Implementation of the 2015 European Society of Cardiology guidelines for the management of infective endocarditis in the Netherlands

A. R. Wahadat · J. W. Deckers · R. P. J. Budde · J. T. M. van der Meer · E. H. Natour · J. ten Oever · A. L. J. Kortlever-van der Spek · B. H. Stegeman · N. J. Verkaik · J. W. Roos-Hesselink · W. Tanis

Abstract Because the occurrence of infective endocarditis (IE) continues to be associated with high mortality, a working group was created by the Dutch Society of Cardiology to examine how the most recent European Society of Cardiology (ESC) guidelines for IE management could be implemented most effectively in the Netherlands. In order to investigate current Dutch IE practices, the working group conducted a country-wide survey. Based on the results obtained, it was concluded that most ESC recommendations could be endorsed, albeit with some adjustments. For instance, the suggested pre-operative screening and treatment of nasal carriers of Staphylococcus aureus as formulated in the ESC guideline was found to be dissimilar to current Dutch practice, and was therefore made less restrictive. The recently adapted ESC diagnostic criteria for IE were endorsed, while the practical employment of the relevant diagnostic techniques was simplified in an adapted flowchart. In addition, the presence of a multidisciplinary, so-called ‘endocarditis team’ in tertiary centres was proposed as a quality indicator. An adapted flowchart specifically tailored to Dutch practice for microbiological diagnostic purposes was constructed. Lastly, the working group recommended the Stichting Werkgroep Antibioticabeleid (SWAB; Dutch Working Party on Antibiotic Policy) guidelines for IE treatment instead of the antibiotic regimens proposed by the ESC.

Keywords Infective endocarditis · Microbiological diagnosis · Disease management · Cardiac imaging · Infection · Prosthetic heart valves

Background and introduction

One of the oldest cardiac diseases, infective endocarditis (IE), remains one of the most fatal manifestations of heart disease [1]. Despite considerable progress in diagnosis and treatment, the in-hospital mortality of IE continues to be about 20%, essentially unchanged during the past decades [2].

The importance of IE is reflected in the frequent publication of new guidelines, for instance by the
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**Prevention and prophylaxis**

Although widespread antibiotic prophylaxis for IE has long been considered effective, the policy for liberal use of antibiotic prophylaxis has gradually changed to more restricted indications. Of note, the 2008 guidelines of the National Institute of Health and Clinical Excellence (NICE) from the UK recommended that antibiotic prophylaxis should be abandoned completely [3]. However, this recommendation was revised after a patient with aortic valve prosthesis died from IE after undergoing a dental procedure without—in line with the NICE guidelines—the use of prophylaxis. The NICE guidelines from 2016 recommend dentists to inform the patient about the level of risk and let him or her decide whether or not to receive antibiotic prophylaxis [4]. The strategy currently endorsed by the American College of Cardiology (ACC), American Heart Association (AHA) and ESC reserves antibiotic prophylaxis for individuals with cardiac disease at high risk of IE, e.g. for patients with a prosthetic valve, a history of IE, or with cyanotic congenital heart disease undergoing a dental procedure with a high risk of bacteremia (usually involving perforation of the gingiva) [1, 5]. Of course, proper oral hygiene is strongly promoted universally. The working group decided to endorse the recommendations of the ESC guidelines on prophylaxis in high-risk subjects without changes or comments [1].

Nasal carriers of *Staphylococcus aureus* have more infections after cardiac surgery [6], and the pre-operative eradication of this micro-organism is thus important. To this end, two options are available. In the first, all subjects—without additional testing—are treated locally with an antibiotic ointment, usually mupirocin. Another option is to screen every patient, and to treat *S. aureus* carriers only. The ESC guidelines recommend only the latter procedure. But the merits of the two methods are of course comparable, and this is—at least according to the survey—reflected by the concomitant use of both approaches for de-colonisation of *S. aureus* in Dutch hospitals. Therefore, the text of the recommendation in Tab. 7 of the guidelines was (slightly) adapted as follows: ‘Preoperative screening and/or treatment of nasal carriage of *Staphylococcus aureus* is recommended before elective surgery in order to treat carriers’ [6] was deleted.

