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Sexual desire, mood disorders and sleep disturbances in female BMS patients: A controlled study

Stefania Leuci 1 | Noemi Coppola 1 | Daniela Adamo 1 | Felice Crocetto 2 | Biagio Barone 2 | Stefania Baldares 1 | Federica Canfora 1 | Michele Davide Mignogna¹

Correspondence

Felice Crocetto, Department of Neuroscience, Reproductive and Odontostomatological Sciences, Urology and Andrology Unit, School of Medicine, University of Naples Federico II, Via Sergio Pansini 5, 80131 Naples, Italy. Email: felice.crocetto@unina.it

Abstract

Background: Burning mouth syndrome is a chronic orofacial pain with intraoral burning and other oral dysaesthetic symptoms that significantly affects the quality of life. The aim of this study is to evaluate the sexual desire in women with BMS and to investigate the possible related factors.

Methods: A case-control study was performed. BMS patients were enrolled according to the International Classification of OroFacial Pain criteria. Demographic variables were collected. We evaluated pain with the Numeric Rating Scale (NRS), Visual Analogue Scale (VAS) and Total Pain Rating Index (T-PRI), anxiety and depression using the Hospital Anxiety and Depression Scale (HADS-A e HADS-D), sleep disturbances with Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS), and sexual desire using Sexual Desire Inventory (SDI).

Results: A total of 50 BMS women and 50 healthy controls were enrolled. Compared with the controls, the BMS patients showed higher scores in the NRS (7,81 ± 1,71 vs. 0,14 \pm 0.40; p < 0.0001), TPR-I (10,50 \pm 4,86 vs. 0,36 \pm 1,06; p < 0.0001), HADS-A (11,86 \pm 2,85 vs. 3,90 \pm 2,81; p < 0.0001), HADS-D (8,04 \pm 3,18 vs. 1,42 \pm 1,86; p < 0.0001) and PSQI (9,04 \pm 2,62 vs. 4,64 \pm 3,27; p < 0.0001). The mean SDI in the study group was significantly lower compared to healthy controls $(32,36 \pm 14,45 \text{ vs. } 69,70 \pm 19,94; p < 0.0001)$. No correlation was found between SDI and others items explored.

Conclusion: In line with previous studies, anxiety, depression and sleep disturbances are more common in BMS patients than in healthy population. This pilot study demonstrates for the first time an association between BMS and low sexual desire.

KEYWORDS

BMS, orofacial chronic pain, quality of life, sexual desire

Stefania Leuci and Noemi Coppola contributed equally to this manuscript.

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¹Department of Neuroscience, Reproductive and Odontostomatological Sciences, Oral Medicine Unit, University of Naples Federico II, Naples, Italy

²Department of Neuroscience, Reproductive and Odontostomatological Sciences, Urology and Andrology Unit, University of Naples Federico II, Naples, Italy

1 | INTRODUCTION

Chronic orofacial pain is one of the main reasons for which patients need medical assistance, representing about 10% of pain in the orofacial region. Among painful cranial neuropathy, burning mouth syndrome (BMS) is included. 1 It is a well-known chronic painful condition (>3 months), characterized by burning or other dysaesthetic sensations in absence of clinical examination findings. The prevalence of BMS range between 1,7% and 3,7% in the general population, with a higher prevalence in women.² Besides burning, BMS patients also complain of xerostomia, itching, stinging, pain, dysgeusia, sand sensation, and paresthesia.² Any intraoral site can be involved; of all the oral mucosa, the tongue appears to be the one most frequently involved site, followed by lips and palate.³ Although the pathogenesis of BMS is still unclear, the role of central and peripheral neuropathy in the onset of the disease is widely documented.⁴ Also psychological factors play a key role in the development of BMS and various studies reported the associations between BMS and mood disorders and/or sleep disturbances. 5,6 Therefore, the quality of life of affected patients is poor compared to the general population. In addition to intraoral discomfort, anxiety, depression and sleep disturbances, also the overlap of multiple chronic painful conditions, are already documented in literature, 7,8 and a reduction in sexual desire (SD) can drastically worsen the quality of life. In fact, sexuality contributes significantly to quality of life and well-being. SD is part of sexual dysfunction that encompasses also orgasmic dysfunction, ejaculatory dysfunction, and sexual pain-penetration disorder. Sexual problems are multifactorial; biological, psycological and socio-cultural factors are involved in the genesis of sexual dysfunction. The type of sexual dysfunction changes according to gender; among men, premature ejaculation and erectile dysfunction are the most common sexual dysfunctions, while for women, the loss of SD is the most frequent sexual problem. 11 The correlation between changes in SD and chronic pain is known; in fact, an association has been reported between low SD and low back pain, fibromyalgia, chronic pelvic pain, and others chronic illnesses, such as celiac disease. 12-14 However, the link between sexual dysfunction and chronic pain, that in most cases is associated with mood disorders, is not yet well known. Considering that the prevalence of sexual dysfunction in patients with chronic pain is high and its negative impact on quality of life, the aim of this study was to investigate the presence of low SD among female BMS patients compared to healthy controls. Furthermore, we explored possible factors that can influence SD in patients with BMS, that is, pain intensity, anxiety, depression and sleep disorders.

