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STUDY DESIGN

Digital consults to optimize guideline-directed therapy: design of a pragmatic multicenter randomized controlled trial

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Abstract

Aims Many heart failure (HF) patients do not receive optimal guideline-directed medical therapy (GDMT) despite clear benefit on morbidity and mortality outcomes. Digital consults (DCs) have the potential to improve efficiency on GDMT optimization to serve the growing HF population. The investigator-initiated ADMINISTER trial was designed as a pragmatic multicenter randomized controlled open-label trial to evaluate efficacy and safety of DC in patients on HF treatment.

Methods and results Patients (n = 150) diagnosed with HF with a reduced ejection fraction will be randomized to DC or standard care (1:1). The intervention group receives multifaceted DCs including (i) digital data sharing (e.g. exchange of pharmacotherapy use and home-measured vital signs), (ii) patient education via an e-learning, and (iii) digital guideline recommendations to treating clinicians. The consults are performed remotely unless there is an indication to perform the consult physically. The primary outcome is the GDMT prescription rate score, and secondary outcomes include time till full GDMT optimization, patient and clinician satisfaction, time spent on healthcare, and Kansas City Cardiomyopathy Questionnaire. Results will be reported in accordance to the CONSORT statement.

Conclusions The ADMINISTER trial will offer the first randomized controlled data on GDMT prescription rates, time till full GDMT optimization, time spent on healthcare, quality of life, and patient and clinician satisfaction of the multifaceted patient- and clinician-targeted DC for GDMT optimization.

Keywords Heart failure; Clinical trial; Guideline adherence; Digital health

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Trial registration: *NCT05413447.*

Introduction

Heart failure (HF) affects more than 64 million people worldwide.[1] In 2012, the global economic burden associated with HF was estimated to be $108 billion annually, and this concerning economic burden is projected to rise due to an increasing prevalence.[2] In this growing HF epidemic, the number of healthcare professionals managing HF remains limited and thereby poses a challenge to deliver optimal care.

The prognosis of patients with HF has improved considerably since the introduction of several HF therapies a few decades ago.[3] Current recommendations for the treatment of patients with HF with reduced ejection fraction (HFrEF) in the 2021 European Society of Cardiology Guidelines for the di-

agnosis and treatment of acute and chronic HF include the following guideline-directed medical therapy (GDMT): beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), angiotensin receptor–neprilysin inhibitor (ARNI) as a replacement for ACE or ARB, and mineralocorticoid receptor antagonists (MRAs), along with sodium–glucose cotransporter-2 inhibitors (SGLT2-is).[3,4] In HFrEF patients, the estimated aggregate benefit is greatest for a combination of beta-blocker, ARNI, MRA, and SGLT2.[5] It is advised to set up GDMT with rapid sequencing and avoid delays.[6–14] Nonetheless, there is a substantial proportion of GDMT underuse where slow optimization, low target dose achievement, and/or discontinuation have been reported.[1,15,16] Furthermore, race/ethnicity, gender, and socio-economic status also impact GDMT use.[17] The explanation for the structural worldwide underuse of GDMT is multifactorial and includes inter-doctor and inter-hospital variation. Digital consults (DCs) including (i) digital exchange of remote measurements, (ii) tailored digital summaries of important clinical information and guideline recommendations, and (iii) the exchange of an e-learning on HF and medication in HF might be useful to improve GDMT prescriptions.

There are various types of DCs and remote care.[18–21] Many types of DC have the potential to improve efficiency on GDMT optimization to serve the growing HF population.[22] Especially during the COVID-19 pandemic, a lot of experience has been gained with video consults (VCs).[23,24] Even in older patients, VCs have been suggested as an additional tool both (i) to supporting self-caring patients with cardiovascular disease to maintain their independence and improve the management of their cardiovascular disease and (ii) to improving the prevention, detection, and management of frailty and supporting collaboration with caregivers.[25] In inflammatory bowel disease, a multifaceted digital intervention has been proven efficacious and safe.[26] In this trial, we chose to adopt this multifaceted approach to achieve the most optimal result of DC in HFrEF patients. Previous studies have indicated that a remote strategy for GDMT optimization might be useful to improve GDMT usage. However, multicenter randomized controlled trials (RCTs) on triple or quadruple GDMT optimization are lacking. Hence, the Assessment of Digital consults on clinical Impact and Efficiency using an RCT (ADMINISTER) was designed to evaluate efficacy and safety.

