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Original research paper

MARS-5 *vs*. MARS-10: Optimizing pharmacist-led adherence assessment in clinical heart failure practice

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ABSTRACT

Optimising medication adherence is essential for effective heart failure (HF) management, yet nonadherence remains common, particularly among hospitalised and advanced-stage patients. This study evaluated the internal consistency reliability and score association of the Medication Adherence Report Scales, MARS-5 and MARS-10, self-report questionnaires in clinical pharmacist-led adherence assessments in hospitalised HF patients. Tools were administered during structured pharmacist-led interviews. To complement quantitative findings, four clinical cases were presented to illustrate the clinical relevance of adherence assessment in real-world HF management. Results showed a strong association between MARS-5 and MARS-10 (n = 70) responses (unweighted Cohen's kappa 0.820 (95 % CI 0.683–0.957; $p < 0.001$) for categorizing patients as nonadherent or adherent and Pearson's r coefficient of 0.899 (95 % CI 0.847–1.000; $p < 0.001$) for continuous score correlation), supporting–score association and flexible use in clinical settings, with MARS-5 reliably identifying nonadherence (defined as score < 20 for MARS-5 and ≤ 8 for MARS-10), with potentially reduced respondent burden due to fewer items. Serious clinical complications were documented in nonadherent patients (41.43 % by MARS-5 and 35.71 % by MARS-10), illustrated through selected cases including stent thrombosis, embolic stroke, graft dysfunction, and deterioration in glycaemic control. These findings indicate the potential of MARS-5 as a practical, time-efficient tool for routine adherence assessment in acute settings. Case analyses underscore the critical role of the clinical pharmacist in proactively identifying nonadherence and enabling timely, targeted interventions to mitigate risk and improve patient outcomes in HF care.

Keywords: heart failure, clinical pharmacist, medication adherence, MARS-5, MARS-10

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INTRODUCTION

Adherence is defined as the extent to which a patient's behaviour corresponds with the agreed recommendations from a healthcare provider (1). Medication adherence, as a key component of overall adherence, which encompasses numerous health-related behaviours (*e.g.* following dietary and physical activity recommendations and regular monitoring), plays a central role in the effective management of chronic diseases. Among these conditions, cardiovascular diseases (CVDs) are particularly impacted by suboptimal adherence because they require long-term, often complex pharmacotherapy regimens aimed at controlling symptoms, preventing acute events, and improving survival (2, 3). The presence of multiple comorbidities such as hypertension, diabetes, and chronic kidney disease, combined with polypharmacy and frequent treatment adjustments, increases the risk of both intentional and unintentional nonadherence. Moreover, many cardiovascular drugs act preventively and are asymptomatic in their benefit, leading patients to underestimate their importance, which further contributes to poor adherence. According to the latest global estimates, CVDs remain the leading cause of death, accounting for approximately 17.9 million deaths per year, equivalent to 32 % of all global deaths (4). Nonadherence exacerbates the burden of CVDs, contributing to increased rates of hospitalisations, emergency department visits, and mortality, while placing substantial economic pressure on healthcare systems (5).

Within the broad spectrum of CVDs, heart failure (HF) presents a particularly formidable challenge in terms of medication adherence. According to the latest position paper from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), HF affects around 63 million people worldwide, with 5-year mortality rates > 50 % in advanced HF (6). The substantial prevalence of HF imposes a significant economic burden on healthcare systems, with the estimated annual cost of 33.14 billion United States dollars (USD) in the European Union and 30.7 billion USD in the United States (7). Despite improvements in therapy and better adherence of prescribers to clinical guidelines (8), the prevalence of HF continues to rise, along with associated morbidity and mortality. The American College of Cardiology (ACC)/American Heart Association (AHA) and the ESC guidelines emphasise the importance of adherence to medications due to their remarkable effect in reducing morbidity and mortality in HF (9, 10). Yet, despite therapeutic advances, medication adherence remains alarmingly suboptimal. Estimates suggest that only 40 to 60 % of patients with HF adhere to their treatment regimens (11).

Nonadherence in HF has been linked to adverse clinical outcomes, including increased all-cause mortality and higher rates of cardiovascular hospitalisations (12, 13). Worsening of HF is often related to nonadherence, accounting for approximately 10 % of hospitalisations and conferring a 10 % higher risk of readmission (14). Nonadherent patients have been shown to be twice as likely to require hospital admission compared to those who adhere to their medication (13). Furthermore, inadequate adherence compromises symptom control (13), undermining the benefits of guideline-directed medical therapy and accelerating disease progression. Contrariwise, reductions in nonadherence are found to result in fewer hospital admissions, readmissions and less mortality (12–14). Ruppar *et al.* suggested that medication adherence should be addressed in regular follow-up visits with HF patients, and interventions to improve adherence should be a key part of HF self-care programs (15). Data is scant for levels of adherence or the effect of medication nonadherence in Croatian patients with HF, inviting research on this population of vulnerable patients. Measuring

