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### **Scientific Research Report**

# Differences in the Knowledge and Experience of Physicians and Dentists About Medication-Related Osteonecrosis of the Jaw in Osteoporotic Patients

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### ABSTRACT

Aim: Prevention of medication-related osteonecrosis of the jaw (MRONJ) in patients with osteoporosis requires the cooperation of physicians and dentists. We investigated the knowledge, experience, and behaviour related to medical and dental cooperation for MRONJ prevention in patients with osteoporosis between physicians and dentists practising in the Shiga prefecture. Materials and methods: We conducted a cross-sectional study to investigate the cooperation between practising physicians and dentists for preventing osteonecrosis of the jaw (ONJ) in patients with osteoporosis using 2 separate questionnaires from July 28, 2018, to February 3, 2019, in Shiga prefecture, Japan. Results: Of 461 dentists who were sent the questionnaires at their dental clinics, 307 (67%) responded via fax. Of 846 physicians who were sent the questionnaire at their clinics, 378 (45%) responded via fax. Of these, 268 (32%) were finally analysed because 110 (13%) physicians had never treated patients with osteoporosis; 50% dentists and 24% physicians were familiar with the MRONJ position paper in Japan, and 39% dentists and 9% physicians had encountered MRONJ in their clinical practice. A total of 30% physicians had requested oral health care by a dentist before administering bone-modifying agents (BMA) therapy. The knowledge and experience of MRONJ differed between doctors and dentists. Conclusion: The behaviour of doctors and dentists was insufficient to enable medical and dental cooperation for the prevention of MRONJ in patients with osteoporosis. The lack of cooperation between physicians and dentists during osteoporosis treatment in the Shiga prefecture in Japan is documented in this study.

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### Introduction

Bone-modifying agents (BMA) such as bisphosphonate and denosumab are widely and safely used as first-line therapy for osteoporosis; they reduce the bone loss and risk of morbidity and mortality resulting from osteoporotic fractures.<sup>1</sup> However, after Marx et al<sup>2</sup> and Ruggiero et al<sup>3</sup> reported osteonecrosis of the jaw (ONJ), it has been known as an intractable, although rare, complication associated with the use of intravenous and oral bisphosphonates. Although this

E-mail address: yamori@belle.shiga-med.ac.jp (M. Yamori). https://doi.org/10.1016/j.identj.2020.12.005 report was published more than 15 years previously, there is no standardised therapeutic protocol for medicationrelated osteonecrosis of the jaw (MRONJ). MRONJ prevention remains the main goal that can be achieved with treatment of the dental lesions using a multidisciplinary approach before initiating antiabsorption therapy, followed by continuous monitoring of the dental disease.<sup>4</sup> Because MRONJ treatment is generally difficult, no optimal therapeutic strategy has been established.<sup>5</sup> The Japanese position paper that was revised in 2016 states that the key factor in preventing MRONJ in patients with osteoporosis is the close collaboration between dentists and physicians.<sup>6</sup> After the publication of the position paper, educational activities, such as lectures, were held in Japan in accordance with the contents.

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The survey of the Japanese Osteoporosis Society for physicians in 2015 indicated that 62% did not require dentists to perform oral health care before the administration of BMA, and 72% reported no cooperation between physicians and dentists.<sup>7</sup> These results suggest that lack of communication and interaction between physicians and dentists in the treatment of patients with osteoporosis may be responsible for the ongoing increase in the incidence of MRONJ in Japan.<sup>6</sup>

Previous studies were performed on physicians of the Japanese Osteoporosis Society who specialised in the treatment of osteoporosis.<sup>7,8</sup> Few studies have investigated the prevention of MRONJ in patients with osteoporosis with both physicians and dentists in the same area. The knowledge and experience of physicians and dentists influence their clinical practice behaviour. Medical and dental cooperation is established by their actions. Evaluation of the knowledge and experience of physicians and dentists regarding MRONJ prevention in patients with osteoporosis will assist in understanding the issues hindering cooperation between physicians and dentists. Therefore, the current study investigated the knowledge, experience, and behaviour related to cooperation between physicians and dentists treating MRONJ in patients with osteoporosis in the Shiga prefecture.

