Comparative Retrospective Analysis of ASCVD Score and Lipoprotein(a) in Predicting Outcomes of Acute Coronary Syndrome

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BACKGROUND
Cardiovascular diseases (CVDs) remain a substantial global health burden, with prevalence nearly doubling from 271 million cases in 1990 to 523 million in 2019. (Roth, 2020) The ASCVD (Atherosclerotic Cardiovascular Disease) 10-year risk score has been widely utilized for assessing the risk of acute coronary syndrome (ACS). (Goff, 2014) However, this tool does not account for all contributory risk factors, including lipoprotein(a) [Lp(a)] which is an emerging marker implicated in predicting ACS risk. (Grundy 2019) Elevated Lp(a) levels are associated with calcific aortic valve stenosis, peripheral artery disease, ischemic stroke, and coronary atherosclerosis. (Tsao, 2023) (Goldsborough, 2022) Lp(a) has huge potential for utility however there remains no clear consensus on how to optimally incorporate Lp(a) levels into standardized risk stratification tools of ACS like ASCVD.

PURPOSE
The goal of this study is to elucidate the complex interactions Lp(a) has with ACS risk factors and demonstrate its utility when used in conjunction with ASCVD risk scoring to augment predictive power in risk stratifying patients likely to suffer from future ACS events.

METHODS
Retrospective analysis was performed. Patients were selected from Trinity Health centers. A total sample size of 1408 patients aged 40-75 years were collected. The primary end point was ACS including those who suffered ST elevation myocardial infarction (STEMI), NON-ST elevation

myocardial infarction (NON-STEMI), coronary arterial bypass graft (CABG), and previous coronary stent(s) placement. Patient information included natal sex, race, age, total cholesterol, HDL cholesterol, history of smoking, diabetes, and history of hypertension treatment were collected. The population was further stratified by Lp(a) levels (according to Heart UK study guidelines) and ASCVD Risk Levels (according to 2013 ACC/AHA). Lp(a) values were reported as nmol/L from two major commercially available labs—LabCorp and Quest Diagnostic. Measuring Lp(a) in nmol/L versus milligrams per deciliter (mg/dL) provided for consistent comparisons across populations. Data analysis was completed with IBM SPSS version 29.0 including spearman rank correlation, chi-square analyses, and linear regression models.

RESULTS

Lp(a) is an emerging risk factor for atherosclerotic cardiovascular disease with growing evidence supporting its predictive value, especially in high-risk groups. (Wong 2022, Borrelli 2021) Several key challenges have impeded the development of a unified approach to Lp(a) risk assessment, including significant variability in circulating Lp(a) concentrations across different populations and ethnic groups. (Tsimikas 2017) An additional challenge is the standardization of Lp(a) assays. The gene that codes for production of lp(a), LPA, has wide variability resulting in some individuals who produce larger components within Lp(a) particle itself. This causes the ratio of particle mass compared to molecular weight to vary across individuals. Thus, the conversion of measuring units between traditional milligrams per deciliter (mg/dL) has room for error. (Alebna 2023, ACC) Whether Lp(a) should be evaluated as a separate risk factor or integrated into existing risk calculators remains a standing issue for debate (Matsuura 2019). Despite the lack of consensus and need for future studies, there is huge potential for Lp(a) to serve as a main player in screening tools for cardiovascular risk assessment in primary care and specialty care settings.

TABLES/FIGURES

Table 1

Cardiovascular risk classification conferred by Lipoprotein(a).

Lp(a) level nmol/L[a]	CV Risk Impact
< 32	Low
32-90	Minor
90-200	Moderate
200-400	High
> 400	Very High

a Cutoffs derived from Copenhagen General Population Study [20].

Table 2

2013 10-year ASCVD risk percentage stratification.

ASCVD 10-year risk %a	ASCVD Risk Impact

< 5	Low
5-7.5	Borderline Risk
7.5-20	Intermediate Risk
> 20	High Risk

Table 3
Breakdown summary of patient demographics

Variable	N=1408	%
Age		
40-50	403	28.62
51-60	405	28.76
61-70	442	31.39
70+	158	11.22
Natal Sex		
Female	684	48.58
Male	724	51.42
Race		
Black	85	6.04
Other	378	26.85
White	945	67.12

Table 4
Frequency and percentage of patients with comorbidities.

