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# Evaluation of Hypertriglyceridemia in Critically Ill Patients With Coronavirus Disease 2019 Receiving Propofol

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**OBJECTIVES:** To report the prevalence of, and evaluate risk factors for, the development of hypertriglyceridemia (defined as a serum triglyceride level of > 400 mg/dL) in patients with coronavirus disease 2019 who received propofol.

**DESIGN:** Single-center, retrospective, observational analysis.

**SETTING:** Brigham and Women's Hospital, a tertiary academic medical center in Boston, MA.

**PATIENTS:** All ICU patients who with coronavirus disease 19 who received propofol between March 1, 2020, and April 20, 2020.

**INTERVENTIONS:** None.

**MEASUREMENTS AND MAIN RESULTS:** The major outcome of this analysis was to report the prevalence of, and risk factors for, the development of hypertriglyceridemia in patients with coronavirus disease 19 who received propofol. Minor outcomes included the development of acute pancreatitis and description of propofol metrics. Of the 106 patients that were included, 60 (56.6%) developed hypertriglyceridemia, with a median time to development of 46 hours. A total of five patients had clinical suspicion of acute pancreatitis, with one patient having confirmatory imaging. There was no difference in the dose or duration of propofol in patients who developed hypertriglyceridemia compared with those who did not. In the patients who developed hypertriglyceridemia, 35 patients (58.5%) continued receiving propofol for a median duration of 105 hours. Patients who developed hypertriglyceridemia had elevated levels of inflammatory markers.

**CONCLUSIONS:** Hypertriglyceridemia was commonly observed in critically ill patients with coronavirus disease 2019 who received propofol. Neither the cumulative dose nor duration of propofol were identified as a risk factor for the development of hypertriglyceridemia. Due to the incidence of hypertriglyceridemia in this patient population, monitoring of serum triglyceride levels should be done frequently in patients who require more than 24 hours of propofol. Many patients who developed hypertriglyceridemia were able to continue propofol in our analysis after reducing the dose.

**KEY WORDS:** acute respiratory distress syndrome; analgesia and sedation; coronavirus disease 2019; lipids; pancreatitis; propofol



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Propofol is a rapidly acting, titratable medication that is commonly used for sedation in mechanically ventilated, critically ill patients. Propofol is minimally water soluble and is therefore available only as an oil-in-water emulsion (1, 2). Particularly when administered at high doses for prolonged durations, it has been associated with various adverse effects, including bradycardia, hypotension, infection, propofol-related infusion syndrome, and hypertriglyceridemia (2–13). Additionally, hypertriglyceridemia may lead to other unwanted outcomes, such as clotting of continuous renal replacement therapy filters or extracorporeal membrane oxygenation (ECMO) circuits, elevated liver enzymes, or pancreatitis (4, 14–19).

The true incidence of both hypertriglyceridemia and pancreatitis associated with propofol are still unknown (18). Various risk factors, such as age, ICU length of stay (LOS), administration of other drugs that may cause hypertriglyceridemia, as well as the dose and duration of propofol, have been associated with the development of elevated triglyceride levels (7, 18).

Patients who are diagnosed with coronavirus disease 2019 (COVID-19) may develop respiratory distress that requires mechanical ventilation, with some progressing to acute respiratory distress syndrome (ARDS) (20–26). Propofol is an attractive sedative in these patients since it is rapid acting and easily titratable. Additionally, propofol is effective for decreasing respiratory drive, allowing for lung protective ventilator strategies, such as the utilization of low tidal volumes, higher positive end-expiratory pressures, and prone positioning (1, 20). While the metabolic derangements secondary to COVID-19 have yet to be fully described, various reports have been published demonstrating hypertriglyceridemia patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), possibly secondary to various therapies (27, 28).

The purpose of this analysis is to report the prevalence of, and evaluate risk factors for, hypertriglyceridemia in patients with COVID-19 who are mechanically ventilated and receiving propofol. Our analysis aimed to describe propofol utilization in patients with COVID-19, specifically in patients who developed hypertriglyceridemia, and evaluate potential negative consequences of continuation of propofol therapy with elevated triglyceride levels.