### Methods

### Questionnaire-based survey

We conducted a cross-sectional study to investigate the cooperation between practising physicians and dentists for preventing ONJ in patients with osteoporosis using 2 separate questionnaires. We explained the main points of the survey at the regular meetings of the medical association and dentists association and obtained consent for the survey. From July 28, 2018, to February 3, 2019, the anonymous, selfadministered, structured questionnaire was sent to 846 clinics belonging to 9 local medical associations and 461 clinics belonging to 7 local dental associations in the Shiga prefecture in Japan. Physicians who had never treated patients with osteoporosis were excluded (eg, specialty in paediatrics, ophthalmology, otolaryngology, dermatology, plastic surgery, psychiatry). This survey targeted dentists who are engaged in general dentistry. Dentists specialising in oral maxillofacial surgery and paediatric dentistry were excluded. The survey did not require the physicians and dentists to provide any personal information, and subject consent was implied if they provided the completed questionnaire. The questionnaire included the following 7 important clinical queries for each physician and dentist:

### Queries for dentist (QD)

QD-1. Do you know medication-related ONJ (MRONJ)?

QD-2. Do you know the latest MRONJ position paper published in Japan?

QD-3. Have you had any personal experience with MRONJ during your practice?

QD-4. Have you ever had any problems during the treatment of patients who are taking BMA? (multiple-choice questions)

### (1) No

(2) Explain the patients about MRONJ

(3) Indications for invasive procedures, such as tooth extraction

(4) Discontinuation of BMA during dental treatment

(5) Other

QD-5. Have patients ever visited your dental clinic under the instructions of their doctor before BMA therapy?

QD-6. Have you ever consulted about patients during BMA therapy with their doctor?

QD-7. Do you have good cooperation with medical professionals during the treatment of osteoporosis with BMA therapy?

#### Queries for physician (QP)

QP-1. Do you know medication-related ONJ (MRONJ)?

QP-2. Do you know the latest MRONJ position paper published in Japan?

QP-3. Have you had any personal experience with MRONJ during your practice?

QP-4. Are you explaining about MRONJ while prescribing BMA to osteoporotic patients?

QP-5. Have you requested oral health care by a dentist before BMA therapy?

QP-6. Have you ever been consulted by a dentist about a patient during BMA therapy?

QP-7. Do you have good cooperation with dentists during the treatment of osteoporosis with BMA therapy?

Frequency distributions and descriptive statistics were generated for all the study variables. Fisher exact test was performed to detect significant associations among categorical variables. This study did not require ethics approval from the Shiga University of Medical Science ethics committee because it did not involve individual data or interventions in the protocol and results. This questionnaire survey was conducted as per the principles of the Declaration of Helsinki and the ethical guidelines of epidemiological research of the Ministry of Health, Labor and Welfare in Japan.

### Results

### Respondents

Of the 461 dentists who were sent the questionnaire at their dental clinics, 307 (67%) responded via fax. Of the 846 physicians who were sent the questionnaire at their clinics, 378 (45%) responded via fax. Finally, 268 (32%) subjects enrolled in the study after excluding 110 (13%) physicians who had never treated patients with osteoporosis. Of the 268, 52 respondents (32%) had worked in the orthopaedics field as specialists who prescribe osteoporotic medicine in Japan.

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### Responses

The results are divided into knowledge and experience, collaboration, and other. For the query with multiple-choice responses (QD-4), the number of responses and the total number of respondents were not matched. The results of each query for dentists and physicians are shown here.

### Knowledge and experience regarding MRONJ

Knowledge of MRONJ (QD-1, 2 and QP-1, 2). The same questions were asked to dentists and physicians about their knowledge of MRONJ.

QD-1, QP-1: Do you know medication-related ONJ (MRONJ)? A total of 296 dentists (96%) and 253 physicians (94%) knew about MRONJ (Figures 1 and 2).

QD-2, QP-2: Do you know the latest MRONJ position paper published in Japan?

Among dentists, 153 (50%) were familiar with the position paper, whereas 151 (49%) were unaware. Three (1%) subjects did not respond. Among the physicians, 65 (24%) were familiar with the position paper and 198 (74%) were unfamiliar. Five (2%) subjects did not respond. The proportion of respondents who knew about the latest position paper of the Japanese Society for Bone and Mineral Research (JSBMR) was significantly lower for physicians than for dentists (P < .01) (Figures 1 and 2).

