


# Application of recommended therapies among patients with heart failure during the Syrian conflict: reality and barriers

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## Abstract

**Aims** Lower socio-economic status may delay and even prevent the application of guideline-directed heart failure (HF) therapy for most patients. This study aims to evaluate the feasibility and possible difficulties facing the application of this treatment during the current Syrian conflict.

**Methods and results** A questionnaire on HF management and feasibility of recommended HF therapy was addressed to physicians practising cardiology in Syria. The questionnaire consisted of 30 questions and focused on the quality of HF management and awareness of recommended drug and device therapy for HF among physicians practising cardiology in Syria. A total of 228 physicians participated in the survey. Awareness of recommended medical and device therapy of HF was very high among participants (98% and 95%, respectively). The majority of participants (>75%) believe that more than half of HF patients do not receive optimal medical HF therapy. Ninety per cent of participants believe that <10% of patients with an appropriate indication for device therapy receive it. More than 75% of participants believe that the cost of medications, alone or in combination with other medical causes, represents the major problem facing the application of optimal HF medical therapy. More than 95% of participants reported that cost alone, or in combination with unavailability, is the primary reason why patients with appropriate indications are not offered device therapy.

**Conclusions** Despite the high level of awareness of recommended HF therapies among Syrian cardiologists, the majority of HF patients are still undertreated. Financial difficulties and lack of resources are the main causes of this problem.

**Keywords** Heart failure; Management; Syrian crisis; Lower socio-economic status

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## Introduction

Heart failure (HF) is a globally progressive condition.<sup>1</sup> All epidemiological parameters of HF are consistently increasing, making it as one of the most rapidly growing cardiovascular (CV) conditions.<sup>1,2</sup> Therefore, HF represents a substantial burden on healthcare systems worldwide.<sup>1–3</sup>

Recently, there is an emerging concern raised on the idea that advances and positive trials in HF have little meaning if

not widely implemented.<sup>1</sup> However, not all patients get the opportunity to benefit from the wide array of indicated medical or device-related HF treatments.<sup>1</sup> In many countries, where HF care is less organized, with delays in follow-up and poor access to cardiology specialists, the application of this complex array of therapy may not be possible.<sup>1,4,5</sup> Certainly, emerging studies are showing that many logistic factors are associated with little or non-use of evidence-based HF therapy, such as lower socio-economic status as measured

by education, income, and marital status, follow-up of treatment by non-cardiologists in addition to providing care in smaller towns and rural areas.<sup>1,4,5</sup> It is known that economic factors may delay and even prevent the application of guideline-directed HF therapy for most patients.<sup>6,7</sup> Furthermore, low socio-economic status has a measurable and significant effect on outcomes of HF patients.<sup>8</sup>

The Syrian crisis has negatively affected the Syrian health-care systems and has led to undertreatment of many CV conditions, including HF.<sup>9–11</sup>

This research aimed to evaluate the quality of HF management in Syria as well as the possible difficulties, which obstacle offering an optimal therapy to HF patients from the prospective of treating physicians.

## Methods

We created a questionnaire in a written and electronic form about management of HF in Syria. The questionnaire was directed to physicians who are practising cardiology in Syria. The written form of the questionnaire was distributed among the 400 physicians who participated in the annual congress of Syrian Cardiovascular Association, which took place in Damascus, Syria, between the 26th and 28th of November 2021. The electronic form was created using an online survey tool (surveymonkey<sup>®</sup>) and was shared via social media 1 week following the congress between the 29th and 5th of December 2021, using a Facebook group called Syrian Heart Society, which contains physicians practising cardiology in Syria. The questionnaire consisted of 30 questions and focused on the quality of treatment of HF, the awareness of European Society of Cardiology (ESC) guidelines-recommended treatment among participating physicians, and feasibility of and possible difficulties, which may face the application of this treatment considering the political and economic conflict. In the absence of national cardiology guidelines in Syria, the ESC guideline was used as it is the most widely used guideline and standard for cardiology practice in Syria. The original and an English translation of the questionnaire including the answers is provided as Supporting Information S1 and S2.

