

Clinical Presentation and Mortality of Spontaneous Intracerebral Hemorrhage Patients with Hypothyroidism



Alexandra L. Czap^{1*}, Ilene Staff Ph.D³ and Louise D. McCullough M.D.^{2,3}



1. University of Connecticut School of Medicine Farmington, CT; 2. University of Connecticut Health Center Departments of Neurology and Neuroscience, Farmington, CT; 3. Stroke Center at Hartford Hospital, Hartford, CT.

Background

- Intracerebral Hemorrhage (ICH) accounts for 10-15% of all strokes annually and is a leading cause of disability and mortality.
- Validated baseline predictors of ICH outcome include hematoma volume, ICH location, evidence of amyloid and advanced age.
- Hypothyroidism affects 5% of the US population. It is associated with an increased risk of atherosclerosis, vascular diseases and coagulopathies.
- Non-thyroidal illness syndrome (NTIS) or low T3 syndrome is extremely common. Leads to changes at all levels of the hypothalamic-pituitary-thyroid axis during stress and systemic illness which may increase mortality.
- Patients with hypothyroidism have an increased risk for ischemic stroke, but paradoxically have more favorable outcomes once a stroke occurs.
- The incidence of hypothyroidism, and its possible effects on clinical outcomes has not been reported in patients with ICH.

Methods

- Retrospective analysis of the Stroke Center at Hartford Hospital (SCHH) database from January 2004 through April 2010.



Figure 1. Selection of Spontaneous ICH Patient Population Flow Chart.

- ICH patients with ICD-9 code of hypothyroidism or history of hypothyroidism compared to non-hypothyroid counterparts admitted to the SCHH.
- Hypothyroid patients were subdivided into 2 groups based on receiving in hospital thyroid replacement medication or not.
 - Treatment medications include: levothyroxine (Synthroid, Levothroid, Levoxyl, Tirosint, Triostat, Unithroid), liothyronine (Cytomel), porcine thyroid (Armour Thyroid, Nature-Throid, NP Thyroid), and liotrix (Thyrolar).
- Parameters Assessed:
 - Stroke severity based on ICH Score, NIH Stroke Scale (NIHSS), Glasgow Coma Score (GCS).
 - Stroke outcome based on NIHSS change, environmental change, modified Barthel Index (mBI), in-hospital mortality and survival assessment over 3 and 12 months.
- Groups were first analyzed using crosstabs and chi-square tests. For the multiple comparisons, oneway ANOVA with Scheffe and univariate log regression. Multivariate logistic regression analysis was performed for outcome measures.

Patient Demographics

	Non-Hypothyroid (n=432)	Hypothyroid with meds (n=36)	Hypothyroid without meds (n=25)	P-value Between Groups
Age (years)	70.4 ± 14.0	75.7 ± 11.9	78.4 ± 9.4	.002
Gender				.006
Male	53.6%	27.8%	40.0%	
Female	46.4%	72.2%	60.0%	
History of				
Hypertension	77.7%	75.0%	80.0%	NS
DM	24.6%	22.2%	36.0%	NS
Heart Dx	31.3%	33.3%	32.0%	NS
Stroke	17.2%	8.3%	24.0%	NS
TIA	7.2%	8.3%	16.0%	NS
Smoking	15.8%	16.1%	13.6%	NS
Medications				
Aspirin	28.7%	25.0%	56.0%	.012
Coumadin	13.2%	13.9%	12.0%	NS
Statins	30.6%	47.2%	48.0%	.030
ACE I	22.9%	8.3%	20.0%	NS
Origin Location				.003
Home	19.5%	22.2%	12.0%	
ALF	1.4%	11.1%	0.0%	
ECF	3.7%	0.0%	4.0%	
Transfer Hospital	16.9%	30.6%	12.0%	
Not Coded	58.5%	36.1%	72.0%	
Blood Pressure				
Systolic (mmHg)	180.8 ± 36.7	173.7 ± 37.7	172.6 ± 36.4	NS
Diastolic (mmHg)	97.3 ± 23.1	90.9 ± 23.2	91.9 ± 26.1	NS
WBC count (x10 ³ /uL)	9.6 ± 3.9	10.5 ± 5.9	9.4 ± 3.3	NS
Glucose (mg/dl)	148.5 ± 67.6	144.3 ± 78.7	138.4 ± 48.7	NS
Coagulation Studies				
INR	1.3 ± 0.9	1.3 ± 0.7	1.3 ± 0.7	NS
PT (sec)	13.5 ± 4.8	13.8 ± 5.1	14.3 ± 4.9	NS
PTT (sec)	27.1 ± 6.0	27.3 ± 5.2	26.7 ± 4.8	NS

