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What size of vegetation is an indication for surgery in endocarditis?

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Abstract

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was whether the of vegetations in endocarditis is an indication for surgery. Altogether, 102 papers were found using the reported search; 16 papers were identified that provided the best evidence to answer the question. The authors, journal, date, country of publication, patient group, study type, relevant outcomes and results were tabulated. The vegetation size was classified into small (<5 mm), medium (5–9 mm), or large (≥10 mm) using echocardiography and a vegetation size of ≥10 mm was a predictor of embolic events and increased mortality in most of the studies with left-sided infective endocarditis. For large vegetations—that commonly resulted from the failure of antibiotics to decrease the vegetation size during 4–8 weeks' therapy—and complications such as perivalvular abscess formation, valvular destruction and persistent pyrexia necessitated surgical intervention. In a multicentre prospective cohort study of 384 consecutive patients with infective endocarditis, it was observed that a vegetation size of >10 mm and severe vegetation mobility were predictors of new embolic events. Equally, a meta-analysis showed that the echocardiographic detection of a vegetation size of ≥10 mm in patients with left-sided infective endocarditis posed significantly increased risk of embolic events. In another prospective cohort study of 211 patients, it was observed that there was an increased risk of embolization with vegetations of ≥10 mm. In similarly another study of 178 consecutive patients with infective endodarditis assessed by echocardiographic study, it was found out that there was a significantly higher incidence of embolism with a vegetation size >10 mm (60%, $P<0.001$). When using the area of the vegetation, a vegetation size of >1.8 cm^2 predicted the development of a complication. Assuming that the vegetation was a sphere, the calculated diameter will be 8 mm when using $4\Omega r^2$ for the area. However, for right-sided infection endocarditis, a vegetation size of >20 mm was associated with a higher mortality when compared with a vegetation size of ≤20 mm. There is strong evidence to suggest that a vegetation size of ≥10 mm especially for left-sided infective endocarditis is an indication for surgery.

Keywords: Vegetation size • Infective endocarditis • Echocardiography • Surgical intervention

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the journal *Interactive CardioVascular and Thoracic Surgery* [1].

THREE-PART QUESTION

In [patients with a vegetation secondary to endocarditis] what size is [an indication for surgery] in order to prevent [embolisation].

CLINICAL SCENARIOS

You are seeing a 67-year old diabetic patient with endocarditis. He has mild mitral regurgitation but the vegetation is 1.20 mm in size on the echo. He has undergone a week of antibiotic treatment and seems quite stable. He has suffered no embolic episodes but the cardiologists feel that the vegetation should be removed. The patient would rather see if it shrinks with further antibiotic treatment and asks if this would be safe.

SEARCH STRATEGY

The literature search was carried out using the U.S. National Library of Medicine's MEDLINE® database, scrutinizing a period from 1966 to March 2012, inclusive, using the PubMed interface. The search parameters were: (vegetation[All Fields] AND size[All Fields]) AND ('surgery'[Subheading] OR 'surgery'[All Fields] OR 'surgical procedures, operative'[MeSH Terms] OR ('surgical'[All Fields] AND 'procedures'[All Fields] AND 'operative'[All Fields]) OR 'operative surgical procedures'[All Fields] OR 'surgery'[All Fields] OR 'general surgery'[MeSH Terms] OR ('general'[All Fields] AND 'surgery'[All Fields]) OR 'general surgery'[All Fields]) AND ('endocarditis'[MeSH Terms] OR 'endocarditis'[All Fields]). The reference citations of the articles found through these searches were also reviewed for relevant articles.

