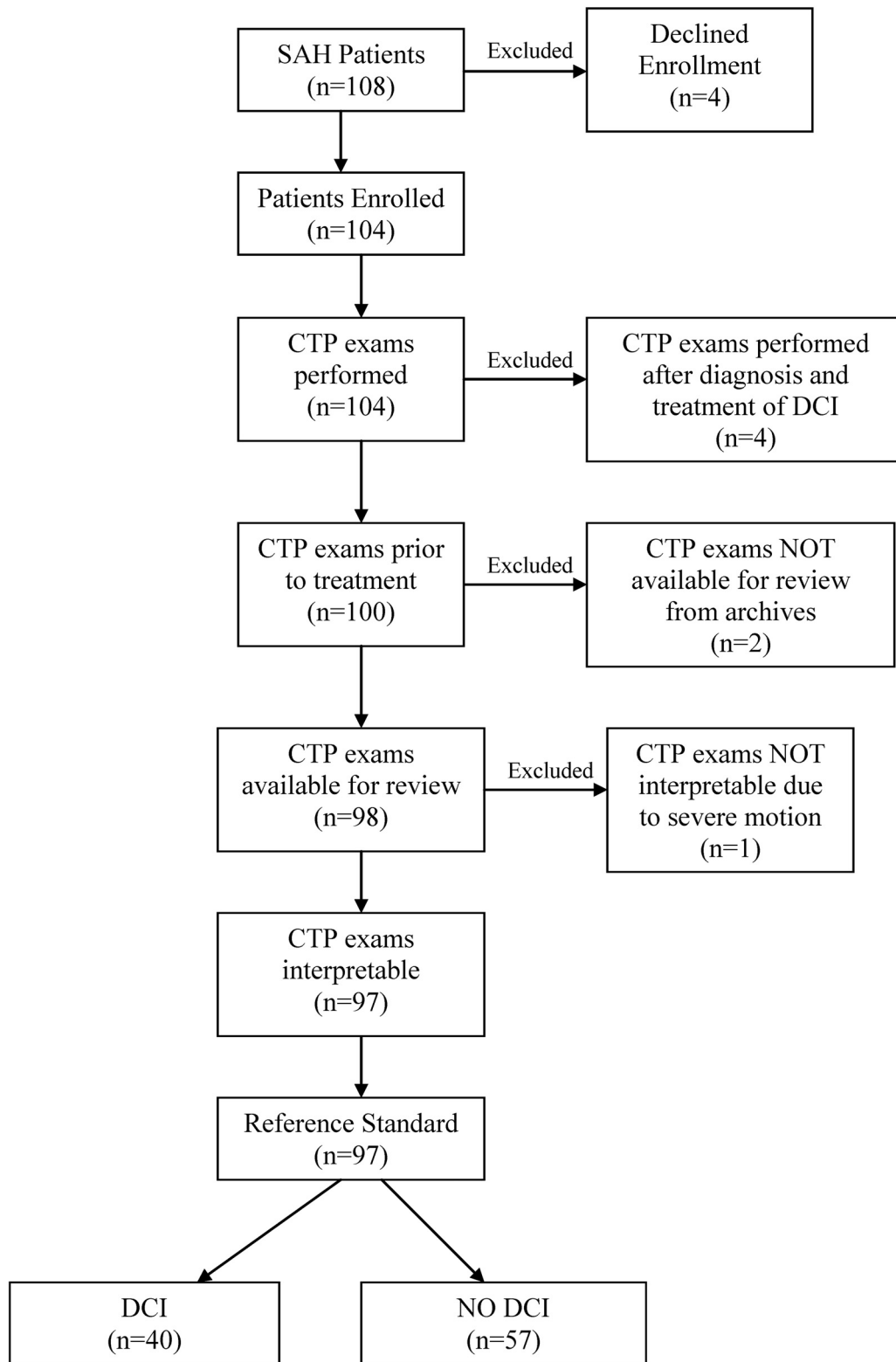
DCI
(n = 1)

NO DCI
(n = 35)

