ORIGINAL ARTICLE

Enhanced Heart Failure Management: Impact of the therapeutic unit for heart failure (TUNI-HF) on mid-term prognosis

Unité thérapeutique d'insuffisance cardiaque (UTIC) : Impact sur la prise en charge et sur le pronostic à moyen terme

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Abstract

Introduction: Chronic heart failure (CHF) is a global and increasing problem responsible of uncontrolled rates of mortality and readmission. A therapeutic Unit of heart failure (TUNI-HF) was established to assume a treatment optimization, comorbidities management and education in order to improve heart failure (HF) prognosis.

Aim: This study aimed to describe the impact of the TUNI-HF on treatment optimization, mortality and readmission rates at 12 months in patients with heart failure with reduced ejection fraction (HFrEF).

Methods: A retrospective study was conducted in the military hospital of Tunis, Tunisia. Two groups were compared: Group "C" included patients followed from March 2018 for 12 months with usual care. Group "U" included patients followed from Mars 2021 for 12 months in the TUNI-HF.

Results: Groups "C" and "U" enrolled 108 and 110 patients respectively. At baseline, patients' characteristics were comparable. Prescription rates of guideline directed medical treatment (GDMT) at optimal doses were low in two groups. After 12 months, prescription rates of beta-blockers (BB) and mineralocorticoid receptor antagonist (MRA) were higher in group "U". In addition, optimal doses of BB, renin angiotensin aldosterone system inhibitors (RAASI) and MRA were more achieved in the same group "U". Loop diuretics were less prescribed in the group "U" and cardiac implantable devices rate was higher in the same group. Kaplan Meier analysis showed significantly lower rates of readmission and all-cause mortality rates in the group "U".

Conclusion: The management of HF in a specialized unit, compared with usual care, was associated with a better treatment optimization and a reduction in mortality and readmission rates.

Key words: Hospital Unit, Mid term prognosis, Management, Heart failure with reduced ejection fraction

Résumé

Introduction: L'insuffisance cardiaque chronique (ICC) constitue un problème de santé publique mondial en constante progression, responsable de taux de mortalité et de réadmission non contrôlés. Une Unité Thérapeutique d'insuffisance cardiaque (UTIC) a été mise en place dans le but d'optimiser le traitement, de prendre en charge les comorbidités et d'assurer l'éducation des patients, afin d'améliorer le pronostic de l'insuffisance cardiaque.

Objectif: Cette étude visait à évaluer l'impact de l'UTIC sur l'optimisation du traitement et les taux de mortalité et de réadmission à 12 mois chez des patients présentant une insuffisance cardiaque à fraction d'éjection réduite (HFrEF).

Méthodes: Une étude rétrospective a été menée à l'Hôpital Militaire de Tunis, en Tunisie. Deux groupes ont été comparés : le groupe « C » incluait des patients suivis pendant 12 mois à partir de mars 2018 dans le cadre de la prise en charge classique ; le groupe « U » comprenait des patients suivis pendant 12 mois à partir de mars 2021 au sein de l'UTIC.

Résultats: Les groupes « C » et « U » comprenaient respectivement 108 et 110 patients. À l'inclusion, les caractéristiques des patients étaient comparables. Les taux de prescription des médicaments recommandés à doses optimales étaient faibles dans les deux groupes. Après 12 mois, les taux de prescription des bêta-bloquants (BB) et des antagonistes de l'aldostérone (AA) étaient plus élevés et l'atteinte des doses optimales de BB, de bloqueurs du système rénine-angiotensine-aldostérone (BSRAA) et d'AA était plus constatée dans le groupe « U ». Dans ce même groupe, les diurétiques de l'anse étaient moins prescrits et le taux de dispositifs cardiaques implantables était plus élevé. L'analyse de Kaplan-Meier a montré des taux significativement plus faibles de réadmission et de mortalité toutes causes confondues dans le groupe « U ».

