ONLINE SUPPLEMENT

A Comparison of Acute Hemorrhagic Stroke Outcomes in two Populations: The Crete-Boston Study

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Supplemental Methods

Imaging studies

All patients included in this study had CT-documented acute ICH. Brain imaging studies, obtained in the Cretan and Boston center, were compared directly regarding the location and volume of the ICH. For this, scans from Boston were sent to Crete in digital form, after removal of all patient-related information. The location of the ICH was independently determined (by EP, AN and CV) taking into consideration the following: hematomas located either entirely in the basal ganglia or in the thalamus or those extending to adjacent structures (cerebrum or brainstem) were included under basal ganglia and thalamus categories, respectively; hematomas spanning both the basal ganglia and the thalamus were included under the basal ganglia category; hemorrhages involving the cerebral lobes, the brainstem or the cerebellum were assigned to these categories only when confined to these structures. Hematoma volume was calculated using the ABC/2 formula, which has been shown to offer a good approximation of the actual hematoma volume.[1]

Assessment of adverse outcomes

Significant medical events during hospitalization of Cretan patients, such as pulmonary embolism, deep venous thrombosis, gastrointestinal tract hemorrhage, and infections requiring intravenous antibiotics, were recorded. Also, blood glucose levels were closely monitored.

Statistical analysis

Multiple logistic regression analysis was performed with backward selection in an initial dataset of variables that included sex, age (per 5-year increments), volume (in a logarithmic scale) and location (lobar versus non-lobar) of ICH, GCS on admission, hypertension, diabetes mellitus, coronary artery disease, antiplatelet, anticoagulant and statin use, smoking in the previous five years and dexamethasone administration.

Supplemental Tables

Table S1.A. Dexamethasone dosing of Cretan patients (n=340)	
Total DxM Dosage received (mg)	
Mean ± SD	113.8 ± 83.3
Treatment duration (days)	
Mean ± SD	9.0 ± 5.7
Initial DxM Dose:	
no of patients treated (%)	
8 mg	5 (1.8%)
12 mg	12 (4.2%)
16 mg	121 (42.6%)
24 mg	88 (31.0%)
32 mg	58 (20.4%)

Table S1.B. Patient characteristics and initial dexamethasone dosing				
	16 mg (n=121)	**24 mg (n=88)**	**32 mg (n=58)**	**P**
Age-yrs: Mean ± SD	72.3 ± 11.7	73.9 ± 12.5	73.4 ± 13.3	0.651
Male sex –no. (%)	69 (57.0%)	48 (54.5%)	37 (63.8%)	0.532
GCS score-mean ± SD	12.5 ± 3.4	11.1 ± 4.2	9.6 ± 4.4	<0.001
mRankin-mean ± SD	4.0 ± 1.2	4.3 ± 1.1	4.5 ± 1.0	0.012
Hematoma volume (ml)				
Mean ± SD	21.3 ± 34.0	38.0 ± 43.4	63.0 ± 67.5	<0.001