## Statistical analysis

Completed written questionnaires were collected and digitally scanned. Data from the written and electronic forms were entered into a Microsoft Excel spreadsheet. The number and percentage of each response were analysed using Microsoft Excel.

## Results

### Participating physicians

A total of 228 physicians participated in the survey (193 in written form and 35 in online form). A total of 170 participants (74.5%) were younger than 40 years old, 28 participants (12.3%) were between 40 and 50 years old, and 30 participants (13.1%) were older than 50 years old. A total of 41.7% of participants were certified cardiologist, 51.3% were cardiologist in training, and 7% were internists. Place of practice was distributed among private office (30.7%), teaching hospitals (39.9%), and community hospitals (29.4%). Sixty per cent of participants reported seeing approximately 10 to 20 patients with HF daily. Most physicians estimated the number of HF patients to be one-quarter of the patients they treat daily.

### Application of medical HF therapy

Almost all participants reported to be aware of the guidelines-recommend four foundational HF drugs [angiotensin-converting enzyme inhibitors (ACEi)/angiotensin receptor neprilysin inhibitor (ARNI), beta-blockers (BB), mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 inhibitors (SGLT2i)].<sup>3</sup> However, 74% of participants stated that less than half of patients with HF with reduced ejection fraction (HFrEF) receive the four foundational HF drugs, which known to improve prognosis (*Figure 1*).

In addition, 85% of participants reported that less than half of patients with HF with mildly reduced ejection fraction (HFmrEF) received the above medications (*Figure 1*). When a new patient is diagnosed with HFrEF, approximately 60% of participants would start all four medications simultaneously. More than 70% would start ACEi rather than ARNI (*Figure 2*).

Regarding iron therapy, only 40% of participants check the iron status of their patients, with 30% doing so only in patients with overt anaemia. About 25% do not check iron status in their patients at all (*Figure 3*). The great majority of participants >80% reported that less than a quarter of HF patients are treated with ivabradine (*Figure 3*).

