



# Is Operative Management Effective for Non-Bacterial Diffuse Sclerosing Osteomyelitis of the Mandible?

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**Purpose:** Operative management has been reported to show varying degrees of therapeutic effects for non-bacterial diffuse sclerosing osteomyelitis of the mandible (DSOM). The purpose of this study was to retrospectively analyze and summarize the operative outcomes for non-bacterial DSOM.

**Methods:** In this retrospective cohort study, patients with non-bacterial DSOM who received operative treatment were enrolled at the Peking University Hospital of Stomatology between 2012 and 2019. The primary predictor variables were the type of operative treatment and number of operations. The outcome variables were operative outcomes (symptom relief or ineffective) and time to recurrent symptoms after operations. Other study variables were demographics, including sex, age, and non-bacterial DSOM onset time. The  $\chi^2$  test and Kaplan–Meier model were used to evaluate differences.

**Results:** The sample was composed of 72 patients with a mean age at onset of  $26.1 \pm 17.8$  years and showed a female predilection. Decortication was performed for 68 patients with non-bacterial DSOM, and 4 patients underwent segmental mandibulectomy. Symptom relief was achieved in 37 (54.4%) patients after the first decortication, and the median time to symptom recurrence was 2.0 months. Furthermore, the longest time to symptom recurrence was not more than 6 months in all patients. Among the 4 patients who underwent segmental mandibulectomy, 2 who received fibula repair experienced recurrence of symptoms at 4 and 5 months after the operations, respectively, and their normal mandible and the transplanted fibula also presented with imaging manifestations of osteomyelitis.

**Conclusions:** Decortication and segmental mandibulectomy were not effective for non-bacterial DSOM. This finding is consistent with the results of other reports, and this condition may be best managed non-operatively by rheumatologists.

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Diffuse sclerosing osteomyelitis of the mandible (DSOM) is a chronic nonsuppurative osteomyelitis of the mandible that can develop at any age. Sueti et al<sup>1,2</sup> summarized the diagnostic criteria for DSOM as follows: patient complaints of pain and swelling of the mandible without fistula formation; radiographic findings

compatible with osteomyelitis for the affected site; histological specimens showing chronic inflammation; recurrent exacerbations of the symptoms despite long-term antibiotic therapy; and no clear underlying cause.

At present, the etiology of DSOM remains unclear. Some researchers believe that DSOM is caused by

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bacterial infection; however, no clear infection route and pathogenic bacteria have been identified.<sup>3-5</sup> A few other studies have suggested that DSOM is a type of chronic tendoperiostitis caused by overuse of the masticatory muscles.<sup>6-8</sup> Some researchers considered it to be an autoinflammatory disease, and named it “chronic non-bacterial osteomyelitis of the mandible,” which can occur alone or present as a manifestation of syndromes (chronic recurrent multifocal osteomyelitis; synovitis, acne, pustulosis, hyperostosis and osteitis syndrome).<sup>1,9,10,11</sup>

For bacterial osteomyelitis, complete debridement, removal of dead bone and other infected tissue, and removal of the identified source of infection, in general, can help achieve the goal of complete cure. However, what role does operative treatment play for non-bacterial DSOM? Is non-bacterial DSOM management similar to that of bacterial osteomyelitis? Can operations help achieve the goal of non-bacterial DSOM cure? According to the literature, operative therapy of non-bacterial DSOM includes decortication, saucerization, debridement, and partial resection of the mandible, and all of these operations have been reported to have varying degrees of therapeutic effects.<sup>4,9,12-15</sup>

The purpose of this study was to analyze and summarize the operative outcomes for non-bacterial DSOM. We hypothesized that the outcome of operative management was ineffective.

## Materials and Method

### STUDY DESIGN AND SAMPLE

To address the research objective, the investigators designed and implemented a retrospective cohort study. The data on patients with non-bacterial DSOM who had received operative treatment after hospitalization at the Department of Oral and Maxillofacial Surgery, Peking University Stomatological Hospital from 2012 to 2019 were collected. The study included patients diagnosed as having non-bacterial DSOM with complete case information with follow-up records for at least half a year, and excluded patients whose case data were incomplete or had no follow-up records. The study protocol was in accordance with the Declaration of Helsinki, and the regional Ethical Review Board of Peking University School and Hospital of Stomatology approved this study.

