Changes in the Levels of Nutrition in Patients with Neuromuscular Disease Admitted to Hospital with Dysphagia
— Analysis Using Functional Oral Intake Scale (FOIS) —

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Abstract

[Purpose] In neuromuscular diseases (NMD), dysphagia progresses under their recognition, resulting in severe respiratory complications, such as choking or aspiration pneumonia. In this study, we investigated the levels of nutrition before and after admission to a hospital, and after videoendoscopic evaluation of swallowing (VE) in NMD, and the factors associated with nutrition level after the VE.

[Methods] The subjects were 25 patients with NMD. We retrospectively investigated them by questionnaires, bedside evaluation sheets, and VE evaluation sheets. The levels of nutrition before and after admission to a hospital, and after the VE evaluation, were scored with the Functional Oral Intake Scale (FOIS-before, FOIS-after, FOIS-VE, respectively). We compared those FOIS scores, and tested which factors in the evaluation sheets were associated with the FOIS-VE.

[Results] Pneumonia or fever, and appetite loss were the top reasons for admission. The FOIS-after and FOIS-VE were significantly less than FOIS-before ($p<0.05$). The FOIS-VE was significantly correlated with "food residue", "voluntary cough", and "wet hoarseness" in the bedside evaluation sheets, and "saliva retention" in the VE evaluation sheets.

[Conclusion] The present study demonstrated that the nutrition level in NMD patients significantly decreased through hospital admission. The findings in this study indicate that screening tests and oropharyngeal evaluations at adequate timings are needed to prevent severe complications. The factors associated with FOIS-VE could be indicators to identify inadequate nutrition levels.

Key words : nutrition level, neuro-muscular disease, videoendoscopic evaluation of swallowing, functional oral intake scale (FOIS)

原　著

全身麻酔下歯科治療後の歯科保健管理の中断要因の検索

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要旨：目的：本研究は，障害者の歯科保健管理の維持をアウトカムとした地域連携クリニカルパスの開発のために，全身麻酔下歯科治療後に3年間の歯科保健管理が維持できなかった者の要因をレトロスペクティブに検索した．

対象と方法：対象は，全身麻酔下の歯科治療を経験した131名の障害者であった．診療記録から年齢，障害の種類，初診時の発達年齢，初診時の口腔内診査への適応性，現在歯数，齲蝕歯数，通院時間，歯科保健管理の継続の有無について調査した．データ解析は，歯科保健管理の継続者群（3年間）と中断者群（3年未満で中断）の管理状況を従属変数としてロジスティック解析を行った．

結果および考察：歯科保健管理の中断要因について初診時の口腔内診査への適応性が抽出できた．初診時の口腔内診査時に自発的に開口を維持し，拒否行動がなく適応できた群は，拒否行動があった群よりも中断しやすい傾向（調整オッズ比6.5，95%CI：2.1-20.3）が認められた．このことから，口腔内診査に適応できる者の保護者は，子どもの口腔内状態について不安を抱いていない可能性があり，歯科保健管理の重要性を理解しなくなったことが中断する理由として考えられた．歯科保健管理の中断を避けるために，初診時の口腔内診査時に適応できる者には，毎回の定期検診時に現在の状況を確認し，良いところを見つけ，患者本人と保護者へ良いところを褒める（陽性強化）ことにより次回来院への動機付けを行うことが重要であると考えられた．

Key words：Oral health management, General anesthesia, Special needs, Dental treatment

緒　言

保護者が障害者に付き添って，遠方の障害者歯科の高次医療機関へ通院することは困難な場合があるため，障害者の歯科管理は，高次医療機関でなく，かかりつけ歯科医で行われることが望ましいと思われる．歯科管理を受けている障害者に歯科治療の必要性があるときは，かかりつけ歯科医で治療を受けることになるが，発達年齢が3歳未満の障害者は，トレーニングを行っても歯科治療が困難である[1]．そのために静脈内鎮静法や全身麻酔の適応になることが多く[2]，高次医療機関との連携が重要となる．歯科治療が困難な障害者は，地域のかかりつけ歯科医で定期検診を行い，歯科治療が必要なときに高次医療機関を受診するという歯科保健管理システムが必要となる．このシステムは，歯科治療が困難な障害者にも良質な歯科医療を効率的かつ安全に，そして適正に提供することができるものとなる．かかりつけ歯科医と高次医療機関の連携による歯科保健管理のために患者情報を共有する必要があるが，そのためのツールとして地域連携クリニカルパスが有用とされている[3]．クリニカルパスとは，医療工程管理の道具であり，医療を標準化し，経済的，効率的，そして質の向上につながるものである．歯科治療が困難な障害者のために既存の歯科疾患を治療することから，歯科保健管理の継続，そして歯科治療の必要があるときの対応までの循環型の地域連携クリニカルパスは，地域医療機関と高次医療機関をつなぐものとなる．障害者歯科医療においては地域連携クリニカルパスを使っての継続的な歯科保健管理が目標となるが，歯科保健管理を中断する患者もいる．歯科保健管理の中断は，地域連携クリニカルパスのアウトカムとしての歯科保健管理の継続という標準的な経過とずれたものとなる．標準的な経過とのずれをバリアンスと呼び，クリニカルパスを構築するためにはバリアンスデータを分析し，改善しなければならない．全身麻酔下歯科治療後に歯科保健管理を中断する患者の要因があらかじめ推測できれば，中断への対応を検討し，地域連携クリニカルパスに反映できると思われる．しかしながら，クリニカルパス作成のための調査[4~6]では，歯科保健管理が中断となる患者の要因は明らかになっていない．