Results

	Non-Hypothyroid (n=432)	Hypothyroid with meds (n=36)	Hypothyroid without meds (n=25)	P-value Between Groups
ICH Score	1.65 ± 1.3	1.43 ± 1.1	1.71 ± 1.2	NS
Volume Pt	37.3%	20.0%	29.2%	NS
Intravent. Pt	44.5%	33.3%	41.7%	NS
Age Pt	31.0%	44.4%	60.0%	.004
Infratent. Pt	11.7%	22.2%	8.3%	NS
GCS Pt (s)	34.7%	20.6%	28.0%	NS
NIHSS Admit	9.9 ± 7.5	5.9 ± 5.9	10.0 ± 8.1	.011
Mortality				NS (.066)
In Hospital	31.6%	13.9%	24.0%	
3 months	39.4%	33.3%	40.0%	
12 months	42.0%	41.7%	40.0%	
Modified Barthel				
PreAdmit	19.2 ± 2.1	19.0 ± 1.6	17.1 ± 4.9	.002
Admit	10.5 ± 7.1	10.0 ± 7.7	8.9 ± 6.5	NS
3 months	15.9 ± 5.9	17.0 ± 4.0	14.5 ± 5.6	NS
12 months	16.1 ± 5.7	15.7 ± 3.7	--	NS
Discharge Location				NS
Home	19.0%	25.7%	8.0%	
Acute Rehab	14.3%	8.6%	20.0%	
Subacute Rehab	28.2%	40.0%	40.0%	
ECF, Hospice, Death	38.5%	25.7%	32.0%	
Environment Change				0.19
Improve/Same	11.4%	32.0%	4.5%	
Worse	21.1%	16.0%	13.6%	
Not Coded	67.5%	52.0%	81.8%	
Discharge to Worse	75.5%	68.6%	72.0%	NS
NIHSS Discharge	5.1 ± 6.0	5.6 ± 6.7	4.3 ± 5.5	NS
Change in NIHSS	-2.4 ± 4.4	0.6 ± 4.1	-1.1 ± 1.9	.037