### VARIABLES

The predictor variables studied were the type of operative treatment, including decortication and segmental mandibulectomy, and the number of operations. The outcome variables measured were operative outcomes and time to symptom recurrence. Since the surgical procedures were associated with postoperative wound pain and required subsequent

antibiotic therapy, the operative outcomes were evaluated 1 month after the operations. If the duration of pain relief was longer than 1 month after the operations, the operations were considered to have provided relief. If the postoperative pain symptoms persisted or recurred within a month, the operations were considered ineffective. The other variables were patient demographics, including sex, age, and non-bacterial DSOM onset time.

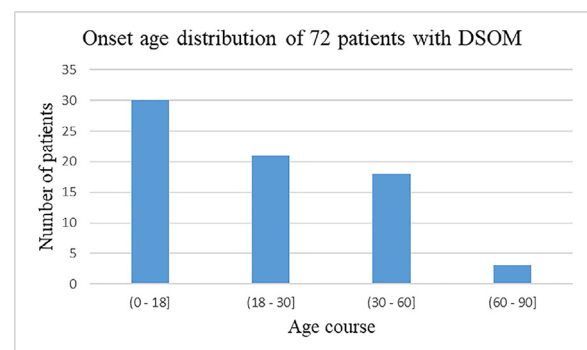
### DATA ANALYSES

Data were analyzed using SPSS v24.0 (IBM, Armonk, NY, USA). The  $\chi^2$  test was used to determine differences in the operative outcomes of the number of decortication procedures in  $2 \times 3$  tables. The Kaplan–Meier model was used to calculate the probability of symptom relief and the probability of ineffectiveness as a function of time. The differences between the Kaplan–Meier curves were tested for significance by the log-rank test.  $P < .05$  was considered significant.

## Results

From 2012 to 2019, 72 patients with non-bacterial DSOM who received operative treatment met the inclusion criteria. Of these, 68 patients underwent decortication to remove the reactive bone and the buccal cortical bone in the lesion area, and the remaining 4 patients underwent segmental mandibulectomy. The age at onset ranged from 4 to 69 years, and the mean age at onset was  $26.1 \pm 17.8$  years. The age distribution is shown in Figure 1. DSOM showed a female predilection, and 44% of the patients were male while 56% were female. The locations of the lesions were as follows: 33 on the left side, 31 on the right side, and 8 on both sides.

Among the patients who underwent decortication, 45 were treated once, 17 were treated twice, 2 were



**FIGURE 1.** Onset age distribution of 72 patients with non-bacterial DSOM. DSOM, diffuse sclerosing osteomyelitis of the mandible.

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**Table 1. OPERATIVE OUTCOMES AFTER DECORTICATION.**

Times of Decortications	First	Second	Third	Greater Than or Equal to Fourth	<i>P</i>
Number of patients	68	23	6	3	
Operative outcomes					.266*
Relief	37(54.4%)	8(34.8%)	2(33.3%)	3(75%)	
Ineffective	31(45.6%)	15(65.2%)	4(66.7%)	1(25%)	
Time range to symptom recurrence (mo)	1-6	2-3	1-3	1-1.5	
Median time to symptom recurrence (mo)	2.0	2.5	2.0	1.0	

\*The  $\chi^2$  test was used to determine differences in  $2 \times 3$  tables, in which the group that underwent 3 decortication procedures was combined with the adjacent group that underwent 4 or more procedures.

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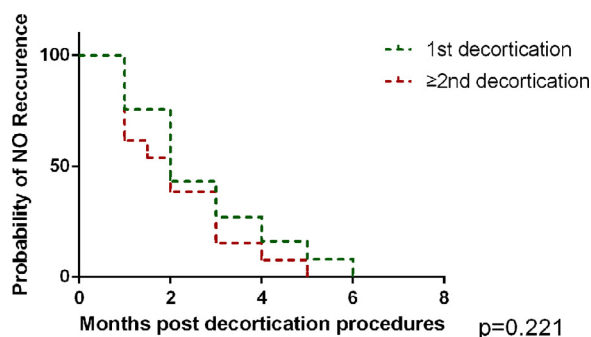
treated thrice, and 4 were treated 4 times or more. Pain disappeared or was alleviated after the operation in only some of the patients; however, the symptoms recurred after a period of time. The outcomes of decortication are shown in Table 1. The times of decortication procedures showed no significant differences in relation to the operative outcomes ( $P = .266 > .05$ ). Moreover, the possibility of no recurrence showed no significant differences ( $P = .221 > .05$ ) between the first decortication and the second or additional decortication procedures (Fig 2). Of the patients who showed effective results in the first decortication, the time to symptom recurrence was not more than 3 months in 73.0% of the patients, and the longest time to symptom recurrence was not more than 6 months in all patients. Among the patients who showed effective results in the second or additional decortication procedures, the time to symptom recurrence was not more than 3 months in 84.6% of the patients, and the longest time to symptom recurrence was not more than 5 months in all patients (Fig 2). After 1 or more decortication procedures, the imaging examination showed varying

