Correlation analysis between biochemical markers, pain perception, low back functional disability, and muscle strength in postmenopausal women with low back pain

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Abstract:
Objective: To analyze the correlation between cortisol, creatine kinase (CK), estradiol, pain perception, low back functional disability, and abdominal and lumbar muscle strength in postmenopausal women with low back pain. Methods: The sample consisted of eleven postmenopausal women (age: 55.09 ± 6.7 years; range between 44 and 66 years old; body mass: 63.07 ± 9.78 kg; height: 1.55 ± 0.07 m; BMI: 26.01 ± 2.67 kg/m²) with pain and functional lumbar incapacity. Blood collection for analysis of the basal serum levels of cortisol and estradiol was performed using the chemiluminescence method, and the enzymatic method was applied for CK analysis. The pain perception and the perception of lumbar functional incapacity were determined through the Visual Analogue Scale (VAS) and the Roland-Morris Questionnaire (RMQ), respectively. The abdominal strength and the strength of the spine extensor muscles were analyzed by an isometric test. Results: The Pearson correlation showed a highly significant negative correlation between the estradiol levels and the VAS (r = -0.725; p = 0.012). The cortisol presented a significant negative correlation with the strength scores of the spine extensors (r = -0.764; p = 0.006). The participants’ age presented significant negative correlation with cortisol (r = -0.764; p = 0.006). The participants’ age presented significant negative correlation with cortisol (r = -0.668; p = 0.025) and with the lumbar score (r = -0.601; p = 0.051). No significant differences were found in RMQ, CK, and the abdominal score (p ≥ 0.05). Conclusions: Postmenopausal women with higher age tend to present higher serum cortisol levels and lower levels of lumbar strength. Moreover, greater levels of cortisol are related to smaller levels of lumbar strength. Lower estradiol levels tend to represent higher pain perception in postmenopausal women with low back pain. Key Words: aging, menopause, spine, cortisol, creatine kinase, estradiol.

Introduction
Menopause is a stage of a woman’s life and its main characteristic is the complete interruption of menstruations (Takahashi & Johnson, 2015). The cessation of the menstrual cycle results from the progressive reduction in estrogen levels, which is the main cause of climacteric. During this period, women tend to present unpleasant signs and symptoms such as increased body mass, hot flashes, cold sweats, insomnia, osteoporosis, psycho-emotional disorders and cardiovascular disease (Tairova & Lorenzi, 2011). As life expectancy increases, it is estimated that women will spend approximately 40% of their lives in the postmenopausal phase (Takahashi & Johnson, 2015).

The postmenopausal hormonal environment is associated with loss of muscle and bone mass (Takahashi & Johnson, 2015), which can occur without any symptoms and the woman feels fine until a fracture occurs (Ilona, Taina, Mirela, Eugenia, & Mihaela, 2010). This way, the reduction of the sex hormones (like estrogen and progesterone) levels can be a risk factor for the degeneration of the intervertebral discs of the lumbar spine (Lou et al., 2017). One of the components of the estrogen is the estradiol. This sex and steroid hormone can be related to the skeletal muscle, the connective tissue, bone tissue, and tendon tissue (Pingel et al., 2012; Osakabe et al., 2001). Thus, the declines in the organic form and function inherent to the aging process tend to cause low back pain. This pain is experienced by most people during life and tends to become chronic with age and relapse (Botov, Shnyakin, Osipov, & Tatyana, 2018).

Low back pain is a health problem with a major socioeconomic impact. This pain is considered chronic if it persists for more than three months (Almeida & Kraychete, 2017). Such pain causes functional and labor
disabilities (Leite, Luciano, Martins, Wajchenberg, & Puertas, 2010; Momsen, Jensen, Nielsen, & Jensen, 2014), representing a growing economic burden due to increasing days of absenteeism from work, loss of productivity, and cost of treatment (Alzahrani et al., 2019). According to the study conducted by the Global Burden of Disease (GBD, 2018), low back pain is the leading cause of years lived with disability (YLD). In most cases, this syndrome has an unknown origin (Hartvigsen et al., 2018).