Stroke Severity

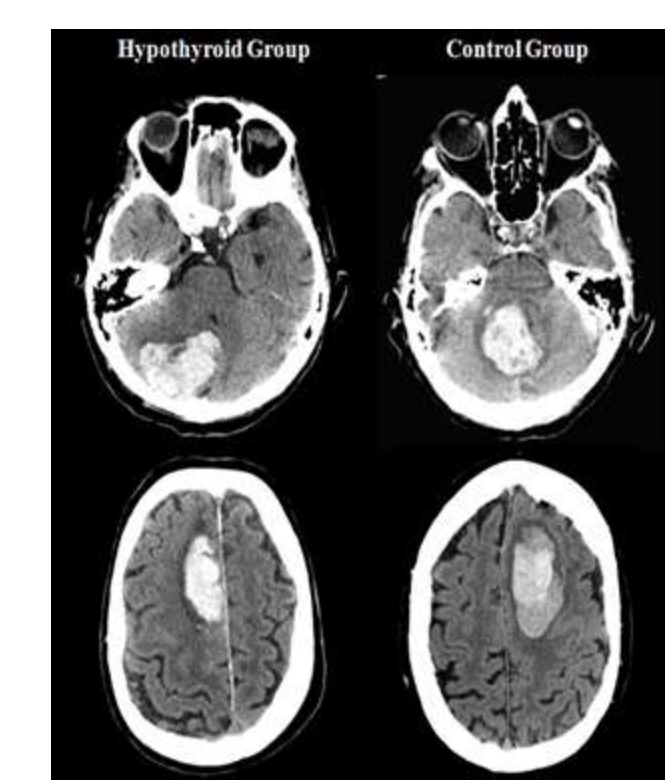
