表4　CRPS患者と非CRPS疼痛疾患患者の背景

		非CRPS疼痛疾患(Jp) (n=146)	CRPS(Jp) (n=195)	CRPS(US) (n=123)
CRPS typeⅡの割合			21.50%	32.00%
女性		51.40%	65.10%	64.50%
年齢		56.8±16.6*	47.8±16.0*	41.1±10.0
原因	手術		31.80%	23.70%
	裂傷		8%	18.60%
	骨折		20.90%	16.10%
鈍的損傷			23.40%	26.20%
上肢症例の割合		58.20%	65.60%	48.30%
罹病期間(月)		37.4±55.7	29.8±42.3	24.8±24.9
VAS(現在)		5.1±2.7	5.5±2.4	
VAS(1週間で最大)		6.9±2.5	7.4±2.3	

CRPS(Jp)と非CRPS疼痛疾患(Jp)は本邦での患者を示す．CRPS(US)は米国でのCRPS患者の背景を示す．

VAS：visual analogue scale；0＝疼痛なし～10＝想像できる最大の疼痛

*Mann-Whitney test：$p<0.05$

〔文献13)より引用・改変〕

表5　本邦のCRPS患者と非CRPS疼痛疾患患者のCRPSチェックリストに基づく症状／徴候

		CRPS(n=195)		非CRPS疼痛疾患(n=146)	
評価項目		徴候(%)	症状(%)	徴候(%)	症状(%)
灼熱痛		NA	64.6	NA	39
知覚過敏		NA	45.6	NA	21.9
皮膚温変化		36.4	73.8	18.5	32.2
皮膚色調変化		60.5	74.4	10.3	22.6
発汗異常		36.4	48.7	5.5	13.7
浮腫		47.7	84.1	9.6	39.7
萎縮性変化	爪	25.6	26.2	4.1	5.5
	体毛	13.3	17.4	0	1.4
	皮膚	39	42.1	13	15.1
筋力低下		81	83.1	54.8	56.2
振戦		21.5	30.3	11.6	16.4
ジストニア		16.9	21	4.8	8.2
関節可動域制限		75.4	75.4	31.5	46.6
痛覚過敏		60	NA	23.3	NA
アロディニア		62.6	NA	21.2	NA

症状とは患者本人が自覚する所見を意味し，徴候は医療者が評価する所見を意味する．

NA：not applicable(チェックリスト中に該当する項目がないことを意味する)

表6　CRPS type 1とtype 2についての因子分析の結果

	CRPS 1＆2(195例)	Type 1のみ(153例)	Type 2のみ(42例)
第一成分	萎縮性変化(徴候) 萎縮性変化(症状)	関節可動域制限(症状) 関節可動域制限(徴候)	症例数が少なく，統計解析ができなかった
第二成分	関節可動域制限(徴候) 関節可動域制限(症状)	萎縮性変化(徴候) 萎縮性変化(症状)	
第三成分	痛覚過敏(徴候) アロディニア(徴候) 知覚過敏(症状)	知覚過敏(症状) アロディニア(徴候) 痛覚過敏(徴候)	
第四成分	発汗異常(症状) 発汗異常(徴候)	発汗異常(徴候) 発汗異常(症状)	
第五成分	浮腫(徴候) 浮腫(症状)	浮腫(徴候)	

症状とは患者本人が自覚する所見を意味し，徴候は医療者が評価する所見を意味する．

を対象に，感覚障害，発汗異常，皮膚温異常，皮膚色調変化，萎縮性変化，浮腫，関節拘縮，運動障害の有無をチェックリストに沿って自覚症状と他覚徴候に分けて評価した(表4，表5)．続いて，チェックリスト評価項目についての因子分析の結果(表6)をもとに判別分析を行い，臨床用指標と研究用指標の2つの指標を提案した(表7)[8),9)]．

医療者だけでなく患者の間にも認められるCRPSの判定をめぐる臨床的な混乱を収束するために，今後はCRPSという病名を用いる際にはこの判定指標に則って判定されたい．この本邦版CRPS判定指標は治療方針の決定や予後予測，専門医への紹介基準などを目的に作成したものであり，決して患者の病態の重症度や後遺障害の有無の判定指標ではない．

CRPSを判定する際には，医療者個々がこの判定指標が作成された前提と2つの但し書きを十分に理解して活用することが重要である．

Ⅳ　CRPS type 1とtype 2の判別について

神経障害性疼痛は，1994年，IASP(国際疼痛学会)によって「神経系の一次的な損傷や機能障害によって引き起こされる疼痛 pain initiated or caused by a primary lesion or dysfunction in the nervous system」と定義[4)]され，神経障害性疼痛の基礎医学的・臨床的概念が整理された一方で，臨床的にはどのような疾患を神経障害性疼痛に含めるか？　の議論が不十分であり，さらに“神経系の機能障害”という言葉が広い意味をもつため侵害刺激の持続(例：炎症性疼痛)による神経可塑的変化から引き起こされる痛覚過敏や神経変性疾患などによる運動障害(例：痙縮)によって引き起こされる筋骨格系の疼痛も神経障害性疼痛に含まれてしまうなど，臨床に即した神経障害性疼痛の定義には議論の余地があった．

そこで2008年，IASP神経障害性疼痛分科会(Neuropathic Pain Special Interest Group：NeuP SIG)は，神経障害性疼痛を「体性感覚系に対する損傷や疾患によって直接的に引き起こされる疼痛pain arising as a direct consequence of a lesion or disease affecting the somatosensory system」と再定義し[10)]，IASPによって正式に承認されている[11)]．このことをふまえてCRPSの判定に関する注意点としては，CRPS type 1は神経障害性疼痛の再定義と診断ガイドライン(図2)[10)]に基づいて判断すると神経障害性疼痛には含まれないことがあげられる(図3)．当然のことではあるが，新定義に従ってもCRPS type 2は神経障害性疼痛に含まれる．本邦ではCRPS type 2症例が単独で統計分析に堪える症例

表7　厚生労働省CRPS研究班から提唱された本邦版CRPS判定指標

臨床用CRPS判定指標

A　病期のいずれかの時期に，以下の自覚症状のうち2項目以上該当すること．
ただし，それぞれの項目内のいずれかの症状を満たせばよい．
1. 皮膚・爪・毛のうちいずれかに萎縮性変化
2. 関節可動域制限
3. 持続性ないしは不釣合いな痛み，しびれたような針で刺すような痛み(患者が自発的に述べる)，知覚過敏
4. 発汗の亢進ないしは低下
5. 浮腫

B　診察時において，以下の他覚所見の項目を2項目以上該当すること．
1. 皮膚・爪・毛のうちいずれかに萎縮性変化
2. 関節可動域制限
3. アロディニア(触刺激ないしは熱刺激による)ないしは痛覚過敏(ピンプリック)
4. 発汗の亢進ないしは低下
5. 浮腫

研究用CRPS判定指標

A　病期のいずれかの時期に，以下の自覚症状のうち3項目以上該当すること．
ただし，それぞれの項目内のいずれかの症状を満たせばよい．
1. 皮膚・爪・毛のうちいずれかに萎縮性変化
2. 関節可動域制限
3. 持続性ないしは不釣合いな痛み，しびれたような針で刺すような痛み(患者が自発的に述べる)，知覚過敏
4. 発汗の亢進ないしは低下
5. 浮腫

B　診察時において，以下の他覚所見の項目を3項目以上該当すること．
1. 皮膚・爪・毛のうちいずれかに萎縮性変化
2. 関節可動域制限
3. アロディニア(触刺激ないしは熱刺激による)ないしは痛覚過敏(ピンプリック)
4. 発汗の亢進ないしは低下
5. 浮腫

