Using Radiological Data to Estimate Ischemic Stroke Severity

Jason J. Sico, MD;[1,2,3] Michael S. Phipps, MD;[4,5];John Concato, MD;[3,6,7] Cynthia Brandt, MD, MPH; [8] Carolyn K. Wells, MPH;[3,7] Albert C. Lo, MD, PhD;[9,10] Stephen E. Nadeau, MD;[11,12] Linda S. Williams, MD;[13,14] Mark Gorman, MD;[15] John L. Boice, MD;[17] and Dawn M. Bravata, MD;[13,16]

AFFILIATIONS

1. Neurology Service, VA Connecticut Healthcare System, West Haven, CT
2. Department of Neurology and Center for NeuroEpidemiological and Clinical Neurological Research, Yale University School of Medicine, New Haven, CT
3. Department of Internal Medicine, Yale University School of Medicine, New Haven, CT
4. Department of Neurology, University of Maryland, Baltimore, Maryland
5. Department of Epidemiology and Public Health, University of Maryland, Baltimore, Maryland
6. Medicine Service, VA Connecticut Healthcare System, West Haven, CT
7. Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System, West Haven, CT
8. Department of Anesthesiology, Yale University School of Medicine, New Haven, CT
9. Department of Neurology, Warren Alpert School of Medicine and Departments of Neurosciences, Community Health, and Engineering at Brown University, Providence, RI
10. Providence Veterans Administration Medical Center, Providence, RI
11. Neurology Service, Malcolm Randall VA Medical Center, Gainesville, FL
12. Department of Neurology, University of Florida School of Medicine, Gainesville, FL
13. VA Health Services Research and Development (HSR&D) Center for Health Information and Communication (CHIC) and the HSR&D Stroke Quality Enhancement Research Initiative (QUERI); Richard L. Roudebush VA Medical Center, Indianapolis, IN
14. Department of Neurology, Indiana University School of Medicine, and Regenstrief Institute, Indianapolis, IN
15. Department of Neurology, University of Vermont School of Medicine, Burlington, VT
16. Department of Internal Medicine, Indiana University School of Medicine, and Regenstrief Institute, Indianapolis, IN
17. Medical Service, Boise VA Medical Center

GRANT SUPPORT

This project was supported by the Department of Veterans Affairs (HSR&D CDA 11-262 and

Merit IIR-01-10403) and Max Patterson Stroke Research Fund at Yale University.

CORRESPONDENCE

Jason J. Sico, MD

950 Campbell Avenue

VA Connecticut Healthcare System, Attn: Neurology – 127

This is the author's manuscript of the article published in final edited form as:
Sico, J. J., Phipps, M. S., Concato, J., Brandt, C., Wells, C. K., Lo, A. C., … Bravata, D. M. (2016). Using Radiological Data to Estimate Ischemic Stroke Severity. Journal of Stroke and Cerebrovascular Diseases, 25(4), 792–798. http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2015.12.002

West Haven, CT 06516

Telephone: (203) 932-5711, X-4724

Fax: (203) 937-3464

E-mail: Jason.sico@yale.edu

RUNNING TITLE

Radiographic Predictors of Stroke Severity

Goal: Risk-adjusted post-stroke mortality has been proposed for use as a measure of stroke care quality. Although valid measures of stroke severity (e.g., the NIH Stroke Scale) are not typically available in administrative datasets, radiology reports are often available within electronic health records. We sought to examine whether admission head computed tomography data could be used estimate stroke severity.

Materials and Methods: Using chart review data from a cohort of acute ischemic stroke patients (1998-2003), we developed a radiographic measure (Brain Imaging Score) of stroke severity in a two-thirds development set and assessed in a one-third validation set. The retrospective NIH Stroke Scale was dichotomized as: mild/moderate (<10) and severe (≥10). We compared the association of this radiographic score with NIH Stroke Scale and in-hospital mortality at the patient-level.

Findings: Among 1348 stroke patients, 86.5% had abnormal findings on initial head computed tomography. The c-statistic for the Brain Imaging Score for modeling severe stroke (development, 0.581; validation, 0.579) and in-hospital mortality (development, 0.623; validation, 0.678) were generated.

Conclusion: Although the c-statistics were only moderate, the BIS provide significant risk stratification information with a two-variable score. Until administrative data routinely includes a valid measure of stroke severity, radiographic data may provide information for use in risk adjustment.