そこで本研究は，障害者歯科医療のための地域連携クリニカルパスの開発のために，全身麻酔下歯科治療後に3年間の歯科保健管理が維持できなかった者の中断要因をレトロスペクティブに検索した．

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対象および方法

対象は，2007年1月1日から2008年12月31日までに松本歯科大学病院特殊診療科にて全身麻酔下歯科治療を実施し，全身麻酔後の歯科保健管理の説明を行い，3〜6カ月ごとの定期検診を勧めた131名（平均年齢11.5±9.8歳）であった．本研究は，平成14年文部科学省・厚生労働省告示第2号　疫学研究に関する倫理指針を遵守して行い，松本歯科大学研究等倫理審査委員会の承認後に研究を行った（許可番号 0131号）．

患者の全身麻酔下歯科治療が行われている間，歯科衛生士と栄養士が保護者に対して20〜30分間，口腔内状態と今後の歯科疾患の予防法について説明した．そのなかで歯科保健管理の重要性とシステムについて説明した．さらに全身麻酔下歯科治療の1カ月後の予後診査においても，定期検診を軸とした歯科保健管理について歯科医師より再度説明した．

調査項目の年齢，障害の種類，初診時の発達年齢（遠城寺式乳幼児分析的発達検査），初診時に評価された口腔内診査における適応性（初診時適応性：表1）は，診療記録から調査した．初診時の口腔内診査用紙から現在歯数，齲蝕歯数を調査し，保護者への問診票から通院にかかる時間を調査した．全身麻酔下歯科治療後の定期検診記録から歯科保健管理の継続の有無，全身麻酔下歯科治療後に紹介元の歯科医療機関へ歯科保健管理を依頼した場合は，依頼した歯科医療機関に問い合わせを行い，歯科保健管理の継続の有無を電話にて聴取した．なお歯科保健管理は，3年間にわたり定期検診（3〜6カ月ごと）が継続して行われた場合を継続管理とし，3年間継続した受診がなされていない場合を中断と判定した．

データ解析は，歯科保健管理の継続群と中断群（管理状況）で各項目の比較を行った（単変量解析）．カテゴリカルデータはχ^2検定を，歯数は等分散検定後にWelch検定あるいはStudentのt検定を行い，p値が0.15未満を多変量解析の独立変数の候補とした．さらに独立変数の項目ごとの独立性を検討するために，それぞれの独立変数の候補の項目ごとにχ^2検定を行い，相関行列表を作成し，交絡因子について検討した．項目間のp値が0.05以上で独立性が得られた項目を独立変数とした．なお0.05未満の場合は，管理状況（継続・中断）とのp値が最も低い項目を多変量解析の独立変数とした（独立性の検討）．選択された項目を独立変数とし，管理状況（継続・中断）を従属変数としてロジスティック回帰分析を行った．統計解析は，統計ソフトSPSS 18.0 for Windowsを用いて行った．

表1　初診時の口腔内診査における適応性の判定基準

適　応；診査の妨げになる行動がなく，指示に従って開口を維持できる
不適応；診査の妨げになる行動がみられる

結　果

1. 単変量解析

歯科保健管理を3年間継続した者は131名中102名（77.9%），中断した者は29名（22.1%）であった．管理状況（継続・中断）と各項目についてχ^2検定を行った結果，p値が0.15未満であった項目は，てんかん，心疾患，初診時適応性，発達年齢では手の運動，基本的習慣，対人関係，発語，言語理解であった．年齢，精神遅滞，自閉症，広汎性発達障害（自閉症以外），Down症候群，脳性麻痺，運動障害，喘息，移動運動，齲蝕歯数，乳歯齲蝕歯数，永久歯齲蝕歯数，管理機関，通院時間は，p値が0.15以上で有意差がみられなかった（表2）．

2. 項目間の関連性

各項目間で独立性がみられたのは，心疾患であった．他の項目は相互に関連性がみられ，管理状況と単相関で最もp値が低かった初診時適応性が従属変数として抽出された（表3）．