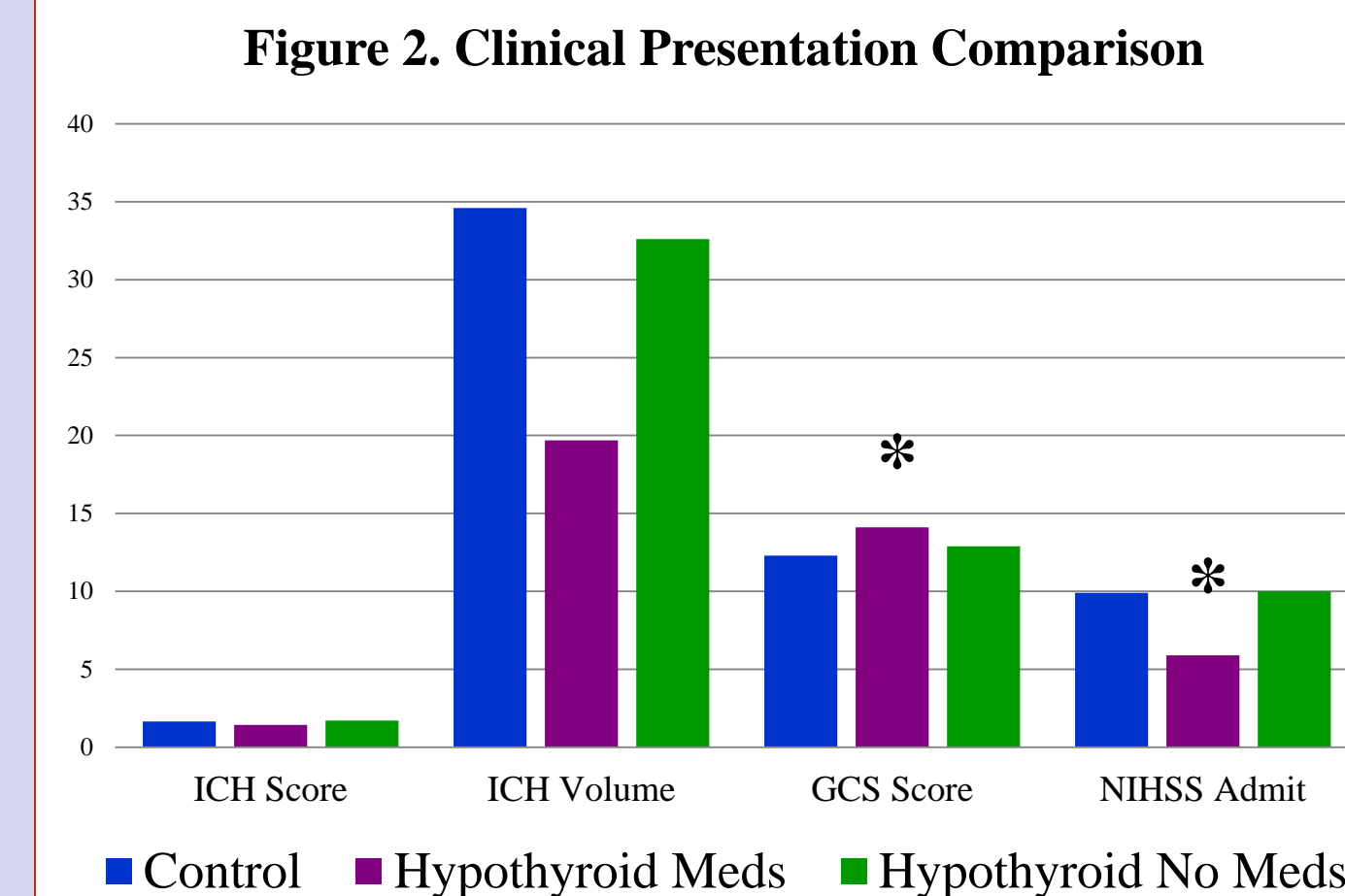
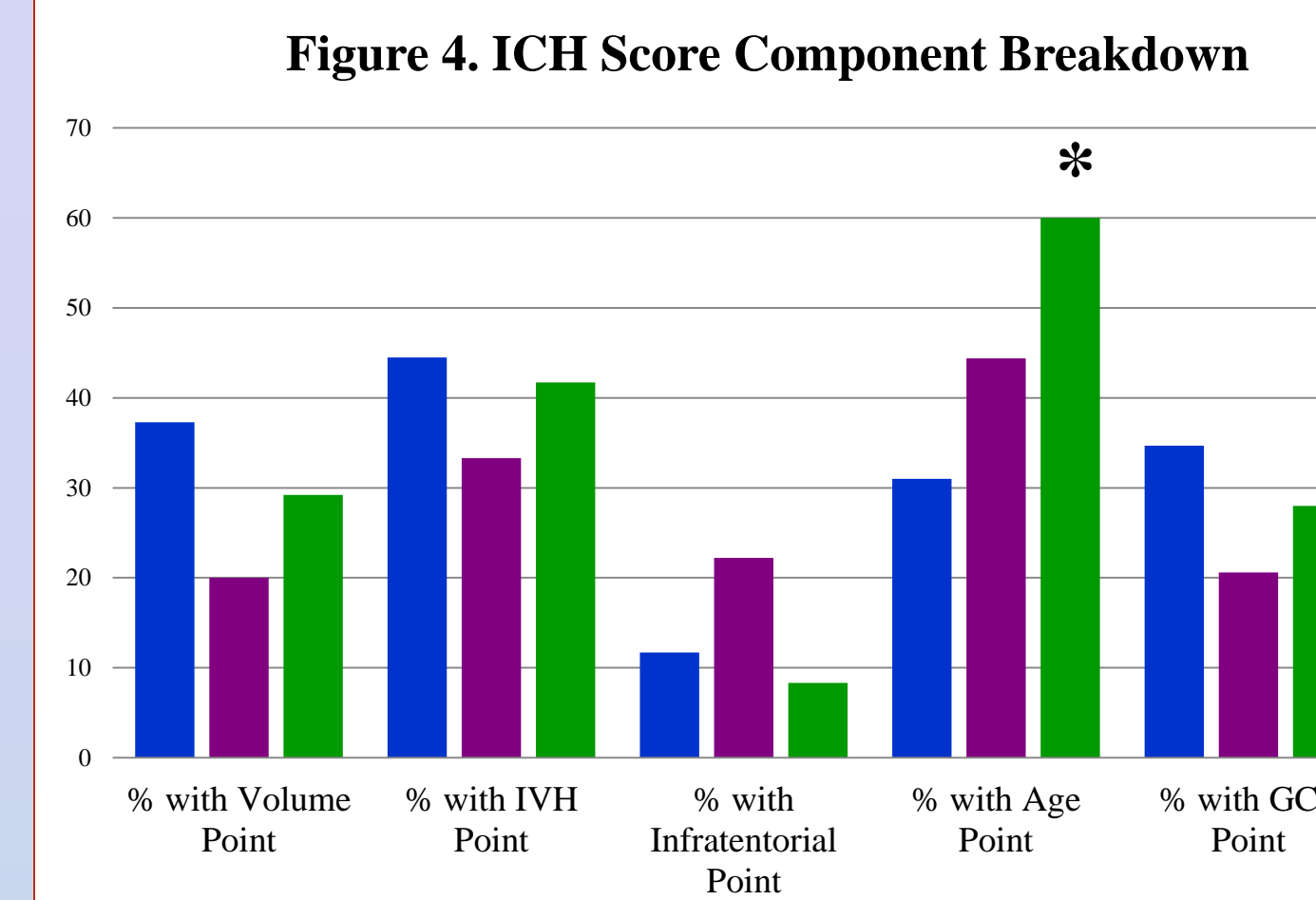