INTRODUCTION

Stroke severity is one of the strongest predictors of post-stroke mortality at the patient level.[1-3] The National Institutes of Health Stroke Scale (NIHSS) is a valid and commonly used prospective measure of stroke severity. The addition of the NIHSS to claims-based 30-day acute ischemic stroke hospital mortality risk models has been shown to improve model discrimination and change mortality performance rankings for hospitals care for Medicare beneficiaries.[4] Healthcare organizations, such as the Centers for Medicare and Medicaid Service (CMS), routinely use 30-day mortality following acute ischemic stroke to evaluate hospital care quality.[5] Unfortunately, the NIHSS is neither documented in routine clinical practice for all stroke patients and nor is currently readily accessible in administrative data.

Predicting stroke severity using commonly gathered and readily accessible data from ischemic stroke patients could be useful for risk adjustment of post-stroke mortality. The retrospective NIHSS (rNIHSS) can be constructed from chart review data with excellent reproducibility and validity;[3] however, the neurological examination data needed to construct an rNIHSS are also not available in administrative data. Even within the robust Department of Veterans Affairs (VA) electronic medical record system, the rNIHSS cannot be efficiently extracted from chart data. In contrast, brain imaging is obtained routinely during the evaluation of patients with stroke.[6] Certain findings on initial head computed tomography (CT; e.g., hypodensity) have been associated with poor stroke outcomes (e.g., stroke severity and mortality).[7-11] Radiology reports of brain imaging studies are readily accessible across VA Medical Centers (VAMC), and therefore could be text-mined, potentially providing a means for obtaining information about stroke severity.

We sought to examine whether admission brain imaging data could be used to estimate stroke severity (based on the rNIHSS). As a secondary analysis, we evaluated the association of radiographic data with in-hospital mortality. We hypothesized that we could identify radiographic features that were associated with severe strokes and that the presence of those radiographic features would be associated with an increased risk of in-hospital mortality.

Materials and Methods

Patients and Setting

This study is a secondary analysis of medical record review data from the Quality Evaluation in Stroke and Transient Ischemic Attack (TIA; QUEST) study.[12] Briefly, this retrospective cohort included patients who were admitted with ischemic stroke or TIA at any of three VA or two non-VA hospitals, during the years 1998-2003, if they had a neurological symptom onset within 2 days of admission, had a neurological deficit on admission (rNIHSS ≥ 2), and were at least 18-years old. Patients were excluded from the QUEST study if they were residing in a skilled nursing facility at the time of stroke symptom onset, were already admitted to the hospital at the time of stroke symptom onset, were transferred from another acute care facility, or were not admitted to the hospital. For this study, we restricted the analysis to stroke patients, and also excluded patients who were: without brain imaging (n=1) and whose brain imaging results were not known (n=3). Since most patients receive a head CT at initial presentation over other imaging modalities, we excluded patients when the first brain imaging study obtained was not a CT (n=14; Figure 1).

Definitions

Brain imaging data were abstracted directly from radiology reports of the initial brain CT. A review of our coding algorithm is available as (Table 1). Stroke onset-to-initial CT time was

available in 57% of the cohort and indicated that 87% of studies were performed within 24 hours (Table 2). Based on a literature review and clinical practice, location of infarct, presence of edema, and any evidence of new or old hemorrhage were considered *a priori* as potential variables in the analysis.[8;9;13-17] As symptom onset cannot be reliably extracted from existing administrative data or unstructured chart review data, we did not take into account the time interval between symptom onset to brain imaging. Because infarct volume was not routinely available in radiology reports, we were unable to assess this variable. We based infarct location on: vascular distribution (e.g., middle cerebral artery [MCA]), individual lobe(s) involved (e.g., frontal), and other location (e.g., thalamus; see Figure 1). The variables that were considered in the analysis are listed under "Radiographic Findings" in Table 1. A rNIHSS was calculated for each patient from admission neurological examination data. We dichotomized stroke severity on the basis of the rNIHSS into mild/moderate (<10) and severe (≥10), as patients with severe strokes are less likely to have a better clinical outcome.