Study design

We designed a prospective investigator-initiated pragmatic multicenter RCT to evaluate the effect of DC on GDMT optimization, time spent on healthcare, and quality of care. Furthermore, we evaluate satisfaction of the DC intervention on the level of both the patient and clinician. The design of the study is shown in *Figure 1*. The primary hypothesis of this study is that DC improves GDMT prescription rates. Secondary hypotheses are that DC improves quality of life (QoL) and reduces time spent on healthcare for patients. The study is being conducted at four centers in the Netherlands, with a case mix of two academic tertiary referral centers (University Medical Center Utrecht and Amsterdam UMC, both at location AMC and at location VUmc) and two non-academic hospitals (Cardiology Center of the Netherlands and Red Cross Hospital). The sites and local principal investigators are listed in *Table 1*. Patient enrolment for this study is done after informed consent was acquired. The local medical ethics committees issued a waiver for this study because two routine treatments are compared (DC or standard) and the patient burden is limited to only two questionnaires. The authors

Figure 1 Flowchart of study procedures and outcomes of the ADMINISTER trial. GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction.

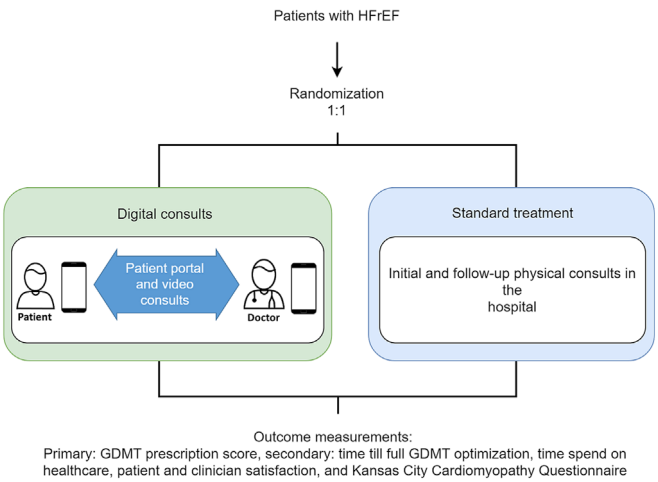


Table 1 Participating locations with corresponding principal investigator

Location	Principal investigator
Amsterdam University Medical Centers (AUMC) location AMC	Mark J. Schuuring
Amsterdam University Medical Centers (AUMC) location VUmc	M. Louis Handoko
Cardiology Center Netherlands (CCN)	Michiel M. Winter
Red Cross Hospital	Maarten A. C. Koole
University Medical Center Utrecht (UMCU)	Pim van der Harst

are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents. The trial is registered at ClinicalTrials.gov Identifier NCT05413447. Results will be reported in accordance to the CONSORT statement.[27]

Patient selection

Patients diagnosed with HFrEF (defined as left ventricular ejection fraction ≤ 40) above 18 years of age from four participating centers in the Netherlands are eligible for this study. Inclusion and exclusion criteria are listed in *Table 2*. All different aetiologies of HF may be included in this study as patients with HFrEF because they share similar up-titration schemes of GDMT. Patients with New York Heart Association class II or higher are included. Patients who do not understand the Dutch language are excluded. Patients with an active COVID-19 infection are excluded as well. Cardiologists and nurses are allowed to not include patients based on suspected unsuitability for participation in this trial. The reasons for nurses and cardiologists to not include patients are as follows: difficult telephone accessibility, terminal diagnosis, suspected difficulty in comprehending the study, and participation in other studies. Patients will be recruited from both the ward and outpatient clinics. If a patient meets all inclusion criteria and is not violating any of the exclusion criteria, the patient is provided a detailed explanation of the study and is asked for informed consent.

Randomization

Patients are randomly assigned to a DC or standard care (*Figure 1*). Randomization is performed by the investigator using a computerized randomization tool (Castor EDC). Patients are randomly assigned in 1:1 ratio stratified by HF de novo, established HF, and hospital. A variable block randomization algorithm with block sizes of 2, 4, and 6 is used.

Digital consult as multifaceted intervention

Patients randomized to the DC intervention receive a multifaceted intervention constituting of the following actions.