Table 1: Best Evidence papers

Author, date, journal, country Study Type (level of evidence)	Patient group	Outcome	Key result	Comments
Rohmann (1992), Eur Heart J, Germany [2] Prospective cohort study (level 3)	281 patients with IE. The prognostic value of ascertaining the site of vegetations evaluated	Risk of embolic Risk of abscess Surgical Intervention Mortality Risk factors for embolism	MV vs AV 25 vs 9.7% 0 vs 6% 5.5 vs 11% 0 vs 1.6% Vegetation size (VS) of >10 mm	TOE assessed the clinical outcome Mean follow up of 14 months
Vilacosta (2002), J Am Coll Cardiol, Spain [3] Prospective cohort study (level 3)	217 episodes of left-sided IE that were experienced among a cohort of 211 prospectively recruited patients	Increased risk of embolization with increasing VS The increased VS at follow-up showed a higher risk for embolization Risk factors for embolism	RR 3.77, 95% CI 0.97 to 12.57; ($P = 0.07$) RR 2.64, 95% CI 0.98– 7.16; $P = 0.02$ VS of ≥10 mm) when the organism was staphylococcus ($P = 0.04$)	TOE and TTE used in assessment Failure of antimicrobial treatment is assessed by increasing VS during therapy
Mugge (1989), J Am Coll Cardiol, Germany [4] Prospective cohort study (level 3)	105 patients with active IE, disease-associated complications defined as severe heart failure (New York Heart Association class IV), embolic events and in-hospital death were correlated to the VS	The correlation of VS with endocarditis-associated complications with a vegetation diameter	Patients with a VS >10 mm had a significantly higher incidence of embolic events than did those with a VS ≤10 mm (22 of 47 vs 11of 58; ($P < 0.01$)	TOE and TTE used in assessment No correlation between VS and location of endocarditis or infective organism
Hecht (1992), Ann Intern Med, USA [5] Retrospective study (level 4)	121 patients intravenous with IE. The presence of a right-sided valve vegetation assessed	Mortality rate	VS >20 mm vs ≤20 mm (33 VS 1.3%; $P < 0.001$)	RSIE assessed Observer blinded study No follow-up
Thuny (2005), Circ, France [6] Prospective cohort study (level 3)	A multicentre study, including 384 consecutive patients (aged 57 ± 17 years) with definite IE using the Duke University criteria	Predictor of 1-year mortality	VS >15 mm (adjusted RR = 1.8; 95% CI, 1.10–2.82; $P = 0.02$)	TOE used in assessment Multicentre study No follow-up
Robbins, (1986), Am J Med [7] Retrospective study (level 4)	This study evaluated the prognostic value of VS in 23 episodes of RSIE in 21 patients	Indication for surgery	No surgery for VS of <10 mm, while VS of ≥10 mm required surgery for persistent pyrexia ($P < 0.05$)	RSIE assessed
Nunes (2010), J Infect Dis, Brazil [8] Prospective cohort study (level 3)	62 patients with IE during a 7-year period. The Cox proportional hazards model was used to identify predictive factors for death	The overall in-hospital mortality	VS >13 mm was the only independent predictor of in-hospital mortality (hazard ratio 1.05 per mm; 95% CI 1.003–1.110; $P = 0.038$)	TOE was used in assessment Prospective study No follow-up
Martin-Davilla (2005), Am Heart J, Spain [9] Retrospective study (level 4)	493 cases of IE. VS was available in 111 cases	Variables associated with mortality	VS > cm ($P = 0.014$; OR 10.2; 95% CI 1.6–78.0)	RSIE No follow-up Not too sure about the role of early surgery
Wong (1983), Arch Intern Med, USA [10] Prospective cohort study (level 3)	34 patients with clinical IE. Vegetations were identified in 16 patients (47%) by M-mode and in 27 patients (87%) by 2D echocardiography	Classification of VS 1 Small 2 Medium 3 Large Incidence of surgery	<5 mm 5 mm–9 mm >10 mm >10 mm (44% vs 0%)	Small sample size Advocated useful classification No follow-up Usefulness of different echocardiographic mode

Continued

Table 1: (*Continued*)