Development and Validation

We divided the cohort into a random two-third sample for development, with the other one-third retained for validation. Logistic regression models with backward elimination were constructed in the development cohort to model both rNIHSS ≥10 and in-hospital mortality. When modeling rNIHSS ≥10, only two variables remained after backward elimination with a significance of $p<0.05$: hypodensities in the MCA distribution and in the temporal lobe. Presence of edema was the last variable eliminated at a $p<0.0540$. Because of this observed relationship to rNIHSS and because the previous literature has suggested that brain edema is associated with increased stroke severity, we initially kept the edema variable in the model.[8] However, the inclusion of edema did not improve discrimination of stroke severity; therefore we removed it

from the scoring system. We used the adjusted odds ratios (ORs) from the MCA and temporal lobe hypodensity variables to construct a scoring system that ranged from 0-3 (referred to in this manuscript as the Brain Imaging Score, or BIS; see Table 1 for listing of candidate radiographic variables). We then tested the BIS in our validation cohort. C-statistics were used to assess model performance.

Missing data were rare; imputations were not made for missing data. All analyses were conducted using SAS 9.2 (Cary, North Carolina). Institutional Review Board (IRB) approval was obtained for this research.

Results

Among the 1348 patients with a head CT, 1166 (86.5%) had an abnormal study; radiographic findings included focal hypodensity, edema, hemorrhage, and periventricular white matter disease (Table 3). Focal hypodensity (development: n=93 [10.2%]; validation: n=44 [10.1%]) or edema (development: n=72 [7.9%]; validation: n=37 [8.6%]) occurred uncommonly.

The development and validation sets were similar with regard to patient demographics, past medical history, proportion with severe stroke (35.2% versus 35.6%), the presence of edema, and in-hospital mortality (6.0% versus 7.6%) within tiers of NIHSS with the exception that patients in the development cohort with less severe stroke were more often male (65.0% vs. 51.9%; $p<0.0001$). When comparing patients with mild/moderate versus severe strokes within the development set, patients with severe strokes were older (73.1 versus 70.5 years; $p=0.004$) with congestive heart failure (17.7% versus 10.6%;$p=0.002$), atrial fibrillation (27.0% versus 15.0%; $p<0.0001$) and higher modified APACHE-III scores (12.4 versus 8.7; $p<0.0001$). Imaging obtained from patients with severe strokes more frequently demonstrated involvement

of: middle cerebral artery (16.5% versus 2.9%), parietal lobe (13.7% versus 5.6%), frontal lobe (11.8% versus 4.9%), temporal lobe (8.4% versus 2.2%; p<0.0001 for all).

The timing from symptom onset to head CT was available in 763 patients. A fairly large proportion of patients received relative early CT scans after symptom onset. For example, patients with rNIHSS:<10 (n=453; 23.8%) and with rNIHSS≥10 (n=310;41.9%) received a head CT less than three hours from symptom onset (Table 2).

The association between the BIS and both severe stroke (rNIHSS ≥10) and in-hospital mortality are shown in Table 2. As the BIS increased from 0 to 3, the proportion with severe strokes increased from 31.1% to 82.4% (p for trend=<0.0001) in the development set; a similar trend was observed in the validation cohort (31.6% to 66.7%;p for trend=<0.0001;Table 4). The gradient was monotonic in the development set but not in the validation set. As the BIS increased from 0 to 3, the proportion of patients dying during the hospital stay increased from 4.5% to 23.5% (p for trend=<0.0001) in the development set; a similar trend was observed in the validation set (4.6% to 44.4%; p for trend=<0.0001); the gradient was also not monotonic in the validation set.

The c-statistic for the BIS was similar between the development and the validation sets in modeling rNIHSS≥10 (0.581 and 0.579, respectively) and in-hospital mortality (0.623 and 0.678, respectively). By way of comparison, in this cohort, the c-statistic for the association of rNIHSS with in-hospital mortality was 0.84.

Discussion

This study demonstrates that a simple approach based on radiographic findings on initial head CT provide considerable stroke severity stratification utilizing a few variables. Although

only a minority of patients had focal hypodensities on admission imaging, the BIS was associated with both severe strokes and in-hospital mortality.

