Psychiatric Outcomes Following Ketamine Administration for Orthopedic Surgical Anesthesia

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For the full paper and citations in *Frontiers in Anesthesiology*, scan here:

Introduction

- What is ketamine and what are the common medical settings in which we see its use?
- Ketamine has different indications and effects in the psychiatric and anesthetic worlds.
- What are the negative side effects seen in its use?
- We looked at its use in orthopedic surgery and observed the psychiatric side effects of various patient populations.

Methods

- This was a retrospective analysis of the TriNetX health database looking specifically at patients undergoing orthopedic surgeries with anesthesia.
- We used CPT codes to identify patients having surgery on various joints/bones including but not limited to spine, shoulder, hip, and knee.
- We then performed four total group analyses between cohorts of patients receiving ketamine and cohorts not receiving ketamine.
- We had three sets of analysis based on age stratification and one ageless: pediatric (<18 years), adult (18–60 years), elderly (>60 years), and a reference analysis of all patients.
- We observed and compared outcomes in the 30-day postoperative period involving diagnoses of various psychiatric-related disorders.

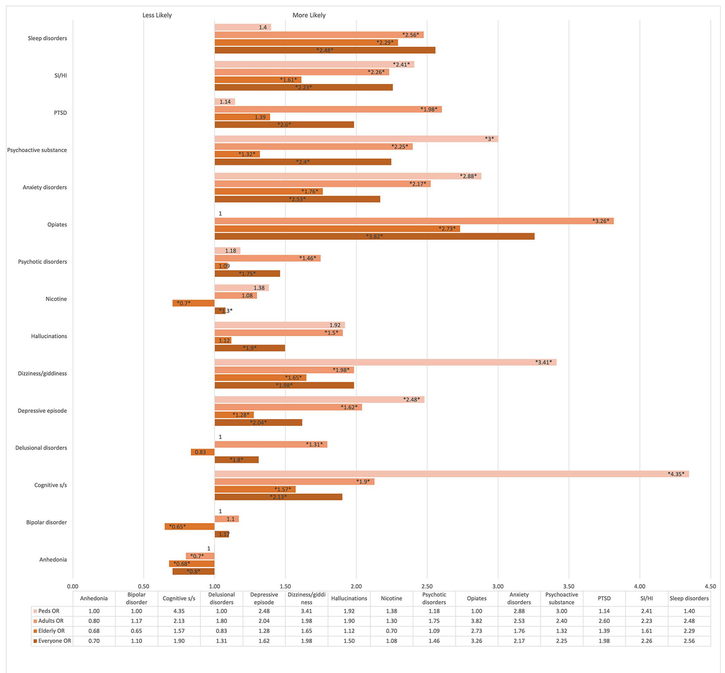
Results

Table 1. Event risk and odds ratio by cohort age.

