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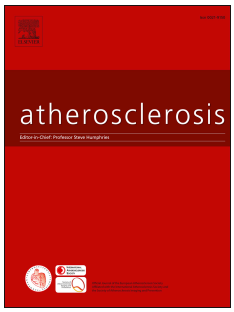

Higher low-density lipoprotein cholesterol levels are associated with decreased mortality in patients with intracerebral hemorrhage

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Higher low-density lipoprotein cholesterol levels are associated with decreased mortality in patients with intracerebral hemorrhage

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Abstract

Background and aims: The relationship between lipoprotein levels, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and clinical outcome after intracerebral hemorrhage (ICH) remains controversial. We sought to evaluate the association of lipoprotein cholesterol levels and statin dosage with clinical and neuroimaging outcomes in patients with ICH.

Methods: Data on consecutive patients hospitalized with spontaneous acute ICH was prospectively collected over a 5-year period and retrospectively analyzed. Demographic characteristics, clinical severity documented by NIHSS-score and ICH-score, neuroimaging parameters, pre-hospital statin use and doses, and LDL-C and HDL-C levels were recorded. Outcome events characterized were hematoma volume, hematoma expansion, in-hospital functional outcome, and in-hospital mortality.

Results: A total of 672 patients with acute ICH [(mean age 61.6±14.0 years, 43.6% women, median ICH score 1 (IQR: 0-2)] were evaluated. Statin pretreatment was not associated with neuroimaging or clinical outcomes. Higher LDL-C levels were associated with several markers of poor clinical outcome and in-hospital mortality. LDL-C levels were independently and negatively associated with the cubed root of hematoma volume (linear regression coefficient -0.021, 95% CI: -0.042−-0.001; p=0.049) on multiple linear regression models. Higher admission LDL-C (OR 0.88, 95% CI 0.77 – 0.99; p= 0.048) was also an independent predictor for decreased hematoma expansion. Higher admission LDL-C levels were independently (p <0.001) associated with lower likelihood of in-hospital mortality (OR per 10mg/dL increase 0.68, 95% CI: 0.57– 0.80) in multivariable logistic regression models.

Conclusions: Higher LDL-C levels at hospital admission were an independent predictor for lower likelihood of hematoma expansion and decreased in-hospital mortality in patients with acute spontaneous ICH. This association requires independent confirmation.

Introduction

The relationship between lipoprotein cholesterol levels [low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)] and clinical outcomes in patients with acute intracerebral hemorrhage (ICH) remains controversial. Early epidemiological studies suggested an association between lower cholesterol levels and death after stroke [1]. Subsequent studies further evaluated LDL-C with associations noted between lower LDL-C levels and ICH risk [2], hematoma growth [3], and mortality [4-6].

As the primary agent responsible for lowering lipid levels, the role of statins in ICH incidence and hematoma volume expansion has generated controversy. This was particularly highlighted after statins were found to be associated with increased rates of hemorrhagic transformation in ischemic stroke [7] and higher incidence of cerebral microbleeds in ICH [8]. However, recent studies have also provided observational evidence showing statin use improving clinical outcomes after ICH [9,10] and not increasing the likelihood of cerebral microbleeds [11].

The relationship between statin use and dosing, lipoprotein levels, hematoma volume, and clinical outcome remains unclear due to inconsistencies in the existing literature and failure to systematically evaluate both clinical and neuroimaging outcomes in individual patients. To clarify this relationship, we sought to evaluate the association of lipoprotein cholesterol levels with clinical and neuroimaging outcomes in patients with acute ICH.

Materials and methods

Patient selection and study protocol

Institutional review board approval was obtained for the conduct of a prospective cohort study evaluating functional and neuroimaging outcomes in adult patients with acute,

spontaneous, non-traumatic ICH in a tertiary-care stroke center. All data was prospectively collected as per hospital registry protocol for acute (< 24 hours) ICH and retrospectively reviewed for accuracy by blinded neurologists (YK, KD, AK, NG). Consecutive patients with ICH were initially identified by ICD code, which spanned a five-year period (from January 2011 to December 2015). Inclusion criteria were as follows: spontaneous etiology for ICH and adult age ($\geq$ 18 years old). Exclusion criteria were as follows: nonspontaneous etiologies of ICH (including traumatic ICH, metastatic lesion with associated hemorrhage, ICH resulting from venous sinus thrombosis, and ICH resulting from underlying vascular lesions), ICH due to supratherapeutic international normalized ratio (INR) in the setting of prehospital anticoagulation or coagulopathy (threshold INR $\geq$ 1.7), and thrombocytopenia (platelets < 50,000/mm^3).

