The New Strategy in Infective Endocarditis: Early Surgery Based on Early Diagnosis. Are We Too Late, When Early Surgery is Best?

Running title: Erbel; Early surgery for infective endocarditis

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Patients with infective endocarditis (IE) have a poor prognosis due to complications including congestive heart failure, paravalvular abscess formation, central and peripheral embolism, and hemorrhagic stroke.\(^1\) Patients with IE and congestive heart failure (CHF) have a mortality as high as 50\%.\(^1\) The poor prognosis seems not be improved during recent years.\(^2\) In Sweden 7.603 patients with IE received a close follow-up with assessment of the 30-day mortality and 5-year follow-up including autopsy in all fatal events sampled from 1997 to 2007.\(^2\) During the observation period no change of mortality was found despite an increase of the incidence of IE from about 7-7.5/100.000 to 8-8.5/100.000 inhabitants.\(^2\) In order to provide a contemporary picture of the presentation, etiology, and outcome of infective endocarditis (IE) a worldwide International Collaboration on Endocarditis-Prospective Cohort Study (ICE PCS) was started in 58 hospitals in 25 countries in 2000.\(^3\) In this issue of Circulation, Chu VH et al\(^4\) report the recent 2008–2012 results of the ICE-PCS database of 1296 IE patients with left sided IE. The hospital mortality for surgery, performed in only 661 (77%) of 863 patients with indications for surgery, reached 14.8% and the 6-month mortality 17.5% compared to 26% and 31.4 %, respectively, when no surgery was provided.\(^4\)

Transesophageal echocardiography (TEE) opened a new window to the heart.\(^5\) TEE was found to be superior to transthoracic echocardiography (TTE) particularly for the diagnosis of infective endocarditis (IE).\(^6\)-\(^8\) Using TEE sessile or mobile masses, attached to the cardiac valves, could be detected in patients with IE even when TTE was negative and even well before destruction of the valve leaflets.\(^6\)-\(^8\) High resolution and image quality enabled the detection of vegetation even in patients with good TTE image quality.\(^6\) The vegetation location as well as the size and mobility of the vegetation were found to be of diagnostic and prognostic value.\(^8\),\(^10\) In addition complications of IE like abscess formation,\(^9\) paravalvular leakage in patients with
prosthetic valves could be visualized.\textsuperscript{10} The development of biplane and later multi-plane and rotational TEE further improved the diagnostic accuracy as well as the wide spread use of the new TEE technology.\textsuperscript{11} The sensitivity of TEE reached 82\% and 96\%,\textsuperscript{6, 12} and the specificity 98\%, positive and negative predictive accuracy 88 and 100\%, respectively.\textsuperscript{6, 12}

TEE induced a paradigm change, when the previously used Beth Israel criteria, later called von Reyn criteria,\textsuperscript{13} with which the diagnosis of “definite IE” was made only when overt destruction of the valve was confirmed by surgery or autopsy, were replaced by the Duke criteria, presented in 1994.\textsuperscript{14} Now echocardiography was assigned to provide clinical criteria for the “definite” diagnosis of IE with signs of endocardial involvement of the disease including masses, abscess formation and new partial dehiscence of prosthetic valves or new valvular regurgitation. The Duke criteria reached a higher sensitivity than the Beth Israel (von Reyn) criteria\textsuperscript{15, 16} which enabled the diagnosis of “definite IE” in only one third of patients with endocarditis.\textsuperscript{14-17} And more IE patients were deemed to be appropriate for surgery.\textsuperscript{15} The wide spread use of the Duke criteria lead to a refinement of the major criteria strengthening the role of echocardiography for the diagnosis of prosthetic valve IE. So-called “minor” echocardiographic criteria were no longer used.\textsuperscript{18}

The modified Duke criteria were included in the 2005 AHA scientific statement on infective endocarditis.\textsuperscript{19} The flow chart on the approach to the diagnostic use of echocardiography included TEE for patients with moderate to high clinical suspicion or candidates with technically difficult TTE images. It was recommended that echocardiography be performed as soon as possible (<12h) after initial evaluation. TEE was preferred but TTE used as first line, if TEE was not immediately available. If TEE was not performed initially, it should be obtained after a positive TTE and as soon as possible in high risk patients for complications as
well as after 7-10 days, if the suspicion for endocarditis persisted without the confirmation of the diagnosis “IE” or a worsening clinical course. Potential need for surgical intervention was described for specific TTE/TEE features (Table 1). However, the role of surgery to prevent systemic embolization was regarded as complex. Surgery was seen to be indicated in the setting of recurrent emboli (≥2) and persistent vegetation despite appropriate antibiotic therapy. The greatest benefit was seen in the early phase of IE, in case of involvement of the anterior mitral leaflet and during the first 2 weeks of antimicrobial therapy.