Conclusion: La prise en charge de l'ICC au sein d'une unité spécialisée, comparée à la prise en charge classique, est associée à une meilleure optimisation thérapeutique ainsi qu'à une réduction des taux de mortalité et de réadmission

Mots clés: Unité hospitalière, programme thérapeutique, défaillance cardiaque, pronostic

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Background

Chronic heart failure (CHF) is a global health problem affecting approximately 64 million individuals in 2017 (1). Its prevalence has surged in recent years and it is predicted that it would rise by 46% overall during the next ten years, with an estimated 8 million additional cases by 2030 (2). North Africa, central Europe and the Middle East present the highest prevalence rates (3). Despite the advancements in treatment modalities, the five-year survival rate is only 56.7% (4), 20% of patients are readmitted within the same year, and over 80% within five years (2). In Tunisia, its prognosis is poor, characterized by repeated rehospitalizations and a still worrying mortality rate. According to the national registry of heart failure (NATURE-HF), the one year mortality reached 11% and the rate of mortality and rehospitalization was approximately 17% in patients with CHF (5).

The economic burden of CHF is substantial, primarily due to in-hospital care, which accounts for 60% of the total expenditure (6).

The suboptimal control of morbidity and mortality rates can be attributed to several factors. Therapeutic inertia, characterized by the failure to initiate or intensify therapy when indicated, plays a signs with heart ificant role. Additionally, the complexity of managing HF and non-compliance with dietary recommendations and treatment regimens exacerbates the situation, leading to poor health outcomes despite the availability of effective treatments.

In response to these challenges, the updated guidelines recommend a multidisciplinary management of HF due to its complexity (7)(8).

This global and uncontrolled problem has been identified in the cardiology department of the military hospital in Tunis, and a HF unit adapted to local properties, called the Therapeutic Unit for Heart Failure (TUNI-HF), has been established in March 2021. This unit employs a multidisciplinary program focused on optimizing treatment regimens, managing comorbidities, and providing therapeutic education to patients and their families. The goal is to enhance quality of life while reducing mortality and rehospitalization rates.

In this study, we aimed to describe the effect of the TUNI-HF on HF management and rates of readmission and mortality at 12 months in patients with heart failure with reduced ejection fraction (HFrEF).

Methods

A retrospective observational study was conducted in the Cardiology Department of the military hospital in Tunis, Tunisia. Patients were divided into two groups: those treated before the establishment of TUNI-HF and those treated after. For patients with ischemic etiology, left ventricular ejection fraction (LVEF) was assessed beyond the sixth week post-myocardial infarction (myocardial stunning). The other non-inclusion criteria included age less than 18 years, advanced CHF (INTERMACS profile < 5), short-term life-threatening extra-cardiac disease, and chronic kidney disease requiring dialysis. Exclusion criteria comprised fewer than two visits or hospitalizations during follow-up and non-exploitable data. All survival patients included in the study were informed and their explicit consent were obtained by signing an informed consent form. For died patients, we obtained the consent of their families.

Group “C” (Usual Care):

Group "C" included consecutive patients hospitalized between March 2018 and February 2019 for HFrEF and followed by usual care for one year. It involved cardiologist visits every 3 to 6 months, with routine biological tests (creatinine, electrolytes). The Follow-up of the last patient included was finished in February 2020 before the COVID-19 waves in Tunisia.

Group “U” and TUNI-HF Program

Group "U" comprised consecutive patients hospitalized between March 2021 and February 2022 for HFrEF and subsequently managed under the TUNI-HF program for one year. This multidisciplinary program focused on treatment optimization, comorbidity management, and therapeutic education. The TUNI-HF team included two cardiologists, a nurse specializing in HF management, a dietitian, and a psychologist, with referrals to other specialties as needed (e.g., endocrinology, nephrology). Guideline Directed Medical Therapy (GDMT) optimization was based on ESC guidelines of 2021 (7) and the clinical practice guide carried out by the national authority for assessment and accreditation in healthcare (INEAS) in 2021 and updated in 2022 (9). Visits were planned every Monday. Patients were initially seen biweekly with up-titration of treatments, until achieving the optimal or maximal recommended dose, followed by visits every 1 to 3 months in the absence of incidents. Routine biological assays (creatinine, electrolytes) and electrocardiograms were done every visit. Supplementary tests like cell blood count, liver tests or NTproBNP were performed in particulars cases. A transthoracic echocardiography was performed initially, and repeated if necessary to evaluate left ventricle filling pressure, left and right ventricles function … A six-minute walk test was conducted initially in absence of contraindication and repeated after 3 and 6 months based on special recommendations (10)(11).

