**UPDATE IN RADIOLOGY**

**Cam-type deformities: Concepts, criteria, and multidetector CT features**

J.M. Mellado, N. Radi

* Hospital Royo Villanova, Zaragoza, Spain
** Laboratorio de Bioarqueología y Osteología Forense, Departamento de Ciencias Biológicas, Geológicas y Medioambientales, Universidad de Bolonia, Bolonia, Italy

Received 4 June 2014; accepted 3 November 2014

**KEYWORDS**
Anatomic variants; Multidetector computed tomography; Magnetic resonance imaging; Femur; Femoroacetabular impingement

**Abstract** Interpreting imaging studies of a painful hip requires detailed knowledge of the regional anatomy. Some variants of the proximal femur, such as cam-type deformities, can course asymptomatically or cause femoroacetabular impingement. The principal numerical criterion for defining cam-type deformities, the alpha angle, has some limitations. In this article, we review the anatomic variants of the anterior aspect of the proximal femur, focusing on cam-type deformities. Using diagrams and multidetector CT images, we describe the parameters that are useful for characterizing these deformities in different imaging techniques. We also discuss the potential correspondence of imaging findings of cam-type deformities with the terms coined by anatomists and anthropologists to describe these phenomena.

© 2014 SERAM. Published by Elsevier España, S.L.U. All rights reserved.

**PALABRAS CLAVE**
Variantes anatómicas; Tomografía computarizada multidetector;

**Resumen** Para interpretar correctamente los estudios radiológicos de una cadera dolorosa se requiere conocer detalladamente la anatomía regional. Algunas variantes del fémur proximal, como las deformidades tipo cam, pueden cursar de forma asintomática o causar un síndrome de choque femoroacetabular. El ángulo alfa, principal exponente numérico de estas deformidades, tiene algunas limitaciones. Nuestro objetivo es revisar las variantes...
Introduction

In 1965, Murray suggested that some minor variants or deformities of the proximal femur can accelerate hip arthrosis. New terms were coined for these deformities (head tilt, pistol grip, post-slip), based on their radiographic appearance and the possible relation with epiphysiodesis. The concept femoroacetabular impingement arises from these and other observations, a controversial entity that has contributed to popularizing the variability of proximal femur in orthopedics and radiology forums. Within femoroacetabular impingement (FAI) two subgroups are distinguished, the cam type and the pincer type, each with specific radiologic findings and differentiated surgical treatments.

The cam type deformity, described in 2001, is an anatomical variant of the proximal femur. The word cam refers to a mechanical element, usually oval, which is attached to an axis at a point that is not its geometric center. The term cam is used in medical literature to describe a lack of sphericity in the femur head, occasionally associated with other minor deformities. Our understanding of the deformity comes from radiologic and intraoperative observations. The surgical hip luxation and arthro-resonance in multiple radial planes have turned out to be of great help in this sense. However, the variable appearance of the cam type deformity in the different modalities or projections makes its characterization complex.

On the other hand, the variants of proximal femur have been studied thoroughly by anatomists and anthropologists for over a century. Research in cadavers has generated a large number of descriptive terms. Most of these variations correspond to three basic typologies: the prominent one (Poirier accessory facet), the flat or hardly prominent one (Angel’s reactive plate) and the excavated one (Allen’s cervical fossa). In their clarifying revision, Villotte and Knüsel group the two latter terms, plate and fossa, suggesting that many cam type deformities could correspond to the accessory facet. More recently, Radi et al. sub-categorized the plate and the fossa and proposed a simplified terminology based on the review of an identified wide skeletal collection.

Our goal is to review the defining criteria of cam type deformities, illustrating the concepts with diagrams and diagnostic images. We focused our attention on multidetector computed tomography (MDCT), effective to assess it qualitative and quantitatively, with usual applications and specific programs (such as Clinical Graphics). Also the MDCT generates extremely realistic 3D reconstructions that can be compared with the specimens from the osteological medical literature. Ultimately we tried to illustrate the variability inherent to the deformity itself, seeking its potential correspondence with some of the concepts described in the osteological medical literature (Table 1).