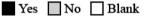
Experience of MRONJ (QD-3, QP-3). The same question was presented to dentists and physicians about their experience of MRONJ.

QD-3, QP-3: Have you had personal experience with MRONJ in your practice?

Among dentists, 120 (39%) had treated patients with MRONJ during their practice, whereas 180 (59%) had never treated a patient with MRONJ. Seven (2%) subjects did not respond. Among the physicians, 25 (9%) reported having treated a patient with MRONJ during their practice, and 240 respondents (90%) had never treated a patient with MRONJ. Three (1%) subjects did not respond. The proportion of physicians who had a personal experience with MRONJ was significantly lower than the proportion of dentists who had (P < .01) (Figures 1 and 2).

Behaviour for patients with osteoporosis related to medical and dental cooperation

Explanation to patients about MRONJ by physicians (QP-4). QP-4: When you prescribe BMA to osteoporotic patients, are you explaining about MRONJ?



QD-1. Do you know medication-related ONJ (MRONJ)?

QD-2. Do you know the latest MRONJ position paper published in Japan?

QD-3. Have you had any personal experience with MRONJ during your practice?

QP-5. Have you requested oral health care by a dentist before BMA therapy?

QD-6. Have you ever consulted about patients during BMA therapy with their doctor?

QD-7. Do you have good cooperation with medical professionals during the treatment of osteoporosis with BMA therapy?

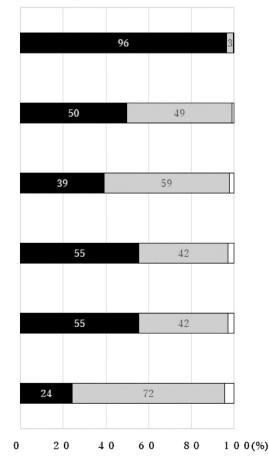


Fig. 1 – Dentists' responses to questions about MRONJ (QD-1, 2, 3, 5, 6, and 7) (n = 307).

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### Yes No Blank

QP-1. Do you know medication-related ONJ (MRONJ)?

QP-2. Do you know the latest MRONJ position paper published in Japan?

QP-3. Have you any had personal experience with MRONJ during your practice?

QP-4. Are you explaining about MRONJ while prescribing BMA to osteoporotic patients?

QP-5. Have you requested oral health care by a dentist before BMA therapy?

QP-6. Have you ever been consulted by a dentist about a patient during BMA therapy?

QP-7. Do you have good cooperation with dentists during the treatment of osteoporosis with BMA therapy?

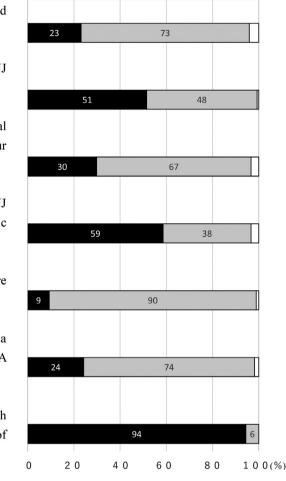


Fig. 2 - Physicians' responses to questions about MRONJ (QP-1, 2, 3, 4, 5, 6, and 7) (n = 268).

A total of 157 respondents (59%) explained MRONJ to their patients, whereas 102 (38%) did not provide any such explanation. Nine (3%) subjects did not respond (Figure 2).

Problems for dentists in treating patients during BMA therapy (QD-4). QD-4: Have you ever had any problems with the treatment of patients who are taking BMA? (multiple-choice questions)

Fifty-seven respondents (19%) had never experienced problems with the treatment of patients who were taking BMA, and 250 respondents (81%) reported having faced challenges in such cases. There are 461 answers in total regarding the problems for dentists in treating patients during BMA therapy in this multiple-answer question. Of these 461 answers, 104 (23%) reported that they found it challenging to explain MRONJ to patients; 199 (43%) reportedly found it difficult to understand the indications for invasive procedures, such as tooth extraction; 147 (32%) stated having issues while making a decision about discontinuation of BMA during dental treatment; and 11 (2%) reported other issues (Figure 3). Consultation by dentists before BMA therapy (QD-5, QP-5). QD-5: Have patients ever visited your dental clinic under the instruction of their doctor before BMA therapy?