degrees of mandibular deformation, and the mandible continued to show osteolysis and sclerosis. With the recurrence of symptoms in some patients, the lesions continued to progress and the scope of osteolysis increased on imaging, as shown in Figure 3.

Four patients underwent segmental mandibulectomy, including 1 who received segmental mandibulectomy alone and 3 who underwent fibula repair after partial mandibular resection. The patient who underwent segmental mandibulectomy alone had received 8 decortications, and finally underwent segmental mandibulectomy. The symptoms did not improve after the operations, and the imaging findings showed that the lesions continued to progress. Because of the multiple operations and lesion progression, most of the mandible in this patient was lost, which seriously affected facial appearance and function. Among the 3 patients who underwent fibula repair after segmental mandibulectomy, 2 received decortications once before segmental mandibulectomy. In 1 patient, the fibula was removed after failure, the mandibular defect was not repaired, and the symptoms recurred 1 year later. In the other 2 patients, symptoms recurred 4 and 5 months after operations. Imaging examination revealed that in addition to the lesion on the originally normal side of the mandible, osteomyelitis appeared in the transplanted fibula, as shown in Figure 4. The data of the 4 patients who underwent segmental mandibulectomy are presented in Table 2.

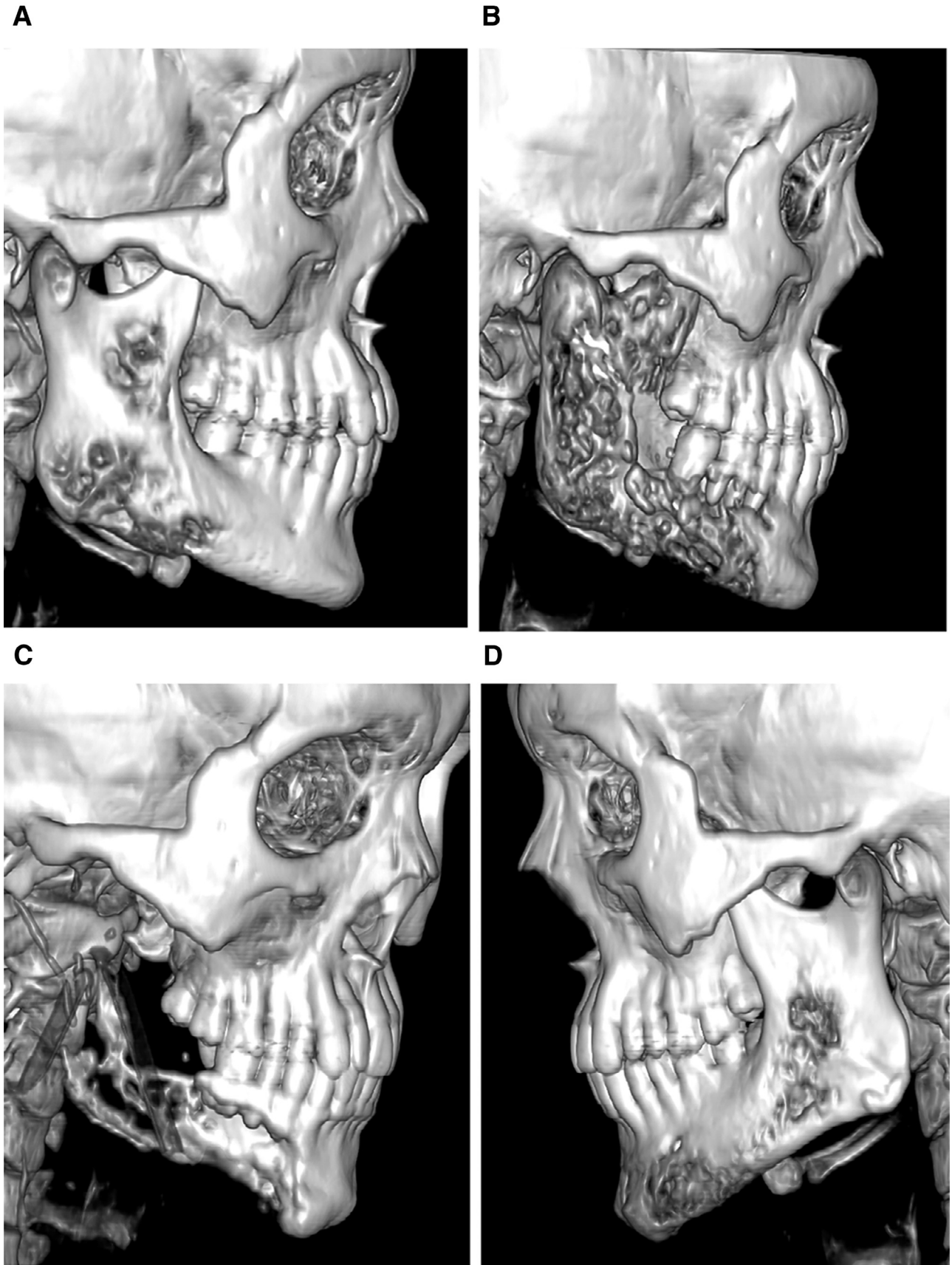
## Discussion

Non-bacterial DSOM is a nonsuppurative inflammatory disease with a relatively low incidence rate and unknown etiology. The distribution of the non-bacterial DSOM demonstrated an almost exclusive involvement of the mandible in the craniomaxillofacial region, but the disease has been reported to occur in the zygomatic arch in 1 case.<sup>16</sup> In this study, the