Figure 3. Comparison of Imaging Studies
ICH Volume calculated using formula (AxBxC)/2; where A = longest axis (cm), B = longest axis perpendicular to A (cm) and C = # of slices x slice thickness (cm).



	ICH Score
GCS Score	3-4: 2, 5-12: 1, 13-15: 0
ICH Volume (cc)	≥ 30: 1, < 30: 0
Intraventricular Hemorrhage	Yes: 1, No: 0
Infratentorial Origin	Yes: 1, No: 0
Age (years)	≥ 80: 1, < 80: 0
Total ICH Score	0-6

Multiple Comparison Analysis

	Non-Hypothyroid vs Hypothyroid with meds	Non-Hypothyroid vs Hypothyroid without meds	Hypothyroid with meds vs Hypothyroid without meds
ICH Score	NS	NS	NS
ICH Volume	NS	NS	NS
GCS Score	.021	NS	NS
NIHSS Admit	.011	NS	NS
Mortality			
In Hospital	.033	NS	NS
3 months	NS	NS	NS
12 months	NS	NS	NS
Modified Barthel			
PreAdmit	NS	.002	.035
Admit	NS	NS	NS
3 months	NS	NS	NS
NIHSS Change	.045	NS	NS

In Hospital Mortality Multivariate

	B	S.E.	Wald	df	Sig.	Exp(B)
Non-Hypothyroid			4.416	2	.115	
Hypothyroid with Meds	-1.031	.501	4.236	1	.040	.357
Hypothyroid no Meds	-.261	.492	.281	1	.596	.770
Gender	.535	.208	6.732	1	.009	1.713
Age	.012	.008	2.667	1	.102	1.013
ASA	-.601	.236	6.470	1	.011	.548
Constant	-2.220	.632	12.333	1	.000	1.09

Hypothyroid variable significant.

Age, gender, aspirin use additional significant variables.

