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Guidelines

2023 SFMU/GICC-SFC/SFGG expert recommendations for the emergency management of older patients with acute heart failure. Part 1: Prehospital management and diagnosis

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1. Abbreviations

ACS acute coronary syndromes
AHF acute heart failure
BNP B-type natriuretic peptide
ED emergency department
ECG electrocardiogram
ESC European Society of Cardiology
GICC-SFC Groupe insuffisance cardiaque et cardiomyopathies de la Société française de cardiologie
GRADE Grading of Recommendations Assessment, Development and Evaluation
HF heart failure
HFpEF heart failure with preserved ejection fraction
HFrEF heart failure with reduced ejection fraction
LVEF left ventricular ejection fraction
NEWS National Early Warning Score
NOVICA-3 De novo Insuficiencia Cardiaca Aguda 3
NT-proBNP N-terminal pro-B-type natriuretic peptide
OPTIMIZE-HF Organized Program To Initiate Lifesaving Treatment In Hospitalized Patients With Heart Failure
PE pulmonary embolism
PICO population, intervention, comparison, outcomes
PPV positive predictive value
PROTECT study Placebo-Controlled Randomized Study of the Selective A1 Adenosine Receptor Antagonist Rolofylline for Patients Hospitalized With Acute Decompensated Heart Failure and Volume Overload to Assess Treatment Effect on Congestion and Renal Function
SFGG Société française de gériatrie et gérontologie
SFMU Société française de médecine d'urgence
TTE transthoracic echocardiography

2. Background

Acute heart failure (AHF) is a complex, multifactorial syndromic condition that, until now, did not have a consensual definition [1,2]. The difficulties in agreeing on a consensual definition of AHF also apply to research, since depending on the application of the field of investigation, the target populations concerned and the therapeutic goals or pathophysiological knowledge sought, the elements defining heart failure (HF) vary, especially among older patients. Thus, although the advent of echocardiography has made it possible to characterize disturbances in myocardial relaxation and altered ventricular filling, marking the birth of the concept of HF with preserved ejection fraction (HFpEF) versus HF with reduced ejection fraction (HFrEF), the different clinical presentations do not always make it possible to determine whether myocardial failure corresponds to a disease of ventricular filling of vascular origin [3].

AHF is most often characterized by dyspnoea, lower limb oedema and/or intense asthenia. It is a common presentation in emergency departments (EDs) and has become a major public health problem as its incidence and prevalence rise in line with an aging population in all developed countries. AHF represents a growing medico-economic burden and is associated with high morbidity and mortality [4]. Currently, AHF is the main reason for hospital admissions in patients aged > 65 years and acute cardiogenic pulmonary oedema accounts for approximately 1% of ED visits [3,4], involving approximately 200,000 patients per year in France (including 5% of the French population aged 75–85 years and 10% of those aged > 85 years) [5]. HF is a progressive pathology linked to aging, with mortality rising by 10% each year [6]. Indeed, the mortality rate remains appalling, reaching up to 12% during the hospital stay, 8–20% in the 2 months following hospitalization for an episode of AHF, and reaching 25–50% in the first 5 years after initial diagnosis. Moreover, mortality is increased in the presence of associated comorbidities such as anaemia, hypercholesterolemia or renal dysfunction, all of which become more frequent with age [3,4,6,7].

3. Methods

A group of 29 experts from the Société française de médecine d'urgence (SFMU; French Society of Emergency Medicine), the Groupe insuffisance cardiaque et cardiomyopathies de la Société française de cardiologie (GICC-SFC; Group of Heart Failure and Cardiomyopathy of the French Society of Cardiology) and the Société française de gériatrie et gérontologie (SFGG; French Society of Geriatrics and Gerontology) was convened. The main objective of the expert panel was to provide recommendations on the emergency management of AHF in older patients (aged > 75 years). The authors used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method to assess the level of evidence in the literature with grading from "No recommendation" to "Expert opinion" to "Moderate recommendation (G1)", and "Strong recommendation (G2)" and with level of evidence scaling from "Low (−)" to "High (+)" [8]. The potential drawbacks of making strong recommendations in the presence of only low-level evidence were highlighted and some recommendations with insufficient evidence were not graded. Five areas were discussed: prehospital management, diagnosis of AHF, therapeutics, pathway of care and ethics, of which the first two are included herein. For each area, the expert panel formulated questions according to the population, intervention, comparison, outcomes (PICO) model [9] and an extensive literature search was performed. The analysis of the literature and the formulation of recommendations were conducted according to the GRADE method [8].