Patient education was based on the INEAS clinical practice guide of chronic heart failure management 2021. Therapeutic education was conducted through discussions between patients and nurses, as well as between patients and physicians. It aimed to improve knowledge about names, indications, dosages, and posology of prescribed drugs, as well as their common side effects. On a practical level, patients were educated on how to adjust diuretic dosages and what they must do in case of alarm signs. Hygienic and dietary measures were explained to patients and their families by the dietitian (Appendix figure 1). At every visit, the educational level was assessed using a specific grid (Appendix figure 2).

Endpoints

The primary endpoints were readmission rates and all-cause mortality at one year. The readmission rate was defined as the proportion of patients who had at least one readmission for HF within the year following inclusion, calculated over the total number of surviving patients. The all-cause mortality rate was defined as the proportion of patients who died during follow-up, calculated over the total number of included patients. Secondary endpoints included the prescription rates of GDMT (Beta blockers, Renin Angiotensin Aldosterone Inhibitors and Mineralocorticoid Antagonists) and the rate of implantable cardiac device utilization (Resynchronization therapy and Implantable cardiac defibrillator). The prescription of Sodium-Glucose Transport Protein 2 (SGLT2) inhibitors was not assessed in the group "C" because this class wasn't recommended before 2021.

Statistical Analysis

Data analysis was performed using IBM SPSS version 24 software. Categorical variables were expressed as numbers and percentages. For quantitative variables, we checked the normality of the distribution by the Kolmogorov-Smirnov test and the Shapiro-Wilk test. Continuous variables that were normally distributed were expressed as means and standard deviations, while those that were not normally distributed were expressed as medians and interquartile ranges (IQR). The alpha risk was set at 5% for all statistical analyses. Qualitative variables were compared using the Chi-square test or Fisher's exact test for small sample sizes. Quantitative variables were compared using Student's T-test for means and the Mann-Whitney U test for medians. Kaplan-Meier survival analysis was used to analyze mortality and rehospitalization rates, with comparisons made using the log-rank test.

Results

From March 2018 to February 2019 and from March 2021 to February 2022, a total of 378 and 449 patients were admitted with heart failure with reduced ejection fraction (HFrEF), respectively. Out of these, 108 patients were included in the first group (Group C, usual care), and 110 patients were included in the second group (Group U, TUNI-HF program). The selection of patients is detailed in figure 1.

Baseline characteristics of patients in both groups were comparable, as detailed in Table 1.

Regarding treatments, the prescription rates were comparable between the two groups: more than 70% for BB and RAASI and more than 40% for MRAs. However, both groups exhibited low rates of achieving optimal doses, as shown in table 1.