Stroke Outcome

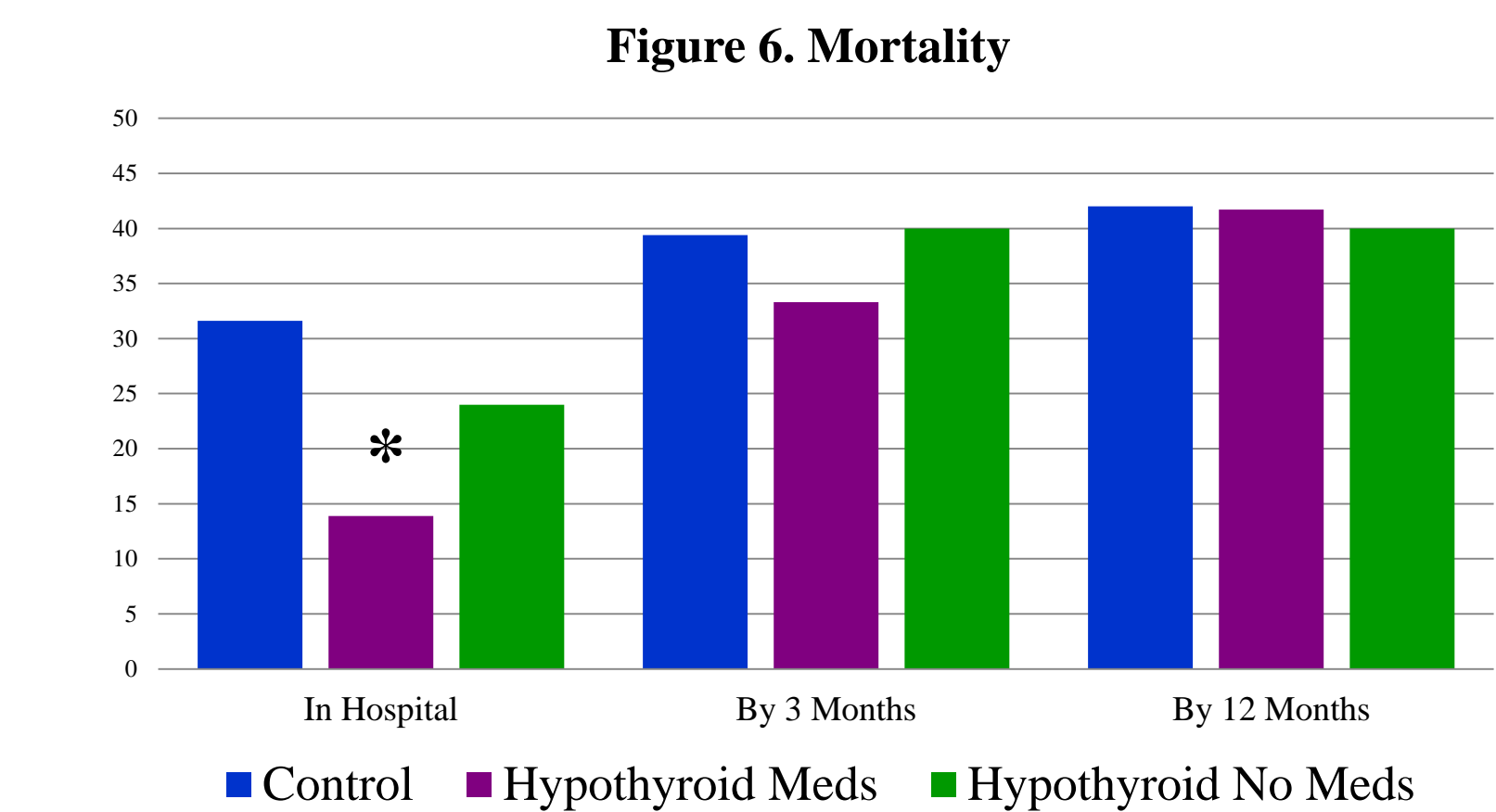


Figure 7. Environment Change

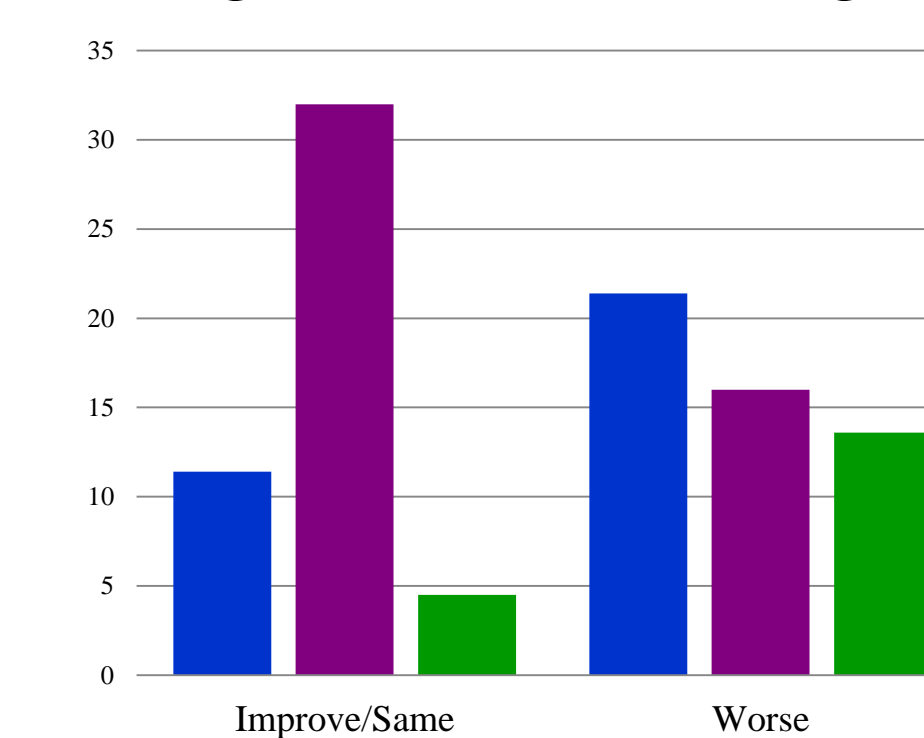
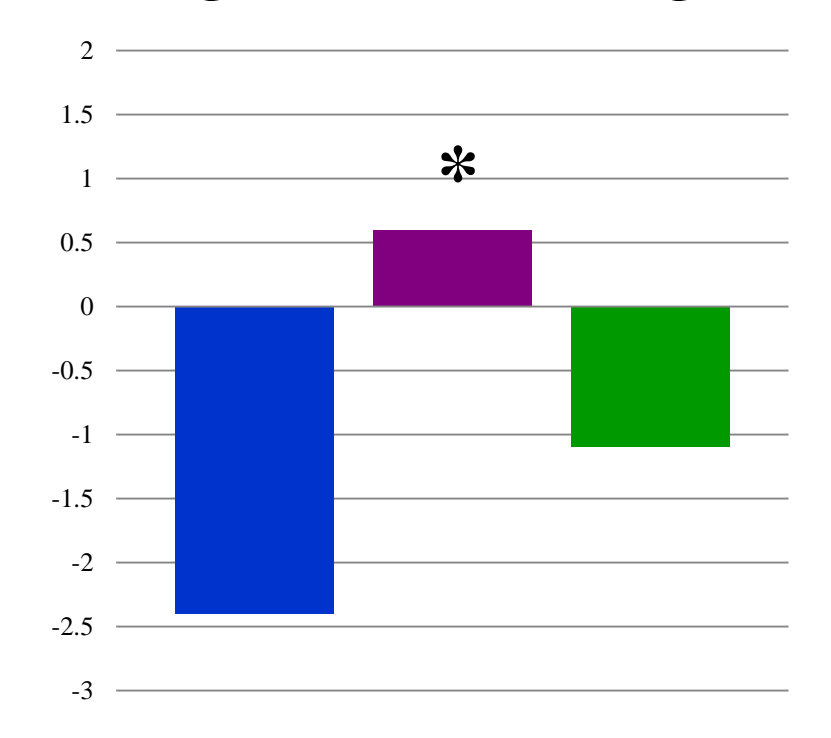


Figure 8. NIHSS Change



Conclusions

- ICH patients with a history of hypothyroidism that received in-hospital hormone replacement had less severe clinical deficits on presentation as seen by lower NIHSS and higher GCS when compared to the euthyroid control group.
- Lower ICH volumes were seen in the hypothyroid patients which likely contributes to improved acute outcomes.
- Hypothyroid patients with in-hospital thyroid replacement had decreased in hospital mortality and better discharge disposition when compared to the euthyroid group.
- Hypothyroidism and physiological normalization of the hypothalamic-pituitary-thyroid axis with thyroid replacement improved outcomes after ICH. Treatment of ICH patients who demonstrate a decrease in thyroid function as a result of acute illness may improve mortality. Studies examining TSH levels are ongoing.

Funding Sources: University of Connecticut School of Medicine, Hartford Hospital Small Grant Program

Acknowledgements: Dr. Lauren Sansing, Gil Fortunato
IRB Approval: "Variability in stroke outcomes across the population" LEE0018889