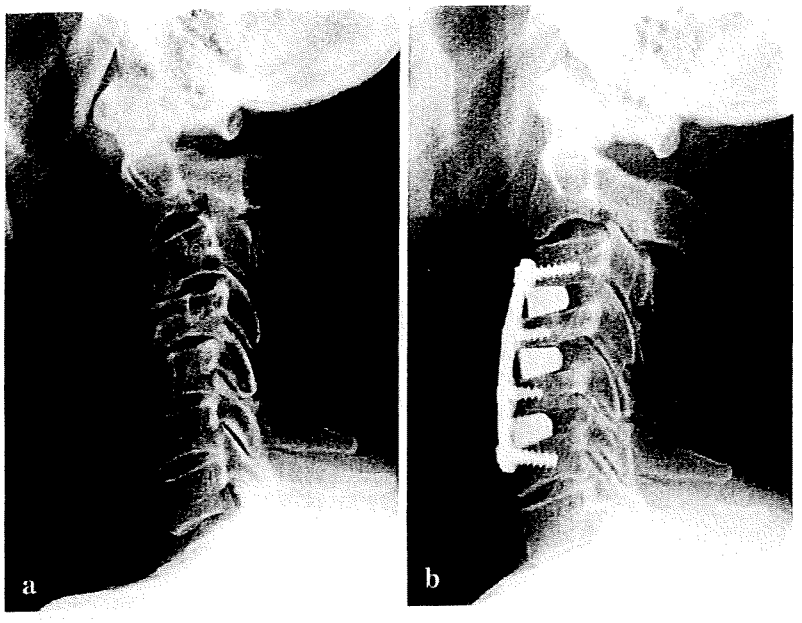

図 6　症例 3，C3-6 分節除圧固定術，人工骨使用
a：術前 X 線像
b：術後 X 線像
C4 および C5 椎体の下位終板も除圧のため削った．除圧後に頸椎を後屈させ，ハイドロキシアパタイトの人工骨を挿入し，プレート固定により前弯位を保持した．

管前後径は 11.5 mm と発育性脊柱管狭窄が認められた．MRI では C4/5 高位で著しい脊髄圧迫と髄内輝度変化，C3/4 および C5/6 で軽度の脊髄圧迫を認めた（**図 4**）．脊髄造影では C4/5 高位でいったん不全ブロックがあり，C3/4 および C5/6 で前方からの硬膜管圧迫を認めた．脊髄は，前屈位でも前方から骨棘により圧迫されており，後方からの除圧には限界があると考えられた（**図 5**）．

手術は C3/4 では後縦靭帯を浮かすように除圧し，C4/5 および C5/6 では後方骨棘を除去した．骨棘切除のために，いずれの椎体も下の終板を削らざるをえなかった．人工骨は各椎間とも前方 8 mm，後方 6 mm のものを使用し，プレートは C6 椎体を fix，C3 椎体を variable screw で固定した（**図 6**）．手術時間は 5 時間 15 分，出血量は 84 m*l* であった．術後 1 年の JOA スコアは 10.5 点と改善が不十分であるが，C4/5 高位の脊髄萎縮が影響していると考えている．

考　察

I 手術適応について

CSM の手術治療における前方法と後方法の選択には，患者側および術者側のさまざまな因子が関与し，優劣は一元的にいえない．厳密にはすべての症例を対象とした無作為比較試験を行うことで決定するしかないが，いまだそこまでの研究はなされていない．

2004 年の Cervical Research Society の参加者 91 名を対象に行われたアンケート調査によれば，側面中間位 X 線上の C2-7 の側面 alignment が 5 度を超える後弯を呈する場合には，無作為比較試験に適さないと回答する人が多かった[3]．また，頸椎後方手術の術後成績において，13 度を超える局所後弯は成績悪化因子とされており[10]，後方手術の術中超音波検査でも 12 度までの後弯度であれば除圧が確認されたという報告もある[2]．われわれのデータでも，局所後弯が 3 度超えた場合には，後方法の長期成績は前方法よりも有意に劣っていた[5]．つまり，CSM のうち，局所後弯が強いケースにおいては，なんらかの alignment の改善が必要な点についてすでにコンセンサスがあると考えられる．そこで，われわれは後弯を伴う CSM に対しては，OPLL に対する手術と同様に，前方除圧固定術を適応してきた．

前方法では 2 椎間までは比較的合併症が少ないが，3 椎間以上になると呼吸器管理および移植骨のトラブルが増すために，避けられることが多い[7]．しかし，呼吸管理に関しては，プレート内固定により早期からの離床や体位交換が可能と

なって，以前と比較するとかなり容易になった[9]．

また，移植骨については，CSMではOPLLとは異なり椎体亜全摘の必然性がないため，分節ごとに移植するか，あるいは椎体亜全摘を限局して適応できる．この分節固定あるいは椎体亜全摘と分節固定の組み合わせ（ハイブリッド固定）により，4〜5椎間の除圧固定であっても，後方のinstrumentationを追加することなく，前方単独での処置が可能とされている[6]．われわれのデータでも，術後1年以上経過した3椎間以上の広範囲前方除圧固定術において，分節固定あるいはハイブリッド固定14例では移植骨のトラブルは発生していない（未発表データ）．

一方，前方除圧固定術の適応のうえでは，いくつかの考慮すべき問題がある．全頸椎にわたって著しい発育性脊柱管狭窄症がある場合には，上下の到達範囲に限界があるため除圧が不十分になる可能性がある．また，後方法術後の後弯症のように椎間関節が強直している場合には，まず後方から関節切除を加えなければならない．この場合には前・後方の合併手術を行う[8]か，椎弓根スクリューを用いて後方から一期的に除圧と矯正を行うことになる．さらに，隣接椎間障害の可能性や採骨部の合併症もありうる．採骨部合併症は，近年，チタンケージと局所骨の組み合わせや，本稿で提示した人工骨の利用により解決しつつある[10]．

2 手術のポイント

実際の手術で留意すべき点は，頸椎ポジションを除圧前後で変化させること，除圧時に終板軟骨を可及的に温存すること，後方の骨棘を確実に切除することである．

全身麻酔の導入後に頸椎のポジションを取るが，最初から矯正位を取る必要はない．頸椎前面の展開ができる程度の広がりがあれば十分であり，極端な頸椎後屈位は術中の麻痺悪化の原因となる．われわれは，脊髄モニタリングにより，術中のみならず，最初の頸椎肢位設定後にも脊髄症の悪化がないことを確認している[11]．最終的に十分な除圧が得られたのちに，手術台を操作して頸椎の後屈を強くする．その結果，椎間板腔の前方部分が広がり，頸椎配列が前弯となるので，この状態で骨移植とプレート固定を行う．

除圧では，骨棘形成が比較的軽度であれば椎体終板は可及的に温存する．海綿骨に切れ込めば，移植骨の沈み込みの要因となり，矯正損失をもたらす．しかし，症例3のように，後方すべりや後方骨棘が著明な場合には，終板を切除して十分な視野を確保しなければならない場合もある．

後療法に関しては，現在のところ，頸椎カラーのみの外固定であるが，大きな矯正損失や偽関節は発生していない．

まとめ

局所後弯を伴うCSMに対して，除圧とともにalignment矯正を行う場合，前方からの分節固定術は良好な矯正と安定した長期成績が得られる手術である．

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MCP-1 expressed by osteoclasts stimulates osteoclastogenesis in an autocrine/paracrine manner

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ABSTRACT

Monocyte chemoattractant protein-1 (MCP-1) is a chemokine that plays a critical role in the recruitment and activation of leukocytes. Here, we describe that multinuclear osteoclast formation was significantly inhibited in cells derived from MCP-1-deficient mice. MCP-1 has been implicated in the regulation of osteoclast cell-cell fusion; however defects of multinuclear osteoclast formation in the cells from mice deficient in DC-STAMP, a seven transmembrane receptor essential for osteoclast cell-cell fusion, was not rescued by recombinant MCP-1. The lack of MCP-1 in osteoclasts resulted in a down-regulation of DC-STAMP, NFATc1, and cathepsin K, all of which were highly expressed in normal osteoclasts, suggesting that osteoclast differentiation was inhibited in MCP-1-deficient cells. MCP-1 alone did not induce osteoclastogenesis, however, the inhibition of osteoclastogenesis in MCP-1-deficient cells was restored by addition of recombinant MCP-1, indicating that osteoclastogenesis was regulated in an autocrine/paracrine manner by MCP-1 under the stimulation of RANKL in osteoclasts.

Osteoclasts are multinuclear cells derived from hematopoietic stem cells or monocyte/macrophage lineage cells [1]. Since osteoclasts are unique cells responsible for bone resorption, the control of osteoclast function or differentiation is critical to protect bones from bone diseases. Osteoclast formation is highly stimulated in destructive bone diseases such as rheumatoid arthritis (RA), multiple myeloma and bone metastasis [2–4]. Macrophage colony stimulating factor (M-CSF) and receptor activator of nuclear factor kappa B ligand (RANKL) have been reported to be expressed in osteoblast/stroma cells [5,6], and described to play a pivotal role in regulating osteoclastogenesis through their receptors, c-Fms and RANK, respectively, which are expressed in osteoclast progenitor cells [7–9]. Various factors such as vitamin D, PTHrP and PGE2 were reported to indirectly stimulate osteoclast differentiation through the upregulation of RANKL in osteoblast/stroma cells [6,10,11], however, the existence of an autocrine/paracrine system that stimulates osteoclastogenesis remains largely unclear.

