Risk Factors With Intravenous Sedation for Patients With Disabilities

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The purpose of this study was to identify the risk factors associated with low peripheral oxygen saturation (SpO_2) and delayed recovery of dental patients with disabilities after intravenous sedation. A total of 1213 patients with disabilities were retrospectively investigated with respect to demographic parameters and sedation conditions. Multivariate logistic analyses were conducted for patients with an SpO_2 <90% and a recovery period of >60 minutes to identify the risk factors for poor sedation conditions. A significant odds ratio related to decreased SpO_2 was observed for age, sex, midazolam and propofol levels, concurrent use of nitrous oxide, cerebral palsy, Down syndrome, and mental retardation. The most problematic patients were those diagnosed with Down syndrome (odds ratio, 3.003–7.978; 95% confidence interval; $P < .001$). Decision tree analysis showed an increased risk of decreased SpO_2 in males with Down syndrome or after administration of >0.493 mg/kg propofol in combination with midazolam. An increased risk of delayed awakening was seen in patients aged less than 21 years and in males administered >0.032 mg/kg of midazolam. Intravenous sedation for dental patients with disabilities, particularly those with cerebral palsy, Down syndrome, or mental retardation, increases the risk of decreased SpO_2. In addition, delayed recovery is expected after midazolam administration.

Key Words: Dental sedation; Low peripheral oxygen saturation; Delayed recovery.

Dental practices are currently challenged by the rapidly growing number of patients with intellectual or physical disabilities.[1,2] Excessive mental strain during dental treatment can cause systemic complications such as vasovagal reflex, neurogenic shock, pain shock, and hyperventilation. Furthermore, patients with cardiovascular diseases, including cerebrovascular disorders, or decreased vital organ reserve capacity can encounter serious complications. A strategy for relieving mental strain is important for safe dental treatment of such patients, and to this end, intravenous sedation is often used.[3,4] However, when using intravenous sedative drugs that have strong systemic actions on the central nervous, respiratory, and circulatory systems, systemic management to ensure patient safety is a prerequisite.[5,6]

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Table 1. Cross-Tabulation of Decreased Peripheral Oxygen Saturation (SpO_2) and Each Item*

	SpO_2 (%)						
	≥90		*<90*		*Total*		
Item	*No.*	*%*	*No.*	*%*	*No.*	*%*	*P value*
Gender							
Male	564	56.6	141	65.3	705	58.2	.022
Female	432	43.4	75	34.7	507	41.8	
Anesthetics							
Midazolam	253	25.4	29	13.4	282	23.2	<.001
Propofol	355	35.6	55	25.5	410	33.8	
Midazolam and propofol	389	39.0	132	61.1	521	43.0	
Combined with nitrous oxide							
(–)	607	60.9	143	66.2	750	61.8	.144
(+)	390	39.1	73	33.8	463	38.2	
Autism							
(–)	701	70.3	160	74.1	861	71.0	.283
(+)	296	29.7	56	25.9	352	29.0	
Cerebral palsy							
(–)	802	80.4	174	80.6	976	80.5	.969
(+)	195	19.6	42	19.4	237	19.5	
Down syndrome							
(–)	947	95.0	173	80.1	1120	92.3	<.001
(+)	50	5.0	43	19.9	93	7.7	
Epilepsy							
(–)	763	76.5	173	80.1	936	77.2	.258
(+)	234	23.5	43	19.9	277	22.8	
Mental retardation							
(–)	368	36.9	60	27.8	428	35.3	.011
(+)	629	63.1	156	72.2	785	64.7	
Dental phobia							
(–)	875	87.8	200	92.6	1075	88.6	.043
(+)	122	12.2	16	7.4	138	11.4	
Abnormal gag reflex							
(–)	959	96.2	214	99.1	1173	96.7	.031
(+)	38	3.8	2	0.9	40	3.3	
Asthma							
(–)	977	98.0	214	99.1	1191	98.2	.281
(+)	20	2.0	2	0.9	22	1.8	
Hypertension							
(–)	964	96.7	215	99.5	1179	97.2	.022
(+)	33	3.3	1	0.5	34	2.8	
Alzheimer's							
(–)	955	95.8	208	96.3	1163	95.9	.733
(+)	42	4.2	8	3.7	50	4.1	
Diabetes							
(–)	947	95.0	205	94.9	1152	95.0	.962
(+)	50	5.0	11	5.1	61	5.0	
Dysautonomia							
(–)	982	98.5	215	99.5	1197	98.7	.224
(+)	15	1.5	1	0.5	16	1.3	
Dementia							
(–)	984	98.7	215	99.5	1199	98.8	.294
(+)	13	1.3	1	0.5	14	1.2	
Total	997		216		1213		

* Seven items had statistically significant correlation with decreased SpO_2 as per the chi-square test.

