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RESEARCH ARTICLE

BLITZ-HF: a nationwide initiative to evaluate and improve adherence to acute and chronic heart failure guidelines

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Aims To assess adherence to guideline recommendations among a large network of Italian cardiology sites in the management of acute and chronic heart failure (HF) and to evaluate if an ad-hoc educational intervention can improve their performance on several pharmacological and non-pharmacological indicators.

Methods and results BLITZ-HF was a cross-sectional study based on a web-based recording system with pop-up reminders on guideline recommendations used during two 3-month enrolment periods carried out 3 months apart (Phase 1 and 3), interspersed by face-to-face macro-regional benchmark analyses and educational meetings (Phase 2). Overall, 7218 patients with acute and chronic HF were enrolled at 106 cardiology sites. During the enrolment phases, 3920 and 3298 patients were included, respectively, 84% with chronic HF and 16% with acute HF in Phase 1, and 74% with chronic HF and 26% with acute HF in Phase 3. At baseline, adherence to guideline recommendations was already overall high for most indicators. Among acute HF patients, an improvement was obtained in three out of eight indicators, with a significant rise in echocardiographic evaluation. Among chronic HF patients with HF and preserved or mid-range ejection fraction, performance increased in two out of three indicators: creatinine and echocardiographic evaluations. An overall performance improvement was observed in six out of nine indicators in ambulatory HF with reduced ejection fraction patients with a significant increase in angiotensin receptor–neprilysin inhibitor prescription rates.

Conclusions Within a context of an already elevated level of adherence to HF guideline recommendations, a structured multifaceted educational intervention could be useful to improve performance on specific indicators. Extending this approach to other non-cardiology healthcare professionals, who usually manage patients with HF, should be considered.

Keywords Acute heart failure • Chronic heart failure • Adherence • Registry • Guidelines

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Introduction

Despite significant advances in diagnosis and therapy over the past 20 years, patients with heart failure (HF) continue to experience poor prognosis. Clinical registries and surveys including patients with chronic HF (CHF) and acute HF (AHF) have demonstrated that adherence to guideline recommendations remains at least sub-optimal.[1–3] Nevertheless, initiatives aiming at targeting guideline implementation, such as the Get With The Guidelines® (GWTG) initiative of the American Heart Association,[4] are rare and should be adopted.

Consequently we conducted the BLITZ-HF study, a quality improvement initiative, with the participation of more than 100 Italian cardiology sites of the Italian HF Network of the National Association of Hospital Cardiologists (ANMCO). The two principal aims were: (i) to evaluate adherence to selected and clinically relevant class I recommendations as reported in the 2016 European Society of Cardiology (ESC) HF guidelines[5] during routine clinical care in both AHF and CHF; and (ii) to verify if a specific multifaceted HF educational intervention, which included face-to-face investigator training meetings and the adoption of an innovative web-based clinical data management programme, could improve adherence to guideline recommendations during a second enrolment period.

Methods

BLITZ-HF is a multicentre, cross-sectional, national study designed to evaluate the extent to which cardiologists adhere to 2016 ESC HF guidelines and whether an implementation intervention could improve guideline adherence. This was evaluated through a multifaceted intervention which included an educational web programme for patient clinical management and face-to-face training meetings (*Figure 1*). No specific protocols for evaluation, management, and/or treatment besides guideline recommendations were put forth during the study. The participating cardiologists were responsible for adopting diagnostics, pharmacological treatments or therapeutic procedures and were requested to justify those decisions in apparent discordance with guideline recommendations (e.g. drug contraindications or intolerance).

The study was conducted through four phases:

- *Phase 1*, a 3-month cross-sectional survey which included subjects admitted for AHF, as well as all CHF outpatients evaluated at the participating centres. Patients' data were collected through an innovative web programme with pop-up reminders on guideline recommendations (see online supplementary material for further details).
- *Phase 2*, four face-to-face educational meetings were held in Milan, Bologna, Rome and Catania over a 2-day period. These meetings included lectures from Italian leading cardiologists in the field of HF and benchmarking discussions sharing Phase 1 results, aiming at improving awareness regarding the contents and the implementation of current guidelines, focusing on diagnostic issues, medical therapy optimization and device implantation. As shown in *Figure 1*, site attendance rate was high (96.2%) with a mean number of investigators from each centre of 1.3 ± 0.5.
- *Phase 3*, a post-intervention cross-sectional survey identical to Phase 1.
- *Phase 4*, a longitudinal follow-up involving all patients included in the study in Phase 1 and 3 with visits at 6 and 12 months from discharge for AHF patients and at 6 and 12 months from enrolment for CHF patients (data not shown).

Site selection is shown in online supplementary *Figure S1*. Of the nearly 450 sites belonging to the Italian ANMCO HF Network, 173 accepted to participate in the study, but only 123 participated in the first enrolment phase (Phase 1) while 106 sites participated in both enrolment phases (Phase 1 and 3) with a nationwide distribution representative of different geographical areas and available hospital facilities (coronary care unit, cath lab, cardiac surgery). Therefore, for the purpose of the present study, only patients enrolled in sites participating in both enrolment phases were considered.

Data collection

In both Phase 1 and 3, information on demographic characteristics, clinical features, medical history, laboratory examinations, diagnostic procedures, pharmacological and non-pharmacological treatments was recorded. Data were collected using the web-based system *IN-HF online Software*, used in Italian sites since 1995, enriched with the above described educational features with pop-up reminders of guideline recommendations.

Patient selection

All patients of any sex, aetiology of HF, level of ejection fraction (EF), New York Heart Association (NYHA) class, with written informed consent either evaluated in the ambulatory setting (CHF) or during admission for acute (*de novo* or worsening) HF were considered for enrolment in the study in its two 3-month enrolment phases (8 March–4 September 2017 and 24 December 2017–9 April 2018). The diagnosis of HF (both acute or chronic) was defined locally following the ESC guidelines.[5] For AHF patients, intravenous therapy (diuretic, vasodilators, vasopressors) was required for enrolment. Main exclusion criteria were age <18 years, and inclusion in other registries or trials that could influence, by protocol, the clinical management of patients.