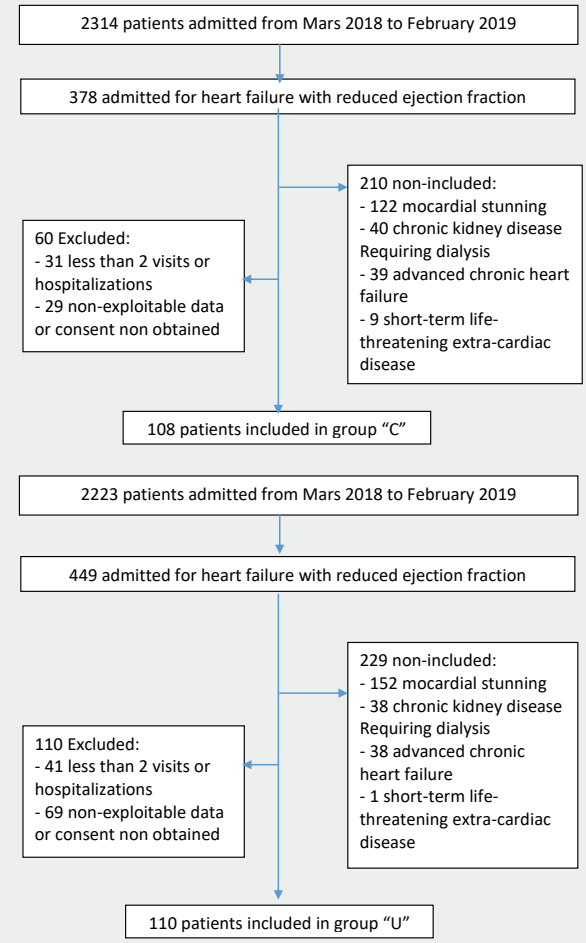

Figure 1. Flow chart of patients' selection

Prescription rates of HFrEF treatments at 12 months

During follow-up in the group "U", SGLT2 inhibitors and angiotensin receptor/neprilysin inhibitor (ARNI) were introduced in 67,9% and 35% of cases respectively. For BB and MRA, novel prescription or up-titration were done in 75.4% and 71,9% in cases respectively.

After 12 months, the prescription rates of beta-blockers (BB) and mineralocorticoid receptor antagonists (MRAs) were higher in Group "U." Additionally, optimal doses of BB, renin-angiotensin-aldosterone system inhibitors (RAASI) and MRAs were more frequently achieved and the prescription of loop diuretics was lower in the same Group.

For non-pharmacological treatment, rate of cardiac implantable devices was higher in the group "U", as detailed in table 2:

Cardiovascular events at 12 months

All-cause mortality and readmission rates at 12 months were lower in the group "U": 6.4% versus 14.8%, (p=0.03; OR 2.55; IC 95%: 1 – 6.49) and 42.7% versus 81.5% (p<0.001; OR=5,9;IC 95% : 3,07 – 11,39;) as shown in figures 2 and 3.

Table 1. Baseline characteristics

	Group "C" N=108	Group "U" N=110	p value
Age (years)	64 ± 8.6	63,5 ± 9.6	0.6
Male (%)	72.2	82.7	0.07
CAD (%)	60.2	65.7	0.4
DM (%)	48.1	56.4	0.2
Hypertension (%)	52.8	55.5	0.7
CKD (%)	24.5	27.8	0.6
NYHA II – III (%)	90.7	90.9	0.4
SBP (mmHg)	120 (IQR 110–140)	120 (IQR110 –140)	0.8
DBP (mmHg)	70 (IQR 60-80)	70 (IQR 70-92)	0.2
HR (bpm)	80 (IQR 74,5–94,5)	80 (IQR 70–92)	0.2
AF (%)	25.9	22.7	0.6
LBBB (%)	30.3	27.5	0.6
Hb (g/dl)	12.6 ± 2.1	13 ± 1.9	0.6
Ferritin (ng/ml)	66 (IQR 45 – 95)	56 (IQR 32-92)	0.2
GFR (ml/min)	71.7 ± 25.3	75.4 ± 27.7	0.2
NT proBNP (ng/l)	3220 (IQR 1295–5000)	2778 (IQR 980 – 4912)	0.2
LVEF (%)	33.5 ± 6.42	30 ± 6.27	0.2
BB (%)	75.9	84.5	0.1
BB optimal doses	21.7	16.4	0.3
RAASI (%)	86.1	78.2	0.1
RAASI optimal doses (%)	33.6	27.4	0.3
MRA (%)	45.4	40.9	0.9
MRA optimal doses (%)	18.7	20	0.5
SGLT2 inhibitors (%)	-	0.9	-
ARNI (%)	-	0	-
Diuretics (%)	87	82.9	0.5
Ivabradine (%)	0.9	2.7	0.8