2 | MATERIAL AND METHODS

2.1 | Study design

This was a prospective, observational and descriptive case-control study carried out at the Oral Medicine Unit, Federico II University of Naples, between October 2021 and March 2022. The study protocol

was approved by the local Ethics Committee (No. 125/19). It was conducted according to the guidelines of the World Medical Association Declaration of Helsinki (World Medical Association, 2013) and follows STROBE guidelines for the reporting of observational studies.

2.2 | Participants

BMS patients and healthy controls, matched by age and gender, were consecutively enrolled during their first visit with an oral medicine specialist and a general dentist respectively. The general procedure and requirements were explained and written informed consent was obtained from all participants. Potentially eligible participants were identified on the basis of the following inclusion and exclusion criteria.

The inclusion criteria for BMS group were as follows:

- 1. Female >18 years old
- 2. Patients to have been in a sexual relationship for >1 year
- 3. Diagnosis of BMS according to the International Classification of OroFacial Pain criteria for the study group (Table 1)
- 4. No abnormalities in laboratory findings
- 5. No history of psychiatric disorder

The inclusion criteria for healthy controls were as follows:

- 1. Female >18 years old
- 2. Patients without oral lesions
- 3. Patients without a history of BMS
- 4. No abnormalities in laboratory findings
- 5. Patients without a history of treatment with psychotropic drugs

The exclusion criteria for both groups were as follows:

- 1. <18 years old
- Pregnancy or menopause, due to the very frequent onset of menopausal-related sexual problems
- Comorbidities such as diabetes-mellitus, urinary infection or other genito-urinary diseases that could have altered their sexual function during the previous month
- 4. History of urologic or pelvic surgery

TABLE 1 Diagnostic criteria of BMS from the International Classification of OroFacial Pain

- A Oral pain fulfilling criteria B and C
- B Recurring daily for >2 h per day for >3 months
- C Pain has both of the following characteristics:
 - 1. Burning quality
 - 2. Felt superficially in the oral mucosa
- Oral mucosa is of normal appearance, and local or systemic causes have been excluded
- E Not better accounted for by another ICOP or ICHD-3 diagnosis

5. Use of psychotropic drugs in the past 3 months

The sociodemographic and medical data and BMS characteristics of the patients were recorded during a standardized interview. Each participant in the study underwent a conventional oral examination to rule out other oral diseases. Afterwards, the following questionnaires were administered anonymously prior to the beginning of ant treatment for BMS.

2.3 | Sexual desire

The "Sexual Desire Questionnaire 2" (SDI-2) was used. The SDI-2 is a self-report tool to assess dyadic and solitary SD comprising 13 items: three items measure the frequency of sexual thoughts ranging from "not at all" (0) to "many times a day" (7), ten items measure subjective SD rated on an 8-point Likert scale ranging from "no desire" (0) to "strong desire" (8). The total score can range from 0–101 and higher scores indicate higher SD.

2.4 Depression and anxiety

The "Hospital Anxiety and Depression Scale" (HADS) is a self-assessment scale to detect states of depression and anxiety in patients in non-psychiatric settings. HADS consists of two subscales: HADS-A for anxiety with 7 items and HADS-D for depression with 7 items. The patients rate each item on a 4-point Likert scale with a range from 0 ("not at all") to 3 ("most of the time"). The total score can range from 0 to 21 for each subscale and higher scores indicate greater severity with the following interpretation: 0–7 normal, 8–10 possible case, 11–21 probable case of mood disorder.