medication adherence in HF is essential given its impact on the abovementioned outcomes. In the absence of a single gold-standard method, clinicians and researchers rely on direct or indirect assessment approaches, each with specific advantages and limitations. Among indirect methods, self-reported adherence questionnaires are commonly used in both clinical and research settings for their affordability, simplicity and emphasis on the patient's perspective. Among these tools, Medication Adherence Report Scale (MARS) stands out as a validated instrument for assessing self-reported medication adherence (16). Developed by Horne and colleagues, MARS is available in two formats: the full-length MARS-10, comprising ten items, and the shorter MARS-5 version of the questionnaire, which retains five core items of the original questionnaire. Although both versions are validated self-report instruments for assessing medication adherence, their comparative performance has not been investigated in hospitalised HF patients, a population with complex pharmacotherapy regimens and high risk of nonadherence. Furthermore, there is limited evidence on their use within pharmacist-led adherence assessments in acute-care settings. This study, therefore, aimed to provide preliminary psychometric evidence on the internal consistency, reliability and score association between these two instruments, serving as a foundation for future validation and clinical implementation studies.

A growing body of evidence supports the integration of clinical pharmacists into multidisciplinary HF teams as an effective strategy to optimise pharmacotherapy, reduce hospital readmissions, and improve patient outcomes (7, 17, 18). Among various aspects of pharmaceutical care, assessment and management of medication adherence is one of the most extensively studied and important areas (7). This role is further strengthened when supported by validated, time-efficient adherence assessment tools, especially in an acute care setting where cognitive and logistical demands are high. In this context, identifying the most practical instrument for routine pharmacist-led adherence assessment is essential.

At the University Hospital Centre (UHC) Zagreb, integration of a clinical pharmacist into the cardiology department, initiated in 2022 as part of a pilot project to implement clinical pharmacy services within the UHC Zagreb, offered insight into adherence patterns of hospitalised patients with HF. This initiative was prompted by the increasing complexity of pharmacotherapy in advanced HF patients and by growing international evidence supporting the role of the clinical pharmacist in multidisciplinary cardiac care teams. Through routine patient interviews, the pharmacist observed frequent signs of nonadherence, ranging from missed doses to misconceptions about medications. Many of those observations occurred among patients with advanced HF awaiting or supported by left ventricular assist device (LVAD) or heart transplantation. These direct clinical experiences raised questions about how best to assess adherence in this group of patients.

To address this gap, the present study aimed to compare MARS-5 and MARS-10 self-report questionnaires administered during clinical pharmacist-led interviews in hospitalised HF patients. The primary aim was to compare the internal consistency and score association between the MARS-5 and MARS-10 questionnaires in hospitalised HF patients. As a secondary aim, four clinical cases were presented to illustrate the clinical relevance of adherence assessment in routine pharmacist-led practice. By identifying whether the shorter MARS-5 scale performs comparably to MARS-10 in this specific population, this study seeks to support evidence-based recommendations for routine adherence screening in pharmacist-led HF care.

EXPERIMENTAL

Study design and patients

This prospective observational cross-sectional study was conducted between August and October of 2022, and enrolled patients ≥ 18 years of age with cardiovascular diseases, hospitalised in the Clinical unit of post-intensive care, heart failure and transplantation cardiology, Division of intensive cardiology care, arrhythmia, and transplantation cardiology, Department of Cardiovascular Diseases, University Hospital Centre Zagreb. In total, 70 patients were included in the study. The sample size was determined based on the expected number of eligible hospitalised patients during the pre-defined three-month study period and the feasibility of conducting structured pharmacist-led interviews. Therefore, no formal sample size calculation was performed due to the exploratory nature of the study. Patients were recruited using a consecutive sampling approach, including all eligible hospitalised adults with a confirmed diagnosis of CVD who met the inclusion criteria and provided informed consent during the study period.

Data collection

Data sources included a structured interview with a clinical pharmacist and a review of available patients' medical documentation collected through patient interview, hospital electronic health records and patient medical archives of the Division of intensive cardiology care, arrhythmia, and transplantation cardiology, Department of Cardiovascular Diseases, University Hospital Centre Zagreb. The structured pharmacist-patient interview gathered sociodemographic data (age, sex, hight, weight, body mass index, smoker's status, number of pack years); primary cardiovascular diagnosis (*i.e.* post-transplant status, LVAD implantation, HF, coronary heart disease, valvular disease…), the New York Heart Association (NYHA) functional status, ejection fraction (EF); comorbidities; diagnosis timeline (year of diagnosis and duration); clinical laboratory values; systolic and diastolic blood pressure; healthcare utilization due to cardiovascular disease worsening; details on pharmacotherapy. Additionally, during the interview, two medication adherence scales were used, MARS-5 and MARS-10. Both questionnaires were simultaneously administered by a clinical pharmacist during structured face-to-face interviews with each participant. Clinical data collected through the interview were further completed and verified by the clinical pharmacist (study investigator) using the hospital electronic health records and archives to confirm accuracy of comorbidities, diagnostic procedures, laboratory results and pharmacotherapy details.

