Atherogenic Index of Plasma and Triglyceride/High-Density Lipoprotein Cholesterol Ratio Predict Mortality Risk Better Than Individual Cholesterol Risk Factors, Among an Older Adult Population

To the Editor: Atherogenic index of plasma (AIP), a logarithmically transformed ratio of triglycerides (TGs)/high-density lipoprotein cholesterol (HDL-C), is considered a marker of plasma atherogenicity[1] based on observed strong ($r>.7$), positive associations between AIP and cholesterol esterification rates, lipoprotein particle size, and remnant lipoproteinemia.[2,3] Previous work supports the utility of this parameter, demonstrating its positive association with cardiovascular disease (CVD) risk.[4,5] Notably, evidence indicates that AIP may be more closely associated with CVD risk than are other atherogenic indices[4] or individual lipoproteins cholesterol concentrations alone.[5]

The purpose of the present study was to assess whether the predictive value of AIP extended to mortality risk among a sample of older US adults, when compared with individual cholesterol risk factors (eg, triglycerides, total cholesterol [TC], low-density lipoprotein cholesterol (LDL-C), and HDL-C) or the TG/HDL-C ratio.[3] This has yet to be evaluated in the literature and is a worthwhile investigation, considering that CVD remains the leading cause of mortality among US adults.

Data from the 1999-2006 National Health and Nutrition Examination Survey were used, with follow-up through 2011. The sample included 1341 older adults (ages 65-85 years) who did not die during the first 12 months of follow-up and had not, at the time of entry into the database, had a physician-diagnosis of congestive heart failure, coronary artery disease, heart attack, stroke, emphysema, or chronic bronchitis. The median follow-up period was 91 months (interquartile range, 68-118 months). Among the 1341 participants, 399 died during the follow-up period. For the entire sample, over 123,909 person-months of follow-up there was an incidence rate of 3.2 (95% CI, 2.91-3.55) deaths per 1,000 person-months. All-cause deaths were assessed, as opposed to CVD deaths (or other cause-specific deaths), because only 62 of the deaths were attributed to CVD.

The AIP was assessed from a blood sample and calculated as $\log_{10}$(TG/HDL-C), with TG (mg/dL/88.57) and HDL-C (mg/dL/38.67) expressed in mmol/L. In a multivariable Cox proportional hazard model (covariates shown in the Table footnote; Schoenfeld's residuals were used to verify the proportional hazards assumption), and as shown in the Table (model 1), TC, LDL-C, HDL-C, and TG were not associated with an increased mortality risk when expressed as a continuous variable. Similarly, when TC (>200 mg/dL; hazard ratio [HR], 0.89; 95% CI, 0.67-1.17), LDL-C (≥100 mg/dL; $HR_{adjusted}$, 0.78; 95% CI, 0.55-1.11), HDL-C (<40 mg/dL; $HR_{adjusted}$, 1.12; 95% CI, 0.78-1.60), and TG (>200 mg/dL; $HR_{adjusted}$, 1.18; 95% CI, 0.86-1.63) were expressed as binary variables, results were unchanged. Notably, however,

TABLE. Multivariable Cox Proportional Hazard Model Evaluating the Association Between Cholesterol Parameters and All-Cause Mortality Risk, 1999-2006 NHANES (N=1341; 60-85 y)[a]

Cholesterol parameters	Weighted mean (95% CI)	HR (95%CI)	
		Model 1[b]	Model 2[c]
TC (mg/dL)	210.4 (207.80 to 213.19)	0.99 (0.61 to 1.58)	0.998 (0.99 to 1.01)
LDL-C (mg/dL)	124.4 (122.06 to 126.77)	1.00 (0.63 to 1.61)	0.9995 (0.99 to 1.01)
HDL-C (mg/dL)	57.54 (56.47 to 58.61)	1.00 (0.62 to 1.61)	NA
TG (mg/dL)	142.77 (138.16 to 147.37)	1.00 (0.91 to 1.10)	NA
TG/HDL-C (mmol/L)	1.24 (1.19 to 1.30)	NA	1.13 (1.02 to 1.25)
AIP, >0.24 vs ≤0.24	0.01 (−0.01 to 0.02)	NA	1.29 (1.03 to 1.63)

[a]AIP = Atherogenic index of plasma; HDL-C = high-density lipoprotein cholesterol; HR = hazard ratio; LDL-C = low-density lipoprotein cholesterol; MET = metabolic equivalent of task; MVPA = moderate-to-vigorous physical activity; NA = not applicable (not entered into the model); NHANES = National Health and Nutrition Examination Survey; TC = total cholesterol; TG = triglyceride.