Conscious sedation is generally preferred to maintain independent breathing and biological defense mechanisms such as coughing and swallowing reflexes. However, dental treatment of patients with disabilities may require behavioral control, especially in the case of mentally challenged individuals with strong treatment refusal reactions. In these cases, deeper levels of intravenous sedation are a safer option.

Table 2. Results of Logistic Regression Analysis for Decreased Peripheral Oxygen Saturation ($SpO_2 < 90\%$)*

Item	Crude Odds Ratio	95% Confidence Interval		P Value	Multivariate Adjusted Odds Ratio	95% Confidence Interval		P Value
		Lower Limit	Upper Limit			Lower Limit	Upper Limit	
Age	0.997	0.987	1.008	.621	1.022	1.008	1.037	.002
Gender (female/male)	0.694	0.511	0.944	.020	0.591	0.419	0.834	.003
Treatment time (min)	1.012	1.003	1.021	.009	1.002	0.992	1.013	.654
Midazolam (mg/kg)	1.233	1.088	1.397	.001	591.212	15.831	22079	.001
Propofol (mg/kg)	1.331	1.163	1.524	<.001	1.495	1.279	1.748	<.001
Combined with nitrous oxide	0.795	0.583	1.083	.145	0.637	0.455	0.893	.009
Cerebral palsy	0.993	0.685	1.439	.969	1.577	1.048	2.373	.029
Down syndrome	4.708	3.036	7.300	<.001	4.895	3.003	7.978	<.001
Mental retardation	1.521	1.100	2.104	.011	1.910	1.271	2.869	.002

* The crude odds ratios demonstrated 6 factors that showed a statistically significant correlation with decreased SpO_2. After adjusting the odds ratio, 8 factors were found to have statistically significant correlations. Step-up procedure (likelihood ratio).

Depending upon the individual case, increased drug doses can cause deep sedation until the patient becomes completely unconscious, which is a deeper degree of sedation compared with conscious sedation.[6,7] If this deep sedative state overrides the nervous system, basic defense mechanisms may also be lost. Therefore, careful perioperative management, similar to that for general anesthesia, is necessary.

Therefore, dental treatment of mentally or physically impaired patients using intravenous anesthetics requires careful perioperative management, similar to general anesthesia. Unfortunately, there is little information available on the disabilities and sedation conditions particularly at risk of causing low peripheral oxygenation and delayed recovery.[8,9]

In this study, we investigated and analyzed the risk factors that may be involved in causing decreased peripheral oxygen saturation (SpO_2) and delayed recovery, including age, sex, treatment duration, type of disability or disease, and type and dose of anesthetic, in dental patients with disabilities.

METHODS

Over the past 7 years, a total of 1335 patients with disabilities received dental treatment under deep intravenous sedation at the dental care division of the National Medical and Educational Consulting Center and at the National Welfare Foundation for Disabled Children. The 122 patients who were administered flumazenil, a benzodiazepine antagonist used for reversal of deep sedation, were excluded from the study. Therefore, this retrospective study included 1213 patients.

The electronic records of each patient were analyzed with respect to demographic data, type of disabilities, and sedation conditions. The types of mental disabilities listed in these records were Alzheimer disease, autism, cerebral palsy, Down syndrome, dysautonomia, dementia, dental phobia, and mental retardation. The types of physical disabilities included epilepsy, asthma, hypertension, diabetes mellitus, and abnormal gag reflex.

The sedation conditions listed in these records were nitrous oxide combination, treatment duration, drugs and their levels used in intravenous sedation, and recovery time required from the end of surgery to regaining consciousness.

