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Appropriateness rating for the application of optimal medical therapy and multidisciplinary care among heart failure patients

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Abstract

Aims Clinical guidelines for improving the patients' quality of care vary in clinical practice, particularly in super-aging societies, like in Japan. We aimed to develop a set of appropriate-use criteria (AUC) for contemporary heart failure (HF) management to assist physicians in decision making.

Methods and results With the use of the RAND methodology, a multidisciplinary writing group developed patient-based clinical scenarios in 10 selected key topics, stratified mainly by HF stage, age, and renal function. Nine nationally recognized expert panellists independently rated the clinical scenario appropriateness twice on a scale of 1–9, as 'appropriate' (7–9), 'may be appropriate' (4–6), or 'rarely appropriate' (1–3). Decisions were based on clinical evidence and professional opinions in the context of available resource use and costs. An interactive round-table discussion was held between the first and second ratings; the median score of the nine experts was then assigned to an appropriate-use category. Most clinical scenarios without strong evidence were evaluated as 'may be appropriate'. Frailty assessments in elderly patients (age \geq 75 years), regardless of the HF stage, and advanced care planning in patients with stage C/D HF, regardless of age, were considered 'appropriate'. For HF with reduced ejection fraction, beta-blocker administration in elderly patients (age \geq 75 years) with heart rate < 50 b.p.m. and mineral corticosteroid receptor antagonist use in elderly patients (age \geq 75 years) with an estimated glomerular filtration rate < 30 mL/min/1.73 m² were considered 'rarely appropriate'.

Conclusions The HF management AUC provide a practical guide for physicians regarding scenarios commonly encountered in daily practice.

Keywords Appropriate-use criteria; Clinical scenarios; Heart failure; RAND

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Introduction

Heart failure (HF) is a rapidly growing, epidemic problem worldwide and is associated with high morbidity, mortality, and cost. ^{1,2} Heart failure societies provide clinical practice guidelines with recommendations applicable to patients with HF, to improve patients' quality of care. ^{1,3,4} However, care remains variable in many situations encountered in everyday practice, owing to a paucity of evidence from

large randomized clinical trials (RCTs) regarding factors such as the appropriate timing of advanced care planning (ACP) and a wide range of clinical patterns that are excluded from RCTs (e.g. advanced age or chronic kidney disease). This raises questions regarding the appropriate timing for as well as the overuse or underuse of HF management.

care remains variable in many situations encountered in To identify critical practical barriers and gaps in care and everyday practice, owing to a paucity of evidence from knowledge, several scientific statements have been

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developed to summarize the current findings in areas with incomplete evidence. ^{5,6} Unfortunately, these efforts have demonstrated that a lack of evidence in this field is pervasive, with inconclusive evidence regarding important outcomes, such as the quality of life, physical function, and maintenance of independence, in patients with advanced age and concomitant disease, making it difficult to identify appropriate interventions. Accordingly, there is a critical need for more practical guidance in areas with incomplete evidence to transform clinical guideline recommendations into clinically actionable information.

Appropriate-use criteria (AUC) have been developed in various fields (e.g. the fields of coronary revascularization and imaging) to complement clinical practice guidelines.^{7,8} The AUC scientifically summarize the expert consensus, serving as practical guidance for assessing and better understanding variability in opinion.^{9,10} AUC have been applied in real-world clinical practice, along with various registries, and they demonstrated the strong possibility of the overuse of percutaneous coronary intervention in real-world practice^{11,12}; this has contributed to a decline in revascularization for inappropriate indications.¹³

However, to date, there are no AUC in HF management. Physicians and caregivers often have to make decisions without adequate evidence or a consensus expert opinion in cases with advanced age or chronic kidney disease, suggesting that the need for AUC is the greatest in such vulnerable populations. Therefore, the multidisciplinary working group (WG) (i) developed 10 key topics of HF management on the basis of detailed literature review and interactive discussion in the WG; (ii) stratified the key topics into 80 scenarios mainly by HF stage, age, and renal function; and (iii) evaluated the

appropriateness of each scenario by scientifically aggregating the opinion of an expert panel using RAND methodology, to provide a framework for the assessment of practice patterns that will facilitate physician decision making.

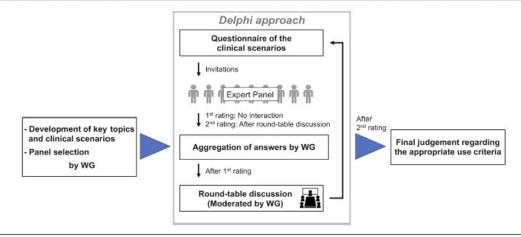
Methods

Briefly, the RAND methodology in the medical field is a qualitative method used for evaluating the appropriateness of various management strategies for which sufficient evidence is not available. ¹⁴ This method entails expert panellists who anonymously reply to repeated questionnaires and subsequently receive feedback from interactive discussion with the panellists (the Delphi approach). The purpose of this procedure is to reduce the variety of responses among the panellists and obtain the most reliable conclusions (*Figure 1*). ^{14,15} An AUC document has two main purposes: (i) as a clinical tool, it can assist physicians in better informing patients of their therapeutic options; and (ii) as an administrative and research tool, it can provide a means of comparing management patterns among physicians.

