

**Supplementary Table**

**Supplementary Table 1** Per-protocol analysis of PSQ scores across postoperative time points

Measure	Time Point	Esketamine Group (n=42)	Control Group (n=38)	p-value			Difference (Control - Esketamine) 95% CI	Adjusted P-values*
				G	T	G*T		
PSQ-Total	Pre-op	4.0 ± 1.5	4.2 ± 0.9	<0.001	<0.001	0.454		
	POD1	3.0 ± 1.1	3.9 ± 1.1				0.2 (0.3 to 1.3)	0.001
	POD2	3.0 ± 1.0	3.6 ± 1.1				0.2 (0.1 to 1.0)	0.027
	POD7	2.9 ± 1.0	3.4 ± 1.3				0.3 (-0.0 to 1.0)	0.078
PSQ-Minor	Pre-op	3.3 ± 1.6	3.4 ± 1.1	<0.001	<0.001	<0.001		
	POD1	2.3 ± 0.9	3.1 ± 1.0				0.2 (0.4 to 1.2)	<0.001
	POD2	2.3 ± 0.8	2.9 ± 1.1				0.2 (0.3 to 1.1)	0.002
	POD7	2.3 ± 0.9	2.6 ± 1.1				0.2 (-0.2 to 0.7)	0.187
PSQ-Moderate	Pre-op	4.8 ± 2.0	5.1 ± 0.8	0.003	0.281	0.989		
	POD1	3.9 ± 1.5	4.7 ± 1.3				0.8 (0.2 to 1.4)	0.013
	POD2	3.6 ± 1.1	4.4 ± 2.3				0.8 (0.00 to 1.6)	0.045
	POD7	3.5 ± 1.2	4.2 ± 1.5				0.7 (0.1 to 1.3)	0.030

Data are mean ± SD; PSQ scores were analyzed by two-way repeated-measures ANOVA to examine Group (G), Time (T), and Interaction (G×T) effects.

**Note:** \*Bonferroni correction for three comparisons. Model: Linear mixed model with random intercept for patient; fixed effects: group, time, group×time interaction, and preoperative PSQ-total score as covariate. Missing data were handled by last observation carried forward (LOCF) imputation.

**Supplementary Table 2.** Intention-to-Treat sensitivity analysis of PSQ scores across postoperative time points

Measure	Time Point	Esketamine Group (n=42)	Control Group (n=42)	p-value			Difference (Control – Esketamine) 95% CI	Adjusted P-values*
				G	T	G*T		
PSQ-Total	Pre-op	4.0 ± 1.5	4.2 ± 0.8	0.001	0.056	0.506		
	POD1	3.0 ± 1.1	3.8 ± 1.0				0.7 (0.3 to 1.2)	0.006
	POD2	3.0 ± 1.0	3.7 ± 1.2				0.7 (0.2 to 1.2)	0.018
	POD7	2.9 ± 1.0	3.4 ± 1.2				0.4 (-0.0 to 0.9)	0.221
PSQ-Minor	Pre-op	3.3 ± 1.6	3.5 ± 1.1	0.003	0.144	0.024		
	POD1	2.3 ± 0.9	3.0 ± 1.0				0.8 (0.3 to 1.2)	0.001
	POD2	2.3 ± 0.8	2.9 ± 1.0				0.6 (0.2 to 1.0)	0.008
	POD7	2.3 ± 0.9	2.6 ± 1.1				0.2 (-0.2 to 0.7)	0.816
PSQ-Moderate	Pre-op	4.8 ± 2.0	5.2 ± 0.8	<0.001	0.177	0.855		
	POD1	3.9 ± 1.5	4.6 ± 1.2				0.7 (0.1 to 1.3)	0.046
	POD2	3.6 ± 1.1	4.5 ± 2.2				0.9 (0.2 to 1.7)	0.049
	POD7	3.5 ± 1.2	4.3 ± 1.5				0.8 (0.2 to 1.3)	0.034

Data are mean ± SD; PSQ scores were analyzed by two-way repeated-measures ANOVA to examine Group (G), Time (T), and Interaction (G×T) effects.