3. ロジスティック回帰分析

心疾患と初診時適応性を独立変数とし，従属変数を管理状況としてロジスティック回帰分析を行った結果，管理状況には初診時適応性のみに有意な相関が認められた（表3）．初診時適応性の調整オッズ比は6.5（95%CI：2.1-20.3）であった．口腔内診査に適応する者は，不適応の者と比較して6.5倍中断する傾向がみられた．心疾患の調整オッズ比は0.388（95%CI：0.09-1.76）であり，有意ではなかった（表4）．

考　察

障害者は適切な歯科保健管理により，未処置齲蝕歯が歯科疾患実態調査で報告された健常者のデータより有意に少なく[7]，適切な歯科保健管理は，障害者の口腔の健康維持のために必要である．しかしながら現実には全身麻酔後継続的な歯科管理を中断する例が少なくない．本研究において全身麻酔下歯科治療後の3年間の歯科保健管理の継続に影響する要因を検索した結果，継続管理の

表2　定期検診継続群と中断群の比較

項目	カテゴリー	継続群	中断群	p
症例数		102	29	
年齢		11.1±9.4	12.8±1.1	0.41
疾患名				
精神遅滞	あり	47	10	0.27
	なし	55	19	
自閉症	あり	38	8	0.34
	なし	64	21	
広汎性発達障害（自閉症以外）	あり	48	10	0.23
	なし	54	19	
てんかん	あり	32	4	0.101
	なし	70	25	
Down 症候群	あり	6	4	0.31
	なし	96	25	
脳性麻痺	あり	10	1	0.48
	なし	92	28	
運動障害	あり	24	5	0.47
	なし	78	24	
喘息	あり	8	1	0.68
	なし	94	28	
心疾患	あり	4	4	0.13
	なし	98	25	
発達				
移動運動	3歳未満	53	14	0.73
	3歳以上	49	15	
手の運動	3歳未満	59	11	0.06
	3歳以上	43	18	
基本的習慣	3歳未満	61	10	0.02
	3歳以上	41	19	
対人関係	3歳未満	75	16	0.05
	3歳以上	27	13	
発語	3歳未満	77	17	0.07
	3歳以上	25	12	
言語理解	3歳未満	71	16	0.14
	3歳以上	31	13	
その他				
齲蝕歯数		8.5±5.3	8.9±5.3	0.77
乳歯齲蝕歯数		5.1±4.9	4.7±5.4	0.71
永久歯齲蝕歯数		3.4±5.9	4.2±6.0	0.55
初診時適応性	適応	48	25	0.0004
	不適応	54	4	
管理機関	大学	85	23	0.62
	開業歯科医院	17	6	
通院時間	30分未満	35	7	0.63
	1時間未満	24	8	
	1時間30分未満	23	9	
	2時間未満	11	4	
	2時間以上	9	1	

中断要因として初診時の口腔内診査への適応性が抽出された．初診時に口腔内診査に拒否行動がなく，適応できる障害者は，拒否行動がみられる者と比較して6.5倍中断する可能性があることが認められた．中断は，障害者である子どもと，連れてくる保護者とに要因があると思われる．

子どもの要因としては，発達が挙げられる．口腔内診査に拒否行動を示すか否かは発達に依存し，2歳6カ月未満の発達レベルでは，口腔内診査[8]と介助磨き[9]に対して拒否行動を示す傾向がある．本研究でも初診時の口腔内診査時の適応性と対人関係の発達とは関連がみられ，過去の報告[8,9]と同様であった．しかしながら，歯科保健管理の中断は，障害者自身ではなく，保護者に依存する行動である．発達レベルが低い障害者は，介助磨きにも適応しないので，保護者自身で十分に磨けなかったり，口腔内を十分に見ることもできない．そのために障害者である子どもの口腔内状態に不安をもつだけでなく，さらに齲蝕になった際の治療困難に対する不安などがあるために，定期検診の重要性を十分に理解し，歯科保健管理を継続させてきたものと考えられる．すなわち初診時の口腔内診査に不適応であることが保護者の不安や心配につながり，保護者の定期検診を継続する動機付けにつながったと考えられた．また発達レベルが低い障害者は，3年間変わらずに口腔内診査に対して不適応であった可能性があり，保護者は，歯科保健管理の必要性を感じていたとも考えられた．つまり全身麻酔後の継続管理には子どもの発達と保護者の危機感が影響していると考えられた．

一方，口腔内診査に適応できる障害者の保護者は，上記の不安が少なく，継続した歯科保健管理の重要性を感じることが少なくなり，中断にいたったと考えられた．口腔内診査に適応できる発達年齢は2歳6カ月以上[8,10]であり，歯科治療への適応は3～4歳以上[1,2]であるので，口腔内診査の適応性だけで歯科治療の適応性を判断するのは困難であることを保護者へ伝え，予防とそのための歯科保健管理の重要性を伝えておくことが重要であると考えられた．