Table 2 Inclusion and exclusion criteria

Inclusion criteria
Age $>$ 18 years
HFrEF (LVEF $\leq$ 40%), all aetiologies
NYHA class II or higher is included
Exclusion criteria
Dutch language barrier
No GDMT optimization possible
Active COVID-19 infection

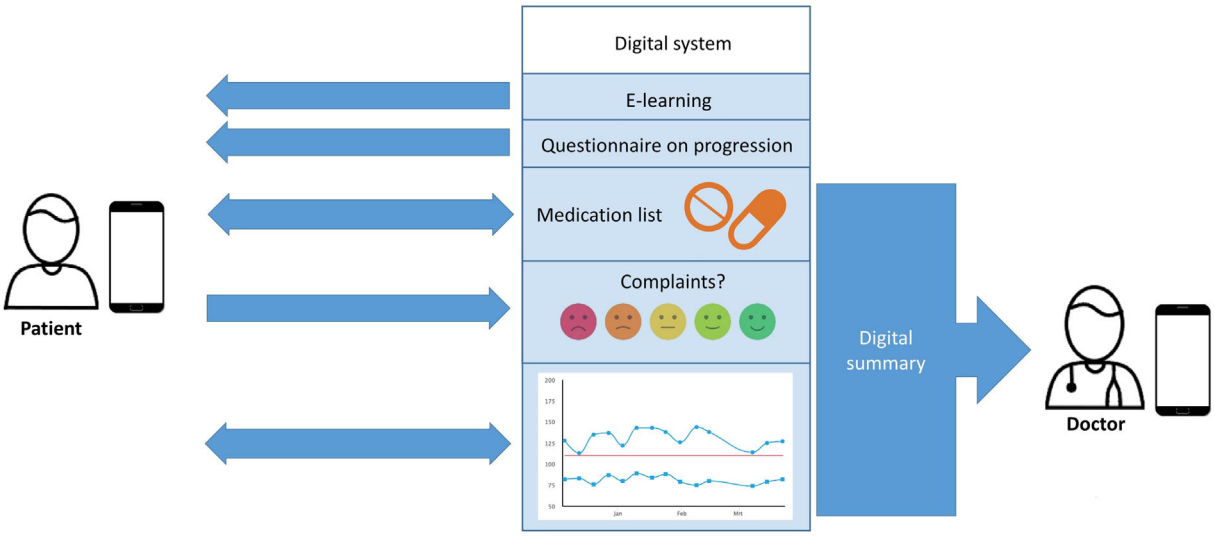
GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Preparing the digital consult

A researcher collects home-measured heart rate (HR) and blood pressure (BP), results of an e-learning, information on medication, and relevant lab results digitally and passes all this information to the medical professionals using existing healthcare portals. This information will be combined with tailored information on guideline recommendations for a patient with a particular focus on GDMT optimization (see *Figure 2*). Conditional guideline recommendations are not taken into account in this study in order to be able to apply the same intervention to all patients and keep the provided e-learning and guideline recommendation to the medical professionals relatively short for all patients. The data are shared in the following way:

1. Pharmacotherapy use and home-measured vital signs are shared and exchanged using Castor EDC. If the patient has no BP monitor, it is provided to them for the duration of the study. Dedicated portals such as the MyChart (Epic, Verona, WI, USA) are encouraged to patients but are not mandatory for the trial.
2. Questionnaires to assess symptoms are sent to patients via Castor EDC.
3. Patients receive education on HF via an e-learning emailed to patients in the intervention group. This is based on information of http://www.heartfailurematters.com. It is only available in Dutch and also accessible via http://www.administer-trial.com/ with a password. The standard care group does not receive the password. The patient also receives information on the latest development in medication for HF and its benefits.

Figure 2 Information flow of digital consults in the ADMINISTER trial.



Performing the digital consult

The first consult in planning and all follow-up consults over a period of 12 weeks after the first consult (which is the baseline) will preferably be held via video (Microsoft Teams, Redmond, WA, USA) or via telephone. The use of a real-time video is however encouraged as it preserves important aspects of communication that cannot be accommodated over the telephone, such as visual interaction and non-verbal cues.[23] However, consults in person are also allowed in the intervention group if deemed necessary by the treating clinician.

Control group

If the patient is drawn into the control group, the patient will receive standard care. Clinicians are free to use all standard modes of communication and are not specifically encouraged to use remote types of communication. The trial is open labelled as it is immediately apparent when a patient is allocated to the treatment group and clinicians need to know when to use the treatment strategy in the treatment group. Clinicians are not informed about the assignment of a patient to the control group to optimally capture remote practice.

Clinical data

Clinical data of participants are collected to describe the patient population. These include data from medical history, vital parameters, 12-lead electrocardiogram, trans-thoracic echocardiography, and laboratory markers at baseline.

