ASSOCIATION BETWEEN LIPID LEVELS AND THE RISK OF HEMORRHAGIC STROKE AMONG WOMEN

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OBJECTIVES

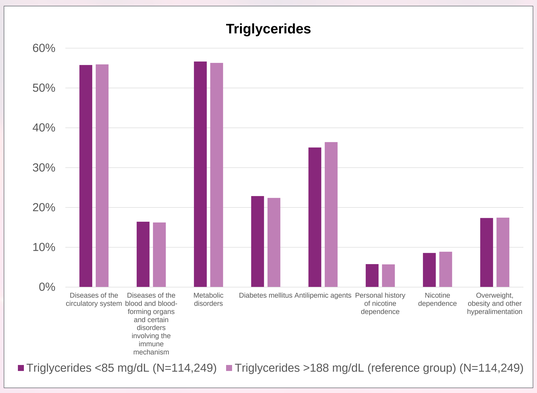
Low low-density lipoprotein cholesterol (LDL-C) levels and low triglyceride levels were associated with an increased risk of hemorrhagic stroke, in the Women's Health Study[1]. This study aims to replicate these results, in a real world setting.

METHODS

Real world data, comprised of electronic medical records from approximately 40 million U.S. patients were analyzed. The population was restricted to females aged 45 years of age and older, who had a lab value after Jan, 1st 2000 and a second recorded lab value at least one month after the first one. LOINC codes for laboratory tests were used to define unique cohorts. The LOINC codes 12951-0 Triglyceride [Mass/volume] in Serum or Plasma by Calculation 3043-7, Triglyceride [Mass/volume] in Blood and 2571-8 Triglyceride [Mass/volume] in Serum or Plasma were used for the triglygerides cohorts. For the LDL-C cohorts, the LOINC codes 13457-7 Cholesterol in LDL [Mass/volume] in Serum or Plasma by calculation, 49132-4 Cholesterol in LDL [Mass/volume] in Serum or Plasma by Electrophoresis, 2089-1 Cholesterol in LDL [Mass/volume] in Serum or Plasma18262-6, Cholesterol in LDL [Mass/volume] in Serum or Plasma by Direct assay and 18261-8 Cholesterol in LDL [Mass/volume] in Serum or Plasma ultracentrifugate, were used.

Five cohorts with the ranges of LDL-C levels: <70 mg/dL, >70-99.9 mg/dL, >100-129.9 mg/dL [reference range], >130-159.9 mg/dL and >160 mg/dL were defined. Similarly, four cohorts for triglyceride levels were defined, with ranges <85 mg/dL, >85-124 mg/dL, >124-188 mg/dL, and >188 mg/dL [reference range]).The index event for the analysis was set as two occurrences of the same lab value range, at least a month apart, for LDL-C and also for triglycerides, with an observation period of one day to one year after the index event. The primary outcome, hemorrhagic stroke, was defined using ICD-10 diagnosis codes I61 nontraumatic intracranial hemorrhage and I60 nontraumatic subarachnoid hemorrhage. Comparisons between each cohort (with an aforementioned defined lab range) and the reference range (Ref.) were performed for the triglycerides and for the LDL-C groups.

Measures of association for each comparison, which include a risk difference, a risk ratio and an odds ratio, were calculated and propensity score matching used to balance cohorts and adjust for 9 of the most likely confounders (Table 2). Confounders that were matched on include age at index, as well as cardiovascular disease, diabetes mellitus, metabolic diseases, obesity, nicotine dependence and use of antilipemic agents (Table 2). Propensity scores were matched 1:1 using a nearest neighbor greedy matching algorithm, with a caliper of 0.25 times the standard deviation, resulting in balanced, matched cohorts (Figure 1).



