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Assessing Opportunities to Improve Sedation/Analgesia Use in Neonatal Patients on Extracorporeal Membrane Oxygenation (ECMO)

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Background

Sedation is used during ECMO to prevent agitation. Analgesia is used to dampen pain perception as neonatal procedural pain related stress is associated with later altered neurodevelopment with poorer perceptual reasoning and visual perception. Common sedatives/analgesics used during ECMO are opiates and benzodiazepines. Studies have shown that lipophilic drugs such as Fentanyl and Midazolam are significantly sequestered in the circuit suggesting opportunities to improve delivery for pain.

Objective

To identify opportunities to improve sedation/analgesia drug treatment in ECMO patients.

Methods & Analysis

- We performed a retrospective chart analysis of all NICU patients receiving ECMO between 2015-20 and assessed the sedative/analgesia type and dose and clinical complications.
- We collected patient demographics, medication type and dose, days to wean, length of hospital stay, mortality, medical complications at discharge and MRI results.
- Statistical analysis included chi-square, two-tailed T-test, and ANOVA, with values considered significant if $p < 0.05$.

Results

Patients on ECMO in CHOR NICU 2015-20 (n=49)	
Birth Gestational Age – wks ± SD	37.6 ± 3.6
Birth weight – grams ± SD	3023 ± 939
Sex	
Female – n (%)	22 (49)
Race	
African American – n (%)	23 (47)
White – n (%)	16 (33)
Hispanic – n (%)	2 (4)
Other – n (%)	8 (16)

Table 1. Patient Demographics. Data presented as Means (SD) and percentages where appropriate.

