Morphometric findings in avascular necrosis of the femoral head

DIANA KAMAL1), RODICA TRĂISTARU2), D. O. ALEXANDRU3), C. K. KAMAL1), D. PIRICI4), O. T. POP4), D. GH. MĂLĂESCU5)

1)University of Medicine and Pharmacy of Craiova
2)Department of Physical Medicine and Rehabilitation
3)Department of Medical Informatics
4)Research Center for Microscopic Morphology and Immunology
University of Medicine and Pharmacy of Craiova
5)Faculty of Nursing, "Constantin Brâncuşi" University, Targu Jiu

Abstract
Avascular necrosis of the femoral head is an illness with a controversial etiology, the trigger event being the suppression of blood flow to the femoral head. The disease affects mostly young adults within their third and fifth decade, the majority of the patients being men. The main risk factors are trauma, chronic alcohol consumption, smoking, corticotherapy. The main goal of our study is to describe the morphometric changes found in the bone tissue of patients diagnosed with avascular necrosis of the femoral head, with different risk factors, by comparing the area of bone trabeculae inside the area of necrosis with that from the adjacent viable tissue. The morphometric study used biological material from 16 patients with ages between 29 and 57 years, who underwent surgery for avascular necrosis of the femoral head. They were admitted in the Orthopedics Department at the Emergency County Hospital in Craiova between 2010 and 2011 and were split into four groups. Group I presented trauma as the main risk factor, Group II had corticotherapy as the defining risk factor, Group III presented chronic alcohol consumption and Group IV was represented by the patients who smoked and exhibited chronic alcohol consumption. There was not a significant statistical difference between the areas of bone trabeculae of the four groups when we compared viable bone tissue to the necrotized one. Knowing the risk factors of the avascular necrosis of the femoral head is critical to the management of the disease, because diagnosing it in an early stage is a necessity for obtaining a good result for conservative treatment.

Keywords: avascular necrosis, femoral head, corticotherapy, morphometry.

Introduction
Avascular necrosis of the femoral head is an illness with a controversial etiology, the trigger event being the suppression of the blood flow to the femoral head. The disease affects mostly young adults within their third and fifth decade, the majority of the patients being men [1, 2]. In order to diagnose the disease in an early stage, the physician must have a high-grade of suspicion regarding patients with risk factors. The main risk factors are trauma, chronic alcohol consumption, smoking, corticotherapy. The relative frequency of the most common causes for avascular necrosis of the femoral head is alcoholism (20–40%), corticosteroid therapy (35–40%), and idiopathic causes (20–40%) [3]. Understanding the risk factors is more important in patients with avascular necrosis of the femoral head in one of the joints, because 50–60% of all patients develop avascular necrosis of the femoral head in both hip joints. This group of patients must be rigorously investigated [3]. Diagnosing the disease in an early stage is important for an optimal result in the outcome of classic treatment approach [4].

In this study, we aimed to describe the morphometric changes found in the bone tissue of patients diagnosed with avascular necrosis of the femoral head, with different risk factors, by comparing the area of bone trabeculae inside the area of necrosis with that from the adjacent viable tissue.

Materials and Methods

The studied group had 16 patients, aged between 29 and 57 years, admitted in the Orthopedics Department in the Emergency County Hospital of Craiova, between 2010 and 2011, and diagnosed with, followed by arthroplasty surgery. Information like age, sex, risk factors, and the debut of the disease were obtained from patient charts for statistical purposes.

Inclusion criteria were the main risk factors that the patients presented (trauma, corticosteroid therapy, chronic alcohol consumption, smoking and alcohol intake).

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The biological material needed for the study consisted of bone fragments harvested from the head and neck of the femur, obtained after the hip surgery that the 16 patients included in our study underwent.

All the patients signed an informed consent form in which it was explained the purpose of the research, the way the biologic material obtained from the hip surgery...
and the personal data obtained from their charts will be further used in the study.

The fragments were cut into 2 to 5 mm sections. The resulting pieces were kept in 10% neutral formalin solution for two weeks. The bone fragments were first decalcified before being processed for the classical histological technique for paraffin inclusion and the result was a series of 4–5 μm sections, which could be stained and studied using the optical microscope. The histological samples were stained using Hematoxylin–Eosin and trichromic (Goldner–Szeckeli) stains. The samples containing the decalcified bone tissue were inspected using a Nikon Eclipse (Nikon, Apidrag, Romania) optical-electronic microscope and significant aspects were picked up using the integrated 5-megapixel CCD camera on the microscope.

For completing the morphometric study, we chose images of the bone trabeculae from the area of necrosis and from areas with viable tissue from all the patients in the study. The area of bone trabeculae was determined using ImageProPlus software from Media Cybernetics, on images, which were modified using Adobe Photoshop for differentiating bone structure from other cellular elements.

Statistical analysis was performed using Microsoft Excel (Microsoft Corp., Redmond, WA, USA), together with the XLSTAT add-on for MS Excel (Addinsoft SARL, Paris, France). Because the study involved a numerical comparison between more than two small groups of patients, the non-parametric Kruskal–Wallis test was primarily used, although we also used the ANOVA test, mainly for the post hoc comparison (Tuckey HSD test) between pairs of groups.