Ethics considerations

The study was approved by the Ethical Committee of the UHC Zagreb (8.1-22/232-2, 02/013 AG), and all participants provided written informed consent prior to inclusion. Before the analysis data were coded and anonymised to ensure data confidentiality. Authors of the MARS-5 and MARS-10 scales were contacted to obtain written permission to use and translate the questionnaires. This study was conducted in accordance with all applicable guidelines for ethical research, including the principles outlined in the Declaration of Helsinki, the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP), the Health Care Act of the Republic of Croatia, and the Patients' Rights Act of the Republic of Croatia (19, 20).

Questionnaire adaptation and scoring

The questionnaires were translated into Croatian following the Brislin forward-backward translation model, performed independently by two bilingual researchers familiar with medical terminology. The translated versions were then back-translated to English to ensure semantic and conceptual equivalence. Minor linguistic adjustments were made to improve clarity and ease of use. No additional cognitive debriefing or expert panel review was conducted, as the study aimed to apply and compare the existing instruments rather than perform full cultural validation. The reliability of Croatian versions of the MARS-5 and MARS-10 scales was evaluated by determining internal consistency (Cronbach's alpha). This approach provided preliminary psychometric evidence regarding the comparability of both scales in hospitalised HF patients.

The MARS-10 scale consists of ten "yes" or "no" statements, with each "no" being scored with a 1 and each "yes" with a 0. Scores range from 0 to 10, and higher scores indicating better adherence. Authors of the original scale suggest scores of 5 or less should be interpreted as "nonadherence" (21). MARS-5 scale, a shortened and adapted version of MARS-10, consists of five statements and five possible answers: "always" (scored as 1), "often" (scored as 2), "sometimes" (scored as 3), "rarely" (scored as 4), and "never" (scored as 5). Scores for each statement are summed to give a total score (ranging from 5 to 25), with higher scores indicating higher levels of adherence. Based on previous studies, as well as a generally accepted threshold, a cut-off score below 20 was considered indicative of nonadherence (16, 22).

For descriptive comparison, both instruments were dichotomised into adherent and nonadherent categories using the 80 % cut-off (MARS-5 < 20, MARS-10 < 8), whereas all statistical analyses were performed using continuous scores to retain variability.

While the MARS-5 questionnaire does not formally distinguish between intentional and unintentional nonadherence, individual items conceptually reflect these domains (*e.g.*, forgetfulness or missing out the doses as unintentional, and dose alteration or discontinuation as intentional). As the study was conducted through pharmacist-led interviews, this interpretation was further informed by the pharmacist's professional judgement and patient interaction during the interview. For the purposes of this study, total scores were used to represent overall adherence behaviour.

Clinical case presentations

The four clinical cases were purposively chosen to illustrate different medication adherence patterns and clinical presentations: unintentional nonadherence, intentional nonadherence, adherence, and discrepant MARS-5 and MARS-10 scores. For categories of nonadherence, two patients with the lowest scores were chosen, one for each type of nonadherence. For the category of discrepant scores, the patient with the biggest difference in scores was presented. If more than one patient was found with identical scores within a category, the choice was made based on patient characteristics (to ensure similar patients were compared), clinical importance of pharmacist intervention, and availability of clinical data needed for case presentation.

Outcome measures

The primary outcome measures were the psychometric parameters of the MARS-5 and MARS-10 questionnaires, specifically internal consistency reliability (Cronbach's

alpha) and score association between the two instruments (Pearson's *r* for continuous measurement, Cohen's kappa for categorical classification).

The secondary outcomes included the descriptive presentations of four clinical cases to illustrate the clinical relevance of adherence assessment in routine pharmacist-led practice. These cases were not included in the statistical analyses, as their purpose was to qualitatively demonstrate different adherence patterns and the practical application of the study findings.

Statistical analysis

Descriptive statistics were conducted to describe the frequencies of patient characteristics. The normality of the distribution of numerical variables was tested by the Kolmogorov-Smirnov test. Non-normally distributed numerical variables were presented as the median and interquartile range (IQR), and normally distributed numerical variables were presented as the mean and standard deviation (SD). Categorical variables were presented as percentages and the difference between groups was tested using the Chi-squared test, and in instances with less than 10 cases per cell Fisher-Freeman-Halton exact test was used. The Kruskal-Wallis test was used to test the differences between continuous variables with respect to adherence. To assess the strength and direction of correlation between MARS-5 and MARS-10 continuous scores, the Pearson correlation coefficient (*r*) was calculated, and to evaluate the association between categorising patients as adherent and nonadherent based on MARS scores unweighted Cohen's kappa was employed. A kappa value > 0.80 was considered a strong level of agreement between scales (23). Internal consistency was determined *via* Cronbach's alpha testing. The scales were considered reliable if Cronbach's alpha was > 0.70 (24–26). Due to the nature of the study design, test-retest reliability could not have been assessed.

