Morning awakening with headache: Association with somatization and depression in craniomandibular disorders and bruxing behavior subjects.

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Abstract:
Introduction: Morning awakening with headache and facial pain are common disturbances in patients with craniomandibular disorders and sleep bruxing behavior. There is paucity of studies regarding etiology and mechanisms of these disorders.

Goals: Test the hypothesis that scores in depression and somatization and greater number of painful sites on awakening in the morning are observed more frequently in those subjects with Craniomandibular Disorder, bruxing behavior and current history of morning awakening with headache as compared to those with no Craniomandibular Disorders and no current history of morning awakening with headache.

Methods: Clinical examination and self-report, description and history of the chief complaint, a set of questionnaires, the Beck Depression Inventory, The Rief and Hiller instrument, criteria for sleep, mixed, daytime bruxing behavior and for Craniomandibular disorders were used to evaluate Craniomandibular Disorders and bruxing behavior subjects reporting morning awakening with headache (n=50), Craniomandibular Disorders and Bruxing Behavior subjects without morning awakening with headache (n=50) and subjects with no Craniomandibular Disorders and no history of morning awakening with headache (n=57). Kruskal-Wallis statistics with Dunn’s and Tukey-Kramer Multiple comparison test were used to analyze data.

Results: Mean depression scores were about 16.3 (SD=6.4, range=7–33); 15.6 (SD=6.7, range=5–35), and 7.2 (SD=5.3, range=0–19) in the subgroups with Craniomandibular Disorders with bruxing behavior and morning awakening with headache, Craniomandibular Disorders, bruxing behavior no awakening with headache and No Craniomandibular Disorders No awakening with headache, respectively. Tukey-Kramer multiple comparison test (p<0.0001): Craniomandibular disorders + Bruxing Behavior + Awakening with headache subgroup versus Craniomandibular Disorders + Bruxing Behavior No awakening with headache subgroup (p<0.05); Craniomandibular Disorders + Bruxing Behavior + Morning awakening with headache subgroup versus No Craniomandibular Disorders No awakening with headache subgroup (p<0.001); Craniomandibular Disorders + Bruxing Behavior No awakening with headache subgroup versus No Craniomandibular Disorders No awakening with headache subgroup (p<0.001). Mean scores in somatization were as follows: Craniomandibular Disorders + Bruxing Behavior + Morning awakening with headache subgroup : 13.7, SD=3.8, range=8–21; Craniomandibular Disorders + Bruxing Behavior No Awakening with Headache subgroup: 13.2, SD=4.7, range=7-28; No Craniomandibular Disorders no Awakening with Headache subgroup: 5.4, SD=3.4, range=0-11. Kruskal-Wallis statistics (p<0.0001), an extremely significant difference: Craniomandibular Disorders + Bruxing Behavior + Morning awakening with headache subgroup versus Craniomandibular Disorders + Bruxing Behavior No awakening with headache subgroup (p<0.05); Craniomandibular Disorders + Bruxing Behavior + morning awakening with headache subgroup versus No Craniomandibular Disorders No morning awakening with headache subgroup (p<0.001); Craniomandibular Disorders + Bruxing Behavior No Awakening with headache subgroup versus No Craniomandibular Disorders No Awakening with Headache subgroup (p<0.001). Mean scores in pain sites on awakening in the morning were as follows: Craniomandibular Disorders + Bruxing Behavior + Morning awakening with headache subgroup 8.1 (SD=1.9, range 6–13); Craniomandibular Disorders + Bruxing Behavior No morning awakening with headache subgroup 7.0 (SD=2.2, range=4–12); No Craniomandibular Disorders No morning awakening with headache subgroup (1.5, SD=1.4, range=0–4). Kruskal-Wallis and Dunn’s statistics (p<0.0001), an extremely significant difference: Craniomandibular Disorders + Bruxing
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Behavior + Morning awakening with headache subgroup versus Craniomandibular Disorders + Bruxing Behavior No morning awakening with headache subgroup (p>0,05); Craniomandibular Disorders + Bruxing Behavior + Morning awakening with headache subgroup versus No Craniomandibular Disorders No Awakening with headache subgroup (p<0,001); Craniomandibular Disorders + Bruxing Behavior No morning awakening with headache subgroup versus No Craniomandibular Disorders No morning awakening with headache subgroup (p<0,001).

