

The impact of transoesophageal echocardiography in elderly patients with infective endocarditis

Abbreviated title: The impact of TEE in elderly patients with IE

Tweet: Old patients who did not undergo TEE during the treatment of IE had poorer functional, nutritional and cognitive statuses, had less often previously known valvular disease, less often perivalvular abscess, were less often operated on and had a poorer prognosis than patients who had TEE.

Marie-Paule B. N'cho-Mottoh^a, Marie-Line Erpelding^b, Claire Roubaud^c, François Delahaye^d, Thibaut Fraisse^e, Marina Dijos^c, Pierre-Vladimir Ennezat^f, Arnaud Fluttaz^g, Benjamin Richard^h, Corinne Beaufortⁱ, Pierre Nazeyrollas^j, Camille Brasselet^k, Olivier Pineau^l, Pierre Tattevin^m, Elodie Curlierⁿ, Bernard Lung^o, Emmanuel Forestier^g, Christine Selton-Suty^{a,*}

^a *University Hospital of Nancy-Brabois, 54511 Vandœuvre Les Nancy, France*

^b *CHRU-Nancy, INSERM, Université de Lorraine, CIC, Epidémiologie Clinique, 54000 Nancy, France*

^c *University Hospital of Bordeaux, 33000 Bordeaux, France*

^d *Hospital Louis Pradel, 69500 Bron, France*

^e *Alès Hospital, 30100 Alès, France*

^f *University Hospital of Grenoble, 38700 La Tronche, France*

^g *Chambéry Hospital, 73000 Chambéry, France*

^h *Annecy Hospital, 74370 Epagny Metz-Tessy, France*

ⁱ *University Hospital of Poitiers, 86000 Poitiers, France*

^j *University Hospital of Reims, 51100 Reims, France*

^k *Clinique Courlancy, 51100 Reims, France*

^l *Villeneuve St Georges Hospital, 91560 Crosne, France*

^m *University Hospital of Rennes, 35000 Rennes, France*

ⁿ *University Hospital of Guadeloupe, Les Abymes 97142, France*

^o *Bichat-Claude Bernard Hospital, 75018 Paris, France*

* Corresponding author. Cardiology Department, CHU Nancy-Brabois, 54511 Vandoeuvre les Nancy, France.

E-mail address: c.suty-selton@chu-nancy.fr (C. Selton-Suty).

Twitter handle: @Marie_Paule11

Journal Pre-proof

ABSTRACT

Background: Infective endocarditis (IE) increasingly involves older patients. Geriatric status may influence diagnostic and therapeutic decisions.

Aim: To describe transoesophageal echocardiography (TEE) use in elderly IE patients, and its impact on therapeutic management and mortality.

Methods: A multicentre prospective observational study (ELDERL-IE) included 120 patients aged ≥ 75 years with definite or possible IE: mean age 83.1 ± 5.0 ; range 75–101 years; 56 females (46.7%).

Patients had an initial comprehensive geriatric assessment, and 3-month and 1-year follow-up.

Comparisons were made between patients who did or did not undergo TEE.

Results: Transthoracic echocardiography revealed IE-related abnormalities in 85 patients (70.8%).

Only 77 patients (64.2%) had TEE. Patients without TEE were older (85.4 ± 6.0 vs 81.9 ± 3.9 years; $P = 0.0011$), had more co-morbidities (Cumulative Illness Rating Scale-Geriatric score 17.9 ± 7.8 vs 12.8 ± 6.7 ; $P = 0.0005$), more often had no history of valvular disease (60.5% vs 37.7%; $P = 0.0363$), had a trend toward a higher *Staphylococcus aureus* infection rate (34.9% vs 22.1%; $P = 0.13$) and less often an abscess (4.7% vs 22.1%; $P = 0.0122$). Regarding the comprehensive geriatric assessment, patients without TEE had poorer functional, nutritional and cognitive statuses. Surgery was performed in 19 (15.8%) patients, all with TEE, was theoretically indicated but not performed in 15 (19.5%) patients with and 6 (14.0%) without TEE, and was not indicated in 43 (55.8%) patients with and 37 (86.0%) without TEE ($P = 0.0006$). Mortality was significantly higher in patients without TEE.

Conclusions: Despite similar IE features, surgical indication was less frequently recognized in patients without TEE, who less often had surgery and had a poorer prognosis. Cardiac lesions might have been underdiagnosed in the absence of TEE, hampering optimal therapeutic management. Advice of geriatricians should help cardiologists to better use TEE in elderly patients with suspected IE.

Keywords:

Infective endocarditis

Transoesophageal echocardiography

Elderly

Geriatric assessment

1. Abbreviations

CIED cardiac implantable electronic device

CIRS-G Cumulative Illness Rating Scale-Geriatric

IE infective endocarditis

TAVI transcatheter aortic valve implantation

TEE transoesophageal echocardiography

TTE transthoracic echocardiography

Journal Pre-proof

2. Background

Infective endocarditis (IE) is a rare but severe disease that increasingly involves elderly patients. Indeed, more than one third of patients with IE are aged > 70 years in developed countries [1, 2]. IE has been associated with less pronounced clinical symptoms and delayed diagnosis in the elderly [3], but more complications and higher mortality [3, 4].