Each of the above mentioned items was cross-tabulated for patients with intraoperative minimum SpO_2 <90% and those with delayed awakening. Consciousness was evaluated depending on its recovery; recovery of vital signs, swallowing function, and the ability to drink and urinate independently; and Romberg test results. Patients who required ≥60 minutes to achieve this state after the end of treatment were included as subjects. Following the chi-square test, multivariate logistic regression and decision tree analyses were performed. To determine the factors involved in decreased SpO_2 and those affecting delayed recovery, multivariate logistic regression analysis was performed. Statistical analysis was performed using a stepwise method (step-up procedure: likelihood ratio) for each disease and the following explanatory variables: age, gender, treatment duration (from the start of anesthesia to the end of the treatment), and type and level of drugs. IBM SPSS Statistics 19 (IBM, Tokyo, Japan) was used as the statistical software. All values are expressed as mean ± SD, and differences with $P < .05$ were considered statistically significant.

RESULTS

We included 1213 patients (705 male, 508 female) with a mean age of 36 ± 14 years (range, 9–83 years) in our

Table 3. Cross-Tabulation of the Recovery Time and Each Item*

	Recovery Time to Awake After Treatment (min)						
	<60		*≥60*		*Total*		
Item	*No.*	*%*	*No.*	*%*	*No.*	*%*	*P Value*
Gender							
Male	640	57.0	65	72.2	705	58.2	.005
Female	482	43.0	25	27.8	507	41.8	
Anesthetics							
Midazolam	255	22.7	27	30.0	282	23.2	.026
Propofol	391	34.8	19	21.1	410	33.8	
Midazolam and propofol	477	42.5	44	48.9	521	43.0	
Combined with nitrous oxide							
(–)	697	62.1	53	58.9	750	61.8	.312
(+)	426	37.9	37	41.1	463	38.2	
Autism							
(–)	800	71.2	61	67.8	861	71.0	.472
(+)	323	28.8	29	32.2	352	29.0	
Cerebral palsy							
(–)	898	80.0	78	86.7	976	80.5	.131
(+)	225	20.0	12	13.3	237	19.5	
Down syndrome							
(–)	1,041	92.7	79	87.8	1,120	92.3	.099
(+)	82	7.3	11	12.2	93	7.7	
Epilepsy							
(–)	866	77.1	70	77.8	936	77.2	.885
(+)	257	22.9	20	22.2	277	22.8	
Mental retardation							
(–)	399	35.5	29	32.2	428	35.3	.527
(+)	724	64.5	61	67.8	785	64.7	
Dental phobia							
(–)	992	88.3	83	92.2	1,075	88.6	.305
(+)	131	11.7	7	7.8	138	11.4	
Abnormal gag reflex							
(–)	1,085	96.6	88	97.8	1,173	96.7	.763
(+)	38	3.4	2	2.2	40	3.3	
Asthma							
(–)	1,104	98.3	87	96.7	1,191	98.2	.220
(+)	19	1.7	3	3.3	22	1.8	
Hypertension							
(–)	1,090	97.1	89	98.9	1,179	97.2	.508
(+)	33	2.9	1	1.1	34	2.8	
Alzheimer disease							
(–)	1,076	95.8	87	96.7	1,163	95.9	.696
(+)	47	4.2	3	3.3	50	4.1	
Diabetes							
(–)	1,068	95.1	84	93.3	1,152	95.0	.460
(+)	55	4.9	6	6.7	61	5.0	
Dysautonomia							
(–)	1,107	98.6	90	100.0	1,197	98.7	.624
(+)	16	1.4	0	0.0	16	1.3	
Dementia							
(–)	1,109	98.8	90	100.0	1,199	98.8	.617
(+)	14	1.2	0	0.0	14	1.2	
Total	1,123		90		1,213		

* The factors of gender and type of anesthetic had statistically significant correlations with the recovery time as per the chi-square test.

study. Mean time from the start of sedation to the end of treatment was 43.0 ± 19.8 minutes, and the mean time required from the end of treatment to recovery of consciousness was 33.0 ± 18.5 minutes. The drugs used for intravenous sedation were midazolam (23.2%; 0.07 ± 0.36 mg/kg) or propofol (33.8%; 1.69 ± 0.99 mg/kg). When midazolam and propofol were used in combination (43.0%), the mean doses were 0.68 ±

Table 4. Results of Logistic Regression Analysis for Recovery Time (≥60 minutes)*