## MATERIALS AND METHODS

This was a retrospective, observational analysis conducted at Brigham and Women's Hospital. Mass General Brigham Institutional Review Board approval was obtained prior to initiation of this study (protocol number 2019P002658). We identified consecutive adult patients with COVID-19 that were admitted to any ICU and received propofol (10% oil-in-water lipid emulsion) while mechanically ventilated. Patients had to receive at least 4 hours of propofol and have at least one serum triglyceride level drawn while receiving propofol to be included in the analysis. The decision to exclude less than 4 hours of continuous infusion propofol was made to eliminate patients who only received propofol for procedural sedation; however, we intended to include patients who may have received relatively short durations of propofol to capture the rapid increase in triglycerides that have been noted in patients with COVID-19. Patients were excluded if they had a diagnosis of pancreatitis or concern for pancreatitis (defined as lipase > 60 U/L or amylase > 125 U/L with consistent CT findings or clinical examination and documentation of pancreatitis by medical team) at admission, or if they transferred from an outside hospital and had received propofol for greater than 24 hours. Hypertriglyceridemia, to be consistent with previous literature, was defined as a serum triglyceride level of greater than 400 mg/dL (7). Additionally, median triglyceride levels were categorized according to the American Heart Association/American College of Cardiology hypertriglyceridemia management guidelines: borderline high: 150 to 199 mg/dL, high: 200 to 499 mg/dL, and very high: greater than or equal to 500 mg/dL (29). Severe hypertriglyceridemia was defined as a serum triglyceride level greater than 1,000 mg/dL.

Pertinent patient data were collected, such as Acute Physiology and Chronic Health Evaluation II score on ICU admission, baseline demographics, relevant past medical history, and nutritional requirements. Baseline laboratory values were defined as available within 1 year of admission. Day 1 of laboratory values and therapies was defined as the first day the patient received propofol. Propofol metrics, such as daily dose, cumulative dose, and duration of infusion, were collected. Daily median propofol rate was calculated using total propofol volume, hours of infusion, and the order weight.

Interruption or discontinuation of propofol due to elevated triglycerides, along with specifics regarding reinitiation of the infusion, were recorded based on both laboratory results and documentation by care teams in electronic medical records. Daily levels of triglycerides, lipase, amylase, creatine kinase, and lactate were collected when available. At our institution, the maximum dose allowed in the ICU is 83 μg/kg/min, and it is recommended to monitor triglyceride levels every 48–72 hours for patients requiring prolonged infusions. In patients in which triglyceride levels are elevated, evaluation of triglyceride and lipase levels is warranted. The maximum levels of inflammatory laboratory values related to COVID-19, such as ferritin, lactic acid dehydrogenase (LDH), C-reactive protein (CRP), D-dimer, and aspartate aminotransferase (AST), were collected for each patient. All patients who had baseline triglyceride values available were evaluated for an increase of greater than or equal to 50% from baseline during propofol therapy. In patients that developed hypertriglyceridemia, documentation of the time to hypertriglyceridemia, lipase at the time of hypertriglyceridemia, average rate of propofol for 6 hours prior, and documentation of pancreatitis were collected. Propofol rate and triglyceride levels were assessed in a subgroup of patients that continued to receive propofol for greater than 24 hours despite developing hypertriglyceridemia. The development of pancreatitis was determined based upon the definition mentioned above, along with high clinical suspicion documented in the patient medical record. The administration of IV or enteral nutrition, along with medications that may affect triglyceride levels, was documented.

Continuous data were analyzed using paired *t* test (parametric data, expressed as mean [SD]) or Mann-Whitney *U* test (nonparametric data, expressed as median [interquartile range (IQR)]) when appropriate. chi-square test or Fisher exact test was used when appropriate for categorical data. We used a logistic regression model to investigate the association of various risk factors with the development of hypertriglyceridemia in patients with COVID-19 who received propofol. Data are presented in odds ratio (OR) and 95% CI. We included variables with *p* value of less than 0.1 from the univariate analysis, unless removed based on clinical experience or data availability. D-dimer, CRP, LDH, and AST were log transformed for the analysis.

## RESULTS

Overall, 128 patients who tested positive for SARS-CoV-2 and received propofol in one of several ICUs dedicated to patients with COVID-19 were screened, of which 22 were excluded for the following reasons: transfer from outside hospital with propofol administered for greater than 24 hours ($n$ = 13), zero triglyceride levels drawn during admission ($n$ = 8), and acute pancreatitis at admission ($n$ = 1). Baseline characteristics of the 106 patients that were included are displayed in **Table 1**.