Conclusion: CMDs subjects with sleep or mixed bruxing behavior demonstrated higher scores in depression, somatization and painful sites as compared with the control subgroup. Craniomandibular disorders and bruxing behavior subjects reporting awakening with headache did not present higher scores in depression, somatization and painful sites as compared to those with Craniomandibular Disorders, bruxing behavior but without morning awakening with headache.

Keywords: Craniomandibular Disorders, Bruxing Behavior. Depression. Somatization. Morning Awakening with Headache.

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I. Introduction

Craniomandibular Disorders (CMDs) is a set of collective terms used in Dentistry and Medicine to describe a number of clinical signs and symptoms involving the masticatory muscles (MM), temporomandibular joints (TMJs) and adjacent anatomic musculoskeletal structures, resulting in very specific signs and symptoms including a complaint of pain, impaired jaw movements, joint noises, tenderness to palpation and headache.[1] It has been reported that a number of factors contribute to the development of CMDs being bruxing behavior (BB) one of the most common pathological elements responsible for a number of signs and symptoms in many components of the stomatognathic system.[2] BB is a very complex oral jaw behavior described as the habit of grinding, clenching, bracing or gnashing the teeth with no functional purposes usually observed at night and/or during the day. BB is also defined as a complex motor and neurophysiological disorder thought to occur in different stages of sleep.[3] Because strong forces can be applied on many components of the masticatory system, BB may affect many muscles of the craniofacial complex, shoulder and neck structures innervated by the trigemino-cervical complex.

Depression is a very common psychological and/or psychiatric disorder characterized by displeasure, sadness, pessimism, loss of energy and vitality, retardation, lowered social interest and a certain neglect in interpersonal relationships and is often associated with a low threshold for stress and anxiety[4]. CMDs and myofascial pain (MPD) patients usually feel overwhelmed and demoralized from the perception of helplessness, hopelessness and lack of control over their symptoms including pain[4]. Depression is observed frequently in MPD and CMDs patients.[6,5] Somatization is defined as the tendency of some “psychosomatic” individuals to experience and communicate psychological distress in the form of bodily symptoms which encourage those patients to seek frequent medical help. Somatization is also defined as the transformation of psychological conflicts into bodily complaints. Subjects’ symptoms usually represent a powerful intra-psychic defense against emotional and psychological instability.[6]

The study of nocturnal BB has experienced a dramatic increase in dental and medical interest in the last 20 years. Because diurnal and nocturnal BB may cause a number of signs and symptoms adjacent and far from the masticatory system, such observation has encouraged experimental and clinical studies to evaluate signs and symptoms, mechanisms, the role of somatization and even pharmacological management of this disorder. Awakening with headache, facial and TMJ pain, insomnia and even somatization are now being studied in depth so as to establish the role of somatization on sleep BB and how sleep BB may contribute to the development of pain in many anatomic areas in the cranial facial and cervical complex. Waking up with headache is traditionally associated with sleep disorders[3]. There may be a close association between headache of the common migraine type, sleep BB and depression[8]. However, there is a paucity of studies correlating sleep BB, somatization, depression, morning awakening with headache and facial pain. Thus, this study is aimed at:

1. Test the hypothesis that CMDs and BB subjects reporting morning awakening with headache demonstrate higher scores in depression, somatization and painful sites as compared with CMDs and BB with no awakening with headache subjects and with No CMDs no awakening with headache individuals.
II. Material and Methods