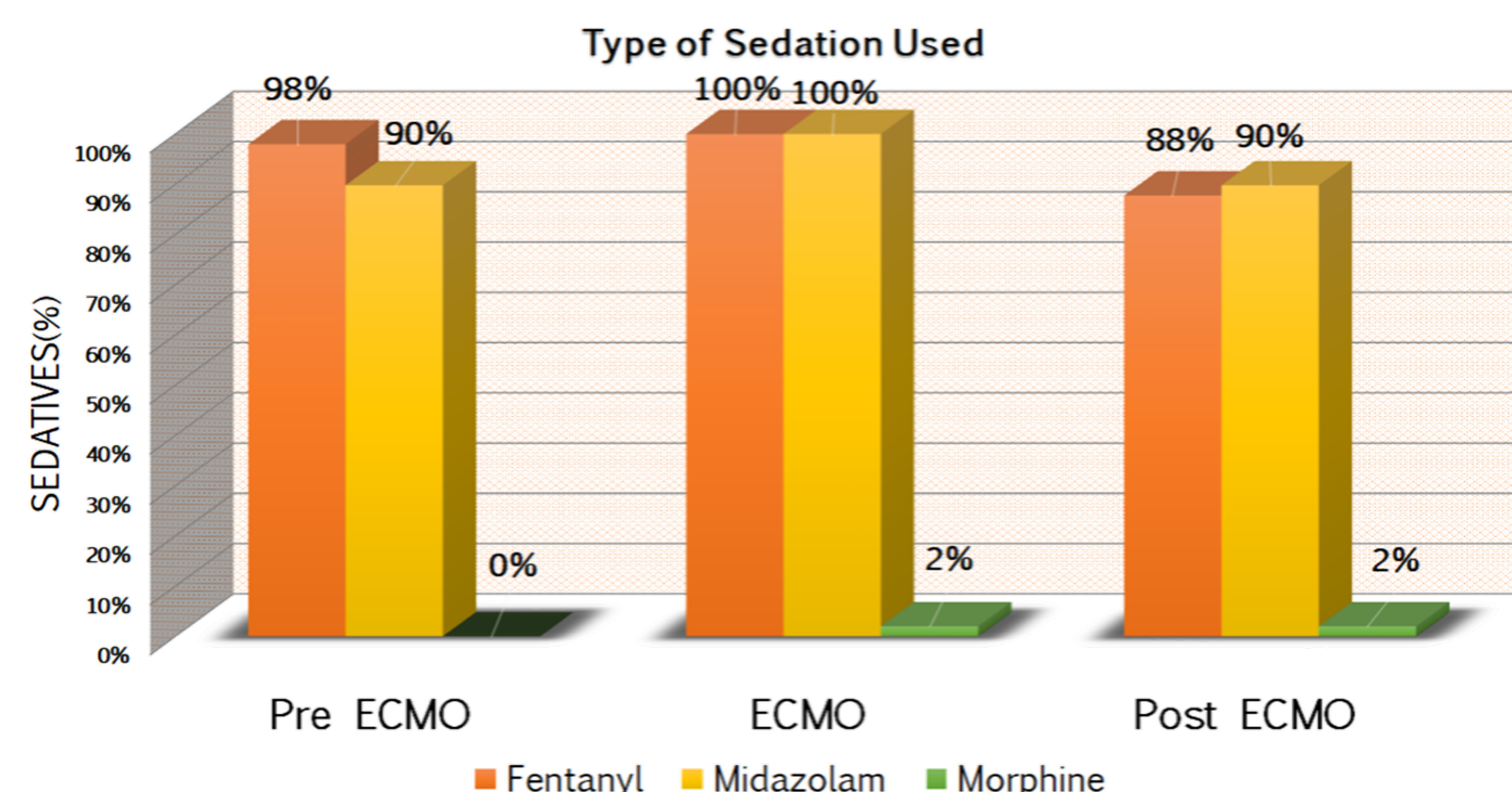


Figure 1. Sedation and Analgesia used for ECMO Patients (n =49)