All ICHs were initially admitted to the intensive care unit (ICU). As per hospital protocol, patients were treated with intravenous pushes of enalapril, hydralazine, or labetalol and escalated to continuous nicardipine infusion to reach a goal SBP < 140 mmHg during the first 24 hours after admission. If clinically stable, SBP parameters were relaxed to SBP goal < 160 mmHg after 24 hours of admission. As per hospital protocol and unless contraindicated or on a different prehospital statin dose, all patients with ICH were given a medium-dose statin within 24 hours of admission after swallow evaluation or feeding tube insertion. Intensive statin pretreatment was defined as patients taking the maximum dose of their respective statin [12].

Demographic characteristics, past medical history, premorbid modified Rankin scores (mRS), and baseline radiological and clinical parameters were prospectively collected. Baseline clinical severity was documented with National Institutes of Health Stroke Scale (NIHSS) scores. Clinical outcome endpoints included mRS at discharge, hospital length of stay, and in-hospital mortality. Favorable functional outcome at discharges was defined as mRS 0-2. All

laboratory values—INR, glucose, platelets, LDL-C, HDL-C—were obtained within 24 hours of hospitalization.

Mortality analysis

Causes of mortality were delineated as follows. Cerebral herniation occurred when the patient reached a comatose state from herniation, was not formally declared brain dead, and passed away from cardiac death after palliative extubation. Brain death occurred when patients met clinical criteria which included loss of brainstem reflexes and apnea testing confirmation or ancillary testing for cerebral circulatory arrest. Spontaneous cardiac arrest occurred during an unanticipated cardiac arrest, unrelated to their primary ICH. Finally, palliative care occurred when the patient remained extubated for longer than 24 hours and was transitioned to comfort measures with subsequent death.

Imaging characterization: ICH volume, and hematoma expansion

Follow-up head computed tomography (CTH) was acquired within 6 to 24 hours of initial CTH. ICH volume as noted in baseline CTH was measured as delineated by the ABC/2 score [13]. Hematoma expansion was defined as >33% expansion or >12.5 ml hematoma volume growth on serial CT scans taken within a 48-hour span [14-16].

Statistical analysis

We presented continuous parametric data using their mean values together with their corresponding standard deviations (SDs). We used median values with their corresponding

interquartile ranges (IQR) for the presentation of non-parametric data and percentages for all dichotomous variables.

Univariate and multivariate regression analyses were used to evaluate the associations between baseline characteristics and admission hematoma volume, hematoma expansion, functional dependence at hospital discharge (mRS scores 3-6), in-hospital mortality among included patients. In all univariate analyses, a threshold of p <0.1 was used to identify candidate variables for inclusion in multivariate regression models that tested statistical significance hypothesis using the likelihood ratio test with an alpha value of 0.05 [17]. We reported all associations as linear regression coefficients in linear regression models and odds ratios (ORs) in logistic regression models, respectively, with their corresponding 95% confidence intervals (95% CI). In all simple and multiple linear regression analyses, baseline hematoma volume was cube root transformed for each patient to satisfy statistical assumptions regarding normality of the distribution, as previously described [18]. The Stata Statistical Software Release 13 for Windows (College Station, TX, StataCorp LP) was used for all statistical analyses.

Results

A total of 803 patients were identified as ICH by ICD code; of these patients, 672 met inclusion criteria [mean age 61.6 ±14.0 years, 43.6% women, median ICH score 1 (IQR: 0-2)]. Baseline characteristics for the study population are included in Table 1. Prehospital statin use was documented in 25.8% and prehospital intensive statin use was documented in 3.4% of the study population (mean admission LDL-C: 100.3 ±36.3 mg/dl; mean admission HDL-C: 52.6 ±18.6 mg/dl).

Associations between demographic variables and the cubed root of hematoma volume at admission are shown in Table 2. Several demographic variables were associated with cubed root of hematoma volume on simple linear regression analysis: Caucasian race, history of hypertension, history of hyperlipidemia, coronary artery disease, past history of stroke, admission glucose, admission LDL-C, subcortical location for ICH, admission systolic blood pressure (SBP), and admission NIHSS. Multiple linear regression analyses identified the following independent predictors of admission hematoma volume: history of stroke, admission LDL-C, subcortical location of ICH, and admission NIHSS. More specifically, LDL-C levels (p= 0.049) were independently and negatively associated with the cubed root of hematoma volume (linear regression coefficient:-0.021, 95% CI -0.042 – -0.001) on hematoma volumes after adjusting for potential confounders.

The following variables were related to hematoma expansion on initial univariate logistic regression models (Table 3): Caucasian race, history of coronary artery disease, admission LDL-C, and admission hemoglobin A1c. However, only higher admission LDL-C emerged as an independent predictor of lower likelihood of hematoma expansion on multivariate logistic regression analyses (OR per 10mg/dL increase: 0.88, 95% CI 0.77 – 0.99, p= 0.048).