Outcome measures

Primary outcome

The primary outcome is a GDMT prescription rate score. This is calculated by the received dose divided by the target dose at 12 weeks after the first consult. The score will range per pharmacotherapy between a maximum of 1 (corresponding with the optimal treatment according to the guidelines) and a minimum of 0 (corresponding with not administering the medicine). The maximum score per patient is 6 (all 'foundational four' pharmacotherapy constituting GDMT at target dose, a switch to ARNI, and adequate iron status). GDMT prescriptions include the following:

1. ACE/ARB/ARNI dose;
2. because ARNI is recommended as a replacement for ACE, an extra score of 1 is added for a replacement of ACE with ARNI;
3. beta-blocker dose;
4. MRA dose;
5. SGLT2-i dose; and
6. intravenous iron administration dose if the patient has iron insufficiency defined by ferritin $<$ 100 ng/mL or ferritin $<$ 300 ng/mL with transferrin saturation $<$ 20%.[3] For patients with periodic screening for iron deficiency and appropriate supplementation, a score of 1 is allocated.

Contraindications to the prescribed medications are determined by a cardiologist, and a valid contraindication will count as 1. Common contraindications are as follows:

1. systolic BP $\leq$ 90 mmHg (contraindication for all four drugs);
2. symptomatic hypertension;

3. estimated glomerular filtration rate (eGFR) $\leq$ 30 mL/min/1.73 m^2 (contraindication for ACE/ARB/ARNI and MRA);
4. eGFR $\leq$ 20 mL/min/1.73 m^2 (contraindication for SGLT2-i);
5. potassium $>$ 5 mmol/L (contraindication for ACE/ARB/ARNI and MRA);
6. HR $\leq$ 60 b.p.m. (contraindication for beta-blockers); and
7. allergy to a medication group.

Secondary outcomes

The following secondary outcomes will be collected:

1. For the patients who reach optimal GDMT, the time till full GDMT optimization will be reported.
2. The patient is asked to fill in their time spent on healthcare during the study period. This is performed directly from Castor EDC as part of a questionnaire and filled in by the patient.
3. The QoL will be evaluated with the Kansas City Cardiomyopathy Questionnaire at the start and end of the trial period. This is a validated questionnaire.[28]
4. Satisfaction of the patient is evaluated with the Net Promoter Score (NPS).[19] To determine this score, the patient is asked to fill in a score (1–10) indicating the likelihood that he or she will recommend the provided healthcare to a friend or colleague. NPS is distributed via Castor EDC as part of the questionnaires sent to the patient.
5. Satisfaction of the HF nurses and clinicians with DC is evaluated with the NPS as well. To determine this score, the cardiologist is asked to fill in a score (1–10) indicating how likely it is that he or she will recommend the currently provided healthcare to a colleague. Castor EDC will be used to distribute the questionnaires to the participating cardiologists and nurses.
6. Data on the safety of DC are acquired by reporting hospitalizations during the trial period. Decreases of eGFR below 30 and hypokalaemia $>$ 5.0 mmol/L are recorded as well to assess safety.
7. The healthcare consumption including the frequency of remote consults and physical consults (PCs) will be recorded to assess the efficiency of the remote consults.

Statistical considerations

The required sample size is calculated from a superiority perspective, using the primary outcome. Division into de novo and established HF is done because of differing reasons for potential under treatment and different baseline values. It is uncertain if the benefit of the intervention will differ between strata and is therefore assumed to be equal for all strata. According to the sample size calculation in nQuery (Statsols, Los Angeles, CA, USA), a sample size of 71 in the control and intervention groups will have 80% power to detect a difference in means of 0.36 (the difference between a Group 1 mean, μ_1, of 2.26 and a Group 2 mean, μ_2, of 1.9) assuming that the common standard deviation is 0.76 using a two-group *t*-test with a 5% two-sided significance level. The sample size calculation is based on 53 patients treated for HFrEF in 2022 between 01 January 2022 and 20 March 2022. To facilitate a 5% dropout, in total, 150 patients will be enrolled. This sample size seems feasible given the number of visiting patients with HFrEF. The treatment effect is estimated to be a 0.36 increase in the primary outcome. This constitutes to one in three patients receiving the target dosage for one medicine or getting an order for iron screening after 12 weeks of being in the intervention group.