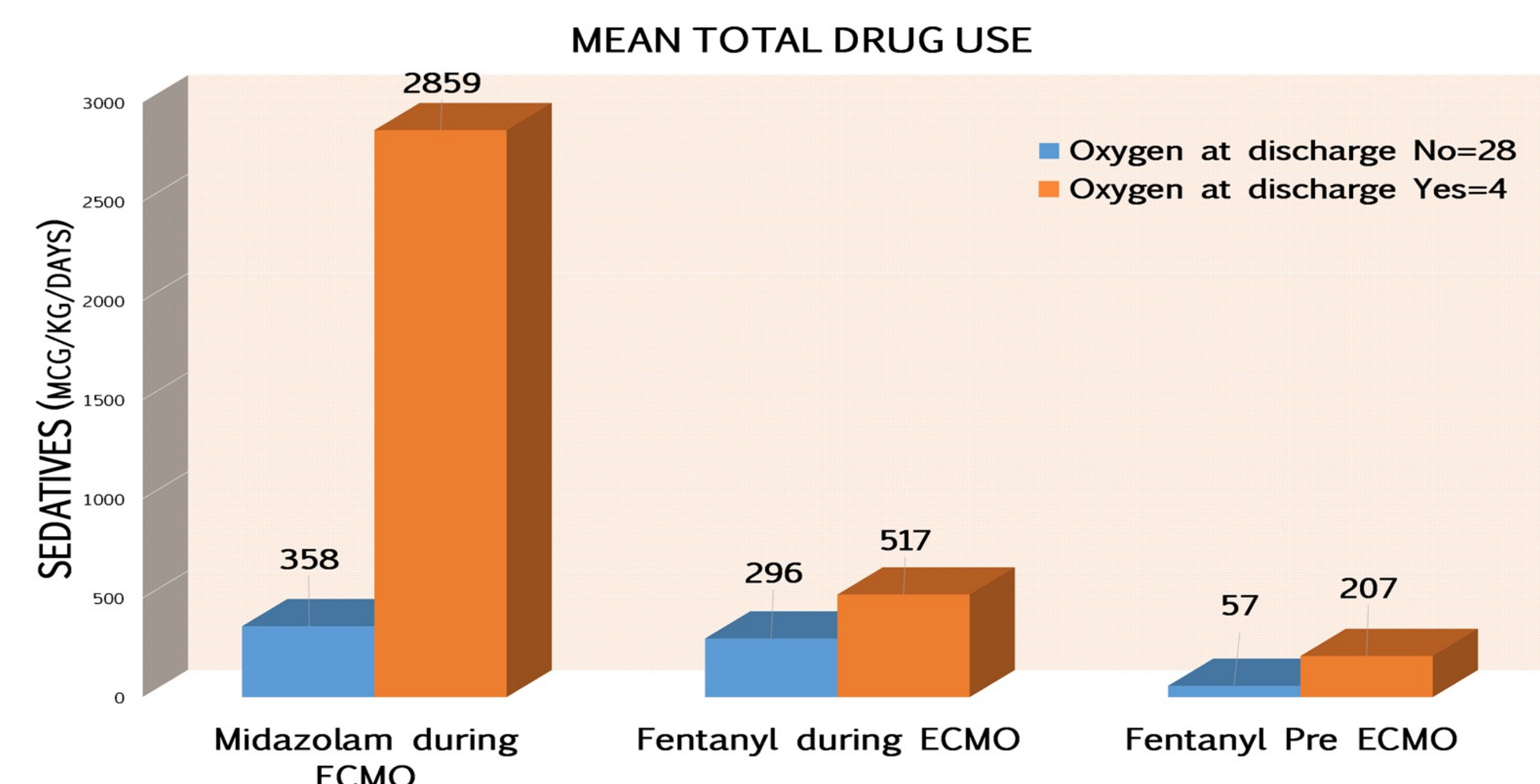


Figure 2. Sedation/Analgesia and Oxygen at Discharge (n =49)