Cam-type deformities in orthopedic and radiologic medical literature

FAI is an entity typical of young, active adults that occurs with hip pain, limitation of movement range, suggestive physical examination and early hip arthrosis. In cam type FAI an anterior femoral neck with prominent contour repeatedly impacts the acetabular notch during hip flexion in abduction and internal rotation causing anterosuperior labral and chondral damage (Figs. 1 and 2). In pincer type FAI both the acetabular retroversion and the deep coxa originate anterosuperior labrum lesions, and in advanced stages, labral and chondral lesions are present in the posteroinferior quadrant. In addition, in pincer type FAI there is sclerosis or cortical excavation in the anterosuperior side of the femoral neck. The cam and pincer FAI types often coexist.

Ganz et al. have established the theoretical and practical foundations of FAI. Many other researchers have taken up the challenge of sub-categorizing and validating the most diverse aspects of FAI. In spite of great academic efforts, FAI continues to pose a number of uncertainties. The exact cause of cam type deformity is unknown, as well as its actual prevalence, its actual usefulness as a FAI radiological marker, the optimal surgical indication, the natural history of non-operated FAI or the possible effectiveness of preventive surgery in asymptomatic patients with this deformity.

The idiopathic cam type deformity is an extension of the epiphysis towards the anterosuperior portion of the femoral neck. In its most common manifestation, it is an osseous prominence lacking epiphyseal sphericity (cam) and a decrease of head–neck offset. Both features are closely linked to each other, but they are not equivalent and they do not occur necessarily in constant proportions. The cam type FAI hypothesis suggests that there is an anomalous FAI when the curvature radius of the femoral head surpasses the curvature radius of the acetabulum. This can happen with several types of femoral deformity though the shape of the acetabular contour also plays a role. In a simplified manner, it can be claimed that there are 3 cam type deformities: (a) predominance of prominence; (b) predominance of...
offset loss, and (c) prominence with offset loss and epiphyseal retroversion (pistol grip deformity) (Fig. 3). The latter has a shape similar to that of epiphysiolysis, but with less accentuated features. These three categories do not cover the whole spectrum of possible variations or represent a validated classification, but they serve the purpose of drawing the attention to the most relevant parameters.

Characterizing the cam type deformity requires a standardized radiographic technique and systematic evaluation.38 Anterior–posterior and axial projections (conventional or Lauenstein) can prove useful (Fig. 1). However, lateral projections with horizontal rays (cross-table, at a 15° internal rotation), Dunn at 90° and Dunn at 45° are more effective because they split the greater trochanter,
The most commonly used measurements are the alpha angle, described in MRI to assess the femoral sphericity deficit, and Eijer’s ratio, described in lateral radiography to assess offset loss. The alpha angle identifies the potentially relevant cam type deformity from the clinical point of view when it reaches values above a specific cut point on an adequate plane. The alpha angle is optimally assessed in planned MR images with double obliquity (parallel to the cervical axis, but with a 45° radial orientation, equivalent to the 1:30 h point) (Fig. 6). The ideal cut point to characterize the deformity is still under discussion, although values >60° improve significantly the effectiveness for identification purposes of the prominences clinically associated with FAI. In any case, the alpha angle is hard to measure, it cannot be estimated subjectively and it is influenced by several geometric factors. Measuring the Eijer ratio is also difficult because the distances assessed are small. For all the above, it is recommended to combine the quantitative and qualitative criteria.

During the last few years new quantitative parameters or modifications from the existing ones have been proposed. In the coronal plane, the triangular index stands out, too complex to be used clinically (Fig. 4C). The anatomical alpha angle has been proposed for the axial plane, which takes into account epiphyseal retroversion on tracing the reference lines (Fig. 5B). The beta angle, measured in 90° Dunn projection, assesses the relation of sphericity deficit with the anterior acetabular lip (Fig. 5A). The angle of torsion specifically quantifies epiphyseal retroversion with respect to the axis of the femoral neck with higher values in the cam type deformity associated with FAI (Fig. 5C). On the other hand, femoral neck anteverision with respect to the posterior bicondylar line shows significantly lower values in patients with cam type FAI than in patients suffering from pincer type FAI. The profusion of new indexes, angles and measurements in recent publications seem to reflect not only the limitations of the original criteria, but also the deformity’s intrinsic variability. In this same line some authors suggest that the cam type deformity is much more than just a protuberance. According to this view, the deformity would entail a multiplicity of dimorphic traits, including large, spheroid femoral head, broad, short femoral neck, increase of the...
Cam-type deformities: Concepts, criteria, and multidetector CT features