Table 4 shows the univariate and multivariate associations of baseline characteristics with functional dependence (mRS-scores of 3-6) at hospital discharge. The following four variables were independently related to functional outcome at hospital discharge: age, history of smoking, admission SBP, and admission NIHSS. Although admission LDL-C was associated with functional independence in initial univariate analyses, the former association did not retain its statistical significance in multivariate logistic regression models (OR 0.94, 95% CI 0.86 – 1.02, p= 0.153).

Table 5 shows the univariate and multivariate associations of baseline characteristics with in-hospital mortality. The following four variables emerged as independent predictors of in-hospital mortality: history of chronic kidney disease, admission LDL-C, admission HDL-C, and admission NIHSS. Higher admission LDL-C levels were independently associated (p <0.001) with lower likelihood of in-hospital mortality (OR per 10mg/dL increase: 0.68, 95% CI 0.57 – 0.80) in multivariate logistic regression analyses adjusting for potential confounders (Table 5). Every 10 mg/dl increase in admission LDL-C was related to a decrease in the odds of in-hospital mortality by 32% (95% CI: 20%-43%).

Discussion

The greatest uncertainty regarding the association between lipoprotein levels, statin use, and clinical outcomes in acute ICH, center around the lipoprotein lowering effects of statins weighed against their neuroprotective, anti-inflammatory effects. We chose to evaluate these potential predictors simultaneously—lipoprotein levels and statin dosage—and identified several independent associations using the following clinical outcome variables: initial hematoma volume, hematoma expansion, functional independence at hospital discharge, and mortality at hospital discharge.

First, statin pretreatment and prehospital intensive statin use was not associated with any of the clinical outcomes in our analyses. A trend associating statin use with higher odds of functional independence at hospital discharge was noted, but this relationship did not reach statistical significance. As larger meta-analyses, published since SPARCL [7] have shown statin use to be associated with reduced mortality in ICH [9,10], our study may have been underpowered to detect a similar association. However, our findings are in line with more recent studies that

failed to document any association between statin pretreatment and admission hematoma volume or hematoma expansion [19]. This somewhat unexpected finding suggests a lesser influence on the neuroprotective and anti-inflammatory effects of statins that promote clinical outcome after ischemic strokes [20]. As LDL-C and to some extent HDL-C, had more robust associations with clinical outcomes, this questions whether lipoprotein cholesterol levels, rather than prehospital statin use, play a larger role in clinical outcomes after ICH.

Second, in accordance with prior studies, we found higher LDL-C levels associated with smaller hematoma volumes, smaller probability of hematoma expansion, and lower mortality. The mechanism for the role of higher LDL-C in preventing mortality may lie in these associations as hematoma expansion [16] and larger initial hematoma volume [21] are well-known predictors of mortality after ICH. Potential unifying chronic and dynamic mechanisms may account for these associations. One potential chronic unifying mechanism may be the association of LDL-C with lower presence of cerebral microbleeds [22]. Cerebral microbleeds and their relationship with LDL-C may ultimately link all of these associations because they negatively impact clinical outcomes in patients with ICH by promoting hematoma growth [3], recurrent ICH [23] and larger perihematomal edema volumes [24]. More dynamically, longitudinal studies of lipoprotein levels show a decline in LDL-C preceding spontaneous ICH [25], which further suggests that LDL-C levels rather than prehospital statin use play a more definitive mechanistic role in ICH incidence and outcome.

HDL-C levels provided less consistent results as HDL-C was not associated with hematoma expansion or clinical outcome at hospital discharge, but were associated with lower mortality. Although lower HDL-C levels have been associated with increased ICH incidence [26,27], the question of ICH incidence was not within the scope of this study.

Several limitations of the present study need to be acknowledged. First, clinical outcomes (mRS and mortality) were evaluated at discharge and not in a prolonged subacute time frame to maximize clinical recovery after ICH. However, a subsequent three month follow-up evaluation would have likely improved functional outcome as it would reflect clinical improvements made after rehabilitation and physical therapy. Second, data was collected retrospectively in a single tertiary care center and this may have introduced bias. However, variables were prospectively inputted and were included in larger database in which study personnel was blinded to the study hypothesis. Finally, although the role of statin use was evaluated, a complex interplay of mechanisms preclude definitive relationships being made between statin use, lipoprotein levels, and clinical outcomes. These include the association between statin use and genetic polymorphisms in effecting lipoprotein levels [28], effects of complementary enzymes such as acetylcholinesterase and butyrylcholinoesterase in lowering lipoprotein levels [29], and pleiotropic effects of statins including anti-inflammation and angiogenesis [30].