2.5 | Sleep

The "Pittsburgh Sleep Quality Index" (PSQI) and the "Epworth Sleepiness Scale" (ESS) were used. The PSQI is a self-report questionnaire that measures sleep quality over the previous month. It consists of seven domains with a total of 19 items. For each domain, the score can range from 0 (no difficulty) to 3 (severe difficulty). The sum of the single domains produces a global score of sleep quality that ranges from 0 to 21 and a score >5 is an indicator of sleep disturbance. The ESS is a self-administered questionnaire to measure the subject's general level of daytime sleepiness consisting of eight items on a 4-point Likert scale (0–3). The ESS score can range from 0 to 24, where a cutoff of >10 represents greater daytime sleepiness.

2.6 | Pain

The "Numerical Rating Scale" (NRS) and the "Visual Analogue Scale" were used to assess pain or discomfort. The NRS is a horizontal line

TABLE 2 Sociodemographic characteristics and risk factors of the sample

| Demographic variables | BMS patients | Healthy controls | | | |
|-----------------------------------|-----------------|---------------------|--|--|--|
| Age (mean years ± SD) | 45,68 ± 6,7 | 44,56 ± 7,11 | | | |
| Education level (mean years ± SD) | 14,52 ± 2,66 | 14,52 ± 3,63 | | | |
| Job status (n; %) | | | | | |
| Employed | 25 (50) | 35 (70) | | | |
| Housewife | 16 (32) | 6 (12) | | | |
| Unemployed | 7 (14) | 8 (16) | | | |
| Retired | 1 (2) | 0 | | | |
| Students | 1 (2) | 1 (2) | | | |
| Body mass index (mean ± SD) | 24,74 ± 3,98 | 23,6 ± 3,11 | | | |
| Risk factors (n; %) | | | | | |
| Smoking status | | | | | |
| Yes | 14 (28) | 15 (30) | | | |
| No | 36 (72) | 35 (70) | | | |
| Alcohol consumption | | | | | |
| No | 37 (74) | 44 (88) | | | |
| Yes | 13 (26) | 6 (12) | | | |

with a single 11-point numeric scale in which 0 represents "no pain" and 10 "worst pain imaginable". Scores range from 0–10 and higher scores indicate greater pain intensity. The "Total Pain Rating Index" (T-PRI) is a measure of the quality of pain. It consists of 15 items from the original McGill Pain Questionnaire and each item ranges from 0 to 3. The total score of T-PRI can range from 0 to 45 and a higher score indicates worse pain.

2.7 | Statistical analysis

All data were collected and subjected to statistical analysis performed with SPSS software (version 25, SPSS Inc., Chicago, IL). Descriptive statistics of the two cohorts were obtained using t-test for independent samples for continuous variables, reporting means and standard deviation, while Fisher exact test was used for categorical variables, reporting absolute numbers and percentages. We successively used one-tailed Mann–Whitney U test on total scores of the compiled questionnaires in order to compare BMS patients versus healthy controls. Statistical significance was assumed for p < 0.05.

3 | RESULTS

A total of 50 female BMS patients and 50 healthy controls were enrolled in the study. All patients successfully completed both questionnaires autonomously. The sociodemographic characteristics of both groups are reported in Table 2. There are no statistically significant differences in relation to marital status, years of education, risk

TABLE 3 Frequency of underlying systemic diseases and concomitant drugs used in BMS patients and healthy controls

| | , | | | | |
|---------------------------|---|--------------------------------------|--|--|--|
| | BMS patients frequency (%) | Healthy controls frequency (%) | | | |
| Systemic diseases | | | | | |
| Hypertension | 12 (24) | 8 (12) | | | |
| Hypercholesterolemia | 12 (24) | 3 (6) | | | |
| Cardiovascular diseases | 5 (10) | - | | | |
| Diabetes | 2 (4) | - | | | |
| Respiratory diseases | 1 (2) | 1 (2) | | | |
| Gastrointestinal diseases | 6 (12) | 2 (12) | | | |
| Endocrinopathies | 9 (18) | 16 (32) | | | |
| Malignancies | 5 (10) | 2 (12) | | | |
| Neurological diseases | - | 1 (2) | | | |
| Others | 16 (32) | 3 (6) | | | |
| Drugs | | | | | |
| Antihypertensives | 16 (32) | 8 (12) | | | |
| Simvastatin | 6 (12) | 3 (6) | | | |
| Metformin | 1 (2) | - | | | |
| Antiplatelets | 2 (4) | - | | | |
| Oral anticoagulant | 2 (4) | - | | | |
| Bisphosphonates | 1 (2) | - | | | |
| Levothyroxine sodium | 11 (20) | 10 (22) | | | |
| Proton pump inhibitors | 9 (18) | 3 (6) | | | |
| Others | 2 (4) | 4 (8) | | | |
| | | | | | |

factors, such as smoking and alcohol, and employment between the two groups.