As with many other diseases, geriatric status may influence diagnostic management, therapeutic decision-making and prognosis of IE [5, 6].

Transoesophageal echocardiography (TEE) improves the diagnosis of IE, particularly in patients with intracardiac devices [7]. However, TEE is not systematically performed in patients with suspected IE, as shown by the recent EURO-ENDO registry, where only 59% of patients underwent TEE. Furthermore, older age may influence the performance of TEE, as it is an invasive procedure that is sometimes difficult to perform in patients with cognitive disorders or agitation [5].

The aim of this study was to describe the use of TEE in elderly patients treated for IE, and the differences in therapeutic management and mortality according to the performance or not of TEE.

3. Methods

A prospective multicentre study (ELDERL-IE) was conducted between March 2015 and April 2016 in 14 primary and tertiary care hospitals in France [8]. The current study is a post hoc analysis from this initial cohort.

Eligible patients were those aged ≥ 75 years and being treated for possible or definite IE according to the Duke criteria modified by Li [9], who agreed to participate and underwent an initial comprehensive geriatric assessment performed by a geriatrician during the first week after admission.

In brief, the comprehensive geriatric assessment described the patient's status 2 months before hospital admission and at the beginning of hospitalization, and included the following data: functional status, assessed by the Activities of Daily Living score (range 0 to 6) [10], the Instrumental Activities of Daily Living score (range 0 to 8) [11] and the ability to walk; nutritional status, assessed by body mass index and the Mini Nutritional Assessment score (range 0 to 30) [12]; and cognitive status, assessed by the Mini Mental Status Examination score (range 0 to 30) [13]. Co-morbidities were summarized using the Charlson Comorbidity Index [14] and the Cumulative Illness Rating Scale-Geriatric (CIRS-G) [15].

Information on IE was collected as described previously [16]. This information included demographic data, co-morbidities, IE characteristics, therapeutic management and follow-up. The definitions of these variables were the same as those used in previous French epidemiological studies on IE. Surgery was categorized as a three-component variable: surgery performed; surgery not performed despite a theoretical indication; and surgery not performed without a theoretical indication.

Once completed, case report forms were validated by an expert team in each region, including the diagnosis of possible or definite IE according to the Duke criteria modified by Li [9]. Follow-up was performed at 3 and 12 months during an on-site consultation. For patients who did not attend follow-up visits, vital status and date of death, if appropriate, were collected through civil registries; so, vital status at 3 months and 1 year was known for all patients.

This study was registered with ClinicalTrials.gov (Identifier: NCT02910856), and received ethics approval from the Comité Consultatif sur le Traitement de l'Information en Matière de Recherche dans le Domaine de la Santé (CCTIRS n°14.699). All patients gave their informed consent [8].

3.1. Statistical analysis

Patients were divided into two groups according to the performance of TEE. Quantitative variables are described as means \pm standard deviations, and qualitative variables are expressed as numbers and percentages. For comparisons, parametric tests were used (Student's *t* test for quantitative variables; the χ^2 test for qualitative variables). Non-parametric tests, such as the Wilcoxon test for quantitative variables and Fisher's exact test for qualitative variables, were used whenever necessary. Kaplan-Meier survival curves according to the performance of TEE were built and compared by the log-rank test. A significance threshold of 0.05 was used. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc, Cary, NC, USA).

4. Results

4.1. Patient characteristics

Among the 120 patients included in the ELDERL-IE study, only 77 (64.2%) had TEE. Transthoracic echocardiography revealed abnormalities related to IE in 85 patients (70.8%), with vegetations found in 81 (67.5%), abscesses in 17 (14.2%) and severe regurgitation in 21 (17.5%). As reported in the princeps paper [8], reasons for not performing TEE were: no change to therapeutic

plans anticipated in 29 cases; transthoracic echocardiography (TTE) considered of sufficient quality in 19 cases; and patient refusal and restlessness in eight cases.

Compared with patients who had TEE, patients without TEE were older (85.4 ± 6.0 vs 81.9 ± 3.9 years; $P = 0.0011$), were more likely to be aged > 85 years (55.8% vs 26.0%; $P = 0.0011$) and had more co-morbidities as assessed by the CIRS-G score (17.9 ± 7.8 vs 12.8 ± 6.7 ; $P = 0.0005$) (Table 1). Repartition of underlying heart disease was significantly different between the two groups, with a lower rate of valvular prosthesis (20.9% vs 41.6%) and a higher rate of no previously known underlying valvular disease (60.5% vs 37.7%) in patients without versus those with TEE ($P = 0.0363$). However, there was a similarly high rate of cardiac implantable electronic devices in the two groups (20.9% vs 23.4%).

4.2. Geriatric comprehensive assessment

Table 1 displays the results of the comprehensive geriatric assessment according to the performance of TEE. At admission, patients without TEE had poorer functional status (Activities of Daily Living score 2.2 ± 1.8 vs 3.6 ± 2.1 ; $P = 0.0004$), nutritional status (Mini Nutritional Assessment score 15.9 ± 6.2 vs 18.8 ± 5.9 ; $P = 0.0222$) and cognitive status (Mini Mental Status Examination score 17.5 ± 7.5 vs 21.6 ± 6.5 ; $P = 0.0063$) compared with patients who had TEE. Functional status was already significantly altered 2 months before diagnosis.