著者らの医療機関では，紹介患者の場合，歯科治療後に紹介元へ引き続き歯科保健管理を依頼することにしている．23名の患者を紹介元（開業歯科医院）へ依頼したが，紹介元での歯科保健管理は，歯科保健管理の中断に影響を与えていなかった．これは，地域で障害のある患者を受け入れ，検診や保健指導を積極的に行い，地域の医療機関と保護者との信頼関係が構築されていることを反映しているものと考えられた．

また，今回の調査対象者のなかには，大学病院への通院時間が片道2時間以上かかる患者もいたが，通院時間

表3　項目間の関連性（相関行列）

項目名	てんかん	心疾患	初診時適応性	手の運動	基本的習慣	対人関係	発語	言語理解	管理状況
てんかん	*	0.57	0.44	<0.01	<0.01	0.32	0.19	0.18	0.1019
心疾患	*	*	0.13	0.85	0.92	0.93	0.55	0.97	0.1286
初診時適応性	*	*	*	0.07	0.03	<0.01	0.02	0.08	0.0004
手の運動	*	*	*	*	<0.01	<0.01	<0.01	<0.01	0.06
基本的習慣	*	*	*	*	*	<0.01	<0.01	<0.01	0.02
対人関係	*	*	*	*	*	*	<0.01	<0.01	0.05
発語	*	*	*	*	*	*	*	<0.01	0.07
言語理解	*	*	*	*	*	*	*	*	0.14

数字：p値

表4　中断の要因（ロジスティック回帰分析）

	オッズ比	95% CI	p
心疾患 （心疾患あり）	0.388	0.09-1.76	0.22
初診時適応性 （口腔内診査に適応）	6.5	2.1-20.3	0.001

は，歯科保健管理の中断に影響を与えていなかった．これは，前述のとおり，紹介された患者は地域で管理され，大学病院を受診した患者は全員が大学での管理を希望し，結果的に保護者が希望した医療機関であったので，通院時間が長くても，患者の保護者にとっては無理がないと考えられた．

初診時の乳歯齲蝕歯数や永久歯の齲蝕歯数は，歯科保健管理の中断に影響を与えていなかった．また初診時の齲蝕歯数が多い者でも歯科保健管理を中断する可能性があり，齲蝕歯数は，保護者に歯科保健管理の重要性を理解させるのに十分ではなかったものと考えられた．また障害の種類とは関連がなかったのは，障害とその重症度は多種多様であり，障害の種類だけで口腔内診査への適応性や歯科治療の困難性を判断できるものではないので，歯科保健管理の継続に影響を与えなかったと考えられた．

地域連携クリニカルパスのアウトカムである歯科保健管理を継続させるために，口腔内診査へ適応性を示す障害者には，なんらかの対策を講じる必要性があると思われた．本研究では，患者の要因を検討したが，保護者の要因も検索し，検討していく必要がある．少なくとも今回の結果から，初診時の口腔内診査に適応する者に対しては，毎回の定期検診時に現在の状況を十分に伝え，歯科疾患リスクの評価と課題提示，そして常日頃のホームケアの良いところを指摘し，患者本人と保護者へ陽性強化することが歯科保健管理の維持にとって重要であると考えられた．とくに陽性強化は，行動を起こすための最も重要かつ中心的なものとされている[11]．初診時の口腔内診査に適応する患者本人と保護者へ陽性強化を心がける必要があるが，この陽性強化は，初診時の適応，不適応にかかわらず，すべての患者と保護者に配慮すべきことと考えられる．

結　論

障害のある患者に対して全身麻酔下歯科治療を実施し，定期検診を軸とした継続的な歯科保健管理を勧めたものの3年間の歯科保健管理が維持できなかった患者の要因について検索した．その結果，初診時の口腔内診査の際に拒否行動がない者は，拒否行動があった者より中断する傾向（調整オッズ比6.5）が認められた．地域連携クリニカルパスのアウトカムである歯科保健管理を継続させるために，口腔内診査に適応性を示す障害者には，なんらかの配慮が必要であることが示唆された．

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Factors Related to the Interruption of Oral Health Management after Dental Treatment under General Anesthesia

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Oral health management by periodic dental check-ups is important for people with special needs. We explain the need for oral health management of persons with special needs after dental treatment under general anesthesia. However, there are some people with special needs that do not visit dental clinics for oral health management. The factors related to the interruption of oral health management after dental treatment under general anesthesia are unknown.

This study retrospectively investigated the factors that contributed to patients discontinuing their oral health management after dental treatment under general anesthesia. With the results from this study we may be able to design a clinical pathway for the prevention of dental diseases in patients with disabilities after dental treatment under general anesthesia.

