

# Validation of High-Sensitivity Troponin I Method in Acute Coronary Syndrome Patients

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## ABSTRACT

**Purpose:** Patients with chest pain or suspected Acute Coronary Syndrome (ACS) who visit emergency departments (ED) rely on the medical staff to quickly risk stratify, diagnose, and treat their condition. Physicians routinely rely on cardiac bio-markers to accurately diagnose and treat patients with chest pain or ACS. Stratus CS is an acute care diagnostics instrument for measuring troponin I levels in patients presenting with suspected myocardial ischemia. The ability to quickly and accurately determine these levels could potentially both improve patient outcomes and save hospital resources by increasing patient throughput. The objective of this research study was to determine if differences in length of stay (LOS) and mortality exist between patients in whom the Stratus CS was used and patients in whom it was not used. **Methods:** Data from three hospitals within the Premier Research Database, a U.S. nationally representative hospital database, were used. The study population included inpatients aged 18 and older, discharged between January 2003 and May 2011, having a principal diagnosis code for myocardial infarction (MI) (ICD-9-CM 410.xx) or Intermediate Coronary Syndrome (ICD-9-CM 411.1) with an emergency admission. A Stratus CS user was defined as a person that had an inpatient visit where the Stratus CS device was billed. T-test analysis was used to evaluate differences in unadjusted LOS. A multivariate gamma regression model for LOS was run adjusting for gender, 3M™ All Patient Refined™ (APR) severity of illness, hospital bed size, diabetes, acute renal failure, chronic renal failure, and heart failure. Chi-square tests were used to evaluate unadjusted differences in mortality, and logistic regression was used to model mortality adjusting for APR severity of illness, diabetes, acute renal failure, and chronic renal failure. **Results:** A total of 3,561 Stratus CS users and 2,256 non-Stratus CS users were included in the study. The mean age of both the Stratus CS user and non-Stratus CS user groups was 67.5(SD 14.7) years. There was an even distribution of patients across both Stratus CS users and non-Stratus CS users with regard to gender, APR severity of illness levels, risk of mortality, and those covered by Medicare. The most frequently occurring physician specialty for both groups was internal medicine, followed by cardiovascular physicians. Unadjusted mean LOS was significantly shorter for Stratus CS users than non-Stratus CS users (mean 4.8 ± 5.5 days versus 5.4 ± 6.6 days, P=0.0002). Shorter LOS for Stratus CS users was supported by regression analysis results (P <0.0001). Unadjusted mortality was lower for Stratus CS users as well (5.1% versus 7.4%, P=0.0004). Adjusted odds of mortality was estimated to be 52% greater for non-Stratus CS users than for Stratus CS users (OR=1.52, 95% CI 1.182-1.944, P=0.0010). **Conclusions:** Patients for whom Stratus CS was used during their inpatient treatment experienced shorter lengths of stay and lower mortality in both unadjusted and adjusted analyses. This research supports the proposition that the quicker the bio-markers are returned to the physician, the faster they can make a diagnosis and treatment decision, which then may improve outcomes for these patients and throughput for the hospital.

## Purpose

Chest pain symptoms in emergency department patients account for around 10% of all visits, which is approximately 119 million visits, annually.<sup>1</sup> Chest pain symptoms can be misleading, resulting in discharge of patients with underlying acute coronary syndrome (ACS).<sup>2</sup> In a large multicenter study, 1.9 percent of patients with Acute Myocardial Infarction were not admitted, resulting in 25 percent of these cases ending in death or serious complications.<sup>3</sup> Physicians routinely rely on cardiac bio-markers to accurately diagnose and treat patients with chest pain or ACS which can reduce potential complications.<sup>4</sup>

## Methods

**Data Source** This study comprised a retrospective analysis of data from the Premier Research Database. The database is a census of all inpatients and hospital-based outpatients from a geographically diverse cohort of hospitals. It contains records on approximately 90 million patients across over 490 hospitals.

**Study Patients** The study population included inpatients aged 18 and older, discharged between January 2003 and May 2011, having a principal diagnosis code for Myocardial Infarction or Intermediate Coronary Syndrome with an emergency admission within three hospitals in the database allowing for a pre-post analysis. A Stratus CS User was defined as a person that had an inpatient visit where the Stratus CS device was billed.