Event—ICD10 code	Event N	Absolute risk	Risk diff.	Odds ratio	95% CI	*P*-value
Opioid related disorders—F11						
Everyone	600	0.30%	+0.2%	3.26	(2.77–3.85)	***0.00***
Peds (<18)	10	0.10%	0%	1.00	(0.42–2.4)	1.00
Adult (18–60)	423	0.40%	+0.3%	3.82	(3.11–4.69)	***0.00***
Elderly (>60)	181	0.20%	+0.1%	2.73	(2.07–3.61)	***0.00***
Nicotine dependence—F17						
Everyone	1,257	0.80%	+0.1%	1.08	(0.99–1.17)	0.07
Peds (<18)	32	0.20%	0%	1.38	(0.81–2.36)	0.23
Adult (18–60)	921	1.20%	+0.3%	1.30	(1.18–1.43)	***0.00***
Elderly (>60)	329	0.50%	−0.2%	0.70	(0.61–0.81)	***0.00***
Other psychoactive substance disorder—F19						
Everyone	909	0.50%	+0.3%	2.25	(2–2.53)	***0.00***
Peds (<18)	30	0.20%	+0.1%	3.00	(1.47–6.13)	***0.00***
Adult (18–60)	658	0.70%	+0.4%	2.40	(2.09–2.76)	***0.00***
Elderly (>60)	239	0.30%	+0.1%	1.32	(1.09–1.6)	***0.01***
Non-mood psychotic disorders—F20-29						
Everyone	1,916	0.90%	−0.3%	1.46	(1.36–1.57)	***0.00***
Peds (<18)	13	0.10%	0%	1.18	(0.53–2.64)	0.68
Adult (18–60)	1,127	1.10%	+0.5%	1.75	(1.58–1.93)	***0.00***
Elderly (>60)	820	1.00%	+0.1%	1.09	(0.99–1.2)	0.09
Delusional disorders—F22						
Everyone	485	0.20%	+0.1%	1.31	(1.14–1.5)	***0.00***
Peds (<18)	10	0.10%	0%	1.00	(0.42–2.4)	1.00
Adult (18–60)	288	0.30%	+0.1%	1.80	(1.48–2.18)	***0.00***
Elderly (>60)	202	0.20%	0%	0.83	(0.69–1)	0.05
Bipolar disorder—F31						
Everyone	214	0.10%	0%	1.10	(0.91–1.34)	0.33
Peds (<18)	10	0.10%	0%	1.00	(0.42–2.4)	1.00
Adult (18–60)	162	0.20%	0%	1.17	(0.93–1.47)	0.17
Elderly (>60)	51	0.10%	0%	0.65	(0.46–0.92)	***0.02***
Depressive episode—F32						
Everyone	2,166	1.30%	+0.5%	1.62	(1.51–1.73)	***0.00***
Peds (<18)	109	0.60%	+0.3%	2.48	(1.75–3.52)	***0.00***
Adult (18–60)	1,212	1.50%	+0.7%	2.04	(1.86–2.25)	***0.00***
Elderly (>60)	894	1.40%	+0.3%	1.28	(1.16–1.41)	***0.00***
Anhedonia—R45.84						
Everyone	571	0.30%	−0.20%	0.44	(0.382, 0.513)	***0.00***
Peds (<18)	24	0.10%	−0.10%	0.42	(0.199, 0.869)	***0.02***
Adult (18-60)	365	0.40%	−0.20%	0.45	(0.373, 0.539)	***0.00***
Elderly (>60)	194	0.20%	−0.10%	0.62	(0.494, 0.778)	***0.00***
Other anxiety disorders—F41						
Everyone	3,097	1.90%	+1%	2.17	(2.04–2.31)	***0.00***
Peds (<18)	268	1.50%	+1%	2.88	(2.28–3.65)	***0.00***
Adult (18–60)	1,670	2.10%	+1.3%	2.53	(2.31–2.75)	***0.00***
Elderly (>60)	1,225	1.90%	+0.8%	1.76	(1.61–1.93)	***0.00***
PTSD—F43.1						
Everyone	375	0.20%	+0.1%	1.98	(1.67–2.36)	***0.00***
Peds (<18)	16	0.10%	0%	1.14	(0.56–2.34)	0.71
Adult (18–60)	297	0.30%	+0.2%	2.60	(2.1–3.23)	***0.00***
Elderly (>60)	65	0.10%	0%	1.39	(0.96–2.02)	0.08
Sleep disorders not substance or psych related—F51						
Everyone	363	0.20%	+0.1%	2.56	(2.11–3.1)	***0.00***
Peds (<18)	14	0.10%	0%	1.40	(0.62–3.15)	0.42
Adult (18–60)	198	0.20%	+0.1%	2.48	(1.91–3.21)	***0.00***
Elderly (>60)	160	0.20%	+0.1%	2.29	(1.74–3.04)	***0.00***
Altered cognition—R41						
Everyone	3,21	1.90%	+0.9%	1.90	(1.8–2.01)	***0.00***
Peds (<18)	557	3.10%	+2.4%	4.35	(3.6–5.24)	***0.00***
Adult (18–60)	1,387	1.50%	+0.8%	2.13	(1.94–2.33)	***0.00***
Elderly (>60)	1,642	2.20%	+0.8%	1.57	(1.46–1.7)	***0.00***
Dizziness/giddiness—R42						
Everyone	2,574	1.40%	+0.7%	1.98	(1.86–2.12)	***0.00***
Peds (<18)	446	2.40%	+1.7%	3.41	(2.82–4.15)	***0.00***
Adult (18–60)	1,215	1.30%	+0.6%	1.98	(1.8–2.18)	***0.00***
Elderly (>60)	956	1.30%	+0.5%	1.65	(1.49–1.83)	***0.00***
Hallucinations—R44.3						
Everyone	684	0.30%	+0.1%	1.50	(1.33–1.69)	***0.00***
Peds (<18)	23	0.10%	+0.1%	1.92	(0.96–3.86)	0.06
Adult (18–60)	359	0.40%	+0.2%	1.90	(1.6–2.27)	***0.00***
Elderly (>60)	320	0.40%	0%	1.12	(0.95–1.31)	0.17
Suicidal/homicidal ideation—R45.85						
Everyone	406	0.20%	+0.2%	2.26	(1.95–2.62)	***0.00***
Peds (<18)	10	0.10%	+0.1%	2.41	(1.15–5.03)	1.00
Adult (18–60)	206	0.20%	+0.2%	2.23	(1.86–2.68)	***0.02***
Elderly (>60)	206	0.20%	+0.1%	1.61	(1.29–2.02)	***0.00***