Outcomes for the entire cohort, as well as for patients who developed ($n$ = 60) and did not develop ($n$ = 46) hypertriglyceridemia, can be found in **Table 2**. The overall median duration of propofol administration was 167 hours (IQR, 71.5–278.5 hr) and the median maximum triglyceride level 456 mg/dL (IQR, 250–602 mg/dL). Of the 106 patients that were included, 60 (56.6%) developed hypertriglyceridemia, and seven patients (6.6%) had severe hypertriglyceridemia (Table 2). The median time to the development of hypertriglyceridemia was 46 hours, with no difference seen in propofol exposure at 48 hours (8.1 vs 6.8 g; $p$ = 0.218). A total of five patients had clinical suspicion of acute pancreatitis, with one patient having confirmatory imaging. The median cumulative dose of propofol in the entire cohort was 34.6 g and the median rate of propofol at the time of the development of hypertriglyceridemia was 58 μg/kg/min. Maximum triglyceride and lipase levels can be found in Table 2.

Of the 39 patients who had propofol discontinued secondary to elevated triglyceride levels, 25 patients (64.1%) were restarted on propofol during their ICU course. The median triglyceride and lipase levels at the time of discontinuation were 579 mg/dL and 71 U/L, respectively. Propofol was held for a median duration of 74 hours and reinitiated at a lower dose in 22 of 25 patients (Table 2).

Median daily triglyceride levels and rates of propofol were compared in patients who developed and did not develop hypertriglyceridemia (**Fig. 1**). Of the 60 patients with hypertriglyceridemia, 35 patients (58.5%) continued receiving propofol for a median duration of 105 hours. Daily serum triglyceride levels and propofol administration rates of these 35 patients are shown in **Figure 2**. Overall, of the 48 patients with baseline triglyceride levels available, 41 patients (85%)

**TABLE 1.**
**Baseline Characteristics**

| Variable | All Patients, *n* = 106 | Developed Hypertriglyceridemia, *n* = 60 | Did Not Develop Hypertriglyceridemia, *n* = 46 | *p* |
|---|---|---|---|---|
| Acute Physiology and Chronic Health Evaluation II[a] | 21 (17–28) | 21 (17–28) | 21 (16–28) | 0.4332 |
| Gender (male)[b] | 67 (63.2) | 39 (65.0) | 28 (60.1) | 0.6620 |
| Age[a] | 66 (56–75) | 60 (52–69) | 70 (66–79) | 0.0001 |
| Weight (kg)[a] | 80.3 (69.7–98.2) | 80.0 (70.2–97.4) | 81.6 (69.2–99.0) | 0.3387 |
| Body mass index[a] | 27.8 (24.8–32.2) | 28.0 (25.0–32.0) | 27.8 (23.9–32.5) | 0.4777 |
| Comorbidities[b] | | | | |
| Hyperlipidemia | 51 (48.1) | 28 (46.7) | 23 (50.0) | 0.7335 |
| Diabetes mellitus | 46 (43.4) | 28 (46.7) | 18 (39.1) | 0.4378 |
| Coronary artery disease | 18 (17.0) | 6 (10.0) | 12 (26.1) | 0.0287 |
| End-stage renal disease, hemodialysis | 13 (12.3) | 10 (16.7) | 3 (6.5) | 0.1145 |
| Alcohol abuse | 5 (4.7) | 4 (6.7) | 1 (2.2) | 0.2795 |
| Hypothyroidism | 4 (3.8) | 3 (5.0) | 1 (2.2) | 0.4491 |
| Lupus | 3 (2.8) | 1 (1.7) | 2 (4.3) | 0.4093 |
| Bone marrow transplant | 1 (.94) | 0 | 1 (2.2) | 0.2512 |
| Baseline triglyceride[a], *n* = 48 | 119 (78–181) | 141 (113–216), *n* = 25 | 107 (70–152), *n* = 23 | 0.0121 |
| Parenteral or enteral nutrition[b,c] | 100 (94.3) | 57 (95.0) | 43 (93.5) | 0.7368 |
| Parenteral | | 0 | 2 | |
| Enteral | | 57 | 42 | |

[a]Reported as median (interquartile range).
[b]Reported as *n* (%).
[c]Patients may have received both therapies.

had a greater than 50% increase (Table 2). While there was a trend toward the development of hypertriglyceridemia in patients who received tocilizumab, no differences were observed in concomitant medications in patients who developed hypertriglyceridemia compared with those who did not, with the exception of IV insulin (Table 2).