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., USA), and p values < 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Participants' characteristics

Of the 70 included patients, 80 % (56) were male, with a mean age of 59.20 ± 11.71 years (ranging from 21 to 85 years). The majority of patients (67.14 %) were characterised as overweight, based on the calculated body mass index (BMI) over 25, with a median BMI value of 27.60 kg m^{-2} (IQR 24.24–30.76). More than half were non-smokers (52.9 %), 28.6 % past smoker, and 18.6 % had an active smoking status. Details on patients' characteristics can be found in Table I.

All patients were diagnosed with HF but were primarily treated for other cardiovascular diagnoses, which led to or progressed from HF. Primary cardiovascular diagnoses were categorised into five classes, according to leading diagnosis in hospital electronic health records: post-heart transplant (HTx) (24.3 % patients), post-LVAD implantation (8.6 %), HF (58.6 %), coronary artery disease (CAD) (5.7 %), and other (2.8 %). Slightly less than two-thirds of patients (n = 43, 61.46 %) were identified as having HF with reduced ejection fraction (EF). Median duration of primary cardiovascular diagnosis was 4.5 years (IQR 1.04–8.75).

Table I. Participants' characteristics

	Participants (n = 70)	
Age (y), mean ± SD	59.20 (± 11.71)	
Sex, *n* (%)	Female	14 (20.0)
	Male	56 (80.0)
BMI (kg m^{-2}), median (IQR)	27.60 (24.24–30.76)	
Smoker's status, *n* (%)	Nonsmoker	37 (52.9)
	Active smoker	13 (18.6)
	Past smoker	20 (28.6)
Pack years, median (IQR)	0 (0–21.88) years	
Primary cardiovascular diagnosis, *n* (%)	HTx	17 (24.3)
	Post LVAD implantation	6 (8.6)
	HF	41 (58.6)
	Coronary heart disease	4 (5.7)
	Other	2 (2.9)
Duration of primary cardiovascular diagnosis (y), median (IQR)	4.5 (1.04–8.75)	
Classification of HF based on EF, *n* (%)	HFpEF	27 (38.57 %)
	HFrEF	43 (61.43 %)
Ejection fraction (%), median (IQR)	35 (22.25–55)	
Comorbidities, median (IQR)	3 (2–4)	
Medication, mean ± SD	10.51 ± 3.40	
Polypharmacy[a]	97.14 %	

BMI – body mass index, EF – ejection fraction, HF – heart failure, HFpEF – HF with preserved ejection fraction, HFrEF – HF with reduced ejection fraction, HTx – heart transplant, IQR – interquartile range, LVAD – left ventricular assist device, SD – standard deviation; [a] polypharmacy – concomitant use of 5 or more medicines

On average, patients were taking 10.51 ± 3.40 medications (ranging from 4 to 18), and almost all were exposed to polypharmacy (97.14 %). When it comes to medication classification, patients used a total of 111 different medicines from 12 different anatomical therapeutic chemical classification groups (ATC) (27). The three most represented medication groups included medication used for the cardiovascular system (36.94 %), alimentary tract and metabolism (12.61 %), and nervous system (10.81 %). Other details on the used pharmacotherapy can be seen in Table II.

MARS-10 or MARS-5 to evaluate medication adherence?

Reliability analysis of the MARS-5 questionnaire, assessed *via* Cronbach's alpha testing, showed high internal consistency for the entire scale (α = 0.91; 95 % CI 0.877–0.941). Item-total correlations for MARS-5 were 0.79 for question 1, 0.759 for question 2, and 0.850,

Table II. Medication use based on ATC classification

	ATC groups	Number of different medicines	Number of patients prescribed
A	Alimentary tract and metabolism	14 (12.61 %)	57 (81 %)
B	Blood and blood-forming organs	10 (9 %)	57 (81 %)
C	Cardiovascular system	41 (36.94 %)	70 (100 %)
G	Genitourinary system and sex hormones	3 (2.7 %)	8 (11.43 %)
H	Systemic hormonal preparations	3 (2.7 %)	22 (31.48 %)
J	Anti-infectives	8 (7.2 %)	12 (17.14 %)
L	Antineoplastic and immuno-modulating agents	6 (5.4 %)	19 (27.14 %)
M	Musculoskeletal system	3 (2.7 %)	21 (30 %)
N	Nervous system	12 (10.81 %)	19 (27.14 %)
R	Respiratory system	9 (8.12 %)	10 (14.28 %)
S	Sensory organs	1 (0.9 %)	1 (1.43 %)
V	Various	1 (0.9 %)	1 (1.43 %)

ATC – Anatomical Therapeutic Chemical Classification

0.853 and 0.695 for questions 3–5, respectively. The average inter-item correlation for the MARS-5 scale was 0.691. Similarly, internal consistency for the MARS-10 scale was considered good with Cronbach's alpha of 0.85 for the entire scale (95 % CI 0.809–0.892). Item-total correlations for MARS-10 ranged from 0.247 to 0.793, while the average inter-item correlation was 0.345. There was no change in Cronbach's alpha values if any of the items were dropped from either scale.

