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Evaluation of the 2023 Duke-ISCVID and 2023 Duke-ESC Clinical Criteria for the Diagnosis of Infective Endocarditis in a Multicenter Cohort of Patients With *Staphylococcus aureus* Bacteremia

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Background. The Duke criteria for infective endocarditis (IE) diagnosis underwent revisions in 2023 by the European Society of Cardiology (ESC) and the International Society for Cardiovascular Infectious Diseases (ISCVID). This study aims to assess the diagnostic accuracy of these criteria, focusing on patients with *Staphylococcus aureus* bacteremia (SAB).

Methods. This Swiss multicenter study conducted between 2014 and 2023 pooled data from three cohorts. It evaluated the performance of each iteration of the Duke criteria by assessing the degree of concordance between definite *S. aureus* IE (SAIE) and the diagnoses made by the Endocarditis Team (2018–23) or IE expert clinicians (2014–17).

Results. Among 1344 SAB episodes analyzed, 486 (36%) were identified as cases of SAIE. The 2023 Duke-ISCVID and 2023 Duke-ESC criteria demonstrated improved sensitivity for SAIE diagnosis (81% and 82%, respectively) compared to the 2015 Duke-ESC criteria (75%). However, the new criteria exhibited reduced specificity for SAIE (96% for both) compared to the 2015 criteria (99%). Spondylodiscitis was more prevalent among patients with SAIE compared to those with SAB alone (10% vs 7%, $P = .026$). However, when patients meeting the minor 2015 Duke-ESC vascular criterion were excluded, the incidence of spondylodiscitis was similar between SAIE and SAB patients (6% vs 5%, $P = .461$).

Conclusions. The 2023 Duke-ISCVID and 2023 Duke-ESC clinical criteria show improved sensitivity for SAIE diagnosis compared to 2015 Duke-ESC criteria. However, this increase in sensitivity comes at the expense of reduced specificity. Future research should aim at evaluating the impact of each component introduced within these criteria.

Keywords. infective endocarditis; Duke criteria; echocardiography; *Staphylococcus aureus*; bacteremia.

In recent years, significant strides in microbiology and imaging techniques have greatly improved our capacity to diagnose infective endocarditis (IE). Early and precise identification of IE is crucial for enhancing patient outcomes [1–3]. For the purpose of standardized IE diagnosis in research settings, the Duke criteria were introduced in 1994 and have since undergone multiple revisions [3–6]. In 2015, the European Society of Cardiology (ESC) updated these criteria, integrating ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for diagnosing prosthetic valve IE and cardiac CT for both native and prosthetic valve IE [3]. In 2023, both the ESC and the International Society for Cardiovascular Infectious Diseases (ISCVID) issued distinct revisions to the criteria [4, 5]. Although both sets of criteria updated the cardiac predisposing factors and the utilization of ^{18}F-FDG PET/CT for diagnosing both native and cardiac implantable electronic device (CIED) lead IE, they differed in other aspects. The 2023 Duke-ESC criteria introduced leaflet thickening as a major imaging criterion and included hematogenous septic osteoarticular complications as a minor vascular criterion [4]. On the other hand, the 2023 Duke-ISCVID criteria incorporated more changes, especially in the microbiological criterion by updating the list of microorganisms considered typical, and introducing of a new surgical major criterion

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[5]. The 2023 Duke-ISCVID clinical criteria showed increased sensitivity compared to the 2015 Duke-ESC criteria [7]. However, they also displayed a decrease in specificity. Moreover, it is important to note that these evaluations assessed the overall impact of the modifications and did not separately measure the specific value added by each change [7].

Despite these extensive modifications, *Staphylococcus aureus* remained a consistent pathogen for IE across all revisions [3–6]. Given that *S. aureus* remained unchanged during the revisions, our study aimed to assess the additional benefit of the modifications introduced by the 2023 Duke-ESC and 2023 Duke-ISCVID criteria when compared to the 2015 Duke-ESC criteria among patients with positive blood cultures for *S. aureus* [3–5]. Through the assessment of the effects of each modification, our goal was to offer a more detailed understanding of the usefulness and significance of the changes introduced in the latest versions.