Figure 4  Characterization of cam type deformity in an anterior-posterior projection. (A) Alpha angle. (B) Murray’s ratio a/b and neck/head ratio c/d. (C) Triangular index, where e is the short radius, f is half the short radius, g is perpendicular to f, and h is calculated through Pythagoras’ theorem. When in an anterior-posterior X-ray (magnification ≤ 1.2) the long radius h is greater than or equal to the short radius e plus 2, we usually speak of femoral asphericity. (D) Neck length of i; depth of superior j and inferior offset k.

Figure 5  Characterization of a cam type deformity in an axial projection. (A) Nötzli’s alpha angle and Wyss’ beta angle. (B) Bouma’s anatomical alpha angle (αa) and posterior displacement of epiphyseal center a. (C) Epiphyseal torsion angle. (D) Lateral (b) and posterior (c) extension of anterior epiphysis. Depth of anterior d and posterior e offset and Eijer’s ratio d/f.

head–neck ratio, decrease of the anterior and posterior offset and occasional epiphyseal retroversion.13

MDCT allows us to study cam type deformities quantitatively and qualitatively. It discriminates between cam type deformities with anterior prominence as a predominating feature (Fig. 7) and those with a more flat profile (Fig. 8). Also it shows the lateral extension of the joint surface, whose outer limit often surpasses the fissure line (Figs. 7 and 8). MDCT’s quantitative study options include densitometries. In cam type deformities,

Table 2  Characterization of cam type deformity based on anterior-posterior projections.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Orientative reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral sphericity deficit</td>
<td>Exceeds the circumferential morphology &gt; 2 mm16</td>
</tr>
<tr>
<td></td>
<td>Rectifies the usual curved contour45</td>
</tr>
<tr>
<td></td>
<td>The fissure scar extends horizontally towards the femoral neck12</td>
</tr>
<tr>
<td></td>
<td>In controls the reference values are 62° (males) and 52° (females)54</td>
</tr>
<tr>
<td></td>
<td>In epiphyseolysis the cut value is &gt; 1.35i</td>
</tr>
<tr>
<td></td>
<td>In cam, long radius ≥ short radius + 2i44</td>
</tr>
<tr>
<td>Superior offset decrease</td>
<td>Disappearance of superior offset (convex contour)7</td>
</tr>
<tr>
<td></td>
<td>Comparison with inferior offset (less useful than the anterior offset)34</td>
</tr>
<tr>
<td>Other associated traits</td>
<td>In cam, average value 1.59 ± 0.11, lower than in controls13</td>
</tr>
<tr>
<td></td>
<td>Cut value &lt; 1.27 associates arthrosis35</td>
</tr>
<tr>
<td></td>
<td>In cam, average value 24.9 ± 2.9 mm (short wide neck13</td>
</tr>
<tr>
<td></td>
<td>In cam, cut value &lt; 1252.25</td>
</tr>
</tbody>
</table>