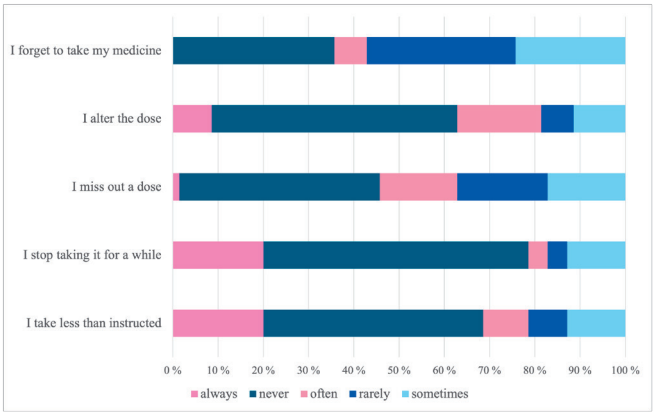

Fig. 1. Answers to the MARS-5 questionnaire.

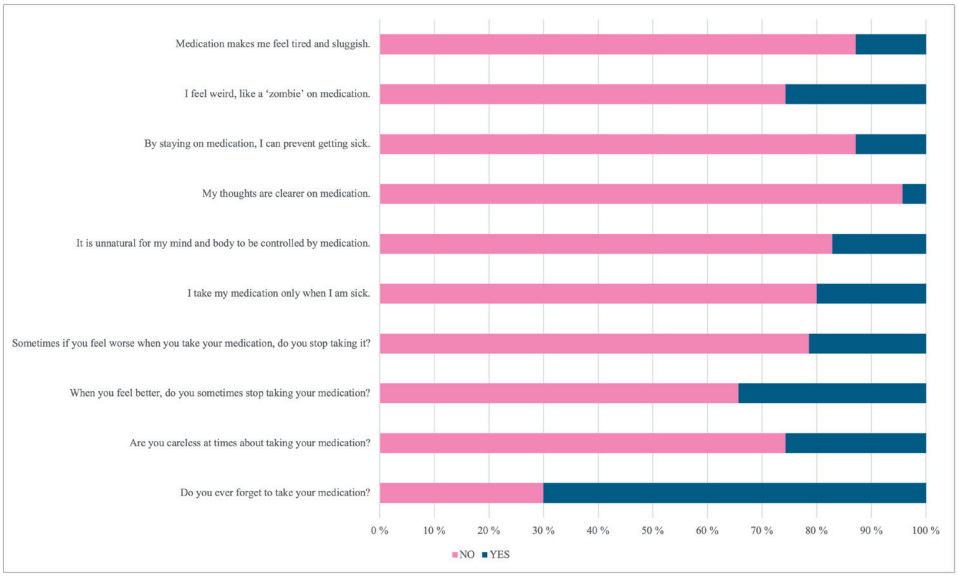

Fig. 2. Answers to the MARS-10 questionnaire.

Both MARS-5 and MARS-10 classified comparable proportions of patients as adherent (58.57 % *vs*. 64.29 %, respectively), with no statistically significant difference in overall classification rates ($\chi^2(1) = 1.50$; $p = 0.22$).

Median score for MARS-5 was 21.50 (IQR 13– 25.00) with a range from 8 to 25. Out of 41.43 % nonadherent patients, 65.62 % (n = 19/29) were identified as being intentionally nonadherent, and 34.48 % unintentionally nonadherent. Fig. 1. brings a detailed representation of answers to each item from the MARS-5 questionnaire.

Median score for MARS-10 was 9 (IQR 6–10) with scores ranging from 1 to 10. Details on answers to specific items of the MARS-10 questionnaire can be seen in Fig. 2.

A systematic review of the HF population in the Middle East reported an average nonadherence rate of 60 % with rates measured with MARS-10 reaching 77 % in hospitalised patients (28), a cross-sectional studies in Jordan found that 47 % to 92.5 % of outpatients exhibited moderate to poor adherence (29, 30), research on the Swiss population of hospitalised HF patients marked a nonadherence rate of 26.4 % (31), while Ethiopian authors report a 17.7 % nonadherence rate for hospitalised chronic HF patients (32). Notably, adherence rates reported in the literature vary considerably, often reflecting differences in study population, settings, and the measurement tool used to assess adherence (33). These data underscore the importance of using a targeted, real-world adherence assessment tool in the HF population to ensure easier comparison on one hand, and on the other, to accentuate the need for continuous assessment of medication nonadherence and employment of person-centred interventions to improve clinical outcomes (33).