The systemic diseases of the study participants and the drugs used are summarized in Table 3. The most frequent comorbidity was essential hypertension for patients and controls without statistically significant differences between patients and healthy controls.

The frequency and the location of the oral symptoms for BMS patients are the following: oral burning was found in 40 patients (80%); of these, in 7 patients (14%) oral burning was found as single symptom. Thirty patients (60%) reported at least two additional oral symptoms. The most frequently involved sites in patients who complain of burning were the tongue (28 pts), lips (14 pts) and palate (12 pts).

NRS, T-PRI, HADS-A, HADS-D, PSQI and SDI scores showed a statistically significant difference between the BMS patients and controls (*p*-value <0.001). No significant statistical difference was found in relation to ESS (*p*-value 0.249) (Table 4).

The majority of BMS patients showed a higher score in the intensity and quality of pain (NRS 7.81 \pm 1.71; TPR-I 10.50 \pm 4.86), borderline abnormal/abnormal score for anxiety (HADS-A 11.86 \pm 2.85) and depression (HADS-D 8.04 \pm 3.18). Sleep disturbances were reported in 47 BMS patients (94%) and in 21 healthy controls (42%) (9.04 \pm 2.62 vs. 4.64 \pm 3.27; *p*-value <0.001).

The analysis of SDI showed a significantly lower SD in BMS patients than in the control group. Overall, the mean score of SDI was 32.26 ± 14.45 for BMS patients versus 69.70 ± 19.94 for healthy controls (*p*-value <0.001) (Table 4).

There is no significant correlation between SDI and total scores of the NRS, T-PRI, HADS-A, and HADS-D (Table 5).

4 | DISCUSSION

In this study, we investigated whether BMS could be associated with sexual disorders. To the best of our knowledge, this is the first study that explores the impact of BMS on SD. Interestingly, the results showed significantly lower SD scores in women with BMS when compared with healthy control women. This supports the hypothesis that BMS can negatively affect the sexual life. In line with the literature, 15 in our cohort the most common symptom was burning, and the most frequently involved site was the tongue. A very high score in pain intensity was found in our patients, demonstrating that the intensity of "pain" is the key symptom. In according with the literature our results showed a higher prevalence of anxiety, depression, and sleep disturbance in BMS group than in the control group. In fact, several studies reported mood disorders in BMS patients, highlighting that psychological factors are directly associated with BMS. 3,16,17 The results of our study showed that among BMS patients a higher proportion of women experienced lack of/low SD compared with healthy women. Our data did not indicate a link between SD and anxiety, depressive symptoms, and sleep disturbances, but exclusively between BMS and SD. It is reasonable to hypothesize that the high incidence of anxiety, depression and sleep disorders in our cohort of patients biased the statistical correlation between these data and SD. Moreover, the limited sample size could contribute to the lack of statistical significance. On the contrary, statistical data, if confirmed by further studies, could indicate that BMS has a negative impact on SD in an independent manner with a still unknown pathogenetic pathway. So, this study provides clear insights into the association of BMS with low SD; however, the underlying pathophysiologic mechanisms are unclear. The hypoactive SD disorder is the most prevalent female sexual dysfunction with a prevalence ranging from 7 to 12% in the general population. 18 Low libido is associated with poor health-related quality of life, an altered emotional state with the prevalence of negative feelings and less happiness.¹⁹ Although the decrease in SD is multidetermined, being the result of biological, environmental, sociological processes, the psychological factors play a key role. 18,19 In fact, several studies showed an association between low SD and emotional disorders, including depression, anxiety, and fatigue. 19,20 These comorbidities are shared with many chronic conditions; in fact, sexual dysfunction in chronic pain, such as low back pain and fibromyalgia, is widely documented. 12,13,21 The relationship between sexual dysfunction, psychological variables, and chronic pain is complex, as well as the reasons for the association. Most of the studies focused on a bidirectional relationship between mood disorders linked to chronic pain and SD,