4.3. IE characteristics

Table 2 displays the comparison of IE characteristics between patients with and without TEE. Location of IE, clinical presentation and IE complications were similar in the two groups (Table 2). Regarding microbiology, there was a non-significant trend towards a higher rate of *Staphylococcus aureus* IE (34.9% vs 22.1%; $P = 0.13$) and a lower rate of unusual pathogens (0% vs 10.4%; $P = 0.0494$) among patients without TEE.

Regarding imaging, patients without TEE also underwent cerebral imaging or positron emission tomography-computed tomography less frequently, although not significantly so. At echocardiography, there was a trend towards a lower frequency of criteria of IE in the group without TEE: any criteria (62.8% vs 75.3%; $P = 0.15$); vegetation (60.5% vs 71.4%; $P = 0.22$); and perforation (2.3% vs 13.0%;

$P = 0.10$). Furthermore, the presence of an abscess (4.7% vs 22.1%; $P = 0.0122$) and severe regurgitation (7.0% vs 23.4% $P = 0.0234$) were less often reported in patients without TEE.

4.4. Treatment and outcome

Table 3 displays the comparison of therapeutic management and follow-up between the groups with and without TEE. Surgery was performed in only 19 patients (15.8% of the total population), all from the TEE group. The repartition of the surgery variable according to its three components was significantly different between the two groups ($P = 0.0006$), with a higher prevalence of non-operated patients without indication in the group without TEE (86.0% vs 55.8%). The additive EuroScore was not significantly different between groups, but its component calculated on operation-related factors was higher in patients without TEE (3.7 ± 0.7 vs 3.3 ± 0.9 ; $P = 0.0134$). Mortality rates were significantly higher in the group without TEE at month 3 (51.1% vs 22.1%) and at year 1 (58.1% vs 33.8%; $P = 0.0044$) (Fig. 1).

5. Discussion

Compared with patients who underwent TEE during the hospitalization for an IE, patients aged > 75 years who did not undergo TEE: (1) were older, with more co-morbidities and poorer functional, nutritional and cognitive statuses; (2) more often had no history of valvular disease or valvular prosthesis, but had similar rates of cardiac implantable electronic devices (CIEDs); (3) less often had recognized features of IE on echocardiography; (4) less often had a recognized indication for surgery and surgery performed; and (5) had a poorer prognosis.

The impact of IE on functional and cognitive status in the elderly has been poorly studied. The ELDERL-IE study revealed that IE dramatically impaired the functional status of the oldest patients. Together with nutritional status, functional status was the only variable associated with mortality, independent of the cardiac and infectious characteristics of IE [8]. All variables measured by the comprehensive geriatric assessment were more severely impaired in patients without TEE than in those with TEE. Furthermore, co-morbidities as assessed by the CIRS-G were more frequent in patients without TEE than in those with TEE.

These findings illustrate the impact of functional status and autonomy on indications and performance of investigations. Doctors are probably less prone to perform semi-invasive imaging

procedures, such as TEE, in old and frail patients [5]. However, the discussion about whether to perform a semi-invasive procedure, such as TEE, which has an impact on patient care, should be discussed with the patient or their family caregivers. Karlawish et al. insisted that advanced care planning is important before older patients are no longer able to make informed medical decisions [17]. Even for older patients who are cognitively impaired, obtaining their consent is essential. No cognitive assessment is available to determine whether a patient has the capacity or not to give consent, especially during a period of acute disease. In our study, however, there was a quite low rate of TEE refusal by the patients.

In most cases, cardiologists made the decision about whether or not to perform TEE themselves, considering that TTE was of sufficient quality or that TEE would not change their therapeutic decision. This type of decision is probably multifactorial, taking into account age, underlying heart disease, functional status, co-morbidities and, of course, the results of TTE.

TEE is often not performed in patients for whom cardiac surgery will never be possible, whatever the reason. Non-performance of TEE could then be considered as a preference misdiagnosis, and not as a medical misdiagnosis, given that doctors do so because they believe in their expertise to make good decisions for the patients. In order to avoid such preference misdiagnoses, Mulley et al. suggested following a three-step reasoning strategy: adopting a state of mind of scientific detachment; formulating the clinical diagnostic issue; and engaging the patient in a conversation to clarify their choice [18]. However, this is not always possible with older patients.

It is well known that TEE has better sensitivity than TTE in the diagnosis of IE echocardiographic specific features. TEE allows better diagnosis of intracardiac abscesses [19] and more accurate quantification of regurgitation when TTE is of suboptimal quality [20]. This lower sensitivity of TTE alone explains, at least in part, the lower rates of IE-specific features identified in the patients who did not have TEE. The better performance of TEE over TTE has been particularly emphasized in case of IE on valvular prostheses or CIEDs. Although lower than in the TEE group, the proportion of intracardiac material was high among patients without TEE (20.9% of valvular prostheses and 20.9% of CIEDs). So, it may be hypothesized that some of those patients with material who did not undergo TEE had cardiac lesions that were not seen by TTE. Actually, patients without TEE had significantly fewer intracardiac abscesses and severe regurgitation than those who had TEE, and (non-significantly) fewer vegetations and perforations.