Item	Crude Odds Ratio	95% Confidence Interval Lower Limit	95% Confidence Interval Upper Limit	P Value	Multivariate Adjusted Odds Ratio	95% Confidence Interval Lower Limit	95% Confidence Interval Upper Limit	P Value
Age	0.979	0.961	0.997	.019	0.986	0.967	1.004	.132
Gender (female/male)	0.511	0.317	0.822	.006	0.528	0.325	0.859	.010
Treatment time (min)	1.001	0.987	1.014	.897	0.999	0.985	1.013	.870
Midazolam (mg/kg)	1.342	1.114	1.616	.002	244.789	2.145	27931	.023

* The crude and multivariate adjusted odds ratios for age, gender, and amount of midazolam showed a statistically significant correlation with the recovery time. Step-up procedure (likelihood ratio).

0.04 mg/kg and 1.35 ± 0.85 mg/kg, respectively. Nitrous oxide was also used in 463 patients (38.2%) sedated with each drug used alone or in combination. Table 1 represents the impact of the type of sedation on SpO_2 during dental treatment. Among the 1213 patients, 216 (17.8%) exhibited SpO_2 <90%. Chi-square analysis revealed a significant effect of sedation type on the regulation of SpO_2 ($P < .001$). Among the mental and physical disabilities listed in the records, Down syndrome, mental retardation, dental phobia, abnormal gag reflex, and hypertension were all associated with lower oxygenation during dental treatment under intravenous sedation (Table 1).

Multivariate logistic regression analyses revealed significant odds ratios for cerebral palsy, Down syndrome, mental retardation, age, sex, and all sedation protocols (Table 2). Again, the most significant findings were observed in patients diagnosed with Down syndrome, with an adjusted odds ratio of 4.895–3.003 (95% confidence interval; $P < .001$). In total, these analyses suggest that patients with mental disabilities are particularly at risk of oxygen deprivation during dental treatment under intravenous sedation in the following ascending order according to disability type: cerebral palsy < mental retardation < Down syndrome.

Ninety of the 1213 patients (7.4%) required a longer recovery period, and patients with a delay of ≥60 minutes were cross-tabulated according to the type of drug and disease (Table 3). The chi-square test showed significant differences for sex and the type of sedative.

To determine the factors affecting delayed recovery, multivariate logistic regression analysis was performed. A significant difference was found for sex and midazolam levels (Table 4).

In addition, to verify the possibility of drug interactions among midazolam, propofol, and nitrous oxide, the factor of drug interaction was added as a factor to the results from Tables 2 and 4, and these results are shown in Tables 5 and 6. For the variables included under drug interactions, each mean was converted to 0 and the

Table 5. Results of Logistic Regression Analysis for Decreased Peripheral Oxygen Saturation (90%), Including Interaction Terms of Anesthetics*

Item	Crude Odds Ratio	95% Confidence Interval Lower Limit	95% Confidence Interval Upper Limit	P Value	Multivariate Adjusted Odds Ratio	95% Confidence Interval Lower Limit	95% Confidence Interval Upper Limit	P Value
Age	0.997	0.987	1.008	.621	1.022	1.007	1.036	.003
Gender (female/male)	0.694	0.511	0.944	.020	0.588	0.417	0.831	.003
Treatment time (min)	1.012	1.003	1.021	.009	1.003	0.993	1.014	.520
Midazolam (mg/kg)	1.233	1.088	1.397	.001	1362.883	30.596	60709	<.001
Propofol (mg/kg)	1.331	1.163	1.524	<.001	1.505	1.281	1.768	<.001
Combined with nitrous oxide	0.795	0.583	1.083	.145	0.721	0.508	1.024	.067
Cerebral palsy	0.993	0.685	1.439	.969	1.642	1.088	2.479	.018
Down syndrome	4.708	3.036	7.300	<.001	4.724	2.884	7.740	<.001
Mental retardation	1.521	1.100	2.104	.011	1.782	1.182	2.689	.006
Midazolam * propofol	0.204	0.010	4.268	.305	0.195	0.012	3.237	.254
Midazolam * nitrous oxide	9.899	0.010	10062	.516	0.131	0.000	222	.592
Propofol * nitrous oxide	0.740	0.548	1.000	.050	0.749	0.554	1.013	.060
Midazolam * propofol * nitrous oxide	188.846	1.085	32867	.046	13.048	0.054	3177	.360

* Step-up procedure (likelihood ratio).