Results

The study included 16 patients diagnosed with avascular necrosis of the femoral head, stages III and IV, with ages between 29 and 57 years, with a mean age of 40 years. The groups of patients were composed of only male patients.

The entire group was divided into four separate groups according to risk factors: the first group presented trauma as a main risk factor, the second group was affected by corticosteroid therapy, the third one suffered from chronic alcoholism and the fourth one had smoking and alcohol consumption as a risk factor. Every group was composed of four patients to facilitate comparison.

The microscopic images showed common elements in all four groups but also differences. These images varied with the same group and even with the same individual, according with the area that was studied (area of necrosis or viable tissue) (Figures 1–4).

Figure 1 – Necrotized trabecular bone area, patient from Group I (HE staining, ×40).

Figure 2 – Viable trabecular bone, patient from Group I (HE staining, ×40).

Figure 3 – Necrotized trabecular area, patient from Group II (HE staining, ×40).

Figure 4 – Viable trabecular bone, patient from Group II (HE staining, ×40).
All the samples had similar morphological alterations consisting of replacement of the normal bone tissue with extensive areas of fibrosis, narrowing of the bone trabeculae inside the area of necrosis.

We compared the area of the bone trabeculae inside the area of necrosis with the adjacent viable tissue, in all four patients groups. We noticed that patients in the same group had similar values in the area of necrosis and the viable tissue area. Regardless of the group, all patients presented narrow bone trabeculae in the area of necrosis in comparison with normal tissue.

We compared the ratio between the areas of the bone trabeculae in the necrotized area and the area of the bone trabeculae in viable tissue, on samples from all four groups). The highest ratio was found in members of Group I and the smallest in members of Group II. The area ratio of Groups III and IV were similar, both with values between Groups I and II (Tables 1 and 2, Figure 5).

Table 1 – Summary data for the percentage of viable tissue for the four studied groups

<table>
<thead>
<tr>
<th>Category (Group)</th>
<th>Mean [%]</th>
<th>St. dev. [%]</th>
<th>C.V. [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>40.36</td>
<td>10.88</td>
<td>26.96</td>
</tr>
<tr>
<td>II</td>
<td>27.85</td>
<td>6.59</td>
<td>23.66</td>
</tr>
<tr>
<td>III</td>
<td>38.38</td>
<td>4.37</td>
<td>11.39</td>
</tr>
<tr>
<td>IV</td>
<td>33.24</td>
<td>5.97</td>
<td>17.95</td>
</tr>
</tbody>
</table>

Table 2 – Results of testing the statistical significance of the means’ differences

<table>
<thead>
<tr>
<th>Kruskal–Wallis test p-value</th>
<th>ANOVA test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.051 Measurements do not differ significantly</td>
<td>0.064 Means’ difference is not significant</td>
</tr>
</tbody>
</table>

Our study included 16 patients, diagnosed with avascular necrosis of the femoral head, stages III and IV. On samples from patients diagnosed in stage III, we observed the presence of bone sequester in the necrotic area and interruptions of the femoral head contour with joint space preserved. In stage IV patients, we noticed the collapse of the femoral head with joint space narrowed or absent and arthritic changes in the acetabulum.

The clinical examination along with paraclinical investigations gave us the information for including the patients in one of the four stages. We used the Ficat scale, and the staging was done based on symptoms, X-ray and MRI images [5].

Avascular necrosis of the femoral head is a disease with an incomplete etiology theory. There are multiple causes incriminated in the development of this illness. Avascular necrosis of the femoral head can be either primary (idiopathic) or secondary (traumatic or non-traumatic) [1, 3, 6–11].

Our study group was split into four groups based on the risk factors as it follows: Group I had trauma as a primary risk factor, Group II were patients with corticosteroid therapy in their history, Group III was represented by patients with chronic alcohol consumption and Group IV, which had smoking and alcohol as a main risk factor. Each group had four patients in order to easily compare the groups.

Avascular necrosis of the femoral head is mostly idiopathic and secondary to trauma. Smoking and alcohol consumption and also corticosteroid therapy are incriminated in the development of the disease.

Morphological abnormalities were found in all the patients, as replacement of the normal bone tissue with extensive fibrous areas, narrowing of the bone trabeculae in the area of necrosis.

There were no statistically significant differences (p>0.05) in the percentage of trabecular bone area among the four groups (Kruskall–Wallis p-value >0.05, ANOVA p-value >0.05).

One of the limitations of our study was the small number of patients. The Kruskal–Wallis test result was very close to the critical value, so, if a larger number of patients would be used, the differences could prove significant.

Performing the post hoc analysis, we found no statistically significant differences between the pairs of groups, but the comparison of I vs. II Groups had a p-value of 0.055, very close to the critical threshold.