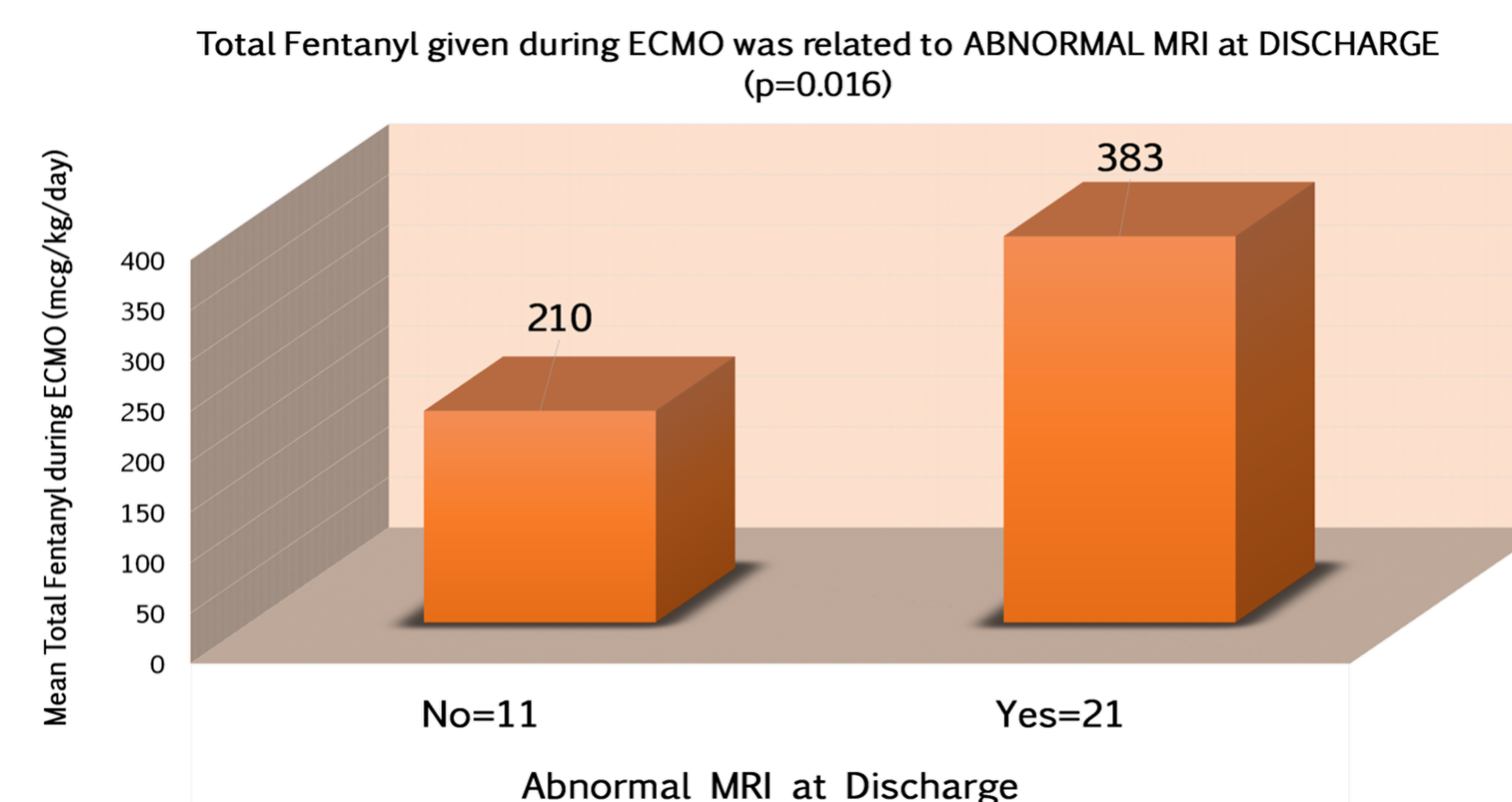


Figure 3. Fentanyl Dose and Abnormal MRI at Discharge (n =32)

Complications Post ECMO Sedation			
Feeding Tube at Discharge	Yes (n=11)	No (n=21)	
Length of Stay (Mean ± SD days)	90.73 ± 96.33	41.24 ± 29.34	$p=0.036$
Time to wean off Midazolam post ECMO (Mean ± SD days)	38.36 ± 62.27	8.74 ± 9.07	$p=0.049$
Total Midazolam given during ECMO (Mean ± SD mg/kg/days)	1.61 ± 0.63	1.03 ± 0.77	$p=0.041$
Total Fentanyl given during ECMO in (Mean ± SD mcg/kg/days)	420.71 ± 188.55	272.72 ± 196.29	$p=0.049$

Table 2. Sedation and Analgesia used (n =49)