4. Prehospital management of AHF in older patients

4.1. Question 1

In the prehospital emergency setting, is there any prognostic or diagnostic score that can help to manage older patients with AHF?

4.1.1. Rationale

Dyspnoea is a frequent reason for emergency calls, and AHF is one of the main causes requiring prehospital emergency care. Whatever the prehospital emergency care system, emergency

medical services with paramedics or on-board emergency physicians, numerous studies and guidelines have suggested that accurate, early diagnosis can improve patient prognosis [1,2,10]. Indeed, survival is increased in patients who receive early treatment (odds ratio [OR] 2.51, 95% confidence interval [CI] 1.37–4.55; $P < 0.01$) [11], but mortality is raised in patients with inappropriate treatment, and could double in older adults [12–14].

Aetiological scores are recommended by the European Society of Cardiology (ESC) [1,2]. The GASP4Ar score incorporates age and requires N-terminal prohormone-B-type natriuretic peptide (NT-proBNP) measurement, which limits its use in prehospital settings [15]. The National Early Warning Score (NEWS), a clinical score based on vital parameters only, has not been evaluated in diagnostic terms [16]. The Brest score, based on 11 simple and readily available variables, aims to determine the diagnostic probability of AHF causing dyspnoea, but has yet to be validated in an independent cohort, and has never been validated in the prehospital setting [17].

4.1.2. Experts' answer

There is insufficient evidence to recommend the use of diagnostic or prognostic scores in the prehospital setting for older patients with suspected AHF.

4.1.3. Experts' recommendation

None.

4.2. Question 2

Can telemedicine be used to reduce the need to transport older patients with AHF to hospital?

4.2.1. Rationale

Telemedicine encompasses several entities: teleconsultation, tele-expertise, remote medical monitoring and tele-counselling. The use of telemedicine platforms has risen considerably with the development of outpatient care for patients with HF. The literature on telemedicine in HF is very heterogeneous and focuses mainly on patients' cardiology follow-up who do not require emergency care. Compared with the usual care pathway involving several care providers (nurses, general practitioners, cardiologists, etc.), the telemedicine-based pathway of care includes the monitoring of acute decompensation and emergency care of patients with HF. According to a meta-analysis by Lin et al. [18], telemonitoring may be associated with a reduction in-hospital admission rates and mortality. In a meta-analysis by Zhu et al. [19], telemonitoring was associated with a reduction in the total number of all-cause hospitalizations (OR 0.82, 95% CI 0.73–0.91; $P = 0.0004$) and cardiac hospitalizations (OR 0.83, 95% CI 0.72–0.95; $P = 0.007$). Remote monitoring resulted in a statistically significant reduction in the risk of all-cause mortality (OR 0.75, 95% CI 0.62–0.90; $P = 0.003$) [19]. However, the odds of HF-related mortality did not differ significantly from that of conventional healthcare (OR 0.84, 95% CI 0.61–1.16, $P = 0.28$). Furthermore, although it seems that telemedicine can make a positive contribution to the early identification of acute decompensation in patients with HF in these meta-analysis [18,19], there are still few studies specific to the elderly. In 2020, a randomized controlled trial assesses the effect of a telemonitoring programme versus standard care in preventing all-cause death or unplanned hospitalization at 18 months and found no difference between the two groups (rate ratio 0.97, 95% CI 0.77–1.23; $P = 0.80$) [20].

4.2.2. Experts' answer

The experts suggest using a telemedicine device to detect and assess emergency situations in older patients with AHF.

4.2.3. Experts' opinion

Strong agreement.

5. Diagnosis of AHF in older patients

5.1. Question 1

In older patients with AHF, should we systematically look for triggering factors?

5.1.1. Rationale

Triggering factors for AHF are found in 45–75% of cases [21–25]. In a cohort of over 15,000 patients suffering from AHF, precipitating factors were identified in 8784 patients (55%) [21]. A single trigger was identified in 7764 patients (49%), while in 1020 patients (6%), a combination of two or more triggers was identified [21]. In the OPTIMIZE-HF (Organized Program To Initiate Lifesaving Treatment In Hospitalized Patients With Heart Failure) study, which included almost 50,000 patients, the three most frequently identified triggers were pulmonary infections (15%), myocardial ischaemia (15%) and arrhythmia (14%) [22]. The authors emphasized the need to determine a precipitating factor during hospitalization [22] as in the NOVICA-3 (De novo Insuficiencia Cardiaca Aguda 3) cohort study, Miró et al. [23] showed that detection of AHF triggers is feasible on admission to the ED.