Outcomes

The primary endpoint was adherence improvement to the specific performance measures detailed in *Table 1* according to disease phase (acute or chronic) and HF phenotype: HF with reduced EF (HFrEF, EF <40%), HF with preserved EF (HFpEF, EF ≥50%) (23.9%) and HF with mid-range EF (HFmrEF, EF 40–49%).

Statistical analysis

Considering the explorative and fully observational nature of the current study, no formal sample size calculation was performed. Nevertheless, we planned to enrol at least 5000 patients in order to have sufficient information on a few subgroups of patients for whom a specific focus could be considered of interest (i.e. patients with preserved EF, different clinical profiles at hospital admission, and chronic obstructive pulmonary disease [COPD] or diabetes). Data analysis was mainly aimed at comparing the degree of adherence to guideline recommendations between the two enrolment periods. Categorical variables were

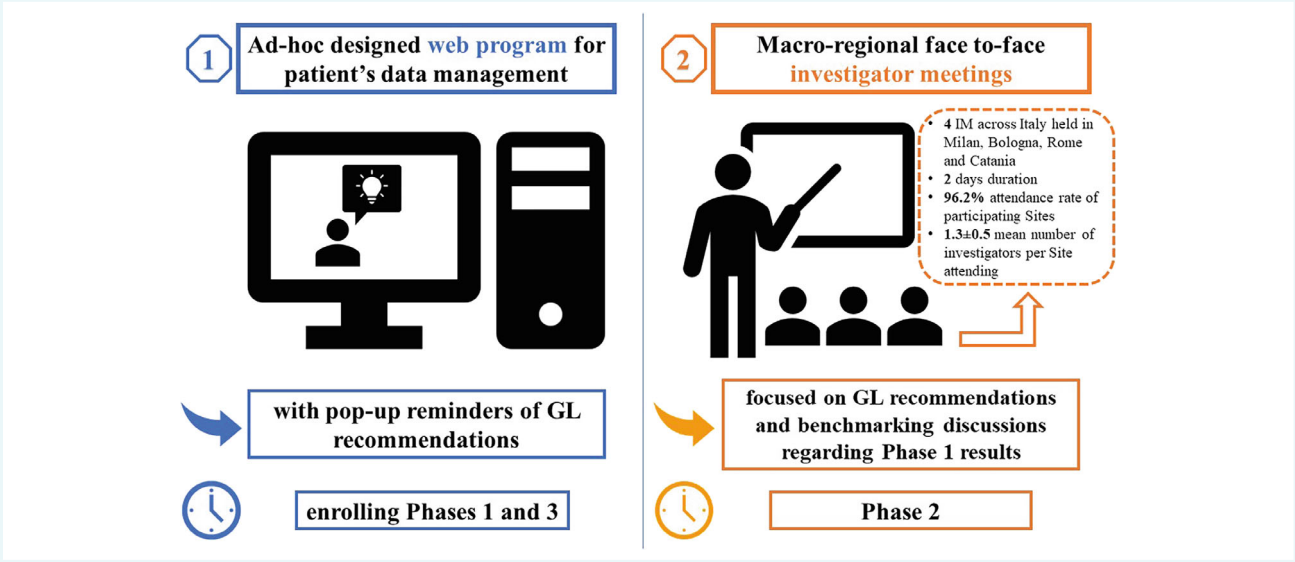

Figure 1 Components of educational intervention to improve adherence to guideline (GL) recommendations. IM, Investigator Meeting.

Table 1 Individual performance measures: recommendations, contraindications/intolerance

HF category and performance measures	Contraindications/intolerance
AHF	
Discharge OAT prescription in AF patients	History of major bleeding
EF in-hospital evaluation	
Creatinine in-hospital evaluation	
NP evaluation on admission	
Discharge ACE-I/ARB/ARNI prescription in HFrEF patients	Angioedema; severe CKD or AKI; symptomatic hypotension
Discharge BB prescription in HFrEF patients	Symptomatic bradycardia, AV block, reversible airway obstruction, asthma, stage IV POAD
Discharge MRA prescription in patients with EF <35%	Severe CKD or AKI; hyperkalaemia
Discharge scheduled cardiological evaluation within 4 weeks	
CHF – HFrEF	
OAT prescription in AF patients	History of major bleeding
EF evaluation	
Creatinine evaluation	
ARNI prescription	Angioedema; severe CKD or AKI; symptomatic hypotension
ACE-I/ARB/ARNI prescription	Angioedema; severe CKD or AKI; symptomatic hypotension
BB prescription	Symptomatic bradycardia, AV block, reversible airway obstruction, asthma, stage IV POAD
MRA prescription in patients with EF <35%	Severe CKD or AKI; hyperkalaemia
BB + ACE-I/ARB/ARNI + MRA prescription	See above listed drug specific contraindication
Ivabradine in SR patients with HR ≥70 bpm and EF ≤35%	
ICD primary NYHA class II–IV	Life expectancy <1 year
CRT-P/D: LBBB, NYHA II–IV	Life expectancy <1 year
CHF – HFmrEF and HFpEF	
OAT prescription in AF patients	History of major bleeding
EF evaluation	
Creatinine evaluation	

ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AKI, acute kidney injury; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; BB, beta-blocker; CHF, chronic heart failure; CKD, chronic kidney disease; CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; EF, ejection fraction; NP, natriuretic peptide; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ICD, implantable cardioverter defibrillator; LBBB, left bundle branch block; MRA, mineralocorticoid receptor antagonist; OAT, oral anticoagulant; POAD, peripheral occlusive artery disease; SR, sinus rhythm.
Severe CKD: estimated glomerular filtration rate <30 ml/min (CKD-Epidemiology Collaboration formula). AKI defined by the presence of one of the following: increase in serum creatinine by ≥0.3 mg/dl (≥26.5 μmol/L) within 48 h; or increase in serum creatinine to ≥1.5 times from baseline, which has occurred within the prior 7 days; or urine volume <0.5 ml/kg/h for 6 h. Hyperkalaemia: >5.5 mEq/L.

reported as percentages, and compared between phases of enrolment by Chi-square test; continuous variables were reported as means and standard deviations (SD), and compared by *t*-test or analysis of variance (ANOVA), if normally distributed, or by Mann–Withney U test or Kruskal–Wallis U test if not normally distributed. Furthermore, because some clinical characteristics of patients enrolled in the two phases resulted statistically different, when the indicators of adherence were significantly different between the two phases at univariate analysis, adjusted multivariable analyses (logistic regression) were performed, considering in the model the enrolment phase and the different characteristics as covariates. A *p*-value <0.05 was considered statistically significant. All tests were two-sided. Analyses were performed with SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

Regulatory considerations

The protocol was submitted to local ethics committees according to current national regulations and the study started at each site only upon the receipt of approval by the ethics committee and local authorities.