※但し書き1
1994年のIASP(国際疼痛学会)のCRPS診断基準を満たし，複数の専門医がCRPSと分類することを妥当と判断した患者群と四肢の痛みを有するCRPS以外の患者とを弁別する指標である．臨床用判定指標を用いることにより感度82.6%，特異度78.8%で判定でき，研究用判定指標により感度59%，特異度91.8%で判定できる．

※但し書き2
臨床用判定指標は，治療方針の決定，専門施設への紹介判断などに使用されることを目的として作成した．治療法の有効性の評価など，均一な患者群を対象とすることが望まれる場合には，研究用判定指標を採用されたい．
外傷歴がある患者の遷延する症状がCRPSによるものであるかを判断する状況(補償や訴訟など)で使用するべきではない．また，重症度・後遺障害の有無の判定指標ではない．

米国から提唱された判定指標にならい，本邦版CRPS判定指標でも臨床用指標と研究用指標の2種類を作成した．本邦版CRPS判定指標の使用にあたっては，但し書き1，2を十分に理解して使用すること．

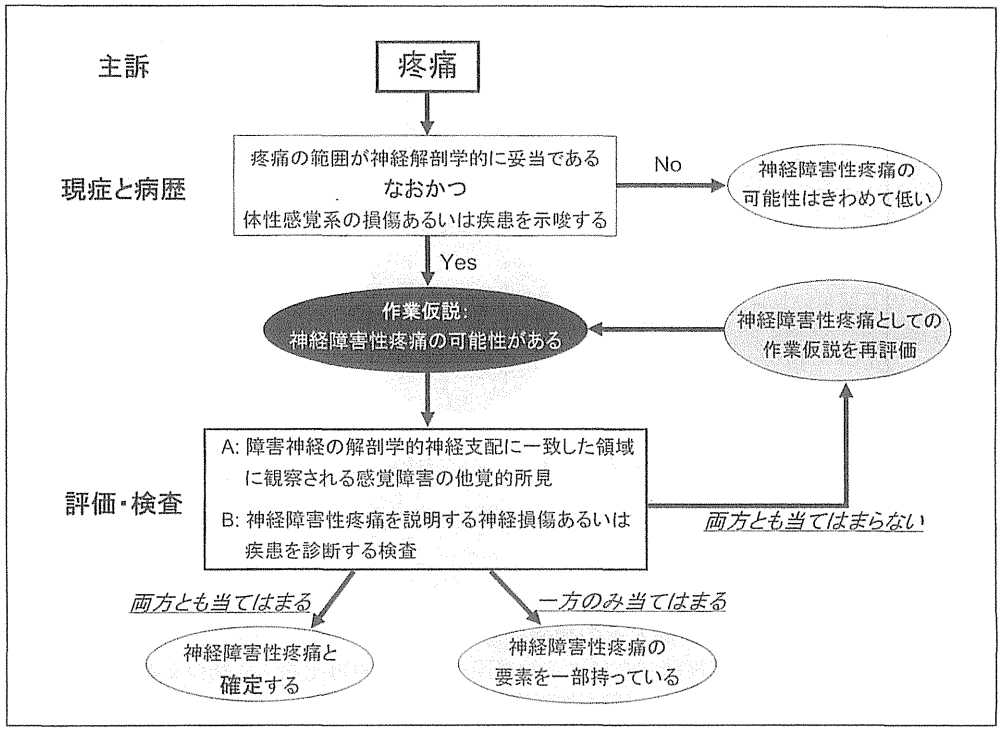

図2　国際疼痛学会神経障害性疼痛分科会から提唱された神経障害性疼痛の診断ガイドライン

〔文献10)より引用・改変〕

数が集まらずCRPS type 1とtype 2をそれぞれ独立して統計分析を行わなかったため，本邦でのデータからはtype 1とtype 2の分類の必要性について論じることはできない．しかし，CRPS type 1単独群とCRPS type 1とtype 2の混合群では因子分析の結果に大きな差はなかった(表6)．この結果はCRPS type 2が加わってもCRPS患者の特徴的な症状／徴候に差はなかったことを意味し，CRPS type 2もCRPS type 1とほぼ同様の症状／徴候を呈していることが示唆される．加えて，米国で行われたCRPS判定指標に関する同様の研究では，神経損傷の有無(type 1症例とtype 2症例)によって症状／徴候に差がなかったとされ[12]，米国版判定指標では神経損傷の有無の区別は設けられていない[13]．したがって，CRPSの判定に限っていえば，神経損傷の有無を問う必要はない(神経損傷の有無にかかわらず浮腫などの特徴的な症状／徴候は起こりうることを意味する)．

また，本邦のCRPS患者を対象にクラスター分析を行うと，ほぼすべての症状／徴候がそろった患者群と浮腫以外の症状／徴候が観察されない患者群，発汗異常を主とする患者群の3群に分かれ，これらの患者群には罹病期間との相関が認められなかった[8]．このことからは，少なくとも本邦におけるCRPS患者では罹病期間が長くなればCRPS症状／徴候が多彩になるわけではないことが示唆される．

おわりに

CRPSは治療抵抗性のこともあり，患者自身に心理的な問題があると評価されることも少なくない．しかし，CRPS患者に対する網羅的な心理評価を行った研究では“CRPS性格”と呼べるようなものはなく，患者の抑うつ状態，不安，怒りがCRPSの疼痛と疼痛に随伴する問題行動に関連していることを

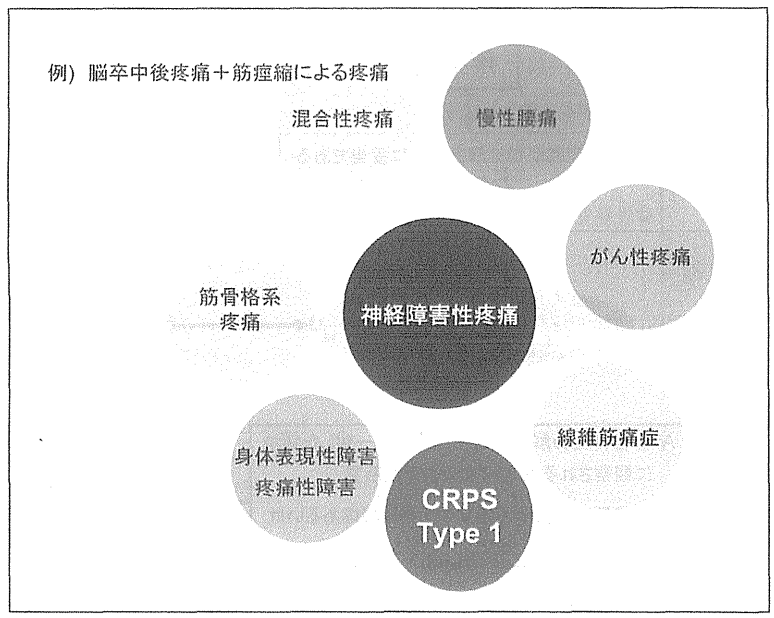

図3　神経障害性疼痛とその類縁疾患
2008年国際疼痛学会による神経障害性疼痛の再定義[11]に基づくと，CRPS type 1は神経障害性疼痛には含まれない．
〔文献16)より引用・改変〕

明らかにしている[14]．CRPSの診療にあたっては医療者が診断名をつけることに執心したり，抑うつ症状や不安の訴えに対して抗うつ薬や抗不安薬だけで対処するという短絡的な薬物療法だけでなく，CRPSについての教育を通じて患者自身が痛みに対する自己管理能力を高められるようにすることが重要である[15]．

謝辞　本稿は厚生労働省CRPS研究班(班長：大阪大学大学院医学系研究科生体統御医学講座麻酔集中治療医学 眞下節教授)の議事をもとに執筆した．CRPS研究班の先生方にこの場を借りてお礼申し上げます．

