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EDITORIAL

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About vegetation size and its clinical implications

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The following questions may arise when facing a patient with left-sided infective endocarditis (IE) and vegetations.

Does vegetation size matter?

Embolic events are frequent and life-threatening complications of IE. They are usually related to fragmentation and systemic embolization of cardiac vegetations. Theoretically, the larger the vegetation, the greater the risk of embolism [1]. In a rather recent meta-analysis of 21 studies including 6646 patients and 5116 measured vegetations, patients with vegetation size greater than 10 mm had significantly increased odds of embolism and mortality [2]. To further correlate embolic events with vegetation size these authors found that odds were greater with a cutoff of 15 mm [2]. Other authors have found that the risk of neurological complications is particularly high in patients with very large (> 30 mm length) vegetations [3]. Thus, the answer is yes, vegetation size matters.

What do the guidelines say?

Echoing previous studies and to prevent embolic events, the American Heart Association guidelines suggest considering surgery in patients with severe valve regurgitation and vegetations > 10 mm (class IIa, level of evidence B). Surgery may also be considered when the vegetation size is > 10 mm, particularly when involving the anterior leaflet of the mitral valve and when associated with other relative indications for surgery (class IIb, level of evidence C) [4]. The European Society of Cardiology guidelines recommend surgery in left-sided persistent vegetations > 10 mm after one or more embolic events despite appropriate antibiotic therapy (class I, level of evidence B). Surgery may also be considered in isolated left-sided large (> 15 mm) vegetations and no other indication for surgery (class IIb, level of evidence C) [5]. Thus, in the current guidelines there is no class I recommendation based exclusively on the vegetation size. The closest to it is the case of isolated, left-sided, very large vegetations (> 30 mm) (class IIa, level of evidence B) [5].

How accurate is the measurement of vegetation size?

Echocardiography, particularly transesophageal echocardiography (TEE), plays a key role in identifying those vegetations more prone to embolize. In this issue of "Cardiology Journal", Cabezón Villalba et al. [6] evaluate the interobserver variability in the measurement of vegetation diameter and its impact on surgical indication when considering the guideline cutoff points. This is a pertinent and relevant research study in which two echocardiographers independently measured the maximum diameter of 76 vegetations in 67 consecutive patients with definite left-sided native valve IE by TEE.

The interobserver interclass correlation coefficient in the measurement of vegetations diameter was 0.757 (0.642–0.839) indicating moderate reliability. Disagreement between operators were

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estimated by the kappa coefficient and the observed concordance. When the cutoff point of 10 mm was considered, disagreement between the experts was found in 18% of cases, whereas with a cutoff of 15 mm, disagreement was found in 25% of cases. In the absence of another indication for surgery, depending on who had measured the vegetations, the indication for surgery would have varied in 43% of the patients. The authors conclude, quite correctly, that the variability of the measurement of vegetations diameter by TEE is high, and consequently, the IE surgical indication based on a cutoff vegetations diameter should be taken with caution.

Is there a better option to measure the vegetations embolic risk?

Real-time three-dimensional-TEE allows a better characterization of vegetations than two--dimensional-TEE [7, 8]. This may end up with a more accurate assessment of the vegetation size and morphology which might lead to a better prediction of the embolic risk in patients with IE.

Has surgery demonstrated a benefit in patients with isolated large vegetations?

It becomes clear that in left-sided IE, large vegetations identify patients with poor outcomes. However, surgery has not been clearly associated with a better prognosis in patients with large vegetations if they do not present with another predictor of poor outcome such as heart failure or uncontrolled infection [9, 10]. Furthermore, surgery in patients with native left-sided IE and isolated large vegetations without any other indication for surgery has been associated with excess mortality [11]. A rather recent study showed that patients with large vegetations (> 10 mm) had higher 6-month mortality. However, after propensity adjustment, the association with higher mortality persisted only in patients with large vegetations managed medically rather than surgically [12]. These findings challenge whether vegetation size alone should be an indication for surgery. In any case, although surgery might be effective in reducing the risk of embolism, the operative risk must be balanced against this benefit.

What can we do to decrease the patient's embolic risk?

Several studies have shown a markedly decreased risk of embolic events in the second week after initiation of targeted antimicrobial therapy [1, 3, 13, 14]. Thus, prompt initiation of an appropriate antibiotic therapy is the most effective known method to reduce embolic events.

Conclusions

In summary, this remarkable investigation of Cabezón Villalba et al. [6], shows that the interobserver variability of the length of a vegetation is high enough to affect the surgical indication in an unacceptable number of patients. As the authors wisely state, vegetation size cannot be regarded as the sole parameter to estimate the embolic risk in IE. This issue requires a multiparametric approach [1]. Hence, currently, vegetation size as the only surgical reason should be more the exception (very large vegetations) rather than the rule [15].

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