**Microbiological diagnosis**

Positive blood cultures remain the cornerstone of IE diagnosis. At least three sets with sufficient volume should be taken at 30-min intervals, and sampling preferably be obtained from a peripheral vein. When a micro-organism has been identified and appropriate antimicrobial treatment is commenced based on susceptibility results, blood cultures should be repeated every 48–72 h until blood cultures remain sterile to

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**Table 1** Selection of recommendations by the working group with regard to the European Society of Cardiology (ESC) guidelines. SWAB Stichting Werkgroep Antibioticabeleid (Dutch Working Party on Antibiotic Policy)

| Topic                                                      | Recommendations in ESC guidelines | Recommendation by the working group |
|------------------------------------------------------------|-----------------------------------|-------------------------------------|
| Antibiotic prophylaxis                                     | Reserve antibiotic prophylaxis for high-risk individuals undergoing dental procedures | No change or comment by the working group |
| Prevention of infection before cardiac or vascular interventions | Screen every patient and treat *Staphylococcus aureus* carriers only pre-operatively | Pre-operative screening and/or treatment of nasal carriage of *Staphylococcus aureus* is recommended before elective surgery in order to treat carriers [4] |
| Microbiological diagnosis                                  | Use the recommendation as presented in the ESC guidelines | Use flowchart as presented in Fig. 1 [1] |
| Diagnostic imaging and criteria                            | Use diagnostic ESC criteria and the recommendation presented in the guidelines | Use diagnostic ESC criteria and the flowchart as presented in Fig. 2 [1] |
| Endocarditis team                                          | Centres without cardio-thoracic facilities must consult the regional endocarditis team in cases of (suspected) IE | No change or comment by the working group |
| Antimicrobial therapy                                      | Antimicrobial therapy according to the ESC guidelines | Antimicrobial therapy according to SWAB guidelines [6] |
| Surgery                                                    | Indication and timing of surgery as presented in the guidelines | No change or comment for the indication of surgery |
| Discharge                                                  | Transthoracic echo after completion of therapy Regular follow-up including blood samples Good oral health maintenance | No change or comment by the working group |

[4] Different recommendation made by the working group compared with the ESC guidelines
verify the effectiveness of the therapeutic regimen. Blood-culture-negative IE refers to IE in which no causative micro-organism can be identified using standard culture methods. In such instances, bacteria such as Bartonella spp. or Coxiella burnetii, fungi or fastidious bacteria may be in play and additional diagnostic testing may be required. Table 12 and Fig. 2 in the ESC guidelines refer to these circumstances. However, some microbiological tests included therein are not available in the Netherlands. The working group has therefore developed a flowchart adapted to Dutch practice (Fig. 1).

**Diagnostic imaging and criteria**

While the modified Duke criteria, which rely heavily on positive blood cultures and findings compatible with IE at echocardiography [7], remain the mainstay for diagnosing IE, current guidelines reflect the increasing importance of more advanced imaging techniques [1]. In particular, computed tomography (CT), positron emission tomography with CT (PET-CT) and magnetic resonance imaging have emerged as valuable additional imaging techniques that provide complementary diagnostic information to echocar-
diography [1]. Available data—also from the Netherlands—indicate increased diagnostic accuracy when these techniques are added to the modified Duke criteria, especially in prosthetic valve endocarditis (PVE) [8–10]. The guidelines provide detailed recommendations on the use of various imaging techniques in both native valve IE and PVE, as well in the diagnosis of cardiac-device-related endocarditis [7, 8]. The working group has combined the text and figures that describe these recommendations in the ESC guidelines into a single scheme (Fig. 2).

The diagnostic accuracy of the modified Duke criteria—which merge the presence of an infective syndrome and endocardial involvement, classically employing echocardiography—is only moderate, in particular in IE of a prosthetic valve [1, 11, 12]. Advanced imaging techniques—as described above—may not only be helpful in the detection of endocardial lesions when added to echocardiography, but also in establishing the presence of (clinically silent) vascular phenomena such as embolic events and infectious aneurysm [13]. Acknowledging this, the most recent ESC guidelines have added the identification of paravalvular lesions by CT and, in the setting of PVE, abnormal activity near the site of the prosthesis on 18F-fluorodeoxyglucose (18F-FDG) PET/CT or radiolabelled leucocyte single photon emission computed tomography (SPECT)/CT, as a ‘major’ criterion for IE. The currently applicable two major and five minor criteria for IE are described in Tab. 2. Examples of pos-