Each patient signed informed consent to the study. Personal data were encrypted to be transferred anonymously to the central server and patients were identified in the electronic case report form by numerical codes. The main database was secured according to current standards to ensure both ethical and integrity requirements of the data. In order to maintain strict security, each investigator/study personnel received a unique login and password to enter patient's information.

Results

Of the 7276 patients enrolled by the sites participating in both Phase 1 and 3, 58 were excluded due to missing data regarding vital status, qualifying EF, or discharge treatment. Therefore, the study population was composed of 7218 patients. As shown in online supplementary *Figure S1*, during the two enrolment phases, 3920 and 3298 patients were included, respectively, 84% with CHF and 16% with AHF in Phase 1, and 74% with CHF and 26% with AHF during Phase 3.

Acute heart failure

Clinical characteristics of AHF patients in the two enrolment phases are shown in *Table 2*. Mean age was 73 ± 12 years. Female gender accounted for about one third of cases. More than half of patients had *de novo* HF. The majority of patients (57.9%) presented with HFrEF, followed by HFpEF (23.9%) and HFmrEF (18.2%). Nearly 40% had a history of atrial fibrillation (AF) and at least moderate chronic kidney disease (CKD) and one fifth had a history of COPD and peripheral arterial occlusive disease. Clinical characteristics of patients enrolled in the two phases were similar, with some differences in type of presentation (*de novo* HF vs. worsening CHF), implanted devices, history of CKD and clinical parameters (systolic blood pressure and heart rate).

Performance measures in acute heart failure patients

Performance measures evaluated in patients hospitalized for AHF are shown in *Figure 2A*. In-hospital echocardiographic evaluation increased significantly from 98.7% to 100% and variation was maintained after adjustment for those variables which were significantly different in the two enrolment phases (online supplementary *Table S1*). Evaluation of creatinine was performed in 97.8% of patients in both phases, whereas natriuretic peptide assessment on admission increased from 59.5% to 64.1%, though without reaching statistical significance ($p = 0.07$). Prescription of oral anticoagulants to patients with AF was above 83% and did not improve in Phase 3. Looking at discharge pharmacological treatments in patients with HFrEF, we observed a good prescription rate of guideline-directed medical therapies (GDMT): a beta-blocker (BB) was prescribed in 87% of patients at discharge with a modest increase in Phase 3; almost three quarters of patients were discharged on an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACE-I/ARB) or an angiotensin receptor–neprilysin inhibitor (ARNI), and this percentage did not rise in Phase 3. According to guideline recommendations, a mineralocorticoid receptor antagonist (MRA) prescription was evaluated in patients with an EF <35% showing a high prescription rate (77%) in Phase 1 that did not change in Phase 3. Finally, the discharge schedule of a cardiology ambulatory evaluation within 4 weeks was overall poor (<50%) and did not improve.

Chronic heart failure

Clinical characteristics of CHF patients according to EF value in the two enrolment phases are shown in *Table 3*. Considering the overall population of 5724 CHF patients enrolled in the two phases, 53.2% had HFrEF, 26.2% HFmrEF and 20.6% HFpEF. Mean age was 70 ± 12, 70 ± 13 and 74 ± 13 years, respectively ($p < 0.0001$). Clinical characteristics of patients enrolled in the two phases were overall similar, with some differences in implanted devices, comorbidities (e.g. COPD and CKD) and systolic blood pressure in the HFrEF subgroup; systolic and diastolic blood pressure and heart rate in HFmrEF patients; mean age and COPD prevalence among HFpEF patients.

Performance measures in chronic heart failure patients

Performance measures evaluated in ambulatory CHF patients with HFmrEF and HFpEF as well as their variation between the two enrolment phases are shown in *Figure 2B*.

In HFmrEF patients, both creatinine and echocardiographic evaluations increased although not significantly between Phase 1 and Phase 3. Prescription of oral anticoagulants to patients with AF was overall high (>90%) and did not significantly change over time.

In HFpEF patients, evaluation of creatinine increased although not significantly from 66.1% to 68.1%, whereas an echocardiographic evaluation increased significantly from 72.3% to 79.0% (unadjusted $p = 0.008$; adjusted $p = 0.01$; online supplementary *Table S1*).

Performance measures evaluated in ambulatory CHF patients with HFrEF as well as their variation between the two enrolment

Table 2 Baseline clinical characteristics of patients with acute heart failure

	Phase 1 (n = 625)	Phase 3 (n = 869)	p-value
Age, years, mean ± SD	72 ± 12	73 ± 12	0.10
Age >75 years, %	46.1	50.9	0.07
Female sex, %	33.1	37.3	0.10
De novo HF, %	52.3	58.3	**0.02**
Diabetes, %	37.6	34.3	0.19
Ischaemic aethiology	42.1	43.3	0.65
EF classification, %			0.33
HFrEF	9.8	56.5	
HFmrEF	8.1	18.3	
HFpEF	2.1	25.2	
Device, %			**<0.0001**
No	76.2	85.5	
CRT-P	1.6	0.5	
CRT-D	6.9	0.5	
ICD	15.3	8.8	
Clinical presentation			0.78
NYHA class III–IV, %	75.8	74.2	
Acute pulmonary oedema, %	21.4	22.9	
Cardiogenic shock, %	2.8	2.9	
History of atrial fibrillation, %	41.6	37.4	0.10
COPD, %	22.9	19.3	0.10
CKD, %	41.3	35.7	**0.03**
POAD, %	16.0	19.1	0.12
SBP, mmHg, mean ± SD	129 ± 28	132 ± 28	**0.02**
DBP, mmHg, mean ± SD	77 ± 16	77 ± 16	0.26
HR, bpm, mean ± SD	91 ± 27	92 ± 24	**0.02**
HR >70 bpm, %	80.7	85.0	**0.03**
Hb <12 g/dl, % (available for 1462 patients)	36.8	36.3	0.85
eGFR <30 ml/min, % (available for 1461 patients)	13.1	12.6	0.78

