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Can Autofluorescence Guide Surgeons in the Treatment of Medication-Related Osteonecrosis of the Jaw? A Prospective **Feasibility Study**

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Purpose: The main limitation of surgical treatment of medication-related osteonecrosis of the jaw (MRONJ) is difficulty in defining resection margins. The aim of this study was to compare the efficacy of the surgeon's experience and autofluorescence-guided bone surgery to delimit resection margins for necrotic bone.

Materials and Methods: MRONJ requiring surgical treatment was classified according to American Association of Oral and Maxillofacial Surgeons staging. To detect vital bone and resection margins, patients of each stage were randomly assigned to 1 of 2 surgical groups: an autofluorescence-guided surgery (AF) group and a conventional surgery (non-AF) group based on the surgeon's experience. Bone samples from the 2 groups were analyzed histopathologically. The main outcomes were defined as the absence of bone exposure or infection at the time of evaluation. Infection was defined as the presence of swelling, pain, or numbness in the area. Measurements were collected preoperatively and 1 week, 1 month, 6 months, and 1 year after surgery. Statistical analysis included descriptive statistics and the Fisher exact test to evaluate eventual differences between the 2 surgical protocols.

Results: The 36 patients (21 women and 15 men) included in this study were equally divided into 2 groups according to the surgical protocol: 18 patients in the non-AF group and 18 in the AF group. Thirty-nine lesions were included in this analysis: 20 lesions in the non-AF group and 19 in the AF group. Histopathologic examination confirmed the necrotic nature of all bone samples. Statistical analysis showed no differences in necrotic bone exposure or signs of infections between the 2 surgical protocols at different times (P > .05).

Conclusions: Although the VELscope appears to be useful in guiding bone resection margins in patients with MRONJ, autofluorescence does not appear to be superior to conventional surgical techniques in mucosal healing and quality of life.

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Medication-related osteonecrosis of the jaw (MRONJ) is a recurring complication in patients treated with bisphosphonates and other antiresorptive drugs such as denosumab or antiangiogenic drugs. These drugs are widely used in the prevention and treatment of bone metastasis and other diseases that alter bone structure, such as osteoporosis, Paget disease, and malignant hypercalcemia. Clinically, MRONJ is characterized by necrotic lesions with bacterial superinfection that causes persistent bone exposure within the oral cavity for a minimum period of 8 weeks and progressive involvement of the jaws.

There are many opinions about the best treatment for patients with MRONJ. In its position paper, the American Association of Oral and Maxillofacial Surgeons (AAOMS) performed MRONJ staging to define the most appropriate treatment for each degree of severity.^{2,4} However, many studies have analyzed the effectiveness of surgical and conservative treatment.⁸ Various investigators have concluded that conservative treatment is indicated for lower stages of the disease and that a surgical strategy should be reserved for the most serious cases. 9-11 In contrast, other studies have found that surgery is a paramount choice in patients with a high degree of MRONJ to remove exposed necrotic bone, but that it is equally necessary for less serious cases to limit bone removal and avoid other pathologic consequences. 12 Furthermore, conservative therapy alone hinders progression of the disease and relieves symptoms but does not act on the cause. 13-16

When osteonecrosis is present, surgical treatment is paramount, especially in patients undergoing injective therapy. Wucosal integrity and bone exposure can affect quality of life independently from infection or pain. Complete removal of necrotic bone is the main goal of surgical treatment and an incomplete sequestrectomy easily leads to recurrence. 12,16,18,19 In contrast, healthy bone should be preserved to avoid other pathologic consequences. There is a wide debate on the best surgical method to define the margins of the osteonecrosis.

Although several radiologic examinations can be supportive, ²⁰ many investigators have considered bone fluorescence a useful method to distinguish viable from necrotic bone. ²¹⁻²³

In the treatment of MRONJ, recent studies have shown promising results for fluorescence-guided bone surgery. ^{24,25} This technique is easy to perform, reproducible, and highly standardized. ¹²

In particular, during surgical debridement, the VELscope (visually enhanced lesion scope) fluorescence lamp (LED Dental, White Rock, BC, Canada) can be used intraoperatively as a guide for delimiting resection margins of necrotic bone in patients with MRONJ. Using direct fluorescence, the VELscope facilitates early recognition and management of lesions that are not clinically visible.

Its light emission excites specific amino acids of collagen. ²⁶ In physiologic conditions, these natural fluorochromes react, exhibit marked autofluorescence, and highlight the presence of vital bone. Conversely, pathologic tissues are characterized by a loss of autofluorescence and appear much darker than the surrounding areas. ^{12,27-29}

Some investigators have published promising results for this technique aiding surgeons in the complete removal of necrotic bone. ¹⁷ It provides an objective and reproducible tool to establish the transition between vital and necrotic bone during surgical procedures.

Because the surgeon's experience in detecting vital and necrotic bone is traditionally used for surgical treatment of MRONJ,³⁰ it would be interesting to evaluate the usefulness of only autofluorescence in bone surgery using the VELscope device.

The aim of this study was to evaluate the efficacy of autofluorescence-guided bone surgery compared with conventional surgery based on the surgeon's experience to delimit resection margins for necrotic bone in patients with MRONJ, with the success rate based on the absence of infection and bone exposure at scheduled follow-up examinations.

Materials and Methods

STUDY SAMPLE AND VARIABLES

This study followed the Declaration of Helsinki on medical protocol and ethics and the regional ethical review board of Central Calabria (reference for the Magna Graecia University of Catanzaro, Catanzaro, Italy) approved the study. A specific informed consent form was prepared and successively submitted to patients included in the protocol. The study was designed as a prospective randomized monocentric clinical trial.

From April 2015 to May 2016, patients with MRONJ requiring surgical treatment were enrolled in the study. MRONJ was classified according to the AAOMS staging (Table 1).²

Although the sample size was not calculated because of the preliminary concept of this study, 36 enrolled patients formed a relevant sample. To create a homogeneous study population, each surgical group included the same number of patients with the same severity of MRONJ lesions. Patients with stage 1 MRONJ were surgically treated when they showed no improvement after a conservative approach using systemic antimicrobial therapy and topical antiseptic treatment. Patients of each stage were randomly assigned to 1 of 2 surgical groups by an independent resident senior. The first group was the

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