Biochemical markers such as creatine kinase (CK) and cortisol have been used as indirect markers of muscle damage as they are a useful and sensitive means for assessing any increase in muscle stress (Foschini, Prestes, & Charro, 2007; Vale et al., 2009). Cortisol is responsible for many catabolic processes in the organism and is released as a pulsatile stress hormone in the bloodstream. In stressful and painful situations, cortisol causes a catabolic state in the metabolism. Individuals with chronic pain who are exposed to permanent stress tend to have elevated cortisol levels compared to healthy people (Eichler, Rachinger-Adam, Kraft, & Azad, 2019). Thus, these biochemical markers of stress and muscle damage (cortisol and CK) may be related to low back pain.

Therefore, the present study aimed to analyze the correlation between cortisol, CK, estradiol, pain perception, low back functional disability, and abdominal and lumbar muscle strength in postmenopausal women with low back pain.

Materials and Methods

Participants
The present research is a cross-sectional correlational descriptive study (Thomas, Nelson, & Silverman, 2012). The sample consisted of postmenopausal women with low back pain. The following inclusion criteria were adopted: a) present perception of lumbar disability and low back pain (defined as pain between the lower ribcage and the gluteal folds); b) nonspecific low back pain characterized by the absence of signs of a serious underlying condition (such as cancer, infection or tail syndrome), spinal stenosis or radiculopathy or other specific spinal cause (such as vertebral compression fracture or ankylosing spondylitis) (Chou et al., 2007); c) no history for at least three months of regular practice of physical exercise. The exclusion criteria were: a) presenting any type of acute or chronic condition that could be aggravated during the test battery; b) be under the use of antidepressant or sedative medications that may be a risk factor for the proposed tests; c) have undergone physical therapy or acupuncture treatment within the past three months. The sample was obtained by stratification from a clinic located in the west zone of Rio de Janeiro, Brazil, the Rheumatological and Physiatric Orthopedic Center (CORF). Thus, the volunteers were recruited via the CORF database, through institutional email or telephone contact. Those who indicated their intention to participate were scheduled for individual face-to-face interviews with the research team, which performed the data collection in a standardized manner.

All subjects were invited to participate voluntarily in the research and signed the informed consent before participation in the study, according to the norms of Resolution no. 466/2012 of the Brazilian National Health Council. The study was approved by the institutional ethics committee (Approval Number 1.360.167).

Procedures

Anthropometric assessment
In the anthropometric evaluation, to measure body mass, height and body mass index (BMI) calculation, a Filizola® mechanical scale (Brazil), 100 g precision and 150 kg capacity, were used with a stadiometer, precision of 0.5 cm. BMI was calculated as the ratio between body mass (kg) and height squared (m²). All measurements were made by a single evaluator according to the International Standards for Anthropometric Assessment (ISAK) protocol (Marfell-Jones, Stewart, & Ridder, 2012).

Pain perception assessment
The intensity of low back pain perception was assessed using the Visual Analogue Scale (VAS) (Langley & Sheppeard, 1985; Scott & Huskisson, 1979). In this linear scale, ranging from 0 to 10 cm, the left extremity (0) corresponds to no pain at all and the right extremity (10) corresponds to unbearably intense pain. The participants were asked to indicate their level of pain by adding a mark on the VAS.

Assessment of the perception of low back functional disability
The Roland-Morris questionnaire (RMQ) was applied to evaluate the functional status of the lumbar spine (Roland & Morris, 1983) through the translated, adapted and validated version for Brazil (Nusbaum, Natour, Ferraz, & Goldenberg, 2001). The RMQ is a subjective scale for individuals who present low back pain. It consists of 24 self-reported affirmations on patient status. The patients mark “yes” or “no” to the statements accordingly to their physical states. Every marked statement as “yes” is scored as 1 point. The total score varies between zero (absence of incapacity) and 24 (maximum incapacity). A value of 11.4 is considered a mean score and scores over 14 are considered to indicate significant disability (Nusbaum et al., 2001).
Assessment of abdominal and lumbar strength