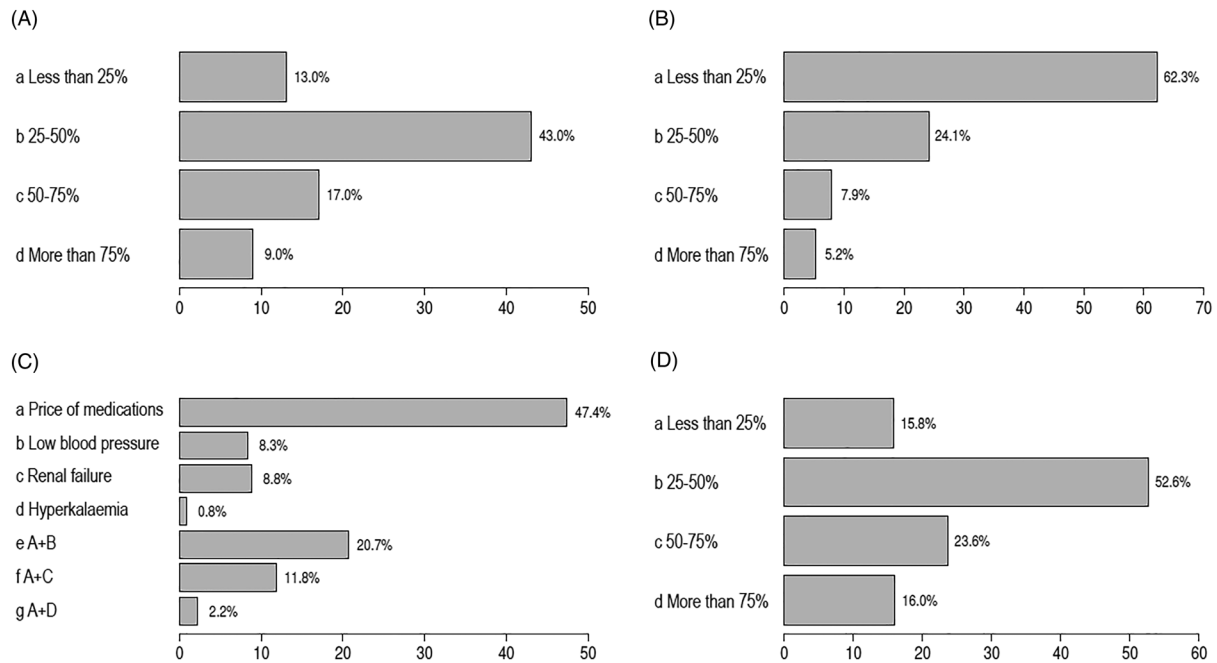
### Application of device therapy

Regarding device therapy, 89% of participants stated that the number of patients receiving an internal cardiac defibrillator therapy (ICD) was <10% of those with an established indication. Similarly, 96% reported that the number of participants receiving cardiac resynchronization therapy (CRT) was also <10% of patients with an appropriate indication (*Figure 4*).

### Diagnostic tests and regular follow-up

Eighty-seven per cent of participants reported arranging follow-up before discharging patients with acute HF. Approximately 60% of participants arrange regular follow-up visits

**Figure 1** Reality and barriers of application of the four foundational HF therapy. (A) Proportion of HF with reduced ejection fraction (HFrEF) patients, with an appropriate indication, who are receiving the four foundational HF drugs? (B) Proportion of HF with mildly reduced ejection fraction (HFmrEF) patients, with an appropriate indication, who are receiving the four foundational HF drugs? (C) What is the most common cause for not putting HF patients on the four foundational HF drugs? (D) What is the percentage of patients who are financially able to afford the cost of HF medications?



every 3 to 6 months, whereas approximately 30% see patients every 6 weeks to 2 months (Figure 5). Regarding determination of brain natriuretic peptide (BNP) levels, only 15% of participants determine BNP levels regularly by their patients. About 30% use it only to confirm the HF diagnosis, and ~43% determine BNP levels only in the case of worsening of symptoms. About 15% stated not to use BNP at all in their practice (Figure 5).

#### Difficulties facing the application of optimal HF therapy

As noted above, more than 75% of participants reported that fewer than half of patients actually receive the four basic HF medications despite appropriate indications (Figure 1). About 48% of participants stated that the price of medications is the main reason that prevents them from prescribing all medications to their patients. More than 30% cited the price of the drug in combination with other reasons, such as hypotension, renal failure, or hyperkalaemia, as a reason for not using these drugs in all patients (Figure 1). Also, more than half of the participants reported the price of the drugs as a reason for not starting patients with newly diagnosed HF on all four drugs simultaneously. In addition, 60% of patients indicated that the high price of ARNI was the main reason for preferring ACEi at the start of HF therapy (Figure 2). About 40% of participants believe that more than half of HF patients are financially unable to pay for their medications. Another

50% believe that 25–50% of patients are financially unable to do so. Regarding device therapy, more than 85% of participants cited cost and unavailability as the main reasons for not using these therapies (Figure 4).