Bold, Italic and underlined values indicate a p-value of $p < 0.05$.

- Figure 1 contains the odds ratio for each outcome of interest, where numbers <1 indicate a reduced risk and numbers >1 indicating increased risks, and asterisks denoting a statistically significant difference.
- Eleven of 15 outcomes had results for specific events, including cohort size, absolute risk, odds ratio with 95% confidence interval, and p-values are compiled in Table 1.



	Anhedonia	Bipolar disorder	Cognitive s/s	Delusional disorders	Depressive episode	Dizziness/giddiness	Hallucinations	Nicotine	Psychotic disorders	Opiates	Anxiety disorders	Psychoactive substance	PTSD	SI/HI	Sleep disorders
Peds OR	1.00	1.00	4.35	1.00	2.48	3.41	1.92	1.38	1.18	1.00	2.88	3.00	1.14	2.41	1.40
Adults OR	0.80	1.17	2.13	1.80	2.04	1.98	1.90	1.30	1.75	3.82	2.53	2.40	2.60	2.23	2.48
Elderly OR	0.68	0.65	1.57	0.83	1.28	1.65	1.12	0.70	1.09	2.73	1.76	1.32	1.39	1.61	2.29
Everyone OR	0.70	1.10	1.90	1.31	1.62	1.98	1.50	1.08	1.46	3.26	2.17	2.25	1.98	2.26	2.56

Figure 1. Odds ratio comparing cohorts receiving ketamine to matched peer cohorts. *Asterisked* values indicate a statistically significant 95% CI.

- In 406,384 patients studied, nearly every measured event displayed an increased risk for patients receiving ketamine as part of their anesthesia.
- Apart from anhedonia, which had a decreased risk of occurrence, every event displayed increased incidence in at least two of the cohorts.
- For all but one event, nicotine use, the significant differences between groups were in concordance with each other.

Conclusions

- Nearly every measured event displayed an increased risk for patients receiving ketamine in at least 2 cohorts.
- Anhedonia and nicotine use were the major outliers.
- There were different major outcomes for different age groups. Considerable differences in the outcomes for pediatric vs. elderly.
- Ketamine should be investigated further in different age groups and with corresponding psychiatric outcomes as current research is still limited.

Implications/Considerations

- Cohorts with “no difference” or minor risk changes as a result of pre-test probability of disease given age.
- Differences between groups could also be explained by difference in the administration of ketamine and the nature of orthopedic procedures.
- Those without disease were excluded from the start, again possibly changing outcomes.
- Not to change practice as a result of this, but to keep in mind as future data arises.

Disclosures

- I declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.