The subjects were 131 persons with special needs who had received dental treatment under general anesthesia. Age, type of disability, and developmental age were examined from medical records. Behavioral adaptations to the oral examination, the number of present teeth and decay examinations were investigated from initial oral examination visitation records. The amount of time that it took to go to the dental hospital was investigated via a questionnaire filled out by the parents. The discontinuation of oral health management was determined from oral examination records taken from a period of three years. The factors related to the discontinuation of oral health management for three years were analyzed using logistic regression analysis.

The factors related to the discontinuation of oral health management for three years after dental treatment under general anesthesia were associated with behavioral adaptations to the oral examination at initial visitation. The adjusted odds ratio (OR) for behavioral adaptations to the oral examination was significant (OR＝6.5, 95%CI, 2.1-20.3). Special needs children with good behavioral adaptations to the oral health examination after treatment under general anesthesia discontinue oral health management 6.5 times more than those with poor behavioral adaptations. It was thought that the parents of a person who has good behavioral adaptations to an oral examination doesn't have anxiety about their oral condition, and doesn't understand the importance of oral health management.

Midazolam Is Associated With Delay in Recovery and Agitation After Ambulatory General Anesthesia for Dental Treatment in Patients With Disabilities: A Retrospective Cohort Study

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Purpose: Some patients with intellectual disabilities (IDs) who undergo total intravenous anesthesia (TIVA) have complications associated with the anesthesia such as prolonged recovery. The purposes of this study were to estimate the frequency of TIVA complications among patients with IDs and to identify factors associated with TIVA complications.

Materials and Methods: This study was designed as a retrospective cohort study. Study samples were selected from the clinical records of patients with IDs who underwent ambulatory general anesthesia in a special dental clinic at the Okayama University Hospital, Okayama, Japan. Predictor variables were patient background, anesthesia-related variables, and dental treatment. Outcome variables were delayed recovery and the complication of agitation. Factors affecting delayed recovery and complications were examined with multivariable analysis.

Results: We enrolled 106 cases (81 male and 25 female patients) in this study. The mean age was 23.9 years. Serious complications were not observed in any cases. The amount of intravenous midazolam was an independent determinant of delayed recovery. Oral midazolam contributed to delayed recovery, although it is very useful for induction in patients with a high level of fear. Oral midazolam and a younger age were independent predictors of agitation.

Conclusions: Intravenous midazolam may not have an advantage in ambulatory general anesthesia. Oral midazolam contributes to delayed recovery and is an independent predictor of agitation.

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General anesthesia (GA) has been used in dentistry for patients with intellectual disabilities (IDs) because of their difficulty in cooperating with dental treatments.[1-6] In addition, ambulatory GA is preferable to hospitalization for these patients and their families because it is hard for them to become accustomed to new circumstances such as a hospital. In ambulatory GA, it is important to control recovery time and prevent complications.

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Recently, short-acting intravenous (IV) anesthetics have been developed. In particular, total intravenous anesthesia (TIVA), consisting of remifentanil and propofol, is considered superior to other anesthetics for ambulatory GA because it enables easy control of anesthesia depth, and allows earlier recovery from GA.[3,7] In addition, because propofol has a strong antiemetic effect, it leads to a comfortable recovery state.[8] Nevertheless, in some cases, it still takes a longer time to recover. Because patients with IDs have various backgrounds, interactions of several factors are considered to be involved in the recovery state. To reduce delayed recovery and/or complications, it would be useful to clarify any independent factors for these outcomes, which was the purpose of our study.

We hypothesized that there are 1 or more variables associated with the outcomes of delayed recovery and complications that can be manipulated by the clinician. The specific aims of the study were to measure, to compare, and to estimate some of these variables of interest by use of retrospective multivariate analysis of dental treatments given to patients with IDs under ambulatory GA.

Materials and Methods

STUDY DESIGN/SAMPLE

To address the research purpose, we designed and implemented a retrospective cohort study. The study population was composed of all patients presenting for evaluation and management of dental treatment under ambulatory GA in the clinic of Special Needs Dentistry at Okayama University Hospital, Okayama, Japan, from December 2009 to November 2010. To be included in the study sample, GA with tracheal intubation had to be maintained with TIVA consisting of remifentanil and propofol. Patients were excluded as study subjects if hospitalization was planned.

VARIABLES

Primary predictor variables were divided into 3 groups as follows: patient specific (age, gender, height, weight, body mass index, cerebral palsy, autism, epilepsy, and mental disorders); anesthetic technique (duration of injection, induction procedure, amount of midazolam by mouth [per body weight], amount of IV midazolam [per body weight], amount of propofol [per body weight], mean rate of propofol infusion [per body weight], and remifentanil infusion rate [per body weight]); and surgical/dental treatment (duration of treatment, long treatment [>100 minutes], and type of treatment). A mental disorder was defined by patient use of psychotropic drugs.