#### Awareness of guidelines-recommended medical and device therapy

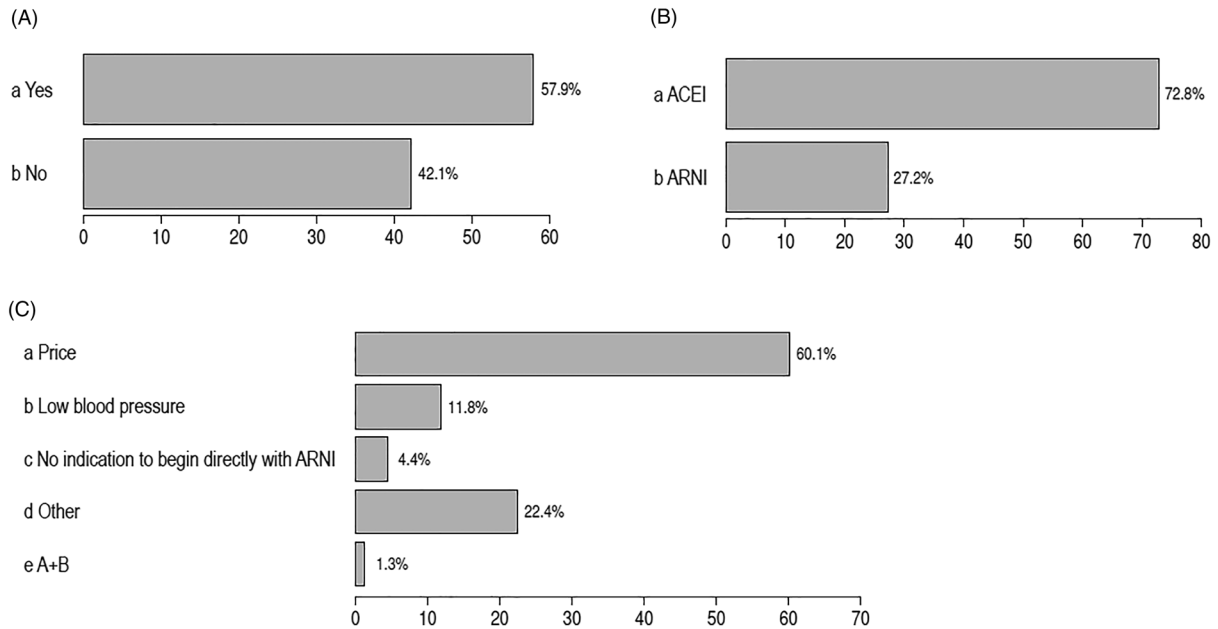
Almost all participants indicated that they are aware of the guidelines-recommended therapy of HF. Less than 5% of participants believe that there is no real benefit to offering ICD or CRT therapy to patients with HF (Figure 4).

## Discussion

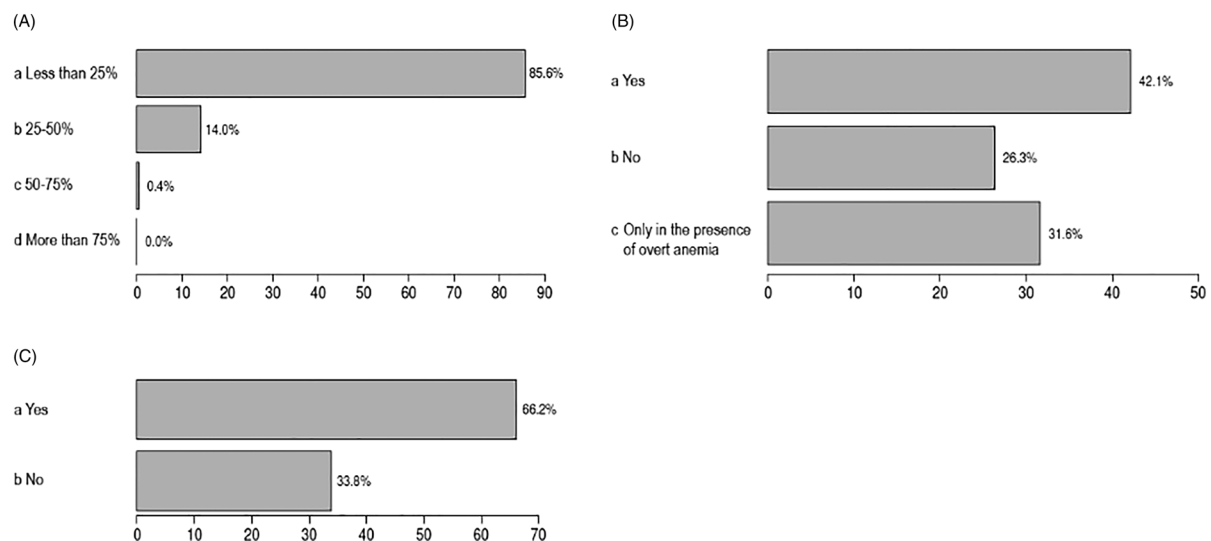
This survey investigated the implementation rate of recommended care for patients with HF in Syria. The primary findings of this study were as follows: (i) The majority of participants are aware of the optimal HF therapy according to current ESC guidelines. (ii) Less than half of HFrEF patients receive the four foundational HF medications, and only ~10% of all patients receive an ICD or CRT. (iii) The main reason for poor implementation of HF treatment is mainly due to cost issues and lack of local availability and experience.