Initial stroke severity, as measured by the NIHSS, strongly predicts important clinical measures as length of hospitalization, functional outcomes, discharge destination and mortality.([6;17]) A minority of stroke patients receiving their care at VA (27.7%)([18]) and Get With the Guidelines Stroke-Participating hospitals (45.1%)([4]) had a documented NIHSS within the medical record, whereas stroke patients at these facilities commonly received brain imaging at presentation (95.0%).([18])

Because the NIHSS or other validated measure of stroke severity are not typically available from administrative data, whereas the results from radiographic reports are routinely available, radiographic reports may be amenable to such data acquisition methods as natural language processing. Thus, radiographic-based approaches to estimating stroke severity may provide a feasible solution to the problem of not having a measure of stroke severity for risk adjustment in administrative data. Although some stroke patients have normal early head CT results, the prevalence of early ischemic changes on head CT has been reported to range from 31% to 87%.([13;14]) ([19])

Several studies have examined brain imaging findings on initial head CT and their prognostic utility in predicting stroke severity and mortality.([2;8]) In the National Institute of Neurological Disorders and Stroke (NINDS) recombinant-tissue plasminogen activator (rt-PA) Trial, the authors found that early ischemic changes were associated with worse baseline NIHSS.([7]) Further, the presence of edema or mass effect on initial head CT not only increased the risk of hemorrhagic conversion after rt-PA, but also increased mortality. Others have reported that as the degree of hypoattenuation or hypodensity increased, stroke severity

worsened.(9) In the European Cooperative Acute Stroke Study (ECASS), the presence and extent of a hypodensity on first head CT was associated with both severe disability. Using first head CT data from 12,550 participants in the International Stroke Trial, visible infarction independently predicted death within 14 days.(14) This prior work, demonstrating that head CT scan results can prognosticate outcomes, lends support to the notion that radiographic reports can serve as surrogates for stroke severity to be used in risk adjustment.

It is not surprising that radiographic infarcts within the MCA distribution (either alone or with temporal lobe involvement) were associated with both rNIHSS and mortality in our data. Many components of the NIHSS can be referred to lesions within the MCA distribution.(20) Vascular lesions visible within the MCA distribution via angiography are predictive of NIHSS scores ≥10.(21) Lesions on the CT scan within the MCA territory are associated with increased mortality, especially if more than one-third of its distribution is involved.(8) We were not able to comment in this study on the percentage of MCA involvement because this estimation was not routinely documented in radiographic reports.

The association between temporal lobe involvement and stroke severity, and especially the association with in-hospital mortality was relatively unexpected. Some previous studies have associated temporal lobe hypodensities with poor outcomes. For example, Kreiger et al found that the presence of a temporal lobe hypodensity was associated with increased risk of fatal brain swelling.(22) Also, right hemisphere insular cortex strokes have been associated with increased rates of arrhythmias and disinhibition of sympathetic control dampening, which may lead to higher mortality rates.(23;24)

Several limitations to this study are worth noting. First, the findings of this study only apply to an early head CT and not to other imaging modalities, such as Magnetic Resonance

Imaging (MRI). However, MRI is less frequently performed than head CT as the initial imaging modality when patients present for stroke evaluation. Following American Heart Association/American Stroke Association guidelines, most patients with acute neurological change and focal deficits receive a non-contrast CT scan as part of their initial evaluation; therefore, this is frequently accessible data.([6;14]) Second, because of our sample size, we were unable to risk adjust for other important predictors of mortality. Therefore, our scoring system predictions of in-hospital mortality are unadjusted, and should be interpreted as such. Third, because radiology data were taken from radiology reports and images were not re-reviewed as part of this study, positive imaging findings may have been under or over-reported. Although CT scans are officially read by attending radiologists, some may have been read by general radiologists and others by neuroradiologists. Inter-observer agreement regarding early signs of ischemic infarction is improved with level of training and experience; however, in routine practice, a general radiologist is more likely to read a head CT than a neuroradiologist.([10;14]) Fourth, variability may exist in how findings are reported by a radiologist. For example, a given lesion could be correctly reported either as a focal hypodensity in the frontal lobe or in the MCA distribution. Fifth, the data analyzed were collected in 1998-2003, and current advances in CT imaging and radiological interpretation may result in more patients with evidence of infarct reported on initial head CT. Fifth, as described above, we do not have data on the extent of MCA involvement or the laterality of focal hypodensities, thereby limiting our ability to assess how these may be related to stroke severity.([8;23;24]) Finally, the cohort only included patients with a rNIHSS of ≥2, therefore, future studies should confirm our findings in a cohort that also includes patients with a rNIHSS of 0 or 1.