Sample
Clinical charts from patients referred consecutively to the Department of Orofacial Pain UNIRG University Dental School, are usually stored into a database for future studies of variables of specific interest. All referred patients were evaluated by a specialist in the field (OFM). Some pre-requisites were used to store clinical charts in the database are the following: 1) Patients should be examined comprehensibly by a specialist, 2) Examination should follow diagnostic criteria accepted in the field of orofacial pain and CMDs, for instance, criteria for CMDs and BB, 3) Only those cases with complete information should be stored in the database, 4) Psychological tests used for depression anxiety, somatization and others should be those widely accepted to gather psychological information, for instance, BDI, TMAS and so forth, 5) Examination in every subject follows the same protocol and subjects sign a formal consent allowing researchers to use their material in future studies. Following these guidelines, we retrieved the first 50 clinical charts of patients presenting information about morning awakening with pain, BB and CMDs (subgroup CMDs+ BB+ AHWA+); 50 clinical charts with information about CMDs, BB and no morning awakening with headache (subgroup CMDs+ BB+ No AWHA) and 57 clinical charts from subjects with no signs and symptoms of CMDs, BB and no personal report of morning awakening with headache (subgroup No CMDs No AHWA). These 157 charts were reviewed retrospectively. In these three subgroups of subjects, data about depression, somatization and painful sites on awakening in the morning, was obtained. All patients were examined initially as clinical cases and stored, then, their clinical charts were retrospectively reviewed by the same examiner (OFM).

Inclusion criteria for CMDs: A complaint of pain, difficulties to perform jaw movements, joint noises, tenderness to palpation of the TMJs and masticatory muscles, and/or headache of musculoskeletal origin.

Inclusion criteria for daytime BB: Daytime BB: Patient’s report of catching himself or herself clenching the teeth during the day, fatigue of the masticatory muscles following eating and/or talking. For Sleep BB: Patients’ report of catching himself or herself grinding or clenching the teeth at night, patient’s relatives or friends report of observing the patient grinding the teeth at night, patients report of jaw locking, facial and or TMJ pain on awakening in the morning, a report of sore teeth on awakening in the morning. Criteria for Mixed BB: A combination of signs, symptoms and report of grinding or clenching the teeth at night and during the day.

Inclusion criteria for morning awakening with headache: A complaint of headache on awakening in the morning reported as occurring occasionally frequently or very frequently. The type of headache was also diagnosed.

Exclusion criteria: Individuals presenting with psychological, psychiatric and/or cognitive disorders, those presenting with some form of epilepsy including Parkinson disease and those with severe motor and/or cognitive difficulties unable to respond properly to questionnaires.

III. Measures

Beck Depression Inventory: The Beck Depression Inventory or BDI is a robust and reliable instrument used worldwide to gather information about depression. The instrument consists of 21 self-reported groups of four statements graded by the degree of severity assessing recent depressive symptoms. Typically, the subject responds in 10-20 minutes to the instrument.

Rief and Hiller questionnaire: The Rief and Hiller questionnaire was used to gather information about somatization in CMDs and BB subjects and in those with no CMDs and No BB. This instrument has 32 self-reported questions organized hierarchically by the frequency of each reported sign, symptom or disorder. The questionnaire evaluates complaints in many organs and systems of the body.

IV. Statistical analysis
Kruskal-Wallis statistics followed by Dunn’s test and the Tukey-Kramer multiple comparison tests were used to analyze data. Significance was accepted if p<0.05.

V. Outcome
This investigation evaluated a subgroup of 50 CMDs and BB reporting morning awakening with headache (CMDs + BB+ AHWAH), 50 CMDs and BB no awakening with headache (CMDs + BB No AHWA) and 57 no CMDs subjects reporting no awakening with headache (No CMDs No AHWA). Mean age in the CMDs + BB + AHWA was about 33,9 (SD=10,5, range 17-63), 37,0 SD=12,2, range 14-56 in the CMDs + BB No AHWA and 32,5 (SD=14,4, range=13-73) in the No CMDs No AHWA subgroup. There was a statistically and significant difference when age was compared in the subgroups, (Kruskal-Wallis and Dunn’ statistics p=0,04): CMDs + BB No AHWA versus No CMDs No AHWA (p<0,05). See Table 1 for further details.
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Mean BDI in the CMDs + BB + AWHA was about 16.3 (SD=6.4, range=7-33), 15.6 (SD=6.7, range=5-35) in the subgroup with CMDs +BB No AWHA and 7.2 (SD=5.3, range=0-19), in the No CMDs No AWHA subgroup. There was a statistically and extremely significant difference when the subgroups were compared (Tukey-Kramer multiple comparison test p<0.0001): CMDs +BB +AWHA subgroup versus CMDs + BB No AWHA subgroup (p>0.05); CMDs + BB+ AWHA+ subgroup versus no CMDs No AWHA subgroup (p<0.001); CMDs+ BB+ No AWHA versus No CMDs No AWHA subgroup (p<0.001). See Table 2 for additional details.