本稿の内容は日本臨床麻酔学会第28回大会(2008，京都)シンポジウム「神経障害性疼痛に関する最近の話題」で発表した．本稿は住谷昌彦，柴田政彦，眞下節，山田芳嗣，厚生労働省CRPS研究班「CRPSの診断と治療：Current Diagnosis Criteria of CRPS in Japan and Search for Clinical Treatment Evidence of CRPS」(Anesthesia 21 Century 10：1935-1940, 2008)および住谷昌彦，柴田政彦，山田芳嗣，眞下節「神経障害性疼痛における医療連携」(宮崎東洋，北出利勝編：慢性疼痛の理解と医療連携．真興交易医書出版部，東京，2008，14-22)の内容と一部重複しているが，各出版社より転載の許諾を得ている．

注1)：因子分析
複数の構成要因から成る対象群のなかで，相関関係にあるいくつかの要因を合成(圧縮)していくつかの成分を抽出し，対象群の特性を求める方法．抽出された成分のうち，それぞれの正の相関についてと負の相関についてとを数値化することによって，どの要因とどの要因が共通に観察されるか？，あるいはどの要因とどの要因が独立して存在しているか？ を評価できる．
注2)：判別分析
異なる2群を統計学的に区別する一般的なルール(条

件文)を導き出す方法．因子分析と判別分析を組み合わせることによって判定指標を作成する手法は，病理学的に客観的な異常を証明し得ない精神科疾患や頭痛などの機能的疾患を対象に用いられている．

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Comprehensive Diagnostic Criteria for Complex Regional Pain Syndrome in the Japanese Population

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Complex regional pain syndrome (CRPS) is a syndrome that describes a broad spectrum of sensory, motor and autonomic-like features with unproven etiology. The International Association for the Study of Pain (IASP) diagnostic criteria of CRPS show high sensitivity but poor specificity. Here, using statistical pattern recognition methods, we suggest a new set of CRPS criteria offering acceptable sensitivity and high specificity for the Japanese population : A standardized sign/symptom checklist was used in patient evaluations to obtain data on CRPS-related signs/symptoms in 195 patients meeting the IASP criteria. We grouped CRPS-related signs/symptoms into five distinct subgroups (trophic change, motor dysfunction, abnormal pain processing, asymmetric sudomotor activity and asymmetric edema). Given patients' ability to discriminate between CRPS and non-CRPS etiology, modifying the IASP criteria could increase clinical diagnostic accuracy in the Japanese population.

Key Words : Complex regional pain syndrome, Japanese CRPS Research Group, Diagnostic criteria, Factor analysis, Discriminant function analysis

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Case Report

Oral Local Anesthesia Successfully Ameliorated Neuropathic Pain in an Upper Limb Suggesting Pain Alleviation through Neural Plasticity within the Central Nervous System: A Case Report

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Neural blockades are considered an alternative to pharmacotherapy for neuropathic pain although these blockades elicit limited effects. We encountered a patient with postbrachial plexus avulsion injury pain, which was refractory to conventional treatments but disappeared temporarily with the administration of the local anesthetic lidocaine around the left mandibular molar tooth during dental treatments. This analgesic effect on neuropathic pain by oral local anesthesia was reproducible. Under conditions of neuropathic pain, cerebral somatotopic reorganization in the sensorimotor cortices of the brain has been observed. Either expansion or shrinkage of the somatotopic representation of a deafferentated body part correlates with the degree of neuropathic pain. In our case, administration of an oral local anesthetic shrank the somatotopic representation of the mouth, which is next to the upper limb representation and thereby expanded the upper limb representation in a normal manner. Consequently, oral local anesthesia improved the pain in the upper limb. This case suggests that pain alleviation through neural plasticity within the brain is related to neural blockade.

1. Introduction

Neuropathic pain typically appears following peripheral nerve injury due to neuropathies, plexopathies, and trauma to selected sites within the central nervous system (CNS). Recently, evidence-based recommendations of pharmacological treatments for neuropathic pain have been proposed based on both positive and negative results from multiple randomized controlled trials. However, approximately 10–15% of all neuropathic pain patients are refractory to pharmacotherapy. For these cases, more invasive pain-management interventions, such as intrathecal drug delivery, neurostimulation, or neural blockade, may be used. Ideally, blocking neural transmission, either temporarily by using local anesthetics or permanently by surgical nerve ablation, can reduce neuropathic pain; however, no neural blockades have been found to be consistently successful [1]. Here, we report on a case of a patient with postbrachial plexus avulsion injury pain whose neuropathic pain had been refractory to several evidence-based pharmacotherapies and interventions, such as spinal cord stimulation, cervical epidural blockade, and brachial plexus blockade. His pain could be well controlled by oral local anesthesia, suggesting pain alleviation through neural plasticity within the CNS.

2. Case Report

A 49-year-old man, who had a left brachial plexus avulsion injury 10 years before, experienced severe neuropathic pain in his left upper limb immediately after the trauma. The patient complained of continuous burning, pressing, and

tingling pain in the upper limb. From the beginning of the perception of the pain in his upper limb, he felt illusory perceptions of fingers touching his face although he did not perceive pain or any other sensory deficits in the face. He had been treated several times for the pain through left brachial plexus blockades and cervical epidural blockades, with no success. His neuropathic pain decreased slightly when taking pregabalin and with the application of cervical spinal cord stimulation (SCS), but it remained severe. He did not have any pain or trigger areas in the face getting caries of the teeth. He once underwent a dental treatment for his left mandibular molar tooth. When local anesthesia was applied around the left mandibular molar tooth (3 mL, 0.5% lidocaine), he felt the enlargement of that region, which was followed by an immediate disappearance of his neuropathic pain. At that time, the illusory finger sensations in the face disappeared. Approximately 2 hours after the dental treatment, the neuropathic pain returned and gradually increased to predental treatment levels. A nonsteroidal anti-inflammatory drug, loxoprofen, completely ameliorated the dental pain but was not effective against the neuropathic pain. Since then, the patient had 3 dental treatments, and local anesthesia around the left molar tooth consistently ameliorated his neuropathic pain. Analgesic effects consistently lasted for several hours following the administration of the local anesthesia. His neuropathic pain was able to be mildly controlled by a combination of pregabalin, SCS, and local anesthesia around the left molar tooth although the molar tooth had completely improved. The use of oral local anesthesia for breakthrough neuropathic pain had been especially effective.

We obtained the patient's consent to report his progress, in accordance with the Declaration of Helsinki.

3. Discussion

Under conditions of neuropathic pain, particularly for deafferentation pain following massive nerve injury, such as postamputation phantom limb pain, postbrachial plexus injury pain, or postspinal cord injury pain, cerebral somatotopic reorganization in the sensorimotor cortices of the brain is observed. Following deafferentation of an upper limb by nerve injury, the somatotopic region corresponding to the upper limb in the sensorimotor cortices shrinks, and the somatotopic region responding to the facial region, which is located next to the upper limb, expands (Figure 1(a)) [2, 3]. The degree of shrinkage of the upper limb representation correlated linearly with the severity of the neuropathic pain [4]. Further, expansion of the somatotopic representation of the affected body part correlated with pain alleviation through neurorehabilitation techniques [5–7]. Therefore, somatotopic reorganization in the sensorimotor cortices closely relates to pathophysiological mechanisms underlying neuropathic pain and its alleviation.