It is well known that the presence of abscesses and perforations has a poor prognosis, with a 2-fold increase in 1-year mortality [21]. Higher mortality would have been expected in the TEE group, but this was not the case, for several reasons. Cardiac lesions might have been underdiagnosed in the absence of TEE. All patients operated on had TEE, and mortality at 3 months and 1 year was lower in this group.

As underlined by the National Academies of Medicine, getting the right diagnosis is a key aspect of health care – it provides an explanation of a patient's health problem, and informs subsequent health care decisions [22]. A proper and accurate diagnosis leads to better, more appropriate and less costly therapy [23]. This is particularly true in the field of surgical indication for IE, and the results of our study are in accordance with this dogma. All operated patients had TEE, with a proper and accurate diagnosis of cardiac lesions. The proportion of non-operated patients with theoretical indication was higher in patients who had TEE, where the decision of non-performance of surgery was taken after obtaining a complete echocardiographic diagnosis with TEE. Finally, the proportion of non-operated patients without recognized theoretical indications was higher in the group without TEE, where fewer features of surgical indications were evidenced by TTE alone, and where indications for surgery might have been unrecognized in some cases.

The proper recognition of surgical indication is of utmost importance in terms of prognosis. Surgery has long been shown to improve the prognosis of selected patients with IE. In our study, the prognosis of patients without TEE who were less often operated on was poorer at both the 3-month and 1-year follow-up compared with patients who had TEE. Some studies have observed that age is associated with higher mortality rates [4, 24], whereas others have been unable to show that age, *per se*, is a prognostic factor [25, 26]. These contradictory results might be explained by the small number of older patients included in those studies, and by the use of different definitions of older adults. The conclusion from these studies should be that it is all the co-morbidities associated with age that influence prognosis, rather than age itself. Patient age is only one among the many variables that should be analysed before taking the decision about whether or not to perform surgery in older patients with IE, and the decision-making process regarding surgery for IE in the elderly should involve two steps. The first step would be to establish the theoretical operative indication according to guidelines, and TEE is then of the utmost importance, by describing precisely the cardiac lesions that should or should not lead to surgery; the second step would then be to discuss the benefit-risk ratio

within the Endocarditis Team. Usual surgery risk scores only take into account the crude age of the patient, and none of them investigates the level of frailty of the patient. So, the help of a geriatrician is of real added value, as some patients with a discouraging initial profile might nevertheless benefit from surgery if they are adequately managed, especially regarding nutrition, cognition and mobilization.

The underuse of surgery in elderly patients with IE was emphasized in a recent large nationwide retrospective study by Ragnarsson et al., who showed that the rate of surgery decreased with increasing age, from 46% in the group aged < 65 years to 6% in the group aged \geq 80 years [27]. Interestingly, the authors used propensity score matching, and showed that when patients aged \geq 75 years who underwent surgery were matched with same-age patients who did not undergo surgery, there was better survival associated with surgery. Similarly, another propensity analysis on data from the European Society of Cardiology EURObservational Research Programme's EURO-ENDO registry showed that mortality from surgery in patients aged > 80 years was similar to that of younger patients, after matching on most of the classical risk factors for poor prognosis of IE [28].

Our study has some limitations. It was a prospective study on IE in older adults, with a specific focus on the impact of the involvement of geriatricians; this particularity may have changed patient management and outcome. Furthermore, patients who underwent urgent surgery or were admitted to an intensive care unit were excluded, so our results cannot be extrapolated to such subjects. Multiple comparisons might have led to alpha risk inflation. Further studies are needed to consolidate these results.

6. Conclusion

Although TEE has higher sensitivity for the diagnosis of IE, it was not always performed in older patients, even in the presence of intracardiac material. Cardiac lesions might have been underdiagnosed in the absence of TEE. These findings, together with the specific general and geriatric characteristics of this group, probably explain, in part, the fact that surgical indication was less frequently recognized, and that patients were less frequently operated on when they did not undergo TEE compared with those who had TEE. The poorer prognosis of these patients is then a complex and mixed result of poor general health and geriatric status, underdiagnosis of specific IE features and less invasive therapeutic management.

These results may suggest that performance of TEE should always be discussed in order to optimize the management of older patients, especially in those with intracardiac material. A meticulous multivariable evaluation, including the advice of geriatricians, taking into account patient status before the current hospitalization, should help cardiologists to refine and improve the selection of old patients who could benefit from TEE.

Sources of funding

The initial research project ELDERL-IE, from which these data were analysed, was supported by a grant of the “Fondation Coeur et Recherche” (France) in 2013.

Disclosure of interest

The authors declare that they have no competing interests.