The primary outcome variable was time to recovery. The secondary outcome variable was the complication of agitation. Recovery time was defined as the duration from termination of treatment until permission for discharge. We judged the recovery state of patients using a postanesthetic discharge scoring system,[9] with which activity, vital signs, intake, pain, and bleeding were estimated. Patients were permitted to be discharged when these factors had recovered to the same levels as on admission.

DATA COLLECTION METHODS

Data were collected from the clinical records of patients who could be included by the criteria of this study. Patient information was deidentified and stored appropriately. This study was approved by the Ethics Committee, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University.

ANESTHETIC PROCEDURE

In our facility, chest radiography, blood examination, and electrocardiography are performed as basic screening tests for GA. Fasting times are 6 hours and 2 hours for food and clear water, respectively. Medicines in daily use are taken as usual.

Basically, GA was started with insertion of an IV line. When it was difficult to place, midazolam was given orally or sevoflurane was inhaled as induction for GA and, occasionally, both were used, followed by insertion of an IV line. Remifentanil was started at 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ at first to decrease vessel pain caused by the propofol injection, and propofol was started 1 to 2 minutes later. Propofol was continuously infused in a target-controlled infusion manner, and the target concentration was initially set at 4.0 $\mu g/mL$ in normal adult patients. In obese patients standard weight is calculated as a body mass index of 22. On the basis of standard weight, the infusion rate of remifentanil was determined. In young patients aged under 16 years, propofol was infused at 10 $mg \cdot kg^{-1} \cdot h^{-1}$ (167 $\mu g \cdot kg^{-1} \cdot min^{-1}$) because target-controlled infusion cannot be used because of the basic settings of the infusion pump. In some patients midazolam was injected before other IV anesthetics, with the intention of sedation to lessen the reaction to vessel discomfort caused by the propofol infusion. After loss of consciousness, rocuronium was injected to obtain muscle relaxation, and an endotracheal tube was inserted, usually through the nose.

Patients were continuously monitored with electrocardiography, blood pressure, SpO_2 (noninvasive oxygen saturation of hemoglobin in arterial blood), bispectral index monitoring, and partial pressure of carbon dioxide in an anesthetic circuit. Body temperature was measured every 30 minutes. After intubation, the infusion rate of remifentanil was reduced to 0.10 to 0.20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and the target concentration of propofol was set at 3.0 $\mu g/mL$. Dur-

ing treatment, the bispectral index value was maintained between 40 and 50 by adjusting the target concentration of propofol, according to a previous report.[10] Systemic blood pressure was maintained at no less than 80 mm Hg. During treatment, local anesthetic containing 2% lidocaine and 1:80,000 epinephrine was used if considered necessary. After tooth extraction, IV or suppository nonsteroidal anti-inflammatory drugs were used. After treatment, infusion of both remifentanil and propofol was terminated, and the effect of the muscle relaxant was reversed with vagostigmin. The tracheal tube was removed when spontaneous breathing recovered. Patients were permitted to be discharged, according to the standards given earlier.

DATA ANALYSIS

Data were analyzed with JMP 9.0.0 (SAS Institute, Cary, NC). A linear regression was applied to examine the bivariate regression between the primary outcome variable (time to recovery) and all continuous study variables, whereas 1-way analysis of variance was used between the primary outcome variable and nominal study variables. To extract independent variables affecting the primary outcome, possible predictive variables were selected with stepwise regression, for which the cutoff was $P < .25$, followed by a multiple regression (standard least squares).

A logistic regression was used to test the relationship between the secondary outcome variable (agitation) and continuous variables. The Fisher exact test was used between the secondary outcome variable and nominal variables. After selection with a stepwise regression, for which the cutoff was $P < .25$, a multiple logistic regression (nominal logistic fit) was used to extract independent variables affecting the secondary outcome variable.

Results

We enrolled 106 cases in this study. The patients' backgrounds and summaries of anesthetic data are shown in Table 1. GA was started with an IV line in 72.6% of all cases, whereas inhaled anesthetic and oral midazolam were used in 18.9% and 13.2%, respectively. Both inhaled anesthetic and oral midazolam were used in 4.7%. No patient was hospitalized unexpectedly after GA. Time to recovery (mean ± SD) was 95.7 ± 26.6 minutes. Major complications did not occur. Because agitation was observed in 20% of cases, we analyzed factors related to the agitation.