Development of key topics and clinical scenarios

First, the multidisciplinary WG performed a systematic literature review to identify important topics of HF management encountered in daily practice that required a few variables necessary for the decision-making process for physicians and caregivers (e.g. age, HF stage, and renal function). The WG estimated that >20 key topics and 100 separate clinical

FIGURE 1 The RAND methodology for the development of appropriate-use criteria for heart failure. This is a qualitative method used for evaluating the appropriateness of various management strategies for which sufficient evidence is not available. This method entails expert panellists who anonymously reply to repeated questionnaires and subsequently receive feedback from interactive discussion with the panellists (the Delphi approach). The purpose of this procedure is to reduce the variety of responses among the panellists and obtain the most reliable conclusions. WG, working group.



scenarios would be required; however, a level of granularity in this framework would be troublesome and unlikely to advance the objective of this study. Accordingly, once the key topics and clinical scenarios were drafted by the two core members (S. S. and S. K.) of the WG, the other WG members (board-certified cardiologists) provided feedback, which led to substantial improvements in the selection of key topics and clinical scenarios. Finally, the WG developed four key topics related to multidisciplinary care and six key topics related to pharmacological therapy and implantable cardioverter-defibrillator (ICD). The 10 key topics are as follows:

Multidisciplinary care in contemporary HF

- 1 Timing of ACP
- 2 Timing of dietary consultations with dietitians
- 3 Timing of frailty assessments
- 4 Timing of rehabilitation consultations with physical therapists Pharmacological approaches and ICDs in contemporary HF
- 5 Administration of an angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) in patients with HF with reduced ejection fraction (HFrEF)
- 6 Administration of a beta-blocker (BB) in patients with HFrEF in sinus rhythm
- 7 Administration of a mineral corticosteroid receptor antagonist (MRA) in patients with HFrEF who remain symptomatic despite treatment with ACEIs and BBs
- 8 Administration of an angiotensin receptor neprilysin inhibitor (ARNI) in patients with HFrEF
- 9 Administration of a sodium-glucose linked co-transporter 2 (SGLT-2) inhibitor in patients with HFrEF
- 10 Placement of an ICD in patients with HFrEF who have class I indications

Regarding multidisciplinary care in contemporary HF, ACP that takes account of preferences for place of death and resuscitation, assessment of nutritious status and dietary consultations with dietitians, monitoring frailty and seeking reversible causes of deterioration of frailty, and cardiac rehabilitation in clinically stable patients with HF to improve functional capacity are all strongly recommended in the clinical guidelines. 1,3,4 However, no clinical guidelines have described the optimal 'timing' of ACP, dietary consultations with dietitians, frailty assessment, and rehabilitation consultations with physical therapists; thus, the WG developed clinical scenarios stratified by the situations frequently encountered in everyday practice. As the HF stage and age would be the top priority when rating the appropriate timing of multidisciplinary care, the WG stratified the key topics of multidisciplinary care by the HF stage and age.

As for the pharmacological therapy for patients with HFrEF, ACEI/ARB, MRA, and ARNI showed efficacy in reducing cardiovascular events in RCTs and are generally

recommended in the clinical guidelines. 1,3,4,16-20 Recently, dapagliflozin showed an efficacy in terms of HF rehospitalization and death for patients with HFrEF.21 However, all of these RCTs excluded patients with impaired renal function glomerular [mostly estimated filtration (eGFR) < 30 mL/min/1.73 m²], raising questions for the appropriateness of administering these medications for patients with impaired renal function. Similarly, BBs showed efficacies in RCTs and were recommended in the clinical guidelines^{22,23}; however, all of these RCTs excluded patients with a lower heart rate (HR) (<60 b.p.m. in the Cardiac Insufficiency Bisoprolol Study II trial and <68 b.p.m. in the Carvedilol Prospective Randomized Cumulative Survival Study trial), raising questions for the appropriateness of administering a BB for patients with lower HR. As the renal function and age are the biggest concern when judging the appropriateness of administering an ACEI/ARB, MRA, ARNI, and SGLT-2 inhibitor as well as HR when judging the appropriateness of administering a BB, the WG stratified the key topics of pharmacological approaches by age, renal function, and HR.

Finally, an ICD is recommended in patients with symptomatic HF and EF \leq 35% despite \geq 3 months of guideline-based medical therapy, regardless of age. 1,3,4 However, the benefit of implementing ICD for eligible patients with a high risk of non-cardiac death is not clear to date. 24 Thus, the WG stratified the appropriateness of the ICD placement by age.