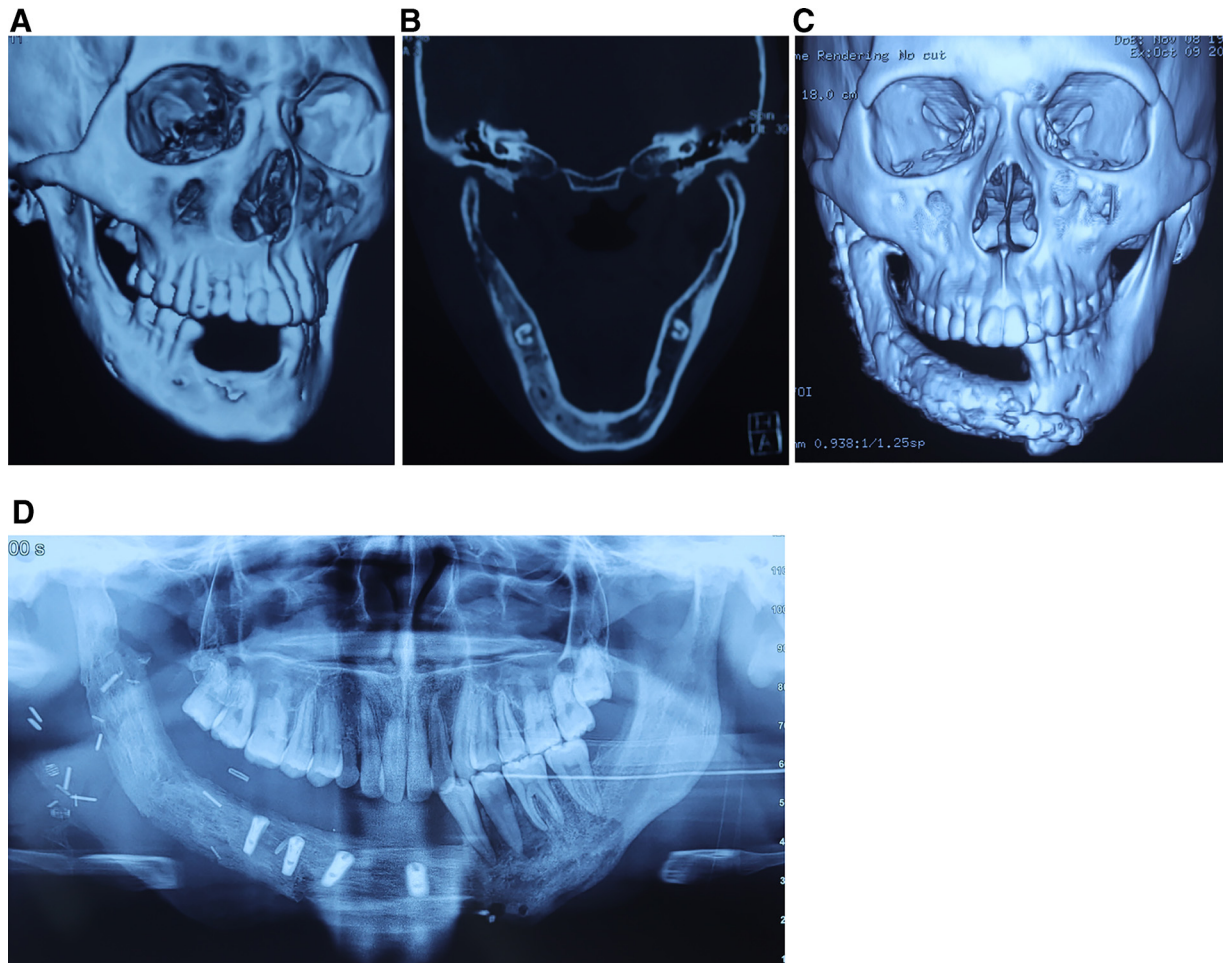


**FIGURE 2.** Probability of no recurrence of non-bacterial DSOM patients with symptom relief by times of decortication procedures. DSOM, diffuse sclerosing osteomyelitis of the mandible.

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**FIGURE 3.** Male, 26 years old. The right mandible showed repeated swelling and pain for 6 months and severe acne on the face, and the diagnosis was suspected to be SAPHO syndrome. The patient was initially treated with antibiotic and corticosteroid. A, CT scan before drug treatment showed cortical destruction of the right mandible; B, CT scan showed continuous progress of bone destruction after 6 months of the



**FIGURE 4.** Male, 20 years old. The right mandible showed repeated swelling and pain for 7 years. The patient had undergone decortication in a local hospital, but the symptoms recurred soon after surgery. Seven months ago, the patient underwent segmental mandibulectomy, fibula repair, and simultaneous implant surgery in the local hospital, and symptoms also recurred at 5 months after the surgery. A and B, CT scan showed non-bacterial DSOM changes in the right mandible before partial mandibular resection; C, CT scan showed that the surface of fibula was rough at 7 months after fibula repair. D, Pantomography showed that the density of the repaired fibula was uneven, and the adjacent mandibular bone was osteolytic at 7 months after fibula repair. DSOM, diffuse sclerosing osteomyelitis of the mandible.

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patient who received segmental mandibulectomy alone also showed pathological changes in the zygoma and zygomatic arch area. In addition to non-bacterial DSOM, there are some other terms for this disease in the literature, such as chronic primary osteomyelitis,<sup>5,17,18</sup> chronic