Table 1. PATIENT BACKGROUND AND SUMMARY OF ANESTHETIC DATA

Category	Variables	Data
Patients	Male/female (%)	76.4/23.6
	Age (mean ± SD) (yr)	23.9 ± 9.3
	Height (mean ± SD) (cm)	155.9 ± 16.5
	Weight (mean ± SD) (kg)	53.9 ± 18.7
	Body mass index (mean ± SD)	21.6 ± 4.8
	Autism (%)	62.3
	Cerebral palsy (%)	19.8
	Epilepsy (%)	44.3
	Mental disorder (%)	24.5
Anesthetic	Induction procedure (%)	
	IV line	72.6
	Inhalation (inhalation of sevoflurane)	14.2
	Oral midazolam	8.5
	Oral plus inhalation	4.7
	Duration of infusion (mean ± SD) (min)	110.1 ± 23.4
	Oral midazolam (mean ± SD) (mg/kg)	0.042 ± 0.112
	IV midazolam (mean ± SD) (mg/kg)	0.025 ± 0.022
	Propofol amount (mean ± SD) (mg/kg)	13.9 ± 3.6
	Propofol rate (mean ± SD) ($mg \cdot kg^{-1} \cdot h^{-1}$)	7.70 ± 1.17
	Propofol rate (mean ± SD) ($mg \cdot kg^{-1} \cdot min^{-1}$)	128.6 ± 19.5
	Remifentanil amount (mean ± SD) (mg/kg)	18.2 ± 5.1
	Remifentanil mode (mean ± SD) ($mg \cdot kg^{-1} \cdot min^{-1}$)	0.164 ± 0.044
Surgical/dental treatment	Treatment time (mean ± SD) (min)	88.0 ± 22.3
	Long treatment time (>100 min) (%)	33.0
	Third molar extraction (%)	34.9
Outcomes	Time to recovery (mean ± SD) (min)	95.7 ± 26.6
	Agitation (%)	20.0

NOTE. Continuous variables are given as mean ± SD, and descriptive variables are given as percent.

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Table 2. ALL STUDY VARIABLES VERSUS PRIMARY OUTCOME VARIABLE (TIME TO RECOVERY) (BIVARIATE REGRESSION)

	Pearson Correlation Coefficient	Confidence Interval		*P* Value
		Lower 95%	Upper 95%	
Age*	−0.222	−0.397	−0.032	.018
Gender†	—	—	—	.816
Height*	−0.073	−0.260	0.120	.443
Weight*	−0.120	−0.304	0.073	.207
Body mass index*	−0.103	−0.288	0.089	.276
Cerebral palsy†	—	—	—	.327
Autism†	—	—	—	.973
Epilepsy†	—	—	—	.463
Mental disorder†	—	—	—	.302
Duration of injection*	0.060	0.060	−0.132	.527
Induction procedure† (IV vs oral and/or inhalation)	—	—	—	.103
Induction procedure† (IV plus inhalation vs oral, oral plus inhalation)	—	—	—	.388
Oral midazolam amount*	0.085	−0.108	0.272	.369
IV midazolam amount*	0.072	−0.121	0.261	.445
Propofol amount*	0.179	−0.017	0.355	.060
Propofol rate*	0.142	−0.050	0.326	.134
Remifentanil amount*	0.100	−0.093	0.287	.290
Remifentanil rate*	0.076	−0.118	0.263	.426
Treatment time*	0.097	−0.097	0.283	.309
Long treatment time (>100 min)†	—	—	—	.334
Third molar extraction†	—	—	—	.656

*Linear regression was used for analysis of continuous variables.
†For nominal variables, 1-way analysis of variance was used to compare groups.

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With a bivariate regression, a significant relationship was observed between time to recovery and age (Table 2). Age, mental disorder, induction procedure, IV midazolam, propofol amount, and dental treatment were selected with stepwise regression. In a multiple regression analysis, the amount of IV midazolam and induction with oral midazolam and/or inhalation of sevoflurane were shown to be independent determinants of time to recovery, but not age (Table 3). Because we suspected that age might be a confounding factor, the relationship between age and induction procedure (IV vs oral and/or inhalation) was examined, and there was a significant relationship ($P < .0001$, 1-way analysis of variance).

In a bivariate regression with the secondary outcome of agitation, there were significant relationships with age, height, weight, cerebral palsy, autism, epilepsy, induction procedure, and oral midazolam (Table 4). Age, epilepsy, induction procedure (IV plus inhalation vs oral, oral plus inhalation), and propofol

Table 3. RESULTS OF MULTIVARIATE REGRESSION (STANDARD LEAST SQUARES) WITH PRIMARY OUTCOME VARIABLE (TIME TO RECOVERY) AS INDEPENDENT VARIABLE

Parameter	Estimate	SE	*t* Value	*P* Value (Probability > |*t*|)
Intercept	89.24	13.87	6.44	<.001
Age	−0.37	0.33	−1.13	.260
Mental disorder	−7.41	6.01	−1.23	.221
Induction procedure (IV vs oral and/or inhalation)	−9.04	3.73	−2.42	.017*
IV midazolam amount	370.85	136.52	2.72	.008*
Propofol amount	1.24	0.72	1.73	.086
Third molar extraction	4.56	2.73	1.67	.098

NOTE. $R^2 = 0.156$.
*Significant parameter.