Panel selection

To prevent bias in the scoring process and ensure an appropriate balance in expertise, the expert panel was intentionally made up of experts from various fields. The nine panellists included five cardiologists working at community tertiary hospitals (in Tokyo, Hyogo, and Nagano), two general practitioners (from Tokyo and Saitama), one occupational therapist (from Hiroshima), and one nurse (from Osaka). All panellists were asked to state declarations of interest that might be perceived as potential conflicts of interest; these are listed in the Acknowledgements section.

First rating: no interaction

In the first round, the panellists were asked to rate each clinical scenario, independently, on a scale of 1–9, by using a Google Form-based answer sheet. The panellists were asked to recognize variability in various patient factors, local practice trends, and a lack of evidence regarding HF management in all possible clinical scenarios. The management was considered appropriate when the potential benefits, in terms of survival or health outcomes (symptoms,

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functional status, and/or quality of life), outweighed the potential negative consequences of the management strategy. 9,14 Scores of 7–9 indicated that the management was considered appropriate for the clinical scenario presented. Scores of 1–3 indicated that the management was considered as rarely appropriate for the clinical scenario, whereas scores in the mid-range (4–6) indicated that the management may be appropriate for the clinical scenario.

Second rating: after round-table discussion at Hiroshima

In the second round, which took place in Hiroshima on October 5, 2019, the panellists participated in an interactive round-table conference under the leadership of the WG (S. S. and S. K.). At the conference, the WG provided the best available evidence regarding each scenario to the expert panel. After confirming the general assumptions and points of confusion, the panellists again independently provided their final rating for each clinical scenario through a Google Form-based answer sheet.

Aggregation and final judgement of appropriateness

When generating the final results, each panellist's rating had equal weight, and the consensus was not coerced. The median numerical score was calculated for each clinical scenario and then allocated to an appropriate-use category, as defined subsequently.

Median Score 7-9: appropriate care (green)

These scores represent an appropriate option for the management of patients in this population. As the benefits generally outweigh the risks, this is an effective option for individual management; however, this may depend on the physical condition of the individual patient and patient-specific preferences.

Median Score 4-6: may be appropriate care (yellow)

These scores reflect options that may occasionally be appropriate for the management of patients in this population, given the variable evidence or agreement with respect to the benefit/risk ratio, potential advantage based on practice experience in the absence of evidence, and/or variability in the population. The effectiveness of the treatment in individual care must be determined by physicians and patients on the basis of additional clinical variables and patient preferences.

Median Score 1-3: rarely appropriate care (red)

These scores reflect options that are rarely appropriate for the management of patients in this population owing to the lack of a clear benefit/risk advantage.

The primary objective of the present report was to provide a tool for assessing the appropriateness of HF management in various clinical scenarios. The consensus among ratings was desirable, but achieving complete consensus among the diverse panellists would have been arbitrary and contrary to the aim of the process.

Agreement was left unquestioned in the final assessment of appropriateness; however, information regarding agreement/disagreement was used by the WG to guide the round-table interactive discussion, emphasizing the panellists' areas of differences. It was also used to assess whether the two rounds of ratings, with a substantial discussion between the ratings, led to some consensus among the panellists.

The degree of agreement between panellists, as described by RAND, was evaluated for each clinical scenario. Agreement among the panellists was defined as the condition in which the ratings of at most two panellists fell outside the range of the 3 points containing the median score; disagreement was defined as the condition in which the ratings of at least three panellists fell in both appropriate and inappropriate categories.

General assumptions

In the clinical scenarios, specific patient groups (e.g. those with dementia, malignancy, high-frailty, do-not-resuscitate status, or co-morbidities likely to increase harm by management) and personal social circumstances (e.g. lack of family support, geographically unable to access medical resources, or personal health insurance issues) were not considered. All patients included in the clinical scenarios were receiving standard care to modify known risk factors, as described in the clinical guidelines, in the setting of standard outpatient clinics. It was acknowledged that, despite the best efforts of physicians, not all patients achieve target goals for cardiac management; however, ongoing efforts and care plans to address risk factors were assumed as continuing. The panellists were required to assess the benefits and risks of management, both with understanding of the feasible resource use and costs, and in the context of an ideal situation in the near future; thus, appropriateness could be categorized as high even though the feasibility was low.

Although the panellists rated the clinical scenarios based on the published literature, many daily HF management practices still remain poorly represented in the literature. Therefore, the panellists had to assume that some of the clinical scenarios had low levels of evidence for guiding rating decisions.

Results

The final ratings for HF management options are listed in Figure 2 (multidisciplinary care) and Figure 3 (pharmacological approaches and ICDs), where green represents 'appropriate' (median score: 7–9), yellow represents 'may be appropriate' (median score: 4–6), and red represents 'rarely appropriate' (median score: 1–3) options. Anonymized individual scores are available in Data S1.