HF is a global health epidemic problem, imposing a substantial burden on healthcare systems across all societies

**Figure 2** Reality and barriers of application of angiotensin receptor neprilysin inhibitor (ARNI) in HF patients. (A) When diagnosing a patient with HF with reduced ejection fraction (HFrEF), do you start simultaneously with the four foundational HF drugs? (B) When diagnosing a patient with HF, do you start with angiotensin-converting enzyme inhibitors (ACEi) or ARNI? (C) What prevents you from prescribing ARNI from the beginning?



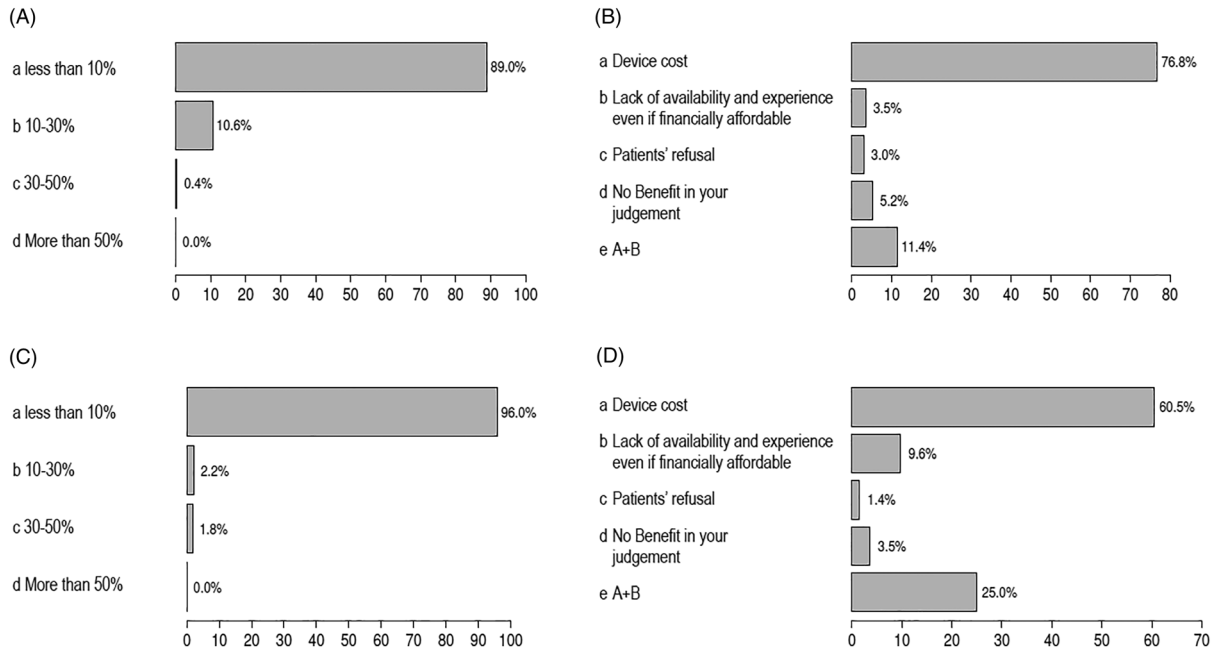
**Figure 3** Reality and barriers of application of other HF therapies. (A) What is the percentage of patients who are receiving ivabradine? (B) Do you determine iron status in patients with HF? (C) Do you give i.v. iron to patients with HF in the case of iron deficiency?