Table 6. Results of Logistic Regression Analysis for Recovery Time (≥60 Minutes), Including Interaction Terms of Anesthetics*

		95% Confidence Interval			Multivariate	95% Confidence Interval		
Item	*Crude Odds Ratio*	*Lower Limit*	*Upper Limit*	*Significant Difference*	*Adjusted Odds Ratio*	*Lower Limit*	*Upper Limit*	*Significant Difference*
Age	0.979	0.961	0.997	0.019	0.986	0.968	1.005	0.162
Gender (female/male)	0.511	0.317	0.822	0.006	0.536	0.329	0.873	0.012
Treatment time (min)	1.001	0.987	1.014	0.897	0.999	0.985	1.013	0.856
Midazolam (mg/kg)	1.342	1.114	1.616	0.002	268.244	2.159	33327	0.023
Midazolam * propofol	0.091	0.001	8.401	0.300	0.095	0.001	8.215	0.301
Midazolam * nitrous oxide	111.508	0.005	2332075	0.353	101.170	0.007	1542473	0.348
Propofol * nitrous oxide	1.116	0.735	1.696	0.605	1.189	0.762	1.854	0.446
Midazolam * propofol * nitrous oxide	0.376	0.000	1463.924	0.817	0.218	0.000	693.539	0.711

* Step-up procedure (likelihood ratio).

product was used as the interaction value to prevent the occurrence of multicollinearity. Multivariate logistic regression analysis using the drug interaction value demonstrated that neither decreased SpO_2 nor delayed recovery showed a significant odds ratio for the factor of drug interaction (Tables 5 and 6).

Similarly, decision tree analysis showed a significantly higher risk of decreased SpO_2 in males with Down syndrome or males administered >0.493 mg/kg of propofol in combination with midazolam. In addition, even patients administered <0.493 mg/kg of propofol for >65 minutes of treatment had a high risk of decreased SpO_2 (Figure 1). A higher probability of delayed recovery was seen in patients aged <21 years and in males administered >0.032 mg/kg of midazolam (Figure 2).

DISCUSSION

Patients with mental and physical disabilities often exhibit maladaptive behavior and are not cooperative during dental treatment, which justifies the use of intravenous sedation for their safety.[3] Compared with general anesthesia, intravenous sedation is easy to perform and is often used in dental treatment.[10,11] However, close monitoring of vital signs is essential because these drugs have strong systemic actions on the nervous, respiratory, and circulatory systems.[5,6] The present study identified the safest sedative and patients at the highest risk of experiencing respiratory depression during and delayed recovery after intravenous sedation for dental treatment.

Among the demographic parameters, gender was the most consistent and significant factor affecting respiratory function and recovery period. Female patients were at lower risk of low SpO_2 and delayed recovery time. There are several reports on sex-related differences with respect to the effects of anesthesia,[12–15] all suggesting that women have lower sensitivity to anesthetics and recover consciousness more rapidly. Some researchers have argued that female hormones such as progesterone may explain these phenomena.[15] Accordingly, male patients should be more closely monitored during dental treatment under intravenous sedation.

Decreased SpO_2 can be caused by occlusion of the upper respiratory tract following motion suppression, sedative drug overdose, or deep sedation[16]; transient glossoptosis caused by choking or cough reflex[17]; or the use of instruments such as those used for maintaining mouth opening during oral manipulations.

This study identified 3 mental disabilities associated with a high risk of poor sedation control during dental treatment in the following descending order: Down syndrome > mental retardation > cerebral palsy. Nearly 50% of patients with Down syndrome exhibit upper-airway obstruction and have congenital heart disease, both risk factors for pulmonary hypertension (review: King et al. 2011[18]). It has been suggested that low SpO_2 is caused by factors such as sleep apnea and upper-airway obstruction due to the presence of a large tongue.[19,20] Therefore, these patients are particularly at risk of cardiovascular complications and low SpO_2 during intravenous sedation. In the case of cerebral palsy and mental retardation, the patients can suffer from upper-airway stenosis.[21,22] Accordingly, the perioperative management of breathing functions is vital during dental treatment under sedation.

Patients who required ≥60 minutes for recovery were included in logistic regression analysis and decision tree analysis that demonstrated midazolam levels to be a risk factor for prolonged recovery time. Midazolam is used during dental treatment for disabled patients,[23,24] especially for its amnesic effect and behavior control, although higher doses can easily result in deep sedation. It is also known to provide a longer duration of action compared with propofol, suggesting delayed recovery.