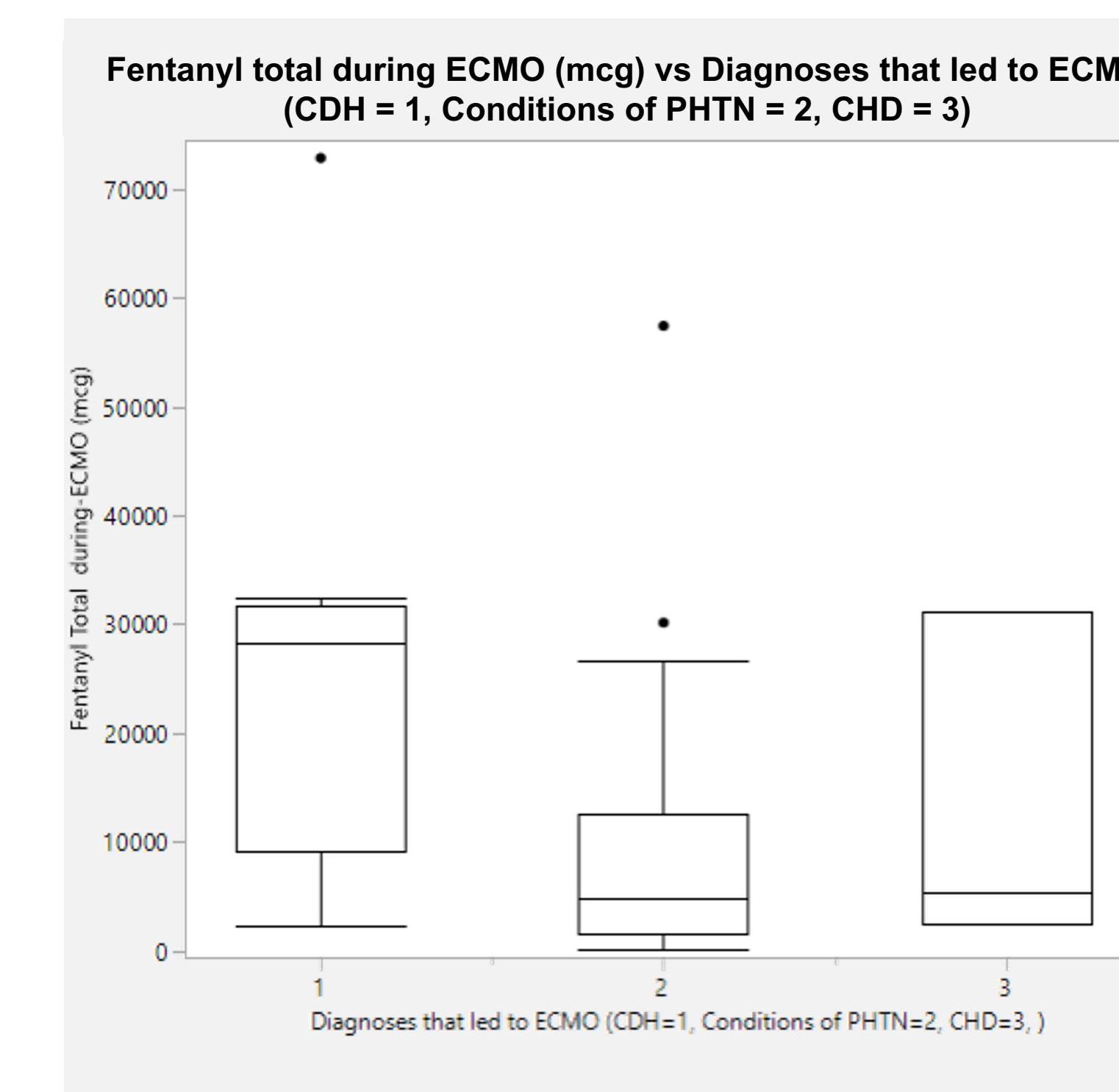


Figure 4. Fentanyl total dose during ECMO by diagnosis leading to ECMO. No significant association between total Fentanyl dose the diagnosis leading to ECMO ($p < 0.01$).