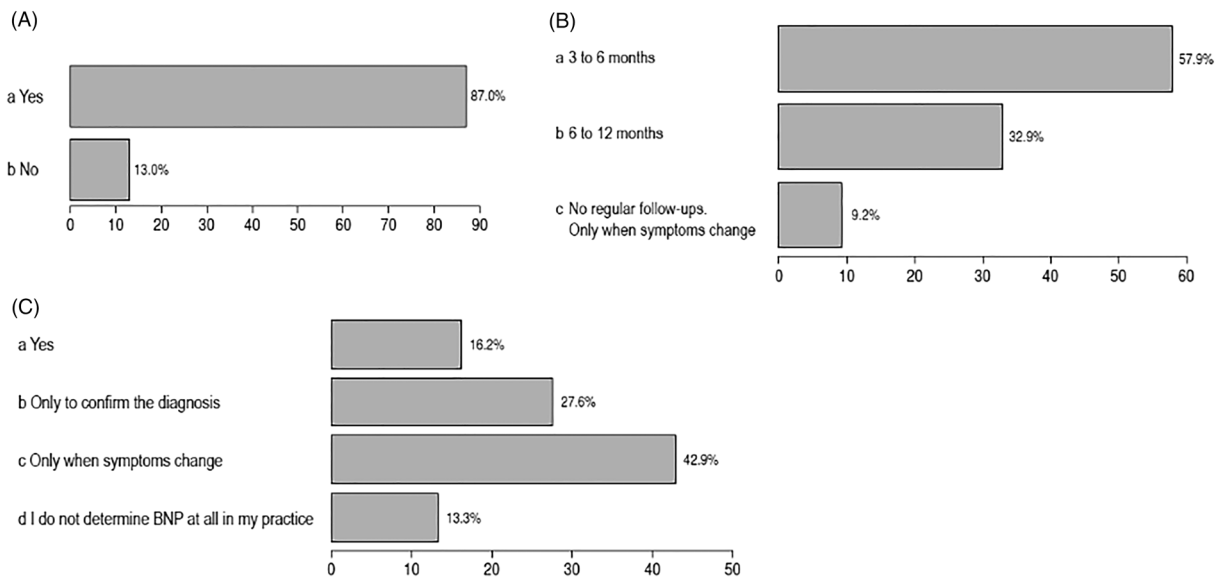
and geographies.<sup>1-3</sup> Recent HF guidelines and recommendations have highlighted the importance of a timely diagnosis treatment for patients with HF to decrease disease progression and improve prognosis.<sup>1-3</sup> Currently, optimization of guideline-directed chronic HF therapy remains the only definitive therapy for HFrEF patients to reduce early death and

hospitalization.<sup>1-3</sup> However, nearly half of the HF patients in our survey do not receive ACEi/ARNI, BB, MRA, or SGLT2i as indicated, and only 40% of physicians regularly check and supplement iron for their patients. In addition, ivabradine was only used in less than a quarter of patients. This highlights the importance of informing and educating

**Figure 4** Reality and barriers of application of devices treatment in HF patients. (A) What is the proportion of patients receiving an internal cardiac defibrillator therapy (ICD), when indicated? (B) What is the cause of that? (C) What is the proportion of patients receiving a cardiac resynchronization therapy (CRT), when indicated? (D) What is the cause of that?



