PUBLICATION INSIGHT

# Elevated serum triglycerides are independently associated with persistent organ failure in acute pancreatitis

H. Nawaz, E. Koutroumpakis , J. Easler , A. Slivka , D. C. Whitcomb , V. P. Singh , D. Y. and G. I. Papachristou
*Am J Gastroenterol.* 2015;110:1497-503.

## CONCLUSION

- Elevated serum triglyceride(TG) levels in patients with acute pancreatitis (AP) are independently and proportionally associated with persistent organ failure.
- Given the substantial differences in clinical outcomes among patients with HTG, it is crucial for clinicians to recognize this risk group.
- Lipotoxicity mediated by elevated triglycerides could serve as a promising target for developing new treatments for severe acute pancreatitis.

## INTRODUCTION

Acute pancreatitis is a common gastrointestinal disorder requiring inpatient admission in the United States. While most cases are mild, a subset of patients (15-20%) develop severe AP characterized by persistent organ failure, leading to significant morbidity and mortality. **Identifying risk factors for severe AP in the early phase is crucial** for appropriate patient triage and targeted therapies. **Hypertriglyceridemia (HTG)** is a major public health problem, affecting over 30% of the U.S. population and is considered the **third most common etiology of AP**.

## METHODS

The study prospectively enrolled 400 AP patients, categorizing them based on their serum TG levels into normal, mild (150–199 mg/dl), moderate (200–999 mg), severe (1.000-1.999 mg/dl) and very severe (> 2.000 mg/dl) HTG. Serum TG levels were measured within 72 hours of hospital admission. The researchers compared demographics, comorbidities, and clinical outcomes across these categories. Univariate and multivariate analyses were conducted to identify independent associations between TG levels and persistent organ failure, adjusting for factors such as age, gender, body mass index (BMI), diabetes, and alcohol etiology.

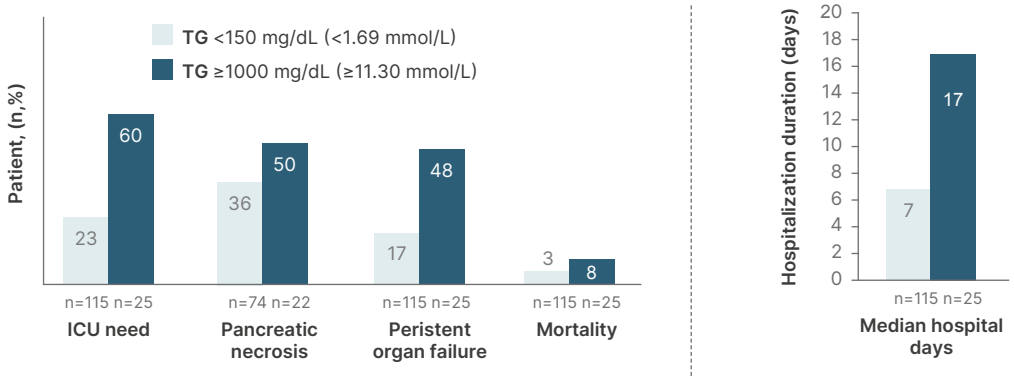
## RESULTS

Out of 400 patients, 201 had serum TG levels measured within 72 hours of admission. Among these, 115 (57%) had normal TG levels, while 86 (43%) had elevated TG levels (20 mild, 41 moderate, and 25 severe/very severe). Key findings include:

- Patients with HTG were younger (median age 44 vs. 52 years), predominantly male (65% vs. 45%), more likely to be obese (57% vs. 34%), and diabetic (38% vs. 17%) compared to those with normal TG levels.
- Persistent organ failure developed in 40% of patients with HTG compared to 17% with normal TG levels ($P<0.001$).
- The rate of persistent organ failure increased with the severity of HTG: 17% in normal TGs, 30% in mild, 39% in moderate, and 48% in severe/very severe HTG ($P<0.001$).

- ICU care was required for 39 patients (45%) with HTG, compared to 27 patients (23%) with normal triglyceride levels (P = 0.001). The median hospital stay was 10 days (range: 5–22) for patients with HTG, versus 7 days (range: 4–15) for those with normal triglyceride levels (P = 0.06). There was no significant difference in the incidence of pancreatic necrosis and mortality between the two groups.
- On multivariate analysis, moderate HTG (odds ratio [OR] 2.6; P=0.04) and severe/very severe HTG (OR 4.9; P=0.009) were independently associated with persistent organ failure.

**Patients with acute pancreatitis (AP) who have HTG have more severe courses and longer hospital stays than normolipemic AP patients**




## DISCUSSION

This study is the first to demonstrate that **elevated serum triglyceride levels early in the disease progression are independently linked to persistent organ failure in acute pancreatitis (AP) patients**, irrespective of the underlying cause. This association is proportional, indicating that higher serum triglyceride levels correspond to an increased likelihood of persistent organ failure. The findings suggest that TG-mediated lipotoxicity plays a critical role in the severity of AP. At the onset of acute pancreatitis (AP), pancreatic injury releases pancreatic lipase into the bloodstream, which hydrolyzes serum triglycerides and adipose tissue, generating free fatty acids. In cases of hypertriglyceridemia (HTG), the excess free fatty acids can exceed the toxic threshold, leading to lipotoxicity, mitochondrial stress, and an inflammatory response, which may result in multi-system organ failure.