The recent 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease recommend early surgery (meaning during initial hospitalization before completion of full therapeutic course of antibiotics) for those (Figure 1) with valve dysfunction causing heart failure, left sided IE caused by Staphylococcus (S) aureus, fungal or other highly resistant organism, heart block, annular or aortic abscess, destructive penetrating lesions, persistent infection as manifested by persistent bacteremia or fevers lasting longer than 5-7 days after onset of therapy (Class I, Level of evidence B). Surgery is recommended in relapsing prosthetic valve IE without other source for portal of infection (Class I, Level of evidence C). For the first time a recommendation is given for patients with recurrent emboli and persistent vegetations despite appropriate antimicrobial therapy (Class IIa, Level of evidence B). For those with mobile vegetations larger than 10 mm in length, early surgery may be considered (Class IIb, Level of evidence B). The new 2014 AHA/ACC guideline also recommends that one base decisions about timing of surgical interventions by consensus of a multidisciplinary team that comprises cardiologists, cardio-thoracic surgeons and infectious disease specialists so as to reduce biases and provide best practice in patients with IE (Class I, Level of evidence B).

In this issue of Circulation, Chu VH et al report the recent results of the ICE-PCS...
database of 1296 IE patients with left sided IE treated between September 2008 and December 2012. A transfer from other hospitals was present in 52% of the included patients. The hospital mortality for surgery reached 14.8% and the 6-month mortality 17.5% compared to 26% and 31.4 %, respectively, when no surgery was provided. Surgery was performed in 661 (77%) of 863 patients within 7 days. Patients who did not have surgery had a higher rate of heart failure, embolic events, abscess formation, severe valvular regurgitation, and larger vegetation size. Only persistent bacteremia was not significantly more often found. Moderate to severe liver disease, stroke prior to decision concerning surgery, and S aureus infection were significant predictors for the non-surgical management. The STS score was not significantly associated with the decision for a surgical treatment.

Poor prognosis, hemodynamic instability, and sepsis, particularly, when S aureus was identified, were associated with an individual not having surgery. In patients with Staphylococcus aureus infection a higher STS-IE score was reported. Most important was the finding that the 6-month survival was very poor for those patients with IE who had an STS score ≥ median, but did not have surgery.4

The authors of this important study should be congratulated on the excellent report, which provides insight into the current diagnosis and treatment of patients with left sided IE. The manuscript is important, because it demonstrates that nearly one quarter of those who have an indication for surgery do not receive the surgical intervention. The recommendation from the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease to involve a multidisciplinary team to guide decision–making is particularly germane in this situation and deserves reinforcement.20

Appropriate early surgery can provide a significant improvement of in-hospital mortality.
and long-term prognosis in IE. At the time of diagnosis, the disease is often quite advanced and in this study by Chu et al, there was already significant valve destruction with new mitral regurgitation in 41.2%, aortic regurgitation in 33.4%, which was severe in one quarter to one fifth of the patient cohort.4 Utilizing TEE as recommended in the new 2014 AHA/ACC guidelines (Figure 1) should allow earlier diagnosis which could thus impact outcome. The ideal situation would be to refer to surgery appropriate patients with IE early enough in their course so that outcomes can be meaningfully improved in this often devastating disease. The current manuscript of Chu et al, in conjunction with the recent AHA/ACC guidelines, provides unique insights that should encourage a multidisciplinary approach to this often devastating disease.

**Conflict of Interest Disclosures:** None.

**References:**


17. Olaison L, Hoguevik H. Comparison of the von Reyn and Duke criteria for the diagnosis of


**Table 1** Echocardiographic Features that suggest Potential Need for Surgical Intervention including the Current Recommendations of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease.\(^{20}\)

<table>
<thead>
<tr>
<th>Vegetation</th>
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<tbody>
<tr>
<td>- Persistent vegetation after systemic embolism</td>
<td>(Class IIa, Level of Evidence: B)</td>
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<tr>
<td>- (Anterior mitral leaflet) vegetation size in length &gt; 10 mm*</td>
<td>(Class IIb, Level of Evidence: B)</td>
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<td>- ≥1 embolic events during the first 2 weeks of antimicrobial therapy*</td>
<td>(Class IIa, Level of Evidence: B)</td>
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<td>- Increase in vegetation size despite appropriate antimicrobial therapy§</td>
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<tr>
<td>Valvular dysfunction</td>
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<tr>
<td>- Acute aortic or mitral insufficiency with signs of ventricular failure§</td>
<td>(Class I, Level of Evidence: B)</td>
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<td>- Heart failure unresponsive to medical therapy§</td>
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<td>- Valve perforation or rupture§</td>
<td>(Class I, Level of Evidence: B)</td>
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<tr>
<td>Perivalvular extension</td>
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<tr>
<td>- Valvular dehiscence, rupture, or fistula§</td>
<td>(Class I, Level of Evidence: B)</td>
<td></td>
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<td>- New heart block&amp;</td>
<td>(Class I, Level of Evidence: B)</td>
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<tr>
<td>- Large abscess or extension of abscess despite appropriate antimicrobial therapy</td>
<td>(Class I, Level of Evidence: B)</td>
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</table>

* Surgery may be required because of risk if embolization; §Surgery may be required because of heart failure or failure of medical therapy; &Echocardiography should not be the primary modality to detect or monitor heart block; Modified version from: Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: Baddour LM et al.\(^{19}\) Copyright 2005, Lippincott William & Wilkins, Hagertown
Figure Legend:

Recommendations for Imaging Studies in NVE and PVE. *Repeat TEE and/or TTE recommended for reevaluation of patients with IE and change in clinical signs or symptoms and in patients at high risk of complications.
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