METHODS

Study Design

In this multicenter Swiss study conducted at both Lausanne University Hospital (CHUV) and University Hospital Zurich (USZ), we adopted a comprehensive approach. We combined data from 3 distinct cohorts:

(i) Retrospective *S. aureus* bacteremia (SAB) cohort of CHUV (January 2015 to December 2021).
(ii) Retro-/prospective cohort of patients with suspected IE of CHUV (January 2014 to December 2017: retrospective inclusion of IE patients; January 2018 to June 2023: prospective cohort of patients with suspected IE).
(iii) Retro-/prospective IE cohort of USZ (January 2014 to December 2017: retrospective cohort of IE patients; January 2018 to December 2022: prospective cohort of IE patients).

Ethical approval for the study was obtained from the Ethics Committees of the Canton of Vaud (CER-VD 2017-02137; CER-VD 2021-02516) and the Canton of Zurich (KEK-2014-0461; BASEC 2017-01140).

Study Participants

We included adult patients (≥18 years old) with positive blood cultures with *S. aureus* from each of the 3 cohorts from January 2014 through December 2022. For the retrospective SAB cohort of CHUV, exclusion criteria included refusal of reuse of the clinical data, and patients who did not undergo echocardiography and either received antibiotic treatment for more than 16 days or passed away within 120 days [8]. Additionally, an exclusion criterion for the CHUV IE cohort was inclusion of the same episode in the CHUV's SAB cohort. We extracted demographic, clinical, imaging, microbiological, surgical, and pathological data from patient's electronic health charts.

Management of SAB and *S. aureus* IE (SAIE)

Following the internal protocols of the institutions, the infectious diseases (ID) consultation service promptly assessed the patient on the same day that blood cultures revealed positive results for *S. aureus*. Physicians were advised to collect 2 sets of blood cultures on day 2 and day 4 after the initiation of therapy as recommended [9]. In the investigation of IE, protocols outlined specific diagnostic approaches contingent on the presence of risk factors such as prior history of IE, the presence of CIED or prosthetic valve, persistent bacteremia for at least 48 hours, embolic events, and community-acquired bacteremia. When any of the aforementioned risk factors were present, it was recommended to undergo both transthoracic echocardiography and transesophageal echocardiography. For patients experiencing nosocomial bacteremia unrelated to catheters and without the above-mentioned risk factors, our protocol mandated the utilization of transthoracic echocardiography alone. In cases of nosocomial catheter-related bacteremia without the specified risk factors, echocardiography was deemed unnecessary [10]. The Endocarditis Teams determined the necessity for additional cardiac imaging studies, such as ^{18}F-FDG PET/CT or cardiac CT on a case-by-case basis.

Evaluation of Different Versions of Duke Criteria

In both centers, an official Endocarditis Team is established since in January 2018. From 2018 onward, a case was categorized as IE in an a posteriori approach at day 60 as discussed by each center's endocarditis team based on clinical, laboratory, microbiological, imaging, surgical, and histopathological results. Prior to 2018, the determination of whether a case constituted IE or not relied on the assessment of 4 IE expert clinicians (M.P.O., P.M., M.v.H., B.H,) that individually reviewed the cases using clinical, laboratory, microbiological, imaging, surgical, and histopathological results. Consensus on classifying a case as IE was achieved only when all four expert clinicians unanimously agreed on the diagnosis. To maintain consistency and ensure continuity in diagnosis, these 4 IE expert clinicians who reviewed cases before 2018 were integral members of the respective endocarditis teams starting from 2018. The rationale for employing an endocarditis team and IE expert clinicians to adjudicate cases of IE is grounded in the multifaceted nature of this medical condition, which demands a comprehensive and specialized approach for accurate diagnosis and management. Cases were categorized as rejected, possible, or definite IE according to the three versions of Duke clinical criteria (2015 Duke-ESC [3], 2023 Duke-ISCVID [5], and 2023 Duke-ESC [4]). To assess their additional value, we emphasized the distinctions between the 2 2023 Duke versions and the 2015 Duke-ESC criteria. Moreover, to assess the individual impact