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ICD, implantable cardioverter defibrillator; POAD, peripheral occlusive artery disease; SBP, systolic blood pressure; SD, standard deviation.

phases are shown in *Figure 2C*. The prescription rate of BBs remained stable and high (almost 95%) in the two phases as did the prescription rate (over 70%) of MRAs which, according to guideline recommendations, was evaluated in patients with an EF <35%. Non-significant performance increases were observed in several indicators: creatinine and echocardiographic evaluation, prescription of oral anticoagulants to patients with AF (close to 90%).

Prescription of an ACE-I/ARB or an ARNI significantly increased from 85.4% to 88.1% (unadjusted $p = 0.03$) as did the prescription of ARNI which doubled from 14.7% to 29.8% (unadjusted $p < 0.0001$). However, only the ARNI prescription increase remained significant after adjustment for different clinical characteristics of patients enrolled in the two phases. Moreover, the prescription rate of the combination of GDMT (BBs plus an ACE-I/ARB/ARNI plus an MRA) also increased from 56.1% to 57.7%, though without reaching statistical significance (online supplementary *Table S1*).

Reasons for non-adherence to recommendations of guideline-directed medical therapies in chronic heart failure patients

In order to identify the causes of true under-treatment, we analysed reasons for non-adherence to GDMT recommendations in ambulatory patients with CHF (*Figure 3*). Among the 410 patients (13.5%) who were not prescribed ACE-I/ARB/ARNI, contraindications or intolerance, which were responsible for more than 90% of the cases of non-prescription, are shown in *Figure 3A*. Main contraindications were severe renal dysfunction, symptomatic hypotension and hyperkalaemia, whereas the main reasons for intolerance were worsening renal function, symptomatic hypotension and cough. Furthermore, 176 (5.8%) HFrEF patients were not prescribed a BB and again in 90% of cases contraindications or intolerance explained this prescription behaviour: main contraindications were bradycardia, hypotension and asthma, while the

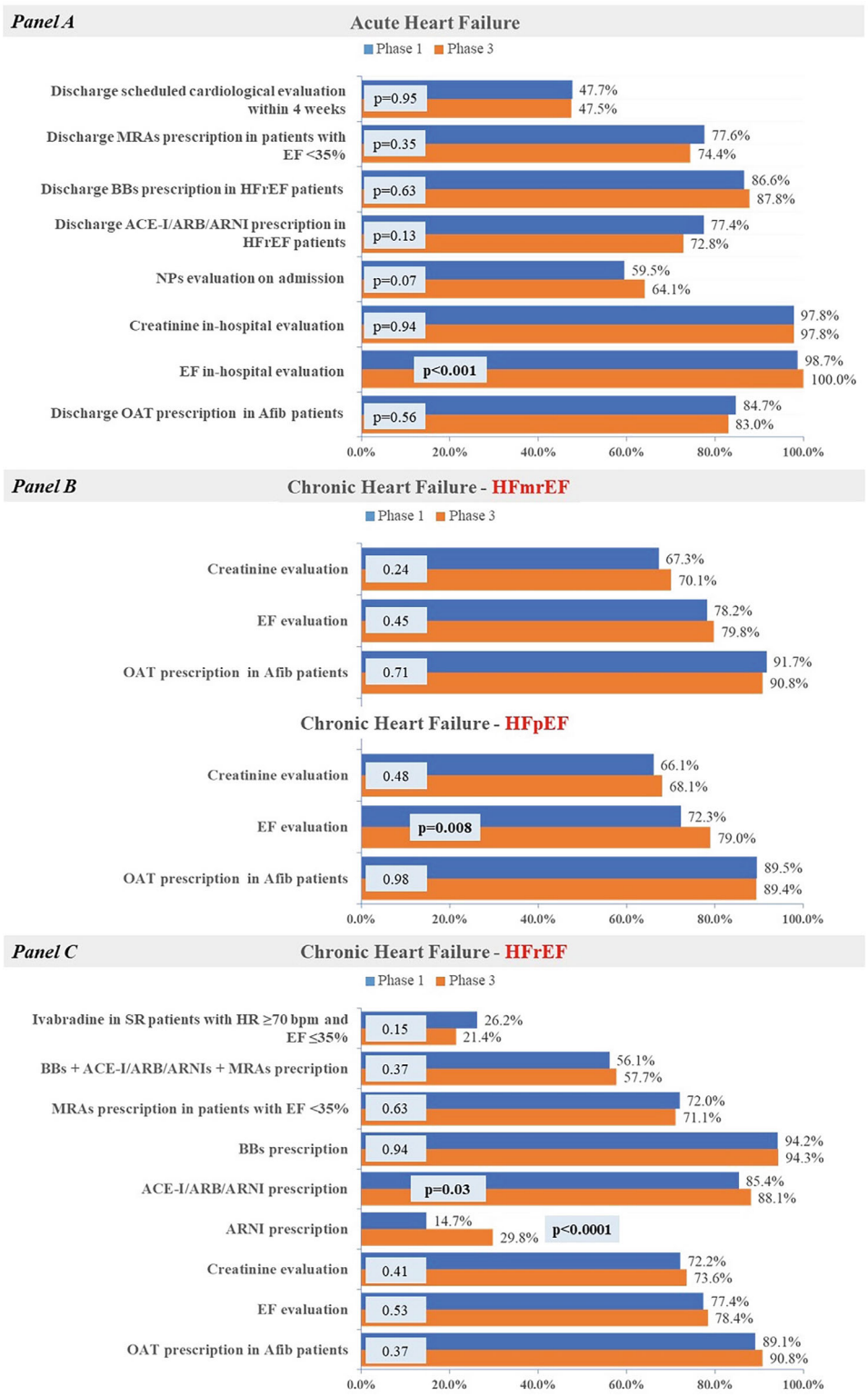

Figure 2 Performance measures according to different cohorts: acute heart failure (AHF) patients (*A*); chronic heart failure (CHF) patients with heart failure with mid-range (HFmrEF) and preserved ejection fraction (HFpEF) (*B*); chronic heart failure (CHF) patients with heart failure with reduced ejection fraction (HFrEF) (*C*). ACE-I, angiotensin-converting enzyme inhibitor; Afib, atrial fibrillation; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; BB, beta-blocker; EF, ejection fraction; HR, heart rate; MRA, mineralocorticoid receptor antagonist; OAT, oral anticoagulant; SR, sinus rhythm