Generally, the clinical scenarios with class I recommendations in clinical guidelines received 'appropriate' recommendations. Overall, the panellists were in agreement for 87% (40/46) of 'appropriate' clinical scenarios (Data S1), suggesting that there were less variations among panellists with regard to these scenarios. Most of the clinical scenarios without strong evidence were evaluated as 'may be appropriate'. The panellists disagreed in 21% (6/29) of the 'may be appropriate' clinical scenarios (Data S1), suggesting a greater variation with regard to these scenarios and the need for further clinical research.

Figure 2 shows the ratings for multidisciplinary care in contemporary HF. In patients with stage C or D HF, the timing of ACP, dietary consultations with dietitians, frailty assessment, and rehabilitation consultations with physical therapists, regardless of age, were evaluated as 'appropriate'. Moreover, frailty assessments in elderly patients with HF (age \geq 75 years) and dietary consultations with dietitians in younger patients with HF (age < 75 years), regardless of HF stage were evaluated as 'appropriate'.

Figure 3 shows the ratings for pharmacological approaches and ICDs in contemporary HF. The clinical scenarios with class I recommendations in clinical guidelines received 'appropriate' recommendations. Most of the clinical scenarios without strong evidence were evaluated as 'may be appropriate'. Importantly, in the setting of HFrEF, the administration of BBs in elderly patients (age \geq 75 years) with a low HR (<50 b.p.m.), the administration of MRAs in elderly patients (age \geq 75 years) and those with low-renal function (eGFR < 30 mL/min/1.73 m²), and the administration of ARNIs in elderly patients (age \geq 85 years) and those with low-renal function (eGFR < 30 mL/min/1.73 m²) were considered to be 'rarely appropriate'.

Discussion

To our knowledge, this is the first report of AUC for HF management. Our main findings were as follows: most clinical scenarios without strong evidence were evaluated as 'may be appropriate'. Frailty assessments in elderly patients (age > 75 years), regardless of HF stage, and ACP in patients with stage C/D HF, regardless of age, were considered as 'appropriate'. For HFrEF, the administration of BBs in elderly patients (age > 75 years) with HR < 50 b.p.m. and the use of MRAs in elderly patients (age > 75 years) with a GFR < 30 mL/min/1.73 m² were considered 'rarely appropriate'. The present report represents the current understanding of HF management and attempts to provide a practical

FIGURE 2 Ratings for multidisciplinary care in contemporary heart failure. Green represents 'appropriate' (median score: 7–9), yellow represents 'may be appropriate' (median score: 4–6), and red represents 'rarely appropriate' (median score: 1–3) options.

	Years	Stage A	Stage B	Stage C	Stage D
Timing of advanced care planning	Age < 75	May be appropriate (5)	May be appropriate (5)	Appropriate (7)	Appropriate (9)
	Age ≥ 75	May be appropriate (5)	May be appropriate (6)	Appropriate (8)	Appropriate (9)
Timing of dietary consultations with dietitians	Age < 75	Appropriate (7)	Appropriate (7)	Appropriate (8)	Appropriate (8)
	Age ≥ 75	May be appropriate (6)	Appropriate (7)	Appropriate (8)	Appropriate (8)
Timing of frailty assessments	Age < 75	May be appropriate (5)	May be appropriate (6)	Appropriate (8)	Appropriate (9)
	Age ≥ 75	Appropriate (7)	Appropriate (7)	Appropriate (8)	Appropriate (9)
Timing of rehabilitation consultations with physical therapists	Age < 75	May be appropriate (4)	May be appropriate (6)	Appropriate (8)	Appropriate (8)
	Age ≥ 75	May be appropriate (4)	May be appropriate (6)	Appropriate (8)	Appropriate (8)

FIGURE 3 Ratings for pharmacological approaches and implantable cardioverter-defibrillators in contemporary heart failure. Green represents the 'appropriate' (median score: 7–9), yellow represents the 'may be appropriate' (median score: 4–6), and red represents the 'rarely appropriate' (median score: 1–3) options. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ICD, implantable cardioverter-defibrillators: MRA, mineral corticosteroid receptor antagonist: SGLT-2 inhibitor, sodium-glucose linked co-transporter 2 inhibitor.