Acknowledgements

The views expressed in this article are those of the authors and do not necessarily represent the view of the Department of Veterans Affairs.

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Table 1: Coding Algorithm for Infarct Location

Acute/subacute infarctions were coded from radiology reports. All applicable locations were coded, and included the following: Middle cerebral artery (MCA), posterior cerebral artery (PCA), anterior cerebral artery (ACA), frontal lobe, temporal lobe, frontal lobe, occipital lobe, white matter, basal ganglia/internal capsule, thalamus, brainstem/cerebellum, other.

A coding algorithm was also generated and is shown below.

If chart states:	**Code:**
anterior choroidal artery (distribution)	basal ganglia/internal capsule
calcarine cortex	occipital lobe
caudate head or caudate nucleus	basal ganglia/internal capsule
cerebellum	brainstem/cerebellum
cerebral peduncle	brainstem
Claustrum	frontal & parietal lobes
corpus callosum	white matter
corona radiata	white matter
extreme (external) capsule	white matter
globus pallidus	basal ganglia/internal capsule
Insula	frontal & parietal lobes
insular ribbon sign* (code Acute infarct)	white matter + frontal
lentiform nucleus	basal ganglia
loss of grey-white differentiation*	white matter + geog. location
MCA artery sign (code Acute infarct)	middle cerebral artery
Medulla	brainstem/cerebellum
midbrain	brainstem/cerebellum
operculum	frontal & parietal & temporal
paracentral lobule	anterior cerebral artery
periventricular/adjacent to ventricle	white matter
Pons	brainstem
post-central gyrus	parietal lobe
pre-central gyrus	frontal lobe
Putamen	basal ganglia/internal capsule
semiovale (anterior, centrum or posterior)	white matter
splenum of corpus callosum	white matter
Striatum	basal ganglia/internal capsule
Subinsula	frontal & parietal lobe
transverse gyrus	temporal lobe
ventricular trigone	white matter

* For these processes, code white matter as well as any geographic location noted.

Table 2: Time from symptom onset to Head CT (N=763)

Time	NIHSS < 10	NIHSS ≥ 10	Total
< 3 hours	108(23.8)	130(41.9)	238(31.2)
3-6 hours	89(19.7)	61(19.7)	150(19.7)
6-12 hours	95(21.0)	38 (12.3)	133(17.4)
12-18 hours	59(13.0)	32(10.3)	91(11.9)
18-24 hours	35(7.7)	20(6.5)	55(7.2)
>24 hours	67(14.8)	29(9.4)	96(12.6)

Table 3. Cohort Characteristics (N=1348)*

Characteristic	Development (N=916) † rNIHSS <10	Development (N=916) † rNIHSS ≥10	P-value	Validation (N=432) ‡ rNIHSS <10	Validation (N=432) ‡ rNIHSS ≥10	P-value
	N=594	N= 322		N=278	N=154	
Demographics						
Age (years): Mean (SD)	70.5(12.7)	73.1 (14.0)	0.004	70.5(13.3)	73.4(13.4)	0.03
Race			0.17			0.64
White	469(79.0)	258(80.1)		213(76.6)	120(77.9)	
Black	85(14.3)	50(15.5)		42(15.1)	27(17.5)	
Hispanic	20(3.4)	10(3.1)		9(3.2)	3(2.0)	
Other/unknown	20(3.4)	4(1.2)		14(5.0)	4(2.6)	
Male Gender	386(65.0)	167(51.9)	0.0001	151(54.3)	70(45.5)	0.08
Past Medical History						
Prior stroke	153(25.8)	80(24.8)	0.76	71(25.5)	43(27.9)	0.60
Prior TIA	96(16.2)	55(17.1)	0.72	49(17.6)	15(9.7)	0.03
Hypertension	431(72.6)	229(71.1)	0.64	205(73.7)	106(68.8)	0.28
Atrial Fibrillation	89(15.0)	87(27.0)	<0.0001	42(15.1)	39(25.3)	0.009
Myocardial infarction	100(16.8)	62(19.3)	0.36	35(12.6)	24(15.6)	0.39
Congestive heart failure	63(10.6)	57(17.7)	0.002	27(9.7)	29(18.8)	0.007
Diabetes	216(36.4)	90(28.0)	0.01	88(21.7)	42(27.3)	0.34
Hyperlipidemia	189(31.8)	87(27.0)	0.13	82(29.5)	36(23.4)	0.17
NIHSS: mean (SD)	5.2(2.1)	17.3(7.4)	<0.0001	5.1(2.1)	17.0(6.3)	<0.0001
Charlson comorbidity score: mean (SD)	2.8(2.2)	3.2(2.5)	0.04	3.0(2.4)	3.0(2.5)	0.54
Non-neurologic disease severity						
Modified APACHE III: mean (SD)	17.6(8.7)	23.6 (12.4)	<0.0001	17.3(8.1)	24.6(12.6)	<0.0001
Independent in Activities of Daily Living	498(83.8)	230(71.7)	<0.0001	235(84.5)	114(74.0)	0.02