The strength of the abdominal muscles was evaluated by the isometric abdominal test. The participant was in the supine position with the hips at 45°, knees at 90° and hands at the side of the body. Both feet rested on the ground. The examiner then asked the participant to move to the final position of each verification level. The participant was instructed to maintain this final position as long as she could. Verification begins with score 1 and progresses sequentially to score 5 according to the following gradation: 1) Unable to lift from the ground anything but her head; 2) With arms extended towards the knees, able to raise the upper body until the upper part of the scapula separates from the ground (holding this position for 1 to 10 seconds); 3) With straight arms, able to raise the upper body until the scapula separates from the ground (holding for 10 to 15 seconds); 4) Arms crossed over the chest, able to raise the upper body until the scapula separates from the table (holding for 15 to 20 seconds); 5) Hands clenched behind the back of the neck, able to raise the upper body until the shoulder blade separates from the ground (holding for 20 to 30 seconds) (Magee & Sueki, 2012).

The strength of the extensor muscles of the spine was evaluated by the isometric test of the extensor spine and the multifidus muscles. The participant starts the test in the pronated position. At the evaluator’s command, she tried to extend the spine to the maximum by lifting her head and torso. The individual should maintain the final position as long as possible. The test score ranges from 1 to 5, as follows: 1) Only a slight muscle contraction without movement; 2) With the hands at the side of the body, the participant extends the lumbar spine, raising the head from the ground (holding for 1 to 10 seconds); 3) With the hands at the side of the body, the participant extends the lumbar spine, raising the sternum from the floor (holding for 10 to 15 seconds); 4) With the hands at the side of the body, the participant extends the lumbar spine, raising the head, chest, and ribs from the floor (holding for 15 to 20 seconds); 5) With hands behind her head, the participant extends the lumbar spine, raising the head, chest, and ribs from the floor (holding for 20 to 30 seconds) (Magee & Sueki, 2012).

Evaluation of the biochemical markers

Basal serum cortisol, CK and estradiol levels were evaluated in a clinical analysis laboratory. The venous blood sample was withdrawn from the antecubital vein at 08.00 am, with at least 12 hours of fasting, using cotton, alcohol, needle, disposable syringe, and sterile tube. Upon arriving in the laboratory, women sat quietly for at least five minutes. The chemiluminescence method for cortisol and estradiol analysis and the enzymatic method for CK analysis were applied (Pardini, 2015).

Statistical analysis

The data were analyzed by the SPSS 23.0 Statistics Software and presented as mean and standard deviation. Pearson’s correlation test was used to analyze the associations between the study variables. The study admitted the value of p ≤ 0.05 for statistical significance.

Results

Eleven postmenopausal women with low back pain, aged between 44 and 66 years old, volunteered for this study. Table 1 shows the sample characteristics, VAS, RMQ, muscle strength scores, and hormonal levels of the study participants.

Table 1. Descriptive characteristics of the sample, scores and biochemical results.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.09</td>
<td>6.70</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>63.07</td>
<td>9.78</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.55</td>
<td>0.07</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.01</td>
<td>2.67</td>
</tr>
<tr>
<td>VAS (score)</td>
<td>7.33</td>
<td>2.29</td>
</tr>
<tr>
<td>RMQ (score)</td>
<td>15.27</td>
<td>3.74</td>
</tr>
<tr>
<td>Cortisol (mcg/dL)</td>
<td>13.69</td>
<td>7.76</td>
</tr>
<tr>
<td>Estradiol (pg/mL)</td>
<td>13.49</td>
<td>2.43</td>
</tr>
<tr>
<td>CK (U/L)</td>
<td>95.64</td>
<td>35.93</td>
</tr>
<tr>
<td>Abdominal strength (score)</td>
<td>4.64</td>
<td>0.50</td>
</tr>
<tr>
<td>Lumbar strength (score)</td>
<td>3.00</td>
<td>0.45</td>
</tr>
</tbody>
</table>