(Continued on next page)
Table 3  Characterization of cam type deformity base don axial or lateral projections.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Orientative reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior sphericity deficit</td>
<td>Exceeds the circumferential contour (&gt;2 mm)&lt;sup&gt;16&lt;/sup&gt;</td>
</tr>
<tr>
<td>Anterior-superior prominence (Fig. 1B)</td>
<td>In controls average value of 47° (males) and 42° (females)&lt;sup&gt;54&lt;/sup&gt;</td>
</tr>
<tr>
<td>Radiographic alpha angle (Frog axial Rx)</td>
<td>In controls average value of 48° (males) and 47° (females) with a reference interval for both genes (95%) of 32–62&lt;sup&gt;42&lt;/sup&gt;</td>
</tr>
<tr>
<td>Radiographic alpha angle (Lateral Rx)</td>
<td>In cam, cut value (at 45°) &gt; 60&lt;sup&gt;48&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tomographic alpha angle (Fig. 5A)</td>
<td>In cam, cut value &gt; 66&lt;sup&gt;55&lt;/sup&gt;</td>
</tr>
<tr>
<td>Anatomic alpha angle (Fig. 5B)</td>
<td>In cam, average value 15.6° (38.7° in controls)&lt;sup&gt;59&lt;/sup&gt;</td>
</tr>
<tr>
<td>Beta angle (Fig. 5A)</td>
<td>In cam, anterior distance exceeds the posterior distance&lt;sup&gt;22,29&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lateral epiphyseal extension (Fig. 5D)</td>
<td>Comparison with posterior offset (same, lesser or absent)&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Anterior offset decrease</td>
<td>In cam, cut value &lt; 8 mm&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>Depth of the anterior offset (Fig. 5D)</td>
<td>In controls average value of 0.19&lt;sup&gt;42&lt;/sup&gt; with a reference interval for both genres (95%) of 0.14–0.24&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td>Radiographic Eijer ratio (Lateral Rx)</td>
<td>In cam, ratio &lt; 0.18&lt;sup&gt;19&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tomographic Eijer ratio (Fig. 5D)</td>
<td>With clinical significance cut value &gt; 2 mm&lt;sup&gt;13&lt;/sup&gt;</td>
</tr>
<tr>
<td>Other associated traits</td>
<td>In cam, cut value &gt; 20&lt;sup&gt;47&lt;/sup&gt;</td>
</tr>
<tr>
<td>Posterior epiphyseal displacement (Fig. 5B)</td>
<td>Similar values in controls and FAI&lt;sup&gt;59&lt;/sup&gt;</td>
</tr>
<tr>
<td>Epiphyseal retroversion with respect to the neck (Fig. 5C)</td>
<td>Lower averages values of cam (10 ± 9) to those of pincer (18 ± 10)&lt;sup&gt;50&lt;/sup&gt;</td>
</tr>
<tr>
<td>Femoral anteverision with respect to the bicondylar line</td>
<td></td>
</tr>
</tbody>
</table>

an increase of underlying trabecular bone density has been demonstrated which presupposes an increase in subchondral rigidity that can accelerate chondral degeneration.<sup>29</sup>

Cam type deformities are highly prevalent in asymptomatic individuals. In fact the overlapping of alpha angles in asymptomatic individuals and in FAI patients has spurred scientific controversy,<sup>12,18,35,42,44,45,48,52,54</sup> moderate skepticism<sup>41</sup> and sarcastic opinions.<sup>13</sup> For the advocates of the FAI concept, we are talking about predisposed individuals that may require specialized orthopedic attention.<sup>27</sup>

For the most reticent ones, the broad angle overlapping between cases and controls could question the theoretical pillars of FAI.<sup>53</sup>

Cam type deformities are more prevalent among males, especially in physically active individuals. They are likely to develop before the fissure closure, as an adaptational expression to a repeated mechanical overload.<sup>28</sup> Many authors claim that the deformity results from a clinically silent epiphysiolysis,<sup>1,31</sup> although this has not been entirely verified and it can occur only in a small proportion of the

Figure 6  (A and B) Characterization of a cam type deformity on radial planes. The measurement of the alpha angle can be obtained on the oblique axial plane with a 3:00h orientation (blue line) through the plane with 1:30 radial orientation (red line), equivalent to 45° better discriminates those patients with FAI patients.<sup>50</sup> The reader can see this figure in color in the electronic version of the article.
Cam-type deformities: Concepts, criteria, and multidetector CT features

Figure 7  Cam type deformity (prominent). 53-year-old asymptomatic man. MDCT with 3D reconstructions (A) anterior–posterior, (B) oblique anterior–posterior and (C) cranio-caudal reconstructions, followed by (D) axial oblique multiplane reconstruction. Prominent cam type deformity with convex contour and regular surface, whose external limit (red arrow) extends the lateral contour of the epiphysis yet it is far from the fissure scar (green arrow). The reader can see this figure in color in the electronic version of the article.