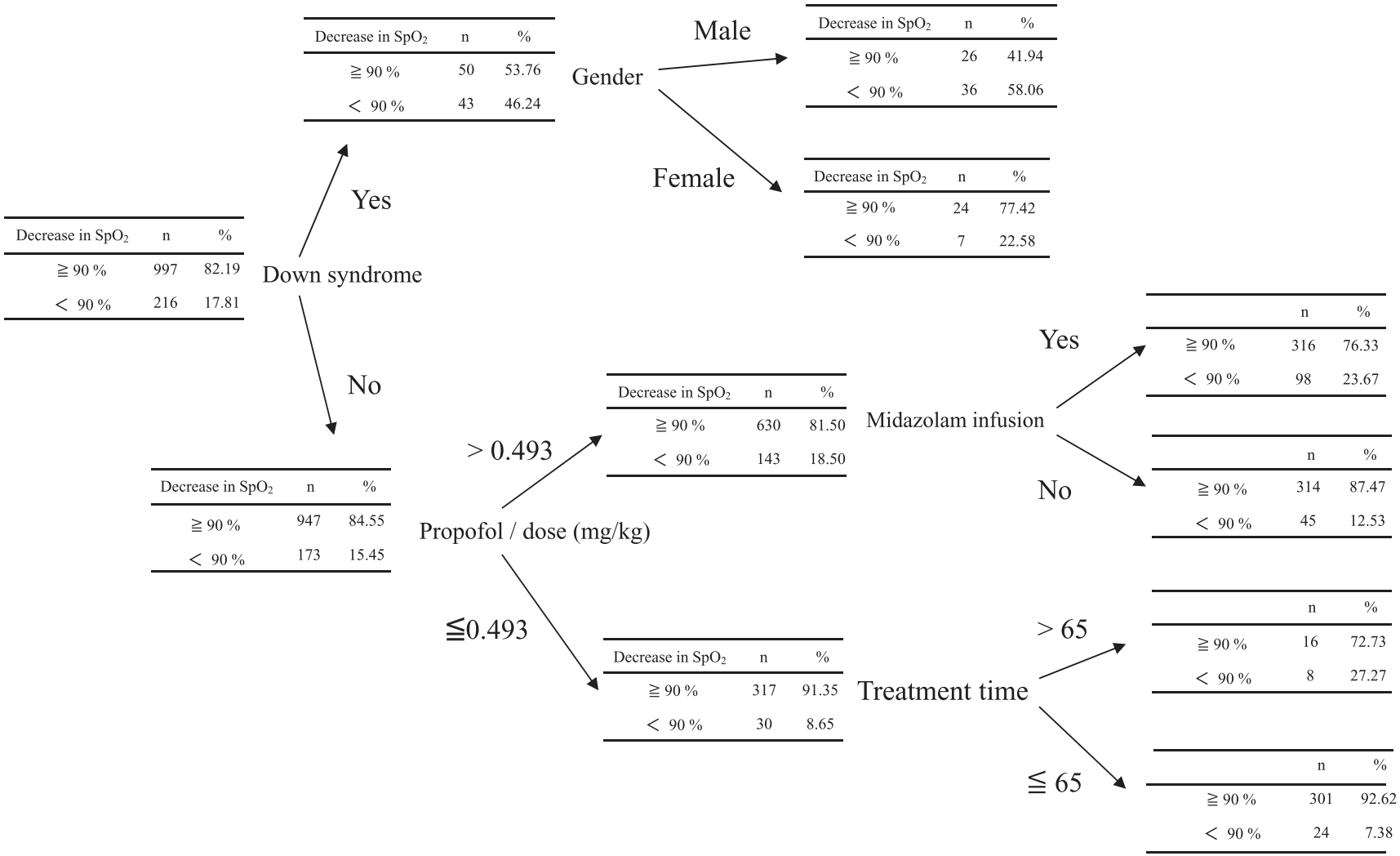

Figure 1. Decrease in peripheral oxygen saturation (SpO_2) was used as an objective variable. Down syndrome was the highest risk factor for decrease in SpO_2.