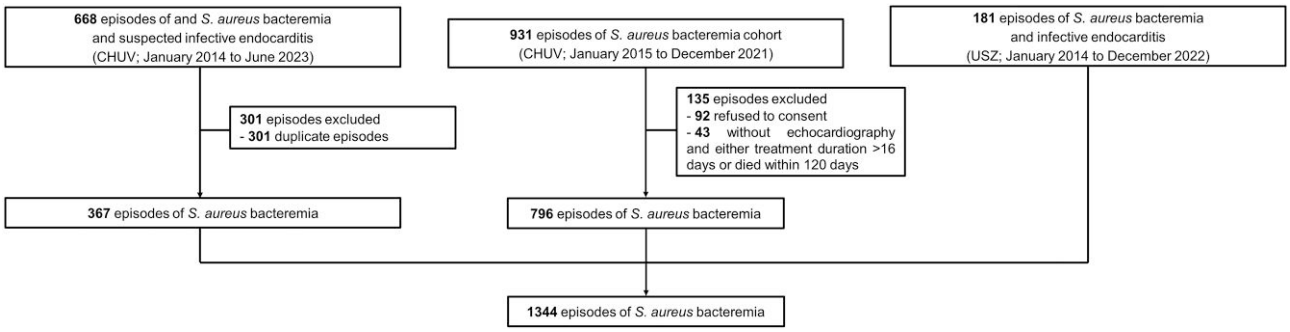

Figure 1. Flowchart of included patients with *S. aureus* bacteremia from the 3 cohorts of Lausanne University Hospital (CHUV) and University Hospital Zurich (USZ).

of each additional characteristic outlined in either the 2023 Duke-ISCVID or 2023 Duke-ESC clinical criteria, we compared the frequencies of these characteristics within the subgroup of patients who had not previously fulfilled the corresponding major/minor criterion according to the 2015 Duke-ESC. For example, to evaluate the real added value of valve leaflet thickening (characteristic added in the 2023 Duke-ESC), we excluded those with valve leaflet thickening who already satisfied the major 2015 Duke-ESC imaging criterion.

Statistical Analysis

SPSS software version 26.0 (SPSS, Chicago, Illinois, USA) was employed for data analysis. Group distinctions were evaluated using Mann-Whitney *U* test for continuous variables and either the χ^2 or the Fisher exact test for categorical variables. The effectiveness of each iteration of the Duke clinical criteria was gauged by assessing the degree of concordance between definite IE cases and the diagnoses made by the endocarditis team [3–5]. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) and accuracy were calculated with a 95% confidence interval (CI). All tests were 2-tailed, and a significance level of $P < .05$ was applied.

RESULTS

Cohort Composition

Out of 1780 eligible episodes with SAB, 1344 episodes were included (796 from retrospective SAB cohort of CHUV, 367 from retro-/prospective cohort of patients with suspected IE of CHUV, and 181 SAIE episodes from retro-/prospective IE cohort of USZ) were included (Figure 1). Among the 1344 episodes with SAB, 486 (36%) also had SAIE based on the endocarditis teams and IE expert clinicians' evaluation. Supplementary Table 1 presents cases classified as IE by the endocarditis teams or IE expert clinicians and treated accordingly, despite not meeting the definite IE criteria outlined in the 2015 Duke-ESC guidelines. Other sources included osteoarticular (248; 19%), catheter-related (190; 14%), skin and soft tissue-related (181; 14%), primary bacteremia with an unknown source (147; 11%), and lower respiratory tract infection (82; 6%).