Table S2. Baseline characteristics of AHS patients on admission

	Crete-Dex (n=340)	**Boston-No Dex (n=510)**	**p**
Age (yr) -			
Mean ± SD	73.1 ± 12.1	72.7 ± 12.3	0.613
Male sex –no. (%)	204 (60·0%)	281 (55.1%)	0.157
Transfer from another hospital–no. (%)	45 (16.0%)	339 (68.5%)	<0.001
Time from onset to ER (h)-mean±SD	9.8 ± 18.1	9.1 ± 19.2	0.672
Time from onset to CT (h)-mean±SD	11.7 ± 18.2	10.7 ± 20.0	0.584
Admission SAP (mmHg)-mean±SD	169.1 ± 28.7	177.8 ± 37.2	0.001
Admission DAP (mmHg)-mean±SD	91.5 ± 18.7	93.1 ± 23.7	0.351
Admission Glucose (mg/dl)-mean±SD	150.5 ± 59.6	155.1 ± 63.9	0.357
GCS score-mean ± SD	11.6 ± 3.9	11.0 ± 4.6	0.062
Location of hemorrhage-no. (%)			0.097
Lobes	102 (30.0%)	194 (38.0%)	
Basal ganglia	134 (39.4%)	159 (31.2%)	
Thalamus	52 (15.3%)	71 (13.9%)	
Brainstem	12 (3.5%)	20 (3.9%)	
Cerebellum	28 (8.2%)	40 (7.8%)	
Multiple/IV	12 (3.5%)	26 (5.1%)	
Intraventricular blood –no. (%)	140 (41.9%)	252 (49.6%)	0.025
Hematoma volume (ml)			
Mean ± SD	35.1 ± 49·0	40.1 ± 50.3	0.109
Median (range)	14.7 (0.1-297.5)	18·4 (0.0-349.9)	
Hematoma max diameter (cm)			0.101
Mean ± SD	4.3 ± 2.1	4.6 ± 2.3	
Anticoagulants-no. (%)	34 (10.5%)	151 (29.6%)	<0.001
Antiplatelets-no. (%)	64 (19.8%)	254 (49.8%)	<0.001
Atrial Fibrillation-no. (%)	45 (13.9%)	143 (28.3%)	<0.001
Diabetes Mellitus -no. (%)	62 (19.1%)	109 (21.6%)	0.383
Hypertension-no. (%)	251 (76.5%)	421 (83.2%)	0.017
Coronary Artery Disease-no. (%)	40 (14.3%)	105 (21.4%)	0.016
Smoking-no. (%)	44 (19.0%)	73 (21.7%)	0.624
Statin use-no. (%)	20 (8.4%)	168 (33.9%)	<0.001
Previous ICH-no. (%)	30 (9.7%)	31 (6.1%)	0.060

Table S3. Intention to treat analysis			
Outcome	**Boston 2003-2009 (n=510)**	**Crete-all 1997-2010 (n=391)**	**P**
Death in hospital-no. (%)	194 (38.0%)	99 (25.3%)	<0.001
Death (30 days)– no. (%)	201 (39.4%)	95 (26.8%)	<0.001
Death (90 days)– no. (%)	223 (43.7%)	110 (33.7%)	0.004
Average in hospital stay Days (mean ± SD)	8.8 ± 11.8	15.2 ± 17.6	<0.001
Mod. Rankin on discharge (mean ± SD)	4.5 ± 1.5	3.9 ± 1.8	<0.001
Mod. Rankin on discharge-no. (%)			<0.001
0	7 (1.4%)	12 (3.6%)	
1	17 (3.5%)	38 (11.3%)	
2	23 (4.7%)	33 (9.9%)	
3	75 (15.2%)	42 (12.5%)	
4	142 (28.9%)	79 (23.6%)	
5	32 (6.5%)	32 (9.6%)	
6	196 (39.8%)	99 (29.6%)	
Serious adverse events-no. (%)			
Pulmonary Embolism	-	2 (0.6%)	
Gastrointestinal Hemorrhage	-	4 (1.3%)	
DVT	-	1 (0.3%)	
Infection		118 (34.1%)	

Includes all AHS patients admitted to the University hospital of Crete during the reporting period, irrespectively whether their IVDxM treatment status is known.

Table S4. In-hospital and 30 day-mortality according to the location of the hemorrhage

	In-hospital, n (%)			30-day, n (%)		
Location	**Crete**	**Boston**	**P**	**Crete**	**Boston**	**P**
Lobar	29/102 (28.4%)	63/194 (32.5%)	0.475	28/92 (30.4%)	66/194 (34.0%)	0.546
Basal Ganglia	**33/134 (24.6%)**	**74/159 (46.5%)**	**<0.001**	**31/119 (26.1%)**	**75/159 (47.2%)**	**<0.001**
Thalamic	**5/52 (9.6%)**	**17/71 (23.9%)**	**0.041**	**6/47 (12.8%)**	**20/71 (28.2%)**	**0.048**
Cerebellar	5/28 (17.9%)	11/40 (27.5%)	0.356	5/27 (18.5%)	11/40 (27.5%)	0.398
Brainstem	4/12 (33.3%)	13/20 (65.0%)	0.082	4/11 (36.4%)	13/20 (65.0%)	0.125
Multiple Territories/ Intra-ventricular	5/12 (41.7%)	16/26 (61.5%)	0.252	4/11 (36.4%)	16/26 (61.5%)	0.160