Table 3 Baseline clinical characteristics of patients with chronic heart failure according to ejection fraction value

	HFrEF (*n* = 3046)			HFmrEF (*n* = 1498)			HFpEF (*n* = 1180)		
	Phase 1 (n = 1791)	Phase 3 (n = 1255)	*p*-value	Phase 1 (n = 825)	Phase 3 (n = 673)	*p*-value	Phase 1 (n = 679)	Phase 3 (n = 501)	*p*-value
Age, years, mean ± SD	70 ± 12	69 ± 12	0.90	70 ± 12	69 ± 13	0.23	75 ± 13	73 ± 14	**0.008**
Female sex, %	19.8	22.5	0.08	29.3	26.0	0.15	48.5	46.5	0.51
Device, %[a]			**0.002**			0.73			0.32
No	36.5	42.3		73.5	71.9		86.4	84.0	
CRT-P	1.4	1.3		1.7	1.2		1.2	0.6	
CRT-D	25.3	20.1		10.4	11.7		5.6	6.1	
ICD	36.8	36.3		14.4	15.2		6.8	9.3	
Atrial fibrillation, %	35.1	34.2	0.59	32.5	35.2	0.27	53.2	49.5	0.21
CKD, %	38.5	34.4	**0.022**	32.0	29.7	0.34	35.2	34.3	0.76
COPD, %	20.8	17.0	**0.008**	18.9	15.8	0.11	23.3	16.6	**0.005**
POAD, %	16.8	14.8	0.14	16.9	13.7	0.09	17.8	16.8	0.64
Diabetes	31.1	30.5	0.73	31.9	32.1	0.93	32.6	28.7	0.16
Ischaemic aethiology, %	51.4	48.8	0.16	39.4	40.0	0.82	23.1	22.8	0.88
NYHA class, %			0.33			0.16			0.95
I	16.0	15.2		26.8	27.5		23.4	24.3	
II	60.2	63.0		59.5	62.6		59.5	59.7	
III	23.1	21.4		13.5	9.7		16.4	15.2	
IV	0.7	0.4		0.2	0.3		0.7	0.8	
SBP, mmHg, mean ± SD	118 ± 17	120 ± 18	**0.02**	124 ± 18	126 ± 19	**0.07**	126 ± 19	126 ± 18	0.97
DBP, mmHg, mean ± SD	72 ± 10	72 ± 10	0.09	73 ± 10	75 ± 10	**0.002**	74 ± 10	74 ± 10	0.99
HR, bpm, mean ± SD	68 ± 12	69 ± 13	0.14	67 ± 12	69 ± 14	**0.003**	69 ± 14	70 ± 13	0.21
HR ≥70 bpm, %	40.6	41.7	0.56	36.7	42.9	**0.015**	45.4	46.5	0.71
Hb <12 g/dl, %[b]	24.2	21.2	0.10	28.3	23.6	0.10	29.7	31.7	0.55
eGFR <30 ml/min, %[c]	10.9	7.0	**0.002**	7.8	6.1	0.32	10.9	9.1	0.40

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ICD, implantable cardioverter defibrillator; POAD, peripheral occlusive artery disease; SBP, systolic blood pressure; SD, standard deviation.

[a]Available for 2937, 1407, and 1104 patients, respectively.

[b]Available for 2127, 988, and 772 patients, respectively.

[c]Available for 2216, 1027, and 790 patients, respectively.

main reasons for intolerance reported by clinicians were bronchospasm, worsening HF, bradycardia and symptomatic hypotension (*Figure 3B*). Finally, 573 patients (28.4%) did not receive an MRA (*Figure 3C*). In Phase 1 clinicians explained this as a result of contraindications or intolerance in 64% of cases, which rose approximately to 66% in Phase 3. Hyperkalaemia and severe renal insufficiency were the most frequent contraindications, wherease hyperkalaemia, worsening renal function and gynecomastia were the more frequently reported causes of intolerance.

Discussion

The main findings of the BLITZ-HF study can be summarized as follows: (i) adherence of participating sites to HF guideline recommendations was high for most indicators; (ii) a multifaceted intervention based on data collection of real-world HF patients with an ad-hoc web-based system together with face-to-face educational investigator meetings was associated with improved adherence to guideline recommendations; (iii) in the setting of AHF, guideline adherence improvement was overall limited and a 4-week discharge follow-up schedule was the indicator with the worst performance; (iv) among CHF patients, we observed a more consistent improvement in several pharmacological and non-pharmacological adherence performance measures; and (v) the choice of evaluating the implementation intervention in the setting of HF specialized cardiologists could have limited the improvement due to an already high performance in guideline adherence.