AF: Atrial Fibrillation; **ARNI**: angiotensin receptor/neprilysin inhibitor; **BB**: Beta-Blockers ;**CAD**: Coronary Artery Disease; **CKD**: Chronic Kidney Disease; **DM**: Diabetes Mellitus; **GFR**: Glomerular Filtration Rate; **Hb**: Hemoglobin level;**HR**: Heart Rate; **DBP**: Diastolic Blood Pressure; **LBBB**: Left Bundle Branch Block; **LVEF**: Left Ventricle Ejection Fraction; **MRA**: Mineralocorticoid Receptor Antagonist; **RAASI**: Renin Angiotensin Aldosterone System Inhibitors; **SBP**: Systolic Blood Pressure; **SGLT2**: Sodium-Glucose Transport Protein 2

Tableau 2. Rates of medical treatments and cardiac implantable devices at 12 months in group "C" and "U"

	Group "C"	Group "U"	p-value
BB (%)	91 (84.3)	102 (94.9)	**0.01**
BB optimal doses (%)	29 (26.9)	87 (80.6)	**<0.001**
RAASI (%)	97 (90.7)	104 (94.5)	0.2
RAASI optimal doses (%)	41 (38.1)	84 (76.4)	**<0.001**
MRA (%)	64 (59.3)	93 (85.3)	**<0.001**
MRA optimal doses (%)	16 (14.8)	78 (71.6)	**<0.001**
SGLT2 inhibitors	-	68 (67.9)	-
ARNI	-	39 (35)	-
Ivabradine (%)	1 (0.9)	10 (9)	**0.002**
Diuretics (%)	101 (94.4)	73 (67.3)	**<0.001**
Cardiac implantable devices (%)	11 (10.8)	23 (20.6)	**0.05**
ICD (%)	3 (2.9)	6 (5.6)	0.4
CRT-D (%)	1 (1)	5 (4.7)	0.2
CRT-P (%)	7 (6.9)	12 (11.2)	0.2

ARNI: angiotensin receptor/neprilysin inhibitor; **BB**: Beta-Blockers; **CRT-D**: Cardiac resynchronization therapy-defibrillator; **CRT-P**: Cardiac resynchronization therapy-pacemaker; **ICD**: Implantable cardioverter defibrillator; **MRA**: Mineralocorticoid receptor Antagonist; **RAASI**: Renin Angiotensin Aldosterone System Inhibitors; **SGLT2**: Sodium-Glucose Transport Protein 2.

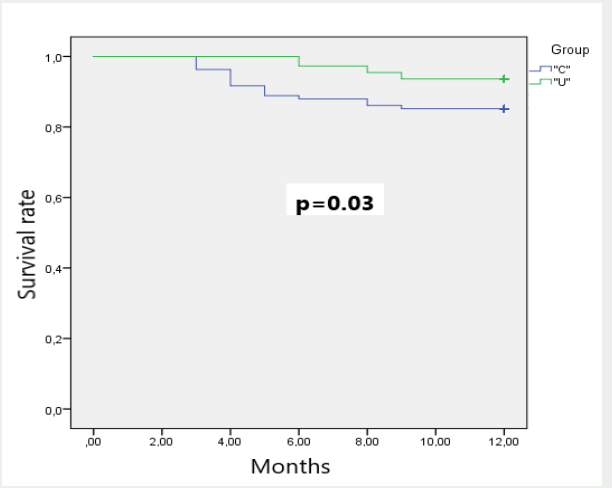

Figure 2. Kaplan–Meier survival curve of patients followed in the TUNI-HF (green line) and those with standard follow-up (blue line)