Infections, particularly pulmonary infections, are the most frequent cause of AHF. Early and correct detection of infection in AHF is difficult, as the typical symptoms of dyspnoea and fatigue can be explained by both aetiologies. In AHF, biomarkers with an infectious spectrum (including C-reactive protein and procalcitonin) do not appear to improve diagnostic sensitivity [26,27].

Myocardial ischaemia can be a trigger for AHF, just as acute coronary syndromes (ACS) can be complicated by AHF, the combination of the two being associated with a poor prognosis [8]. The diagnosis of ACS as the cause of AHF is difficult to distinguish from myocardial damage resulting from AHF [28]. In the event of suspected ACS with a non-qualifying electrocardiogram (ECG), a troponin assay should be performed (see Question 5).

Atrial fibrillation and AHF can exacerbate each other. When atrial fibrillation is the cause of AHF, the outcome appears to be more favourable than in the presence of other contributing factors such as ACS or infection [2,21,29].

Pulmonary embolism (PE) can be a trigger for AHF but, to date, no study has reliably determined the prevalence of PE in patients with AHF. In 2005, Darze et al. [30] conducted a prospective study to assess the prevalence of PE using a systematic diagnostic approach. Of the 198 patients with HF recruited in this study, 18 (9%) were diagnosed with PE. Given the incidence of PE in patients with AHF, it is suggested that PE should be investigated according to clinical probability.

Anaemia is present in approximately 30% of patients with HF [31,32]. Although not strictly speaking a triggering factor, the presence of anaemia worsens the morbidity and mortality of patients with HF. The presence of anaemia should therefore be systematically sought in the ED [1,2,32]. Associated deficiencies should be investigated during hospitalization [1,2].

In the OPTIMIZE-HF study, worsening renal function was associated with higher mortality [22]. Based on daily creatinine measurements, the PROTECT study (Placebo-Controlled Randomized Study of the Selective A1 Adenosine Receptor Antagonist Rolofylline for Patients Hospitalized With Acute Decompensated Heart Failure and Volume Overload to Assess Treatment Effect

on Congestion and Renal Function) also found that a creatinine increase of 26.4 μmol/L (0.3 mg/dL) between two measurements was associated with a poorer prognosis [33]. This notion is even truer is patients aged ≥ 80 years, where a rise in creatinine is strongly associated with prognosis, even in the absence of residual congestive signs [34].

Older patients, particularly women, are more likely to present with HFpEF, with elevated vascular resistance and consequent acute cardiogenic pulmonary oedema in the context of severely elevated blood pressure [35]. Moreover, high blood pressure is associated with a greater probability of HFpEF [36]. Regular monitoring of blood pressure in the ED is therefore essential [10].

ESC recommendations suggest that thyroid function (i.e. thyroid-stimulating hormone level) should be assessed in all HF patients [1,2]. However, this test should not be performed in the ED. In fact, thyroid function testing is part of the initial systematic hospital work-up for HF [2,37].

Non-adherence to pharmacological treatment or a low-salt diet is reported to be a cause of hospitalization in 5–20% of cases [38–41]. A systematic search for such non-adherence enables educational information to be adapted during hospitalization.

5.1.2. Experts' answer 1

Triggering factors such as the presence of an infectious focus, hypertension, ACS, arrhythmia, anaemia, renal failure or non-adherence to treatment should probably be systematically investigated.

5.1.3. Grade

G2+.

5.1.4. Experts' answer 2

The experts suggest that PE should not be systematically investigated.

5.1.5. Experts' opinion

Strong agreement.

5.1.6. Experts' answer 3

The experts suggest that dysthyroidism should not be systematically sought in the ED. This search should be carried out as part of the HF patient's healthcare journey.

5.1.7. Experts' opinion

Strong agreement.

5.2. Question 2

In older patients with AHF, does repeating the ECG or cardiac monitoring improve the diagnosis of the triggering factor?