Implementation strategies

Implementation interventions aim at bridging the gap between evidence and practice. The development of national programmes to measure performance indicators and to provide feedback to individual participating centres has strongly been recommended by international societies. Several implementation interventions have been studied with a broad range of characteristics: type of study (randomized vs. cohort studies), level at which they are delivered

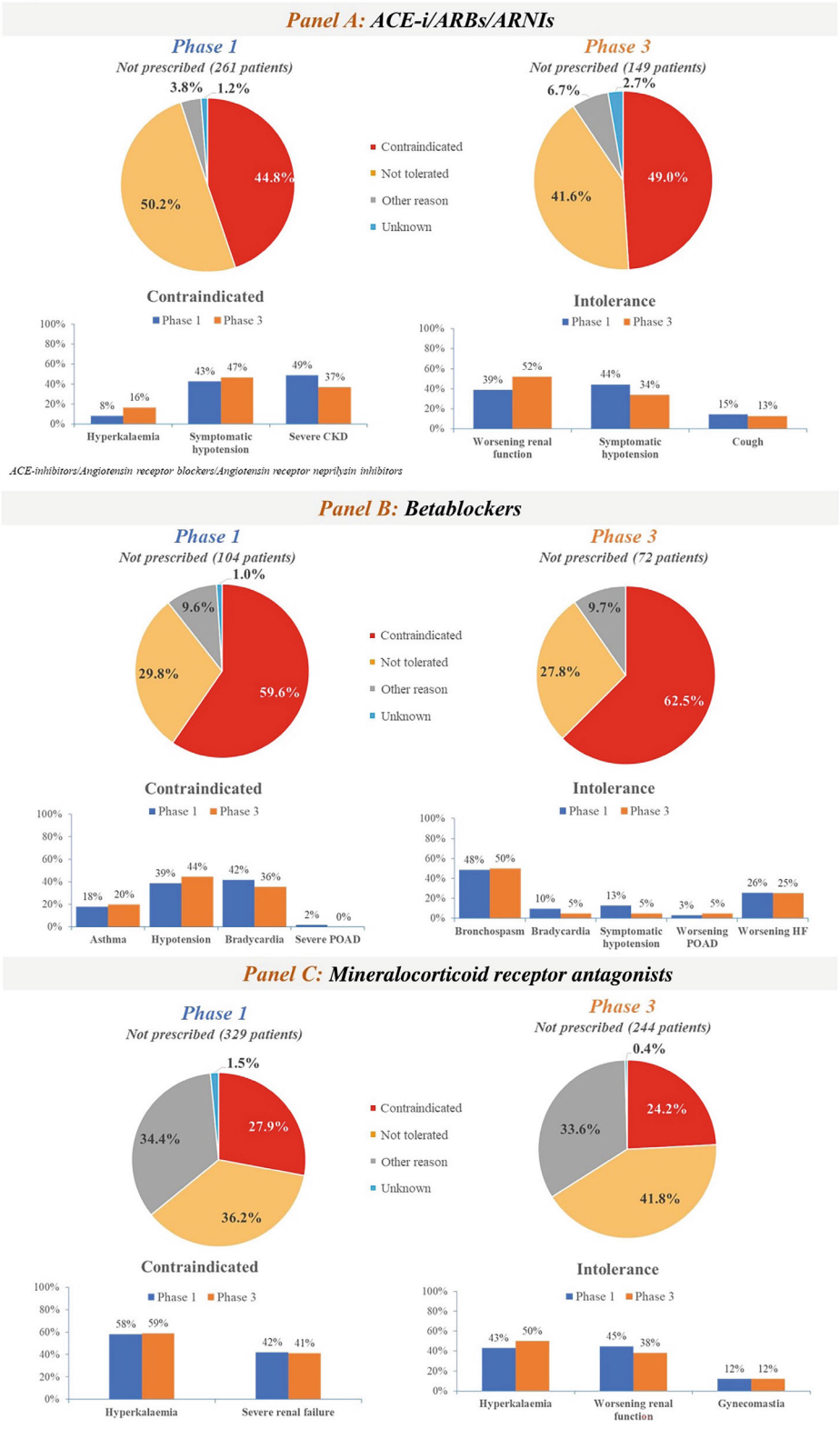

Figure 3 Reasons for guideline-directed medical therapy non-prescription among chronic heart failure patients with heart failure with reduced ejection fraction: angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/angiotensin receptor–neprilysin inhibitor (ACE-I/ARB/ARNI) (*A*); beta-blockers (BBs) (*B*); mineralocorticoid receptor antagonists (MRAs) (*C*). CKD, chronic kidney disease; POAD, peripheral occlusive arterial disease.

(provider, organizational, or health system), patient setting (AHF, CHF, or both), type of intervention (single vs. multifaceted), outcome (treatment prescription and/or target dose achievement, device implantation, patient's education, laboratory and instrumental performance measures).[6–8] On the basis of previous experience with short-term nationwide BLITZ surveys,[9,10] ANMCO has launched the BLITZ HF study which was designed as a provider level implementation intervention study aimed at improving several performance indicators in acute and chronic HF patients. Therefore, BLITZ-HF represents a unique, comprehensive and innovative implementation intervention that comprises different models previously proposed.

Quantitative improvements after Phase 2, characterized by reinforcement of guideline recommendation and benchmarking interventions based on the results obtained in the first enrolment period, were obtained in almost 50% of performance measures. It should be emphasized that participating sites were selected on the basis of their expertise in the management of HF and, therefore, this improvement was obtained in a context of generally high performing sites.

Acute heart failure patients

Among patients with AHF, the increase in performance was overall limited, with a significant rise in in-hospital echocardiographic evaluation together with a trend of improvement in BB prescription and natriuretic peptide assessment. Non-pharmacological indicators were represented by creatinine and echocardiographic evaluations (analysed in both acute and chronic HF patients) as well as the schedule of a cardiology visit within 4 weeks after hospital discharge (for AHF patients). If the first indicator improved in almost all settings and types of HF, a disappointing result was obtained in the follow-up schedule which was the poorest of all performance measures (<50%). Guidelines recommend clinical re-evaluation of AHF patients early after discharge in order to prevent inappropriate early rehospitalizations and improve prognosis.[5] The prognostic implications of a HF hospitalization on the natural history of HF patients[11] and the risks correlated to early readmission during the so-called transition phase[12–14] are well known. Early post-discharge follow-up programmes can effectively reduce this risk.[15] Hence, after having highlighted these topics during the Phase 2 educational interventions, we would have expected improvement in Phase 3 on this performance measure, particularly because of the high percentage of new-onset HF patients that should clearly need to continue post-discharge medical treatment optimization and be educated on disease self-management. Nevertheless, the prognostic impact in terms of early rehospitalization could be limited by the longer length of stay as demonstrated by the data from our previous registry.[16] Furthermore, organizational issues could be improved by an early check with telemedicine or telephone contacts, in the context of an integrated follow-up strategy.