In conclusion, this study highlights that higher LDL-C levels are associated with lower in-hospital mortality in patients with spontaneous ICH. Potential underlying mechanisms of this association may be related to the smaller hematoma volumes and lower likelihood of hematoma expansion that was documented in patients with higher admission LDL-C. Pre-hospital and acute statin intake was not associated with clinical outcome in our dataset. Larger, prospective, multicenter studies further delineating the role of statins and the mechanism between increased LDL-C levels and lower mortality are necessary to independently validate these findings.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Author contributions

Dr. Chang: study concept and design, acquisition of data, analysis and interpretation, writing of manuscript, critical revision of manuscript for important intellectual content

Dr. Katsanos: analysis and interpretation, critical revision of manuscript for important intellectual content

Dr. Khorchid: acquisition of data, critical revision of manuscript for important intellectual content

Dr. Dillard: acquisition of data, critical revision of manuscript for important intellectual content

Dr. Kerro: acquisition of data, critical revision of manuscript for important intellectual content

Ms. Burgess: acquisition of data, critical revision of manuscript for important intellectual content

Dr. Goyal: acquisition of data, critical revision of manuscript for important intellectual content

Dr. AW Alexandrov: critical revision of manuscript for important intellectual content

Dr. AV Alexandrov: critical revision of manuscript for important intellectual content

Dr. Tsivgoulis: study concept and design, analysis and interpretation, critical revision of manuscript for important intellectual content

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Figure Legends

Figure 1. Scatterplot and regression line demonstrating the inverse relationship between the cubed root of baseline hematoma volumes and admission low-density lipoprotein cholesterol levels for patients with intracerebral hemorrhage.

Figure 2. Bar charts and fractional-polynomial prediction line demonstrating the inverse relationship between all-cause mortality frequency and admission low-density lipoprotein cholesterol levels (per 10 unit increase) in patients with intracerebral hemorrhage.

Tables

Table 1: Baseline characteristics of the study population (n=672).

Age (years, mean ±SD)	61.6±14.0
Gender (% female)	43.6%
Race (%)	Caucasian: 27.8% Black: 70.5% Asian: 1% Hispanic: 0.7%
BMI (mean ±SD)	28.9±7.4
ICH score (median, IQR)	1 (0-2)
Mortality (%)	24.1%
Hypertension (%)	86%
Diabetes mellitus (%)	34.8%
Hyperlipidemia (%)	32.4%
Coronary artery disease (%)	12.3%
Congestive heart failure (%)	7.6%
Chronic kidney disease (%)	13.9%
History of stroke (%)	22.6%
Smoking (%)	39.8%
Antiplatelet pretreatment (%)	32.1%
Anticoagulant pretreatment (%)	3.8%
Statin pretreatment (%)	25.8%
Intensive statin pretreatment (%)	3.4%
Admission INR (mean ±SD)	1.11±0.37
Admission glucose (median, IQR)	132 (104-174)
Admission platelets (x1,000, (median, IQR))	217 (177-267)
Admission low-density liprotein cholesterol (mg/dl, mean ±SD)	100.3±36.3
Admission high-density liprotein cholesterol (mg/dl, mean ±SD)	52.6±18.6
Admission hemoglobin A1c (%, median, IQR)	5.7 (5.3-6.4)
Admission Creatinine (median, IQR)	1.1 (0.8-1.4)
Subcortical ICH [a] (%)	69.8%
Admission systolic blood pressure (mmHg, mean ±SD)	183±40
Admission diastolic blood pressure (mmHg, mean ±SD)	103±27
Admission NIHSS [b] score (median, IQR)	8 (2-18)

[a] ICH, intracerebral hemorrhage.

[b] NIHSS, National Institutes of Health Stroke Scale.

Table 2: Simple and multiple linear regression analyses evaluating the association of baseline characteristics with the cubed root of baseline hematoma volume.