Monocyte chemoattractant protein-1 (MCP-1)/Chemokine (C–C motif) ligand 2 (Ccl2) is a chemokine that belongs to the CC chemokine family and plays a critical role in the recruitment and activation of leukocytes during acute inflammation [12]. MCP-1 has been shown to play a critical role in the pathogenesis of arteriosclerosis and other vascular diseases by recruiting monocytes into the arterial wall [13]. MCP-1 has also been reported to be involved in osteoclast differentiation [14–17], however, studies of osteoclast differentiation using MCP-1-deficient mice have not been reported. Since MCP-1 has been implicated in the cell–cell fusion of osteoclasts [14–17], and MCP-1 family ligands share multiple receptors, it is possible that MCP-1 binds to an unknown receptor to stimulate osteoclast cell–cell fusion. Dendritic cell specific transmembrane receptor (DC-STAMP), an orphan seven transmembrane receptor, is essential for cell–cell fusion of osteoclasts, and DC-STAMP-deficient osteoclasts show a complete lack of cell–cell

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fusion [18–20]. DC-STAMP is highly induced in osteoclasts during differentiation [18,21] and is a direct target of NFATc1, an essential transcription factor for osteoclast differentiation [19,22]. Thus osteoclast differentiation and cell–cell fusion are both regulated by the RANKL-NFATc1 axis.

In this study, we describe that among MCP ligands, MCP-1 is specifically expressed in osteoclasts. MCP-1-deficient osteoclasts showed reduced multinuclear osteoclast differentiation and downregulation of NFATc1. Recombinant MCP-1 did not restore defective osteoclast cell–cell fusion in DC-STAMP-deficient cells. MCP-1 did not induced osteoclast differentiation in the absence of RANKL, whereas inhibited osteoclastogenesis in MCP-1-deficient cells was restored by recombinant MCP-1 in the presence of RANKL. Taken together, these findings suggest that MCP-1 expressed in osteoclasts plays a role in regulating osteoclast differentiation in an autocrine/paracrine manner under stimulation by RANKL.

Materials and methods

Mice. All animals were purchased from Japan Crea (Tokyo, Japan) or born and kept under pathogen-free conditions, and cared for in accordance with the guidelines of Keio University School of Medicine. *MCP-1*$^{-/-}$ mice were provided by Dr. Rollins ([23], Dana-Farber Cancer Institute, Boston, MA). *DC-STAMP*$^{-/-}$ mice were prepared as previously described [18,19].

Osteoclast differentiation in vitro. Bone marrow cells were isolated from *MCP-1*$^{-/-}$, *DC-STAMP*$^{-/-}$ or wild-type control mice and cultured in αMEM (Sigma–Aldrich, St. Louis, MO) medium containing 10% FCS in the presence of 50 ng/ml M-CSF (R&D, McKinley Place, MN, USA) at 37 °C in a humidified atmosphere of 5% CO_2 in air. After three days of culture, M-CSF-dependent adherent cells were harvested and cultured in the presence of M-CSF and RANKL (R&D) as previously described [18,19]. In some experiments, recombinant MCP-1 (R&D) was added to the culture. Osteoclastogenesis was evaluated by tartrate resistance acid phosphatase (TRAP) staining as described [24,25].

Microarray. Osteoclasts were formed from osteoclast progenitor cells isolated from wild-type mice, and total RNA was extracted. Oligonucleotide microarrays (GeneChip Mouse Genome 430 2.0 Array, Affymetrix) were used to monitor the relative abundance of transcripts.

Real-time Reverse Transcriptase-PCR. Total RNA was extracted from cultured osteoclasts using an RNeasy kit (Qiagen GmbH, Hilden, Germany), and cDNA was synthesized using the Advantage RT-for-PCR kit (Clontech, Mountain view, CA). *Cathepsin K*, *DC-STAMP* and *NFATc1* transcripts were quantified on ABI PRISM 7000 (Applied Biosystems, Foster City, USA) using TaqMan probes. *GAPDH* was used for sample normalization. Applied Biosystems assay IDs were Mm00484036_m1 (*Cathepsin K*), Mm01168058_m1 (*DC-STAMP*), Mm00479445_m1 (*NFATc1*), and 4352932E (*GAPDH*).

Statistical analysis. *P* values were calculated by the unpaired Student's *t*-test.

Results

MCP-1 is specifically expressed in osteoclasts and plays a critical role in osteoclastogenesis

The expression of the MCP ligands; MCP-1, 2, 3, and 4 were analyzed in murine osteoclasts by GeneChip analysis (Fig. 1A). MCP-1 was highly and specifically expressed in osteoclasts. This result led us to analyze the role of MCP-1 in osteoclastogenesis.

Osteoclast progenitor cells were isolated from MCP-1-deficient or wild-type mice, cultured in the presence of M-CSF and RANKL, and osteoclast differentiation was evaluated by TRAP staining and May-Gruenwald staining (Fig. 1B). Multinuclear osteoclast formation was significantly inhibited in MCP-1-deficient osteoclasts when compared to wild-type osteoclasts (Fig. 1B and C).

MCP-1 did not rescue the defective cell–cell fusion in DC-STAMP-deficient osteoclasts

Since MCP-1 was reportedly involved in osteoclast cell–cell fusion [14–17], MCP-1 was added to the culture to analyze whether it could rescue the inhibited cell-cell fusion of DC-STAMP-deficient osteoclasts (Fig. 2). However, the complete lack of cell–cell fusion in DC-STAMP-deficient osteoclasts was not restored by the addition of MCP-1 (Fig. 2A and B). MCP-1 did not induce cell–cell fusion or TRAP expression in wild-type cells in the absence of RANKL (Fig. 2A and B).

Osteoclast differentiation was inhibited in MCP-1-deficient cells

Since osteoclast cell–cell fusion is induced at the terminal stage of differentiation, the expression of *Cathepsin K* and *DC-STAMP*, a terminal differentiation marker for osteoclasts and an essential molecule for osteoclast cell–cell fusion, respectively, was analyzed

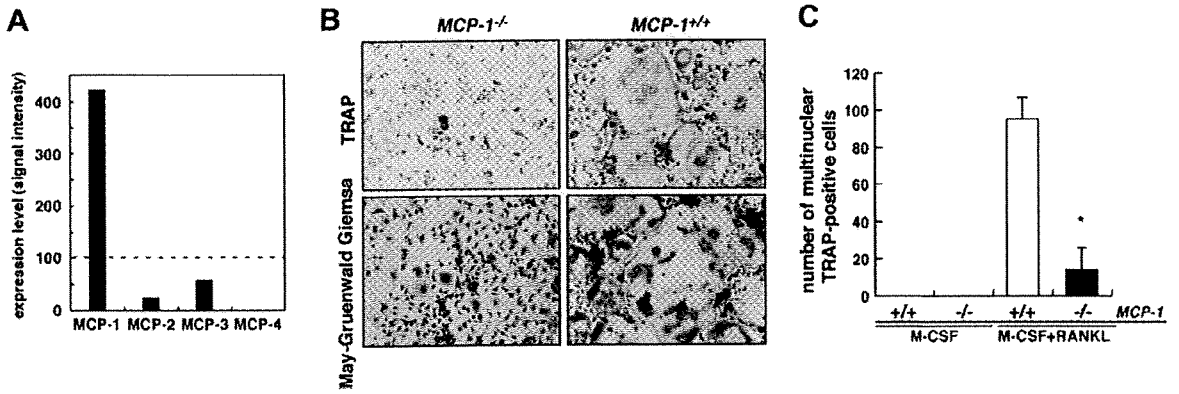

Fig. 1. MCP-1 expressed in osteoclasts plays a role in multinuclear osteoclast formation. (A) Osteoclasts were generated from wild-type osteoclast progenitor cells in the presence of M-CSF (50 ng/ml) and RANKL (25 ng/ml). RNA was extracted and GeneChip analysis was performed. Expression of MCP1, 2, 3, and 4 in osteoclasts is shown. MCP-1 is specifically expressed in osteoclasts. (B and C) Osteoclast progenitor cells were isolated from MCP-1-deficient (*MCP-1*$^{-/-}$) or wild-type (*MCP-1*$^{+/+}$) mice and cultured in the presence of M-CSF (50 ng/ml) and RANKL (25 ng/ml). After 7 days of culture, osteoclastogenesis was evaluated by TRAP staining (upper panel) or May-Gruenwald Giemsa staining (lower panel) (B), and the number of multinuclear TRAP-positive cells containing more than three nuclei was examined (C).