Cohen's kappa agreement analysis yielded a kappa value of 0.820 (95 % CI 0.683–0.957; $p < 0.001$), indicating strong agreement between the two measures when it comes to cate-

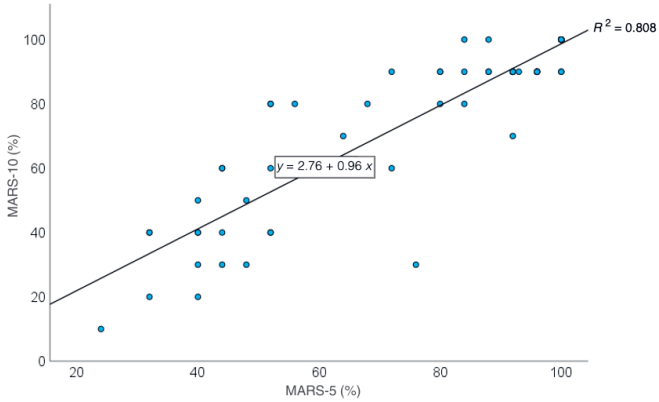

Fig. 3. MARS-10 and MARS-5 correlation.

gorising patients as adherent or nonadherent with a cut-off point of 80 %. Observed percentage agreement was 97.56 % of cases for categorising patients as adherent on both scales, and 82.76 % for categorizing patients as nonadherent. In six cases, there was a discrepancy in categorisation between the two MARS scales. In five instances, MARS-5 categorised patients as nonadherent and MARS-10 as adherent, and in one case, the opposite classification was found. Closer inspection of cases shows that the inconsistency in categorisation was made for patients near or on the cut-off point of 80 % on either of the scales (*i.e.* MARS-5 score of 72 % and MARS-10 score of 80 %). This suggests that special attention should be paid to patients with threshold or borderline adherence as they are at increased risk of crossing into nonadherence and potentially further worsening clinical outcomes (34–36). Similarly, continuous score correlation evaluation shows a very strong positive correlation between medication adherence assessed with MARS-5 and MARS-10 questionnaires, with Pearson's correlation coefficient r = 0.899 (95 % CI 0.847–1.000; $p < 0.001$). A graphic presentation of this finding can be seen in Fig. 3. Observed positive correlations support the notion of their convergent validity and indicate that either version of the MARS questionnaire can be used to evaluate medication adherence behaviours in HF patients. For those with limited time, a shorter MARS-5 can be more appropriate, whereas those who wish to explore additional behavioural aspects of nonadherence, MARS-10 can be used. Specific reasons or contextual indicators for medication nonadherence can be clinically valuable and potentially shape further treatment options (37). Besides behavioural aspects, studies are highlighting the importance of exploring barriers and facilitators of medication adherence. Where MARS scales are not sufficient, there is a potential to use tools which show good correlation with MARS, such as ADHERE-7, and allow for a deeper investigation into reasons for nonadherence (38–40).

Clinical cases

Four clinical cases are presented descriptively to illustrate the clinical relevance of adherence assessment in routine pharmacist-led practice. These cases were not included in the statistical analyses, as their purpose was to qualitatively illustrate different adher-

Table III. Clinical cases

	Patient 1	Patient 2	Patient 3	Patient 4
Age (y)	44	42	52	61
Gender	Male	Male	Male	Male
Primary diagnosis	HF (biventricular ischaemic CMP)	HF (dilated CMP)	HF (biventricular dilated CMP)	HF (biventricular ischaemic CMP)
NYHA Class	III	III	III	III
Year of diagnosis	2022	2018	2015	2021
Duration (y)	0.5	4	7	1
MARS-10 score (%)	30	10	80	90
MARS-5 score (%)	44	24	52	96
Nonadherence type	unintentional	intentional	unintentional	NA
Number of hospitalisations/ED visits due to CVD	3	5	2	4
Major clinical outcome documented alongside nonadherence	Stent thrombosis	Ischemic cerebrovascular event	None	None
Physician opinion	Stent thrombosis was documented following the delay of DAPT introduction associated with nonadherence	Ischemic cerebrovascular event was documented in the context of low reported nonadherence to warfarin The discharge letter contained a note on the importance of taking prescribed medication regularly and as prescribed.	Concerns regarding adherence. The discharge letter contained a note on nonadherence to some of prescribed medication between two latest hospital evaluations.	No concerns regarding adherence.

Pharmacist opinion	Nonadherence may have contributed to stent thrombosis. The patient has a low understanding of his disease and pharmacotherapy. Patient did not collect his prescribed medications from the pharmacy on the day of hospital discharge (Friday), perceiving it as non-urgent. He developed stent thrombosis by the following Monday.	Nonadherence may have contributed to or exacerbated the risk of cerebrovascular events. The patient showed poor engagement with medical staff and consistently disregarded pharmacotherapy guidance. His approach to medication was influenced by personal beliefs and preferences, rather than medical recommendations.	Concerns regarding adherence. Patients' adherence very inconsistent and varies over time. Patient stopped taking some of prescribed medication, altered the doses and missed out doses in the period between the two latest hospital evaluations.	Patient demonstrated good adherence to prescribed pharmacotherapy, with medication-taking behaviour considered adequate and consistent with recommended standards for HF management.