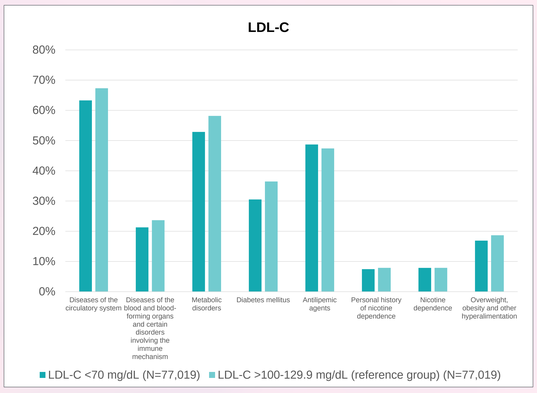


Figure 1. Baseline co-morbidities and medications (after propensity score matching)

Table 1. Baseline characteristics of study participants (before matching)

	Triglycerides ≤85 mg/dL			Triglycerides >188 mg/dL (reference group)			LDL-C <70 mg/dL			LDL-C ≥100-129.9 mg/dL (reference group)		
		Patient Count	% of Count		Patient Count	% of Count		Patient Count	% of Count		Patient Count	% of Count
Age (years)												
Age at index (mean ± sd)	59.6 ± 12.5	255,198	100	60.4 ± 11.5	131,347	100	65.4 ± 12.6	89,563	100	59.5 ± 11.8	248,722	100
Ethnicity												
Hispanic or Latino		7,656	3		10,508	8		2,350	2		5,455	2
Not Hispanic or Latino		130,151	51		74,867	57		47,169	53		154,419	62
Unknown		117,391	46		45,971	35		40,044	45		88,848	36
Race												
White		158,223	62		107,705	82		56,831	64		189,097	76
Black or African American		56,144	22		9,194	7		9,997	11		35,325	14
Asian		22,968	9		2,627	2		16,181	18		6,243	3
Unknown		17,864	7		11,821	9		6,079	7		17,104	7

Table 2. Propensity score matching covariates

Code(s)	Diagnoses/Medications
I00-I99	Diseases of the circulatory system
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
E70-E88	Metabolic disorders
E08-E13	Diabetes mellitus
CV350	Antilipemic agents
Z87.891	Personal history of nicotine dependence
F17	Nicotine dependence
E65-E68	Overweight, obesity and other hyperalimentation
N/A	Age at Index

RESULTS

Two balanced matched cohorts, for the triglycerides and LDL-C groups were generated, with total counts of N=228,498 patients and N=154,038 patients, respectively (Figure 1).

Among women aged 45 years of age and older, patients with triglyceride levels <85 mg/dL had a higher risk of hemorrhagic stroke RR (95% CI) 1.28 (1.09,1.51) compared to those with triglyceride levels >188mg/dL (ref. range) (Table 3). Patients with LDL-C levels <70 mg/dL), compared to those with LDL-C levels >100-129.9 mg/dL (ref. range) had a higher risk for hemorrhagic stroke RR (95%CI) 1.32 (1.09,1.60) (Table 4).

Table 3. Association between triglyceride ranges and risk of hemorrhagic stroke

	Risk Ratio
≤85 mg/dL	1.28 (1.09,1.5)
>85–124 mg/dL	1.13 (0.96,1.32)
>124–188 mg/dL	0.94 (0.79,1.09)
>188 mg/dL	Ref.

Table 4. Association between LDL-C ranges and risk of hemorrhagic stroke

	Risk Ratio (95% CI)
<70 mg/dL	1.32 (1.09,1.60)
≥70–99.9 mg/dL	1.24 (1.07,1.43)
≥100–129.9 mg/dL	Ref.
≥130–159.9 mg/dL	1.08 (0.89,1.31)
≥160 mg/dL	1 (0.77,1.31)

CONCLUSIONS

In this real world analysis, low LDL-C levels and low triglyceride levels were associated with increased risk of hemorrhagic stroke, among women aged 45 years and older.

REFERENCES

1. Rist, P.M. et al.. Lipid levels and the risk of hemorrhagic stroke among women. Nerology. 2019; e2286