Patients' Characteristics

Table 1 provides detailed patient characteristics with a specific emphasis on the advantages of the 2023 Duke-ISCVID and the 2023 Duke-ESC criteria as compared to the 2015 Duke-ESC criteria. Notably, significant new valvular regurgitation was more prevalent in patients with SAIE in comparison to those with SAB (18% vs 3%, $P < .001$). However, when patients who already met the major 2015 Duke-ESC imaging criterion were excluded, the incidence of significant new valvular regurgitation was similar between SAIE and SAB patients (3% vs 2%, $P < .001$). Leaflet thickening was more common among patients with SAIE compared to those with SAB (9% vs 2%, $P < .001$). Yet after excluding patients who already satisfied the major 2015 Duke-ESC imaging criterion, the occurrence of leaflet thickening was comparable between SAIE and SAB patients (4% vs 2%, P .068). Supplementary Table 2 illustrates the comparison of characteristics between episodes with or without SIAE within the subgroup of patients who had not previously met the corresponding major/minor criterion according to the 2015 Duke-ESC criteria.

Evaluation of the Different Versions of Duke Clinical Criteria

Out of 1344 patients with SAB, definitive SAIE was diagnosed in 375 (28%), 424 (32%), and 432 (32%) patients using the 2015 Duke-ESC, 2023 Duke-ISCVID, and 2023 Duke-ESC clinical criteria, respectively. Additionally, 55 (11%) patients were confirmed to have definite IE according to pathologic criteria. Table 2 offers an overview of the performance of the versions of the Duke clinical criteria. Sensitivity for the 2015 Duke-ESC, 2023 Duke-ISCVID and the 2023 Duke-ESC clinical criteria was calculated at 75% (95 CI: 71%–98%), 81% (77%–84%), and 82% (78%–85%), respectively, with specificity at 99% (98%–99%), 96% (95%–97%), and 96% (95%–97%), respectively.

Table 1. Comparison of Episodes With or Without Final Infective Endocarditis Diagnosis Among 1344 Patients With *S. aureus* Bacteremia

