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EDITORIAL COMMENT

# Left atrial appendage thrombus in severe mitral stenosis: Can chamber morphology and thrombus location influence therapeutic choice?

## Trombo no apêndice auricular esquerdo na estenose mitral grave - a morfologia da câmara e a localização do trombo podem influenciar a escolha terapêutica?

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The article by Ashraf et al. published in this issue of the *Journal*[1] focuses on the importance of transesophageal echocardiography (TEE) and cardiac computed tomography (CT) in the evaluation of patients with significant mitral stenosis who are undergoing percutaneous mitral valvotomy. It is a prospective multicenter study, carried out over seven months in Pakistan, in which the presence and location of thrombi in the left atrial appendage (LAA), the morphology of this structure and the influence of anticoagulation were assessed by TEE and then by CT in the evolution and disappearance of thrombi, reassessed by TEE after three months of therapy. The patients were relatively young (mean age 38 years, standard deviation 12 years), and the series is not very large (88 patients).

It is known that, in rheumatic mitral stenosis, atrial thrombi may be in multiple locations in the left atrium (LA), and may even be loose and mobile in the atrial cavity, but in around half of cases are located in the LAA. Their presence is considered a contraindication for percutaneous mitral valvotomy, as they carry the risk of causing periprocedural thromboembolism, with its associated morbidity and mortality. Atrial thrombi are considered an indication for surgery in mitral stenosis. However, a period of anticoagulation can be tried, which may last up to six months.[2] As the catheter or guide can sometimes penetrate the LAA, it is important to avoid proposing a percutaneous approach in this context.[3]

As is well known, mitral stenosis is often the result of valvular alterations caused by rheumatic fever[3] after tonsillitis that was not properly treated and autoimmune changes subsequently developed. Prophylaxis maintained with penicillin every three weeks appears to prevent the development of the disease or new outbreaks of streptococcal infection that worsen valvular lesions.

Nowadays, in developed countries, rheumatic mitral stenosis is rare and degenerative mitral stenosis predominates, often associated with calcification of the valve ring, predominantly in female and elderly individuals.[3] However, in developing countries in Asia, Africa and parts of South America, there are still many episodes of rheumatic fever which cause significant early forms of rheumatic valve disease, with the appearance of severe mitral stenosis at a very young age. It is essential to approach these patients in a structured manner. For example, in pregnant women, increased cardiac output is often associated with significant clinical worsening and may result in the need for early and urgent intervention. In these cases, it is particularly important to evaluate the effect of anticoagulation and to identify which patients have the weakest response to this therapy. This knowledge may lead to an earlier decision to opt for surgery, although this may jeopardize the success of the pregnancy and fetal viability.

Cardiac CT and cardiac magnetic resonance imaging (MRI) studies show that there are different LAA morphologies,

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conventionally divided into four types: cauliflower, cactus, windsock and chicken wing.

In Ashraf et al.'s study,[1] only 27% of patients showed complete thrombus resolution, the highest proportion being in those with cactus-type LAA (66%) and in those with thrombus at the LAA tip, while there was no thrombus resolution in any patients with thrombus at the LAA base. The most frequent LAA type in this study was chicken wing (44%), but, in this morphology, only 14% showed thrombus resolution with anticoagulation, while the cactus type was less prevalent but responded better to anticoagulation. In another study[2] in patients with mitral stenosis and atrial fibrillation (AF), around 94% of thrombi disappeared with oral anticoagulation when they were in the LAA.

In a study by Abanador-Kamper et al.,[4] chicken-wing morphology was seen in only a quarter of patients (25.5%) and windsock predominated (51.5%), and in those who presented thrombi in the LAA, the prevalence of windsock morphology was even higher (62%). In the present study, the most superficial thrombi largely disappeared (62.5%).[1] However, those in the base of the LAA did not change.

More recent, less organized thrombi naturally respond better to oral anticoagulation. On the other hand, most organized, sometimes even calcified, thrombi do not respond well to anticoagulation. Deep thrombi in the LAA can sometimes be confused with the pectineal muscles; it is not always possible to make this distinction based on morphological appearance. It cannot be completely excluded that some of these thrombi, which are located deeply, were incorrectly diagnosed as such, especially since the text does not mention whether the existence of thrombi in the LAA was confirmed in those who underwent surgery.

However, other studies have shown that chicken-wing morphology in patients with non-valvular AF appears to be protective both against the appearance of thrombi[5] and against their recurrence.[6] In a study by Anselemino et al.[7] in patients with non-valvular AF who were candidates for AF ablation, the incidence of the different morphological LAA types was similar to that of Ashraf et al.,[1] with Anselemino et al. also finding chicken wing to be the predominant morphology. Silent cerebral ischemia on brain MRI, which was common in patients in Anselemino et al.'s study, was, in addition to age, related to non-cactus type morphologies – chicken wing, windsock or cauliflower. Thus, in their study also, cactus morphology was less serious.

In some studies, the chicken-wing type is considered to be associated with a lower incidence of thrombi,[4,7] but in one study[4] those with thrombi and this morphology had a higher risk of developing thromboembolic phenomena (42.9% vs. 20% with another morphology). In the population of di Biase et al.'s study[7] with non-valvular AF and a history of transient ischemic attack (TIA)/stroke, patients with chicken wing LAA morphology had a 79% lower previous incidence of TIA/stroke. In Ashraf et al.,[1] although the incidence of chicken-wing morphology was significant, these patients did not appear to respond adequately to oral anticoagulation (at least when it lasted for only three months): only 27% of patients had their thrombi eliminated with anticoagulation. This figure seems very low, especially since the international normalized ratio range chosen was between 2.5 and 3.5 and patients who were not at therapeutic levels were excluded.

In general, it is thought that up to 20% of patients do not respond to therapy. In Ashraf et al.'s study, the proportion of total thrombus resolution, might have been greater if the duration of anticoagulation had been extended to six months, as in other studies,[2] instead of only three months. In the latter study, only 12% responded to oral anticoagulation when the thrombi were located in the body of the left atrium.

Except in urgent symptomatic cases, I consider that waiting three to six months to evaluate the response to oral anticoagulation is feasible, even for thrombi deep in the LAA. In the three months of the study analyzed here, no thromboembolic phenomena were observed, either arterial or venous, although this is independent of the presence of thrombi in the LAA.

We can therefore say that this study highlights the association of LAA morphology and thrombus location with a weaker response to oral anticoagulation in patients with mitral stenosis who are candidates for mitral valvotomy. Awareness of this can sometimes help to opt for an earlier, more invasive strategy against some types of thrombi and/or LAA in patients with significant rheumatic mitral valve stenosis.

However, this series is not very large and there is considerable variability in the results of different series. There appears to be agreement only that the cactus type is associated with the best therapeutic response. So an individualized approach should be adopted for each case.

## Conflicts of interest

The author has no conflicts of interest to declare.

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