Elevated levels of nonfasting triglycerides were associated with increased risk for death, MI, and ischemic heart disease

Nordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A. **Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women.** JAMA. 2007;298:299-308.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★★☆ Endocrinology ★★★★★★☆

QUESTION

Does the level of nonfasting triglycerides (indicative of remnant lipoproteins) predict risk for death, myocardial infarction (MI), and ischemic heart disease in men and women?

METHODS

Design: Cohort from the Copenhagen City Heart Study followed for a mean 26 years.

Setting: Copenhagen, Denmark.

Patients: 6394 men and 7587 women who were 20 to 93 years of age and of Danish descent from the Copenhagen Central Person Register.

Risk factors: Increasing levels of nonfasting triglycerides (< 1 mmol/L [< 88.5 mg/dL], 1 to 1.99 mmol/L [88.5 to 176.1 mg/dL], 2 to 2.99 mmol/L [177.0 to 264.6 mg/dL], 3 to 3.99 mmol/L [265.5 to 353.1 mg/dL], 4 to 4.99 mmol/L [354.0 to 441.6 mg/dL], and ≥ 5 mmol/L [≥ 442.5 mg/dL]). Results were adjusted for age, total cholesterol, body mass index, hypertension, diabetes, smoking, alcohol consumption, physical inactivity, lipid-lowering therapy, and postmenopausal status and hormone therapy in women.

Outcomes: Death, MI, and ischemic heart disease.

MAIN RESULTS

At a mean 26 years, 4087 (64%) men and 3731 (49%) women died, 1102 (17%) men and 691 (9.1%) women had MI, and 1912 (30%) men and 1567 (21%) women had ischemic heart disease. Every 1-mmol/L (88.5-mg/dL) increase in the level of nonfasting triglycerides led to increasing risk for death, MI, and ischemic heart disease in women and death and MI in men (Table).

CONCLUSION

Elevated levels of nonfasting triglycerides were associated with increased risk for death, myocardial infarction, and ischemic heart disease in women and death and myocardial infarction in men.

Sources of funding: Danish Heart Foundation; Danish Medical Research Council; Research Fund at Rigshospitalet; European Union.

For correspondence: Dr. B.G. Nordestgaard, Herlev University Hospital, Herlev, Denmark. E-mail brno@heh.regionh.dk.

Association between increasing nonfasting triglyceride levels and risk for death, myocardial infarction (MI), and ischemic heart disease (IHD) in men and women at a mean 26 years*

Triglyceride level (mmol/L) [mg/dL]	Adjusted hazard ratio (95% CI)†					
	Men (*n* = 6394)			Women (*n* = 7587)		
	Death	MI	IHD	Death	MI	IHD
< 1 [< 88.5]	1.0	1.0	1.0	1.0	1.0	1.0
1 to 1.99 [88.5 to 176.1]	1.2 (1.0 to 1.5)	1.4 (1.0 to 2.1)	1.1 (0.8 to 1.4)‡	1.3 (1.1 to 1.5)	1.7 (1.2 to 2.5)	1.4 (1.1 to 1.8)
2 to 2.99 [177.0 to 264.6]	1.4 (1.1 to 1.7)	1.6 (1.1 to 2.4)	1.3 (0.9 to 1.7)‡	1.6 (1.4 to 2.0)	2.5 (1.6 to 3.9)	1.8 (1.4 to 2.5)
3 to 3.99 [265.5 to 353.1]	1.5 (1.2 to 2.0)	2.3 (1.4 to 3.7)	1.3 (0.9 to 1.9)‡	2.2 (1.7 to 3.0)	2.1 (1.0 to 4.3)	1.8 (1.2 to 2.9)
4 to 4.99 [354.0 to 441.6]	1.6 (1.1 to 2.1)	1.9 (1.0 to 3.4)	1.2 (0.7 to 1.9)‡	1.9 (1.2 to 3.0)	2.4 (1.2 to 3.0)	1.2 (0.6 to 2.5)‡
≥ 5 [≥ 442.5]	1.8 (1.3 to 2.5)	2.4 (1.3 to 4.2)	1.5 (1.0 to 2.4)	3.3 (2.0 to 5.4)	5.4 (2.1 to 14)	2.6 (1.2 to 5.5)

*CI defined in Glossary. All trends for association between increasing triglyceride levels and increasing risk for death, MI, or IHD are significant ($P = 0.03$ for IHD in men, $P < 0.001$ for the rest).

†Adjusted for age, total cholesterol, body mass index, hypertension, diabetes, smoking, alcohol consumption, physical inactivity, lipid-lowering therapy, and postmenopausal status and hormone therapy in women.

‡Not significant.

COMMENTARY

Serum triglyceride levels have never been widely accepted as an important risk factor for coronary heart disease, despite a rather large body of suggestive evidence. One proposed reason for the inconclusive evidence has been that postprandial rather than fasting triglyceride levels have the stronger mechanistic relationship with atherogenesis. The study by Nordestgaard and colleagues addresses this hypothesis by testing the association between nonfasting triglyceride levels and incidence of angina, MI, or death in a cohort study of Danes that began in 1976. The study found significant associations with most endpoints and trends toward stronger associations at higher triglyceride levels. Associations were stronger in women than in men.

Like most epidemiologic studies of chronic disease, this study suggests directions for future research and leaves clinically important questions unanswered. The study did not compare the predictive value of fasting triglyceride levels with that of nonfasting levels or provide suggestions for standardizing postprandial triglyceride measurements. It only partially untangled the confounding effects of age, overweight, and insulin resistance—effects that will become important if we reach the stage of testing treatment for postprandial hypertriglyceridemia. Although participants were selected from a very narrow ethnic range, another study showed similar conclusions without some of the shortcomings of this study (1).

Although intriguing, the results are not ready to be applied clinically. The measurement of nonfasting triglyceride levels should not replace the measurement of fasting levels, and risk for coronary heart disease should continue to be judged by assessing age, sex, systolic blood pressure, presence of diabetes, smoking history, family history in first-degree relatives, and high- and low-density lipoprotein cholesterol levels.

Edward P. Havranek, MD
Denver Health Medical Center
Denver, Colorado, USA

Reference

1. **Bansal S, Buring JE, Rifai N, et al.** JAMA. 2007;298:309-16.