	Simple linear regression analysis		**Multiple linear regression analysis**	
Variable	**Coefficient (95% CI)**	***p***	**Coefficient (95% CI)**	***p***
Age	0.003 (-0.002, 0.008)	0.23	-	-
Gender	-0.120 (-0.27, 0.028)	0.11	-	-
Caucasian race	0.194 (0.029, 0.36)	0.021	0.15 (-0.024, 0.33)	0.089
BMI	-0.001 (-0.011, 0.009)	0.83	-	-
Hypertension	0.216 (0.004, 0.43)	0.046	0.002 (-0.22, 0.23)	0.99
Diabetes mellitus	0.065 (-0.090, 0.22)	0.41	-	-
Hyperlipidemia	-0.245 (-0.40, -0.087)	0.002	-0.062 (-0.22, 0.095)	0.44
Coronary artery disease	0.249 (0.026, 0.47)	0.028	-0.016 (-0.26, 0.23)	0.90
Congestive heart failure	0.180 (-0.095, 0.455)	0.20	-	-
Chronic kidney disease	-0.035 (-0.25, 0.18)	0.75	-	-
History of stroke	-0.257 (-0.43, -0.082)	0.004	-0.26 (-0.44, -0.088)	**0.003**
Smoking	0.025 (-1.012, 0.15)	0.70	-	-
Antiplatelet	0.089 (-0.072, 0.25)	0.28	-	-
Anticoagulant	0.115 (-0.27, 0.51)	0.56	-	-
Statin pretreatment	-0.073 (-0.25, 0.10)	0.41	-	-
Intensive Statin pretreatment	0.391 (-0.676, 0.849)	0.10	-	-
Admission INR	0.099 (-0.12, 0.32)	0.37	-	-
Admission glucose [a]	0.001 (0.001, 0.002)	<0.001	-0.001 (-0.002, 0.001)	0.57
Admission platelets	-0.001 (-0.002, 0.001)	0.18	-	-
Admission low-density liprotein cholesterol [a]	-0.040 (-0.065, -0.016)	0.001	-0.021 (-0.042, -0.001)	**0.049**
Admission high-density liprotein cholesterol [a]	-0.037 (-0.085, 0.010)	0.12	-	-
Admission hemoglobin A1c	-0.014 (-0.69, 0.041)	0.62	-	-
Admission creatinine	-0.012 (-0.056, 0.033)	0.61	-	-
Subcortical intracerebral hemorrhage	-0.360 (-0.52, -0.20)	<0.001	-0.545 (-0.71, -0.38)	<**0.001**
Admission systolic blood pressure [a]	0.020 (0.002, 0.039)	0.031	0.012 (-0.010, 0.034)	0.29
Admission diastolic blood pressure[a]	0.008 (-0.019, 0.034)	0.58	-	-
Admission NIHSS [b]	0.043 (0.038, 0.049)	<0.001	0.048 (0.039, 0.056)	**<0.001**

[a] Per 1mg/dL increase.

[b] NIHSS, National Institutes of Health Stroke Scale.

Table 3: Univariate and multivariate logistic regression analyses evaluating the association of baseline characteristics with the likelihood of hematoma expansion.

	Univariate logistic Regression Analysis		**Multivariate logistic Regression Analysis**	
Variable	**OR (95%CI)**	***p***	**OR (95%CI)**	***p***
Age	1.01 (0.98, 1.02)	0.64	-	-
Gender	0.84 (0.49, 1.44)	0.53	-	-
Caucasian Race	1.61 (0.92, 2.83)	0.096	1.28 (0.52, 3.14)	0.58
BMI	0.99 (0.96, 1.03)	0.83	-	-
Hypertension	1.17 (0.52, 2.61)	0.70	-	-
Diabetes mellitus	0.91 (0.53, 1.57)	0.74	-	-
Hyperlipidemia	1.21 (0.69, 2.11)	0.50	-	-
Coronary artery disease	2.71 (1.40, 5.27)	0.003	1.93 (0.63, 5.85)	0.25
Congestive heart failure	1.52 (0.63, 3.69)	0.35	-	-
Chronic kidney disease	0.93 (0.43, 2.00)	0.85	-	-
History of stroke	0.90 (0.48, 1.68)	0.73	-	-
Smoking	1.03 (0.65, 1.64)	0.89	-	-
Antiplatelet	0.97 (0.55, 1.70)	0.91	-	-
Anticoagulant	1.24 (0.26, 5.97)	0.79	-	-
Statin pretreatment	1.35 (0.76, 2.41)	0.31	-	-
Intensive statin pretreatment	0.46 (0.05, 3.86)	0.472	-	-
Admission INR	0.93 (0.41, 2.10)	0.85	-	-
Admission glucose [a]	1.00 (0.99, 1.01)	0.68	-	-
Admission platelets	0.97 (0.55, 1.70)	0.91	-	-
Admission low-density liprotein cholesterol [a]	0.91 (0.82, 1.01)	0.052	0.88 (0.77, 0.99)	**0.048**
Admission high-density liprotein cholesterol [a]	1.05 (0.89, 1.24)	0.53	-	-
Admission hemoglobin A1c	1.18 (0.98, 1.41)	0.073	1.15 (0.93, 1.43)	0.19
Admission Creatinine	0.96 (0.79, 1.17)	0.70	-	-
Subcortical intracerebral hemorrhage	1.49 (0.80, 2.77)	0.21	-	-
Admission systolic blood pressure [a]	0.97 (0.90, 1.04)	0.36	-	-
Admission diastolic blood pressure [a]	0.95 (0.86, 1.05)	0.35	-	-
Admission NIHSS[b]	1.00 (0.97, 1.03)	0.86	-	-

[a] per 10mg/dL increase

[b] NIHSS – National Institutes of Health Stroke Scale

Table 4. Univariate and multivariate logistic regression analyses evaluating the association of baseline characteristics with the likelihood of functional dependence at hospital discharge (mRS-scores of 3-6).