Concerning the somatotopic reorganization of the face and hand regions, the overlapping of these regions can sometimes induce the following illusion in patients with a deafferentation of a hand: touching the face creates obvious referred sensation of fingers in the face as if the fingers

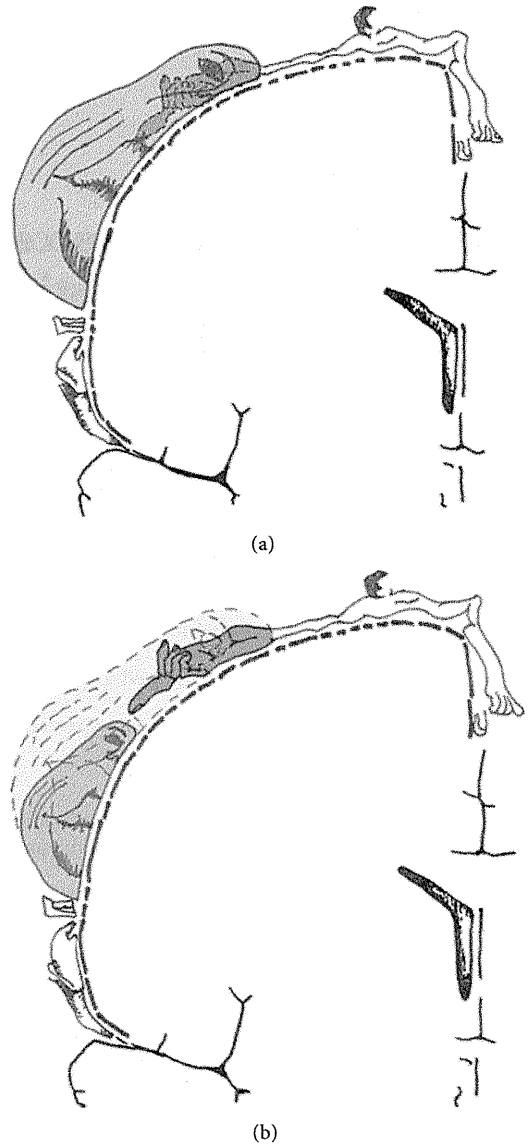

Figure 1: Topographical somatotopic reorganization in the sensorimotor cortices following deafferentation by a brachial plexus avulsion injury (a) and normalization of the reorganization by application of local anesthesia in the mouth (b).

are embedded in the face [8]. We consider one possibility that the analgesic effects of the oral local anesthesia in our case were derived from the neural plasticity in the sensorimotor cortices because our patient perceived a similar illusory sensation of fingers in the face. Deafferentation by local anesthesia, as well as that by nerve injury, shrinks the somatotopic representation of the exposed body part and simultaneously expands the nearby somatotopic representation in the sensorimotor cortices, and these are not associated with subcortical changes [9, 10]. On the basis of this notion, we speculated that, in our case, local anesthesia in the mouth shrank the mouth/face representation and subsequently expanded the somatotopic representation of the hand/upper

limb within the sensorimotor cortices (Figure 1(b)), resulting in amelioration of the neuropathic pain in the upper limb. The disappearance of the illusory finger sensations in the face soon after the oral local anesthesia supported the intimate relationship between analgesic effects of the upper limb pain and cerebral reorganization of hand/upper limb and face/mouth representations.

In general, neural blockades are applied to painful body parts in order to block neural transmission; however, the clinical significance of neural transmission blockades remains unclear for nerve-injured neuropathic pain because of deafferentation. Local anesthesia at an intact limb contralateral to the painful limb has been reported to display clear analgesic effects on postamputation phantom limb pain, suggesting pain alleviation through neural plasticity within the CNS [11]. Thus, several types of local anesthesia or neural blockades on unaffected body parts have distinct clinical significance compared to neural transmission blockades, whereas peripheral nerve blockades shrink the somatotopic area of the exposed body part and seem to have no analgesic effect on neuropathic pain in general. Specific analgesic effects on neuropathic pain from local anesthesia and neural blockade could be derived from CNS plasticity. In the future, functional brain imaging studies examining the relationship between neural blockade application for neuropathic pain and CNS plasticity need to be performed in order to better understand somatotopic reorganization in the sensorimotor cortices induced by neural blockades.

4. Conclusion

For neural blockades, oral local anesthesia is a novel candidate for treating neuropathic pain in the upper limb, and the analgesic effect might be derived from its effects on neural plasticity within the CNS.

Acknowledgments

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ORIGINAL ARTICLE

Impact of remifentanil introduction on practice patterns in general anesthesia

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Abstract
Purpose The introduction of new medicine can change clinical practice patterns and may affect patient outcomes. In the present study, we investigated whether introduction of remifentanil in Japan affected the practice patterns of anesthesia.
Methods Using the Japanese Diagnosis Procedure Combination database, we extracted records of 423,491 patients who underwent surgery with general anesthesia in 243 hospitals before (2006) and after (2007) the introduction of remifentanil, and identified anesthetic agents used for each patient. A hierarchical mixed-effects logistic regression analysis was performed to analyze the factors that affected selection of remifentanil. Further, we compared postoperative length of stay (LOS), in-hospital mortality, and total costs between 2006 and 2007.
Results In 2007, remifentanil was used for up to 41.4% of all general anesthesia, accompanied by a reduction in nitrous oxide use and an increase in total intravenous anesthesia. Female gender, increasing age, and preoperative comorbidities including diabetes mellitus, hypertension, liver cirrhosis, and chronic renal failure were positively associated with the use of remifentanil, whereas accompanying cardiac disease and co-application of epidural anesthesia were negatively associated. In 2007, a similar in-hospital death rate, similar or decreased total costs, slightly reduced duration of anesthesia, and substantially reduced postoperative LOS were seen compared to those in 2006.
Conclusions Our data revealed rapid changes in practice patterns in anesthesia after the introduction of remifentanil in Japan. Remifentanil was used more often in patients with comorbidities and without epidural anesthesia, and its introduction did not affect increase in total medical costs.

Keywords Remifentanil · Anesthetic practice · Postoperative outcome · In-patient medical cost

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Introduction

The introduction of new medical devices such as the drug-eluting stent for angina pectoris [1] or new drugs such as anti-tumor necrosis factor-α antibody for rheumatoid arthritis [2] had a major impact on medical practice patterns over a short time period, affecting not only patient outcomes but also total medical costs, although published reports gave variable results [3].

In anesthesiology, only a limited number of reports show changes in practice patterns in anesthesia [4]. It is

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also not clear to what extent such changes affect medical costs and patient outcome [5].

Remifentanil, a mu-opioid receptor agonist, has a unique pharmacokinetic profile, characterized by rapid equilibration with the central compartment, and a short half-life, independent of infusion duration [6, 7]. Although its use is common in Western countries [8], it was finally approved in Japan in December 2006, and its use in clinical practice commenced in January 2007. The unique pharmacological properties of this novel drug facilitated its rapid assimilation into Japanese clinical procedures, making a considerable impact on anesthetic practice. However, accurate data have not been reported on the expansion of remifentanil use and the subsequent changes in practice patterns in general anesthesia. In addition, the effects of remifentanil introduction on patient outcomes remain unclear.

In the present study, we investigated the proportion of remifentanil use in the first year of its introduction and changes in the patterns of anesthetic drug use. Then, we analyzed factors affecting selection of remifentanil. We also compared duration of anesthesia and total costs as well as postoperative length of stay (LOS) and in-hospital mortality before and after introduction of remifentanil, using the nationwide Japanese administrative claims database, the Diagnosis Procedure Combination (DPC) database.

Materials and methods

DPC database and participants

The DPC is a mixed-case system, similar to the diagnosis-related groups (DRG) in the U.S. Medicare program. It was launched in 2002 by the Ministry of Health, Labor and Welfare of Japan and is linked with a lump-sum payment system. Key objectives of the DPC system are to implement a standardized electronic claims system and to provide transparency of hospital performance [9, 10]. All 82 university teaching hospitals must adopt the DPC system, and community hospitals can voluntarily adopt this system. Data are mainly used for profiling practice patterns, refining case-mix classification, and planning health policies such as resource allocation.