There was no difference in baseline characteristics, cumulative propofol dose at 48 hours after initiation, total propofol exposure during ICU admission, amount of enteral or parenteral nutrition, or duration of propofol administration when comparing patients who developed and did not develop hypertriglyceridemia (Tables 1 and 2). A univariate analysis of risk factors for the development of hypertriglyceridemia can be found in Table 2. Patients who developed hypertriglyceridemia were younger, less likely to have coronary artery disease, and had significantly higher inflammatory markers. We estimated the associations of age, coronary artery disease, tocilizumab use, LDH, ferritin, CRP, AST, and D-dimer to risk of hypertriglyceridemia using a logistic regression model. Increased

**TABLE 2.**
**Outcomes**

| Variable | All Patients, *n* = 106 |
|---|---|
| Prevalence of hypertriglyceridemia[a] | 60 (56.6) |
| Prevalence of pancreatitis[a] | 5 (4.7) |
| Confirmed by CT imaging | 1 (0.9) |
| Duration of propofol (hr)[b] | 167 (71.5–278.5) |
| Total cumulative dose (g)[b] | 34.6 (16.3–55.9) |
| Propofol discontinued due to hypertriglyceridemia | 39 (36.8) |
| Time to hypertriglyceridemia (hr)[b] | 46 (27.8–81.5) |
| Lipase at time of hypertriglyceridemia[b] | 43 (22.5–92.3) |
| Maximum triglyceride level (mg/dL)[b] | 456 (250–602) |
| Maximum lipase level[b] | 31 (9–150) |
| Univariate Analysis of Parameters Associated With Hypertriglyceridemia | |

| Variable | Developed Hypertriglyceridemia, *n* = 60 | Did Not Develop Hypertriglyceridemia, *n* = 46 | *p* |
|---|---|---|---|
| Total cumulative propofol dose at 48 hr (g)[b] | 8.1 (4.8–11.6) | 6.8 (4.8–10.1) | 0.2187 |
| Total propofol dose (g)[b] | 35.0 (17.5–56.2) | 34 (12.4–57.6) | 0.7794 |
| Total propofol duration (hr)[b] | 171 (69.8–273.2) | 161.5 (71.5–296.3) | 0.7414 |
| Propofol held due to hypertriglyceridemia and restarted[a] | 25 (41.7) | NA | 0.2512 |
| Hours held prior to restarting propofol[b] | 74 (37–152) | NA | 0.2512 |
| Rate of propofol at time of hypertriglyceridemia (µg/kg/min)[b] | 58 (42–66) | NA | 0.2512 |
| ICU length of stay (hr)[b,c] | 421 (250.3–615) | 309.5 (156–481) | 0.0198 |
| ICU mortality | 20 (33.3) | 16 (34.7) | 0. 8759 |
| Concomitant medications[a] | | | |
| Statins | 26 (43.3) | 22 (47.8) | 0.6451 |
| Ezetimibe | 0 | 1 (2.2) | 0.2512 |
| Tacrolimus | 0 | 1 (2.2) | 0.2512 |
| Atypical antipsychotics | 31 (51.7) | 18 (39.1) | 0.2772 |
| Steroids | 8 (13.3) | 6 (13.0) | 0.9651 |
| IV insulin | 19 (31.7) | 6 (13.0) | 0.0252 |
| Beta blockers | 14 (25.0) | 16 (41.3) | 0.2804 |
| Tocilizumab | 20 (33.3) | 8 (17.4) | 0.0650 |

(*Continued*)

**TABLE 2. (*Continued*).**
**Outcomes**

| Variable | Developed Hypertriglyceridemia, *n* = 60 | Did Not Develop Hypertriglyceridemia, *n* = 46 | *p* |
|---|---|---|---|
| Maximum triglyceride (mg/dL)[b] | 575 (492–770) | 221 (151–267) | < 0.00001 |
| Maximum triglyceride (mg/dL) breakdown[a] | | | 0.2512 |
| 150–199 (borderline high) | 0 | 21 (45.7) | |
| 200–499 (high) | 16 (26.7) | 25 (54.3) | |
| 500–999 (very high) | 37 (61.7) | 0 | |
| > 1,000 (severe) | 7 (11.6) | 0 | |
| > 50% increase from baseline triglyceride | 23 (92), *n* = 25 | 18 (78.3), *n* = 23 | 0.1779 |
| Maximum lipase[b] | 71 (31–135) | 38 (21–94) | 0.03 |
| Maximum creatine kinase[b] | 827 (410–1,721) | 404 (109–765) | 0.0012 |
| Maximum lactate dehydrogenase[b] | 596 (478–743) | 438 (330–529) | < 0.00001 |
| Maximum ferritin[b] | 2,816 (1,477.8–7,023) | 941 (406–1,700) | < 0.00001 |
| Maximum C-reactive protein[b] | 301 (242.9–301) | 245 (150.2–301) | 0.0011 |
| Maximum aspartate aminotransferase[b] | 133 (85–181) | 79 (53–150) | 0.0045 |
| Maximum D-dimer[b] | 4,001 (3,993.5–4,001) | 3,822.5 (2,540–4,001) | 0.0076 |