**Fig. 2** Flowchart of diagnostic imaging for infective endocarditis in the Netherlands. IE infective endocarditis, TTE transthoracic echocardiogram, TEE transoesophageal echocardiogram, BC blood cultures, 18F-FDG PET/CT 18F-fluorodeoxyglucose positron emission tomography computed tomography, SPECT single photon emission computed tomography, CTA computed tomography angiography, ICE intracardiac echocardiogram, SWAB Stichting Werkgroep Antibiotica Beleid (Dutch Working Party on Antibiotic Policy). a[1, 25]. b[26]. cConsider referring to a tertiary referral centre when there is definite IE and one or more of the following: congenital heart disease in pregnancy, prosthetic valve endocarditis, heart failure, paravalvular extension or uncontrolled infection, embolic events or cerebrovascular accident, arrhythmia or conduction disturbances
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approach adopted in France, with standardised med-
guidelines refer—among other things—to the team
expertise needed to treat complex IE patients. The
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The ‘endocarditis team’

An important addition in the latest ESC guidelines is
the recommendation to establish a multidisciplinary
‘endocarditis team’. Such a team, comprising—at
least—a cardiologist, cardio-thoracic surgeon, infec-
tious diseases specialist, microbiologist and radiolo-
gist/nuclear medicine physician should provide the
expertise needed to treat complex IE patients. The
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cal interventions that were found to improve outcome
relative to earlier experience [14–18]. A comparable
recommendation has been made in the AHA/ACC
guidelines for the management of patients with valvu-
lar disease [19]. In line with the ESC guidelines, the
working group recommended that each of the current
16 Dutch tertiary referral centres with cardio-tho-
racic facilities create a specific regional endocarditis
team. Moreover, the working group proposed to qual-
ify the presence and composition of such a team as
a quality indicator. The working group endorsed the
ESC guidelines recommendation that centres without
cardi-thoracic facilities must consult the regional
endocarditis team in cases of (suspected) IE.

Antimicrobial therapy

There are major differences between European coun-
tries in the use of antimicrobial therapy and conse-
quently in the antibiotic resistance patterns of pathogens. The Netherlands has the lowest rate of
antibiotic use in Europe. The result is a stable level
of antimicrobial resistance, whereas most countries
experience increasing levels each year. European
guidelines for antimicrobial therapy therefore can-
not be simply adhered to but have to be tailored to
individual countries. Recommendations for antibi-
otic therapy in the Netherlands are provided by the
Stichting Werkgroep Antibiotica Beleid (SWAB; Dutch
Working Party on Antibiotic Policy). Importantly,
SWAB recently updated their guidelines for antibiotic
treatment for IE, on the basis of an in-depth compari-
sion of the most recent ESC and the AHA IE guidelines.
In cases of discordance between the recommenda-
tions in these documents, SWAB guidance is based
on a formal literature review on best current Dutch
practice, taking into consideration national resistance
patterns and dosing habits. For all these reasons, the
working group recommended the employment of
the SWAB guidelines for subsequent use in the
Netherlands [20].

Main complications and their management

Heart failure resulting from valvular regurgitation
or obstruction, uncontrolled infection and embolic
events occurring under adequate antibiotic treatment
constitute major complications of IE and may require
surgical treatment [1, 21–24]. The working group en-
dorsed the ESC indications for cardiac surgery with-
out modifications. However, the timing of the surgical
procedure was left to the discretion of the specialists
involved. In accordance with the recommendations
of the ESC guidelines, complex IE patients should
be referred early to a regional centre with cardio-thoracic
facilities. Such cases include, but are not limited to,
IE patients with congenital heart disease, PVE, preg-
nant women, patients with heart failure, uncontrolled
infection, rhythm abnormalities or stroke.

Table 2  Diagnostic criteria for infective endocarditis (IE) according to the 2015 European Society of Cardiology (ESC) guidelines for IE