nonsuppurative osteomyelitis,<sup>5,17,18</sup> and juvenile chronic osteomyelitis when it appears in children and adolescents<sup>4,5,19</sup>. The disease is also considered to be a manifestation of synovitis, acne, pustulosis, hyperostosis and osteitis and chronic recurrent multifocal osteomyelitis in some patients, who, in addition to mandible lesions,

show bone and skin lesions in other parts of the body.<sup>1,10,11</sup>

Eyrich et al<sup>13</sup> thought that, in a strict sense, non-bacterial DSOM merely describes a radiologic appearance of the imaging manifestations of various forms of osteomyelitis. Furthermore, the term non-bacterial DSOM does not accurately reflect the dynamic nature of the disease. In general, in the early stage of the disease, the imaging features are usually dominated by osteolysis or by a mixture of osteolysis and osteosclerosis. In the late or stationary stage of the disease, the imaging features may be dominated by sclerosis.

above-mentioned drug treatment; C, decortication of right mandibular lesions was performed 2 months later. Postoperative CT scan showed that most of the right mandible was missing. D, Three months after decortication, swelling and pain appeared in the left mandible. CT scan showed extensive absorption of the left mandible cortical bone. SAPHO, synovitis, acne, pustulosis, hyperostosis and osteitis.

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**Table 2. GENERAL CONDITIONS AND OUTCOMES IN 4 PATIENTS WHO UNDERGO SEGMENTAL MANDIBULECTOMY.**

Patient	Sex	Age (Yr)	Site	Number of Decortications	Defect Repair	Postoperative Condition	Time of Relief (Mo)
1	M	40	B	8	No	Recurrent	No relief
2	M	25	R	1	Fibula	Remove the fibula	12
3	M	20	R	1	Fibula	Involving the fibula	5
4	M	30	L	0	Fibula	Involving the fibula	4

Abbreviations: M, male; B, bilateral; R, right; L, left.