Journal Pre-proof

References

- [1] Selton-Suty C, Celard M, Le Moing V, Doco-Lecompte T, Chirouze C, Lung B, et al. Preeminence of *Staphylococcus aureus* in infective endocarditis: a 1-year population-based survey. *Clin Infect Dis* 2012;54:1230-9.
- [2] Slipczuk L, Codolosa JN, Davila CD, Romero-Corral A, Yun J, Pressman GS, et al. Infective endocarditis epidemiology over five decades: a systematic review. *PLoS One* 2013;8:e82665.
- [3] Durante-Mangoni E, Bradley S, Selton-Suty C, Tripodi MF, Barsic B, Bouza E, et al. Current features of infective endocarditis in elderly patients: results of the International Collaboration on Endocarditis Prospective Cohort Study. *Arch Intern Med* 2008;168:2095-103.
- [4] Terpenning MS, Buggy BP, Kauffman CA. Infective endocarditis: clinical features in young and elderly patients. *Am J Med* 1987;83:626-34.
- [5] Forestier E, Fraisse T, Roubaud-Baudron C, Selton-Suty C, Pagani L. Managing infective endocarditis in the elderly: new issues for an old disease. *Clin Interv Aging* 2016;11:1199-206.
- [6] High KP, Bradley S, Loeb M, Palmer R, Quagliariello V, Yoshikawa T. A new paradigm for clinical investigation of infectious syndromes in older adults: assessment of functional status as a risk factor and outcome measure. *Clin Infect Dis* 2005;40:114-22.
- [7] Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;36:3075-128.
- [8] Forestier E, Roubaud-Baudron C, Fraisse T, Patry C, Gavazzi G, Hoen B, et al. Comprehensive geriatric assessment in older patients suffering from infective endocarditis. A prospective multicentric cohort study. *Clin Microbiol Infect* 2019;25:1246-52.
- [9] Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Jr., Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;30:633-8.
- [10] Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970;10:20-30.
- [11] Lawton MP. Scales to measure competence in everyday activities. *Psychopharmacol Bull* 1988;24:609-14.

- [12] Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Cederholm T, et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging* 2009;13:782-8.
- [13] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-98.
- [14] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-83.
- [15] Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. *Psychiatry Res* 1992;41:237-48.
- [16] Nanna MG, Peterson ED, Wu A, Harding T, Galanos AN, Wruck L, et al. Age, knowledge, preferences, and risk tolerance for invasive cardiac care. *Am Heart J* 2020;219:99-108.
- [17] Karlawish JH, Casarett DJ, James BD, Xie SX, Kim SY. The ability of persons with Alzheimer disease (AD) to make a decision about taking an AD treatment. *Neurology* 2005;64:1514-9.
- [18] Mulley AG, Trimble C, Elwyn G. Stop the silent misdiagnosis: patients' preferences matter. *BMJ* 2012;345:e6572.
- [19] Habib G, Badano L, Tribouilloy C, Vilacosta I, Zamorano JL, Galderisi M, et al. Recommendations for the practice of echocardiography in infective endocarditis. *Eur J Echocardiogr* 2010;11:202-19.
- [20] Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease: Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Rev Esp Cardiol (Engl Ed)* 2022;75:524.
- [21] Lauridsen TK, Park L, Tong SY, Selton-Suty C, Peterson G, Cecchi E, et al. Echocardiographic Findings Predict In-Hospital and 1-Year Mortality in Left-Sided Native Valve *Staphylococcus aureus* Endocarditis: Analysis From the International Collaboration on Endocarditis-Prospective Echo Cohort Study. *Circ Cardiovasc Imaging* 2015;8:e003397.
- [22] Committee on Diagnostic Error in Health Care, Board on Health Care Services, Institute of Medicine, The National Academies of Sciences, Engineering and Medicine. Improving

- Diagnosis in Health Care. Balogh EP, Miller BT, Ball JR, eds. Washington, DC: The National Academies Press (US); 2015.
- [23] Khullar D, Jha AK, Jena AB. Reducing Diagnostic Errors--Why Now? *N Engl J Med* 2015;373:2491-3.
- [24] Selton-Suty C, Hoen B, Grentzinger A, Houplon P, Maignan M, Juilliere Y, et al. Clinical and bacteriological characteristics of infective endocarditis in the elderly. *Heart* 1997;77:260-3.
- [25] Peled N, Pitlik S, Livni G, Ashkenazi S, Bishara J. Impact of age on clinical features and outcome of infective endocarditis. *Eur J Clin Microbiol Infect Dis* 2006;25:473-5.
- [26] Werner GS, Schulz R, Fuchs JB, Andreas S, Prange H, Ruschewski W, et al. Infective endocarditis in the elderly in the era of transesophageal echocardiography: clinical features and prognosis compared with younger patients. *Am J Med* 1996;100:90-7.
- [27] Ragnarsson S, Salto-Alejandre S, Strom A, Olaison L, Rasmussen M. Surgery Is Underused in Elderly Patients With Left-Sided Infective Endocarditis: A Nationwide Registry Study. *J Am Heart Assoc* 2021;10:e020221.
- [28] Pazdernik M, lung B, Mutlu B, Alla F, Riezebos R, Kong W, et al. Surgery and outcome of infective endocarditis in octogenarians: prospective data from the ESC EORP EURO-ENDO registry. *Infection* 2022;50:1191-202.