**Figure 5** Follow-up of patients with HF. (A) When discharging a patient with decompensated HF, do you set an appointment for follow-up? (B) How long is the period between regular follow-up in patients with HF? (C) Do you routinely determine BNP levels in HF patients?



physicians about all therapy options beyond the four foundational drugs to treat symptomatic HF patients such as ivabradine. Suboptimal rates of initiation of HF-related pharmacotherapy after HF diagnosis have been reported in

previous retrospective analyses.<sup>12,13</sup> Callender *et al.* showed in their meta-analysis an obvious underutilization of evidence-based medications among HF patients in low- and middle-income countries.<sup>14</sup> They highlighted the importance

of developing and implementing quality improvement programmes in evidence-based management of HF in this region.<sup>14–16</sup> Generally, medical care in Syria is provided by the government, which only provides emergency treatment and only in government facilities and cannot provide outpatient care. As a result, patients unfortunately have to buy the medication themselves.

Nevertheless, available data on low-income countries are likely not representative of these entire regions.<sup>13</sup> Systematic data on HF patients are very limited in low-income countries and specifically in the Middle East. Specifically, there is a lack of knowledge about the specific causes of HF, its treatment, and outcomes in these regions. Our findings add an important value to the limited existing data coming from the Middle East. Our results are in line with the results of other studies by confirming that medication uptake rates remain suboptimal in patients with HF<sub>rEF</sub> despite high awareness of physicians. Beyond physician's awareness, patient's adherence to HF medical therapy represents a significant challenge in improving HF patient outcomes.<sup>17</sup> Therefore, patient education plays an important role in achieving better outcomes for our patients.

During the war years, the healthcare system in Syria has been severely damaged, resulting in a significant shortage of medical instruments, medicines, and local doctors capable of performing complex and novel procedures.<sup>9–11</sup> In addition, the current Syrian economic crisis has placed a significant strain on Syrian healthcare system and Syrian patients, leaving more than 70% of patients unable to receive the necessary treatment.<sup>9–11</sup> This has been shown in our analysis as more than 50% and 90% of HF patients are not able to receive the optimal HF drugs or devices due to high costs. Furthermore, we showed that the absence of local physicians' experience in performing CRT or ICD procedure represents an additional challenge on offering this therapy to HF patients. Therefore, development of educational measures to provide training to local physicians in performing those procedures is needed. Furthermore, developing and strengthening national programmes to develop simple measures for CV diseases, such as delivery of appropriate guideline-directed medical therapy (GDMT), could potentially address some of these shortcomings in such regions and play an important part in health-system improvement and lead to improve physician and institutional practices for HF.

Furthermore, in our survey, 51% of participants were in medical training, which reflects the high rate of physicians visiting the national congress to develop their expertise and bring positive change to their practice despite numerous challenges and deep resource shortages facing the medical field in Syria. In addition, around 75% of participants were under 40 years old, which is another indicator of the current situation in our country, where a majority of the doctors practising cardiology are relatively young. In fact, cardiology certification requirements include 2 years of internal medicine

and 3 years of cardiology training. This also shows the unmet need to train and help young doctors in Syria.

## Limitations

Although this survey represents the first study of HF management in Syria, we acknowledge that it has many limitations. The number of participants was limited and may not be representative of practice across the whole country. Therefore, selection bias cannot be ruled out. Furthermore, due to missing data about the location type of the practice (rural vs. urban) and small sample size for teaching vs. general hospitals, performing sub-analysis might not provide significant differences between subgroups. Although this survey-based research adds valuable knowledge about quality of and difficulties facing the care of HF therapy in Syria, it depends only on an approximate estimation of participating physicians and does not replace the need for a national register studies to obtain solid data about the application of optimal therapies among patients with HF. Furthermore, due to the Syrian war, our results only represent practice in Syria and cannot be transferable and comparable to other developing or developed countries.

## Conclusion

Despite the high level of awareness of recommended HF therapy among Syrian cardiologist, a large proportion of HF patients remain undertreated and not well controlled. High costs of therapies, shortage of medical instruments and medications, and the experience of local physicians represent the major causes of this problem.

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## Conflict of interest

None declared.

## Supporting information

**Data S1.** Supporting Information.

**Data S2.** Supporting Information.

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

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