The DPC database comprises discharge abstracts and administrative claims, with data compiled between July 1 and December 31 each year by the DPC Research Group [10–13]. The database initially included 82 hospitals in 2003. The numbers of inpatients and participant hospitals are increasing each year, with around 3 million patients from 926 hospitals in 2007, which represented approximately 45% of all acute care inpatient hospitalizations in Japan [11]. The database includes the following data: unique identification number of each hospital; patient age and sex; diagnoses recorded in the Japanese language together with the *International Classification of Diseases, 10th Revision*; surgical procedures coded with original Japanese codes; drugs and devices used; LOS; in-hospital mortality; and total costs (including costs for hospitalization, surgery, anesthesia, drugs and devices used).

The DPC database corresponds to the Nationwide Inpatient Sample in the United States [14] to some extent but has several advantages [10]. To optimize the validity of the recorded diagnoses, physicians in charge record the diagnoses in reference to the medical charts. Detailed data are available for the treatments administered on a daily basis (e.g., types of drugs administered, duration of anesthesia, volume of blood transfusion). Medical clerks and licensed medical information managers accurately record the dates of each surgery and other procedures and the dates of use of each drug and device. Physicians and hospitals consistently comply with data submission because it is mandatory to obtain DPC-based reimbursement of medical fees.

All patient identifiers have been removed from this database. Because of the anonymous nature of the data, obtaining informed consent from patients was unnecessary. The Institutional Review Board of the University of Occupational and Environmental Health approved this study design.

Data extraction

To compare the pre-remifentanil period (July–December 2006) with the remifentanil treatment period (July–December 2007), we included data from all 243 hospitals that participated in the DPC survey in both years. We extracted data on all surgical patients who underwent general anesthesia in these hospitals, including type of hospital, type of admission, patient age, sex, surgical procedures, duration of anesthesia (min), volume of blood transfusion, postoperative LOS (days), in-hospital mortality, and total costs. General anesthesia was defined as anesthesia for surgery for at least 20 min with volatile anesthetics and/or intravenous anesthetics supplemented with oxygen via a mask including laryngeal mask or endotracheal tube.

We also extracted data regarding medications used for general anesthesia, including barbiturates, nitrous oxide, volatile anesthetic agents, muscle relaxants, hypnotics, and narcotics.

Patients who underwent the following eight classes of surgery in 2007 were subdivided to evaluate differences in distribution of remifentanil among surgical subcategories: cardiac surgery, neurosurgery, thoracic surgery, vascular surgery, general surgery, gynecology, orthopedic surgery, and otolaryngology. When a patient underwent two or more surgeries during the hospitalization, the patient was

classified into one group according to the most recent surgery. If a patient underwent multiple surgeries at the same time, we selected the one surgery that required the most medical resources. Postoperative LOS was determined as the days between the day of the surgery and that of discharge.

Descriptive statistics

The proportions of patients who received each drug were compared between 2006 and 2007. Combinations of remifentanil and fentanyl, and of nitrous oxide and volatile agents, were also compared between the 2 years. Further, postoperative in-hospital mortality, duration of anesthesia, postoperative LOS, and total costs were compared between the 2 years for all populations and eight surgical subcategories.

Logistic regression to determine factors for selecting remifentanil

To determine possible contributing factors for selection of remifentanil, we extracted the data of patients who had general anesthesia with either fentanyl alone or remifentanil and fentanyl in 2007. In the logistic regression model, the dependent variable was set as "remifentanil use" (fentanyl alone = 0; both remifentanil and fentanyl = 1). A hierarchical mixed-effects logistic regression analysis was performed in which age, sex, intraoperative use of epidural anesthesia, comorbidities, and surgical subcategories were set as fixed effects, and sites (described by unique identifiers for all 243 hospitals) were used as random intercepts.

Statistical analysis

We performed univariate comparisons of variables for the two groups, using the Mann–Whitney U test for nonparametric data and the chi-square test for categorical data as appropriate. All statistical analyses were conducted using the SAS 9.1 (SAS Institute, Cary, NC, USA), and P values <0.05 were considered to be significant. The exchange rate was assumed to be 100 yen to 1 U.S. dollar (USD).

Results

Patient demographics

All 243 acute care hospitals that participated in DPC in both 2006 and 2007 were enrolled in this study. A total of 423,491 patients (206,102 in 2006 and 217,389 in 2007) were identified. Overall, 59.6% of patients were admitted to 53 teaching hospitals, while the remaining 40.4% were treated at 190 non-teaching hospitals (Supplemental Tables 1, 2).

Anesthetic drug used

Table 1 shows the use of each anesthetic drug in 2006 and 2007. Remifentanil accounted for 41.4% of all general anesthesia usage in 2007. The proportion of cases in which either fentanyl or remifentanil was used increased from 76.5% in 2006 to 83.3% in 2007. The proportion including remifentanil in 2007 was higher in teaching hospitals than

Table 1 Anesthetic drugs used

Drug	2006 (n = 206,102) (%)	2007 (n = 217,389) (%)	P*
Narcotics			
Remifentanil	0.0	41.4	<0.001
Fentanyl	76.5	71.2	<0.001
Morphine	13.7	13.4	<0.001
Hypnotics			
Barbiturates	18.4	14.9	<0.001
Propofol	72.8	76.9	<0.001
Midazolam	9.4	12.6	<0.001
Nitrous oxide	25.8	14.0	<0.001
Volatile anesthetic agents			
Sevoflurane	79.5	74.2	<0.001
Isoflurane	4.6	3.3	<0.001
Halothane	0.1	0.1	0.732
Muscle relaxants			
Suxamethonium	0.5	1.3	<0.001
Vecuronium	84.2	81.9	<0.001
Rocuronium	0.0	2.6	<0.001
Pancuronium	1.0	0.9	0.158
Others			
Droperidol	12.2	13.9	<0.001
Ketamine	5.1	3.8	<0.001
Diazepam	1.3	1.2	0.023
Combination of fentanyl and remifentanil			
Neither	23.5	16.7	<0.001
Fentanyl alone	76.5	41.9	<0.001
Remifentanil alone	0.0	12.1	<0.001
Both	0.0	29.3	<0.001
Combination of nitrous oxide and volatile agents			
Neither	14.0	21.0	<0.001
Nitrous oxide alone	2.1	1.6	<0.001
Volatile agents alone	60.1	65.0	<0.001
Both	23.8	12.4	<0.001

* P value for the comparison between 2006 and 2007 evaluated with the chi-square test