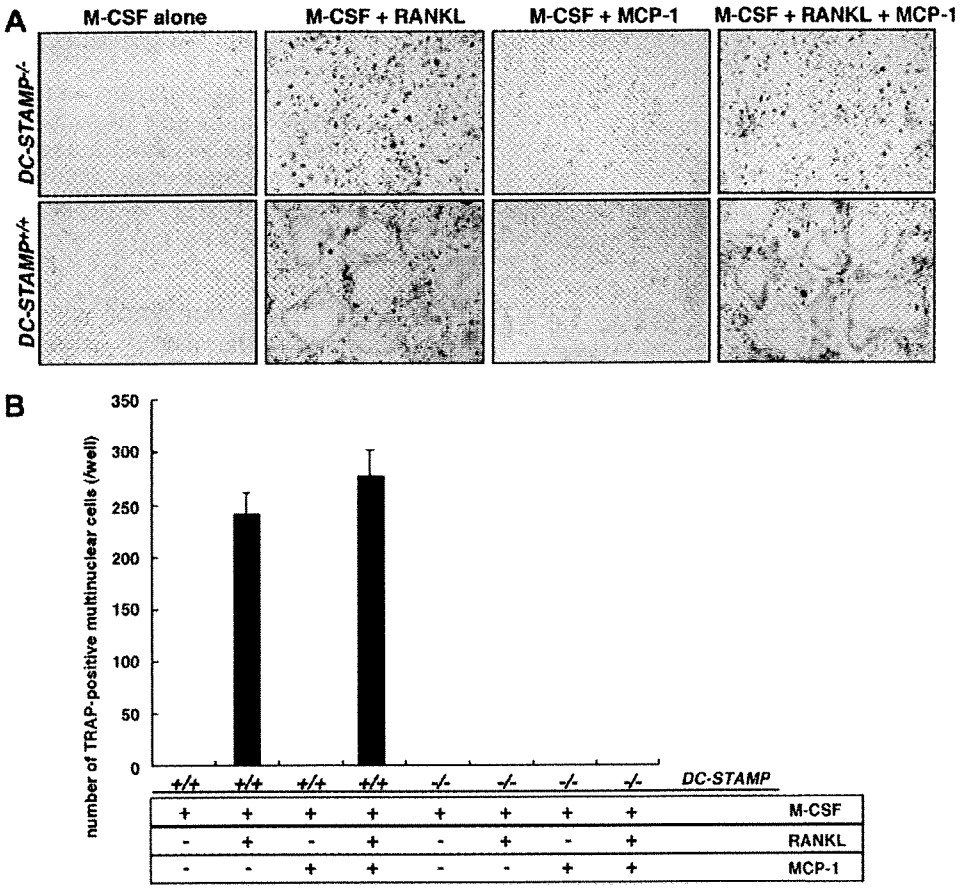

Fig. 2. MCP-1 does not function in DC-STAMP-deficient cells. Osteoclast progenitor cells were isolated from DC-STAMP-deficient (*DC-STAMP* $^{-/-}$) or wild-type (*DC-STAMP*$^{+/+}$) mice and cultured in the presence of M-CSF (50 ng/ml), M-CSF (50 ng/ml) + RANKL (25 ng/ml), M-CSF (50 ng/ml) + MCP-1 (100 ng/ml), and M-CSF (50 ng/ml) + RANKL (25 ng/ml) + MCP-1 (100 ng/ml). After 7 days of culture, osteoclastogenesis was evaluated by TRAP staining (A), and the number of multinuclear TRAP-positive cells containing more than three nuclei was scored (B).

(Fig. 3). *Cathepsin K* and *DC-STAMP* expression was significantly reduced in MCP-1-deficient osteoclasts compared to wild-type osteoclasts, indicating that osteoclastogenesis was inhibited in MCP-1-deficient osteoclasts. Since NFATc1 is an essential transcription factor for osteoclast differentiation and Cathepsin K and DC-STAMP are both direct targets of NFATc1 in osteoclasts [20,26], the expression of *NFATc1* was analyzed in MCP-1-deficient osteoclasts (Fig. 3). The expression of *NFATc1* was significantly downregulated in MCP-1-deficient osteoclasts compared with wild-type osteoclasts (Fig. 3), suggesting that MCP-1 expressed by osteoclasts induces osteoclast differentiation in an autocrine/paracrine manner.

MCP-1 plays a role in regulating osteoclastogenesis under stimulation by RANKL

In order to elucidate the role of MCP-1 in the regulation of osteoclast differentiation, recombinant MCP-1 was added to culture of MCP-1-deficient cells (Fig. 4). The inhibition of osteoclastogenesis seen in MCP-1-deficient cells was restored by the addition of MCP-1 in a dose-dependent manner, indicating that MCP-1 expressed in osteoclasts plays a critical role in regulating osteoclast differentiation. Osteoclast differentiation was not induced by MCP-1 in the absence of RANKL, suggesting that MCP-1 stimulates osteoclastogenesis under stimulation by RANKL (Fig. 4). Taken

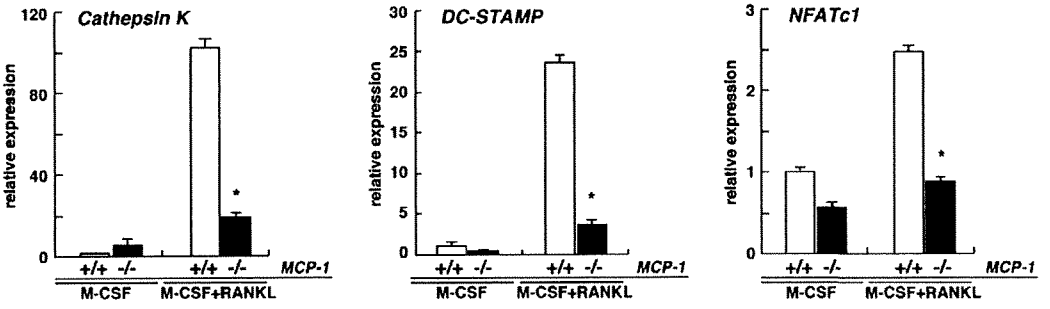

Fig. 3. Osteoclastogenesis is inhibited in MCP-1-deficient cells. Osteoclast progenitor cells were isolated from MCP-1-deficient (black column) or wild-type (white column) mice and cultured in the presence of M-CSF and RANKL. After 7 days of culture, total RNA was extracted, and real time PCR analysis was undertaken to determine the expression levels of indicated genes relative to *GAPDH* ($^{*}P < 0.01$).

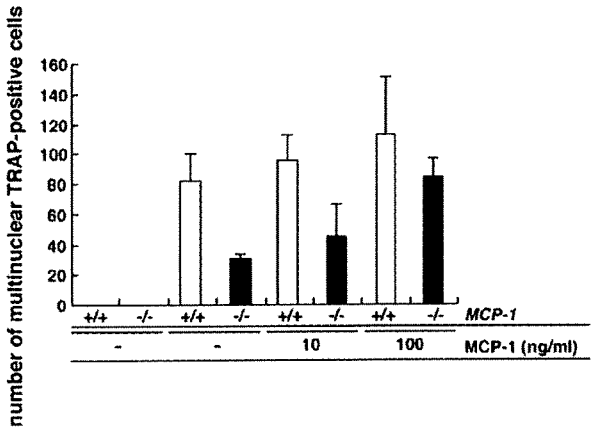

Fig. 4. Reduced osteoclastogenesis in MCP-1-deficient cells is restored by recombinant MCP-1. Osteoclast progenitor cells were isolated from MCP-1-deficient (black column) or wild-type (white column) mice and cultured in the presence of M-CSF (50 ng/ml) + RANKL (25 ng/ml) with or without the indicated concentrations of MCP-1. After 7 days of culture, osteoclastogenesis was evaluated by TRAP staining, and the number of multinuclear TRAP-positive cells containing more than three nuclei was scored.

together, our results indicate that MCP-1 expressed by osteoclasts plays a role in stimulating osteoclastogenesis induced by RANKL in an autocrine/paracrine manner.

Discussion

Osteoclastogenesis is induced by a combination of M-CSF and RANKL, both of which are cytokines expressed by osteoblasts, without osteoblasts/stromal cells [27]. The expression of RANKL in osteoblasts is upregulated by several factors such as vitamin D3 and PGE2 [6,10,11,27], and osteoclast differentiation has been considered to be controlled by microenvironmental factors [27]. The induction of osteoclastogenesis is simulated at sites of inflammation, bone metastasis and tooth eruption [2–4,28], suggesting that some factors may stimulate osteoclast differentiation at the site of bone destruction. In this study, we demonstrated that osteoclastogenesis induced by RANKL was further stimulated by MCP-1 expressed by osteoclasts in an autocrine/paracrine manner. MCP-1 expression has been detected at sites of RA, tooth eruption and bone metastasis where osteoclastogenesis is highly stimulated [29–32].

The most characteristic feature of osteoclasts is multinucleation induced by cell–cell fusion of mononuclear cells. We found that DC-STAMP was essential for cell–cell fusion of osteoclasts, and that osteoclast multinucleation was completely abrogated in DC-STAMP-deficient osteoclasts [18,19]. The multinucleation of osteoclasts through DC-STAMP upregulates their bone resorbing activity, suggesting that DC-STAMP is a molecule expressed by osteoclasts that stimulates osteoclast function [18]. Since DC-STAMP is an orphan receptor, a ligand that stimulates osteoclast cell-cell fusion and function may exist. DC-STAMP is a seven transmembrane receptor, and MCP-1 is known to bind to multiple receptors such as CCR2 and CCR11, both of which are seven transmembrane receptors. MCP-1 has been shown to induce differentiation and cell–cell fusion of osteoclasts [14–17,31], and DC-STAMP is reportedly involved in osteoclast differentiation [21].

Although its function was not demonstrated, MCP-1 expression in osteoclasts has previously been shown by large-scale expression analysis [33,34]. MCP-1 has been shown to induce differentiation without RANKL in human osteoclasts [14,15,31]. In our study, MCP-1 did not induce murine osteoclastogenesis without RANKL, suggesting that the differentiation system or requirement of MCP-1 for stimulating osteoclastogenesis is different between humans and mice; MCP-1 might be more critical for human osteoclastogenesis.

Our study establishes a function for MCP-1 expressed by osteoclasts on osteoclastogenesis. MCP-1 does not induce cell–cell fusion in DC-STAMP-deficient cells, but it plays a role in stimulating osteoclast differentiation under stimulation by RANKL in an autocrine/paracrine manner.

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Comparison of clinical outcome after treatment of hip arthritis caused by MRSA with that caused by non-MRSA in infants

Mitsuaki Mortia, Hiroaki Nakamura and Toshio Kitano

We compared the results of four patients treated for septic arthritis of the hip caused by methicillin-resistant *Staphylococcus aureus* (MRSA) with those of five non-MRSA cases. All four patients with MRSA were neonates when infection occurred, and all four had preceding sepsis and marked swelling of the thigh. The mean duration of follow-up was 5.6 years. At the time of most recent follow-up, all four exhibited severe discrepancy in leg length, and their femoral heads exhibited high-grade deformation according to the Choi classification. In contrast, in the non-MRSA cases, the mean age at infection was 2.2 years and the mean duration of follow-up was 2.9 years. At the most recent follow-up, they exhibited no remarkable discrepancy in leg length and only low-grade deformation of the femoral head. In this study, patients with MRSA showed more marked deformity of the hip and discrepancy of leg length because of lower age and to the presence of organisms resistant to antibiotics. Possible strategies for early diagnosis to prevent poor results after MRSA-induced hip arthritis include the following: (i) ensuring that pediatricians are familiar with the early signs of infection of the hip joint, (ii) aggressive puncture and drainage of pus from the affected joint, and (iii) initial use of antibiotics effective in treating MRSA, especially for patients suspected to have MRSA in the neonatal nursery. *J Pediatr Orthop B* 18:1–5 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: hip joint, methicillin-resistant *Staphylococcus aureus*, septic arthritis

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Introduction

In infants with septic arthritis, treatment in the early stage after definitive diagnosis is a key to satisfactory clinical outcome. Diagnosis is, however, not easy, especially in neonates, as they are unable to complain of symptoms and early signs of infection are often overlooked [1,2].