| | BMS patients mean ± SD | Healthy controls mean ± SD | p-value |
|--------|------------------------|----------------------------|---------|
| NRS | 7,81 ± 1,71 | 1,14 ± 0,40 | <0.001 |
| VAS | 7,59 ± 1,79 | 1,18 ± 0,44 | <0.001 |
| T-PRI | 10.50 ± 4.86 | 1,36 ± 1,06 | <0.001 |
| HADS-A | 11,86 ± 2,85 | 3,90 ± 2,82 | <0.001 |
| HADS-D | 8,04 ± 3,18 | 1,42 ± 1,86 | <0.001 |
| PSQI | 9,04 ± 2,63 | 4,64 ± 3,27 | <0.001 |
| ESS | $3,94 \pm 2,68$ | $5,02 \pm 3,69$ | 0.249 |
| SDI | 32.26 ± 14.45 | 69.70 ± 19.94 | <0.001 |

TABLE 4 Current prevalence of pain, mood, anxiety, sleep disturbances, and sexual desire in the study groups

Abbreviations: ESS, Hospital Anxiety and Depression Scale; HADS-A, Hospital Anxiety and Depression Scale- Anxiety; HADS-D, Hospital Anxiety and Depression Scale- Depression; NRS, Numerical Rating Scale; PSQI, Hospital Anxiety and Depression Scale; SD, standard deviation; SDI, Sexual Desire Inventory; TPR-I, Total Pain Rating Index; VAS, Visual Analogue Scale.

TABLE 5 Pearson's correlations between sexual desire and four variables: pain, anxiety, depression, sleep disorders

| | r curson's correlations between sexual desire and roar variables, party anxiety, depression, steep disorders | | | | | | | | |
|--------|--|--------|---------|---------|---------|---------|---------|-------|--------|
| | | SDI | NRS | VAS | HADS-A | HADS-D | T-PRI | PSQI | ESS |
| SDI | Pearson correlation | 1 | -0.051 | -0.057 | 0.104 | 0.083 | -0.115 | 0.043 | -0.216 |
| | Sig. (2-tailed) | | 0.726 | 0.695 | 0.470 | 0.568 | 0.425 | 0.765 | 0.132 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| NRS | Pearson correlation | -0.051 | 1 | 0.820** | 0.147 | 0.082 | 0.170 | 0.202 | -0.023 |
| | Sig. (2-tailed) | 0.726 | | 0.000 | 0.308 | 0.571 | 0.238 | 0.160 | 0.877 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| VAS | Pearson correlation | -0.057 | 0.820** | 1 | 0.214 | 0.179 | 0.281* | 0.143 | -0.006 |
| | Sig. (2-tailed) | 0.695 | 0.000 | | 0.136 | 0.213 | 0.048 | 0.323 | 0.969 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| HADS-A | Pearson correlation | 0.104 | 0.147 | 0.214 | 1 | 0.455** | 0.394** | 0.053 | -0.151 |
| | Sig. (2-tailed) | 0.470 | 0.308 | 0.136 | | 0.001 | 0.005 | 0.717 | 0.297 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| HADS-D | Pearson correlation | 0.083 | 0.082 | 0.179 | 0.455** | 1 | 0.177 | 0.266 | 0.017 |
| | Sig. (2-tailed) | 0.568 | 0.571 | 0.213 | 0.001 | | 0.219 | 0.062 | 0.907 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| T-PRI | Pearson correlation | -0.115 | 0.170 | 0.281* | 0.394** | 0.177 | 1 | 0.126 | 0.163 |
| | Sig. (2-tailed) | 0.425 | 0.238 | 0.048 | 0.005 | 0.219 | | 0.382 | 0.257 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| PSQI | Pearson correlation | 0.043 | 0.202 | 0.143 | 0.053 | 0.266 | 0.126 | 1 | 0.160 |
| | Sig. (2-tailed) | 0.765 | 0.160 | 0.323 | 0.717 | 0.062 | 0.382 | | 0.268 |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| ESS | Pearson correlation | -0.216 | -0.023 | -0.006 | -0.151 | 0.017 | 0.163 | 0.160 | 1 |
| | Sig. (2-tailed) | 0.132 | 0.877 | 0.969 | 0.297 | 0.907 | 0.257 | 0.268 | |
| | N | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| | | | | | | | | | |