Analysing pharmacological treatment among HFrEF patients, we observed a better performance in GDMT prescriptions rates in the CHF cohort. Among AHF patients, a trend towards a rise in discharge prescription of BBs was observed. Interestingly, the prescription rate of MRAs in AHF patients with an EF ≤35% was higher among AHF patients compared with their CHF counterparts. The use of MRAs in the acute setting as well as potassium-sparing medications (and not only disease modifiers) in a context of decongestion could explain this finding, although this was not confirmed in other registries such as the ESC HF Long-Term Registry.[17] Moreover, the above described disappointing performance in both phases in the schedule of a follow-up visit within 4 weeks after hospital discharge confirms that changing organization strategies is often more difficult than modifying medical treatment habits, nevertheless major efforts should be made to address this issue which currently represents one of the main unmet needs in the management of HF.

Chronic heart failure patients

Among CHF patients with HFpEF, a significant increase in echocardiographic evaluations was observed. Analysing the performance measures in CHF patients with HFrEF, it should be underlined that improvements were evaluated in a context of a high adherence to guideline recommendations. Prescription rates of GDMTs in HFrEF patients were overall high at baseline and higher compared to those observed in other similar contemporary clinical registries. In the CHAMP-HF study among eligible patients with HFrEF, baseline treatments rates with ACE-I/ARB/ARNI, BB, and MRA were 73.4%, 67.0%, and 33.4%, respectively, and therefore significantly lower than ours.[18] ARNI prescription doubled and a significant increase in the prescription of an ACE-I/ARB or an ARNI, which in Phase 3 was close to 90%, was observed. Nevertheless, on multivariable analysis, this difference between the two phases was no longer significant. This was probably influenced by a more preserved kidney function observed in patients included in the second enrolment phase. Furthermore, there were non-significant rises in echocardiographic and creatinine evaluations, and in the use of oral anticoagulants among patients with AF. Finally, the use of an ACE-I/ARB or an ARNI in combination with other strongly recommended treatments, MRAs and BBs, increased in Phase 3 reaching 58%. Considering that this percentage was obtained in HF clinics, it might seem unsatisfactory, nevertheless it might be considered a good performance if we compare it with other HF registries such as CHAMP-HF where this percentage was 21%.[19] Among reasons for lack of implementation of renin–angiotensin–aldosterone system inhibitors (contraindications or intolerance), we found known factors such as hypotension, worsening renal function and hyperkalaemia. Interestingly, the latter could be significantly reduced with the use of the new potassium binders. The efficacy and safety of these drugs in HF patients were recently evaluated in two randomized clinical trials: the DIAMOND trial[20,21] and the PRIORITIZE HF trial[22] both significantly affected by the COVID-19 pandemic with the first recently completed, although with a change in the primary outcome (from a composite of cardiovascular death and cardiovascular hospitalization to mean change in serum potassium from baseline), and the second prematurely interrupted. Furthermore, the prescription of ARNI doubled from Phase 1 to Phase 3 as a consequence of the educational intervention, therefore suggesting that this approach may be useful for the implementation of new treatments in clinical practice. In HFrEF patients with a heart rate

>70 bpm, in the absence of AF, and EF ≤35% the prescription of ivabradine decreased from Phase 1 to Phase 3, although not significantly.

The prescription of oral anticoagulants in patients with AF increased in Phase 3 only in ambulatory HFrEF patients but remained high in the other HF subtypes of ambulatory patients.

The lack of improvement in some performance indicators may have different explanations. In general, the selection of sites with a HF clinic and, therefore, with experience in the management of HF patients could have selected 'high performance sites' with a good guideline adherence already present in the first enrolment phase. Furthermore, when we analysed the performance regarding adherence to GDMTs, we should remember that this was an 'all-comers' registry which included patients of different age, variable comorbidity burden and different phases and severity of the disease ranging from stable NYHA class I in an early stage of the disease to advanced HF patients in whom also the possibility of implementing treatments would also vary significantly. Finally, as above reported, some differences in selected clinical characteristics were observed in the two enrolment phases which might have influenced the results. For example, the higher rate of *de novo* HF patients in the second enrolment phase could have limited treatment implementation at discharge.

Study limitations

Some limitations of our study should be acknowledged. Consecutive enrolment was recommended in the protocol and strongly encouraged during the two enrolment phases, nevertheless no ad-hoc validation was performed to verify this issue and enrolment rate might have been slightly lower than expected in some sites, which may have led to a limited selection bias. Moreover, the performance evaluation was done on two subsequent phases, therefore on different patient cohorts, with no longitudinal evaluation of performance in the same cohort which would have solved the 'still under implementation' bias. Furthermore, the exclusion of patients already enrolled in the previous phase or in a different setting may have altered the epidemiological characteristics of our study population and this should be considered when comparing our data to other national and international registries. As reported above, the setting of HF-oriented specialized cardiology sites could have limited the power of the implementation intervention. Also, due to the non-randomized nature of the intervention, even if the interval between the two enrolment phases was quite limited (3 months), part of the adherence improvement to guideline recommendations could be explained by natural trends in better use of drugs over time. Since informed consent is necessary to be enrolled in almost all studies (both observational and randomized), only patients having signed an informed consent were included in our study as in all the other ones. In any case, this fact can have determined a selection bias. However, it is worth noting that since in this study no diagnostic and/or therapeutic procedures were specifically required by protocol and all procedures/treatments were left to the decision of the attending physician according to clinical practice, the refusal rate to enter this observational study was very limited, minimizing the problem of selection bias. Finally, since the completion of the study and the present publication, new ESC guidelines have been released.[23] Nevertheless most indicators have not changed significantly.

Conclusions

In conclusion, our data show that a structured educational intervention aimed at reinforcing adherence to guideline recommendations associated with benchmarking reports on the performance obtained in the first enrolment phase, may be able to improve clinicians' adherence to HF guidelines on several indicators.