CMP – cardiomyopathy, CVD – cardiovascular disease, DAPT – dual antiplatelet therapy, ED – emergency department, HF – heart failure, HTx – heart transplant, NA – not applicable, NYHA – New York Heart Association

ence patterns and the real-world applicability of the adherence assessment. A summary of the cases is provided in Table III.

In three cases (patients 1, 2 and 4), responses to MARS-5 were consistent with those obtained *via* MARS-10, supporting the adequacy of the shorter questionnaire in detecting both intentional and unintentional nonadherence. Patients classified as nonadherent exhibited serious adverse outcomes, including stent thrombosis and embolic stroke, which were documented in the context of reported nonadherence and may have been exacerbated by suboptimal adherence behaviour. These events were anticipated or supported by physician documentation in discharge letters and follow-up notes, affirming the clinical relevance of adherence assessment.

For example, Case 1 illustrated that unintentional nonadherence in the immediate post-discharge period might be associated with adverse outcomes. The patient, recently hospitalised for acute myocardial infarction and treated with percutaneous coronary intervention, was initiated on dual antiplatelet therapy (DAPT) during hospitalisation and discharged on a Friday with a discharge letter and prescribed medication, including DAPT. However, due to a lack of understanding regarding the urgency of continuing treatment, the patient chose to delay obtaining the prescribed therapy until the following Monday. Stent thrombosis was documented following this delay, representing a preventable complication that might have been avoided with earlier pharmacist intervention.

Case 2 illustrated a patient with a cerebrovascular event due to embolisation from a left ventricular thrombus. Considering the patient's low adherence to warfarin, this event was documented in the medical record as occurring in the context of suboptimal anticoagulation control. While causality could not be established, it is plausible that

inadequate adherence may have contributed to or exacerbated the risk of this adverse outcome.

Case 3 reveals a patient with conflicting MARS scores. This divergence in scores could be explained by misunderstanding and/or misinterpretation of questions, as well as differences in scope of adherence behaviour explored by the scales. For instance, the patient gave contradictory answers to the question of forgetfulness, as well as to taking less medication than instructed or changing the dose of medicine. From a clinical perspective, while major clinical outcomes possibly associated with nonadherence were not observed at the time of clinical visit, early detection of nonadherence is crucial to prevent further downturn/slip/decline/drop into nonadherent behaviour, which could lead to suboptimal therapeutic effectiveness and increased risk of disease progression and poorer health outcomes (35). This contrasting result may indicate that MARS-5 captured subtle aspects of nonadherence not reflected by MARS-10. However, this observation should be interpreted with caution, as differential sensitivity between the two instruments cannot be confirmed from a single case and requires further empirical validation.

In contrast, Case 4 presented an example of a patient with high adherence scores across both scales. The patient consistently followed the prescribed regimen, and no adverse outcomes documented alongside nonadherence were observed during hospitalisation or follow-up. This case supports the utility of both MARS questionnaires in distinguishing between adherent and nonadherent profiles and reinforces the suitability of MARS-5 for efficient routine screening.

Taken together, these case analyses illustrate the potential applicability of the MARS-5 questionnaire as a practical tool for pharmacist-led adherence assessment in hospitalised HF patients. While not intended to establish definitive psychometric conclusions, the findings suggest that MARS-5, despite containing fewer items, effectively identified relevant adherence issues in a manner comparable to MARS-10, without compromising clinical interpretability. Moreover, its brevity may support its routine use in pharmacist-patient consultations to recognise patients who could benefit from targeted interventions, such as enhanced education or closer follow-up, particularly in settings where time or cognitive demands limit the feasibility of longer instruments. Research supports a more proactive role of clinical pharmacists in the care of HF patients, where they can be a key stakeholder in ensuring optimised utilisation of HF medication, addressing nonadherence to guideline-directed medical therapy, and positively affecting patient outcomes (41, 42).

While these cases do not represent the full study population, they reinforce the importance of routine adherence screening in HF care and support the integration of MARS-5 as a practical solution in everyday clinical settings.

Strategic implications and recommendations

Routine use of adherence measures can help healthcare providers proactively identify patients at risk of poor adherence. Objective measures, such as medication serum or urine concentration, have been proven to be useful in monitoring and predicting adherence and clinical outcomes in HF patients (43, 44). Such tests are expensive, complex, and can lead to white coat adherence with patients improving medication-taking behaviour before hospital visits, and do not reveal the context behind medication nonadherence. Where possible, subjective and objective medication adherence measurements should be combined.