Author, date, journal, country Study Type (level of evidence)	Patient group	Outcome	Key result	Comments
Tischler (1997), J Am Soc Echocardiogr, USA [11] Meta-analysis (level 3)	A meta-analysis of which identified by a computerized search of the key words IE and echocardiography A pooled odds ratio was calculated by using the Robins, Greenland, and Breslow estimate of variance	The pooled odds ratio for increased risk of systemic embolization in the presence of a vegetation	VS >10 mm (10 studies, 738 patients) was 2.80 (95% CI 1.95–4.02; $P < 0.01$). The odds ratio of requiring valve-replacement surgery (7 studies, 549 patients) was 2.95 (95% CI 1.90–4.58; $P < 0.01$). The odds ratio of death (6 studies, 476 patients) was 1.55 (95% CI 0.92–2.60; $P = 0.10$)	Meta-analysis without homogeneity
Goldman (1995), Int J Cardiol, USA [12] Retrospective (level 4)	74 patients with IE	VS of >1.8 cm^2	100% specific but only 30% sensitive for predicting the development of a complication	The area of the vegetation calculated
Rohmann (1991), J Am Soc Echocardiogr, Germany [13] Prospective cohort study (level 3)	83 patients with IE monitored for a mean of 74 weeks	Group A vs Group B VS Incidence of complications: Embolic events Perivalvular abscess formation Mortality *Staphylococcus aureus* *Streptococcus viridans*	 Increasing VS (8.2 ± 1.5–11.2 mm; $P < 0.05$) vs decreasing VS (8.3 ± 0.8 to 4.9 ± 0.8 mm $P < 0.05$) 45 vs 2%, $P < 0.05$ 45 vs 17% $P < 0.05$ 13 vs 2% $P < 0.05$ 10 vs 0% $P < 0.05$ 44 vs 11% $P < 0.05$) 33 vs 18% $P < 0.05$	TOE Prospective study Other complications also assessed VS used as a prognostication means
Di Salvo (2001), J Am Coll Cardiol, France [14] Retrospective study (level 4)	178 consecutive patients with IE	Incidence of embolism	VS < 10 mm (60%, $P < 0.001$) Mobile vegetations (62%; $P < 0.001$) RSIE	TOE was used. The incidence of EE compared with respect to other characteristics
Rohmann (1997), Clin Cardiol, Germany [15] Prospective cohort study (level 2)	The effect of antibiotic regimes on VS in 183 patients with IE. The patients were followed for a mean of 76 weeks and had a minimum of two consecutive TOE	Treatment with different antibiotics with corresponding change in VS: 1 vancomycin 2 ampicillin 3 penicillin 4 penicillase-resistant drugs 5 cephalosporin	 45% reduction 19% reduction 5% reduction 15% increase 40% increase	The patients were followed for a mean of 76 weeks TOE was used in assessment
Heinle (1994), Am J Cardiol, USA [16] Retrospective (level 3)	41 patients with IE independently reviewed by 4 echocardiographers blinded to the clinical data. The vegetations were assessed for other characteristics	Incidence of embolic events	50% EE in VS of >10 mm vs 42% VS of ≤10 mm	To determine inter-observer variability of echocardiographic characteristics of vegetations in patients with IE Prospective study
Leitman (2011), Eur J Echocardiogr, Israel [17] Retrospective study (level 4)	146 patients with IE were identified Large vegetations (≥10 mm) occurred in 46 patients	Risk of mortality The strongest independent predictor of mortality	Older patients with large VS had increased risk of mortality 38% ($P < 0.05$) 1 MRSA IE (45%; $P = 0.01$) 2 staphylococcal IE with large VS in older patients (50%, $P = 0.02$) diabetes (25%, $P < 0.02$)	The other factors for predicting mortality was also determined Results not explicit

AV: aortic valve; EE: embolic event; IE: infective endocarditis; MRSA: methicilin resistant *staphylococcus aureus*; MV: mitral valve; RSIE: right-sided infective endocarditis; TOE: transoesophageal echocardiography; TTE: transthoracic echocardiography; VS: vegetation size.

SEARCH OUTCOME

One hundred and two papers were found using the reported search. From these, 16 papers were identified that provided the best evidence to answer the question. The results are tabulated in Table 1.

RESULT

Rohmann *et al*. [2] retrospectively reviewed 281 patients with clinically suspected infective endocarditis (IE) and by multivariate analysis showed that the risk factors for subsequent embolism and in-hospital fatality was with a vegetation size (VS) of >10 mm.