	Univariate logistic Regression Analysis		**Multivariate logistic Regression Analysis**	
Variable	**OR (95%CI)**	***p***	**OR (95%CI)**	***p***
Age	1.02 (1.01, 1.03)	0.004	1.03 (1.00, 1.07)	**0.023**
Gender	1.14 (0.82, 1.58)	0.44	-	-
Caucasian Race	0.92 (0.64, 1.32)	0.65	-	-
BMI	0.98 (0.96, 1.01)	0.11	-	-
Hypertension	1.79 (1.14, 2.80)	0.011	0.88 (0.39, 2.00)	0.77
Diabetes mellitus	1.15 (0.82, 1.63)	0.41	-	-
Hyperlipidemia	0.77 (0.54, 1.09)	0.15	-	-
Coronary artery disease	1.17 (0.70, 1.95)	0.54	-	-
Congestive heart failure	2.03 (0.99, 4.14)	0.052	2.31 (0.55, 9.66)	0.25
Chronic kidney disease	0.75 (0.47, 1.18)	0.21	-	-
History of stroke	1.07 (0.72, 1.58)	0.75	-	-
Smoking	1.37 (1.02, 1.84)	0.036	2.47 (1.33, 4.57)	**0.004**
Antiplatelet	1.38 (0.96, 1.98)	0.081	1.43 (0.73, 2.82)	0.30
Anticoagulant	0.61 (0.27, 1.37)	0.24	-	-
Statin pretreatment	1.40 (0.95, 2.08)	0.090	1.99 (0.95, 4.14)	0.066
Intensive statin pretreatment	0.93 (0.35, 2.43)	0.880	-	-
Admission INR	0.84 (0.54, 1.29)	0.42	-	-
Admission glucose [a]	1.01 (1.00, 1.02)	0.001	1.00 (0.99, 1.01)	0.72
Admission platelets	1.00 (0.99, 1.01)	0.44	-	-
Admission low-density liprotein cholesterol [a]	0.91 (0.86, 0.96)	0.001	0.94 (0.86, 1.02)	0.15
Admission high-density liprotein cholesterol [a]	1.05 (0.94, 1.17)	0.36	-	-
Admission hemoglobin A1c	0.96 (0.84, 1.09)	0.53	-	-
Admission Creatinine	0.98 (0.89, 1.08)	0.73	-	-
Subcortical intracerebral hemorrhage	1.71 (1.21, 2.42)	0.002	1.12 (0.57, 2.21)	0.74
Admission systolic blood pressure [a]	1.08 (1.04, 1.13)	<0.001	1.18 (1.03, 1.36)	**0.016**
Admission diastolic blood pressure [a]	1.07 (1.01, 1.13)	0.033	0.89 (0.72, 1.10)	0.29
Admission NIHSS [b]	1.41 (1.33, 1.51)	<0.001	1.41 (1.30, 1.54)	**<0.001**