Figure legend

Fig.0

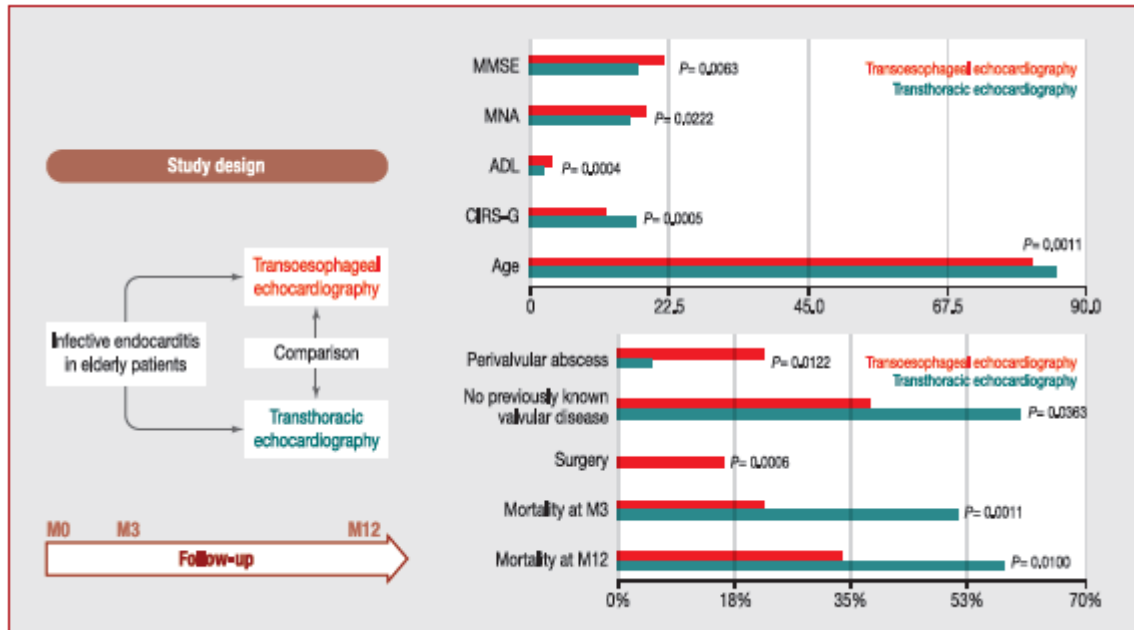
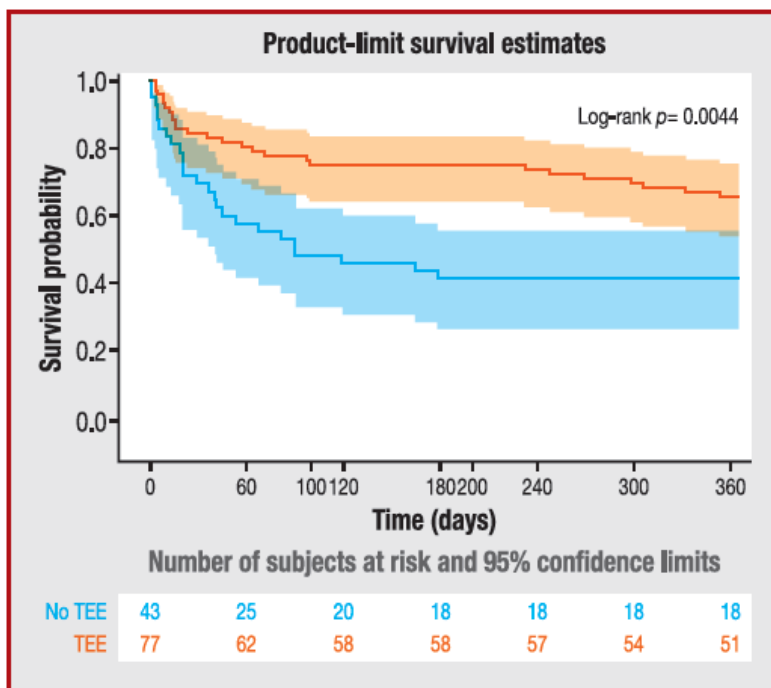


Fig. 1. Kaplan-Meier survival curves and *P* value for comparison with log-rank test.



Central illustration. Elderly patients who did not undergo TEE during the treatment of IE had poorer functional, nutritional and cognitive statuses, less often had previously know valvular disease or

perivalvular abscess, were less often operated on, and had a poorer prognosis than patients who had TEE. ADL: Activities of Daily Living; CIRS-G: Cumulative Illness Rating Scale-Geriatric; M0: month 0; M3: month 3; M12: month 12; MMSE: Mini Mental Status Examination; MNA: Mini Nutritional Assessment.

Journal Pre-proof

Table 1

Patient characteristics and comprehensive geriatric assessment according to the performance of transoesophageal echocardiography.