Radiographic Findings						
Edema	30(5.1)	42(13.0)	<0.0001	16(5.8)	21(13.6)	0.005
Infarct Locations						
Middle Cerebral Artery	17(2.9)	53(16.5)	<0.001	9(3.2)	29(18.8)	<0.0001
Posterior Cerebral Artery	4(0.7)	2(0.6)	0.93	7(2.5)	1(0.6)	0.17
Anterior Cerebral Artery	1(0.2)	2(0.6)	0.25	1(0.4)	0(0.0)	0.46
Basal Ganglia	29(4.9)	21(6.5)	0.30	17(6.1)	11(7.1)	0.68
Thalamus	5(0.8)	6(1.9)	0.18	1(0.4)	5(3.2)	0.01
Parietal Lobe	33(5.6)	44(13.7)	<0.0001	21(7.5)	13(8.4)	0.74
Frontal	29(4.9)	38(11.8)	<0.0001	13(4.7)	12(7.8)	0.18
Temporal	13(2.2)	27(8.4)	<0.0001	6(2.2)	8(5.2)	0.09
Occipital	21(3.5)	16(5.0)	0.29	14(5.0)	5(3.2)	0.39
Brainstem	18(3.0)	3(0.9)	0.04	8(2.9)	7(4.5)	0.36
New hemorrhage	5(0.8)	3(0.9)	0.89	0(0.0)	2(1.3)	0.06
No findings (normal CT)	88(14.8)	39(12.1)	0.26	33(11.9)	19(12.3)	0.89
In-hospital mortality	13(2.2)	42(13.0)	<0.0001	4(1.4)	29(18.8)	<0.0001

*Data are presented as number (column percentage) unless otherwise indicated.

†P-values compare patients with NIHSS<10 to NIHSS≥10 within development set.

‡P-values compare patients with NIHSS<10 to NIHSS≥10 within validation set.

Table 4. Association Data and Stroke Severity/In-hospital Mortality*

		Development Cohort N=916			Validation Cohort N= 432		
Brain Imaging Score	Score	rNIHSS <10	rNIHSS ≥10	P-value †	rNIHSS <10	rNIHSS ≥10	P-value†
Neither MCA nor temporal lobe	0	567(68.9)	256(31.1)	<0.0001	266(68.4)	123(31.6)	<0.0001
Temporal lobe only	1	10(43.5)	13(56.5)		3(60.0)	2(40.0)	
MCA only	2	14(26.4)	39(73.6)		6(20.7)	23(79.3)	
MCA and temporal lobe	3	3(17.7)	14(82.4)		3(33.3)	6(66.7)	
Predicting In-Hospital Mortality‡	**Score**	**In-hospital survival**	**In-hospital mortality**	**P-value**	**In-hospital survival**	**In-hospital mortality**	**P-value**
Neither MCA nor temporal lobe	0	786(95.5)	37(4.5)	<0.0001	371(95.4)	18(4.6)	<0.0001
Temporal lobe only	1	21(91.3)	2(8.7)		4(80.0)	1(20.0)	
MCA only	2	41(77.4)	12(22.6)		20(69.0)	9(31.0)	
MCA and temporal lobe	3	13(76.5)	4(23.5)		5(55.6)	4(44.4)	

*N (Row Percentage)

† P-value for trend from Chi-Square test

‡ Unadjusted mortality

Figure 1: Cohort Schematic (N=1363)