**Note:** \*Bonferroni correction for three comparisons. Model: Linear mixed model with random intercept for patient; fixed effects: group, time, group×time interaction, and preoperative PSQ-total score as covariate. Missing data were handled by last observation carried forward (LOCF) imputation.

**Supplementary table 3** FDR-adjusted P-values for all outcome measures

<b>Outcome Measure</b>	<b>Original P-value</b>	<b>FDR-adjusted P-value</b>	<b>Significance Change</b>
PSQ_total_D1	0.001	0.005	Remained significant
PSQ_total_D2	0.027	0.045	Remained significant
PSQ_total_D7	0.125	0.141	Remained non-significant
PSQ_moderate_D1	0.013	0.029	Remained significant
PSQ_moderate_D2	0.045	0.058	Lost significance
PSQ_moderate_D7	0.030	0.045	Remained significant
PSQ_minor_D1	0.001	0.005	Remained significant
PSQ_minor_D2	0.002	0.006	Remained significant
PSQ_minor_D7	0.938	0.938	Remained non-significant
NRS_rest_30 min	0.582	0.860	Remained non-significant
NRS_rest_6 h	0.280	0.560	Remained non-significant
NRS_rest_12 h	0.238	0.560	Remained non-significant
NRS_movement_30 min	<0.001	0.001	Remained significant
NRS_movement_6 h	0.020	0.073	Lost significance
NRS_movement_12 h	0.938	>0.999	Remained non-significant
HAMD-17	0.125	0.417	Remained non-significant
PGE <sub>2</sub> group	0.931	>0.999	Remained non-significant
PCA_compressions	>0.999	>0.999	Remained non-significant
Rescue_analgesia	0.602	0.860	Remained non-significant

## Supplementary Figure

### Supplementary Figure 1: Pain Sensitivity Questionnaire

#### Pain Sensitivity Questionnaire

##### Instructions

0 = No pain

1–3 = Mild pain

4–6 = Moderate pain

7–9 = Severe but tolerable pain

10 = The most severe pain imaginable (extreme pain)

##### Items

1. Imagine your calf hitting the edge of a hard object (e.g. the edge of a glass coffee table)

hard. How painful would you feel? [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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2. Imagine your tongue being scalded by a very hot drink. [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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3. Imagine mild soreness in your muscles from exercise. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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4. Imagine your finger being caught in a drawer. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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5. Imagine taking a warm water shower. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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6. Imagine your shoulder being slightly sunburned. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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7. Imagine falling off a bicycle and scraping your knee. [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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8. Imagine accidentally biting your tongue or cheek hard while eating. [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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9. Imagine walking barefoot on cool tile floors. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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10. Imagine cutting a small wound on your finger and accidentally sprinkling salt on it.

[Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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11. Imagine a rose thorn pricking the tip of your finger. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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12. Imagine holding an ice pack with your bare hands for a few minutes. [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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13. Imagine shaking hands with someone with normal hand strength. [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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14. Imagine shaking hands with someone with strong hand strength. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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15. Imagine accidentally touching the hot handle of a hot pot (as hot as the pot itself) when lifting it. [Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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16. Imagine being stepped on by someone wearing heavy boots while you are wearing sandals. [Single choice]\*

0	1	2	3	4	5	6	7	8	9	10
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17. Imagine the "funny bone" (ulnar nerve) in your elbow hitting the edge of a table.