In a study performed by Zhang Y et al., in 2010, on 66 patients diagnosed with avascular necrosis of the femoral head, that were shared in three groups according the risk factors (Group A – traumatic caused avascular necrosis of the femoral head, Group B – steroid-induced disease, Group C – alcohol-induced illness), there were no statistically significant differences (p>0.05) in the percentage of trabecular bone area among the three groups [12].

The ratio between the necrotized trabecular area and the healthy trabecular area was the highest in Group I.

Discussion

Avascular necrosis of the femoral head is a disease caused by the disruption of the blood flow to the femoral head, affecting young adults with ages between 30 and 50 years, raising diagnostic and therapeutic issues. Avascular necrosis of the femoral head affects four to eight times more men than women.
Trauma is the most frequent cause of secondary avascular necrosis of the femoral head [3, 6]. Necrosis can develop within the first eight hours following a traumatic event, the cause being blood flow hindering [3]. Femoral neck and head fractures are the most common traumatic causes, which lead to necrosis [6, 7].

After the trauma, superior retinacular vessels can be affected along with the nourishing artery and the round ligament artery. Also, an intra-capular hematoma can develop which causes rising of the pressure at this level, causing articular capsule blood vessel tamponade. After the splaining of the coxo-femoral joint, the blood flow at this level can be cut off due to the rupturing of the round ligament and the artery that accompanies it. The destruction of the articular capsule wrecks the integrity of the blood vessels at this level. Patients can develop avascular necrosis of the femoral head even after a femoral fracture that occurred 10 years earlier.

Local trauma can lead to blood flow obstruction to the femoral head. This vascular cut off can inflict the death of the bone marrow at this level, the destruction of the bone cellular elements and the development of a well defined area of necrosis. These events take place just hours after the traumatic event and the full extent of the alterations is visible in just a couple of days [6].

The ratio between necrotized trabecular bone and healthy, viable tissue in Group II was the lowest of all the four groups.

The corticosteroid therapy was incriminated in the development of avascular necrosis of the femoral head, the femoral head being the most frequent location for this disease. Usually, when the disease appears, it is bilateral. The exact dosage of corticosteroids necessary to induce the disease is unknown but it is considered that high doses, even when they are administered for a short period of time, represent a high risk for developing the disease [6]. In the majority of patients, symptoms appear after approximately three years after initiating the corticosteroid therapy [13]. By discontinuing the corticosteroid therapy, some lesions characteristic to the early stages of the disease can decrease or disappear altogether [14, 15].

There are many mechanisms incriminated in the development of the avascular necrosis of the femoral head in patients under corticosteroid therapy [3], amongst which: the occlusion of small blood vessels produced as a consequence of fat emboli from the liver obstructing them; an increase in intraseous pressure because of large fat cells accumulating in the marrow, without a compensatory loss of bone matrix elements; the hydrolysis of fat emboli into free fatty acids with a toxic effect on vascular endothelia and leading to intra-vascular clotting; angiogenesis inhibition due to a decrease in proteolysis activity through the synthesis of thyroid anti-hormones polyclonal antibodies; the direct toxic effect of corticosteroid therapy on bone cells; transformation of the hematopoietic marrow into fatty marrow, a precursory stage in the development of avascular necrosis of the femoral head and inducing bone cells apoptosis (osteoblasts, osteocytes) [16, 17].

On samples from Groups III and IV, where the primary risk factors were smoking and alcohol consumption, we did not find any particular aspects, other than the ones found in all four groups. The area ratio of Groups III and IV were similar, both with values between Groups I and II.

Individuals consuming less than 400 mL of alcohol per week have three times the risk of developing avascular necrosis of the femoral head than people who do not drink at all. The risk is increased 11 times over in individuals who consume more than 400 mL a week [6, 7, 18]. Alcohol can have toxic effect on bone forming cells, its toxic effect on the liver is well established, and a steatotic liver is a permanent source of asymptomatic emboli [3].

Individuals smoking more than 20 cigarettes a day have a high risk of developing the disease [19]. Smoking has an inhibiting effect on osteogenesis and bone reparation processes [20, 21].

Conclusions

The microscopic images obtained from patients in the four groups, with different risk factors, presented some similarities but also particular aspects found in members from a specific group. There was no significant statistical difference between ratio of the necrotized trabecular area and the normal trabecular area, from the four groups with different risk factors. It must be said that not all individuals presenting with these risk factors will go on to develop the disease because there are significant individual sensibility differences in the general population.

Acknowledgments

Diana Kamal and Constantin Kamal Kamal acknowledge the support received through the project entitled “Doctorate an Attractive Research Career”, contract number POSDRU/1.1.5/S/52826 co-financed by European Social Fund through Sectoral Operational Programme for Human Resources Development 2007–2013.

References

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Corresponding author
Rodica Trăistaru, Department of Physical Medicine and Rehabilitation, University of Medicine and Pharmacy of Craiova, 2–4 Petru Rareş Street, 200349 Craiova, Romania; e-mail: rodicatraistru@hotmail.com

Received: June 26th, 2012
Accepted: November 5th, 2012