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However, since the term has long been used as a diagnostic name for the disease, it is still in use today.

Typical symptoms of non-bacterial DSOM are recurrent pain, swelling, and trismus. It is significantly different from odontogenic osteomyelitis in that there are no internal or external fistulae, abscess, and sequestrum. Because the disease is relatively rare and there is no clear etiology, it is often misdiagnosed clinically. Due to the similar pathological features, non-bacterial DSOM is often misdiagnosed as fibrous dysplasia or fibrous dysplasia with infection. About 10 years ago, quite a few of the patients with this disease in our department were diagnosed as showing fibrous dysplasia with infection and received repeated debridement and antibiotic treatment. With the gradual accumulation of the number of cases of this disease encountered clinically, non-bacterial DSOM was eventually diagnosed uniformly on the basis of its clinical manifestations, imaging manifestations, laboratory tests, and pathological manifestations in our department. In addition, non-bacterial DSOM also needs to be differentiated from ossifying fibroma, osteosarcoma, and other such conditions.<sup>15</sup>

There are many treatment methods available for non-bacterial DSOM. However, to date, they only seem to improve the symptoms, and there is no exact radical cure. The main treatment methods include non-surgical treatment and surgical treatment. Non-surgical treatment includes drug therapy, physical therapy, and hyperbaric oxygen therapy.<sup>7,8,19,20</sup> Surgical treatment includes decortication, saucerization, debridement, segmental mandibulectomy, and segmental mandibulectomy combined with vascularized bone flap repair.<sup>4,12-14,21</sup>

Jacobsson et al<sup>3</sup> reported that 7 non-bacterial DSOM patients underwent decortication and were symptom-free for 6 to 12 months after surgery; and even when relapses occurred, they were less severe than before. Montonen et al<sup>12</sup> reported that 34 non-bacterial DSOM patients underwent 61 decortications. Among them, 18 patients were symptom-free, and the symptoms recurred an average of 9.8 months after surgery. Of these, 12 showed improvement after the first surgical

procedure. In the other 6 patients, decortication had to be performed 2 to 4 times before healing occurred. Ogawa et al<sup>14</sup> reported that 6 non-bacterial DSOM patients were treated with saucerization combined with particulate cancellous bone and marrow grafting. Of these, 3 were symptom-free, and 3 exhibited an improvement in symptoms. In all of our patients, symptoms recurred at 1-6 months after decortication. Swei et al<sup>13</sup> reported that 4 patients with non-bacterial DSOM underwent partial resection of the mandible and repair with iliac bone, but new lesions appeared in the remaining mandible in all cases at 3 to 12 months after surgery. Fibular free flaps were used to repair the defect after hemi-mandibulectomy, and the lesions did not recur during the follow-up period of 6 months.<sup>22</sup> In our study, 2 patients underwent segmental mandibulectomy and fibula free flap repair in local hospitals, but they showed symptoms of pain and swelling, and imaging examination showed that the lesions appeared on the normal mandible and the transplanted fibula at 4 and 5 months after operation.

The surgical results in this group of patients showed that active surgical treatment did not eliminate symptoms for a long time, nor did it delay or stop the disease progression, but it seemed to accelerate the disease process in some cases. On the basis of a literature review and in cooperation with the department of rheumatology and immunology, we gradually changed the treatment method to drug treatment and finally used bisphosphonates to treat patients with non-bacterial DSOM and achieved a stable therapeutic effect.<sup>23</sup>

The results of this study showed that operative treatment for non-bacterial DSOM was ineffective. Irrespective of whether the patients underwent decortication or mandibular segmental osteotomy, only a few of patients' symptoms were improved after the operation, and the symptom relief was not lasting. These results suggest that the treatment of non-bacterial DSOM should not rely on surgery. Bisphosphonates have been used in the treatment of non-bacterial DSOM by many researchers.<sup>24-26</sup> We used pamidronate disodium for the treatment of 43 non-

bacterial DSOM patients, and followed them for 0.5 to 1.5 years after treatment. Most of the patients' pain and swelling symptoms were completely relieved, and the effect was lasting.<sup>23</sup> In addition, some authors reported that biological agents also had an effect on non-bacterial DSOM.<sup>27</sup> These results provide new ideas for the treatment of non-bacterial DSOM.

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