	Years	eGFR > 60	30 ≤ eGFR ≤ 60	eGFR < 30
Administration of ACEI/ ARB in patients with HFrEF	Age < 75	Appropriate (9)	Appropriate (8)	May be appropriate (6)
	75 ≤ age < 85	Appropriate (9)	Appropriate (8)	May be appropriate (6)
	Age ≥ 85	Appropriate (7)	May be appropriate (6)	May be appropriate (5)
Administration of MRA in patients with HFrEF	Age < 75	Appropriate (8)	Appropriate (8)	May be appropriate (5)
	75 ≤ age < 85	Appropriate (8)	Appropriate (7)	Rarely appropriate (3)
	Age ≥ 85	Appropriate (7)	May be appropriate (6)	Rarely appropriate (3)
Administration of ARNI in patients with HFrEF	Age < 75	Appropriate (8)	Appropriate (7)	May be appropriate (6)
	75 ≤ age < 85	Appropriate (8)	Appropriate (7)	May be appropriat (5)
	Age ≥ 85	Appropriate (7)	May be appropriate (5)	Rarely appropriate (3)
Administration of SGLT-2 inhibitor in patients with HFrEF	Age < 75	Appropriate (8)	Appropriate (7)	May be appropriat (5)
	75 ≤ age < 85	Appropriate (8)	Appropriate (7)	May be appropriat (5)
	Age ≥ 85	May be appropriate (6)	May be appropriate (5)	May be appropriat (4)
		HR > 60	50 ≤ HR ≤ 60	HR < 50
Administration of beta-blocker in patients with HFrEF	Age < 75	Appropriate (9)	Appropriate (7)	May be appropriat
	75 ≤ age < 85	Appropriate (8)	Appropriate (7)	Rarely appropriate (3)
	Age ≥ 85	Appropriate (7)	May be appropriate (4)	Rarely appropriate (2)
Placement of ICD in patients with HFrEF who have class I indications	Age < 75	Appropriate (7)		
	75 ≤ age < 85	May be appropriate (6)		
	Age ≥ 85	May be appropriate (4)		

guide for HF management for physicians and patients. Furthermore, these AUC could provide physicians and institutions with performance measurement tools, through which the quality of care can be measured. This may help to standardize and advance the quality of care, thereby improving patient outcomes.^{25,26} It is anticipated that this report will accelerate the translation of scientific evidence into clinical practice.

ACP is not often performed, or is poorly performed, in patients with HF, and no clinical guidelines have described the optimal timing of ACP in patients with HF. ^{1,3,4} A Palliative Care Task Force expert position statement reported that ACP should be adopted according to the patient's readiness to engage in ACP and should not be postponed until end-stage HF. ACP should be considered at transition points during the course of HF, such as at hospital admission, when functional decline occurs despite optimal treatment, and when disease-oriented treatment options have been exhausted. ²⁷ The Supportive and Palliative Care Indicators Tool can also help to identify patients who may adopt ACP, based on the risk of deterioration and death. ²⁸ These statements suggest that further detailed clinical scenarios,

stratified by patient readiness, screening tools, or frailty, are needed in future revisions of this report. Nevertheless, the present report contributes to a growing body of literature on the appropriate timing of ACP.

As frailty is multifactorial and reportedly independently associated with mortality and readmission in elderly patients with HF, ^{29–31} periodical assessments of frailty and identification of reversible causes are strongly recommended for elderly patients with HF.³ However, a definition of the appropriate timing for the assessment of frailty is lacking. Based on the present report, frailty assessments are recommended for elderly patients aged > 75 years with HF of any stage, suggesting frailty as a key indicator for every elderly patient with HF.

BBs reduce morbidity and mortality in patients with HFrEF in sinus rhythm and are recommended in clinical guidelines. 1,3,4 However, because previous RCTs excluded patients with advanced age or low HR, evidence for the use of BBs in these vulnerable populations is limited. 22,23 An observational study has shown that BBs are associated with reduced mortality in patients with HFrEF in sinus rhythm, regardless of HR, but few patients with HR < 65 b.p.m. were

enrolled in that study; hence, it is difficult to evaluate the appropriateness of this finding for many clinical scenarios. ³² Notably, in the present report, the administration of BBs in elderly patients with low HR (<50 b.p.m.) was evaluated as 'rarely appropriate', hopefully supporting physicians' decision making. Moreover, BBs have shown no benefit in terms of hospital admissions and mortality in patients with HFrEF who are in atrial fibrillation and should be considered for HR control in such patients, especially in those with a high HR. ^{3,33,34} Adding clinical scenarios for patients with HFrEF and atrial fibrillation will be our next challenge.

MRAs are recommended for patients with HFrEF who remain symptomatic despite treatment with ACEI and BBs to reduce mortality and HF hospitalization. 18,19 Caution should be exercised when using MRAs in patients with impaired renal function (particularly those with eGFR < 30 mL/min/ 1.73 m²) and advanced age, because of the limited available data. Notably, in the present study, the administration of MRAs in patients with advanced age and low-renal function (eGFR < 30 mL/min/1.73 m²) was considered to be 'rarely appropriate'. Furthermore, the administration of MRAs in younger patients (<85 years) with moderately impaired renal function (30 < eGFR < 60 mL/min/1.73 m²) was evaluated as 'appropriate'. Several reports have recommended the use of MRAs under careful monitoring during the initiation of MRA treatment, and particularly during periods of acute illness, to maximize the benefits and mitigate the risks of MRA therapy. 35,36 Given that only 30-50% of eligible patients receive MRA therapy worldwide, 37,38 continuous efforts are required to improve the administration of MRAs in patients with HFrEF.

The risk of sudden death has declined substantially over the past two decades, owing to the widespread use of guideline-based medical therapy, suggesting the need for new criteria to identify high-risk subgroups of patients who would benefit from ICD implantation in a cost-effective manner. Shadman et al. recently developed a risk assessment model, the Seattle Proportional Risk Model, for improved identification of patients who would benefit most from primary prevention ICD therapy. Further clinical scenarios, including age, poor HF prognosis, and co-morbidities, are needed to assess patients who would gain the greatest long-term overall benefit from primary prevention ICD implantation.