The study by Vilacosta *et al*. [3], of 211 cohort patients who were prospectively recruited, observed increased risk of embolization with increasing VS and that a VS of ≥10 mm had a higher incidence of embolism ($P = 0.04$), even at follow-up.

Mugge *et al*. [4] reviewed 105 patients with IE and observed that patients with a VS of >10 mm had a significantly higher incidence of embolic events than those with a VS ≤10 mm (22/47 vs 11/58; $P < 0.01$).

Hecht *et al*. [5] retrospectively surveyed 121 patients with right-sided infective endocarditis (RSIE). VS >20 mm was associated with a higher mortality when compared with VS of ≤20 mm (33 vs 1.3%, $P < 0.001$).

Thuny *et al*. [6], from their multicentre study of 384 consecutive patients with IE, showed that VS >10 mm and severe vegetation mobility were predictors of embolic events and that VS >15 mm was a predictor of 1-year mortality.

Robbins *et al*. [7] evaluated the prognosis of a predetermined VS in 21 patients with RSIE. The patients with VS of <10 mm required no surgery, while patients with VS ≥10 mm required surgery ($P < 0.05$). Furthermore, a VS of <10 mm corresponded to patients who responded to medical therapy, and a VS of ≥10 mm to those with lower response rate to such treatment.

Nunes *et al*. [8] prospectively analysed the data of 62 patients with IE. On multivariate analysis, a VS of >13 mm remained the only independent predictor of in-hospital mortality (hazard ratio 1.05 per mm; 95% CI 1.003–1.110; $P = 0.038$).

In Martin-Davila *et al*. [9] on review of 493 patients with RSIE, by univariate analysis, it was found that a VS >20 mm and a fungal aetiology were associated with in-hospital mortality and, by multivariate analysis, that a VS <20 mm was also associated with increased mortality ($P = 0.014$; OR 10.2; 95% CI 1.6–78.0).

Wong *et al*. [10] reviewed 34 patients with clinical IE, classifying vegetations into small (<5 mm), medium (5–9 mm), or large (≥10 mm), with large VS having a higher incidence of surgical intervention (44 v 0%).

In Tischler *et al*. [11], meta-analysis revealed that the pooled odds ratio for increased risk of systemic embolization was in presence of a VS >10 mm (10 studies, 738 patients). The analysis supported the hypothesis that left-sided VS of >10 mm posed a significantly increased risk of embolic events.

Goldman *et al*. [12] identified 74 high-risk patients with IE and showed that a VS of >1.8 cm^2 was 100% specific but only 30% sensitive for predicting the development of a complication and that 77% of patients requiring surgery were predicted as having larger VS, amongst other conditions.

Rohmann *et al*. [13] evaluated 83 patients with IE dividing them into group A; patients with constant or increasing VS (8.2 ± 1.5 to 11.2 mm, $P < 0.05$) during the 4–8 weeks of antimicrobial therapy, while group B were patients with decreasing VS (8.3 ± 0.8 to 4.9 ± 0.8 mm, $P < 0.05$). The incidence of complications after diagnosis and onset of therapy was higher in group A than in group B.

Di Salvo *et al*. [14] assessed 178 consecutive patients with IE and found out a significantly higher incidence of embolism with VS <10 mm (60%, $P < 0.001$) and in patients with mobile vegetations (62%, $P < 0.001$). Also, on multivariate analysis, the only predictors of embolism were VS ($P = 0.03$) and mobility ($P = 0.01$).Early surgery was indicated in patients with VS >15 mm and high mobility, irrespective of other parameters.

Rohmann *et al*. [15] evaluated the effect of different kinds of antibiotic regimes on VS in 183 patients with IE, observing that embolic events were more common in patients with VS >10 mm. Also, the highest complication rate was observed when VS significantly increased during the antibiotic treatment.

Heinle *et al*. [16] reviewed the echocardiograms of 41 patients with IE, made independently by four echocardiographers who were blinded to the clinical data with respect to the VS, as well as other parameters. VS >10 mm were associated with a 50% incidence of embolic events, compared with a 42% incidence of embolism in patients with vegetations measuring ≤10 mm.