	No SAIE (n = 858)		SAIE (n = 486)		*P* Value
Demographics					
Male sex, n (%)	605	(71)	358	(74)	.232
Age, median years (IQR)	68	(55–78)	67	(51–76)	.021
Cardiac predisposing factors					
Intravenous drug use, n (%)	58	(7)	74	(15)	<.001
Rheumatic heart disease/hypertrophic cardiomyopathy, n (%)	0	(0)	3	(0.6)	.047
Congenital disease, n (%)	11	(1)	56	(12)	<.001
Prosthetic valve, n (%)	17	(2)	106	(22)	<.001
Prior endocarditis, n (%)	12	(1)	49	(10)	<.001
Minor predisposition criterion (2015 ESC), n (%)	89	(10)	216	(44)	<.001
Moderate/severe valve regurgitation/stenosis, n (%)	95	(11)	96	(20)	<.001
Moderate/severe valve regurgitation/stenosis, n (%)	83	(10)	53	(11)	.510
Cardiac implantable electronic devices, n (%)	59	(7)	160	(33)	<.001
Cardiac implantable electronic devices, n (%)	54	(6)	91	(19)	<.001
Transcatheter aortic valve replacement, n (%)	6	(0.7)	17	(4)	<.001
Transcatheter aortic valve replacement, n (%)	6	(0.7)	15	(3)	.001
Minor predisposition criterion (2023 ISCVID), n (%)	147	(17)	329	(68)	<.001
Heart transplantation, n (%)	5	(0.6)	2	(0.4)	1.000
Heart transplantation, n (%)	5	(0.6)	2	(0.4)	1.000
Left ventricular assist device, n (%)	3	(0.8)	1	(0.4)	.644
Left ventricular assist device, n (%)	0	(0)	0	(0)	…
Minor predisposition criterion (2023 ESC), n (%)	151	(18)	330	(68)	<.001
Microbiological data					
Polymicrobial bacteremia, n (%)	89	(10)	16	(3)	<.001
Major microbiological criterion (all versions), n (%)	649	(76)	439	(90)	<.001
Minor microbiological criterion (all versions), n (%)	209	(24)	47	(10)	<.001
Imaging data					
Positive echocardiography (either TTE or TOE) for vegetation, perforation, abscess, aneurysm, pseudoaneurysm, fistula, n (%)	0	(0)	331	(68)	<.001
Abnormal metabolic activity in ^{18}F-FDG PET/CT in prosthetic valve, n (%)	0	(0)	21	(4)	<.001
Positive cardiac-CT for vegetation, perforation, abscess, aneurysm, pseudoaneurysm, fistula, n (%)	0	(0)	6	(1)	.002
Major imaging criterion (2015 ESC), n (%)	0	(0)	351	(72)	<.001
Abnormal metabolic activity in ^{18}F-FDG PET/CT in native valve or CIED lead, n (%)	0	(0)	24	(5)	<.001
Abnormal metabolic activity in ^{18}F-FDG PET/CT in native valve or CIED lead, n (%)	0	(0)	7	(1)	.001
Significant new valvular regurgitation on echocardiography, n (%)	24	(3)	55	(18)	<.001
Significant new valvular regurgitation on echocardiography, n (%)	24	(3)	11	(2)	.598
Major imaging criterion (2023 ISCVID), n (%)	24	(3)	369	(76)	<.001
Leaflet thickening on echocardiography (either TTE or TOE) or cardiac CT, n (%)	16	(2)	44	(9)	<.001
Leaflet thickening on echocardiography (either TTE or TOE) or cardiac CT, n (%)	16	(2)	17	(4)	.068
Major imaging criterion (2023 ESC), n (%)	16	(2)	373	(77)	<.001
Manifestations					
Setting of infection onset					
Community, n (%)	350	(41)	198	(65)	<.001
Healthcare-associated, n (%)	163	(19)	49	(16)	
Nosocomial, n (%)	345	(40)	58	(19)	
Minor fever criterion (all versions), n (%)	706	(82)	402	(83)	.881
New heart murmur, n (%)	125	(15)	148	(31)	<.001
Vascular phenomena (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions), n (%)	50	(6)	285	(59)	<.001
Cerebral embolic events, n (%)	5	(0.6)	153	(32)	<.001
Non-cerebral embolic events, n (%)	46	(5)	206	(42)	<.001
Minor vascular criterion (2015 ESC), n (%)	50	(6)	285	(59)	<.001
Cerebral abscess, n (%)	0	(0)	3	(0.6)	.047
Cerebral abscess, n (%)	0	(0)	0	(0)	…
Splenic abscess, n (%)	0	(0)	0	(0)	…

Table 1. Continued

	No SAIE (n = 858)		SAIE (n = 486)		*P* Value
Minor vascular criterion (2023 ISCVID), n (%)	50	(6)	285	(59)	<.001
Septic arthritis, n (%)	73	(9)	55	(11)	.100
Septic arthritis, n (%)	71	(8)	26	(5)	.049
Spondylodiscitis, n (%)	56	(7)	49	(10)	.026
Spondylodiscitis, n (%)	51	(6)	24	(5)	.461
Minor vascular criterion (2023 ESC), n (%)	163	(19)	327	(67)	<.001
Minor immunologic criterion (all versions), n (%)	7	(0.8)	75	(15)	<.001
Data on surgery/CIED-extraction/histopathology, n (%)					
Valve surgery performed, n (%)	1	(0.1)	145	(30)	<.001
Macroscopic evidence of IE by inspection (surgery), n (%)	0	(0)	96	(20)	<.001
Major surgery criterion (2023 ISCVID), n (%)	0	(0)	0	(0)	…
CIED-extraction (among 219 patients with CIED), n (%)	5	(9)	70	(44)	<.001
Positive CIED-lead culture (without contact with infected pocket site), n (%)	0	(0)	25	(5)	<.001
Autopsy performed, n (%)	9	(1)	11	(2)	.099
Duke pathological criterion (2015 ESC, 2023 ISCVID), n (%)	0	(0)	55	(11)	<.001
Classifications					
Classification according to 2015 Duke-ESC clinical criteria					
Rejected, n (%)	273	(32)	13	(2)	
Possible, n (%)	575	(67)	108	(22)	
Definite, n (%)	10	(1)	365	(75)	<.001
Classification according to 2023 Duke-ISCVID clinical criteria					
Rejected, n (%)	247	(29)	6	(1)	
Possible, n (%)	579	(68)	88	(18)	
Definite, n (%)	32	(4)	392	(81)	<.001
Classification according to 2023 Duke-ESC clinical criteria					
Rejected, n (%)	227	(27)	3	(0.6)	
Possible, n (%)	596	(70)	84	(17)	
Definite, n (%)	35	(4)	399	(82)	<.001