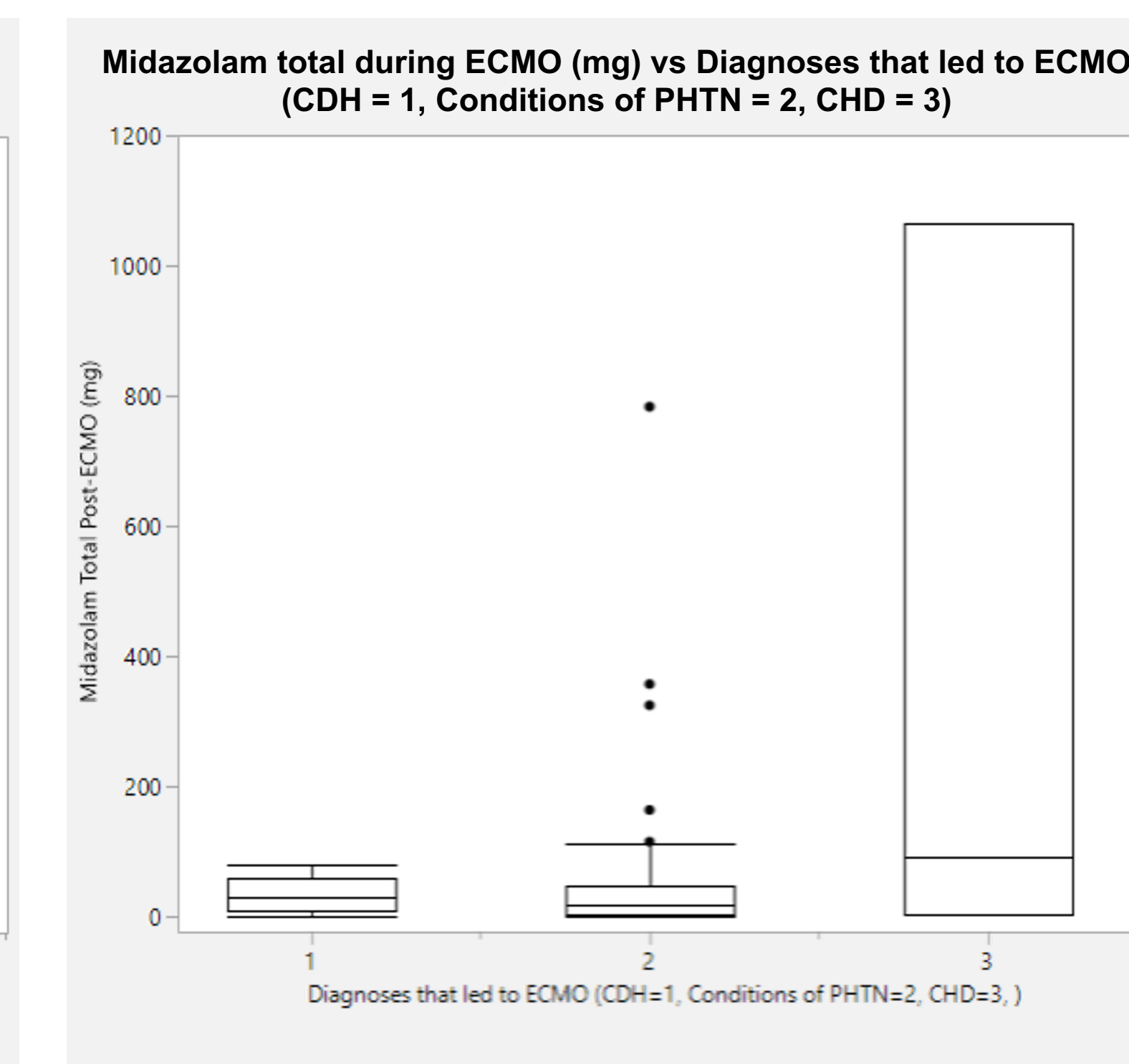


Figure 5. Midazolam total dose during ECMO by diagnoses leading to ECMO. Congenital heart disease is associated with higher total Midazolam dose ($p < 0.01$).

Conclusions

- Fentanyl and Midazolam are commonly used sedation and analgesia agents in neonatal ECMO patients.
- Fentanyl and Midazolam increased dose exposure was associated with greater risk for neurological clinical complications, delay in oral feeding, and need for feeding tube at discharge with prolonged hospitalization in infants receiving ECMO.
- Multivariate analysis is needed to adjust for the diagnosis and the length of ECMO run.
- Further studies are needed to assess serum drug concentrations in ECMO patients to better understand development of drug tolerance, circuit sequestration, and dose exposure, as well as adjust the therapeutic range and decrease sedation and analgesia dosage exposure.

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