[Single choice] \*

0	1	2	3	4	5	6	7	8	9	10
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**Pain Sensitivity Scores:**

PSQ-total \_\_\_\_\_

PSQ-moderate \_\_\_\_\_

PSQ-minor \_\_\_\_\_

## Supplementary Figure 2: 17-item Hamilton Depression Rating Scale (HAMD-17)

### 17-item Hamilton Depression Rating Scale (HAMD-17)

Name: \_\_\_\_\_ ID: \_\_\_\_\_

#### 1. Depressive Mood

- Absent
- Only reported when asked
- Spontaneously described during the interview
- Evident through non-verbal cues (facial expression, posture, voice, or tearing) without verbal expression
- Almost all verbal and non-verbal expressions (facial expressions, actions) reflect this mood

#### 2. Feelings of Guilt

- Absent
- Blames oneself and feels that one has harmed others
- Thinks one has committed a crime, or repeatedly ruminates on past mistakes; believes the illness is punishment for one's mistakes, or has delusions of guilt
- Delusions of guilt accompanied by accusatory or threatening hallucinations

#### 3. Suicide

- Absent
- Feels life is meaningless
- Wishes to be dead, or often thinks about death
- Passive suicidal ideation
- Severe suicidal behavior

#### 4. Difficulty Falling Asleep

- No difficulty
- Reports difficulty falling asleep (cannot fall asleep within 30 minutes of going to bed; note the patient's usual bedtime)

Reports difficulty falling asleep every night

**5. Sleep Maintenance Difficulty (Middle Insomnia)**

Absent

Light sleep with frequent nightmares

Woke up in the middle of the night (before 12:00 midnight, excluding trips to the toilet)

**6. Early Morning Awakening (Terminal Insomnia)**

Absent

Early awakening, 1 hour earlier than usual but can fall asleep again

Cannot fall asleep again after early awakening

**7. Work and Interests**

Absent

Only reports loss when asked

Spontaneously expresses loss of interest in activities, work, or study (e.g., feels listless, hesitant, cannot persist, or needs to force oneself to work or labor)

Participates in ward work or entertainment for less than 3 hours  Stops working due to illness; inpatients do not participate in any activities or cannot complete daily ward tasks without assistance

**8. Retardation (slow thinking/speech, poor concentration, reduced initiative)**

Normal thinking and speech

Mild retardation noted during mental examination

Obvious retardation noted during mental examination

Difficulty conducting mental examination

Complete inability to answer questions (catatonia)

**9. Agitation**

No abnormality

- Slightly fidgety during examination
- Obvious restlessness or frequent small movements
- Cannot sit still; stood up, rubbed hands, bit fingers/hair/lips during examination

#### 10. Psychic Anxiety

- No abnormality
- Reports anxiety only when asked
- Spontaneously expresses anxiety
- Obvious anxiety evident in facial expression and speech
- Obvious panic

#### 11. Somatic Anxiety (physical symptoms of anxiety: dry mouth, bloating, diarrhea, belching, abdominal cramps, palpitations, headache, hyperventilation, sighing, frequent urination, sweating, etc.)

- Absent
- Mild
- Moderate (definite presence of the above symptoms)
- Severe (symptoms above are severe and affect life or require treatment)
- Severe impact on life and activities

#### 12. Gastrointestinal Symptoms

- Absent
- Decreased appetite but eats without encouragement
- Needs urging or persuasion to eat; requires laxatives or digestive aids

#### 13. General Symptoms

- Absent
- Heaviness in limbs, back, or neck; back pain, headache, muscle pain, general weakness or fatigue
- Obvious symptoms

**14. Sexual Symptoms (decreased libido, menstrual irregularities, etc.)**

- No abnormality**
- Mild**
- Severe**
- Uncertain or not applicable to the respondent**

**15. Hypochondriasis**

- Absent**
- Excessive concern about physical health**
- Repeatedly ruminates on health issues**
- Hypochondriacal delusions and often seeks medical attention due to hypochondria**
- Hypochondriacal delusions accompanied by hallucinations**

**16. Weight Loss (assessed by medical history)**

- No weight loss**
- Possible weight loss**
- Definite weight loss**

**17. Insight**

- Knows one is ill and presents with depression**
- Knows one is ill but attributes it to poor diet, environmental issues, overwork, viral infection, or the need for rest**
- Completely denies illness**