In *italics* appear the comparison among episodes with or without SIAE of characteristics within the subgroup of patients who hadn't previously fulfilled the corresponding major/minor criterion according to the 2015 Duke-ESC.

TTE, TOE, 18F-FDG PET/CT, and cardiac CT were performed in 2037 (96%), 1237 (58%), 396 (19%), and 77 (4%) patients, respectively. In CHUV, thoracoabdominal and cerebral imaging for the research of embolic events were performed in 1169 (72%) and 641 (39%) patients, respectively. Valve surgery, CIED extraction, and autopsy were performed in 464 (22%) patients 31 (1%) and 126 (out of 453 patients with CIED; 28%) patients, respectively.

Abbreviations: CIED, cardiac implantable electronic devices; ESC, European Society of Cardiology; ^{18}F-FDG PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; IQR, interquartile range; ISCVID, International Society of Cardiovascular Infectious Diseases; SAIE, *S. aureus* infective endocarditis.

Table 2. Performance of Different Versions of the Duke Clinical Criteria Among 1344 Patients With *S. aureus* Bacteremia

	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy % (95% CI)
2015 Duke-ESC	75 (71–98)	99 (98–99)	97 (95–99)	88 (86–89)	90 (88–92)
2023 Duke-ISCVID	81 (77–84)	96 (95–97)	92 (90–95)	90 (88–91)	91 (90–91)
2023 Duke-ESC	82 (78–85)	96 (95–97)	92 (89–94)	90 (89–92)	91 (89–92)

Abbreviations: CI, confidence interval; ESC, European Society of Cardiology; ISCVID, International Society of Cardiovascular Infectious Diseases; NPV, negative predictive value; PPV, positive predictive value.

Metastatic Osteoarticular Complications

In terms of metastatic osteoarticular complications, the occurrence of septic arthritis was similar between patients with SAIE and SAB (11% vs 9%, $P = .100$). On the other hand, spondylodiscitis was more prevalent among patients with SAIE compared to those with SAB (10% vs 7%, $P = .026$). Nevertheless, when patients meeting the minor 2015 Duke-ESC vascular criterion were excluded, the incidence of spondylodiscitis was comparable between SAIE and SAB patients (6% vs 5%, $P = .461$). Out of the 108 cases of septic arthritis with available data on the onset of local symptoms, it was observed that in 73 cases (68%), patients experienced local symptoms more than 24 hours before the onset of systemic symptoms. In 27 cases (25%), local symptoms appeared simultaneously with

systemic symptoms (within ±− 24 hours of each other), and in the remaining eight cases (7%), local symptoms emerged after the onset of systemic symptoms. For the 88 instances of spondylodiscitis with accessible information on the onset of local symptoms, the following patterns were identified: in 60 episodes (68%) local symptoms began before the onset of systemic symptoms, in 21 episodes (24%), local symptoms and systemic symptoms occurred simultaneously, and in 7 episodes (8%), local symptoms appeared after the onset of systemic symptoms. Supplementary Tables 3 and 4 provide further insights into the associations between septic arthritis and spondylodiscitis and between embolic events and left-heart valve vegetation. It was observed that neither septic arthritis nor spondylodiscitis demonstrated a significant association with either embolic events or left-heart valve vegetation.