Among dentists, 215 (70%) reported that they had experience of referrals before BMA therapy, while 90 respondents (29%) had no such experience. Two (1%) subjects did not respond (Figure 1).

QP-5: Have you requested oral health care by a dentist before BMA therapy?

Among physicians, 80 (30%) had, at some point, requested oral health care by a dentist before they administered BMA therapy, while 179 respondents (67%) had never referred their patient to a dentist for such care. Nine (3%) subjects did not respond (Figure 2).

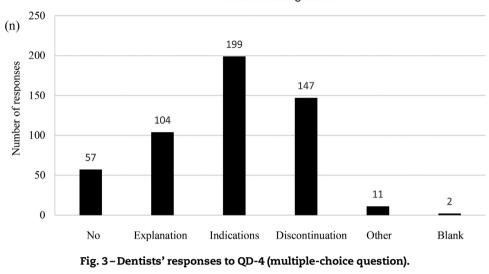
Consultation to physicians during BMA therapy (QD-6, QP-6). QD-6: Have you ever consulted about patients during BMA therapy with their doctor?

Among dentists, 170 (55%) had consulted a physician about patients during BMA therapy with their doctor, whereas 129 (42%) had never consulted. Eight (3%) subjects did not respond (Figure 1).

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NONCOOPERATION IN TREATING OSTEOPOROSIS



QD-4. Have you ever had any problems during the treatment of patients who are taking BMA?

QP-6: Have you ever been consulted by a dentist about a patient during BMA therapy?

Among physicians, 138 (51%) had been consulted by a dentist about a patient during BMA therapy, while 128 (48%) had never been consulted. Two (1%) subjects did not respond (Figure 2). The percentage of dentists who had consulted a physician was similar to the percentage of physicians who reported having been consulted by a dentist during BMA therapy.

#### Cooperation for the prevention of MRONJ

Cooperation during BMA therapy (QD-7, QP-7). QD-7: Do you have good cooperation with medical professionals during the treatment of osteoporosis with BMA therapy?

Among dentists, 74 (24%) cooperated with medical professionals during the treatment of osteoporosis with BMA therapy, whereas 220 (72%) did not report having cooperated. Thirteen (4%) subjects did not respond (Figure 1).

QP-7: Do you have good cooperation with dentists during the treatment of osteoporosis with BMA therapy?

Among physicians, 62 (23%) cooperated with a dentist during the treatment of osteoporosis with BMA therapy, while 195 (73%) did not report such cooperation. Eleven (4%) subjects did not respond (Figure 2).

More than 70% of the respondents, both dentists and physicians, reported that they had experience of good cooperation with the other during BMA therapy.

### Discussion

The prevention of MRONJ in patients with osteoporosis requires the cooperation of physicians and dentists.<sup>6</sup> A questionnaire-based survey was conducted for both physicians and dentists practising in the Shiga prefecture in terms of the knowledge, experience, and behaviour related to medical and dental cooperation for the prevention of MRONJ in osteoporosis patients. To our knowledge, our report is the first to survey both medical and dental professionals in Japanese concerning this issue. We made 2 important clinical observations. First, the knowledge and experience regarding MRONJ differed between physicians and dentists. Second, the behaviour of doctors and dentists did not allow for sufficient cooperation between physicians and dentists to prevent MRONJ in patients with osteoporosis.

First, the knowledge and experience of MRONJ differed between physicians and dentists. MRONJ was first reported more than 15 years previously, and in this survey, almost all physicians and dentists knew about MRONJ. Following the publication of the position paper by the American Association of Oral and Maxillofacial Surgeons (AAOMS) in 2006, many position papers have been published and revised, providing information regarding the most recent cases of diagnosis and treatment. Even though educational activities, such as lectures, were held in Japan in accordance with the contents after the MRONJ position paper that was published in 2016 in Japan,<sup>6</sup> only 50% of the dentists and 25% of the physicians knew about it. Neither physicians nor dentists are sufficiently updated in their knowledge about MRONJ. Physicians were less updated than dentists. Dentists may be more conscious than physicians about updating their knowledge regarding MRONJ because dentists are at risk of being directly involved in its development. To provide good treatment for patients with osteoporosis, it is important that both physicians and dentists have the same basis of knowledge and perform each treatment with common awareness. However, the results of this study did not reflect such standardised knowledge and treatment.