Mean scores in somatization were as follows: 13.7 (SD=3.8, range=8-21), in the CMDs +BB + AWHA subgroup; 13.2 (SD=4.7, range=7-28) in the CMDs + BB No AWHA subgroup; 5.4 (SD=3.4, range=0-11) in the No CMDs No AWHA subgroup. There was a extremely and statistically significant difference when means scores in somatization were compared (Kruskal-Wallis test p<0.0001): CMDs + BB + AWHA versus CMDs + BB No AWHA (p<0.05); CMDs + BB + AWHA versus No CMDs No AWHA (p<0.001): CMDs + BB No AWHA versus No CMDs No AWHA (p<0.001). See Table 2 for additional details.

Mean scores in pain sites in the three subgroups were as follows: 8.1 (SD=1.9, range=6-13) in the CMDs + BB + AWHA subgroup; 7.0 (SD=2.2, range=4-12) in the CMDs + BB+ No AWHA subgroup; 1.5 (SD=1.4, range=0-4) in the No CMDs No AWHA subgroup. There was a extremely and statistically significant difference when the subgroups were compared (Kruskal-Wallis and Dunn’ statistics p<0.0001): CMDs + BB + AWHA subgroup versus CMDs + BB + No AWHA subgroup (p<0.05); CMDs + BB+ AWHA subgroup versus No CMDs No AWHA subgroup (p<0.001); CMDs + BB+ No AWHA versus No CMDs No AWHA subgroup (p<0.001). See Table 2 for additional details.

VI. Discussion

BDI scores were higher and very similar in the subgroups with CMDs awakening and no awakening with headache as compared with the control subgroup which demonstrated lower BDI values. The practical significance of these findings is that according to the classification system for bruxers used in the current investigation, sleep and mixed bruxers were characterized by higher scores in depression. Regarding those CMD and bruxers who reported morning awakening with headache (CMDs+ BB+ AWHA+), both sleep and mixed bruxers were represented in this subgroup probably indicating that higher scores in depression may be observed in sleep and mixed bruxers. Congruent with these findings on depression one investigation evaluated sleep quality in adult patients presenting with sleep related BB and asserted that the mechanism of signs and symptoms in those bruxers indicates an association with psychiatric abnormalities including anxiety and depression. Researchers also reported that morning awakening with headache is a common medical complaint in such bruxers and CMD individuals. Morning awakening with headache and with pain in other anatomic sites in the masticatory system is a common clinical complaint in bruxers and CMDs individuals. Subjects with CMDs, sleep BB and TMJ usually present with a complex personality with high to moderate levels of depression. In consonance with findings in the current investigation, one study evaluated a possible association between anxiety, depression and BB. Researchers reported that scores in anxiety and depression in bruxers were higher as compared with the control subgroup.

Somatization scores were higher in those subjects with CMDs, BB and awakening or not awakening with headache as compared with the control subgroup. This outcome is in line with one study asserting that individuals with painful TMJs and BB exhibit a complex personality associated with higher scores in somatization which make them more vulnerable to complains of pain in multiple anatomic sites. It may be that sleep and mixed BB are closely associated with a major psychiatric, disorder, for instance, somatization. In this regard, somatization may trigger nocturnal BB which in turn leads to pain in multiple sites including facial, TMJ and headache pain on awakening in the morning as nocturnal BB is not controlled or attenuated by protective neurophysiological mechanism. Supporting in part this line of evidence, one investigation indicates that somatization is a more important predictor of myofascial pain symptoms (a common musculoskeletal disorder in the craniofacial region) than sleep bruxism. Individuals complaining of facial pain, headache and CMDs, usually complain of psychosomatic disorders, emotional stress and anxiety. It is likely that under the effects of a major psychiatric construct, for instance, somatization, strong, uncontrolled loading of the supporting structures of the masticatory forces, for instance, TMJ and periodontal ligament, result in pain in multiple sites including toothache, headache, TMJ pain, facial pain and even cervical pain, indicating that sleep and mixed BB may be extremely harmful for the craniofacial complex in many CMDs individuals. Regarding headache in CMDs individuals, 80% of those subjects with CMDs and BB complain of various common headache types including tension-type headache, migraine and occipital neuralgia. Individuals with recurrent headaches have somatization of emotions as a major disorder in their psychological profile. Females were overrepresented in the two subgroups with CMDs and BB and in the control one without CMDs.
In this connection, one investigation\cite{16}, evaluating psychological factors in medical students with or without CMDs, researchers reported that women are likely more prone to express somatic symptoms than men.