[a] per 10mg/dL increase

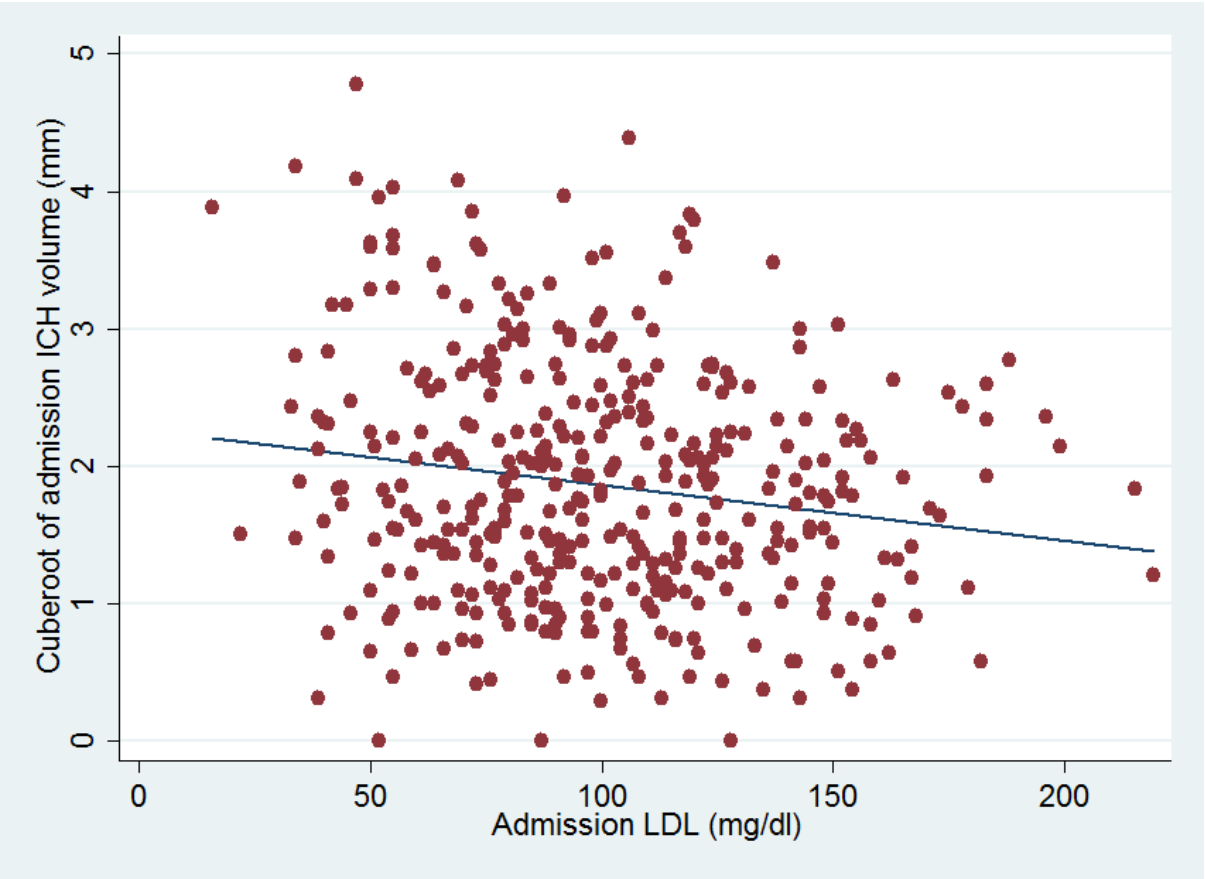
[b] NIHSS – National Institutes of Health Stroke Scale

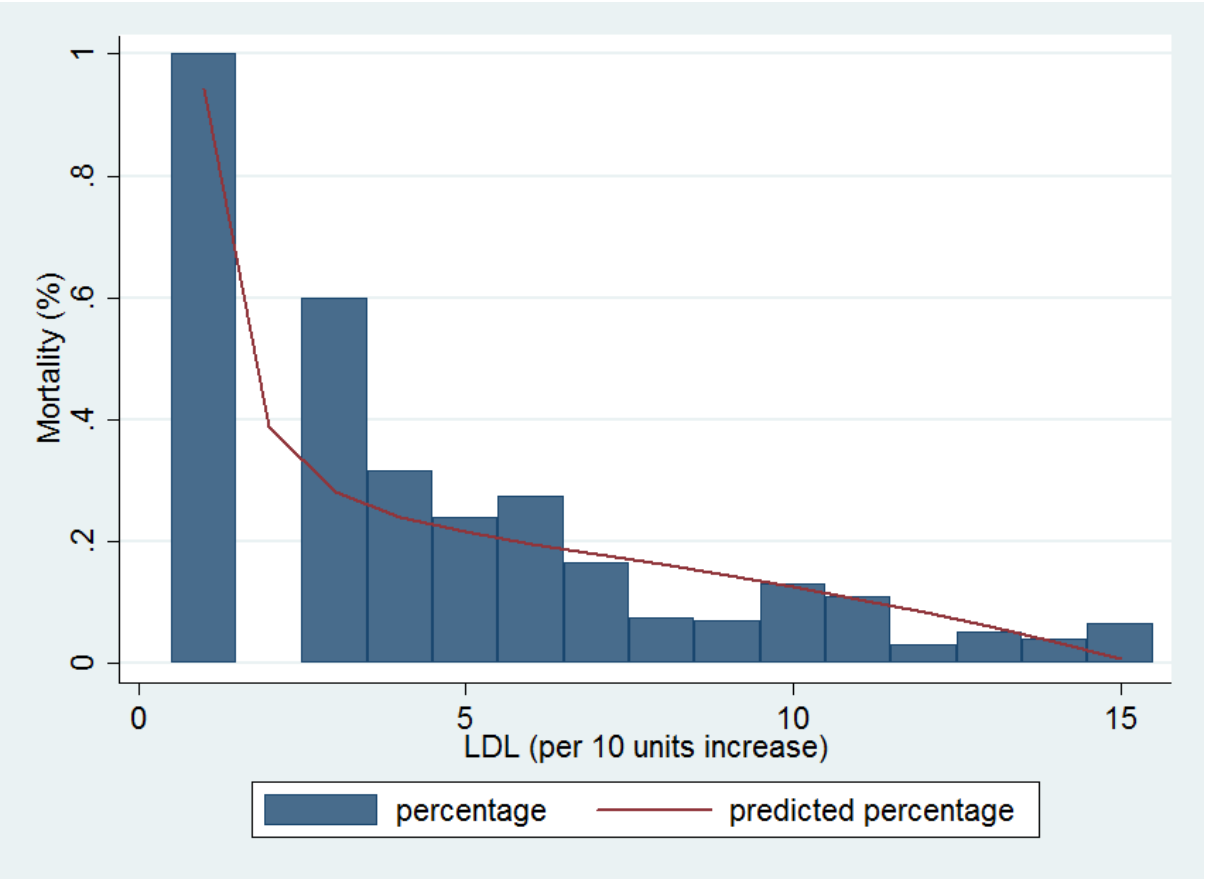
Table 5. Univariate and multivariate logistic regression analyses evaluating the association of baseline characteristics with the likelihood of in-hospital mortality.