Methicillin-resistant *Staphylococcus aureus* (MRSA) infection has been increasing in frequency in hospitals and neonatal nurseries [3,4]. Most of the affected patients in such facilities have been premature infants requiring intensive care [5,6]. Although osteomyelitis and septic arthritis caused by MRSA in infants have increased in frequency [7–9], there have been no follow-up studies of septic arthritis of the hip caused by MRSA. The purpose of this study was to compare the outcome of treatment of septic arthritis of the hip caused by MRSA with that of non-MRSA cases.

Patients and methods

Between June 1994 and June 2006, 11 infants with septic arthritis of the hip were treated in our institution. Of these 11 cases, two cases were lost to follow-up. Therefore, nine cases were included in this study. Four of the nine cases were because of MRSA and five caused by non-MRSA organisms (Table 1). Of the five non-MRSA cases, two had negative cultures, two were caused by methicillin-sensitive *Staphylococcus aureus*, and one was because of penicillin-resistant *Streptococcus pneumoniae*. MRSA cases included three girls and one boy. The age at time of diagnosis ranged from 16 to 29 days after birth, with a mean of 20 days after birth. Thus, all patients were younger than 1 month of age. Duration of follow-up ranged from 1 year 6 months to 8 years 7 months, with a mean of 5 years 7 months.

Non-MRSA cases included two girls and three boys. Age at time of diagnosis ranged from 5 months to 6 years 10 months, with a mean of 2 years 3 months after birth. Duration of follow-up ranged from 1 year 2 months to 4 years, with a mean of 2 years 11 months. We determined the duration of time to definitive diagnosis as well as clinical outcome in each group. In addition, at the time of most recent follow-up, we evaluated discrepancy in leg length on whole-leg plain radiograph and deformation of the proximal femur using the radiographic classification of the hip proposed by Choi [1]. Although this classification is designed for determination of treatment, we used it for grading of deformation as a sequelum of infection.

Results

All of the patients with MRSA were neonates younger than 1 month of age. All four patients had preceding

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Table 1 Results for nine patients with septic arthritis of the hip

Case	Age		Duration of symptoms before diagnosis (days)	Duration from diagnosis to drainage (days)	Joint fluid culture	Follow-up duration	Choi class	LLD (mm)
	Years	Months						
1		<1	4	4	MRSA	8 years 7 months	IV B	10 (220)[a]
2		<1	4	1	MRSA	6 years 6 months	II A	38
3		<1	8	1	MRSA	5 years 8 months	III A	14
4		<1	5	1	MRSA	1 years 6 months	II A	10
5		5	1	1	MRSA	4 years	I A	NR
6	1		2	3	-	4 years	I A	NR
7	1		2	10	-	1 year 6 months	I B	NR
8	1		5	2	PRSP	1 year 2 months	I B	NR
9	6		2	3	MRSA	4 years	I A	NR

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; NR, not remarkable; PRSP, penicillin-resistant *Streptococcus pneumoniae*.
[a]LLD, leg length discrepancy, length of elongation is in parenthesis.

sepsis or bacteremia caused by MRSA. Two of the four underwent continuous drip infusion in the maternity hospital. At the time of diagnosis, all four exhibited swelling of the thigh on the affected side accompanied by lateral deviation of the femoral shaft on plain radiograph. The mean duration from the appearance of early signs to the diagnosis of septic arthritis was 5.3 days. The mean duration from diagnosis to the performance of open drainage was 1.8 days. At the most recent follow-up, all four exhibited marked discrepancy in leg length. In addition, the femoral head was severely deformed and exhibited high-grade changes according to the Choi classification.

Of the five patients with non-MRSA disease, one patient was 5 months old and the other four patients were over 1 year of age. They exhibited fever, pseudoparalysis of the leg, hip joint pain, and limping at the time of diagnosis. The mean duration of symptoms and signs before diagnosis was 2.4 days and the mean duration from diagnosis to the performance of open drainage was 3.8 days, indicating that the mean duration of symptoms before diagnosis was short in comparison with that in the four MRSA cases. All non-MRSA cases exhibited low-grade changes, type I A or B, according to the Choi classification at the most recent follow-up. Representative cases of patients with MRSA disease with longer than 5-year follow-up are described below.

Case presentations

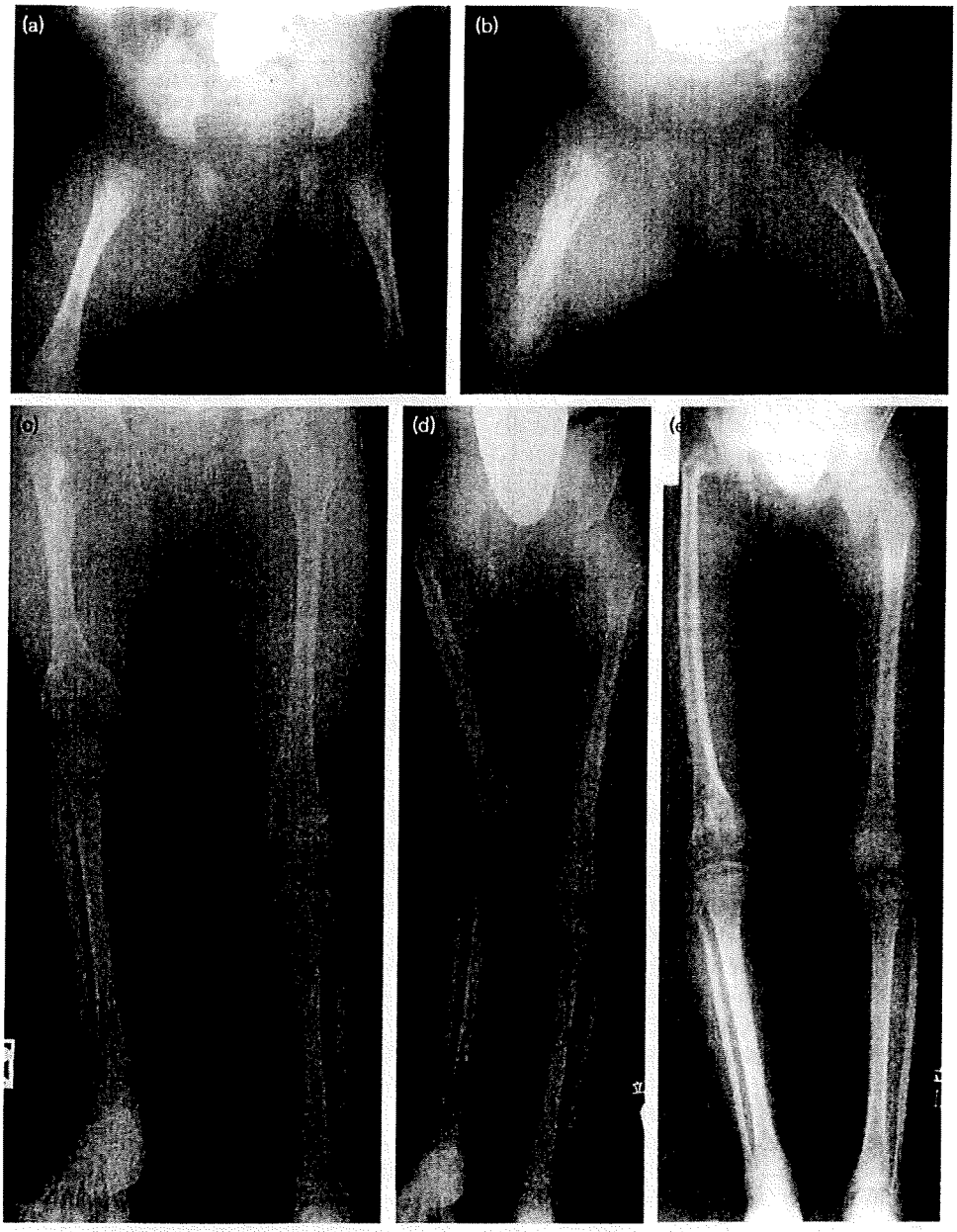
Case 1

A girl, one of triplets, with low body weight was treated with intravenous nutritional infusion because of difficulty with breast-feeding in the neonatal intensive care unit (NICU). She developed an infection in her right hand at 7 days after birth, and the wound was opened to enable drainage of pus. At 16 days after birth, she was referred to our clinic because of elevation of markers of inflammatory reaction in blood and apparent swelling of her right thigh. MRSA was detected on blood culture. At the time of admission, severe swelling was observed in her right thigh. Plain radiograph of the hip showed deviation of the femoral shaft laterally and dislocation of the right hip from its normal position (Fig. 1a). On closed puncture of her right hip, pus was aspirated, after antibiotic administration. On account of lack of improvement with these procedures, open drainage of the hip joint was performed at 19 days after birth. Intraoperative examination revealed disappearance of cartilage on the head of the caput and acetabulum as well as dead bone in the joint. Continuous administration of antibiotics for longer than 1 month induced subsidence of active infection. The femoral head had disappeared and osteomyelitis of the entire right femur was, however, detected (Fig. 1b). At 3 years and 8 months of age, the affected leg was 60 mm shorter than the intact leg (Fig. 1c). We therefore attempted to elongate the right thigh 120 mm with an external fixation device. Following this procedure, the knee on the affected side gradually assumed valgus position and the patella dislocated laterally (Fig. 1d). At the age of 6 years, we attempted to elongate the leg again by 100 mm and correct the deformity with a Taylor Spatial Frame. At the most recent follow-up at 8 years and 7 months of age, deformity of the right hip was type IV B according to the Choi classification, and a 10 mm discrepancy in leg length was observed (Fig. 1e).