[b]This model included TC, LDL-C, HDL-C, and TG in a single model and also adjusted for age (continuous; y), sex, race-ethnicity (Mexican American, white, black, other), physician-diagnosed hypertension (yes/no), physician-diagnosed diabetes (yes/no), body mass index (continuous; kg/m^2), self-reported smoking status (daily, former, never), on cholesterol medication (yes/no), self-reporting meeting physical activity guidelines (yes/no; ≥2000 MVPA MET-min-month).

[c]Adjusted for the same covariates in model 1 but TG and HDL-C were not included in model 2 (LDL-C and TC, along with all the other covariates, were included).

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the TG/HDL-C ratio (eg, the nonlogarithmic form of AIP) was associated with an increased mortality risk ($HR_{adjusted}$, 1.13; 95% CI, 1.02-1.25). When AIP was expressed as a continuous variable, AIP was not statistically significantly associated with mortality risk ($HR_{adjusted}$, 1.29; 95% CI, 0.90-1.86).

However, those with an AIP of more than 0.24 (vs $\leq$0.24)[1] had a 29% increased mortality risk ($HR_{adjusted}$, 1.29; 95% CI, 1.02-1.62) (model 2, Table). Those with a moderate AIP level[1] (AIP of 0.1-0.24 vs AIP <0.1) did not have an increased mortality risk ($HR_{adjusted}$, 0.96; 95% CI, 0.63-1.46).

The present study supports a positive, independent association between TG/HDL-C and elevated AIP with mortality risk. In addition, these findings indicate that AIP, and, in particular, TG/HDL-C may be stronger predictors of mortality than individual cholesterol risk factors.

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"Being Dumped" for Administrative Efficiency

To the Editor: Dr Bostwick's commentary published in the July 2016 issue of *Mayo Clinic Proceedings*[1] is very troubling. As general internists for a combined 80 years, we have both been honored to be able to provide ongoing care for fellow physicians as well as patients who have established important relationships with our own doctors. We both fully understand the issues from both points of view, including the efficiency necessary to successfully run a practice of general internal medicine. However, we feel strongly that the existing relationship established by a patient (in this case a physician) and his doctor takes precedence over any real (or perceived) reduction in "clinical efficiency" resulting from continuity of care.

As Dr Bostwick notes, "an administrative quest…had dictated that [his doctor] no longer commandeer appointment slots designated for external referrals to accommodate the internal patients for whom he provided care." An "appointment slot" for a new patient is very different from one for an established patient. His physician apparently acquiesced with the administrative mandate, or may have had no choice. An alternative option could have been to ask the internist to avoid adding additional "internal patients," which, in time, would have gradually improved the "efficiency" issue. Another alternative would have been to ask the internist to meet with each of his internal patients individually to discuss the issue, and if agreeable, those willing to change physicians could be transitioned in a less stressful manner. Either of these compromises would have allowed for the possibility of maintaining the patient-physician relationship.

Dr Bostwick, as the patient, has written articulately and thoughtfully about his feelings and fears, ending his commentary by saying, "I am terrified I will be dumped again." The *Proceedings* should be credited for publishing this piece because it will undoubtedly lead to important discussion. Hopefully, those discussions will include the deserved emphasis on the doctor-patient relationship, which in our opinion should be considered a higher priority than "clinical efficiency." In the final analysis, we should be reminded of the exemplary guidance provided (for all patients) by the Mayo Clinic primary value statement: "The needs of the patient come first."

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Editor's Note: When publishing a letter that comments on an article published previously in *Mayo Clinic Proceedings*, it is the journal's policy to invite the author(s) of the referenced article to publish a response. Dr J. Michael Bostwick was invited to respond, and although he was supportive of this letter, he felt the content of the letter did not require a reply.

1. Bostwick JM. Dumped: how a quest for administrative efficiency lost a doctor his doctor. *Mayo Clin Proc*. 2016;91(7):833-835.

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Atrial Fibrillation: Interatrial Block May Be an Underdiagnosed and Easily Recognizable Risk Factor

To the Editor I read with interest the excellent article by Morin et al[1] published in the December 2016 issue of *Mayo Clinic Proceedings*. As the authors noted, a myriad of risk factors for atrial fibrillation have been identified.