NA = not available.
[a]Reported as *n* (%).
[b]Reported as median (interquartile range).
[c]ICU length of stay calculated using ICU survivors.

levels of ferritin (OR, 3.43; 95% CI, 1.68–6.98), CRP (OR, 3.97; 95% CI, 1.11–14.2), and D-dimer (OR, 14.3; 95% CI, 1.76–115.8) were independent risk factors for the development of hypertriglyceridemia after logistic regression (**Table 3**).

## DISCUSSION

Propofol is a rapidly acting, titratable medication that is commonly used for sedation in mechanically ventilated, critically ill patients. Patients with COVID-19 may develop respiratory failure requiring mechanical ventilation. Additionally, while various interventions such as administration of low tidal volumes, neuromuscular blockade, and prone positioning help optimize mechanical ventilation and minimize risk of barotrauma in patients who develop ARDS, they may lead to a requirement of increased doses of sedatives and analgesics (30). While propofol offers many advantages to other sedatives in these patients, the risk of hypertriglyceridemia may be significantly increased given the increased propofol exposure with prolonged duration of mechanical ventilation. We observed a markedly increased rate of hypertriglyceridemia in patients with COVID-19 compared with previous studies evaluating patients without COVID-19. To our knowledge, this is the largest analysis evaluating the risk of hypertriglyceridemia with propofol in this patient population.

The true incidence of hypertriglyceridemia associated with propofol is still unknown; however, literature suggests an occurrence between 18% and 45% (13,