Furthermore, physicians and dentists differed greatly in their experience of ONJ in patients with osteoporosis. This survey was conducted in a single region; therefore, the number of patients with osteoporosis who developed MRONJ was considered to be the same. However, there

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was a difference in the experience regarding MRONJ between physicians and dentists, with the physician population being larger than the dentist population. Diagnosis and treatment of MRONJ is mainly performed by dentists. It is suggested that the dentists may not report to physicians the development of MRONJ in their patients. Dentists need to inform physicians regarding the onset of MRONJ in their patients because physicians may then develop a greater awareness regarding MRONJ prevention in patients. Another possibility is that the dentist informed the physicians about the diagnosis, and it did not mature into an action. In that case, it is necessary to educate them to make them more aware of MRONJ.

Second, the behaviour of doctors and dentists was not compatible with cooperation between physicians and dentists for preventing MRONJ in patients with osteoporosis. Explanations of MRONJ by physicians would encourage patients with osteoporosis to pay attention to their oral health. However, physicians do not provide sufficient explanation regarding MRONJ to patients. We found that the types of difficulties that dentists experienced while examining patients with osteoporosis were different from those that they experienced while examining other patients. One such challenge is the difficulty of explaining MRONJ to patients experienced by dentist may have arisen from physicians not educating the patient about MRONJ. Most dentists found it difficult to understand the indication for surgical procedures, such as tooth extraction in patients at risk of developing MRONJ. Dentists also found it difficult to decide whether to withdraw BMA before the surgery because this issue is still under discussion.<sup>6</sup> Prescribing physicians need to better understand the challenges faced by dentists in treating patients with osteoporosis. In addition, 67% of the physicians had never referred a patient for dental treatment before their therapy. This finding was reported at 62% in the previous report,<sup>7</sup> and the results of this study are similar to those, indicating that many physicians still do not refer their patients to dentists before initiating antiabsorption therapy. More awareness in oral health and explanation about MRONJ for patients with osteoporosis are needed for physicians to facilitate a change in their scope of practice. In this study, only 25% of the physicians and dentists did not consult or refer their patients to each other to prevent MRONJ. Further cooperation between physicians and dentists is needed to prevent MRONJ in this region. If dentists and physicians coordinate and communicate more closely with each other, MRONJ could be prevented in patients with osteoporosis, enabling uninterrupted BMA therapy.

Certain limitations of this study should be acknowledged. First, this study may have a selection bias because of the low proportion of respondents. Second, a potential limitation is that this study used self-reported data of participants that may contain inaccuracies. A further possible limitation of the study is that it may not be representative of all dentists and physicians in Japan because it was limited to a certain region of Japan. However, considering that previous studies have reported similar findings for physicians, the present results may indicate the current status of medical and dental collaboration in the treatment of osteoporosis in Japan.

### Conclusion

In conclusion, the present study highlighted the ill-matched situation between dentists and physicians in the knowledge and experience of MRONJ. Neither physicians nor dentists were updated regarding the advancements in the diagnosis and treatment of MRONJ. Physicians had less experience with MRONJ than dentists. It is suggested that dentists did not report to the physician about the development of jaw osteonecrosis in their patients. For their part, physicians did not provide the necessary information about MRONJ to their patients and failed to refer their patient for dental treatment before initiating antiabsorption therapy. Thus, the lack of cooperation between physicians and dentists during osteoporosis treatment in the Shiga prefecture in Japan is documented in the present study.

### Author contributions

Masashi Yamori: conception and design, acquisition of data, analysis and interpretation of data, drafting the manuscript Mitsumasa Tamura: acquisition of data, analysis and interpretation of data Masaki Mikami, acquisition of data, analysis Toshio Mori, acquisition of data, analysis Masaharu Noi: analysis Yoshisato Machida: revising it critically for important intellectual content Shinya Koshinuma: revising it critically for important intellectual content

Gaku Yamamoto: conception and revising it critically for important intellectual content

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### **Conflict of interest**

None disclosed.

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