Characteristic	N=1408	%
Diabetes	334	23.72
Smoking	523	37.14
Treatment of Hypertension	797	56.61
Acute Coronary Syndrome	242	17.19

Table 5
ASCVD risk level of active patients.

ASCVD 10-year Risk %	ASCVD Risk Impact	N=1408	%	Valid %	Cumulative %

< 5	Low	544	38.6	38.6	38.6
5-7.5	Borderline	156	11.1	11.1	49.7
7.5-20	Intermediate	456	32.4	32.4	82.1
> 20	High	252	17.9	17.9	100.0

Table 6

Lipoprotein(a) risk level of active patients.

Lp(a) level nmol/L	CV Risk Impact	N=1408	%	Valid %	Cumulative %
< 32	Low	788	56.0	56.0	56.0
32-90	Minor	286	20.3	20.3	76.3
90-200	Moderate	223	15.8	15.8	92.1
200-400	High	101	7.2	7.2	99.3
> 400	Very High	10	0.7	0.7	100.0

Table 7

Exploratory Chi-Square analysis between risk levels and ASCVD risk score variables.

Variable	df	X^2	p
Natal Sex (Male/Female)			
ASCVD Risk Impact	3	160.710	< .001
Lp(a) CV Risk Impact	4	13.957	< .05
Acute Coronary Syndrome	1	43.308	< .001
Age (40-75 y/o)			
ASCVD Risk Impact	9	828.391	< .001
Lp(a) CV Risk Impact	12	18.662	.097
Acute Coronary Syndrome	3	97.529	< .001
Race (‘White’, ‘Black’, ‘Other’)			

ASCVD Risk Impact	6	17.236	< .05
Lp(a) Risk Impact	8	63.933	< .001
Acute Coronary Syndrome	2	7.680	< .05
Smoker (Yes/No)			
ASCVD Risk Impact	3	205.194	< .001
Lp(a) Risk Impact	4	10.857	< .001
Acute Coronary Syndrome	1	45.439	< .001
Diabetes (Yes/No)			
ASCVD Risk Impact	3	191.169	< .001
Lp(a) Risk Impact	4	3.073	.546
Acute Coronary Syndrome	1	16.680	< .001
Treatment of Hypertension (Yes/No)			
ASCVD Risk Impact	3	277.666	< .001
Lp(a) Risk Impact	4	2.118	.714
Acute Coronary Syndrome	1	88.529	< .001

Table 8

Model 1: Regression coefficients for prediction of acute coronary syndrome.

Variable	B	S.E.	Wald	p	Exp(B)	95% CI for Exp(B)	
						Lower	Upper
ASCVD Risk Impact Level			48.636	< .001			
Borderline	1.638	0.386	18.003	< .001	5.143	2.414	10.958
Intermediate Risk	1.587	0.329	23.277	< .001	4.889	2.566	9.315
High Risk	2.318	0.333	48.458	< .001	10.154	5.287	19.501

Lp(a) Risk Impact Level			4.928	.295		
ASCVD Risk Impact Level * Lp(a) Risk Impact Level			1.649	1.00		

Table 9

Model 2: Regression coefficients for prediction of acute coronary syndrome.

Variable	B	S.E.	Wald	p	Exp (B)	95% CI for Exp (B)	
						Lower	Upper
Sex[a]	0.1719	0.176	16.610	< .001	2.052	1.452	2.899
Age			40.730	< .001			
51-60	0.909	0.282	10.421	.001	2.481	1.429	4.309
61- 70	1.486	0.266	31.289	< .001	4.418	2.625	7.436
71-75	1.681	0.301	31.149	< .001	5.372	2.977	9.695
Race			1.130	.598			
Total Cholesterol Level			18.236	< .001			
Borderline	-1.018	0.272	14.011	< .001	0.361	0.212	0.616
High	-0.870	0.359	5.893	.015	0.419	0.207	0.846
HDL Cholesterol Level			.817	.665			
Lp(a) Level			16.693	.002			
Minor	0.236	0.216	1.188	.276	1.266	0.829	1.934
Moderate	0.729	0.215	11.442	< .001	2.073	1.359	3.162
High	0.835	0.287	8.455	.004	2.304	1.313	4.043
Very High	0.825	0.956	.745	.388	2.282	.350	14.858

Variable	B	S.E.	Wald	p	Exp (B)	95% CI for Exp (B)	
Treatment of Hypertension	0.998	0.204	23.916	< .001	2.712	1.818	4.045
Smoker	0.817	0.160	26.221	<. 001	2.264	1.656	3.096
Diabetes	0.178	0.182	.955	.329	1.195	.836	1.708
Note [a] males							

Figure 1

Odd ratio of developing acute coronary syndrome (ACS) across different levels of the ASCVD (Atherosclerotic Cardiovascular Disease) risk impact level.