5.2.1. Rationale

ECG on admission is a key element in the management of older patients with AHF. It helps exclude the diagnosis of ST-segment elevation myocardial infarction or arrhythmias potentially responsible for this condition [28,42]. AHF is a risk factor for the development of atrial and ventricular arrhythmias, and some treatments have significant pro-arrhythmogenic properties. Furthermore, in the older patient population, there is an increased risk of abnormal ECG on admission regardless of its origin [43]. In 2007, a retrospective study that analysed 9315 ECGs from patients with AHF aged 71 ± 13 years found that < 2% had a normal ECG [43]. In a post-hoc analysis, Benza et al. [44] analysed the occurrence of arrhythmias in 949 patients (median age 65 years) hospitalized for AHF. Six percent of patients presented with a cardiac rhythm disorder, of which 49% were atrial fibrillation or atrial flutter, 32% sustained ventricular tachycardia and 19% ventricular fibrillation [44]. Unfortunately, there are no good-quality studies comparing the value of systematic ECG monitoring versus no monitoring after an initial non-pathological ECG in older patients. Recently, a prospective study by Sweda et al. [45] analysed the ECGs of 1915 patients presenting to the ED with a chief complaint of acute dyspnoea. They found that the median (interquartile range) angle between the QRS axis and the T-wave axis (QRS-T angle) was significantly higher in patients with AHF than in patients with acute dyspnoea of extra-cardiac origin (110° [46–156°] vs. 33° [15–57°]; $P < 0.001$) [45]. However, the area under the curve in the population of patients aged > 75 years was only 0.71 (95% CI 0.67–0.74) [45].

5.2.2. Experts' answer 1

The experts suggest systematically performing an ECG on admission to the ED and repeating it in the event of an intercurrent event.

5.2.3. Experts' opinion

Strong agreement.

5.2.4. Experts' answer 2

The experts suggest performing a second ECG if the patient is hospitalized, on admission into the medical ward and/or before the patient returns home from the ED.

5.2.5. Experts' opinion

Strong agreement.

5.2.6. Experts' answer 3

The experts suggest that older patients with established AHF should not be systematically monitored by electrocardioscope in the ED.

5.2.7. Experts' opinion

Strong agreement.

5.3. Question 3

In the dyspnoeic emergency patient, does natriuretic peptide (B-type natriuretic peptide [BNP] or NT-proBNP) measurement improve the diagnosis of AHF?

5.3.1. Rationale

The diagnosis of AHF in older patients is challenging, particularly due to their heterogeneous symptoms, comorbidities and polypathological nature. In this context, the use of biomarkers to confirm or refute the diagnosis is tempting. In a French study in 26 EDs, Chouihed et al. [6] found that biomarkers were used in > 90% of patients with suspected AHF. Threshold values for BNP (< 100 ng/L) and NT-proBNP (< 400 ng/L) in young and middle-aged patients are often used to exclude HF. However, in older patients, there are many confounding factors that raise the baseline level, including age, but also comorbidities (hypertension, cardiac pathologies, renal or chronic respiratory failure) and triggering factors such as ACS or atrial fibrillation [2,8,21,28,29,46]. While the ability to exclude a diagnosis of AHF for patients with BNP or NT-proBNP values below the defined thresholds seems to be preserved in studies [46–51], the probability that values in older patients are below these thresholds seems low [47]. More generally, the threshold values used in this population have not been established. As long ago as 2004, Maisel et al. [48] reported an age-related difference in BNP levels in a study of 1586 patients without being able to define a precise threshold beyond the age of 70 years. As there was a risk of not recognizing HF, the authors recommended that the threshold should not be modified. Zaphiriou et al. [49] studied

306 patients (mean age 74 years), 104 of whom were diagnosed with HF. They found negative predictive values between 0.87 and 0.97 for BNP and NT-proBNP at the defined thresholds, but positive predictive values (PPVs) of 0.44 and 0.59 respectively [49]. In 2005, Ray et al. [50] reported a moderate discriminatory capacity of BNP at the usual threshold of 100 ng/L for the diagnosis of HF in patients aged > 65 years (PPV = 0.65). At higher thresholds, sensitivity ranged from 0.63 to 0.81 [50]. A study by Plichart et al. [51] focused on patients aged > 80 years who were hospitalized for dyspnoea or desaturation. All patients underwent a BNP assay and a cardiologist who was blinded to the results established a diagnosis according to the recommendations of the ESC. In this study of 383 patients (including 238 with HF), the BNP assay was not discriminatory for the aetiological diagnosis [51]. Furthermore, due to the particularity of its pharmacological action, patients with HF who are taking an angiotensin-receptor neprilysin inhibitor will have an elevated BNP level irrespective of treatment efficacy, and any biological monitoring will need to be carried out using NT-proBNP [1,2].

5.3.2. Experts' answer

In the absence of a validated threshold in this population, BNP and NT-proBNP assays should probably not be used routinely to diagnose AHF in dyspnoeic older emergency patients.