Case 2

A male infant with low body weight, one of twins, had been treated with continuous venous infusion because of low blood sugar in the newborn nursery. At 6 days after birth, fever was noted, and markers of inflammatory reaction in the blood were elevated. After confirmation of MRSA by culture of blood and urine, he was treated with antibiotics. Despite this, swelling of the right thigh was noted, and he was referred to our clinic at 17 days of age (Fig. 2a). On the day of admission, we performed open drainage of the right hip. Intraoperative findings revealed dislocation of the right hip, though the femoral head was not deformed. Several months later, the right hip exhibited deformation and sclerotic change (Fig. 2b). At most recent follow-up at 6 years and 6 months after treatment, deformation of the affected hip was type II A according to the Choi classification. The affected leg was 38 mm shorter than the other leg (Fig. 2c).

Fig. 1

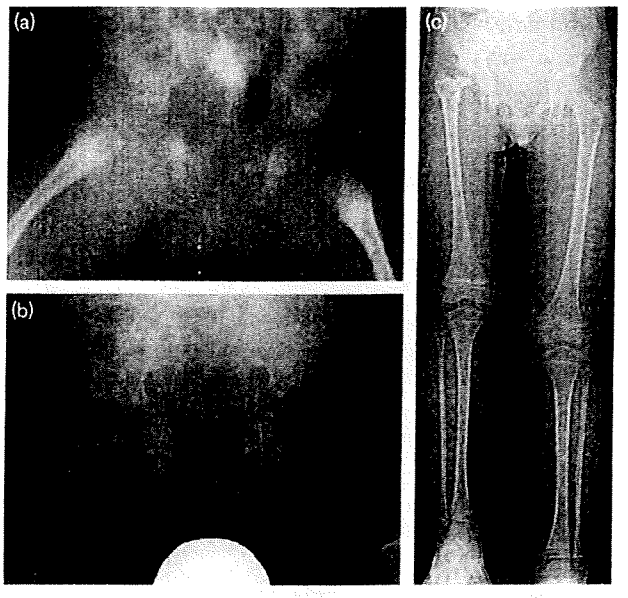


(a) Plain radiograph at 16 days after birth shows lateral deviation of the femoral shaft and dislocation of the right hip. (b) At 1 month after birth, the entire right femur exhibits periosteal reaction. (c) Hip radiograph at 3 years of age reveals disappearance of the right femoral head, dislocation of the right hip, and marked shortening of the right femur. (d) At the age of 6 years and 1 month, discrepancy of leg length is 45 mm. (e) At the most recent follow-up at 8 years and 7 months of age, deformation of the right hip was type IV A according to the Choi classification.

Case 3

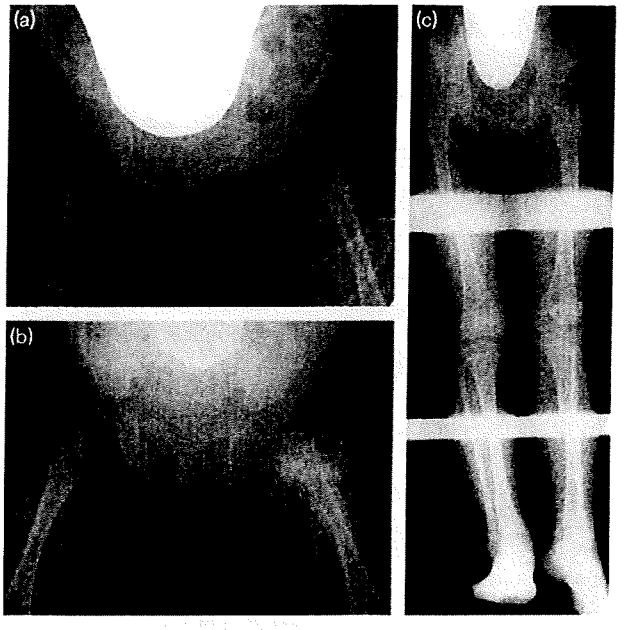
A female infant girl with normal weight was admitted to another hospital because of high fever and abscess formation around the navel at 24 days after birth. On account of elevation of markers of inflammatory reaction in the blood, administration of ampicillin and cefazolin was performed. Blood culture yielded MRSA. At 29 days after birth, the left thigh exhibited swelling, and septic arthritis was diagnosed based on the findings of closed puncture of the right hip. At 32 days of age, the patient was referred to our hospital. Physical examination on the day of admission revealed swelling of the right thigh accompanied by obvious lateral deviation of the femoral shaft and dislocation of the hip on plain radiograph (Fig. 3a). On that day, the infected hip was opened and pus inside the joint was drained. Intraoperative

Fig. 2



(a) This radiograph shows slight dislocation of the right hip and lateral deviation of the right femoral shaft at the time septic arthritis of the right hip was diagnosed. (b) The right hip exhibits deformation and sclerotic change. (c) At the most recent follow-up at 6 years and 6 months of age, deformation of the right hip was type II A. The affected leg was 38 mm shorter than the other leg.

Fig. 3



(a) Marked lateral deviation of the left femoral shaft is noted at 32 days of age. (b) Radiograph shows callus formation in the proximal portion of the left femur at 4 months of age. (c) At the most recent follow-up at 5 years and 8 months of age, deformation of the right hip was type III A according to the Choi classification.

examination revealed complete dislocation of the right hip and disappearance of most of the femoral head. Pus was drained and dead bone was curetted even from the region of the femoral neck. Callus formation in the proximal portion of the left femur was recognized at 4 months of age (Fig. 3b). At the most recent follow-up at 5 years and 8 months of age, Choi classification was type III A and the affected leg was 14 mm shorter than the intact leg (Fig. 3c).

Discussion

In this report, we have described treatment outcomes after septic arthritis of the hip and compared results in MRSA and non-MRSA cases. All MRSA cases exhibited severe deformity of the hip and severe discrepancy in leg length.

The diagnosis of septic arthritis is usually difficult and tends to be delayed in young infants. It is particularly difficult in neonates because the early signs of hip infection are unclear [1,2]. Griffin [10] reported the results of treatment in 64 patients with 67 infected hips, and concluded that early antibiotic treatment combined with open drainage was important in obtaining a good clinical outcome. He also reported that infants and young children were more likely to have poor results because of delay in diagnosis.

Choi evaluated residual deformity after treatment for septic arthritis in 31 children younger than 1 year of age, and concluded that premature birth as well as delay in diagnosis and start of treatment were associated with poor clinical outcome [1].

Recently, MRSA infections have been increasing in frequency in NICUs as well as normal newborn nurseries, and have become a serious problem [6,9,11]. Some reports have described musculoskeletal infections caused by MRSA, and noted that they are difficult to cure [12,13]. However, there have been no detailed reports on septic arthritis of the hip caused by MRSA.

In this study, the results of treatment for MRSA-induced arthritis were unsatisfactory compared with those for non-MRSA cases. Several reasons why the results in our patients with MRSA were not satisfactory are present. First, all were neonates whose cartilage and bone were weak at the time of infection, and early diagnosis was difficult because of the lack of complaints of symptoms. Second, especially in the neonatal nursery, there are no orthopedic specialists, who have special interest in bone or joint infection. Third, the range of antibiotics effective in treating MRSA infection is limited.

As described above, in our series, diagnosis was not made until distinctive signs such as swelling of the thigh and

lateral deviation of the femoral shaft on plain radiograph were noted. Slight swelling, erythema, warm skin on the thigh, pseudoparalysis of the leg, and positioning in slight flexion and external rotation are possible early signs of hip infection. It is thus essential that pediatricians be familiar with the early signs of hip infection and that patients with these signs be referred to orthopedic specialists without delay. The orthopedic specialist must then consider aggressive puncture and drainage, identification of organisms, and corresponding antibiotic administration. Initial use of antibiotics effective against MRSA should be considered without waiting for culture reports in NICU or in the neonatal nursery where surveillance showed MRSA positive.

In cases of septic arthritis of the hip, infection probably starts from the metaphysis and then spreads into the joint as well as bone. It can thus cause osteomyelitis of the femur as in our Case 1, with destruction of the physis of distal femur. In this case, we performed elongation and correction for deformity and discrepancy in leg length. Operations such as Pemberton osteotomy, trochanteric arthroplasty, and arthrodesis, however, might be other treatment options for hip joint deformity as proposed by Choi.

In conclusion, we compared clinical outcomes of septic arthritis of the hip caused by MRSA with non-MRSA cases. Strategies for preventing poor results after MRSA-induced hip joint arthritis in neonates include the following: (i) ensuring that pediatricians are able to detect the early signs of infection of the hip joint, (ii) aggressive performance of puncture and drainage of pus from the affected joint, and (iii) initial use of antibiotics effective against MRSA, especially for patients suspected to have MRSA in the neonatal nursery.

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Quality of Life in Patients Treated Surgically for Scoliosis

Longer Than Sixteen-Year Follow-up

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Study Design. A retrospective study.

Objective. To evaluate the long-term quality of life (QOL) of patients treated surgically for scoliosis.

Summary of Background Data. Measures of long-term outcome after surgery for scoliosis have focused mainly on radiologic changes. However, QOL issues such as working status and marital status are the subjects of greatest concern for patients who will undergo surgical treatment for scoliosis.

Methods. Thirty-two patients treated surgically for scoliosis between 1976 and 1989 were included in this study. The mean duration of follow-up was 21.1 years. Eighteen patients had adolescent idiopathic scoliosis, 8 congenital scoliosis, and 6 symptomatic scoliosis. We evaluated long-term outcome by direct interview with patients. Working status, marital status, and childbearing were determined in addition to clinical and radiologic evaluation. Patients were also asked to fill out the short form (SF)-36 and Scoliosis Research Society (SRS)-22 questionnaires.