SD: standard deviation; BMI: body mass index; VAS: visual analogue scale; RMQ: Roland-Morris questionnaire; CK: creatine kinase.
Table 2 presents the values related to the correlation coefficient (r) between the variables studied. It was observed a highly significant negative correlation between the estradiol levels and the VAS. Hence, lower estradiol levels mean higher pain perception. The cortisol presented a significant negative correlation with the strength scores of the spine extensors. This means that individuals with a high cortisol rate presented low back strength. The participants’ age presented significant correlation with cortisol (the higher the age, the higher the serum cortisol levels) and with the lumbar strength scores (the higher the age, the lower the lumbar strength levels). In the other study variables (RMQ, CK, and the abdominal scores), there was no significant correlation.

Table 2. Correlation analysis of the variables studied.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>VAS</th>
<th>RMQ</th>
<th>Cortisol</th>
<th>Estradiol</th>
<th>CK</th>
<th>AbdScore</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>-0.516</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.104</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>-0.057</td>
<td>0.505</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.868</td>
<td>0.113</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>0.668*</td>
<td></td>
<td>-0.381</td>
<td>-0.243</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.025</td>
<td>0.248</td>
<td>0.472</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>0.498</td>
<td>-0.725*</td>
<td>-0.352</td>
<td>0.571</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.119</td>
<td>0.012</td>
<td>0.288</td>
<td>0.066</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>0.179</td>
<td>-0.207</td>
<td>-0.546</td>
<td>0.063</td>
<td>-0.071</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.599</td>
<td>0.541</td>
<td>0.082</td>
<td>0.853</td>
<td>0.836</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AbdScore</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>-0.492</td>
<td>0.407</td>
<td>0.217</td>
<td>-0.522</td>
<td>-0.575</td>
<td>-0.267</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.124</td>
<td>0.214</td>
<td>0.522</td>
<td>0.100</td>
<td>0.064</td>
<td>0.427</td>
<td></td>
</tr>
<tr>
<td>LumScore</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>-0.601*</td>
<td>0.234</td>
<td>0.000</td>
<td>-0.764*</td>
<td>-0.378</td>
<td>-0.205</td>
<td>0.443</td>
</tr>
<tr>
<td>p-value</td>
<td>0.051</td>
<td>0.488</td>
<td>1.000</td>
<td>0.006</td>
<td>0.252</td>
<td>0.545</td>
<td>0.172</td>
</tr>
</tbody>
</table>

VAS: visual analogue scale; RMQ: Roland-Morris questionnaire; CK: creatine kinase; AbdScore: abdominal score; LumScore: lumbar score.* p ≤ 0.05.

Discussion

The present study analyzed the correlation between cortisol, CK, estradiol, pain perception, low back functional disability, and abdominal and lumbar muscle strength in postmenopausal women with low back pain. The participants presented an RMQ score of over 14, which is compatible with a significant level of low back functional disability (Nusbaum et al., 2001). This characteristic of the sample is in accordance with a study conducted by Lima et al. (2018), who also investigated the low back functional disability in individuals with low back pain. On the other hand, Kofotolis, Kellis, Vlachopoulos, Gouitas, and Theodorakis (2016) and Miyamoto, Costa, Galvanin, and Cabral (2013) had a sample with lower RMQ scores when compared with the present study.

It was observed in the current study that the lower the estradiol level, the higher the VAS, which means greater levels of pain. The postmenopausal estradiol reference value is less than or equal to 32.2 pg/mL (Pardini, 2015). These lower hormone levels may be associated with loss of bone mass (Takahashi & Johnson, 2015), which can represent a risk factor for the deterioration of the intervertebral discs of the lumbar spine (Lou et al., 2017). The practice of resistance training, three times per week, can promote higher bone mineral density in the lumbar spine (Borba-Pinheiro et al., 2016; Borba-Pinheiro et al., 2010). Consequently, the practice of physical exercise is crucial since low back pain is often triggered by trunk muscle weakness resulting from insufficient exercise, obesity, and improper posture (Jang, Cho, & Cho, 2015).