	Whole population (<i>n</i> = 120)	No TEE (<i>n</i> = 43; 35.8%)	TEE (<i>n</i> = 77; 64.2%)	<i>P</i>
Demographic data				
Age (years)	83.1 ± 5.0	85.4 ± 6.0	81.9 ± 3.9	0.0011
Age ≥ 85 years	44 (36.7)	24 (55.8)	20 (26.0)	0.0011
Male sex	64 (53.3)	19 (44.2)	45 (58.4)	0.13
Co-morbidities				
Charlson score	1.8 ± 1.7	2.1 ± 2.1	1.7 ± 1.4	0.88
Age-adjusted Charlson score	5.7 ± 1.7	6.2 ± 2.1	5.4 ± 1.5	0.0371
At least one co-morbidity	69 (57.5)	27 (62.8)	42 (54.5)	0.38
Hypertension	86 (71.7)	35 (81.4)	51 (66.2)	0.08
Diabetes mellitus	40 (33.3)	13 (30.2)	27 (35.1)	0.59
Neoplasia	33 (27.5)	15 (34.9)	18 (23.4)	0.18
Renal failure	26 (21.7)	9 (20.9)	17 (22.1)	0.88
M-2 geriatric assessment				
ADL	5.0 ± 1.7	4.3 ± 2.0	5.4 ± 1.3	0.0003
IADL	4.5 ± 2.9	3.3 ± 2.8	5.1 ± 2.8	0.0019
Walking ability	109 (93.2)	35 (85.4)	74 (97.4)	0.0141
D0 geriatric assessment				
ADL	3.1 ± 2.1	2.2 ± 1.8	3.6 ± 2.1	0.0004
Walking ability	38 (35.5)	6 (16.7)	32 (45.1)	0.0037
MNA total score	17.8 ± 6.1	15.9 ± 6.2	18.8 ± 5.9	0.0222
MMSE score	20.3 ± 7.1	17.5 ± 7.5	21.6 ± 6.5	0.0063
CIRS-G score	14.5 ± 7.5	17.9 ± 7.8	12.8 ± 6.7	0.0005
BMI	25.1 ± 4.8	24.8 ± 5.6	25.2 ± 4.3	0.68
Underlying heart disease				

Native valve disease	24 (20.0)	8 (18.6)	16 (20.8)	} 0.0363
No previously known valve disease	55 (45.8)	26 (60.5)	29 (37.7)	
Valvular prosthesis	41 (34.2)	9 (20.9)	32 (41.6)	
TAVI	6 (10.7)	3 (13.6)	3 (8.8)	0.67
Previous IE	6 (5.0)	3 (7.0)	3 (3.9)	0.67
Stimulating device	27 (22.5)	9 (20.9)	18 (23.4)	0.76
Pacemaker	23 (85.2)	8 (88.9)	15 (83.3)	1.00
Implantable cardioverter defibrillator	4 (14.8)	1 (11.1)	3 (16.7)	1.00

Data are expressed as mean \pm standard deviation or number (%). ADL: Activities of Daily Living; BMI: body mass index; CIRS-G: Cumulative Illness Rating Scale-Geriatric; D0: day of diagnosis IADL: Instrumental Activities of Daily Living; IE: infective endocarditis; M-2: 2 months before diagnosis; MMSE: Mini Mental Status Examination; MNA: Mini Nutritional Assessment; TAVI: transcatheter aortic valve implantation; TEE: transoesophageal echocardiography.

Table 2

Infective endocarditis characteristics according to the performance of transoesophageal echocardiography.

	Whole population (<i>n</i> = 120)	No TEE (<i>n</i> = 43; 35.8%)	TEE (<i>n</i> = 77; 64.2%)	<i>P</i>
Origin of infection				0.55
Community acquired	86 (71.7)	26 (72.2)	60 (81.1)	
Health care related	24 (21.8)	10 (27.8)	14 (18.9)	
Responsible micro-organisms				
Streptococcaceae	65 (54.2)	25 (58.1)	40 (51.9)	0.51
Oral streptococci	13 (10.8)	4 (9.3)	9 (11.7)	0.77
Group D streptococci	21 (17.5)	6 (14.0)	15 (19.5)	0.45
<i>S. pyogenes</i>	7 (5.8)	5 (11.6)	2 (2.6)	0.10
<i>Enterococci</i>	23 (19.2)	10 (23.3)	13 (16.9)	0.40
Other streptococci	1 (0.8)	0 (0.0)	1 (1.3)	1.00
Staphylococcaceae	38 (31.7)	17 (39.5)	21 (27.3)	0.17
<i>S. aureus</i>	32 (26.7)	15 (34.9)	17 (22.1)	0.13
Coagulase-negative staphylococci	6 (5.0)	2 (4.7)	4 (5.2)	1.00
Other micro-organisms	8 (6.7)	0 (0.0)	8 (10.4)	0.0494
> 1 responsible micro-organism	5 (4.2)	1 (2.3)	4 (5.2)	0.65
No identified micro-organism	2 (1.7)	0 (0.0)	2 (2.6)	0.54
Time delay between hospitalization and diagnosis				0.19
< 4 days	80 (67.2)	25 (59.5)	55 (71.4)	
≥ 4 days	39 (32.8)	17 (40.5)	22 (28.6)	
Location of IE				0.42
Aortic valve	39 (32.5)	11 (25.6)	28 (36.4)	
Mitral valve	36 (30.0)	14 (32.6)	22 (28.6)	
Aortic and mitral valves	7 (5.8)	1 (2.3)	6 (7.8)	
Tricuspid valve	4 (3.3)	1 (2.3)	3 (3.9)	
Bilateral IE	3 (2.5)	1 (2.3)	2 (2.6)	