Limitations

Our findings should be interpreted in the context of several limitations and considerations. First, while the AUC have been designed to address many clinical scenarios commonly encountered in daily practice, it would be impossible to include every conceivable patient presentation. For example, the presence of atrial fibrillation and chronic obstructive

pulmonary disease when judging the appropriateness of a BB, and the low blood pressure when judging the appropriateness of an ACEI/ARB or an ARNI would also be a big concern; therefore, we plan to use these co-morbidities as important scenarios in the next update. Second, panellists who had heterogeneous backgrounds might have affected a variety of opinions and the degree of consensus in our study. On the other hand, we would also like to state that the expert panel consisted of various backgrounds could evaluate the HF management with multiple viewpoints, which might prevent bias in rating the appropriateness from the point of patient-centred outcome. For example, nurses were more likely to evaluate that ACP should be implemented in the earlier HF clinical stages than physicians. 40 Accordingly, we believe that the expert panel in our study would be one of our advantages for evaluating the appropriateness from multiple viewpoints. Third, as some clinical scenarios will be reconsidered as new data and field experience become available, it will be necessary to assess and update the clinical scenarios and AUC periodically. Finally, there were disagreements in some clinical scenarios, although these variations in opinion did not affect the appropriateness of the evaluation. Consensus among the panellists was desirable, but further attempts to force consensus would have diluted the real differences of opinion among panellists, and therefore, it was not coerced. In fact, two rounds of ratings with substantial discussion did lead to some improvement in consensus among panellists. Further research using clinical registries is required to accumulate the best available evidence to support clinical decision making.

Conclusions

This report represents the current AUC for HF management, considering real-world situations. It is intended to provide a practical and clinically actionable guide to help physicians make more informed decisions in areas with limited evidence. Further investigations will be necessary to assess how these AUC are used and change HF management in clinical practice after their publication. We will periodically update the criteria as new data and experience become available.

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Conflict of interest

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Supporting information

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

Data S1 Anonymised individual scores of the rating for heart failure management.

References

- Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, Drazner MH, Filippatos GS, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld JA, Masoudi FA, McBride PE, Peterson PN, Stevenson LW, Westlake C. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol 2017; 70: 776–803.
- Sakata Y, Shimokawa H. Epidemiology of heart failure in Asia. Circ J 2013; 77: 2209–2217
- 2209–2217.

 3. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, Gonza'lez-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2016; 37: 2129–2200.
- 4. Tsutsui H, Isobe M, Ito H, Okumura K, Ono M, Kitakaze M, Kinugawa K, Kihara Y, Goto Y, Komuro I, Saiki Y, Saito Y, Sakata Y, Sato N, Sawa Y, Shiose A, Shimizu W. Shimokawa H. Seino Y. Node K. Higo T, Hirayama A, Makaya M, Masuyama T, Murohara T, Momomura SI, Yano M, Yamazaki K, Yamamoto K, Yoshikawa T, Yoshimura M, Akiyama M, Anzai T, Ishihara S, Inomata T, Imamura T, Iwasaki YK, Ohtani T, Onishi K, Kasai T, Kato M, Kawai M, Kinugasa Y, Kinugawa S, Kuratani T, Kobayashi S, Tanaka A, Toda K, Noda T, Nochioka K, Hatano M, Hidaka T, Fujino T, Makita S, Yamaguchi O, Ikeda U, Kimura T, Kohsaka S, Kosuge M, Yamagishi M, Yamashina A. JCS 2017/JHFS 2017 guideline on diagnosis and treatment of

- acute and chronic heart failure—digest version. Circ J 2019; 83: 2084–2184.
- Rich MW, Chyun DA, Skolnick AH, Alexander KP, Forman DE, Kitzman DW, Maurer MS, Mcclurken JB, Resnick BM, Shen WK, Tirschwell DL. Knowledge gaps in cardiovascular care of the older adult population. Circulation 2016; 133: 2103–2122.
- Hein AM, Scialla JJ, Edmonston D, Cooper LB, DeVore AD, Mentz RJ. Medical management of heart failure with reduced ejection fraction in patients with advanced renal disease. JACC Hear Fail 2019; 7: 371–382.
- Wolk MJ, Bailey SR, Doherty JU, Douglas PS, Hendel RC, Kramer CM, Min JK, Patel MR, Rosenbaum I, Shaw LJ, Stainback RF, Allen JM, American College of Cardiology Foundation Appropriate Use Criteria Task Force. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force. J Am Coll Cardiol 2014; 63: 380–406.
- 8. Brindis RG, Douglas PS, Hendel RC, Peterson ED, Wolk MJ, Allen JM, Patel MR, Raskin IE, Hendel RC, Bateman TM, Cerqueira MD, Gibbons RJ, Gillam LD, Gillespie JA, Hendel RC, Iskandrian AE, Jerome SD, Krumholz HM, Messer JV, Spertus JA, Stowers SA. ACCF/ASNC appropriateness criteria for single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI): a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working G. J Am