Results. Twenty-seven patients (84.4%) were or had been engaged in various occupations without marked difficulty. Although none of the male patients was married, 62.5% of the female patients were married. Half of the female patients had delivered babies after surgery, and the mean number of such children was 1.83. On the SF-36, none of the scores for subjects with idiopathic or congenital scoliosis were markedly different from those for age-matched healthy controls. Multivariate logistic regression analysis revealed that marked preoperative Cobb angle and positive sagittal balance at the most recent follow-up were significantly associated with increased odds ratio for poor scores on the SRS-22.

Conclusion. We evaluated long-term QOL in patients treated surgically for scoliosis, and found that it was not impaired, particularly in the case of patients with idiopathic or congenital scoliosis. Larger preoperative Cobb angle and positive sagittal balance at the most recent follow-up were related to poor outcome in QOL as assessed by the SRS-22.

Key words: scoliosis, surgical treatment, quality of life, long-term outcome. **Spine 2009;34:2179–2184**

Outcome measures after surgical treatment in patients with scoliosis have focused mainly on objective parameters such as correction ratio of Cobb angle on plain radiograph. However, these parameters are only weakly related to functional status. Recently published studies suggest that the magnitude of the scoliotic curve and the degree of curve correction in surgically treated patients are weak predictors of outcome scores and patient satisfaction.[1]

QOL measures are now considered essential in the evaluation of surgically treated patients with scoliosis.[2–20] They are especially important in long-term follow-up studies, which can yield reliable information for patients who will undergo scoliosis surgery. One of the subjects of greatest concern for female patients is whether they will be able to have a baby with a normal delivery.[21–25] Danielsson and Nachemson reported long-term outcomes regarding childbearing and sexual life in women treated for adolescent idiopathic scoliosis (AIS), compared with matched control subjects who did not have scoliosis,[21] and found that patients appeared to function well with regard to marital status and number of children.

The Scoliosis Research Society instrument for outcome assessment (SRS-22) was designed to measure outcome after surgery for scoliosis.[26–29] The short form-36 (SF-36) has been the most commonly used questionnaire for evaluation of the physical and mental condition of patients. In this study, we evaluated the status of patients who underwent surgical treatment for scoliosis with both the SRS-22 and SF-36. The aim of this study was to evaluate health-related QOL long-term after surgery for scoliosis, and to identify socio-clinical factors affecting patient QOL.

■ Materials and Methods

Patients

A total of 83 patients were treated surgically for scoliosis between 1976 and 1989 by 1 senior author (H.M.). Two patients died of causes unrelated to scoliosis surgery, 38 patients could not followed due to inability to locate them, 5 lived too far away to visit our clinic, and 6 refused to participate in our study. As a result, 32 patients visited our clinic for direct interview, with a 38.6% follow-up rate. There were 8 men and 24 women. Age at the time of surgery ranged from 10.9 to 22.2 years, with a mean of 15.3 years. The mean duration of follow-up was 21.1 years (range: 16.5–28.9), and the mean age at the most recent follow-up was 36.4 years. For the type of scoliosis, 18 patients had adolescent idiopathic scoliosis, 8 congenital scoliosis, and 6 symptomatic scoliosis. We have defined the symptomatic patients, who had original causes of scoliosis such as neurofibromatosis, cerebral palsy, osteogenesis imperfecta, congenital myopathy, and Marfan syndrome. In this study, there were 2 cases of neurofibromatosis, 1 of cerebral palsy, 1 of osteogenesis imperfecta, 1 of congenital myopathy, and 1 of

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Table 1. Patients Demographics

	Total	Idiopathic	Congenital	Symptomatic
No. patients (male:female)	32 (8:24)	18 (3:15)	8 (3:5)	6 (2:4)
Age at the most recent follow-up (yr)	36.4 (30.6–43.8)	36.4	36.8	35.7
Duration of follow-up (yr)	21.1 (16.5–28.9)	20.6	23.1	19.9
Age at time of surgery (yr)	15.3 (10.9–22.2)	15.9	13.7	15.8
Type of surgery	Harrington: 14 Cotrel-Dubousset: 11 Zielke: 4 Dwyer: 2 C-D and Zielke: 1	Harrington: 7 Cotrel-Dubousset: 8 Zielke: 2 Dwyer: 1	Harrington: 7 Dwyer: 1	Cotrel-Dubousset: 3 Zielke: 2 C-D and Zielke: 1

Marfan syndrome. Twenty-five patients underwent a posterior procedure, 6 patients an anterior procedure and 1 patient underwent a combined anterior and posterior procedure. The instrumentation used was Harrington instrumentation in 14 patients, Cotrel–Dubousset (C-D) 11 patients, Zielke in 4 patients, Dwyer in 2 patients, and C-D with Zielke in 1 patient (Table 1). Harrington instrumentation was used until 1985, and C-D instrumentation since then.

Physical and radiologic examinations were performed at the most recent follow-up. The contents of interview included working status, marital status, delivery status, and number of children. In addition, the patients were asked to fill out questionnaires to evaluate long-term outcome. The evaluation was performed by the first author (K.T.), who was unbiased and not involved in the primary care of the patients.

Physical Examination

The present height and weight were measured and body mass index was calculated. The rib and lumbar humps were measured with a scoliometer. Spinal balance was evaluated with a plumb line from the C7 spinous process to the intergluteal crease, and leg length discrepancy was assessed in millimeters.

Radiologic Evaluation

Standing posteroanterior and lateral plain radiograph examinations of the whole spine were performed. Radiologic evaluation included preoperative Cobb angle, correction ratio with surgical treatment, loss of correction of Cobb angle at the most recent follow-up, lumbar lordosis measured between cranial L1 endplate and caudal L5 endplate, and sagittal balance defined as anterior deviation drawn perpendicularly from the center of the C7 vertebral body to the posterior cranial corner of the sacrum.[30] In addition, the cranial and caudal ends of fusion were evaluated.

Contents of Interview

We interviewed the patients regarding working and marital status. In the case of female patients, number of children, delivery status, and problems during pregnancy were determined. The official Japanese version of the SF-36 was used to evaluate both the physical and mental status of the patients. The SF-36 consists of 36 questions about the general health status of patients, and scores for 8 specific physical and emotional categories were obtained.

The Japanese SRS-22 questionnaire was also filled out. In this questionnaire, there were 5 questions in each of the first 4 domains (function and activity, pain, self-image and appearance, and mental health) and 2 questions regarding treatment satisfaction. All answers were scored from 0 to 5.

Statistical Analysis

We also evaluated factors contributing to the scores on the SRS-22 with multivariate logistic regression analysis. This evaluation was performed with SRS-22 score as an outcome index, and factors reducing SRS-22 score were evaluated. Sex, age, working status, marital status, VAS score, degree of rib hump, preoperative Cobb angle, correction ratio of Cobb angle, loss of correction, Cobb angle at the most recent follow-up, and sagittal balance at the most recent follow-up were selected as explanatory variables for construction of multivariate models. Odds ratios, their 95% confidence intervals (95% CI), and *P* values were calculated with Statistical Analysis System Version 9.1.3 (SAS Institute, Inc., Cary, NC).

Table 2. Clinical Examination and Radiological Evaluation

	Total	Idiopathic	Congenital	Symptomatic
Height (cm)	154.4 (106–174.3)	157.6	155.8	142.9
Weight (kg)	49.3 (27–66.9)	48.9	51.3	48.0
Body mass index (kg/m^2)	20.5 (15.3–32.1)	19.6	21.2	22.5
Rib hump (mm)	19.2 (0–75)	23.8	13.8	12.5
Lumbar hump (mm)	2.8 (0–35)	3.1	3.1	1.7
Plumb line (mm)	11.0 (0–50)	9.1	7.5	21.7
Leg length discrepancy (mm)	8.9 (0–20)	7.5	6.3	18.0
Preoperative Cobb angle (°)	69.8 (32–140)	65.1	54.5	104.7
Postoperative Cobb angle (°)	33.0 (4–95)	30.9	30.5	49.8
Rates of operative correction (%)	53.7 (18.1–107.1)	57.1	46.0	53.5
Cobb angle at the most recent follow-up (°)	41.7 (11–106)	39.5	36.8	60.0
Loss of correction (°)	8.7 (0–42)	8.6	6.3	11.2
Lumbar lordosis (°)	31.7 (7–53)	33.8	31.9	23.8
Positive sagittal balance (mm)	19/32 (21.7)	8/18 (7.9)	6/8 (27.6)	5/6 (62.0)
No. levels of fusion (vertebrae)	9.1 (2–15)	9.8	7.1	9.5

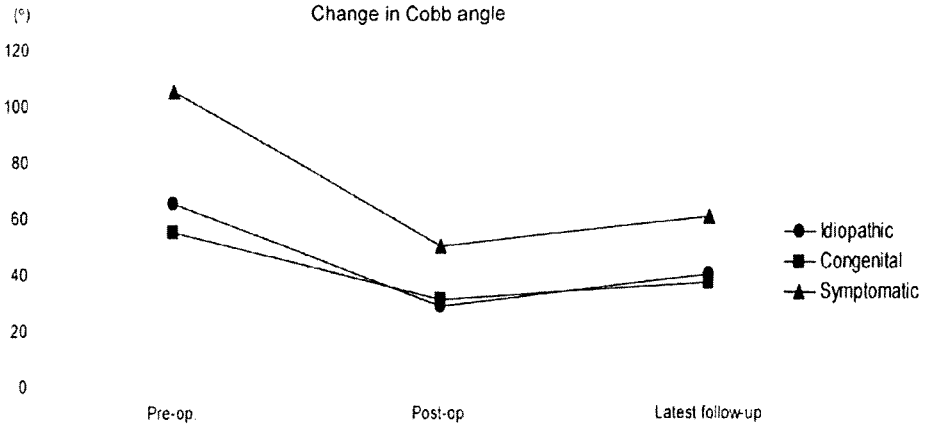

Figure 1. Change in Cobb angle by type of scoliosis. Patients with symptomatic scoliosis had a significantly higher preoperative Cobb angle, but no significant differences were found among the groups in postoperative Cobb angle, ratio of operative correction, Cobb angle at the most recent follow-up, or degree of loss of correction.