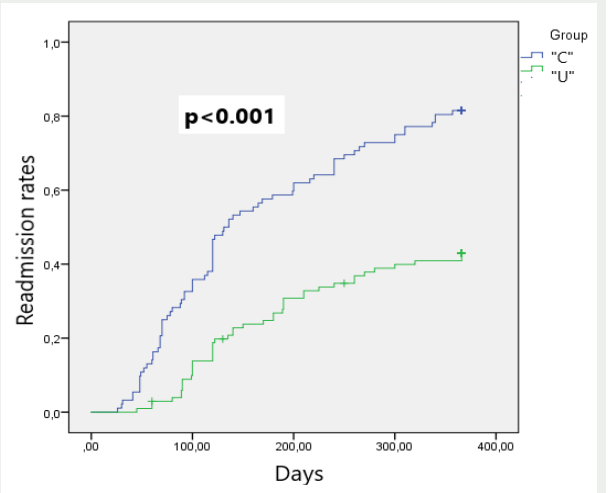

Figure 3. Kaplan–Meier readmission curve of patients followed in the TUNI-HF (green line) and those with standard follow-up (blue line)

Discussion

We conducted a study to evaluate the impact of the Therapeutic Unit for Heart Failure (TUNI-HF) on the management and mid-term prognosis of HF. We Enrolled patients admitted for heart failure with reduced ejection fraction (HFrEF) and followed for 12 months.

The primary endpoints were all-cause mortality and readmission rates at 12 months, while secondary endpoints included the prescription rates of CHF treatments. Patients of group "C" were theoretically followed until February 2020. This fact is important because of the COVID-19 waves in Tunisia which began in august 2020 until march 2021 (12). Consequently, strict measures imposed by the national authorities could have a potential impact on health system in our country (13).

The study sample comprised 108 patients before the establishment of TUNI-HF and 110 patients after. At baseline, patients of group "C" and "U" had many comorbidities such as diabetes (48.1% and 56.4% respectively), coronary artery disease (60.2% and 65.7% respectively) and chronic kidney disease (24.5% and

27.8% respectively) which reflected the complexity of the management of patients with HF in real life. Baseline characteristics were comparable between the two groups. This ensured a balanced comparison between them, allowing for an accurate assessment of the impact of the TUNI-HF program. Concerning GDMT at baseline, prescription rates were approximately 80% for beta-blockers (BB) and renin-angiotensin-aldosterone system inhibitors (RAASI), and 50% for mineralocorticoid receptor antagonists (MRA). These rates were similar to those reported in the Tunisian national registry (NATURE-HF) (5) and other international registries such as ESC HF Long-Term (ESC-HF-LT) registry (14) and ASIAN-HF (15). However, the rates of achieving optimal doses were low in both groups, reflecting a therapeutic inertia that was observed in the national Tunisian registry (15) and in large registries such as CHAMP-HF (United States) (16), CHECK-HF (Netherlands) (17) and BIOSTAT-CHF (11 European countries) (18). Many factors could trigger this inertia. Patients related factors include patients' characteristics (e.g., age, comorbidities, impaired renal function, low blood pressure). Healthcare related factors include the lack of a specialized and structured follow-up with adapted strategies and lack of physicians' awareness (19).

After 12 months, the prescription rates of both medications and their optimal doses increased in Group "U," contrasting with the usual care group. This improvement reflects the impact of TUNI-HF on GDMT optimization, through the initiation of medication in naïve patients or dose adjustments to achieve recommended or maximally tolerated doses, and a structured follow-up to recognize and treat situations that could limit treatment optimization. Similar impacts of HF units on treatment optimization have been reported in several studies. A meta-analysis of 10 randomized clinical trials evaluating the efficacy of HF units in reducing unplanned re-hospitalizations demonstrated increased likelihood of initiating ACE inhibitors/ARBs, ARNIs, BBs, and AAs, and increasing doses of ACE inhibitors/ARBs II. It also showed an increased likelihood of reaching the target dose of ARBs and switching from ACE inhibitors/ARBs to ARNIs (20).

In addition to treatment optimization in TUNI-HF, achieving recommended doses of GDMT was also related to medication adherence by improving knowledge of patients about medications, concept of drug titration, and importance of respecting prescriptions and scheduled visits.