In this sense, another finding of the present study was that the postmenopausal women with low back pain who had a high cortisol level showed low lumbar strength. Besides, the cortisol also presents a correlation with the age of the study sample. In this sense, the postmenopausal women with higher age presented higher serum cortisol levels and lower lumbar strength. Higher levels of this catabolic hormone in the bloodstream may be related to the higher level of deterioration and dehydration that intervertebral discs attempt to present with advancing age (McGill, 2015) and the pain intensity that the participants presented (Eichler et al., 2019).

The other biochemical marker used in the current study was the CK. This enzyme is often described as the best indirect biomarker of muscle damage because these molecules are cytoplasmic and cannot cross the sarcolemmal membrane barrier. Thus, increased serum concentration of these molecules is used as an indication of damage to the muscle membrane and other tissue structures (Smith et al., 1994; Foschini, Prestes, & Charro, 1994).
However, in the present study, there was no significant correlation between CK with the other variables analyzed. Additionally, CK values presented by the participants are within the normal range (33 – 211 U/L for women) (Pardini, 2015). Since the serum CK concentration is subject to physiological variations that affect enzyme activity – such as gender, age, ethnicity, muscle mass, and type of exercise performed (Clarkson & Hubal, 2002) –, the lack of correlation may be related to the absence of physical exercise in the study sample. Strength exercises or other exercises that require predominantly eccentric actions are the ones that most damage muscle tissue, thus having the most effect on CK levels (Foschini, Prestes, & Charro, 2007).

Therefore, the first line in the treatment of nonspecific low back pain should contain nonpharmacological options, such as the practice of physical activity (O’Sullivan, O’Sullivan, & O’Keeffe, 2019). Thus, treatments and exercise programs with an emphasis on the recovery of functional movements, muscle strength and flexibility should be the basis of low back pain prevention and intervention processes (McGill, 2015).

However, the practice of non-specific physical activity has not presented a significant effect on the reduction of low back pain (Marini et al., 2017). In this sense, the Pilates method has been performed in individuals with low back pain. One of the principles of this method is the centralization, which involves the “power house” and, consequently, the lumbar region (Santos, Moser, & Bernardelli, 2015). Thus, postmenopausal women undergoing Pilates classes concomitantly with physical therapy had reduced pain and disability caused by chronic low back pain (Cruz-Diaz et al., 2016). Nevertheless, it is important to emphasize that it is not yet clear in the scientific literature whether Pilates is more effective than other exercises for reducing short-term low back pain, and the evidence for medium-term pain reduction is poor (Yamato et al., 2016).

It is important to highlight that preventive exercise programs with a special focus on the spine should be implemented at an early age to avoid postural problems and pain in childhood, youth, adulthood, and old age (Elena, Ingrid, Šárka & Jan, 2018). In cases where the individual already experiences pain, a program for the functional recovery and retraining of the vertebral column should be practiced to prevent recurrences and/or further complications (Călina et al., 2009).

The limitations of this study include the relatively small sample size, besides, lack information about the diet and sleep quality and quantity of the participants since these variables can interfere in hormonal levels, such as cortisol (Orth & Kovacs, 1998). Therefore, future studies would be necessary to confirm our findings.

Conclusions

In conclusion, the results of this study suggest that lower estradiol levels tend to represent higher pain perception levels and a high cortisol rate correlates with lower lumbar strength in postmenopausal women with low back pain. In addition, the older the postmenopausal women are, the higher tends to be the serum cortisol levels and the lower tends to be the lumbar strength. This way, the data presented in this research article may serve as a reference for a study aimed at investigating the relationship between postmenopause, age, lower back strength, and cortisol.

Future studies should present intervention proposals for the prevention or treatment of low back pain, including the correction of daily postural gestures and exercise programs. Also, it is suggested to use noninvasive methods for the diagnosis of low back pain, such as infrared images examination (thermography).

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Conflicts of interest - The authors have no conflicts of interest to declare.

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