Leitman *et al*. [17] identified 146 patients with IE and observed that older patients with large vegetations had significantly increased risk of mortality 38% ($P < 0.05$). The strongest independent predictor of mortality amongst other factors was large vegetations (43%; $P = 0.01$).

CLINICAL BOTTOM LINE

The studies showed that the risk for embolic events and mortality increased with VS of 10 mm or more for LSIE and 20 mm or more for RSIE and the vegetations of those respective sizes were indications for surgery (44% vs 0%). This was also stated in the recent European guidelines on the prevention, diagnosis, and treatment of infective endocarditis [18].

Conflict of interest: none declared.

REFERENCES

[1] Dunning J, Prendergast B, Mackway-Jones K. Towards evidence-based medicine in cardiothoracic surgery: best BETS. Interact CardioVasc Thorac Surg 2003;2:405–9.
[2] Rohmann S, Erbel R, Gorge G, Makowski T, Mohr-Kahaly S, Nixdorff U *et al*. Clinical relevance of vegetation localization by transoesophageal echocardiography in infective endocarditis. Eur Heart J. 1992;4:446–52.
[3] Vilacosta I, Graupner C, San Roman JA, Sarria C, Ronderos R, Fernandez C *et al*. Risk of embolization after institution of antibiotic therapy for infective endocarditis. J Am Coll Cardiol. 2002;9:1489–95.
[4] Mugge A, Daniel WG, Frank G, Lichtlen PR. Echocardiography in infective endocarditis: reassessment of prognostic implications of vegetation size determined by the transthoracic and the transesophageal approach. J Am Coll Cardiol. 1989;3:631–8.
[5] Hecht SR, Berger M. Right-sided endocarditis in intravenous drug users. Prognostic features in 102 episodes. Ann Intern Med. 1992;7:560–6.
[6] Thuny F, Di Salvo G, Belliard O, Avierinos JF, Pergola V, Rosenberg V *et al*. Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicentre study. Circulation. 2005;1:69–75.

[7] Robbins MJ, Frater RW, Soeiro R, Frishman WH, Strom JA. Influence of vegetation size on clinical outcome of right-sided infective endocarditis. Am J Med 2:165–71.
[8] Nunes MC, Gelape CL, Ferrari TC. Profile of infective endocarditis at a tertiary care centre in Brazil during a seven-year period: prognostic factors and in-hospital outcome. Int J Infect Dis. 2010;5:394–8.
[9] Martín-Davila P, Navas E, Fortún J, Moya JL, Cobo J, Pintado V *et al*. Analysis of mortality and risk factors associated with native valve endocarditis in drug users: the importance of vegetation size. Am Heart J. 2005;5:1099–106.
[10] Wong D, Chandraratna AN, Wishnow RM, Dusitnanond V, Nimalasuriya A. Clinical implications of large vegetations in infectious endocarditis. Arch Intern Med. 1983;10:1874–7.
[11] Tischler MD, Vaitkus PT. The ability of vegetation size on echocardiography to predict clinical complications: a meta-analysis. J Am Soc Echocardiogr. 1997;5:562–8.
[12] Goldman ME, Fisher EA, Winters S, Reichstein R, Stavile K, Gorlin R *et al*. Early identification of patients with native valve infectious endocarditis at risk for major complications by initial clinical presentation and baseline echocardiography. Int J Cardiol. 1995;3:257–64.
[13] Rohmann S, Erbel R, Darius H, Görge G, Makowski T, Zotz R *et al*. Prediction of rapid versus prolonged healing of infective endocarditis by monitoring vegetation size. J Am Soc Echocardiogr. 1991;5:465–74.
[14] Di Salvo G, Habib G, Pergola V, Avierinos JF, Philip E, Casalta JP *et al*. Echocardiography predicts embolic events in infective endocarditis. J Am Coll Cardiol. 2001;4:1069–76.
[15] Rohmann S, Erhel R, Darius H, Makowski T, Meyer J. Effect of antibiotic treatment on vegetation size and complication rate in infective endocarditis. Clin Cardiol. 1997;2:132–40.
[16] Heinle S, Wilderman N, Harrison JK, Waugh R, Bashore T, Nicely LM *et al*. Value of transthoracic echocardiography in predicting embolic events in active infective endocarditis.: Duke Endocarditis Service. Am J Cardiol. 1994;8:799–801.
[17] Leitman M, Dreznik Y, Tyomkin V, Fuchs T, Krakover R, Vered Z. Vegetation size in patients with infective endocarditis. Eur J Echocardiogr. 2012;13:330–8.
[18] Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I *et al*. Guidelines on the prevention, diagnosis,and treatment of infective endocarditis. Eur Heart J 2009;30:2369–413.