■ Results

Clinical Examination

The mean height was 154.4 cm (range, 106–174.3), mean weight 49.3 kg (range, 27–66.9), and mean body mass index 20.5 kg/m^2 (range, 15.3–32.1) at the most recent follow-up (Table 2). The mean degree of rib hump was 19.2 mm (range, 0–75), and the mean degree of lumbar hump 2.8 mm (range, 0–35).

Radiologic Evaluation

Cobb angle improved from a mean of 69.8° (range, 32°–140°) before surgery to 33° (range, 4°–95°) after surgery (Table 2, Figure 1). The mean ratio of operative correction was 53.7% (range, 18.1–107.1). The mean Cobb angle at the most recent follow-up was 41.7° (range, 11°–106°), with a mean of 8.7° (range, °0–42°) in loss of correction over 16-year follow-up. By type of scoliosis, patients with symptomatic scoliosis had a significantly higher preoperative Cobb angle, but no significant differences were observed among the groups in postoperative Cobb angle, ratio of operative correction, Cobb angle at the most recent follow-up, or degree of loss of correction.

By type of instrumentation, the correction ratio with surgical treatment was 50.4% for Harrington instrumentation, 53.1% for C-D, 72.5% for Zielke, 42.1% for Dwyer, and 53.4% for combined C-D and Zielke instrumentation. Mean loss of correction was 6.9° for Harrington instrumentation, 6.6° for C-D, 20.3° for Zielke, 5.5° for Dwyer, and 9.0° for C-D and Zielke.

Mean lumbar lordosis was 31.7° (range, 7°–53°), 19 patients (59.4%) had positive sagittal balance, and the mean degree of deviation was 21.7 mm (range, −45–140). The mean number of levels of fusion was 9.1 vertebrae (range, 2–15).

Additional Surgery

Additional surgery was performed in 5 patients who underwent removal of instrumentation at a mean of 7.6 years after surgery at their own request while asymptomatic. Three patients had revision surgery due to instrument failure within 2 years after the original scoliosis surgery. The first of these patients were idiopathic scoliosis treated with Dwyer instrument. Within 1 year after this operation, the patient required additional instrumentation with Harrington rod system due to breakage of a connection wire. The second of these patients were osteogenesis imperfecta treated with C-D instrumentation, and required revision surgery due to breakage of a rod. This patient was treated with reapplication of C-D instrumentation. The third of these patients were congenital myopathy treated with Zielke instrumentation, and required refixation with C-D instrumentation for progression of thoracic curvature. All patients who underwent required revision surgery had positive sagittal balance at the time of revision surgery as well as at the latest follow-up. The mean positive balance of these patients was 92 mm at the time of revision surgery.

Working and Marital Status

Twenty-seven patients (84.4%) were or had been engaged in various occupations after surgery, such as office work, sales work, factory work, waitressing, receptionist work, work as a telephone operator, and nursing, without marked difficulty (Table 3).

Although none of the male patients with any type of scoliosis and none of the female patients with symptomatic scoliosis were married, 75% of the female patients with adolescent idiopathic scoliosis or congenital scoliosis were married. Of 24 female patients, 12 (50%) had delivered babies after surgery, and had a mean number of children of 1.83 (range: 0–3). The rate of cesarean section was 22.7% and none of the patients had experienced problems during pregnancy or delivery.

Table 3. Working, Marital, and Delivery Status

	Total	Idiopathic	Congenital	Symptomatic
Employed	27/32	17/18	7/8	3/6
Married (male)	0/6	0/3	0/3	0/2
Married (female)	15/24	12/15	3/5	0/4
Deliveries	12/24	9/15	3/5	0/4
No. children	1.83	1.78	2.0	—
Cesarean section	5/22	3/16	2/6	

Table 4. SF-36 Norm-Based Scoring Scores and SRS-22 Scores

	Total	Idiopathic	Congenital	Symptomatic
Physical function	46.0 ± 17.1	53.0	49.4	20.5
Role-physical	48.4 ± 12.6	50.8	51.1	37.5*
Bodily pain	50.1 ± 9.9	50.6	47.8	51.5
General health	48.1 ± 10.5	47.7	49.1	47.9
Vitality	48.3 ± 10.5	48.4	47.6	49.2
Social function	52.8 ± 7.9	53.4	57.1	45.0*
Role-emotional	50.3 ± 10.4	51.4	55.0	41.0*
Mental health	51.7 ± 7.2	51.3	51.8	52.7
SRS-22 total score	84.9 ± 10.5	85.4	87.8	79.5
Function/activity	3.98 ± 0.68	4.10	4.20	3.30*
Pain	4.38 ± 0.64	4.39	4.45	4.23
Self-image/appearance	3.26 ± 0.64	3.13	3.48	3.33
Mental health	3.94 ± 0.56	4.00	3.93	3.80
Satisfaction with management	3.58 ± 1.16	3.67	3.75	3.08

*$P < 0.05$

SF-36 Questionnaire

In the case of symptomatic scoliosis, scores for physical function, role-physical, social function, and role-emotional were significantly low. However, none of the scores for subjects with idiopathic or congenital scoliosis were markedly different from those for age-matched healthy controls (Table 4).

To examine differences in score by type of instrumentation, we summarized the results for Harrington instrumentation, C-D instrumentation, and anterior instrumentation (Zielke or Dwyer). Almost all scores for subjects with anterior instrumentation were lower than those for patients with Harrington and C-D instrumentation.

SRS-22 Questionnaire

The mean total SRS questionnaire score was 84.9 ± 10.5 (range: 65–105) at the most recent follow-up. Overall, scores for self-image and appearance were low despite high scores for function and activity, pain, and mental health. By type of scoliosis, scores for function and activity were significantly low in patients with symptomatic scoliosis (Table 4).

By type of instrumentation, mean total SRS questionnaire score was 88.1 for Harrington instrumentation, 88.6 for C-D, and 73.0 for anterior instrumentation (Dwyer or Zielke). The mean score for anterior instrumentation was significantly lower than those for Harrington and C-D instrumentation. Furthermore, the mean score for patients who had revision surgery was 71.3, and that was significantly lower than that for the others.

By the lowest instrumented vertebra, there was no significant difference in SRS-22 score among distal levels of fusion (Figure 2).

Statistical Analysis

Univariate logistic regression analysis revealed that higher preoperative Cobb angle, higher Cobb angle at the most recent follow-up, and positive sagittal balance at the most recent follow-up were significantly associated with increased odds ratio for poor scores on the SRS-22 (Table 5). Poor SRS-22 score means a score lower than the median of total SRS-22. Total SRS-22 score ranged from 65 to 105, with a median score of 88 points. Therefore, poor SRS-22 score means a score lower than 88 points. Multivariate

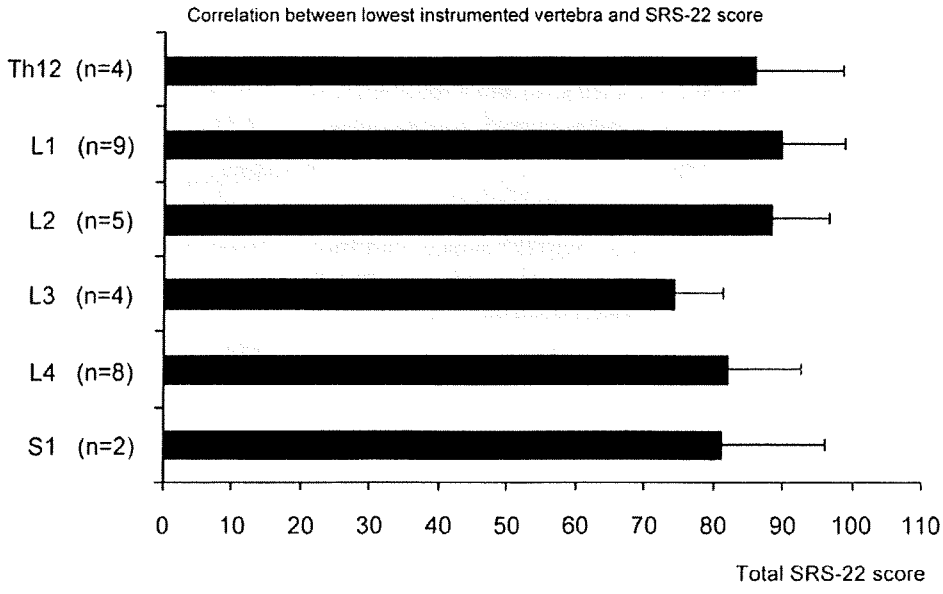

Figure 2. This figure shows relationship between the lowest instrumented vertebra and total SRS-22 score. There was no significant difference in SRS-22 score according to the distal level of fusion.