Table S5. Clinical outcomes					
	Boston (n=510) 2003-2009	**Crete (n=340) 1997-2010**		**Crete (n=190) 2003-2009**	
Blood Glucose (mg/dl) (mean ± SD)					
At 3 days post admission	138.7 ± 43.9	148.1 ± 58.3	0.038	155.8 ± 65.2	0.004
At 6 days post admission	136.7 ± 41.7	146.4 ± 69.1	0.083	154.9 ± 73.4	0.007
At 9 days post admission	150.9 ± 58.3	137.4 ± 68.9	0.080	140.1 ± 64.4	0.226
Serious adverse events-no. (%)					
Pulmonary Embolism	-	2 (0.7%)		1 (0.6%)	
Gastrointestinal Hemorrhage	-	3 (1.1%)		2 (1.2%)	
DVT	-	1 (0.3%)		1 (0.6%)	
Infection	-	105 (33.2%)		59 (33.1%)	

Supplemental Figures

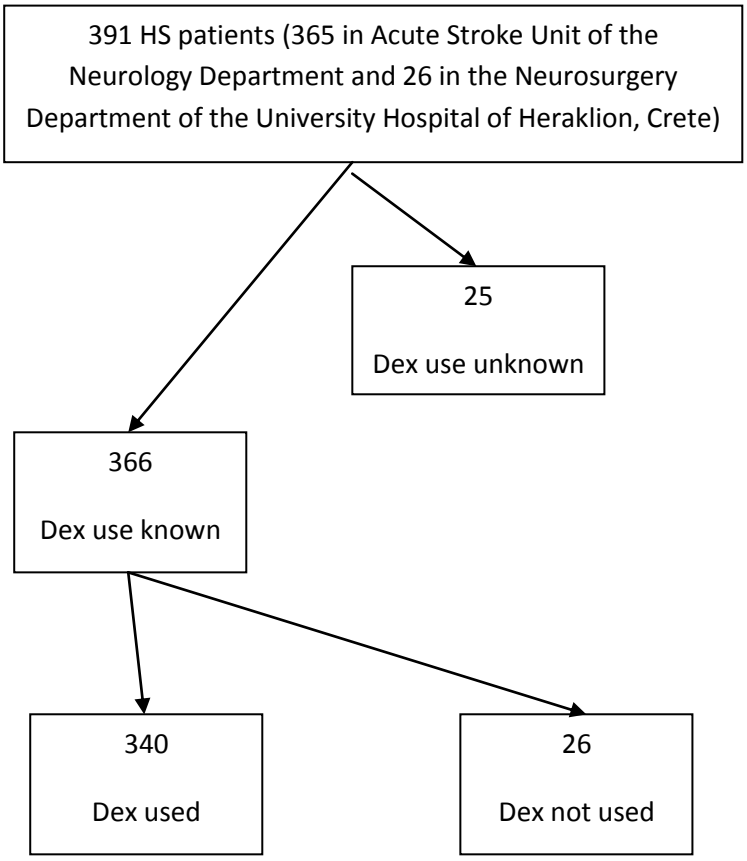

Figure S1. Flow chart of patients from Crete included in the analysis. Dex: Dexamethasone.

