Higher On-admission Serum Triglycerides Predict Less Severe Disability and Lower All-cause Mortality after Acute Ischemic Stroke

Slaven Pikija, MD,* Vladimir Trkulja, MD, PhD,† Lucija Juvan, MD,* Marija Ivanec, MD,* and Dunja Dukši, MD*

Background: High(er) on-admission triglyceride (TG) levels have been suggested as an independent predictor of better outcomes of the acute ischemic stroke. Data regarding poststroke physical disabilities have been contradictory. We aimed to investigate the relationship between fasting on-admission TG and development of disability and all-cause mortality over a 2.5-year period. *Methods:* This prospective observational study included 83 acute ischemic stroke patients (29 cardioembolic; 41% men; median age 76 years) followed-up for 28 to 30 months and assessed for physical disability using the Modified Rankin scale (mRS) at 1 week and 3, 12, and 24 months poststroke. TGs were considered as a continuous and a binary variable (≤1.27 [n = 43] and >1.27 mmol/L [n = 43]). *Results:* Higher TGs (continuous or binary) were independently (default adjustments: stroke type, severity at presentation, age, atrial fibrillation, preindex event antiplatelet use, infarct volume, postindex event antiplatelet, statin and angiotensin-converting enzyme inhibitor use, on-admission fasting cholesterol, mean platelet volume, and glomerular filtration rate) were associated with: (1) higher odds of mRS 0 to 2 (none/mild disability) across the assessments (overall odds ratio [OR] 2.73 [95% confidence interval {CI} 1.15-6.38] and OR 3.57 [95% CI 1.04-12.3], respectively); (2) lower odds of mRS worsening between any 2 consecutive assessments (overall OR 0.44 [95% CI 0.20-0.96] and OR 0.35 [95% CI 0.16-0.77], respectively); (3) lower risk of all-cause mortality (hazard ratio 0.47 [95% CI 0.23-0.96] and hazard ratio 0.45 [95% CI 0.21-0.98], respectively). *Conclusions:* These data suggest that higher fasting TGs on-admission predict less severe disability, reduced disability progression, and all-cause mortality in patients with acute ischemic stroke. **Key Words:** Acute ischemic stroke—disability—serum triglycerides—survival.

Increased fasting serum triglycerides (TGs) are typically caused by a combination of genetic and nongenetic factors. Values <1.7 mmol/L are considered normal, concentrations between 1.7 and 2.3 mmol/L are considered borderline high, values between 2.3 and 5.6 mmol/L indicate hypertriglyceridemia (high), and values >5.6 mmol/L are considered very high.[1] A recent meta-analysis of prognostic studies[2] identified high TGs as an independent risk factor for ischemic stroke. Although a critical cut-off value has not been uniformly identified, the effect is consistent across a range of demographic, (co-)morbidity and lipid profile patient characteristics, and considering all ischemic stroke types. An additional population-based study yielded results that were in line with such a view.[3]

On the other hand, the relationship between TGs determined in ischemic stroke patients on admission (typically 24-48 hours since symptom onset) and stroke

From the *Department of Neurology, County Hospital Varaždin, Varaždin; and †Zagreb University School of Medicine, Zagreb, Croatia.

Received October 2, 2011; revision received March 5, 2012; accepted March 8, 2012.

Drs. Pikija and Trkulja contributed equally to this article.

Address correspondence to Slaven Pikija, MD, Department of Neurology, County Hospital Varaždin, Ivana Meštrovića bb, HR-42000 Varaždin, Croatia. E-mail: spikija@gmail.com.