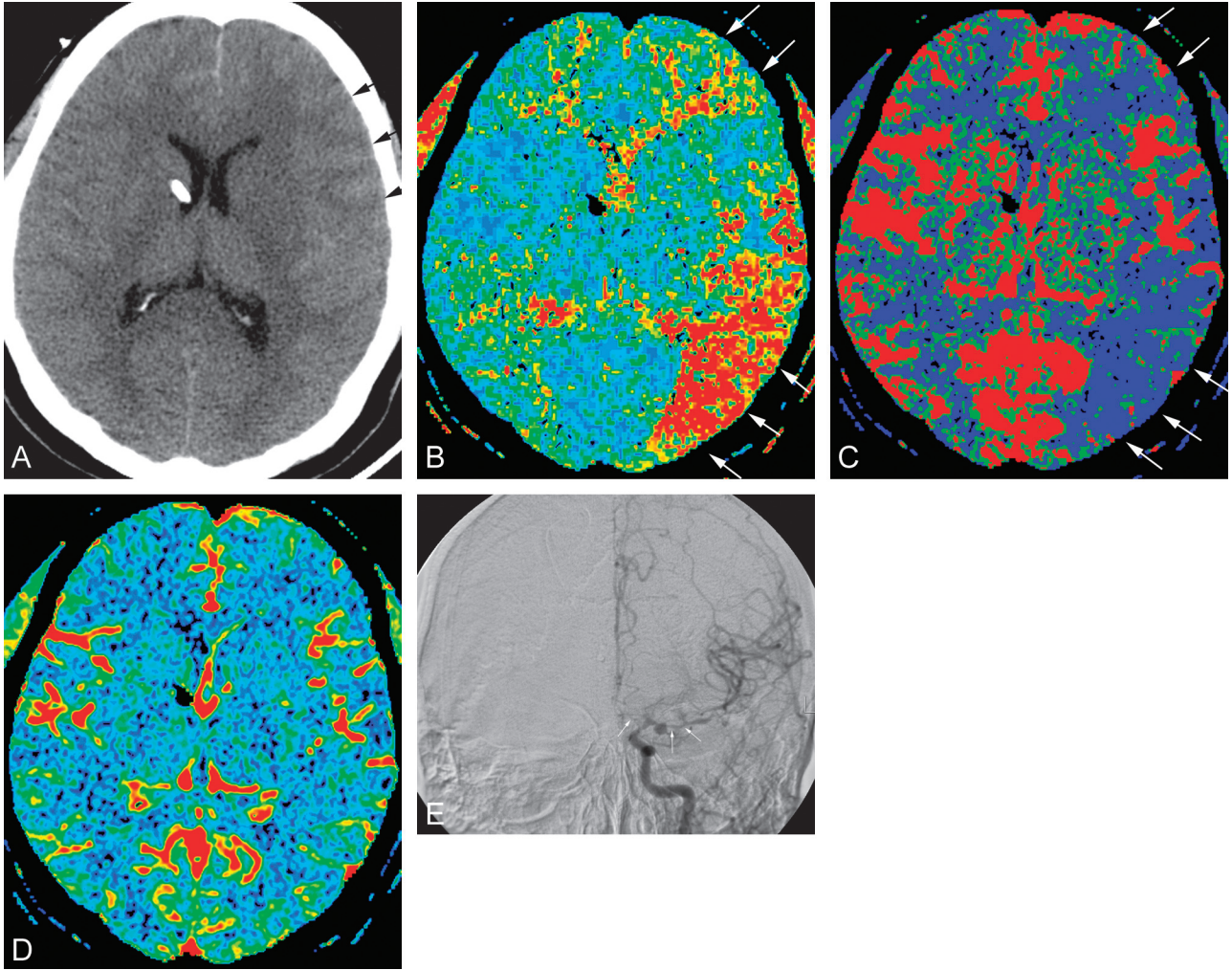
DCI
(n = 3)

NO DCI
(n = 1)

On-line Fig 1. Flow diagram for the reference standard. Note that the assignment of patients in the study by the reference standard at each level is in parentheses.



On-line Fig 2. Flow diagram for patient enrollment.



On-line Fig 3. A 30-year-old woman presented with acute SAH and underwent coil embolization of a left middle cerebral artery (MCA) ruptured aneurysm. The patient developed new right-sided upper-extremity weakness on day 7. *A*, Noncontrast CT of the head demonstrates minimal evolving SAH in the sulci (*arrows*). There is no new hemorrhage, infarction, or hydrocephalus to indicate another cause for the symptoms. *B*, The CTP MTT map demonstrates prolongation (red) in the transit time involving the left anterior and MCA territories (*arrows*). *C*, The CTP CBF map reveals matched areas of reduced (blue) cortical blood flow (*arrows*). *D*, The CTP CBV map has symmetric blood volume without a notable perfusion deficit. *E*, DSA anteroposterior view with injection of the left internal carotid artery performed on day 7 demonstrates marked narrowing of the ACA and MCA (*arrows*), representing severe vasospasm.