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Table 4. ALL STUDY VARIABLES VERSUS SECONDARY OUTCOME VARIABLES (AGITATION [YES OR NO]) (BIVARIATE REGRESSION)

	Odds Ratio	*P* Value
Age*	0.017	.003
Gender†	1.19	>.999
Height*	0.045	.013
Weight*	0.040	.030
Body mass index*	0.143	.172
Cerebral palsy†	0.00	.012
Autism†	3.95	.037
Epilepsy†	0.272	.040
Mental disorder†	0.521	.394
Duration of injection*	0.177	.235
Induction procedure† (IV vs oral and/or inhalation)	0.152	<.001
Induction procedure† (IV plus inhalation vs oral, oral plus inhalation)	9.81	<.001
Oral midazolam amount*	17.9	.001
IV midazolam amount*	0.334	.181
Propofol amount*	0.359	.545
Propofol rate*	3.56	.407
Remifentanil amount*	1.87	.639
Remifentanil rate*	1.90	.649
Treatment time*	0.445	.411
Long treatment time (>100 min)†	1.08	>.999
Third molar extraction†	0.436	.328

*Logistic regression was used for analysis of continuous variables.

†For nominal variables, a contingency table and Fisher exact test (2 sided) were used to compare groups.

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amount were selected with stepwise regression. In a multiple logistic regression analysis, only age and induction procedure (IV plus inhalation vs oral, oral plus inhalation) were independent predictors of agitation (Table 5).

Discussion

The purpose of this study was to determine factors affecting the outcomes, such as delayed recovery and complications, with a retrospective multiple regression analysis. Results show that the amount of IV midazolam and use of oral midazolam and/or inhalation of sevoflurane are independent predictors of delayed recovery, but not age. Because there was a significant relationship between age and induction procedure (IV vs oral and/or inhalation), age is considered a confounding factor.

In our facility, midazolam was often injected before the injection of propofol. Patients who received midazolam before propofol may have been sedated enough to not respond to the discomfort from the propofol injection. However, because fentanyl has been proven to be effective for pain relief,[11-15] starting a continuous infusion of remifentanil 2 to 3 minutes before the propofol injection is more useful for ambulatory GA than midazolam. Thus, IV midazolam does not seem to have an advantage for ambulatory GA consisting of remifentanil and propofol.

In our study, oral midazolam and/or inhalation of sevoflurane was shown to be an independent predictor of prolonged recovery, although oral midazolam was very useful in patients with a high level of fear. Oral midazolam is reported to not affect recovery time in pediatric patients.[4] Because adult patients are included in this study, prolonged recovery may occur at a higher rate in adults after oral midazolam. In addition, oral midazolam was shown to be an independent factor for agitation.

In our facility oral midazolam was used for patients with a high level of fear, which is considered a reason for agitation when they are awake. Inhalation of sevoflurane during insertion of an IV line may be involved with delayed recovery. However, because the direct effect of sevoflurane used only during induction does not seem to prolong recovery, further research on a larger sample size is necessary to clarify this question.

Although administration of midazolam and/or fentanyl is effective,[16,17] because it leads to delayed recovery, complete prevention of agitation should not be the goal in ambulatory GA. Age is an independent determinant of agitation in our results. This may support previous reports on the importance of coopera-

Table 5. RESULTS OF MULTIPLE LOGISTIC REGRESSION (NOMINAL LOGISTIC REGRESSION) WITH SECONDARY OUTCOME VARIABLES (AGITATION [YES OR NO])

Parameter	Estimate	SE	χ^2	*P* Value (Probability > χ^2)
Intercept	2.34	1.45	2.59	.107
Age	−0.08	0.04	5.19	.023*
Epilepsy	−0.67	0.34	3.78	.052
Induction procedure (IV plus inhalation vs oral, oral plus inhalation)	−0.91	0.35	6.81	.009*
Propofol amount	−0.12	0.08	2.41	.121

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tion from parents.[18] Pain control, by use of local anesthetics and nonsteroidal anti-inflammatory drugs during and after dental treatment, is considered important, especially when GA is maintained with remifentanil because it induces hyperalgesia.[19]

In conclusion, in ambulatory GA with TIVA consisting of remifentanil and propofol, the amount of IV midazolam was an independent determinant of delayed recovery. Oral midazolam contributed to delayed recovery, although it is very useful for induction in patients with a high level of fear. Oral midazolam and a younger age are independent predictors of agitation. In the future, a prospective study with a larger sample size among multiple facilities is expected to validate the suggestions raised in this study.

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