## Methods

**Stratus CS** is the only High-Intensity Troponin instrument that meets the less than 10% cardiovascular sensitivity guideline of the American College of Cardiology, and European Society of Cardiology, and simultaneously meets the National Association of Clinical Biochemistry and Centers for Medicare and Medicaid Services requirements for turn-around-time less than 1 hour.

**Study Endpoints** The study endpoints included length of stay (LOS) and inpatient mortality.

**Statistical Analysis** Descriptive statistics were used to summarize the characteristics of the study population (including age, gender, race, geography, outcomes). Univariate analyses included mean, standard deviation, and frequency distribution (N/%). Statistical tests included t-test or chi-square as appropriate. A multivariate gamma regression model for LOS, adjusting for gender, 3M™ All Patient Refined™ (APR) severity of illness, hospital bed size, diabetes, acute renal failure, chronic renal failure, and heart failure between groups was utilized. Logistic regression was used to model mortality adjusting for APR severity of illness, diabetes, acute renal failure, and chronic renal failure.

## Results

**Table 1 – Demographics of Stratus CS Users and non-Stratus CS Users**

	Stratus CS user	Non-Stratus CS user	Total	
<b>Patients</b>	N	3,561	2,256	5,817
<b>Age</b>	Mean(Std Dev)	67.5(±14.7)	67.5(±14.6)	67.5(±14.6)
<b>Age Group</b>	18-34	30 (0.8%)	14 (0.6%)	44 (0.8%)
	35-44	166 (4.7%)	117 (5.2%)	283 (4.9%)
	45-54	545 (15.3%)	357 (15.8%)	902 (15.5%)
	55-64	815 (22.9%)	476 (21.1%)	1,291 (22.2%)
	65-74	756 (21.2%)	457 (20.3%)	1,213 (20.9%)
	75+	1,249 (35.1%)	835 (37.0%)	2,084 (35.8%)
<b>Gender</b>	Male	2,261 (63.5%)	1,394 (61.8%)	3,655 (62.8%)
<b>Race</b>	White	1,846 (51.8%)	1,105 (49.0%)	2,951 (50.7%)
<b>Discharge status</b>	Home	2,905 (81.6%)	1,805 (80.0%)	4,710 (81.0%)
	Expired	182 (5.1%)	166 (7.4%)	348 (6.0%)
	Other	474 (13.3%)	285 (12.6%)	759 (13.0%)
<b>Health Care Coverage Type</b>	Medicaid	170 (4.8%)	75 (3.3%)	245 (4.2%)
	Medicare	1,900 (53.4%)	1,268 (56.2%)	3,168 (54.5%)
	Managed Care/Commercial	1,108 (31.1%)	754 (33.5%)	1,862 (32.0%)
	Other	383 (10.7%)	159 (7.0%)	542 (9.3%)
<b>APR-DRG Severity</b>	Minor	891 (25.0%)	619 (27.4%)	1,510 (26.0%)
	Moderate	1,253 (35.2%)	773 (34.3%)	2,026 (34.8%)
	Major	841 (23.6%)	505 (22.4%)	1,346 (23.1%)
	Extreme	576 (16.2%)	359 (15.9%)	935 (16.1%)
<b>APR-DRG Risk of Mortality</b>	Minor	1,279 (35.9%)	758 (33.6%)	2,037 (35.0%)
	Moderate	971 (27.3%)	650 (28.8%)	1,621 (27.9%)
	Major	796 (22.4%)	523 (23.2%)	1,319 (22.7%)
	Extreme	515 (14.5%)	325 (14.4%)	840 (14.4%)

## Results

### Hospital Characteristics

- All 3 hospitals were classified as urban
  - Two hospitals were classified as non-teaching and 1 was teaching.
  - Bed Size
    - 1 hospital (200-299 beds)
    - 1 hospital (300-499 beds)
    - 1 hospital (500+ beds)