Table 5. Univariate and Multivariate Logistic Regression Analysis to Evaluate the Factors Associated With QOL

	Univariate Analysis			Multivariate Analysis		
Explanatory Variables	OR	95% CI	*P*	OR	95% CI	*P*
Sex (male)	0.85	(0.17–4.20)	0.84	3.47	(0.08–142.9)	0.52
Age	2.14	(0.52–8.85)	0.29	2.49	(0.08–76.9)	0.60
Working status	1.77	(0.42–7.46)	0.43	5.32	(0.18–166.7)	0.33
Marital status	0.98	(0.24–3.95)	0.98	0.06	(0.002–2.68)	0.15
VAS score	1.29	(0.32–5.18)	0.72	0.56	(0.016–20)	0.75
Degree of rib hump	1.29	(0.32–5.18)	0.72	1.39	(0.088–22.2)	0.81
Preop Cobb angle	6.58*	(1.40–31.25)	0.017	83.3*	(1.80–1000)	0.024
Correction ratio of Cobb angle	2.14	(0.52–8.85)	0.29	0.35	(0.01–11.9)	0.56
Cobb angle at the most recent follow-up	5.05*	(1.11–22.73)	0.037	0.40	(0.019–8.55)	0.56
Loss of correction	1.29	(0.32–5.18)	0.72	0.86	(0.038–19.2)	0.92
Positive sagittal balance at the most recent follow-up	4.88*	(1.06–22.22)	0.042	200*	(1.34–1000)	0.038

logistic regression analysis also revealed that higher preoperative Cobb angle and positive sagittal balance at the most recent follow-up were significantly associated with increased odds ratio for poor scores on the SRS-22.

■ Discussion

Correction of spinal deformity with instrumentation is an established procedure in scoliosis surgery, and good clinical outcomes have been reported with it even long-term.[5,6,10,14–18,31,32]

However, measures of long-term outcome in scoliosis surgery have mainly focused on radiologic changes such as correction ratio of Cobb angle and loss of correction. In the Study Group On Scoliosis Orthopedic and Rehabilitative Treatment 2005 Consensus Paper, it was reported that only 5% of studies on scoliosis included a measure of esthetic appearance, 1.48% a measure of health-related QOL, and 1% a measure of disability.[33]

Recently, the development of the SRS patient questionnaire, an adolescent idiopathic scoliosis-specific QOL instrument, has enabled surgeons to measure QOL before and after corrective surgery for scoliosis. The most recent format of the SRS questionnaire (SRS-22) has 22 items and consists of scales for Function and activity, pain, self-image and appearance, mental health, and satisfaction with treatment. The SRS-22 is more versatile than SRS-24, since scoliosis patients with or without surgery and healthy control individuals can complete the questions in all sections.[34,35]

The SF-36 is also the instrument most widely used to evaluate QOL in adult patients.[36] It consists of 8 subscales including physical function, role-physical, bodily pain, general health, vitality, social function, role-emotional, and mental health. However, the SF-36 includes neither a score for self-image nor a factor unique to patients with scoliosis.[27]

Benli *et al* reported long-term findings for a large series of patients treated with Texas Scottish Rite Hospital instrumentation in 109 patients with AIS using the SRS-22 questionnaire.[18] Scores for self-image, mental status, and function domains exhibited inverse correlations with preoperative curve magnitude and loss of correction, but correlated positively with the rate of postoperative correction of Cobb angle. In addition, surgical treatment did not have negative effects on education, occupation, or marriage.

Danielsson and Nachemson reported long-term outcomes regarding childbearing and sexual life in women treated for AIS, compared with matched control subjects who did not have scoliosis.[21] They found that patients functioned well socially in terms of marital status and number of children, and did not have more problems during pregnancy and delivery than a control group. In their study, neither the number of pregnancies nor the age at first pregnancy was affected by scoliosis.

As noted in their article, impacts on working and marital status are of great concern to patients who will undergo surgical treatment for scoliosis. However, there have been very few studies on this, and none in Japan.

In the present study, most of the patients were or had been engaged in various occupations after surgery without marked difficulty. As for marital status, although none of the male patients with any type of scoliosis and none of the female patients with symptomatic scoliosis were or had been married, 75% of female patients with adolescent idiopathic scoliosis or congenital scoliosis were or had been married. This percentage is equal to that for the normal population of Japanese women of the same age (2005 Population Census). Numbers of children had by patients with idiopathic scoliosis and congenital scoliosis were also equivalent to that for the normal population, these patients experienced no problems during pregnancy or delivery, and their rate of cesarean section was nearly equivalent to that in the normal population.

We also evaluated factors reducing SRS-22 scores by calculating odds ratios on multivariate logistic regression analysis. Preoperative Cobb angle and positive sagittal balance at the most recent follow-up were significantly associated with increased odds ratio for poor scores on the SRS-22. Preoperative Cobb angle was a factor consistently noted in some previous studies.[15–18] In addition, positive sagittal balance at the most recent follow-up was identified as a factor contributing to QOL following scoliosis surgery in our study. Glassman *et al* examined 752

patients with adult deformity, and found that the severity of symptoms increased in linear fashion with degree of progression of positive sagittal balance.[30] These findings emphasize the importance of carefully ensuring sagittal plane alignment in the treatment of spinal deformity.

There are some limitations to the present study, which might affect the conclusions drawn from its findings. Because validated patient-oriented instruments were not available 20 years ago, long-term assessment of this type of surgery must be retrospective. The response rate was low, as expected in a study with very long-term follow-up evaluation. Unfortunately, since no control group of untreated patients with scoliosis was available, the final effect of the operative procedure on the natural course of the deformity could not be clearly determined. However, no selection bias could be ascertained among the patients present at follow-up assessment in terms of either demographic or preoperative characteristics.

We evaluated outcome following scoliosis surgery for longer than 16 years. Further investigations with longer follow-up are needed to confirm the findings of this study, which are, however, important for both surgeons and patients.

■ Key Points

- We evaluated long-term quality of life (QOL) in patients treated surgically for scoliosis regarding working and marital status, and also with the scores on the SF-36 and SRS-22.
- Long-term QOL was not impaired after scoliosis surgery regardless of residual deformity.
- Multivariate logistic regression analysis revealed that large preoperative Cobb angle and positive sagittal balance at the most recent follow-up were factors reducing QOL as assessed by the SRS-22.

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Low Back Pain in Patients Treated Surgically for Scoliosis

Longer Than Sixteen-Year Follow-up

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Study Design. A retrospective study.

Objective. To evaluate long-term outcome regarding low back pain (LBP) in patients treated surgically for scoliosis.

Summary of Background Data. Measures of long-term outcome after surgery for scoliosis have focused mainly on radiologic changes. However, subjective symptoms such as LBP after surgical treatment are of great concern to patients who undergo surgical treatment for scoliosis.

Methods. Thirty-two patients treated surgically for scoliosis between 1976 and 1989 were included in this study. The mean duration of follow-up was 21.1 years. Eighteen patients had adolescent idiopathic scoliosis, 8 had congenital scoliosis, and 6 had symptomatic scoliosis. We evaluated long-term outcome by direct interview. Degree of LBP was evaluated by visual analogue scale score and Moskowitz classification in addition to clinical and radiologic evaluation. Patients were also asked to complete the SF-36 questionnaire.

Results. Mean visual analogue scale score at the latest follow-up was 21 (0–80), and 15% of patients had occasional or frequent LBP in Moskowitz classification. On the SF-36, score for bodily pain was not markedly different from that for age-matched controls. Among radiologic findings, level of distal fusion had no effect on the incidence or severity of LBP. Furthermore, preoperative Cobb angle, latest Cobb angle, and degenerative changes of subjacent segment each exhibited no correlation with degree of LBP, either. On the other hand, sagittal balance was a factor affecting LBP following scoliosis surgery.

Conclusion. We evaluated long-term outcomes regarding LBP following scoliosis surgery. Regardless of residual back deformity, LBP was found to be no more frequent than in the normal population in Japan. Positive sagittal balance at the latest follow-up was a factor significantly contributing to LBP following scoliosis surgery.

Key words: scoliosis, surgical treatment, low back pain, long-term outcome. **Spine 2009;34:2198–2204**

Outcome measures after surgical treatment in patients with scoliosis have focused mainly on objective parameters such as correction ratio of Cobb angle on plain radiograph. However, these parameters are only weakly related to functional status. Recently published studies suggest that the magnitude of scoliotic curvature and degree of correction of such curvature in surgically treated patients are only weak predictors of outcome scores and patient satisfaction.[1]

Low back pain (LBP) has been considered an essential issue in the evaluation of surgically treated patients with scoliosis. It is especially important in long-term follow-up studies, which can yield reliable findings for patients who will undergo scoliosis surgery. Although many studies have reported the incidence of LBP after surgery for scoliosis, their results have been quite wide-ranging (from 7% to 66%).[2–19] Furthermore, various factors contributing to LBP reported in previous studies remain controversial to draw the conclusion.[10–19] Long-term outcome regarding LBP is thus a matter of great concern for patients with scoliosis.

We have already reported findings regarding general health-related quality of life such as working status and marital status from our own follow-up of patients.

The aim of the present study was to evaluate long-term outcomes with regard to LBP after surgery for scoliosis, and to identify factors affecting LBP.

■ Materials and Methods

Patients

A total of 83 patients were treated surgically for scoliosis between 1976 and 1989 by 1 senior author (H.M.). Two patients died of causes unrelated to scoliosis surgery, 38 patients could not followed due to inability to locate them, 5 lived too far away to visit our clinic, and 6 refused to participate in our study. As a result, 32 patients visited our clinic for direct interview, with a 38.6% follow-up rate. There were 8 men and 24 women. Age at time of surgery ranged from 10.9 to 22.2 years, with a mean of 15.3 years. Mean duration of follow-up was 21.1 years (range, 16.5–28.9), and mean age at the latest follow-up was 36.4 years. By type of scoliosis, 18 patients were adolescent idiopathic scoliosis (AIS), 8 congenital scoliosis, and 6 symptomatic scoliosis (2 were neurofibromatosis, 1 cerebral palsy, 1 osteogenesis imperfecta, 1 congenital myopathy, and 1 Marfan syndrome). Twenty-five patients underwent a posterior procedure, 6 underwent an anterior procedure, and 1 patient underwent a combined anterior and posterior procedure. The instrumentation used was Harrington in 14 patients, Cotrel-Dubousset (C-D) in 11 patients, Zielke in 4 patients, Dwyer in 2 patients, and C-D with Zielke in 1 patient (Table 1). Harrington instrumentation was used until 1985, and C-D instrumentation subsequently.

Physical and radiologic examinations were performed at the latest follow-up. Patient interview included determination of

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