The prescription rate of loop diuretics was lower in Group "U." This reduction reflected improved congestion signs and exercise tolerance, therefore a reducing in symptomatic treatment. These findings align with results from the STRONG-HF study by Mebazaa et al. (21), which reported lower average daily doses of oral loop diuretics in patients receiving high-intensity care. It can be explained also by concomitant prescription of SGLT2 inhibitors (22).

This reduction in loop diuretic use in asymptomatic or pauci-symptomatic patients is necessary to reduce side effects such as dehydration, renal impairment, electrolyte disorder and hypotension.

The rate of implantable cardiac devices was higher in Group "U," suggesting that TUNI-HF program enhances rhythmic management through more frequent identification of patients eligible for cardiac resynchronization therapy (CRT) and implantable cardioverter-defibrillators (ICD), particularly with the increased use of cardiac MRI to identify high-risk patients (23).

Management of HF in TUNI-HF may reduce all-cause mortality and readmission rates at 12 months compared with conventional care, due to the optimization of pharmacological and non-pharmacological therapies and comprehensive management of comorbidities. Similar results were observed in real life. For example, the creation of the HF unit at René Dubos Hospital (Pontoise, France) in 2002 was associated with a reduction in HF readmission and mortality (24). Several meta-analyses confirmed our findings. A first meta-analysis published in the Cochrane database, including 47 randomized clinical trials with 10869 patients, demonstrated that multidisciplinary management likely reduces all-cause mortality and readmissions compared to usual care (25). Another meta-analysis by Van Spall et al. (26), including 53 randomized clinical trials with 12356 patients, showed that specialized clinics providing transitional care after hospitalization for acute HF significantly decreased mortality and readmissions compared to usual care. A third meta-analysis by Ruppar et al. (27), including 48 studies published between 1996 and 2013, reinforced these findings, indicating that interventions to improve therapeutic optimization reduce the risk of mortality and readmission compared to control groups.

Limitations

Our study has several limitations that merit discussion. The single-center, retrospective design, and relatively small sample size limit the generalizability of our findings to the broader population of patients with heart failure with reduced ejection fraction (HFrEF). However, our results were consistent with those reported in the literature.

Furthermore, we studied the impact of TUNI-HF on patients with HFrEF, but it could be beneficial for all patients with CHF regardless of the LVEF. This fact was demonstrated in STRONG-HF: Rapid up-titration of oral medications for HF and close follow-up reduce 180-day death and HF readmission independently from LVEF (28). Additionally, our focus was on the optimization of medical treatments without assessing potential side effects, which could be more prevalent due to the intensive therapeutic approach. Acute renal failure and hypotension are the most common side effects reported in the literature and may influence treatment optimization and prognosis (29)(30). Furthers studies are required to describe the prevalence of side effects and their impact on prognosis in the TUNI-HF. We suggest that these adverse effects did not significantly impact mortality and readmission rates at 12 months in our study, although this was not directly assessed.

Moreover, the two groups were managed during two periods with different guidelines: Group "C" was managed according to the 2016 ESC guidelines (32), while Group "U" followed the 2021 guidelines. The

introduction of new therapeutic options, such as sodium-glucose cotransporter-2 inhibitors (SGLT2-I) in 2021, was not accounted for in the prescription rate comparison. We propose that therapeutic inertia, rather than updated guidelines, was a primary issue.

The TUNI-HF program also had limitations. It predominantly focused on the organic aspects of HF management, neglecting the mental health component. Depression, affecting approximately 20% of HF patients and associated with poorer outcomes (7), was not studied. Future efforts should include depression and mental health management in the TUNI-HF. In addition, cardiac rehabilitation has not been an important part of our program, even though its benefits are proven to improve the quality of life of patients and reduce readmissions (7).

Conclusion and implications

To the best of our knowledge, this is the first published study in Tunisia and North Africa to describe a structured multidisciplinary program for the management of HF and its impact on prognosis.

The establishment of an accessible and specialized HF units, implementing best practices in disease management, improved the prognosis of HF by offering patient detailed medication reconciliation with a structured and close follow-up, comorbidities management, education in a controlled setting, and overall improved continuity of care.

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