Scores in pain sites on awakening in the morning were higher in the subgroups presenting CMDs, BB, awakening with headache and CMDs + BB no awakening with headache as compared with the control subgroup (those with no CMDs and no awakening with headache). In the last few years there has been a dramatic increased interest in studying the clinical effects of nocturnal or mixed BB on the cervical and masticator musculoskeletal structures\cite{17}. These observations indicate that in terms of pain, the clinical consequences of sleep and mixed BB are observed in anatomic areas close and distant to the masticatory anatomic structures\cite{18}. Although, there is paucity of comparative studies, there seems to be clinical, anatomic and psychological differences when sleep, mixed and diurnal bruxism are compared. These differences include personality factors, intensity and frequency of forces applied to the masticatory system, and anatomic structures overloaded by the intensity of forces in sleep BB. This assumption is echoed in part by one investigation\cite{12} asserting that myofascial pain, a common disorder in CMD subjects, was only detected among subjects with sleep bruxism. Dass and associates\cite{19} evaluated a case of headache associated with sleep-related BB and CMDs. They reported that such patient complained of headache, pain in the teeth, and tender TMJs. Clenching may also occur as a component of sleep bruxism. Bruxism, especially sustained clenching, produces joint pain and occasional headache explained by overloading of the temporomandibular joints\cite{20} but it is likely that overloading causes sustained strain in some masticatory and cervical muscles, thus leading to pain as result of damage and/or reactivation of some distant trigger points in other anatomic areas.

Concurrent with this set of observations, a recent study\cite{21} in bruxers with CMDs indicated that a higher frequency of painful sites on awakening in the morning including headache and cervical pain can be observed in sleep bruxers. Such investigation also reported that most common anatomic painful areas were the face, TMJs, head, neck and teeth. BB is currently considered as a risk factor for both CMDs and headache\cite{22}. Regarding TMJ pain, it has been reported that overloading associated with prolonged tooth clenching may produce an increase in stress in the retrodiscal tissues\cite{22} which are supplied with abundant nerve fibers and blood vessels. The mechanisms responsible for awakening with pain in some cervical and masticatory structures remain poorly understood. However, one investigation\cite{23} defends the notion that such pain is the result of repetitive jaw compression from BB with origin in sympathetic stimulation of the jaw elevators and other muscles during sleep. The number of anatomic sites reported as painful was higher in individuals with more severe BB in one investigation\cite{24}. Noteworthy to mention is that regarding types and mechanisms of headache on awakening in the morning, such pain may be the result of a referred pain mechanism from the TMJ, some masticatory muscles including the temporal and superficial masseter, from cervical muscles most frequently the trapezius muscle and last but no less important, from sensitization of both trigeminal and cervical nerves. Even chronic use of medication may cause headache as most over-the-counter medications and narcotic pain killers wear off in 4-8 hours, making people most vulnerable more frequently early in the morning, more specifically if using excessively these medications\cite{25,26,27}.

\section*{VII. Conclusion}

This investigation evaluated a subgroup of individuals with CMDs, sleep and mixed BB reporting morning awakening with headache, a subgroup with CMDs, sleep and mixed BB reporting no morning awakening with headache and another subgroup with no CMDs and no reporting morning awakening with headache. The CMDs and BB subgroup reporting awakening with headache did not demonstrate higher scores in depression, somatization and painful sites when compared with the CMD and BB subgroup no reporting awakening with headache. However, CMDs an BB subjects reporting or no reporting morning awakening with headache were psychologically and pathologically more disturbed as they demonstrated higher scores in depression, somatization and painful sites when compared with the no CMDs no morning awakening with headache subgroup. New studies using similar samples, criteria and methods, should be carried out to further validate the outcomes reported in the current study.