**Table 2 –Primary ICD-9 Diagnosis Code Distribution of Study Population**

	ICD-9 Description	Stratus CS user	Non-Stratus CS user	Total
		3,561	2,256	5,817
410.01	AMI, anterolateral wall, initial	75 (2.1%)	72 (3.2%)	147 (2.5%)
410.02	AMI, anterolateral wall, subsequent	1 (0.0%)	-	1 (0.0%)
410.10	AMI, anterior wall, unspecified	1 (0.0%)	1 (0.0%)	2 (0.0%)
410.11	AMI, anterior wall, initial	328 (9.2%)	282 (12.5%)	610 (10.5%)
410.12	AMI, anterior wall, subsequent	1 (0.0%)	1 (0.0%)	2 (0.0%)
410.21	AMI, inferolateral wall, initial	87 (2.4%)	69 (3.1%)	156 (2.7%)
410.31	AMI, inferoposterior wall, initial	44 (1.2%)	35 (1.6%)	79 (1.4%)
410.40	AMI, inferior wall, unspecified	3 (0.1%)	1 (0.0%)	4 (0.1%)
410.41	AMI, inferior wall, initial	466 (13.1%)	307 (13.6%)	773 (13.3%)
410.51	AMI, lateral wall, initial	52 (1.5%)	43 (1.9%)	95 (1.6%)
410.61	True posterior wall, initial	9 (0.3%)	3 (0.1%)	12 (0.2%)
410.70	AMI, subendocardial, unspecified	4 (0.1%)	1 (0.0%)	5 (0.1%)
410.71	AMI, subendocardial, initial	2,211 (62.1%)	1,127 (50.0%)	3,338 (57.4%)
410.72	AMI, subendocardial, subsequent	5 (0.1%)	2 (0.1%)	7 (0.1%)
410.80	AMI NEC, unspecified	-	1 (0.0%)	1 (0.0%)
410.81	AMI NEC, initial	54 (1.5%)	103 (4.6%)	157 (2.7%)
410.90	AMI NOS, unspecified	3 (0.1%)	1 (0.0%)	4 (0.1%)
410.91	AMI NOS, initial	134 (3.8%)	139 (6.2%)	273 (4.7%)
410.92	AMI NOS, subsequent	3 (0.1%)	-	3 (0.1%)
411.1	Syndrome, intermediate coronary	80 (2.2%)	68 (3.0%)	148 (2.5%)

### Comorbidities

Stratus CS users had significantly more patients with acute renal failure, chronic kidney disease, and heart failure.

**Table 3 – Study Population Comorbidities**

	Stratus CS user		Non-stratus CS user		
	#	%	#	%	p-value
Diabetes – ICD-9:250.xx	1,143	32.1	717	31.8	0.8013
Acute renal failure – ICD-9:584.xx	424	11.9	199	8.8	0.0002*
Chronic Kidney Disease – ICD-9:585.xx	513	14.4	91	4.0	<.0001*
Heart failure – ICD-9:428	920	25.8	720	31.9	<.0001*

\* Significant at the 0.05 level

**Table 4 – Inpatient Mortality**

	Stratus CS user		Non-stratus CS user		
	#	%	#	%	p-value
Inpatient Mortality (N)	182	5.1	166	7.4	0.0004*

\* Significant at the 0.05 level

## Results

### Mortality Odds Ratio

The adjusted odds of dying was 52% greater for non-Stratus CS users when compared to Stratus CS users (OR=1.52, 95% CI 1.18-1.94, P=0.0010)

### Length of Stay

Both unadjusted (Table 5) and adjusted mean LOS was significantly shorter for Stratus CS users when compared to non-Stratus CS users .

**Table 5 – Length of Stay**

	Total		Stratus CS user		Non-stratus CS user		
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	p-value
Length of Stay (days)	5.04	±5.96	4.81	±5.53	5.41	±6.58	0.0002*

\* Significant at the 0.05 level

## Limitations

Use of observational administrative databases has noted limitations which include selection bias and reliance on accurate and complete ICD-9 coding and billing, as utilized in this study. Our use of statistical methods of modeling to adjust for baseline differences can minimize, but cannot totally account for, all potential confounders. Additionally, diagnostic practice may have changed within the institutions during the Stratus CS study time period.

## Conclusions

Patients for whom Stratus CS was used during their inpatient treatment experienced shorter lengths of stay and lower mortality in both unadjusted and adjusted analyses. This research supports the proposition that early availability of bio-markers enable physicians to make earlier diagnoses and treatment decisions which may improve outcomes for this patient population, as well as increase throughput for the hospital. Further investigations into the impact of the actual timing of the receipt of biomarkers in the decision making process would be beneficial.

## References

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