eComment. Early surgery in preventing stroke in left-sided infective endocarditis

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I read with great interest the article by Okonta *et al.* [1], and I think that the discussion should be primarily focused on early surgery in left-sided infective endocarditis (IE) to prevent stroke. The three main indications for early surgery in IE are heart failure, uncontrolled infection and prevention of embolic events [2]. Although embolic stroke is a major cause of morbidity in patients with IE, the value of early surgery in preventing embolic events still remains controversial.

According to the data analyzed by Okonta *et al.* [1], it is very clear that a vegetation length >10 mm and severe vegetation mobility are the most potent independent predictors of a new embolic event. If we use the term "new embolic event" in relation to the time after the beginning the antibiotic therapy in IE, then the benefits of surgery in preventing embolism may be greatest during the first week of antibiotic therapy. This is because the risk of new embolism is highest during the first days following the initiation of antiobiotic therapy and decreases two weeks thereafter [3].

Although new recommendations of European Society of Cardiology guidelines for IE emphasize the timing of surgery [2], the exact role of early surgical intervention in order to avoid embolic events is still unclear. Vegetation size can be one of the reasons for surgery, but is rarely the only one. In the absence of a previous embolism, surgery is indicated with vegetation length >10 mm and some other predictor of complicated IE (heart failure, uncontrolled infection). Eventually, surgery may be considered in cases with very large (>15 mm) vegetations on the aortic or mitral valve, according to the possibility of valve repair. Cabell *et al.* [4] have demostrated that in native IE, mitral valve IE is associated with higher risk of embolism than aortic valve IE (OR 3.6; 95% CI 1.1-11.6). That is why earlier surgery should be especially emphasized in the cases of mitral valve vegetations.

Finally, one must keep in mind that the major complications with early surgery are valve dysfunction because of tissue inflammation, and the increased risk of recurrent infection resulting in early prosthetic valve endocarditis [5].

Any current conclusions must be open to continuing review as new data become available to allow more enlightened judgements in preventing the risk of embolism in left-sided IE. Some personal conclusions regarding the indication of early surgery in IE include:

i) vegetation lengths >10 mm associated with one of the following conditions: complicated course of IE (haemodynamic deterioration, uncontrolled infection, neurological complication), severe vegetation mobility located on the mitral valve, valve repair appears feasible immediately after antibiotic therapy is started;
ii) vegetation length >15 mm in aortic or mitral valve with or without other complication.

Conflict of interest: none declared

References

[1] Okonta KA, Adamu YB. What size of vegetation is an indication for surgery in endocarditis? Interact CardioVasc Thorac Surg 2012;15:1052–6.
[2] Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I *et al*. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis. Eur Heart J 2009;30:2369–413.
[3] Vilacosta I, Graupner C, San Roman JA, Sarria C, Ronderos R, Fernandez C *et al*. Risk embolization after institution of antibiotic therapy for infective endocarditis. J Am Coll Cardiol 2002;39:1489–95.
[4] Cabell CH, Pond KK, Peterson GE, Durack DT, Corey GR, Anderson DJ *et al*. The risk of stroke and death in patients with aortic and mitral valve endocarditis. Am Heart J 2001;142:75–80.
[5] d'Udekem Y, David TE, Feindel CM, Armstrong S, Sun Z. Long-term of surgery for active infective endocarditis. Eur J Cardiothorac Surg 1997;11: 46–52.