5.3.3. Grade

G2−.

5.4. Question 4

In the dyspnoeic emergency patient, does natriuretic peptide (BNP or NT-proBNP) measurement improve the prognosis of AHF?

5.4.1. Rationale

Results on the use of natriuretic peptide level as a prognostic marker in the ED are not unequivocal. A study of 11,679 patients found a modest predictive effect (HR 1.07, 95% CI 1.05–1.08) of a 30% increase in natriuretic peptide level in older patients (≥ 65 years) who presented to the ED with AHF without atrial fibrillation [52]. The discrepancies surrounding the prognostic properties of this assay are possibly heightened by the variability in the choice of event measured (re-hospitalization, death, time to onset), the timing of the assay (in the ED or in the hospital ward) and – above all – the threshold used, which differs from one study to another and increases with age [53–56]. It should be noted that natriuretic peptide has been included in prognostic models in several studies, with interesting results [57,58]. In contrast to its measurement on admission, its prognostic value at discharge and during follow-up is well established [2].

5.4.2. Experts' answer

Natriuretic peptide measured in the ED should probably not be used as a prognostic factor in older patients consulting for AHF.

5.4.3. Grade

G2−.

5.5. Question 5

Do troponin assays (high-sensitivity cardiac troponin T and high-sensitivity cardiac troponin I) improve diagnosis in older patients with AHF?

5.5.1. Rationale

Numerous studies have shown that elevated troponin levels are associated with increased morbidity and mortality, whether from cardiovascular or other causes. A meta-analysis by Aimo et al. [59] that included 10 studies with a total of 9289 patients aged 66 ± 12 years with HF and elevated troponin levels found increases in all-cause mortality (hazard ratio [HR] 1.48, 95% CI 1.41–1.45), cardiovascular mortality (HR 1.40, 95% CI 1.33–1.48) and cardiovascular hospitalizations (HR 1.42, 95% CI 1.36–1.49) over a mean follow-up of 2.4 years. Troponin measurement in older patients presenting to the ED with AHF also has a goal in the aetiological diagnosis. Indeed, the clinical presentation of an ACS is more likely to be atypical in older patients, with dyspnoea as the main symptom [60]. In this context, the experts reiterate that troponin assays cannot be interpreted independently of ECG analysis, but many factors are likely to raise baseline troponin levels [2,59]. Thus, in a 2012 prospective cohort study, Santhanakrishnan et al. [61] showed, in a small cohort of 51 patients, that those with HFpEF or HFrEF had higher high-sensitivity troponin T levels than the general population (23.7 or 35.6 pg/mL vs. 3.7 pg/mL, respectively) [61]. Furthermore, in a 2013 cohort study of 1514 patients with AHF and renal failure, Pfortmueller et al. [62] found that 382 patients (25%) with moderate to severe renal failure had significantly higher high-sensitivity troponin T levels than patients without impaired renal function (0.028 vs. 0.009 mg/L, $P < 0.0001$). Regarding the confounding factors that may elevate troponin according to the 2020 ESC recommendations [2], age and renal function are considered the most important, with variations of up to 300%. More recently, in a post-hoc study involving a cohort of 46,435 patients who underwent troponin testing in the ED, Lowry et al. [63] found that the specificity and PPV of troponin testing fell sharply with age. Inpatients aged ≥ 75 years, specificity and PPV were 82.6% (95% CI 81.9–83.4%) and 51.6% (95% CI 49.8–53.2%), respectively, much lower than among those aged 50–74 years: 95.5% (95% CI 95.2–95.8%) and 70.1% (95% CI 68.5–71.8%), respectively [63]. These results suggest that two consecutive measurements should be performed to detect real myocardial damage, rather than age-related variability. Overall, troponin measurement in older patients with AHF in the ED appears to be recommended solely for the purpose of aetiological diagnosis, and always in correlation with clinical and ECG analysis [2]. If there is a strong suspicion of ischaemia, and specific management is possible or envisaged, this assay should be repeated once to take account of inter-individual variability and a baseline level that is probably different in this population.

5.5.2. Experts' answer

Older patients with AHF should probably have a troponin assay performed in the ED. This assay is intended for aetiological diagnosis but should always be correlated with clinical findings and ECG analysis and may be repeated only once.

5.5.3. Grade

G2+.

5.6. Question 6

In an older dyspnoeic patient presenting to the ED, does a point-of-care thoracic ultrasound improve the diagnosis of AHF?