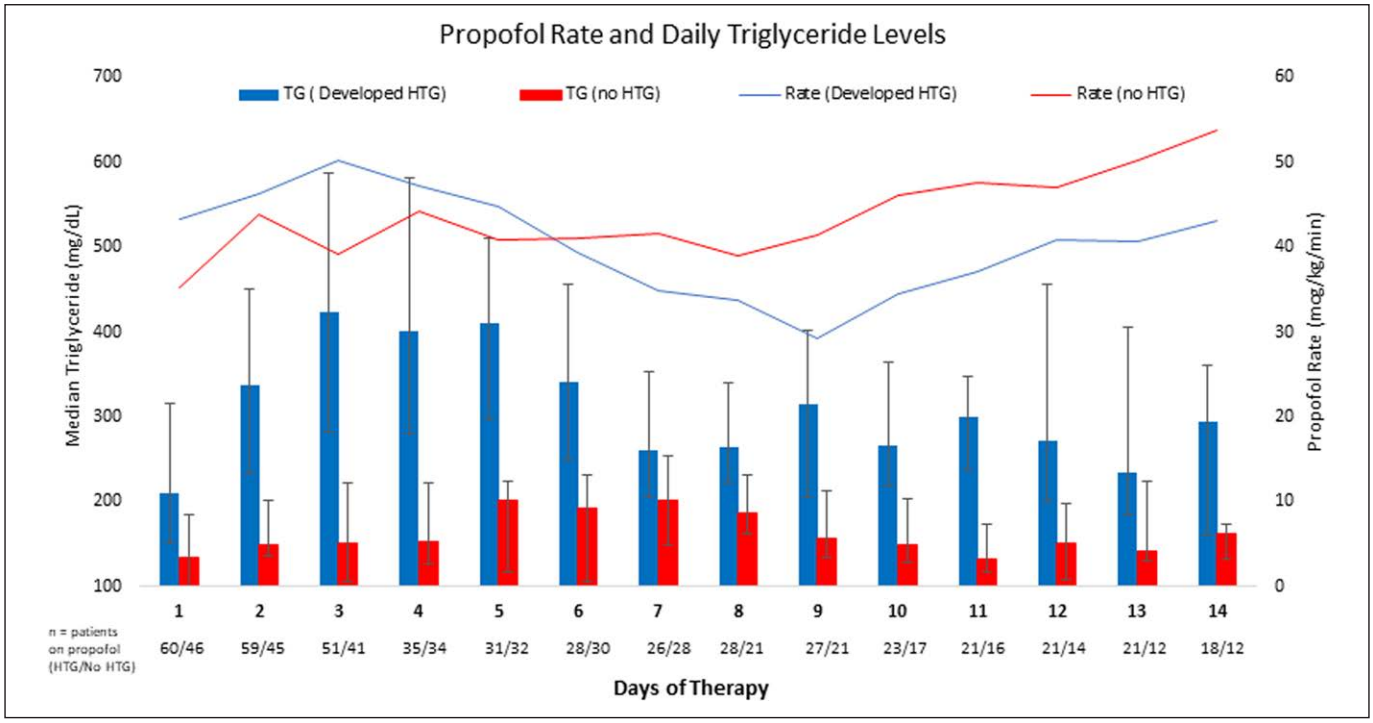


**Figure 1.** Median daily propofol rate and triglycerides (TGs) in patients who did and did not develop hypertriglyceridemia (HTG).

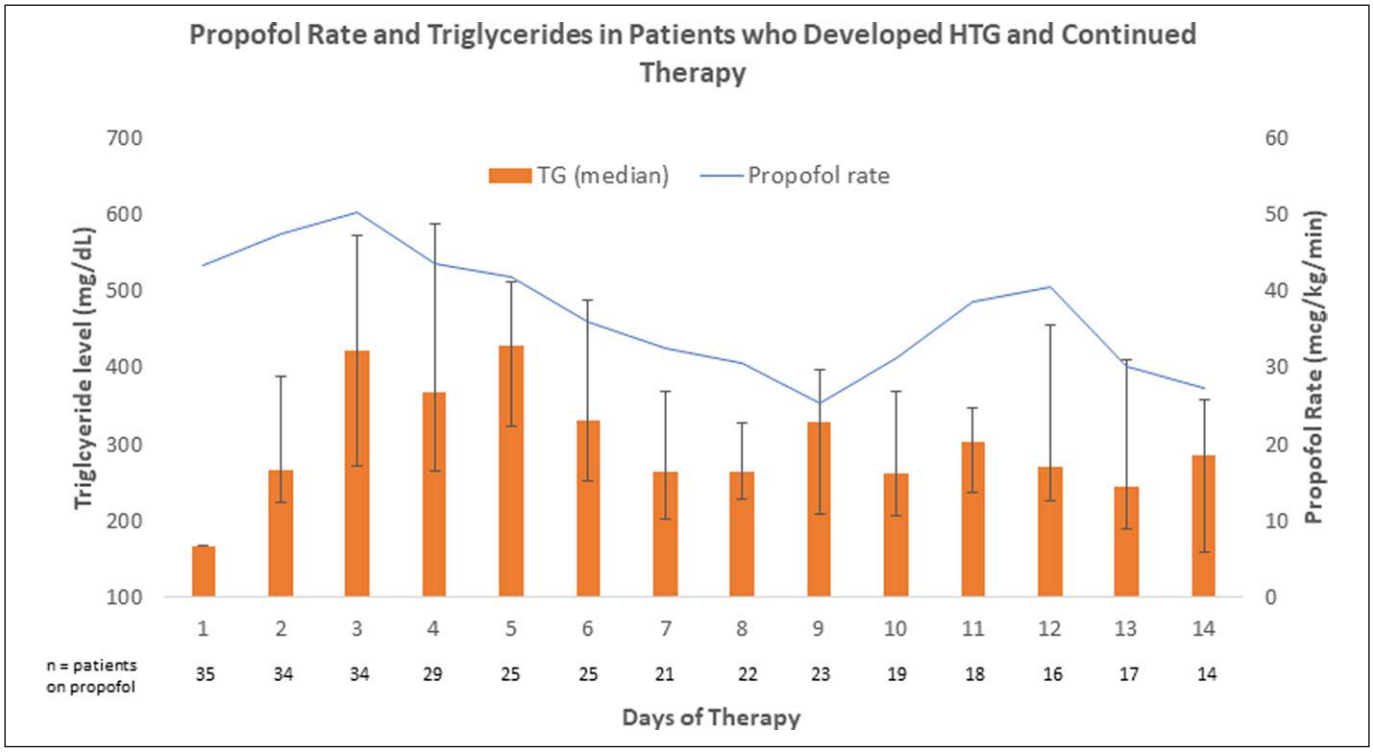


**Figure 2.** Median propofol rate and median daily triglycerides (TGs) in patients who developed hypertriglyceridemia (HTG) and continued propofol greater than 24 hr.