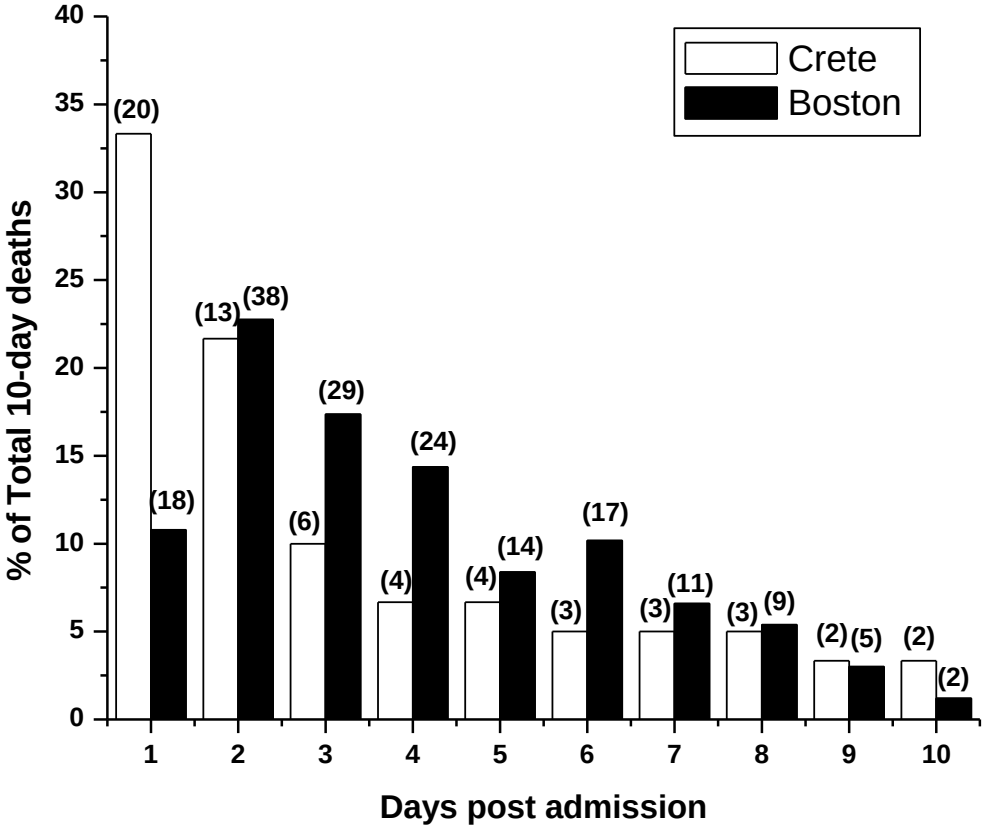

Figure S2. Daily death rates as percentage of the 10-day mortality in Crete and Boston (total number of deaths 60 and 167, respectively). Each successive doublet of columns represents different days post admission (shown under the x axis). The numbers in parentheses above each column represent the number of deaths.

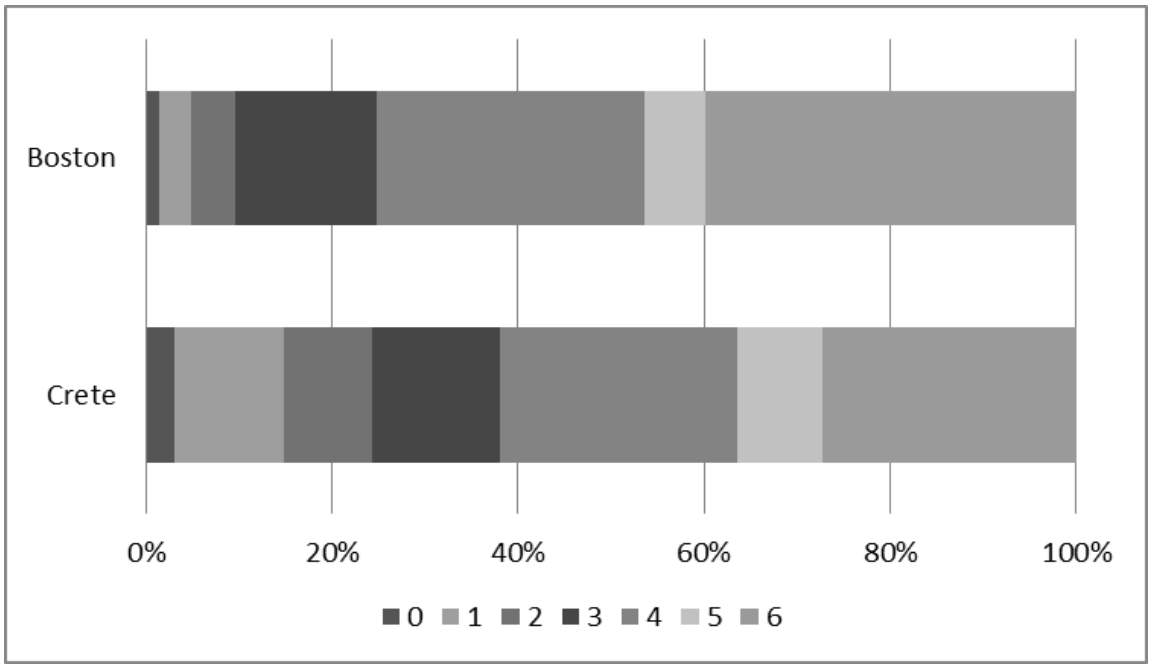

Figure S3. mRankin Scale on discharge for patients with AHS in Boston (upper panel) and Crete (lower panel).

Supplemental References

1) Kothari R, Brott T, Broderick J, Barsan W, Sauerbeck L, Zuccarello M, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke*. 1996; 27: 1304-1305.