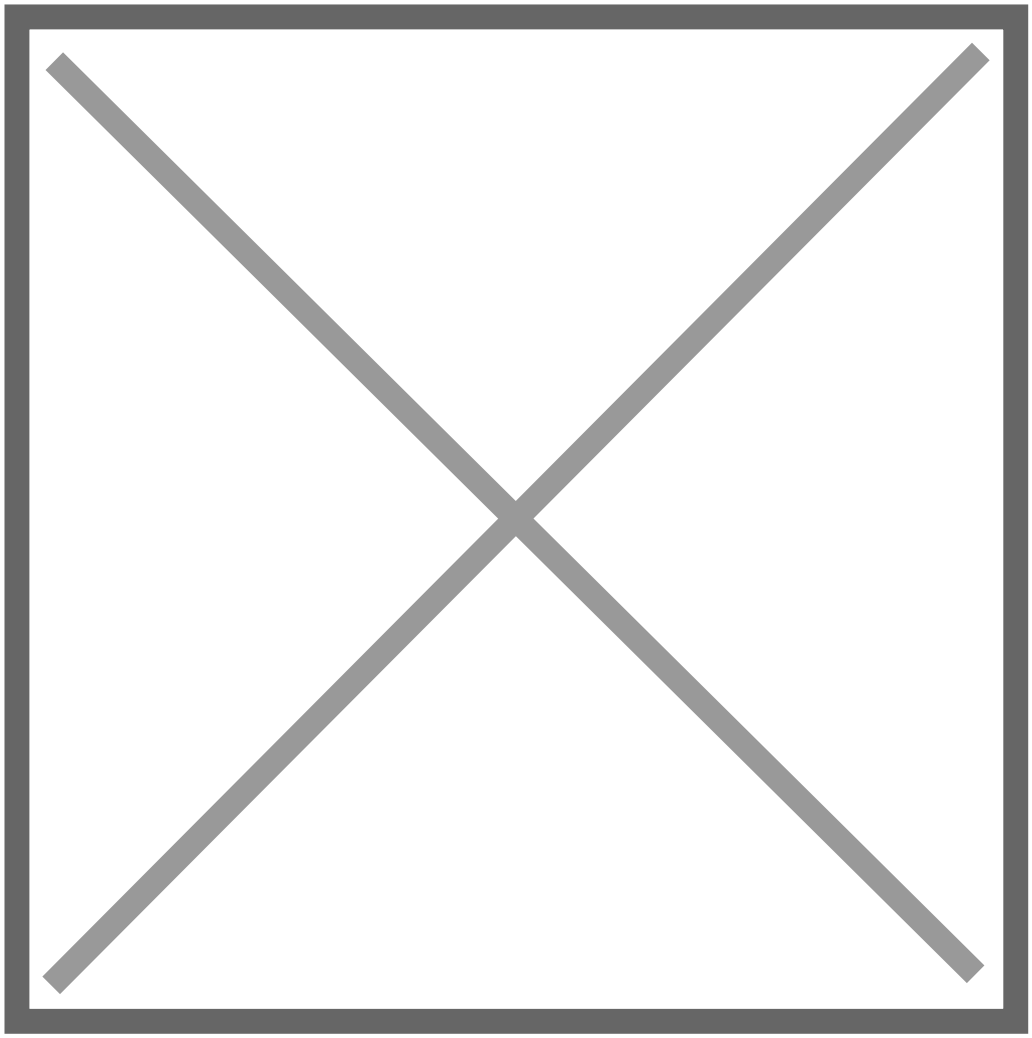
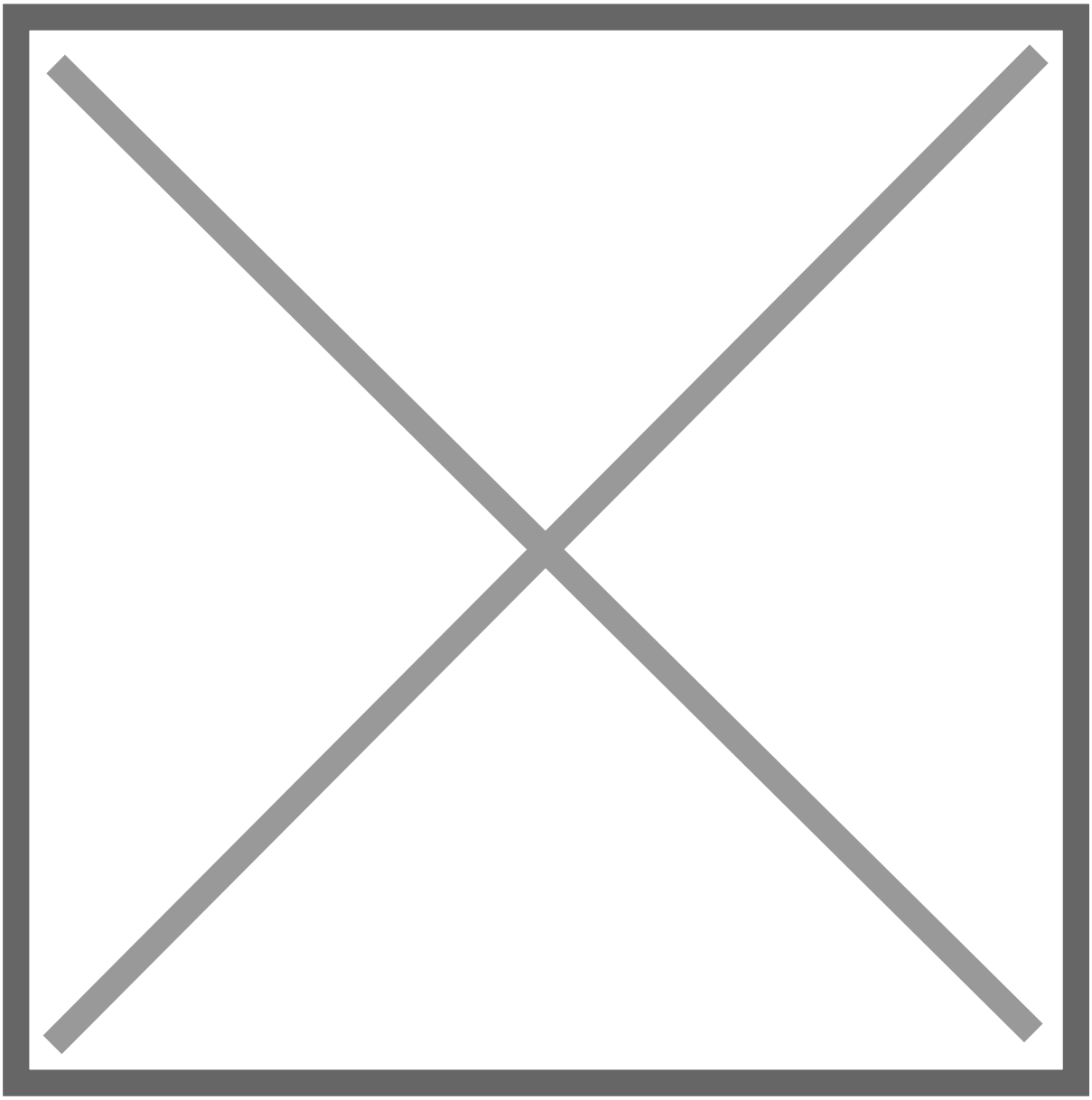


Figure 2
Odds ratio of ASCVD risk calculator categories and Lipoprotein (a) risk impact for ACS



♢ reference categorical variable; ● variable p <0.001; categorical variable non-significance

DISCUSSION

This study demonstrates the robust utility of Lp(a) in ACS risk scoring. When present in moderate or high levels Lp(a) is an additional factor that should be included in ASCVD scoring. Lp(a) can provide unique predictive value in individuals with genetic predispositions. Further studies which tease out the variability of Lp(a) across racial groups and genetic variability are needed to create a more robust screening tool.

CONCLUSION

This study demonstrates the robust utility of Lp(a) in ACS risk scoring. When present in moderate or high levels Lp(a) is an additional factor that should be included in ASCVD scoring. Lp(a) can provide unique predictive value in individuals with genetic predispositions. Further studies which tease out the variability of Lp(a) across racial groups and genetic variability are needed to create a more robust screening tool.

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