5.6.1. Rationale

Numerous studies and three meta-analyses have demonstrated that the presence of a bilateral B-line profile on lung ultrasound, which is more or less associated with impaired left ventricular systolic function, performs very well in the diagnosis of AHF (sensitivity 73–94%, specificity 83–94%), particularly in the congestive state [64–68]. The role of point-of-care thoracic ultrasound could be even more important in an older population, in whom the clinical presentation is sometimes atypical and the biology (NT-proBNP) less specific [69].

The experts highlight three key points:

- the bilateral B-line profile makes the diagnosis of bilateral interstitial lung disease without determining the aetiology (particularly AHF versus bilateral pneumopathy). The clinician must therefore interpret it in the light of the complete clinical picture, and prospective studies are still needed to identify the exact diagnostic thresholds in this population;
- the finding of impaired systolic function on point-of-care thoracic ultrasound, in addition to the bilateral B-line profile, reinforces the probability of AHF. However, the finding of normal left ventricular systolic function does not invalidate this diagnosis, as a significant proportion of AHF patients, particularly older patients, have HFpEF;
- the only way to diagnose AHF without considering left ventricular ejection fraction (LVEF) is to approach left ventricular filling pressures by assessment of the E/e' ratio. Indeed, a simple protocol combining lung ultrasound with measurement of the E/e' ratio offers excellent performance [70]. However, it can only be used by clinicians who have been trained in this practice.

5.6.2. Experts' answer

Clinical point-of-care thoracic ultrasound (pulmonary and cardiac) is probably required to diagnose AHF in older patients with dyspnoea in the ED.

5.6.3. Grade

G2+.

5.7. Question 7

In an older patient presenting to the ED with AHF, does transthoracic echocardiography (TTE) by a cardiologist modify therapeutic management?

5.7.1. Rationale

AHF can occur in the setting of HFpEF or HFrEF. TTE is an important diagnostic tool in the management of patients with AHF. The ESC recommends this examination as Class I and level of evidence C [1,2]. It should be performed on all patients presenting with AHF, on admission and during hospitalization. TTE can be used to assess LVEF and right ventricular function, the size of the heart chambers, the presence of diastolic dysfunction and/or to detect the presence of underlying heart disease such as dilated cardiomyopathy or valvular damage [70–72]. The prognostic value of ultrasound parameters varies between studies, but LVEF, the severity of tricuspid leakage and right ventricular dysfunction are the most important prognostic elements for the occurrence of events at 1 month at the start of hospitalization [73–76]. No parameter other than LVEF appears to be predictive of in-hospital outcome [73]. Although TTE can be used to monitor response to treatment, no study has been carried out to determine the value and timing of repeated TTE, except in the event of a major change in the clinical picture. After in-hospital admission, full cardiac TTE should be performed during hospitalization, when the patient is able to maintain decubitus [71].

5.7.2. Experts' answer

The experts suggest performing a TTE during hospitalization as soon as the patient is able to maintain a decubitus position.

5.7.3. Experts' opinion

Strong agreement.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2024.08.002.

Disclosure of interest

N.P. has received consulting fees from VYGON SA (CPAP-Boussignac), symposia lecture fees and congress invitations from Fisher & Paykel Healthcare SAS (Optiflow), and is involved in an independent clinical research programme for Roche Diagnostics (no fee or grant) and a fundamental research programme for Boehringer Ingelheim GMBH (no fee or grant).

C.D. has received congress invitations from Boehringer, consulting, lecture fee and research grant from Abott, consulting and lecture fees from Abiomed and Satelia, and consulting fees from AstraZeneca.

A.B. has received consultancy fees from Pfizer, Vifor Pharma, Boehringer and AstraZeneca and been involved in symposia for Novartis and Vifor Pharma.

M.P. has received lecture fees from Bristol Myers Squibb, consultancy fees from AstraZeneca and a congress invitation from Novartis.

N.G. has received honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, Lilly, Novonordisk, Novartis, NP Medical, Roche diagnostics and Echosens.

F. Roca has been involved in oral communications for Pfizer, Bayer and Sanofi, consulting and congress invitation from Novartis.

P.J. has received honoraria from AstraZeneca, Bayer, Novonordisk, Novartis, NP medical, Boehringer Ingelheim amd Pfizer.

F.M. has received honoraria from Novartis, Pfizer, Vifor, Boehringer and Bristol Myers Squibb.

T.C. has been involved in consulting for Novartis.

All other authors declare that they have no competing interest.

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