- Coll Cardiol. Elsevier Masson SAS 2005; 46: 1587–1605.
- Dehmer GJ, Grantham JA, Maddox TM, Ms C, Dean LS, Duffy PL, Rigolin VH. ACC/AATS/AHA/ASE/ASNC/ SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease. J Am Coll Cardiol 2017; 69: 2212–2241.
- Inohara T, Kohsaka S, Miyata H, Ueda I. Appropriateness of coronary interventions in Japan by the US and Japanese standards. Am Heart J 2014; 168: 854–861.
- Hannan EL, Cozzens K, Samadashvili Z, Walford G, Jacobs AK, Holmes DR, Stamato NJ, Sharma S, Venditti FJ, Fergus I, King SB. Appropriateness of coronary revascularization for patients without acute coronary syndromes. J Am Coll Cardiol 2012; 59: 1870–1876.
- Inohara T, Kohsaka S, Miyata H, Ueda I, Ishikawa S, Ohki T, Nishi Y, Hayashida K, Maekawa Y, Kawamura A, Higashi T, Fukuda K. Appropriateness ratings of percutaneous coronary intervention in Japan and its association with the trend of noninvasive testing. JACC Cardiovasc Interv 2014; 7: 1000–1009.
- 13. Kirtane AJ, Doshi D, Leon MB, Lasala JM, Ohman EM, O'Neill WW, Shroff A, Cohen MG, Palacios IF, Beohar N, Uriel N, Kapur NK, Karmpaliotis D, Lombardi W, Dangas GD, Parikh MA, Stone GW, Moses JW. Treatment of higher-risk patients with an indication for revascularization. Circulation 2016; 134: 422–431.
- Fitch K, Bernstein SJ, Aguilar M, Burnand B, Lacalle J, Lazaro P, Loo M, McDonnell J, Vader J, Kahan J. The RAND/UCLA Appropriateness Method User's Manual. RAND; 2001.

- Patel MR, Spertus JA, Brindis RG, Hendel RC, Douglas PS, Peterson ED, Wolk MJ, Allen JM, Raskin IE. ACCF proposed method for evaluating the appropriateness of cardiovascular imaging. J Am Coll Cardiol 2005; 46: 1606–1613.
- Group TCTS. Effects of enalapril on mortality in severe congestive heart failure. N Engl J Med 1987; 316: 1429–1435.
- Investigators TS. Effect of enarapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med 1991; 325: 293–302.
- Pitt B, Zannad F, Remme W, Cody RJ, Castaigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med 1999; 341: 709–717.
- Swedberg K, Shi H, Vincent J, Pocock SJ. Eplerenone in patients with systolic heart failure and mild symptoms. N Engl J Med 2011; 364: 11–21.
- McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K, Zile MR. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014; 371: 993–1004.
- 21. McMurray JJV, Solomon SD, Inzucchi SE, Kober L, Kosiborod MN, Martinez FA, Ponikowski P, Sabatine MS, Anand IS, Lohlavek JB, Bohm M, Chiang CE, Chopra VK, De Boer RA, Desai AS, Diez M, Drozdz J, Dukat A, Ge J, Howlett JG, Katova T, Kitakaze M, Ljungman CEA, Merkely B, Nicolau JC, O'Meara E, Petrie MC, Vinh PN, Schou M, Tereshchenko S, Verma S, Held C, DeMets DL, Docherty KF, Jhund PS, Sjöstrand M, Langkilde A-M. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019; 381: 1995–2008.
- Investigators C. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. Lancet 1999; 353: 0-13
- Packer M, Coats AJS, Fowker M, Katus HA, Krum H, Mohacsi P, Rouleau JL, Tendera M, Castaigne A, Roecker E, Schultz M, DeMets D. Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med 2001; 344: 1651–1658.
- 24. Shadman R, Poole JE, Dardas TF, Mozaffarian D, Cleland JGF, Swedberg K, Maggioni AP, Anand IS, Carson PE, Miller AB, Levy WC. A novel method to predict the proportional risk of sudden cardiac death in heart failure: derivation