1052-3057/$ - see front matter

doi:10.1016/j.jstrokecerebrovasdis.2012.03.006

severity/outcomes appears to be just the opposite. Higher on-admission TG levels have been found to be independently associated with milder clinical symptoms at presentation (TG >2.3 mmol/L),[4] lower on-admission infarct volumes (stroke-type adjusted) on computed tomographic (CT) scans of the brain (TG >1.7 mmol/L[5] or by 1 mmol/L increase[6]), and less severe disability 1 week poststroke.[6] Only 1 smaller study suggested, based on a univariate analysis, that TG might be somewhat higher in patients with a more severe clinical presentation.[7] The relationship between the on-admission TGs and long(er)-term outcomes is less clear. Stroke patients showing aspirin resistance apparently have higher TG levels than the aspirin responders; high(er) early poststroke TG levels were therefore suggested as a potentially unfavorable prognostic marker.[8] However, higher on-admission TGs were independently associated with a lower all-cause mortality (over a 6-month period)[9] and, in a recent Korean cohort,[10] with a lower all-cause and cardiovascular mortality (over 5 years). Regarding physical disability, high(er) TG levels were independently associated with better outcomes at 90 days poststroke in 1 study in Chinese patients,[11] whereas no effect on disability at 90 days was reported in 2 other studies in European patients.[12,13] Some studies[5,7,8,10,11] referred explicitly to fasting TGs, whereas in others[4,6,9,12,13] this was not the case. Consequently, the primary objective of the present study was to investigate the relationship between the fasting on-admission TGs and medium-/long-term physical disability in a cohort of ischemic stroke patients not treated with thrombolysis or endovascular procedures.

Methods

This single-center prospective observational study was approved by the local ethics committee (in line with the national policy on observational studies).

Patients

Consecutive patients who presented with signs or symptoms of an acute stroke between July 1, 2008 and December 31, 2008 underwent a standard in-house procedure and were included in the present analysis if the following criteria were met: (1) admission within 36 hours of onset; (2) verified ischemic stroke in line with the standard criteria[14]; (3) age ≥18 years; (4) absence of a severe inflammatory/infective disease; (5) no known malignancy; (6) no previous intracranial surgery; (7) serum glucose, cholesterol, and TGs determined after at least a 10-hour fast but not longer than 48 hours since symptom onset; (8) other blood biochemistry and hematology assessed within 36 hours since symptom onset; (9) not a candidate for[15] and not treated (at other, specialized institutions) with delayed endovascular procedures; and (10) consent (patients/relatives) for anonymous use of data for research purposes. A total of 83 patients met these criteria (144 screened).

Diagnostic Procedures

Patients were examined, and a standard 12-lead electrocardiogram, CT brain scan and blood samples for routine biochemistry, coagulation, and hematology were taken[15,16] (ethylenediaminetetra-acetic acid–treated tubes for hematology to avoid platelet swelling).[6] Stroke patients were admitted to the stroke unit with continuous monitoring until stabilization or for at least 72 hours poststroke, after which they were transferred to the neurology ward. Where indicated, extracranial/transcranial Doppler ultrasound and echocardiography were performed, typically between days 2 and 7 after admission. These and other diagnostic procedures (eg, laboratory including blood oxygenation and toxicology tests, chest radiograph, electroencephalogram, and arteriography) were performed/repeated as indicated until discharge and during follow-up in line with a standard of care for stroke patients.

Treatments

All patients were started on aspirin immediately after their diagnosis (200-300 mg loading dose, 100 mg/day onward). General acute stroke treatment was in line with the guidelines.[15,16] After stabilization (typically from day 5 since admission onward), treatments aimed at secondary prevention were defined in line with the recommendations,[15,16] except that low-dose aspirin remained the exclusive antiplatelet treatment, warfarin was introduced to only 2 patients with atrial fibrillation (otherwise managed with low-dose aspirin and antiarrhythmics), glibenclamide was the predominant oral antidiabetic medication, and the only dyslipidemia treatment were statins (no patient used fibrates). Patients surviving the hospital stay proceeded to rehabilitation programs and all received appropriate lifestyle and dietary instructions. Recombinant tissue plasminogen activator (rt-PA) became available during October 2008 (approved by the National Health Insurance System), but was not used in any of the current patients.

Patient Evaluations and Follow-up

A structured interview (patients/relatives) and medical history review were used to establish preindex event patient characteristics. Hypertension, atrial fibrillation, chronic heart failure, and diabetes mellitus were assessed also based on diagnostic procedures during the in-hospital stay. Strokes were classified as cardioembolic, small artery occlusion (lacunar), large artery atherosclerotic, other determined etiology, and stroke of undetermined/unclassified etiology[17] based on agreement between 2 investigators. On-admission serum creatinine