18). One study of 20 ICU patients compared rates of serum triglyceride levels in patients receiving propofol to those receiving barbiturate and benzodiazepine-based alternatives (31). All patients received parenteral nutrition and propofol was administered at an average rate of 2 mg/kg/hr (33.3 µg/kg/min). This study found triglyceride levels were not statistically significantly different between groups; however, this may be due

**TABLE 3.**
**Multivariate Analysis of Odds for Development of Hypertriglyceridemia**

| Variable | OR (95% CI) | *p* |
|---|---|---|
| Age | 0.423 (0.251–0.713) | 0.001 |
| Coronary artery disease | 0.329 (0.080–1.36) | 0.125 |
| Tocilizumab | 2.08 (0.563–7.65) | 0.273 |
| Ferritin[a] | 3.43 (1.68–6.98) | 0.001 |
| C-reactive protein[a] | 3.97 (1.11–14.2) | 0.034 |
| D-dimer[a] | 14.3 (1.76–115.8) | 0.013 |
| Lactate dehydrogenase[a] | 2.05 (0.563–7.65) | 0.505 |
| Aspartate aminotransferase[a] | 1.02 (0.417–2.50) | 0.963 |

OR = odds ratio.
[a]Log transformed.

to the small sample size and overall low total dose of propofol administered (31). Another study found an overall incidence of hypertriglyceridemia in critically ill patients to be 45%, along with a strong correlation between propofol dose and triglyceride levels (5). However, the study used a definition of hypertriglyceridemia of greater than 2 mmol/L or approximately 180 mg/dL.

Carrasco et al (13) compared 88 patients that received midazolam and propofol for short-, moderate-, and long-term durations. While specific triglyceride levels are not reported, daily lipid levels were obtained in 22 patients, with 10 demonstrating a greater than 50% increase from baseline. The authors note that these values normalized after sedation was discontinued. In another study comparing propofol to midazolam, triglyceride levels were assessed every 72 hours (9). Hypertriglyceridemia leading to discontinuation occurred in 11 of 54 patients who received propofol. In this analysis, the mean triglyceride level when propofol was discontinued was 588 mg/dL and subsequently 328 mg/dL 72 hours later. In our cohort, most patients with baseline triglyceride levels prior to propofol initiation had an increase greater than 50% in triglyceride levels, and 39 patients had propofol discontinued secondary to hypertriglyceridemia. However, 25 patients were restarted on propofol with only five patients discontinuing therapy due to the development of hypertriglyceridemia again. Patients that were restarted on propofol were reinitiated on a lower dose than what they were receiving when they developed hypertriglyceridemia. While there may be specific subgroups of patients with COVID-19 in which the use of propofol should be avoided, such as those with familial chylomicronemia syndrome, our data demonstrate that hypertriglyceridemia may not necessitate propofol discontinuation (32). Instead, providers may use dose minimization strategies, such as sedation goal-directed titrations and opioid rotation, to limit the amount of lipid content that patients receive (33, 34).

Devlin et al (7) found that hypertriglyceridemia, defined as triglyceride 400 mg/dL, occurred in 18% of patients, with 10% of those patients developing pancreatitis. Six of the 29 patients (21%) who had hypertriglyceridemia had levels greater than 1,000 mg/dL, and the median maximum triglyceride level was 696 mg/dL. Age, duration of propofol, ICU LOS, and admission to a medical ICU were identified as risk factors for hypertriglyceridemia; however, none of these remained significant after multivariate logistic regression analysis. The median duration and cumulative dose of propofol prior to hypertriglyceridemia was 54 hours and 15 g, respectively. In our analysis, we observed a significantly higher rate of hypertriglyceridemia in patients with COVID-19. The time to development of hypertriglyceridemia and median maximum triglyceride levels in those who developed hypertriglyceridemia were comparable in our analysis. However, propofol was continued in most patients who developed hypertriglyceridemia despite triglyceride levels greater than 400 mg/dL. Figure 2 displays patients who continued receiving propofol despite high elevated triglyceride levels. Decreasing propofol doses led to overall reductions in triglyceride levels. Optimization of sedation and maintenance of ventilator synchrony in mechanically ventilated patients with COVID-19 is often challenging. Propofol offers many advantages over other sedative options, and discontinuation due to triglyceride levels greater than 400 or 500 mg/dL likely results in the selection of one or more agents that have significant adverse events and may not be ideal in patients with ARDS and prolonged ventilation time (13, 35, 36). We did not observe negative consequences in patients who continued to receive propofol despite elevated triglyceride levels.