\section*{References}


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Table 1: Social and demographic data in the CMDs, BB awakening with headache (CMDs+ BB+ AWHA), CMDs + BB No awakening with headache (CMDs + BB+ No AWHA) and No CMDs No awakening with headache (No CMDs No AWHA) subgroups.

<table>
<thead>
<tr>
<th>GENRE</th>
<th>CMDs+ BB+ AWHA</th>
<th>CMDs+ BB+ No CMDs</th>
<th>CMDs+ BB+ No AWHA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=50</td>
<td>n=50</td>
<td>n=57</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>49</td>
<td>49</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>98</td>
<td>73.7</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>100</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>AGE</td>
<td>33.9</td>
<td>37.0</td>
<td>32.5*</td>
</tr>
<tr>
<td>SD</td>
<td>10.5</td>
<td>12.2</td>
<td>14.4</td>
</tr>
<tr>
<td>Range</td>
<td>17–63</td>
<td>14–56</td>
<td>13–73</td>
</tr>
</tbody>
</table>

*Kruskal-Wallis statistics (p<0.04): CMDs+ BB+ AWHA versus CMDs+ BB+ No AWHA (p<0.05); CMDs+ BB+ AWHA versus no CMDs No AWHA (p>0.05); CMDs+ BB+ No AWHA versus No CMDs No AWHA (p<0.05).

Table 2: Depression, somatization and pain sites scores in the CMDs+ BB+ Awakening with headache+ (CMDs+ BB+ AWHA), CMD+ BB+ No awakening with headache (CMDs+ BB+ No AWHA) and No CMDs No awakening with headache (No CMDs No AWHA) subgroups.

<table>
<thead>
<tr>
<th>BDI</th>
<th>CMDs + BB+ AWHA</th>
<th>CMDs + BB+ No AWHA</th>
<th>No CMDs No AWHA</th>
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</thead>
<tbody>
<tr>
<td>n=50</td>
<td>n=50</td>
<td>n=57</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>16.3</td>
<td>15.6</td>
<td>7.2*</td>
</tr>
<tr>
<td>SD</td>
<td>6.4</td>
<td>6.7</td>
<td>5.3</td>
</tr>
<tr>
<td>Range</td>
<td>7–33</td>
<td>5–35</td>
<td>0–19</td>
</tr>
<tr>
<td>SOMATIZATION</td>
<td>Mean</td>
<td>13.7</td>
<td>13.2</td>
</tr>
<tr>
<td>SD</td>
<td>3.8</td>
<td>4.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Range</td>
<td>8–21</td>
<td>7–28</td>
<td>0–11</td>
</tr>
<tr>
<td>PAIN SITES</td>
<td>Mean</td>
<td>8.1</td>
<td>7.0</td>
</tr>
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<table>
<thead>
<tr>
<th></th>
<th>CMDs+ BB+ AWAHA</th>
<th>CMDs+ BB+ No AWAHA</th>
<th>CMDs+ BB+ AWAHA versus CMDs+ BB+ No AWAHA</th>
</tr>
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<tbody>
<tr>
<td>SD</td>
<td>1.9</td>
<td>2.2</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>Range</td>
<td>6—13</td>
<td>4—12</td>
<td><strong>Kruskal-Wallis test (p &lt; 0.0001): CMDs+ BB+ AWAHA versus CMDs+ BB+ No AWAHA (p &gt; 0.05); CMDs+ BB+ AWAHA versus No CMDs No AWAHA (p &lt; 0.001); CMDs+ BB+ No AWAHA versus No CMDs No AWAHA (p &lt; 0.001).</strong></td>
</tr>
</tbody>
</table>

*Tukey-Kramer multiple comparison test (p < 0.0001): CMDs+ BB+ AWAHA versus CMDs+ BB+ No AWAHA (p > 0.05); CMDs+ BB+ AWAHA versus no CMDs No AWAHA (p < 0.001); CMDs+ BB+ No AWAHA versus No CMDs No AWAHA (p < 0.001).**