This approach might be considered as a model for further and regular evaluations to improve sites' adherence to current guidelines[23], possibly extending this experience from a specialized cardiology setting to other healthcare professionals who routinely manage patients with HF.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Conflict of interest: none declared.

Appendix

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References

1. Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola VP, et al.; EuroHeart Survey Investigators; Heart Failure Association, European Society of Cardiology. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. *Eur Heart J*. 2006;**27**: 2725–36.
2. Tavazzi L, Senni M, Metra M, Gorini M, Cacciatore G, Chinaglia A, et al.; IN-HF (Italian Network on Heart Failure) Outcome Investigators. Di Lenarda A, Mortara A, Oliva F, Maggioni AP; Multicenter prospective observational study on acute and chronic heart failure: one-year follow-up results of IN-HF (Italian Network on Heart Failure) outcome registry. *Circ Heart Fail*. 2013;**6**:473–81.
3. Maggioni AP, Anker SD, Dahlström U, Filippatos G, Ponikowski P, Zannad F, et al.; Heart Failure Association of the ESC. Are hospitalized or ambulatory patients with heart failure treated in accordance with European Society of Cardiology guidelines? Evidence from 12,440 patients of the ESC Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2013;**15**:1173–84.
4. Allen LA, Fonarow GC, Liang L, Schulte PJ, Masoudi FA, Rumsfeld JS, et al.; American Heart Association's Get With The Guidelines Heart Failure (GWTG-HF) Investigators. Medication initiation burden required to comply with heart failure guideline recommendations and hospital quality measures. *Circulation*. 2015;**132**:1347–53.
5. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2016;**18**:891–975.
6. Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. *Am Heart J*. 2011;**161**:1024–30.
7. Fonarow GC, Petereson ED. Heart failure performance measures and outcome: real or illusory gains. *JAMA*. 2009;**302**:792–4.
8. Shanbhag D, Graham ID, Harlos K, Haynes RB, Gabizon I, Connolly SJ, et al. Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review. *BMJ Open*. 2018;**8**:e017765.
9. Olivari Z, Steffenino G, Savonitto S, Chiarella F, Chinaglia A, Lucci D, et al. The management of acute myocardial infarction in the cardiological intensive care units in Italy: the 'BLITZ 4 Qualità' campaign for performance measurement and quality improvement. *Eur Heart J Acute Cardiovasc Care*. 2012;**1**:143–52.
10. Gulizia MM, Cemin R, Colivicchi F, De Luca L, Di Lenarda A, Boriani G, et al.; BLITZ-AF Investigators. Management of atrial fibrillation in the emergency room and in the cardiology ward: the BLITZ AF study. *Europace*. 2019;**21**: 230–8.
11. Bello NA, Claggett B, Desai AS, McMurray JJ, Granger CB, Yusuf S, et al. Influence of previous heart failure hospitalization on cardiovascular events in patients with reduced and preserved ejection fraction. *Circ Heart Fail*. 2014;**7**:590–5.
12. Au AG, McAlister FA, Bakal JA, Ezekowitz J, Kaul P, van Walraven C. Predicting the risk of unplanned readmission or death within 30 days of discharge after a heart failure hospitalization. *Am Heart J*. 2012;**164**:365–72.
13. Desai AS, Stevenson LW. Rehospitalization for heart failure: predict or prevent? *Circulation*. 2012;**126**:501–6.
14. Dharmarajan K, Hsieh AF, Lin Z, Bueno H, Ross JS, Horwitz LI, et al. Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. *JAMA*. 2013;**309**:355–63.
15. Van Spall HGC, Rahman T, Mytton O, Ramasundarahettige C, Ibrahim Q, Kabali C, et al. Comparative effectiveness of transitional care services in patients discharged from the hospital with heart failure: a systematic review and network meta-analysis. *Eur J Heart Fail*. 2017;**19**:1427–43.
16. Di Tano G, De Maria R, Gonzini L, Aspromonte N, Di Lenarda A, Feola M, et al.; IN-HF Outcome Investigators. The 30-day metric in acute heart failure revisited: data from IN-HF Outcome, an Italian nationwide cardiology registry. *Eur J Heart Fail*. 2015;**17**:1032–41.
17. Chioncel O, Mebazaa A, Maggioni AP, Harjola VP, Rosano G, Laroche C, et al.; ESC-EORP-HFA Heart Failure Long-Term Registry Investigators. Acute heart failure congestion and perfusion status – impact of the clinical classification on in-hospital and long-term outcomes; insights from the ESC-EORP-HFA Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2019;**21**: 1338–52.
18. Greene SJ, Butler J, Albert NM, DeVore AD, Sharma PP, Duffy CI, et al. Medical therapy for heart failure with reduced ejection fraction: the CHAMP-HF registry. *J Am Coll Cardiol*. 2018;**72**:351–66.
19. Greene SJ, Fonarow GC, DeVore AD, Sharma PP, Vaduganathan M, Albert NM, et al. Titration of medical therapy for heart failure with reduced ejection fraction. *J Am Coll Cardiol*. 2019;**73**:2365–83.
20. ClinicalTrials.gov. Patiromer for the Management of Hyperkalemia in Subjects receiving RAASi Medications for the Treatment of Heart Failure (DIAMOND). ClinicalTrials.gov Identifier: NCT03888066. https://clinicaltrials.gov/ct2/show/NCT03888066 (7 July 2022).
21. Butler J, Anker SD, Siddiqi TJ, Coats AJS, Dorigotti F, Filippatos G, et al. Patiromer for the management of hyperkalaemia in patients receiving renin-angiotensin-aldosterone system inhibitors for heart failure: design and rationale of the DIAMOND trial. *Eur J Heart Fail*. 2022;**24**:230–8.
22. ClinicalTrials.gov. Potassium Reduction Initiative to Optimize RAAS Inhibition Therapy With Sodium Zirconium Cyclosilicate in Heart Failure (PRIORITIZE HF). ClinicalTrials.gov Identifier: NCT03532009. https://clinicaltrials.gov/ct2/show/NCT03532009 (7 July 2022).
23. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2022;**24**:4–131.