The exact reason for the higher prevalence of elevated triglyceride levels in patients with COVID-19 is

unknown. A report of two cases of hypertriglyceridemia in patients who received tocilizumab for elevated interleukin (IL)-6 levels secondary to COVID-19 was recently published (27). While no baseline triglyceride levels are reported, both patients had triglyceride levels greater than 1,000 mg/dL after receiving tocilizumab. Both patients also received propofol for sedation until or throughout tocilizumab administration, and one of these patients developed acute pancreatitis. The exact mechanism of tocilizumab-induced hypertriglyceridemia is unknown, but it is hypothesized that tocilizumab may interfere with IL-6-mediated uptake of fatty acids from the serum into skeletal muscle (37, 38). Another report of two cases highlighted elevated triglyceride levels possibly secondary to lopinavir/ritonavir (28). It is unknown if these patients received propofol, but the authors mention that the patients had additional risk factors for hypertriglyceridemia. Previous cases of disproportionately elevated triglycerides with standard rates of propofol have been reported in patients with H1N1, although it is unknown if these patients received other medications that may have contributed (6). In our cohort, we did not observe significant differences in the cumulative amount or duration of propofol when comparing patients that developed or did not develop hypertriglyceridemia, which contrasts with previous studies (7).

We did not observe differences in severity of illness, weight, the number of patients with hyperlipidemia at baseline, or the number of patients receiving enteral or parenteral nutrition. We did not specifically collect daily lipid intake, as all ICU patients at our institution are closely monitored by a registered dietician and nutritional requirements are adjusted based on concomitant propofol rates to avoid overfeeding. Specifically, if serum triglycerides are greater than 400 mg/dL lipids are removed from parenteral nutrition, or enteral feeding is adjusted to a low lipid formulation. However, our analysis had only two patients receiving parenteral nutrition, with zero patients in the hypertriglyceridemia group. As noted in previous studies, concomitant medications may alter serum triglyceride levels. Although not statistically significant, a higher percentage of patients in our analysis who developed hypertriglyceridemia were noted to receive IV insulin infusions, which may lead to increased hydrolysis of triglycerides (5–7, 27, 28, 37, 38). However, all patients received IV insulin infusions for the management of hyperglycemia, not for elevated triglyceride levels. Although hyperglycemia was commonly seen in patients with COVID-19, our institutional guidelines favored the use of frequent dosing of subcutaneous insulin aspart, as compared continuous IV infusions, to limit frequent entry into the patient's room for intensive monitoring. The higher use of subcutaneous insulin may limit the triglyceride-lowering effect of insulin therapy. We did find that patients with hypertriglyceridemia had higher inflammatory markers, which remained statistically different upon multivariate regression. Patients with COVID-19 may be at higher risk of hypertriglyceridemia secondary to multiple etiologies, and patients who receive propofol may benefit from increased frequency of monitoring as well as implementation of dose minimization strategies early in their course.

There are several limitations of our analysis. Due to strict isolation precautions and the desire to minimize staff exposure to COVID-19, few CT scans were done in order to assess for pancreatitis. Therefore, while we observed a low rate of suspected pancreatitis, we were not able to reliably use confirmation by imaging as a part of the diagnostic criteria. There are also many patient-specific factors (medications, nutrition, and disease states) that may have had a potential impact on triglyceride levels. Although we aimed to capture and account for the majority of these scenarios, particularly those that we deemed clinically relevant and have been consistently seen in previous literature, there may have been confounders that were not accounted for, such as IV heparin therapy. Additionally, baseline laboratory values, specifically triglyceride levels, were only available in roughly half of our patient population, making it difficult to fully interpret changes in triglyceride levels from baseline. Our study also did not collect data specific to complications with dialysis or ECMO filters in relation to the development of hypertriglyceridemia. Finally, while we correlated propofol discontinuation with elevated triglyceride levels in addition to documentation inpatient charts, the retrospective nature of the analysis limits the accuracy of determining why propofol was discontinued in all cases.

## CONCLUSIONS

Hypertriglyceridemia in patients with COVID-19 who receive propofol is very common and may occur independent of propofol dose or duration. Due to the frequency of hypertriglyceridemia in this patient

population, monitoring of serum triglyceride levels should be done frequently in patients who require more than 1–2 days of propofol. Many patients who developed hypertriglyceridemia were able to continue propofol in our analysis after reducing the dose. Despite the increased rate of hypertriglyceridemia, immediate discontinuation of propofol and use of alternative sedatives may not always be feasible or desirable.

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