DISCUSSION

In 2023, ISCVID and ESC both introduced revisions to the Duke criteria [3–5] resulting in improved sensitivity for IE diagnosis when compared to the 2015 Duke-ESC criteria. After assessing the 2023 Duke-ISCVID version of the clinical criteria, it was observed that sensitivity increased overall, regardless of the causative microorganisms, although specificity decreased [7]. In patients with positive blood cultures for *S. aureus*, each version exhibited a notably higher specificity compared to what was observed in the aforementioned study [7]. This divergence can be attributed to the distinct characteristics associated with SAIE. This particular form of IE is characterized by virulence factors that accelerate vegetation formation, vegetation growth and perivalvular invasion resulting in the emergence of easily detectable lesions [11, 12]. Therefore, in this current study, none of the patients with SAIE met the major surgical criterion introduced by the 2023 Duke-ISCVID version. All patients who exhibited evidence of SAIE during direct inspection in the course of heart surgery had already met the major imaging criterion.

Cardiac lesions such as new valvular insufficiency and leaflet thickening, the former part of the 2023 Duke-ISCVID and the latter of 2023 Duke-ESC, were associated with SAIE [3–5]. However, this correlation lost significance when patients with other typical SAIE valve lesions were excluded. Valvular insufficiency and leaflet thickening are not specific indicators of IE. In contrast, local invasion can lead to complications like perforation, valve prosthesis dehiscence and corda rupture, all of which contribute to valvular insufficiency [13]. In the current study, leaflet thickening was found to be associated with the presence of vegetations. However, leaflet thickening alone did not show a significant correlation with SAIE. This particular lesion can manifest in various conditions, including age-related or myxoid degeneration, inflammatory valvular diseases, amyloidosis, or valve thrombosis, indicating a lack of specificity [14, 15].

In terms of predisposing factors, CIED and transcatheter aortic valve implantation (TAVI) were included in both 2023 Duke versions, as they account for a significant portion of IE cases [16, 17]. As shown in this study, both factors continued to be associated with SAIE even when patients who met the established 2015 Duke-ESC predisposition IE criterion were excluded. In contrast, the incorporation of preexisting moderate or severe valve regurgitation/stenosis or heart transplantation did not improve the accuracy of the 2023 Duke-ISCVID criteria, the latter due to a very limited number of patients at risk.

An additional inclusion in the 2023 Duke-ESC minor vascular criterion was hematogenous osteoarticular complications. This addition led to a decrease in accurate SAIE diagnosis since, when cases with embolic events were excluded, no association with IE was observed. Furthermore, all the vascular phenomena mentioned in the 2015 Duke-ESC criteria are exclusive to embolic events, which is not typically the case with spondylodiscitis [3]. In most instances, spondylodiscitis arises from hematogenous seeding from distant foci unrelated to IE, with urinary-tract and skin infections being the most common sources [18]. In a prior report, IE constituted only 12% of spondylodiscitis cases [18]. Even in instances of IE, the occurrence of spondylodiscitis often arises from hematogenous seeding rather than embolization. There was no association between spondylodiscitis or septic arthritis and the presence of embolic events or vegetation, which strengthens the case for not classifying them as embolic events. Spondylodiscitis typically precedes IE, whereby embolic events are always a consequence of IE. In our study, for both septic arthritis and spondylodiscitis, local symptoms preceded the onset of fever in 68% of cases. However, it is important to note that the presence of these complications should not defer the search for IE in patients with bacteremia. These complications are accounted for in two prediction scores used to diagnose SAIE [8, 19].