Figure 8  Cam type deformity (flat). 49-year-old asymptomatic man. MDCT with 3D reconstructions. (A) Anterior–posterior, (B) oblique anterior–posterior and (C) cranio-caudal reconstructions followed by (D) axial oblique multiplane reconstruction. Cam type deformity with predominantly flat contours, with erased anterior offset and small medial depression (blue arrow). The outer limits of the deformity (red arrow) extends the lateral contour of the epiphysis yet it is far from the fissure scar (green arrow). The reader can see this figure in color in the electronic version of the article.
cases. Cam type deformities can also have a racial and
genetic component. 43

Recent publications suggest that the deformity has mul-
tiple causes, and the patient’s age, sex, bodily habits,
exercises and evolutionary patterns, among other factors
are influential. 46 The deformity can be sub-categorized into:
(a) primary; (b) secondary to development, related to epi-
physiolysis, Perthes’ disease and interventional congenital
hip dysplasia, and (c) acquired—identified with remodeling
associated with hip arthrosis, post-traumatic deformity or a
previous osteotomy. 46 Therefore, cam type deformities can
cause and also be the consequence of arthrosis. 50 And it
can be secondary to epiphysiolysis or have nothing to do
with it. There seem to be several types of deformity. But if
that is the case, maybe not all of them cause FAI and then
it would be necessary to discriminate them with renewed
criteria.

Proximal femur variations in osteological
medical literature

The osteological medical literature contains a large variety
of descriptive terms for the proximal femur, many of which
have fallen into disuse. 5  19 The three basic forms described
by anatomists and anthropologists are Poirier’s accessory
facet, Angel’s reactive plate and Allen’s cervical fossa, with
a variable expression in the anterior–posterior and lateral
or axial planes (Fig. 9).

In the anterior–posterior plane, the distinction between
Poirier’s accessory facet and Angel’s reactive plate is
based on its outer contour; being a priori the facet more

Figure 9  Variability of the anterior facet of the proximal
femur based on the existing osteological medical literature.
On the anterior–posterior plane, (A) Poirier’s accessory facet;
(B) Angel’s reactive plate, and (C) facet or plate with superior
offset loss, similar to cam type deformity. On the axial plane,
(D) not-elevated Angel’s reactive plate, with crest (lateral) and fossa
(medial); (E) flat reactive plate, with crest (lateral) and herni-
ation pit (medial), and (F) prominent plate or facet, similar to
the cam type deformity.

Figure 10  Reactive plate. 40-year-old asymptomatic man.
MDCT with 3D reconstructions. (A) Anterior–posterior, (B) oblique
anterior–posterior and (C) oblique axial, and (D) multiplane axial oblique
reconstructions. Slightly sclerotic hardly appreciable
reactive area. The plate’s external limit (red arrow) is far from the fissure scar (green arrow). The reader can see this figure in
color in the electronic version of the article.
Cam-type deformities: Concepts, criteria, and multidetector CT features

Figure 11 Reactive plates in individuals of different ages. (A and B) 58-year-old man. (C and D) 78-year-old man. Both asymptomatic. MDCT with anterior–posterior 3D (A and C) and multiplane axial oblique reconstructions (B and D). Reactive plates with flat profile (A and B) and convex profile (C and D) (arrows).

Figure 12 Reactive plate and herniation pit. 47-year-old asymptomatic man. MDCT with (A and B) 3D anterior–posterior and (C) multiplane axial oblique reconstructions. Reactive area with slightly elevated profile (green arrows) and underlying herniation pit (red arrows). The reader can see this figure in color in the electronic version of the article.

circumscribed (Fig. 9A) and the plate more extensive and lateral (Fig. 9B). When loss of superior offset is associated (Fig. 9C), the variant is similar to the cam type deformity. Systematization in the lateral or axial plane distinguishes between concave or non-elevated (Fig. 9D), flat (Fig. 9E) and prominent variants (Fig. 9F) being the prominent variant closer to cam type morphology.

Poirier’s accessory facet was defined as a lateral extension of the epiphysis towards the anterosuperior region of the neck (Fig. 9A). It is usually covered by hyaline

Figure 13 Cam type deformity. Specimen from the cadaver of a 59 year-old male. Views (A) frontal and (B) cranio-caudal showing a deformity typical of the cam type (between arrows). Lateral extension of the epiphysis, with a prominent profile, with epiphyseal retroversion and short neck. Source: Identified skeletal collection. La Certosa Cemetery. Museum of Anthropology of the University of Bologna. Bologna, Italy.
cartilage. Its prevalence is unknown because the data published are inconsistent.\textsuperscript{5,6} The accessory facet has a smooth contour, with a profile continuing to the joint surface of the epiphysis in the femoral neck region without apparent transition. It can present a triangular or oval configuration, and it can be hard to identify when it coexists with other variations or degenerative changes. When described like this the facet can correspond to the classical cam type deformity (Figs. 3A,D and 7).\textsuperscript{8,9}