^{**}Correlation is significant at the 0.01 level (2-tailed).

affecting both the quality of life.^{21,22} Undoubtedly, the psychological distress associated with chronic pain affects the sexual life, but other mechanisms may also be at the basis of this association. In recent decades, some studies highlighted the role of central nervous system dysfunctioning in the pathogenesis of BMS, in addition to psychological cause and alterations in the peripheral nervous systems.^{23,24} The structure and brain function of BMS patients was explored with

functional magnetic resonance imaging (fMRI), displaying anatomical and functional changes in the bilateral ventromedial prefrontal cortex, in the anterior cingulate gyrus, in the bilateral thalamus, insula/frontal operculum and in the amygdala. ^{25,26} The majority of BMS subjects showed grey matter changes in the pain matrix. ²⁷ Sexual behavior is regulated by complex interactions of central and peripheral nervous system. Over the ages, the neural mechanisms underlying sexual

^{*}Correlation is significant at the 0.05 level (2-tailed).

behavior have been elucidated. Different brain areas are involved in human sexuality: thalamus, hypothalamus, amygdala, septal region, prefrontal cortex, cingulate cortex, and insula.^{28,29} As stated above, in BMS patients the same brain regions can be affected. Therefore, the low SD in BMS patients could be due to a dysfunction in brain reward systems. Our study is the first to show an association between BMS and low SD. Also, based on the data present in the literature about the pathogenesis of the two disorders, our hypothesis is that the co-occurrence of BMS and reduction of SD is the result of a multifactorial process. Concluding, central neurological alterations shared between the two pathologies, psychological factors and hormonal mediators may be responsible for this association. In fact, as confirmed in the literature, the impairment of mental health plays a key role in SD; in particular, low SD is linked to depression and anxiety. To date, the relationship between sexual dysfunction and psychotic disease is controversial.²⁰ It is well known that BMS patients can experience varying degrees of psychiatric illness, particularly anxiety and depression. So, the reduction of SD in patients with BMS could be an expression of the underlying psychiatric disease, responsible, together with the complex mechanism of interactions described above, for the onset of the BMS. However, some limitations in our study should be noted. First, the low number of patients. Second, we only used the SDI in the absence of other tools to investigate sexual function, including orgasmic function. Third, we have not explored marital satisfaction that affects sexuality. This study is a preliminary investigation, further studies with a larger sample size are needed and the possible association between mood disorders, sleep disturbances and SD in BMS patients must be further investigated. Moreover, studies are underway on the effect of BMS therapy on SD.

5 | CONCLUSION

The results of our study suggest that the female patients with BMS could be investigated concerning sexual health to early diagnose sexual dysfunction, in order to improve treatments and patients' overall health and quality of life. Concluding, the new insights into chronic pain patient suffering make clear once more why clinical management could be intellectually and emotionally complex dealing with the most concealed aspect of human heart. Continuing education, collaboration between specialists, and multidisciplinarity are needed.

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ETHICS APPROVAL

The study protocol was approved by the local Ethics Committee No. 125/19.

AUTHOR CONTRIBUTIONS

Conceptualization, Felice Crocetto and Noemi Coppola. Methodology, Stefania Leuci and Noemi Coppola. Software, Biagio Barone, Federica

Canfora, and Stefania Baldares. Validation, Michele Davide Mignogna and Stefania Leuci. Formal Analysis, Biagio Barone and Stefania Baldares. Investigation, Felice Crocetto, Noemi Coppola and Daniela Adamo. Resources, Noemi Coppola and Felice Crocetto. Data Curation, Biagio Barone, Federica Canfora, and Daniela Adamo. Writing – Original Draft Preparation, Stefania Leuci and Noemi Coppola. Writing – Review & Editing, Michele Davide Mignogna and Stefania Leuci. Visualization, Stefania Leuci. Supervision, Stefania Leuci and Michele Davide Mignogna. All authors gave final approval and agree to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Noemi Coppola https://orcid.org/0000-0002-0030-3621

Daniela Adamo https://orcid.org/0000-0002-3784-4229

Felice Crocetto https://orcid.org/0000-0002-4315-7660

Federica Canfora https://orcid.org/0000-0002-4610-6690

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