The present study has several limitations. First, it included a moderate number of episodes, with the majority being retrospectively included. However, all but 78 (6%) episodes underwent echocardiography. These 78 patients were included under the assumption of having SAB because they had received 16 days or less of antibiotic treatment, which was considered insufficient for potentially undiagnosed IE. Furthermore, they survived for at least 120 days, a timeframe deemed adequate for monitoring any recurrence of bacteremia in case of a misdiagnosis of the initial episode. Moreover, 2 of 3 cohorts included patients with IE or IE suspicion, resulting in a higher incidence of IE within the final cohort (36%) compared to previous studies (7%–14%) [8, 19, 20], potentially leading to selection bias. This overrepresentation of patients with a more severe phenotype could result in a false inflation of the sensitivity of a diagnostic test. Another limitation of our study pertains to the reference standard used, which relied on the

Endocarditis Teams from 2 institutions. The study, conducted from January 2014 to June 2023, witnessed increasing use of advanced imaging and microbiological modalities for IE diagnosis. The evolving understanding and experience within the Endocarditis Team during this period may have contributed to variations in diagnoses, posing a challenge to the consistency of the gold standard over time and limiting external validity. Despite these limitations, conducting such studies is crucial, given the complexities involved, and feasible only in centers with well-established endocarditis teams, as demonstrated in this study. To mitigate this limitation, we included an explanation for cases not classified as definite IE by the 2015 Duke-ESC criteria but identified as such by the Endocarditis Teams and subsequently treated as IE (Supplementary Table 1). Additionally, a limitation arises from both centers being situated in Switzerland. As a result, the findings may be influenced by local management practices, including the mandatory requirement for infectious diseases consultation, use of cardiac imaging modalities such as ^{18}F-FDG PET/CT or cardiac CT, as well as the performance of thoracoabdominal or cerebral imaging studies to investigate embolic events [8]. These approaches may differ widely on a global scale. In this scenario, the particular practices in Switzerland could have played a role in improving the detection of embolic events, thereby enhancing the diagnosis of IE [19–21]. Moreover, only 38% of the operated patients fulfilled the pathological criterion. This can be attributed to several factors. Not all patients underwent early surgery, which impacted the likelihood of obtaining positive culture and pathology results. Additionally, in patients who underwent valvuloplasty, the procedure hindered the extraction of tissue for examination. Finally, both hospitals had detailed protocols for the IE investigation algorithm. However, we cannot entirely dismiss the possibility that specific differences between the hospitals could have impacted the results.

In conclusion, among patients with positive blood cultures for *S. aureus*, both the 2023 Duke-ISCVID and 2023 Duke-ESC clinical criteria for IE showed a slight improvement in sensitivity compared to the 2015 Duke-ESC criteria. The enhanced diagnosis can mainly be attributed to the inclusion of factors such as CIED and TAVI as predisposing factors, along with the detection of abnormal metabolic activity in ^{18}F-FDG PET/CT in native valve or CIED-lead. However, it is crucial to highlight that the increase sensitivity was accompanied by a reduction in specificity in the updated versions. The decrease in specificity is likely due to the inclusion of new variables, such as valvular insufficiency and leaflet thickening, as part of the imaging criterion. Additionally, the addition of hematogenous osteoarticular complications to the category of minor vascular phenomena may have contributed to this decline. Further studies are needed to thoroughly evaluate the accuracy of the new 2023 Duke criteria. These studies should assess both the overall effectiveness of the updated criteria and the influence of each newly introduced variable individually. Furthermore, forthcoming revisions of the Duke criteria should have a stronger foundation in clinical research findings and rely less on expert opinion.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. B. H. and M. P. O. conceived the idea. M. P. O., P. M., M. F., G. T., P. T., M. K., M. V. H., R. B., J. E., B. G., and B. H. collected the patients' data. B. H. and M. P. O. supervised the project. M. P. O. and B. H. performed the analysis. All authors interpreted the results. M. P. O. wrote the first draft of the manuscript. All authors contributed to manuscript revision and read and approved the submitted version.

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