	Univariate logistic Regression Analysis		**Multivariate logistic Regression Analysis**	
Variable	**OR (95%CI)**	***p***	**OR (95%CI)**	***p***
Age	1.00 (0.99, 1.01)	0.80	-	-
Gender	0.95 (0.66, 1.35)	0.77	-	-
Caucasian Race	1.08 (0.73, 1.58)	0.70	-	-
BMI	0.97 (0.95, 1.01)	0.063	1.00 (0.94, 1.07)	0.927
Hypertension	1.75 (0.98, 3.14)	0.059	2.03 (0.28, 14.8)	0.486
Diabetes mellitus	0.98 (0.67, 1.42)	0.91	-	-
Hyperlipidemia	0.55 (0.37, 0.84)	0.006	1.01 (0.36, 2.82)	0.981
Coronary artery disease	1.94 (1.18, 3.18)	0.008	1.86 (0.47, 7.43)	0.378
Congestive heart failure	2.24 (1.24, 4.06)	0.008	1.28 (0.28, 5.89)	0.753
Chronic kidney disease	1.90 (1.18, 3.05)	0.008	5.81 (1.42, 23.8)	**0.014**
History of stroke	0.72 (0.46, 1.13)	0.16	-	-
Smoking	1.44 (1.07, 1.94)	0.017	1.59 (0.79, 3.20)	0.188
Antiplatelet	1.17 (0.80, 1.72)	0.41	-	-
Anticoagulant	1.88 (0.81, 4.35)	0.14	-	-
Statin pretreatment	0.91 (0.60, 1.39)	0.67	-	-
Intensive statin pretreatment	0.68 (0.22, 2.16)	0.517	-	-
Admission INR	1.33 (0.85, 2.10)	0.22	-	-
Admission glucose [a]	1.01 (1.00, 1.02)	<0.001	1.00 (0.99, 1.01)	0.951
Admission platelets	1.00 (0.99, 1.01)	0.80	-	-
Admission low-density liprotein cholesterol [a]	0.76 (0.68, 0.84)	<0.001	0.96 (0.94, 0.98)	**<0.001**
Admission high-density liprotein cholesterol [a]	0.84 (0.71, 1.01)	0.057	0.97 (0.94, 0.99)	**0.011**
Admission hemoglobin A1c	0.94 (0.77, 1.15)	0.54	-	-
Admission Creatinine	1.22 (1.11, 1.35)	<0.001	0.86 (0.63, 1.17)	0.341
Subcortical intracerebral hemorrhage	1.35 (0.90, 2.01)	0.147	-	-
Admission systolic blood pressure [a]	1.07 (1.02, 1.12)	0.003	1.00 (0.99, 1.02)	0.746
Admission diastolic blood pressure [a]	1.05 (0.99, 1.12)	0.10	-	-
Admission NIHSS [b]	1.21 (1.17, 1.24)	<0.001	1.24 (1.17, 1.33)	**<0.001**

[a] per 10mg/dL increase

[b] NIHSS – National Institutes of Health Stroke Scale





Highlights – Atherosclerosis

- The relationship between lipoproteins (LDL, HDL) and outcome in ICH is unclear
- This relationship was studied in a prospective cohort study with 672 patients
- Higher LDL levels were independently associated with lower in-hospital mortality