Stimulating device	4 (3.3)	1 (2.3)	3 (3.9)	
Unknown	27 (22.5)	14 (32.6)	13(16.9)	
Number of vegetations				0.10
0	63 (52.5)	17 (39.5)	46 (59.7)	
1	52 (43.3)	24 (55.8)	28 (36.4)	
2	5 (4.1)	2 (4.6)	3(3.9)	
Clinical symptoms				
Fever	91 (77.1)	32 (76.2)	59 (77.6)	0.86
Heart failure	33 (27.5)	13 (30.2)	20 (26.0)	0.62
NYHA III/IV	13 (12.0)	4 (10.8)	9 (12.7)	1.00
Cerebral complication	18 (15.0)	6 (14.0)	12 (15.6)	0.81
Symptomatic cerebral complication	10 (8.5)	4 (9.8)	6 (7.9)	0.74
Emboli other than cerebral	15 (12.5)	7 (16.3)	8 (10.4)	0.35
Any vascular phenomenon	31 (25.8)	12 (27.9)	19 (24.7)	0.70
Any immunological phenomenon	6 (5.0)	1 (2.3)	5 (6.6)	0.42
Extracardiac complication	48 (40.0)	17 (39.5)	31 (40.3)	0.94
Imaging data				
Cerebral imaging (CT scan or MRI)	82 (68.3)	26 (60.5)	56 (72.7)	0.17
PET-CT	5 (4.2)	0 (0.0)	5 (6.5)	0.16
IE criteria at echo	85 (70.8)	27 (62.8)	58 (75.3)	0.15
Vegetation	81 (67.5)	26 (60.5)	55 (71.4)	0.22
Mean size of vegetation (mm)	11.7 ± 7.4	11.3 ± 10.3	11.9 ± 5.9	0.19
Perforation	11 (9.2)	1 (2.3)	10 (13.0)	0.10
Intracardiac abscess	17 (14.2)	2 (4.7)	17 (22.1)	0.0122
Severe regurgitation	21 (17.5)	3 (7.0)	18 (23.4)	0.0234
LVEF < 45%	38 (31.7)	16 (41.0)	22 (31.4)	0.31

Data are expressed as number (%) or mean ± standard deviation. CT: computed tomography; IE: infective endocarditis; LVEF: left ventricular ejection fraction; MRI: magnetic resonance imaging; PET: positron emission tomography; TEE: transoesophageal echocardiography.

Table 3

Therapeutic management and follow-up according to the performance of transoesophageal echocardiography.

	Whole population (<i>n</i> = 120)	No TEE (<i>n</i> = 43; 35.8%)	TEE (<i>n</i> = 77; 64.2%)	<i>P</i>
Antibiotic therapy				
Duration of antibiotic therapy (days)	38.9 ± 22.1	33.6 ± 23.7	41.9 ± 20.7	0.0330
Use of gentamycin	79 (65.8)	25 (58.1)	54 (70.1)	0.18
Duration of gentamycin therapy (days)	5.6 ± 5.3	3.0 ± 3.0	6.7 ± 5.7	0.0010
Switch to oral antibiotic therapy	24 (20.0)	7 (16.3)	17 (22.1)	0.45
Surgery				
Operated patients	19 (15.8)	0 (0.0)	19 (24.7)	} 0.0006
Non-operated patients with indication	21 (17.5)	6 (14.0)	15 (19.5)	
Non-operated patients without indication	80 (66.7)	37 (86.0)	43 (55.8)	
Additive EuroScore	11.0 ± 2.4	11.4 ± 2.4	10.8 ± 2.3	0.18
EuroScore (patient-related factors)	7.0 ± 1.9	7.1 ± 1.7	6.9 ± 1.9	0.56
EuroScore (cardiac-related factors)	0.6 ± 1.1	0.6 ± 1.0	0.6 ± 1.2	0.41
EuroScore (operation-related factors)	3.4 ± 0.9	3.7 ± 0.7	3.3 ± 1.0	0.0134
Follow-up				
Length of hospital stay (days)	37.5 ± 29.4	33.1 ± 19.6	39.9 ± 33.3	0.66
Death during hospital stay	23 (19.2)	12 (27.9)	11 (14.3)	0.07
Mortality rates (%)				
At 3-month follow-up	32.5 (24.9–41.7)	51.1 (37.4–66.7)	22.1 (14.3–33.1)	
At 1-year follow-up	42.5 (34.2–51.8)	58.1 (44.1–72.9)	33.8 (24.4–45.5)	0.0044
Duke-Li IE classification				0.0404
Definite	91 (75.8)	28 (65.1)	63 (81.8)	
Possible	29 (24.2)	15 (34.9)	14 (18.2)	

Data are expressed as mean ± standard deviation, number (%) or % (95% confidence interval). IE: infective endocarditis; TEE: transoesophageal echocardiography.

Fig. 1