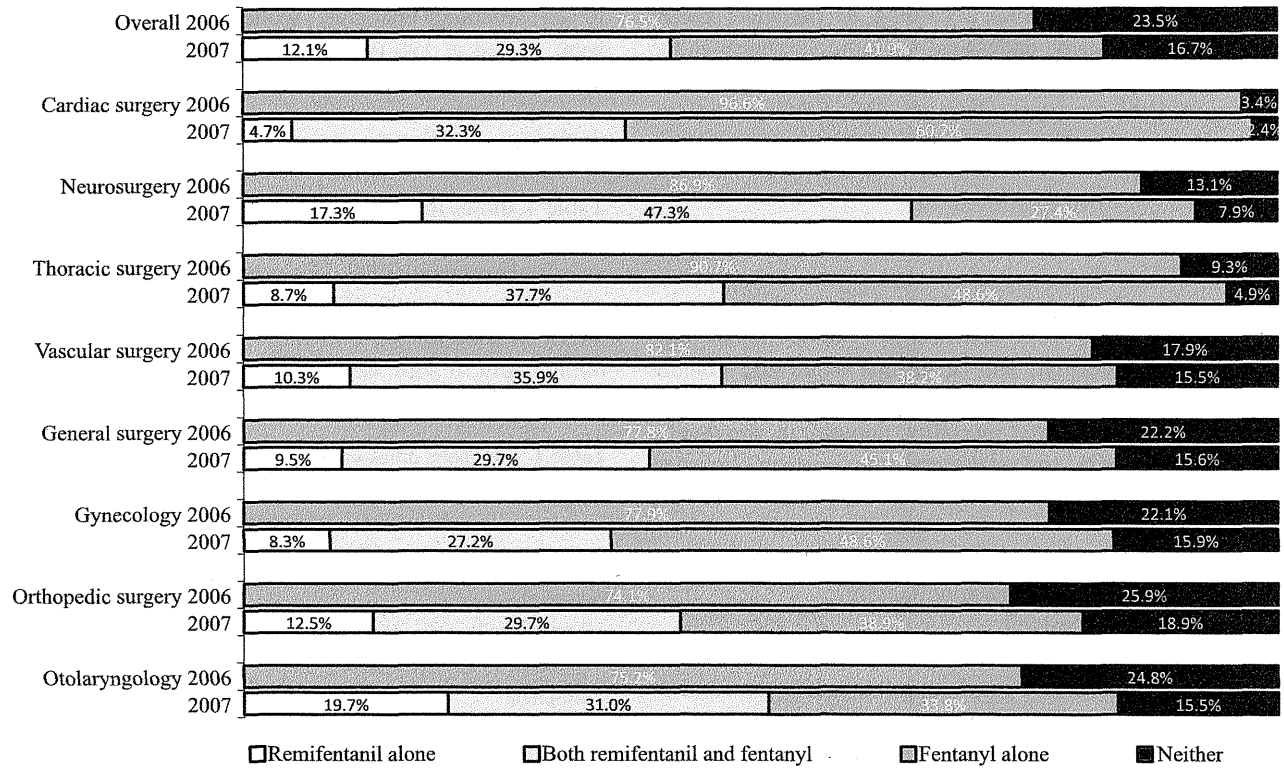

Fig. 1 Combination of remifentanil and fentanyl in each surgical field: percentage of surgeries using fentanyl and/or remifentanil in 2006 and 2007. *Open bars* cases in which remifentanil alone was used; *light gray bars* both remifentanil and fentanyl; *dark gray bars* fentanyl alone; *closed bars* neither remifentanil nor fentanyl

in non-teaching hospitals (48.1% vs. 36.9%, $P < 0.01$). The use of remifentanil in 2007 was exceptionally high in neurosurgery (64.6%) and otolaryngology (50.7%) (Fig. 1). The use of nitrous oxide decreased from 25.9% in 2006 to 14.0% in 2007. The proportion of patients who received neither nitrous oxide nor volatile agents, i.e., those undergoing total intravenous anesthesia (TIVA), increased from 14.0% in 2006 to 21.0% in 2007.

Barbiturate use was lower in 2007 (14.9%) than in 2006 (18.4%), whereas use of propofol was higher in 2007 (76.9%) than in 2006 (72.8%). Vecuronium was used in more than 80% of general anesthesias in both years, whereas rocuronium, which was introduced in September 2007, was utilized in 2.6% of surgeries in that year.

Factors associated with selection of remifentanil

Among 217,389 patients in 2007, 91,097 received fentanyl alone, and 63,739 received both remifentanil and fentanyl. Both patient factors and surgical factors affecting use of remifentanil were analyzed with adjustment for site effects by incorporating hospital identification numbers into the hierarchical mixed-effects logistic regression model. Female sex, increasing age, and comorbidities including diabetes mellitus, hypertension, liver cirrhosis, and chronic renal failure were positively associated with selection of remifentanil. In contrast, cardiac diseases and intraoperative epidural anesthesia were negatively associated with selection of remifentanil. Neurosurgical patients were more than fivefold more likely to receive remifentanil compared with cardiac surgery patients (Table 2).

Postoperative outcomes

Table 3 shows in-hospital mortality, mean duration of anesthesia, mean postoperative LOS, and mean total cost in each surgical field. All outcomes were compared between 2006 and 2007. No significant difference in in-hospital mortality was seen in any surgical subcategory showed between the 2 years. The mean duration of anesthesia was slightly shorter in 2007 than in 2006, and the differences were statistically significant in general surgery, gynecology, and orthopedic surgery. Mean postoperative LOS was shorter in 2007 in all surgical subcategories, and most of these findings were statistically significant, except for otolaryngology cases. Total cost was comparable between the 2 years, except for general surgery and gynecology, which were significantly less in 2007 compared with 2006.

Table 2 A hierarchical mixed-effects logistic regression analysis for selecting remifentanil (fentanyl alone = 0; both remifentanil and fentanyl = 1)

	Odds ratio	95% confidence interval	*P* value
Sex (female)	1.09	1.06–1.12	<0.001
Age	1.02	1.02–1.02	<0.001
Epidural anesthesia	0.36	0.35–0.37	<0.001
Diabetes mellitus	1.07	1.02–1.11	0.006
Hypertension	1.08	1.04–1.13	<0.001
Cardiac diseases	0.91	0.86–0.95	<0.001
Cerebrovascular diseases	1.07	1.00–1.15	0.068
Chronic lung diseases	1.01	0.93–1.08	0.888
Liver cirrhosis	1.19	1.00–1.41	0.049
Chronic renal failure	1.17	1.08–1.27	<0.001
Surgical category			
Cardiac surgery	Reference		<0.001
Neurosurgery	5.49	5.05–5.98	
Thoracic surgery	3.20	2.94–3.47	
Vascular surgery	2.36	2.17–2.58	
General surgery	2.00	1.87–2.13	
Gynecology	2.01	1.86–2.17	
Orthopedic surgery	1.89	1.76–2.02	
Otolaryngology	2.48	2.31–2.76	

Discussion

Population representation

According to the Survey of Medical Institutions 2008 in Japan, the average number of surgeries under general anesthesia throughout the country was 187,097 per month. [Survey of Medical Institutions 2008 (in Japanese). Vital and Health Statistics Division, Ministry of Health, Labour and Welfare, Japan. Available at: http://www.mhlw.go.jp/toukei/saikin/hw/iryosd/08/index.html. Accessed June 14, 2011.] Our data included 423,491 cases in 12 months, representing about 19% of all patients who underwent general anesthesia during the data extraction period in Japan. The age distribution was similar to that in another large database of anesthesia maintained by the Japanese Society of Anesthesiologists [15, 16].

Spread of remifentanil use and factors associated with its selection

Remifentanil was administered in more than 40% of all general anesthesias in the first year of its introduction, an extremely rapid increase in the proportion of its use [17].

Remifentanil was more frequently selected for patients with comorbidities, including hypertension, diabetes mellitus, and liver and kidney disease, presumably because it has advantages over other opioids such as a controllable, strong antinociceptive effect and rapid extrahepatic metabolism and elimination.

Epidural anesthesia was negatively associated with selection of remifentanil. Multiple publications suggest better patient intra- and postoperative condition with epidural anesthesia [18, 19]. It is anticipated that anesthesiologists did not believe it necessary to use remifentanil when they applied epidural anesthesia intraoperatively. The proportion of remifentanil use was higher in the nonepidural group than in the epidural group (45.2% vs. 30.6%). It was also higher in neurosurgery (64.6%) and otolaryngology (50.7%) cases. These results suggest that the pharmacological properties of remifentanil are highly

Table 3 Comparison of in-hospital mortality, average duration of anesthesia, postoperative length of stay, and total cost between 2006 and 2007 in each surgical subcategory

	In-hospital mortality (%)			Duration of anesthesia (min)			Postoperative length of stay (days)			Total costs (USD)		
	2006	2007	*P**	2006	2007	*P*†	2006	2007	*P*†	2006	2007	*P*†
Overall	1.41	1.36	0.242	211	208	<0.001	16.4	15.7	<0.001	12,733	12,648	0.051
Cardiac surgery	4.78	4.53	0.403	407	403	0.111	24.7	24.1	0.039	43,797	43,427	0.327
Neurosurgery	5.46	5.47	0.985	316	314	0.352	28.7	27.6	0.004	23,255	23,193	0.784
Thoracic surgery	1.73	1.69	0.862	259	255	0.296	14.5	14.0	0.046	15,926	15,820	0.669
Vascular surgery	3.59	3.50	0.761	267	262	0.074	24.0	22.6	0.002	18,489	18,458	0.927
General surgery	2.02	2.02	0.952	220	216	<0.001	16.9	16.1	<0.001	12,096	11,935	0.019
Gynecology	0.15	0.12	0.381	163	161	0.043	10.1	9.2	<0.001	7,046	6,951	0.042
Orthopedic surgery	0.66	0.56	0.092	191	188	<0.001	23.0	22.3	<0.001	14,108	14,112	0.957
Otolaryngology	1.33	1.43	0.314	177	174	0.429	12.3	12.1	0.222	8,448	8,555	0.330

LOS length of stay

* *P* value for the comparison between 2006 and 2007 evaluated with the chi-square test. Continuous variables, indicated with †, were evaluated using the Mann–Whitney *U* test

appreciated in those surgeries in which a neuraxial blockade cannot be applied.