- of the Seattle Proportional Risk Model. Heart Rhythm 2015; 12: 2069–2077.
- 25. Fonarow GC, Abraham WT, Albert NM, Stough WG, Greenberg BH, Connor CMO, Pieper K, Sun JL, Yancy C, Young JB. Association between performance measures and clinical outcomes for patients hospitalized with heart failure. JAMA 2007; 297: 61–70.
- 26. Inohara T, Kimura T, Ueda I, Ikemura N, Tanimoto K, Nishiyama N, Aizawa Y, Nishiyama T, Katsumata Y, Fukuda K, Takatsuki S, Kohsaka S. Effect of compliance to updated AHA/ACC performance and quality measures among patients with atrial fibrillation on outcome (from Japanese Multicenter Registry). Am J Cardiol 2017; 120: 595–600.
- 27. Sobanski PZ, Alt-Epping B, Currow DC, Goodlin SJ, Grodzicki T, Hogg K, Janssen DJA, Johnson MJ, Krajnik M, Leget C, Martínez-Sellés M, Moroni M, Mueller PS, Ryder M, Simon ST, Stowe E, Larkin PJ. Palliative care for people living with heart failure: European Association for Palliative Care Task Force expert position statement. Cardiovasc Res 2019; 116: 12–27.
- Highet G, Crawford D, Murray SA, Boyd K. Development and evaluation of the supportive and palliative care indicators tool (SPICT): a mixed-methods study. BMJ Support Palliat Care 2014; 4: 285–290.
- Tanaka S, Kamiya K, Hamazaki N, Matsuzawa R, Nozaki K, Maekawa E, Noda C, Yamaoka-Tojo M, Matsunaga A, Masuda T, Ako J. Incremental value of objective frailty assessment to predict mortality in elderly patients hospitalized for heart failure. J Card Fail 2018; 24: 723–732.
- Cannon JA, Moffitt P, Perez-Moreno AC, Walters MR, Broomfield NM, McMurray JJV, Quinn TJ. Cognitive impairment and heart failure: systematic review and meta-analysis. J Card Fail 2017; 23: 464–475.
- Huynh QL, Negishi K, Blizzard L, Saito M, De Pasquale CG, Hare JL, Leung D, Stanton T, Sanderson K, Venn AJ, Marwick TH. Mild cognitive impairment predicts death and readmission within 30 days of discharge for heart failure. Int J Cardiol 2016; 221: 212–217.
- 32. Kotecha D, Flather MD, Altman DG, Holmes J, Rosano G, Wikstrand J, Packer M, Coats AJS, Manzano L, Böhm M, van Veldhuisen DJ, Andersson B, Wedel H, von Lueder TG, Rigby AS, Hjalmarson Å, Kjekshus J, Cleland JGF. Heart rate and rhythm and the benefit of beta-blockers in patients with heart

- failure. J Am Coll Cardiol 2017; 69: 2885-2896.
- Kotecha D, Holmes J, Krum H, Altman DG, Manzano L, Cleland JGF, Lip GYH, Coats AJS, Andersson B, Kirchhof P, von Lueder TG, Wedel H, Rosano G, Shibata MC, Rigby A, Flather MD. Efficacy of β blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. Lancet 2014; 384: 2235–2243.
- 34. Cleland JGF, Bunting KV, Flather MD, Altman DG, Holmes J, Coats AJS, Manzano L, McMurray JJV, Ruschitzka F, Veldhuisen DJ, Van Lueder TG, Von Böhm M, Andersson B, Kjekshus J, Packer M, Rigby AS, Rosano G, Wedel H, Hjalmarson A, Wikstrand J, Kotecha D. Beta-blockers for heart failure with reduced, mid-range, and preserved ejection fraction: an individual patient-level analysis of double-blind randomized trials. Eur Heart J 2018; 39: 26–35.
- Cooper LB, Hemandez AF. Maximizing benefits and mitigating risks with mineralocorticoid receptor antagonist therapy. Eur J Heart Fail 2018; 20: 1227–1229.
- Agrawal S, Agrawal N, Garg J, Mohandas R, Gupta T, Segal M. Heart failure and chronic kidney disease: should we use spironolactone? Am J Med Sci 2015; 350: 147–151.
- Albert NM, Yancy CW, Liang L, Zhao X, Hernandez AF, Peterson ED, Cannon CP, Fonarow GC. Use of aldosterone antagonists in heart failure. *JAMA* 2009; 302: 1658–1665.
- Takei M, Kohsaka S, Shiraishi Y, Goda A, Nagatomo Y, Mizuno A, Sujino Y, Kohno T, Fukuda K, Yoshikawa T. Heart failure with midrange ejection fraction in patients admitted for acute decompensation: a report from the Japanese Multicenter Registry. J Card Fail 2019; 25: 666–673.
- Shen I, Jhund PS, Petrie MC, Claggett BL, Barlera S, Cleland JGF, Dargie HJ, Granger CB, Kjekshus J, Køber I., Latini R, Maggioni AP, Packer M, Pitt B, Solomon SD, Swedberg K, Tavazzi I, Wikstrand J, Zannad F, Zile MR, McMurray JJV. Declining risk of sudden death in heart failure. N Engl J Med 2017; 377: 41–51.
- Tokunaga-Nakawatase Y, Ochiai R, Sanjo M, Tsuchihashi-Makaya M, Miyashita M, Ishikawa T, Watabe S. Perceptions of physicians and nurses concerning advanced care planning for patients with heart failure in Japan. Ann Palliat Med 2020: 9: 1718–1731.