| Criteria                                      | Major Criteria                                           | Minor Criteria                                           |
|-----------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
|                                               | 1. Blood cultures positive for IE                         | 1. Predisposing heart condition or injection drug use    |
|                                               | a. Typical micro-organisms consistent with IE from 2 separate blood cultures: | 2. Fever defined as temperature >38 °C                   |
|                                               |   – Viridans streptococci, *Streptococcus gaiIlyticus* (Streptococcus bovis), | 3. Vascular phenomena (including those detected by imaging only) |
|                                               |   – HACEK group*, *Staphylococcus aureus*; or             | 4. Immunological phenomena (e.g. Janeway lesions, Oster’s nodes) |
|                                               |   – Community-acquired enterococci, in the absence of a primary focus; or | 5. Positive blood culture but does not meet a major criterion as noted above |
|                                               |   b. Micro-organisms consistent with IE from persistently positive blood cultures: | 1. Predisposing heart condition or injection drug use |
|                                               |   – ≥2 positive blood cultures of blood samples drawn ≥12 h apart; or | 2. Fever defined as temperature >38 °C                   |
|                                               |   – All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or | 3. Vascular phenomena (including those detected by imaging only) |
|                                               |   c. *Coxiella burnetii* phase I IgG antibody titre >1:1024 | 4. Immunological phenomena (e.g. Janeway lesions, Oster’s nodes) |
|                                               | 2. Imaging positive for IE                                | 5. Positive blood culture but does not meet a major criterion as noted above |
|                                               | a. Echocardiogram positive for IE                         | 6. An abnormal activity around the site of prosthetic valve implantation detected by 18F-FDG PET/CT (only if the prosthesis was implanted for >3 months) |
|                                               |   – Vegetation                                            | 7. Paravascular lesions and/or vegetation detected by cardiac CTA |
|                                               |   – Abscess, pseudoaneurysm, intracardiac fistula         | 8. Positive blood culture but does not meet a major criterion as noted above |
|                                               |   – Valvular perforation or aneurysm                      | 9. New partial dehiscence of prosthetic valve            |
|                                               |   – New partial dehiscence of prosthetic valve            | 10. Abnormal activity around the site of prosthetic valve implantation detected by 18F-FDG PET/CT (only if the prosthesis was implanted for >3 months) |
|                                               | 3. Imaging positive for IE                                | 11. Paravascular lesions and/or vegetation detected by cardiac CTA |
|                                               | a. Echocardiogram positive for IE                         | 12. Vasculature phenomena (including those detected by imaging only) |
|                                               |   – Vegetation                                            | 13. Vascular phenomena (including those detected by imaging only) |
|                                               |   – Abscess, pseudoaneurysm, intracardiac fistula         | 14. Vascular phenomena (including those detected by imaging only) |
|                                               |   – Valvular perforation or aneurysm                      | 15. Vascular phenomena (including those detected by imaging only) |
|                                               |   – New partial dehiscence of prosthetic valve            | 16. Vascular phenomena (including those detected by imaging only) |
|                                               | 4. Imaging positive for IE                                | 17. Vascular phenomena (including those detected by imaging only) |
|                                               | a. Echocardiogram positive for IE                         | 18. Vascular phenomena (including those detected by imaging only) |
|                                               |   – Vegetation                                            | 19. Vascular phenomena (including those detected by imaging only) |
|                                               |   – Abscess, pseudoaneurysm, intracardiac fistula         | 20. Vascular phenomena (including those detected by imaging only) |
|                                               |   – Valvular perforation or aneurysm                      | 21. Vascular phenomena (including those detected by imaging only) |
|                                               |   – New partial dehiscence of prosthetic valve            | 22. Vascular phenomena (including those detected by imaging only) |
|                                               | 5. Positive blood culture but does not meet a major criterion as noted above |

IE infective endocarditis, 18F-FDG 18F-fluorodeoxyglucose, PET/CT positron emission tomography/computed tomography, CTA computed tomography angiography

*Haeuophilus, Aggregatibacter, Cardiobacterium, Eikenella, Kingella*
**Fig. 3** Different examples of major imaging diagnostic criteria: two cases of positive transoesophageal echocardiogram (a, b), one case of positive \(^{18}\)F-FDG PET/CT (c, d) and one case of positive cardiac CT (e, f). a A case of a mechanical aortic valve with signs of vegetation (red arrow). The red arrow in b also indicates a vegetation on the aortic valve bioprosthesis, whereas the white arrow indicates a possible abscess of the aortic root. In c (fused PET/CT images) and in d (non-attenuated PET images) the white arrows indicate \(^{18}\)F-FDG uptake around the aortic valve bioprosthesis as a sign of possible infection. The red arrow in e indicates a vegetation on one of the leaflets of an aortic valve bioprosthesis. Finally, the red arrow in f indicates a mycotic aneurysm alongside the aortic valve bioprosthesis.

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