MARS scales could be embedded into hospital electronic health records or systems and used during hospital or outpatient clinic admissions to capture changes in adherence levels, including easier correlation to clinical outcomes.

For easier interpretation of MARS scores, clinically relevant cut-off points need to be used. Whilst evidence indicates cut-off points of 80 % can reliably distinguish patients at higher risk for negative outcomes associated with poorer medication adherence, for HF, a cut-off point of 88 % offers a balance of specificity and sensitivity for predicting clinical outcomes (31, 45, 46). Distinct consideration needs to be given to patients with threshold results who exhibit intentional nonadherence characteristics, as well as those with conflicting scores or answers, for whom a more tailored approach might be necessary (47, 48).

Furthermore, special attention should be given to patients with risk factors of negative outcomes in HF, which could be associated with medication nonadherence and/or polypharmacy (49, 50). This study's population was, in the majority, exposed to polypharmacy in percentages similar to other populations of HF patients (51). Even though a specific number of medicines or exposure to hyperpolypharmacy (concomitant use of 10 or more medicines) was not associated with lower scores on MARS scales for this population, healthcare providers should consider how non-HF-medicine polypharmacy affects adherence to HF treatment and clinical outcomes (51, 52).

Additional studies should explore which patient-reported and patient-specific factors are predictive of nonadherent behaviour in HF, as well as which factors in those with increased risk are best targeted by pharmacist-led multidisciplinary interventions.

Limitations and strengths

This study has several limitations that should be acknowledged. First, its cross-sectional design precludes assessment of adherence changes over time or test-retest reliability. The small sample size (n = 70) and single-centre setting may also limit generalizability. Second, adherence was measured using a self-reported questionnaire without an external criterion measure (*e.g.,* pharmacy dispensing data or clinical outcomes), which introduces potential recall and social desirability bias. The administration of questionnaires through pharmacist-led interviews, although beneficial for clarifying patient responses, deviated from the scales' intended self-completion format and may have introduced additional social desirability bias. Furthermore, while the Brislin translation model was applied for linguistic adaptation, no cognitive debriefing or expert panel review was conducted; therefore, the Croatian versions cannot be considered fully culturally validated. Lack of cognitive debriefing to assess item clarity and patients' potential misinterpretation of certain questionnaire items could have additionally negatively contributed to the high Cronbach's alpha value. Dichotomisation of continuous scores, though useful and often easier to apply for clinical classification, may have reduced measurement precision. A cut-off point of 80 % used for dichotomised categorisation could have led to potential misclassification bias, especially for patients with adherence near the threshold level. Future studies could explore whether varying cut-off thresholds yield consistent categorisation, affect agreement levels between the two scales, and what clinical impact they might have. Regardless, the used cut-off point is widely accepted in research, including in patients with cardiovascular comorbidities (16, 22). Finally, purposive case selection means that the presented case analyses serve only illustrative purposes and should not be interpreted as representative.

Despite these limitations, the study has several important strengths. The dual approach in analysing both the association of continuous data with Pearson's r and agreement between dichotomised categories with Cohen's kappa reduces potential interpretation bias and offers a more comprehensive assessment. It included a high-risk and clinically complex population with advanced HF, including those with LVAD or post-transplant status, who are often underrepresented in adherence research (53, 54). The study was conducted in a real-world clinical environment, reflecting routine pharmacist-led care in hospitalised settings. To our knowledge, this is the first examination of MARS-5 and MARS-10 correspondence in Croatian HF patients, providing valuable preliminary insights to support future large-scale validation studies (55, 56).

CONCLUSIONS

This study provides preliminary evidence of high internal consistency and strong score association between the MARS-5 and MARS-10 questionnaires in hospitalised HF patients. The findings indicate that the shorter MARS-5 may serve as a practical and feasible option for pharmacist-led adherence assessment in clinical settings. Presented cases illustrated the clinical relevance of adherence assessment in identifying patients with suboptimal medication-taking behaviours. These results support further investigations of MARS-5 in larger, multicentre studies to confirm its reliability and clinical applicability.

Ethical approval. – Ethical approval for this study was obtained from the Ethical Committee of the University Hospital Centre Zagreb. Participating subjects were free to decline participation at any time during the study. Data were collected and stored under specific codes with an assurance of anonymity and data confidentiality. All methods were carried out in accordance with relevant guidelines and regulations.

Consent to participate. – Informed consent on participation was obtained from all subjects before data collection.

Availability of data and materials. – The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest. – The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be viewed as a potential conflict of interest.

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Authors contributions. – Conceptualisation, M.M.; methodology, M.M. and I.B.; formal analysis, I.B.; writing, original draft, M.M. and I.B.; writing, review and editing, B.S., M.O.H., P.T., and D.M.; supervision, B.S., M.O.H., and P.T.; resources, B.S. and D.M. All authors have read and agreed to the published version of the manuscript.

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