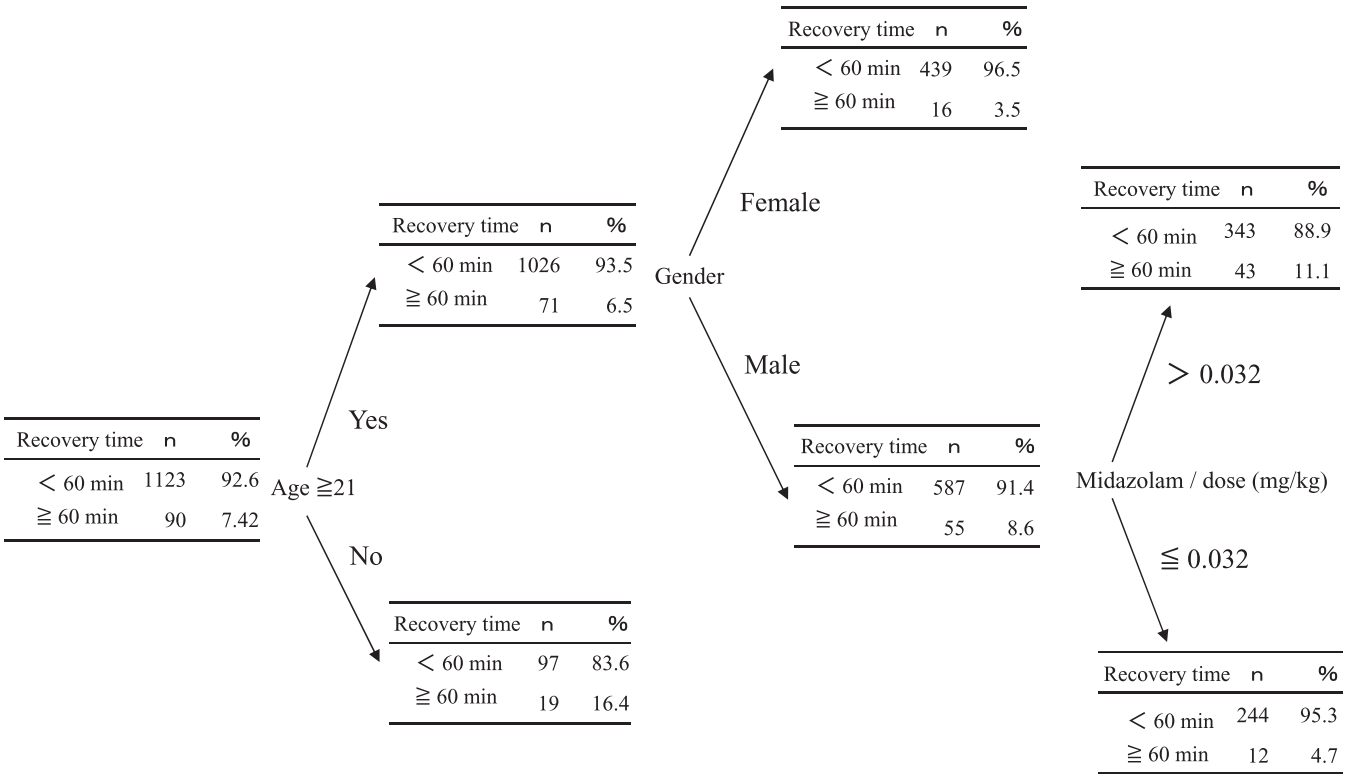

Figure 2. Results of decision analysis for recovery time (≥60 minutes). Recovery time (≥60 minutes) was used as an objective variable. Age and gender were the highest risk factors for prolongation of recovery time.

During dental treatment of patients with mental retardation who show vigorous treatment-refusal actions, a period of deep sedation is intentionally selected for controlling such behavior. In such a scenario, independent maintenance of airways is physiologically difficult. Although spontaneous respiration is maintained, respiration and circulation are depressed and basic defense mechanisms are partially suppressed, resulting in decreased SpO_2.[6] To prevent these signs, oxygen and emergency equipment must be kept ready[6] and consciousness, ventilation, oxygenation, and circulation statuses should be carefully monitored. Along with maintaining the defense mechanisms, airway management has to be carefully performed. Titrated drug administration and precise perioperative systemic management are also very important.

The present study suggests that patients diagnosed with Down syndrome, mental retardation, and cerebral palsy should be more closely monitored during dental treatment under intravenous sedation.

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