Angel’s reactive plate, a fairly more recent concept than that of accessory facet, introduces the idea of adaptational or occupational trait.\textsuperscript{3} It is identified in up to 87% of the specimens. It is more prevalent among males, especially in elderly males.\textsuperscript{7} The reactive plate extends more laterally and inferiorly than Poirier’s facet (Fig. 9B).\textsuperscript{1,5,8,9} It can be covered by fibrocartilage\textsuperscript{8} and it often presents sclerosis and cortical irregularity of a variable-profile (Fig. 9D–F). In MDCT, the reactive plate often adopts a slightly sclerotic appearance not elevated or associated with a minimal decrease of the anterior offset (Fig. 10). When the reactive plate is prominent, it can be similar to the accessory facet. In fact, they can both reflect variable degrees of the same phenomenon.\textsuperscript{9} On the other hand, MDCT allows us to compare reactive plates in individuals of different ages (Fig. 11). The prominent plate, frequent in old age, seems to exaggerate a superficial trait that is present in the early decades of life.

The outer contour of the reactive area can be outlined by an osseous lip or crest\textsuperscript{1,9} (Fig. 9D–F) which is generally easy to identify with MDCT (Fig. 11). When the crest is prominent, the plate takes on an excavated appearance (fossa). Also the plate can present a patent aspect in dry cadaver specimens\textsuperscript{9} possibly unnoticed in MDCT. In its extreme version, cortical patency also transforms into cervical fossa.\textsuperscript{1,9}

Some cortical pores in the reactive area communicate with a small juxtacortical cyst, known as herniation pit.\textsuperscript{58,61} Such a cyst—a concept of radiological origins is recognizable by its radio-lucid appearance with sclerotic edges. Its prevalence ranges between 5 and 12%. Its meaning is controversial, and it can represent a synovial hernia or an intraosseous ganglion. Similar fibrocystic changes have been found in 33% of FAI patients,\textsuperscript{23} although its relevance as FAI radiographic markers is still under discussion. In any case, the pits often appear closely related to the reactive plate focused on the utmost superior and medial margins of the femoral neck (Fig. 12).

Most authors talk about the existence of a direct relation between these skeletal variants of the proximal femur and habits associated with exercise or rest. It is hypothesized that there is a repetitive friction of the femoral neck with contiguous soft tissue structures, such as lower fasciculus of the iliofemoral capsular ligament\textsuperscript{62} or the psoas tendon.\textsuperscript{8,9}

Conclusions

Cam type deformities can have 3 basic configurations: prominent, flat and with epiphyseal retroversion. On the other hand, the variants described in descriptive osteology are summarized in 2: Poirier’s accessory facet (Fig. 13) and Angel’s reactive plate (Fig. 14). The accessory facet is equivalent to the classical cam type deformity.\textsuperscript{8,9} However, the facet and the plate can look like each other, and they can be associated to crests, fossae, pores and pits. As a matter of fact we do not know if the accessory facet and the reactive plate are different entities or extreme versions of a continuous spectrum of variability that is still far from being fully understood.

Ethical responsibilities

Protection of people and animals. Authors confirm that no experiments have been performed on human beings or animals.

Data confidentiality. Authors confirm that the protocols of their institution have been followed on the publication of data from patients.

Right to privacy and informed consent. Authors declare that in this article no data from patients have been published.

Authors

1. Manager of the integrity of the study: JMM.
2. Original idea of the Study: NR.
Cam-type deformities: Concepts, criteria, and multidetector CT features

3. Study design: JMM.
4. Data mining: JMM, NR.
5. Data analysis and interpretation: JMM, NR.
6. Statistical analysis: N/A.
7. Reference search: JMM, NR.
8. Writing: JMM, NR.
9. Critical review of the manuscript with intellectually relevant remarks: JMM, NR.
10. Approval of final version: JMM, NR.

Conflict of interests

Authors declared no conflicts of interests.

Acknowledgement

To Dr. Ignacio Quintana, MD for his collaboration searching for information from medical literature.

References