Cardiac surgery had the smallest impact on the choice of remifentanil, presumably because of the greater surgical insult to patients, who frequently require postoperative mechanical ventilation; therefore, anesthetists can apply a large dose of fentanyl intraoperatively without considering early postoperative emergence and extubation in the operating theater. Coexisting cardiac disease was negatively associated with selection of remifentanil (Table 2). The well-known circulatory suppressive effect of remifentanil [20] may be another reason for the anesthetists to refrain from applying it in cardiac surgery.

Bramhall pointed out three prerequisites for an anesthetic drug to obtain a major share in the market. (Bramhall J. Remifentanil: Clinical use of an evanescent opioid. Available at: http://faculty.washington.edu/bramhall/lectures/opioids/remife~1.htm. Accessed June 14, 2011.) First, the drug must fit a "niche," allowing techniques to be used that were previously impractical; second, the drug must be cost effective; and third, it must have a safer profile than currently available agents. The safety of novel agents is generally extensively evaluated before clinical application, but it is usually difficult to show that the drug is "safer" than other drugs before substantial use. Similarly, the cost-effectiveness of anesthetic drugs cannot be clearly determined before substantial use, because various parameters can affect postoperative medical costs [21]. In contrast, intraoperative clinical advantages of remifentanil are evident even before substantial use. Its unique property as an ultra-short-acting opioid allowed application of new techniques that were previously impractical. For example, it enabled extensive opioid use as primary treatment for intraoperative pain that did not affect early postoperative emergence [22]. Bramhall also stated that the superiority of a drug over others should be assessed quite accurately, even if subjectively, by individual anesthetists in their daily practice. Because other short-acting opioids, i.e., sufentanil and alfentanil, had not been introduced into clinical use in Japan, the effect of remifentanil was likely to have a greater impression on Japanese anesthesiologists, and this may have boosted its penetration into the market.

The Japanese health insurance system does not offer economic incentives to anesthesiologists, and the reimbursement of costs for surgery and anesthesia is based on a fee-for-service system [23]. Therefore, anesthesiologists in Japan choose drugs according to their clinical applicability and convenience, with little economic consideration. Indeed, the present study revealed that sevoflurane was used in an exceptionally large population of general anesthesia cases despite its relatively high costs compared with other volatile agents (Table 1) [24]. Because there was more than a 10-year delay in the clinical application of remifentanil in Japan from Western countries, anesthesiologists should already have been familiar with its pharmacological properties and practical clinical application, thus making it easy for them to bring it into their clinical practice.

Change in patterns of drugs used for general anesthesia

Along with the rapid escalation of remifentanil use, an increase in TIVA and a reciprocal decrease in nitrous oxide use were obvious. Increase in propofol users by 4.1% in contrast to the reduction in barbiturates users by 3.5% may be the consequence of the increase in TIVA population, because propofol, which is the most popular hypnotic for maintenance of TIVA, can also substitute for barbiturates as an induction agent. Remifentanil may be superior to nitrous oxide for pain control with less environmental effect (i.e., contamination of the atmosphere in the operating room) and fewer adverse effects on patients, such as postoperative nausea and vomiting [25]. Other volatile anesthetic agents, specifically sevoflurane and isoflurane, were significantly reduced in use in 2007, but the magnitudes are less than that of nitrous oxide (Table 1). These observations may possibly be the result of their known organ-protective effects [26], recognized by most of the anesthesiologists in Japan, as well as their easy and titratable properties in regular clinical practice.

Impact on patient postoperative outcome and cost

Postoperative LOS was significantly reduced in all the surgeries except for otolaryngology, although the magnitude of surgical insult indicated by duration of anesthesia were relatively similar in both years. However, whether application of remifentanil led to better postoperative recovery is not clear. Currently few publications have reported association between use of remifentanil and better postoperative recovery [27]. Other factors, such as less-invasive surgical techniques and improved perioperative care, which affects enhanced recovery after surgery [28], may have contributed to the reduction in postoperative LOS in surgical patients.

Remifentanil is relatively expensive, a 2-mg vial costing 25.34 USD, about 10 times that of fentanyl (0.1 mg ampule for 2.45 USD) in Japan. Rapid increase in the proportion of remifentanil use was anticipated to cause increase in total costs. However, all surgical subcategories showed similar or less total cost in 2007 compared with 2006. Although multiple factors affect patient postoperative outcome and total costs, we can at least say from the present results that application of remifentanil did not affect increase in total costs. To disclose the possible contribution of remifentanil to better postoperative recovery, further evaluation using a wider dataset or a randomized controlled trial is necessary.

Limitations

Several limitations to this study should be acknowledged. The first is the use of an administrative claims database. Generally, the recorded diagnoses in such databases are less well validated than those in planned prospective surveys. However, several advantages of the data submission processes in the DPC database, such as physician-dependent diagnosis reporting, requirement of data entry via a strict data format, and mandatory submission linked with reimbursement, maximize the accuracy and consistency of reporting. Second, the database does not include actual doses of each anesthetic that might affect patient outcome. Detailed information about patients' signs and symptoms or laboratory data are also missing; thus, it is impractical with the present data to determine whether introduction of remifentanil affected postoperative LOS and in-hospital mortality.

In conclusion, our data revealed a rapid increase in the proportion of surgeries using remifentanil following its introduction in 2007. Comorbidities including diabetes mellitus, hypertension, liver cirrhosis, and chronic renal failure were positively associated and epidural anesthesia and coexisting cardiac diseases were negatively associated with the use of remifentanil. Postoperative LOS was reduced in 2007, and total cost was comparable in the 2 years, indicating higher drug acquisition costs for remifentanil could be offset by reduced postoperative hospital LOS.

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◆症　例

閉塞性動脈硬化症に対する脊髄刺激実施中の末梢組織経皮的酸素分圧の測定が有用であった1症例

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要旨　難治性の閉塞性動脈硬化症に対する脊髄刺激療法で，術中の末梢組織経皮的酸素分圧の測定が有用であった1症例を報告する．65歳の男性で，閉塞性動脈硬化症で足趾の切断術を受けたが，切断部に強い痛みが残存した．外科的腰部交感神経節切除術は無効で，薬物療法で痛みは軽減しなかった．痛みの軽減と局所血流の改善を目的に，脊髄刺激療法を試みた．試験の電気刺激時に痛みは即時的に軽減しなかった．しかし，患肢の末梢組織経皮的酸素分圧が上昇し，足趾切断部から出血しだした．脊髄刺激療法で患肢の血流増加が期待できると判断し，脊髄刺激電極およびジェネレーターを一期的に埋め込んだ．その後，脊髄刺激により下肢痛は軽減し，血管造影で末梢動脈血流が改善した．脊髄刺激療法の適応判断に術中の末梢組織経皮的酸素分圧の測定が有用であることが示唆された．

キーワード　脊髄刺激療法，術中末梢組織経皮的酸素分圧，末梢動脈疾患

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I　はじめに

脊髄刺激療法は外傷性の神経損傷後の痛みや複合性局所疼痛症候群（CRPS），脊椎手術後症候群などの神経障害痛に対する有用性が示されている．狭心症や末梢血管障害のような虚血性疾患に対して，脊髄刺激療法が虚血痛に対する治療のみならず，循環障害に対する治療法としても有用であることが報告されている[1]．

今回われわれは，末梢血管障害の代表的疾患である閉塞性動脈硬化症の患者に対する脊髄刺激電極の挿入術中に患肢の経皮的酸素分圧（$tcpO_2$）が上昇したので，一期的に脊髄刺激ジェネレーターを埋め込んだ症例を報告する．

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J-STAGE早期公開論文（2010年11月8日早期公開）

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II　症　例

65歳，男性，身長163 cm，体重50 kg

主訴：右足部の痛み，しびれ

既往歴：特記事項なし

現病歴：6カ月前から両側足趾の蒼白と右第1趾の擦傷および安静時痛が起こった．右足趾の擦傷が増悪し，右第1趾基部が腫脹した．4カ月前に右足趾全体に浮腫が発現し，右第1趾の黒色化や潰瘍が進行した．安静時痛は数値評価スケール（numerical rating scale：NRS）で7であった．3カ月前に当院血管外科を受診し，血管造影でFontaine IV°の右下肢閉塞性動脈硬化症と診断された．右第1趾周囲の発赤や黒色壊死が急速に進行し，右第1趾切断術を施行されたが，術後も右第1趾切断部に強い痛みが残存した．ブプレノルフィンの持続皮下注（初期用量0.4 mg/日）やブプレノルフィン坐薬（0.2 mg）で痛みを治療したが，痛みは軽減せず，創部の肉芽形成が不良であった．2カ月前に右腰部交感神経節切除術を外科的に施行されたが，右第1趾切断部の痛みは不変であった．

その直後から，われわれが痛みの治療に関与した．

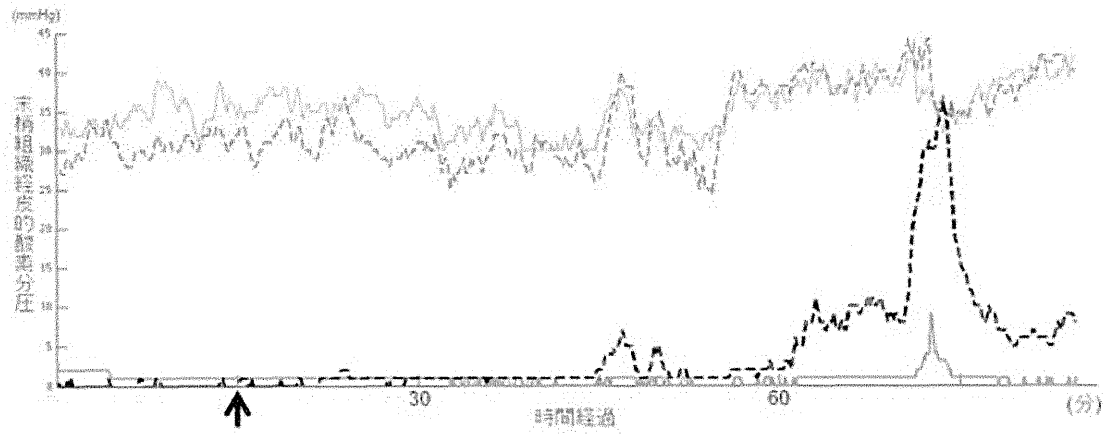

図 1　脊髄刺激療法施行中の末梢組織経皮的酸素分圧測定の経時的変化
太点線は右（患側）足第 1 趾基部，太灰色線は右足第 5 趾基部，細点線は左（健側）足第 1 趾基部，細灰色線は左足第 5 趾基部での測定結果を示す．矢印時点からテスト脊髄刺激を開始した．

0.2％ロピバカインの硬膜外腔持続注入（5 ml/時間），ブプレノルフィン座薬（0.2 mg）を投与したが，痛みは軽減せず，ガバペンチン（初期用量 600 mg/日，3 日ごとに 300 mg/日ずつ増量，維持量 2,400 mg/日）および非ステロイド性抗炎症薬（セレコキシブ 200 mg/日）の内服を開始した．ロピバカインの硬膜外腔持続注入とブプレノルフィンの持続皮下注を漸減中止し，外来通院が可能となった．しかし，NRS で 5 の痛みが持続し，痛みの治療と局所血流改善を目的として脊髄刺激療法を予定した．

患者を手術台上で腹臥位とし，両足部に経皮酸素ガス分圧測定装置［TCM400（ラジオメーター社）］を装着した．第 2/3 腰椎椎間から脊髄刺激電極を第 10 胸椎レベルの硬膜外腔に留置し，電気刺激で右下肢全体に刺激感覚を得られた．さらに，第 4/5 腰椎椎間から脊髄刺激電極を第 1 腰椎レベルの硬膜外腔に挿入し，電気刺激で右第 1 足趾を中心とした足部全体に刺激感覚が得られた．手術室入室時の組織酸素分圧（$tcpO_2$）は左足部 30–40 mmHg に対して右足部 0–2 mmHg（**図 1**）であった．脊髄の試験刺激を開始した後から，右足部の $tcpO_2$ は 10–15 mmHg へと漸増し，最大 30 mmHg に上昇した（**図 1**）．試験刺激開始から 80 分後には，右第 1 趾切断部から出血しだした．試験刺激術中に痛みは即時的に軽減しなかったが，$tcpO_2$ の上昇および右第 1 趾の出血から，右下肢血流増加の効果が期待できると判断し，脊髄刺激ジェネレーターを右下腹部に一期的に埋め込んで手術を終了した．

術後は脊髄刺激療法により，痛みは NRS で 2 と軽減し，ブプレノルフィン坐薬を中止しても痛みは増強しなかった．術後 7 週間目の $tcpO_2$ は，右足部は 18–28 mmHg，左足部は 60 mmHg に上昇していた．術後 8 週間目の下肢血管造影で，下肢血流は増加していた．

III　考　察

脊髄刺激療法は難治性疼痛疾患のみならず，末梢循環障害や狭心症などの非疼痛性疾患にも適応が広がっている．本症例は各種の治療に抵抗性の虚血性疾患であった．局所麻酔薬の硬膜外持続注入は血流改善や痛みの治療に有用とされる．しかし，本症例では詳細な機序は不明であるが，中枢神経系レベルでの侵害受容応答の過剰興奮により硬膜外持続注入に対して抵抗性を示したと推測される．このような理由から痛みの治療だけでなく血流改善を目的として脊髄刺激療法を選択した．

脊髄刺激療法の作用機序は，脊髄での侵害受容性神経伝達物質の分泌抑制や下行性疼痛抑制系の賦活化，局所循環の改善による効果など，複数の鎮痛機序が考えられている．虚血痛に対する鎮痛効果は，脊髄刺激により介在ニューロンを介してカプサイシン受容体含有求心性線維が逆行性に刺激され，CGRP や一酸化窒素が末梢組織中に放出されることによる血管拡張作用との関連が推測されている[2]．さらに，脊髄刺激は自律神経系を直接的に調節し，二次的に交感神経の緊張を低下させ，血管拡張作用を持つことも推測されている[3,4]．

経皮的酸素分圧（$tcpO_2$）は局所組織血流量や皮膚の酸素拡散能および酸素消費量を反映し[5]，末梢組織での微小循環の評価法として広く利用されている．足趾血圧や足関節・上腕血圧比などは，微小循環の変動に対する感度が低く，脊髄刺激療法による治療効果の判定には有用で