For statistical analyses, SPSS 28.0 (SPSS Inc., Chicago, IL, USA) for Windows is used. A two-tailed probability value of $<$0.05 is used as a criterion for statistical significance. Descriptive data will be presented as number with percentage, as mean with standard deviation, or as median with range when appropriate. The primary analysis will be according to the intention-to-treat principle. Chi-squared test for qualitative data and independent *t*-test for quantitative data will be applied to detect differences between the intervention group and the standard care group at baseline if the data are normally distributed. If there are significant differences between groups on parameters that could influence the study outcome, we will perform covariate-adjusted comparisons as a secondary analysis. Differences between baseline and follow-up within groups will be assessed using a paired *t*-test. To detect differences in the outcomes between the DC and standard care groups, again, χ^2 test and independent *t*-test will be applied.

Data management

A Data Privacy Impact Assessment was performed by the hospital's data protection officer. All patient data will be stored in the electronic record system (Castor EDC) allowing for safe and transparent record keeping. This policy is in accordance with Dutch regulations. Access to Castor EDC is only granted to employees involved in this trial. To limit missing data, reminders are sent to participants to fill in their questionnaires. In cases where missing data are unavoidable and data could not be retrieved, imputation can be used to still perform a proper analysis.

Timeline and trial enrolment

Patients will be enrolled in the study from September 2022. The end of enrolment is expected in December 2023.

Discussion

The current study is the first investigator-initiated pragmatic multicenter RCT that evaluates the effect of DC on HFrEF pa-

tients with indication for GDMT optimization. A heterogeneous group of patients, clinicians, and clinical practices is included to maximize the applicability of these results to everyday practice. As GDMT optimization is recommended for all patients with HFrEF, a diverse selection of patients with a wide variety of different aetiologies for HFrEF and treated by different clinicians seems appropriate in this trial. Pilot studies on the assessment of DC are promising so DC has the potential to improve efficiency on GDMT optimization. The ADMINISTER trial will offer the first robust data of GDMT prescription rates, time till full GDMT optimization, time spent on healthcare, patient and clinician satisfaction, QoL, and safety.

Efficacy of digital consults

E-learning and exchange of digital information in heart failure

In patients with HF, there are three RCTs with more than 100 patients in which the effects of digitally exchanging e-learning and other digital information are measured.[29–32] In an RCT by Ross *et al*. on 117 patients with HF, the effect of a platform containing access to electronic medical records, information about the disease of the patient, and a messaging system for communicating with the nursing staff is tested.[29] Self-efficacy, health status, patient satisfaction with doctor–patient communication, adherence to medications, and adherence to the medical regiment were assessed using questionnaires. In this study, a better adherence to medical advice for the patients using the platform was reported (P = 0.02 accounted for multiple testing); the other metrics were not significantly different. In an RCT by Brennan *et al*., patients gained access to specific aspects of a digital platform with a messaging system, patient-specific information, and the ability to track relevant health parameters.[30] The patients received access to a part of the platform based on the needs of the patient as assessed by a nursing staff. In the 146 included patients, the health status, QoL, self-management capabilities, and satisfaction with nursing care were measured using questionnaires. A short-term improvement in health status and QoL in patients who gained access to a portal was reported. The other metrics were not significantly different. Dang *et al*. assessed the feasibility of a digital platform among patients with HF in an RCT with 102 included patients.[31] In 53 of these patients, the QoL, HF knowledge, and self-management capabilities were measured. An improvement in QoL was found. In conclusion, different studies and, thus, different platforms resulted in different improvements as assessed with questionnaires. However, key success factors of these platforms for the exchange of an e-learning and other digital information have not yet been identified.

Remote consults

Performing a consult with VCs has been shown to save patients time by eliminating travel time and retaining similar time spent on consult and waiting time for the doctor. The time saved is reported to be on average between 39 and 121 min, depending on the hospital.[33–35] Satisfaction regarding VCs is reported to be equal to PCs.[23,36] However, several studies have reported that in 71–97% of the patients receiving VC, patients would like future appointments to also be a VC.[23,33] In non-cardiac patients, VCs have been shown to be non-inferior to standard care for guideline adherence of patients with obstructive sleep apnoea, monitoring of chronic wounds, and cognitive behaviour therapy for insomnia.[37–39] The implementation of VC in routine clinical practice has however remained limited. This is hypothesized to both be a result of increase in workload associated with familiarization with the technique and be a result of doctors falling back on what they are used to do, what they are trained to do, and what they enjoy.[23,40] Three studies have compared the effectiveness of VC to standard care in cardiology.[41–43] Two of those comparisons occurred during an emergency upscaling of VCs due to the COVID-19 pandemic. Yuan *et al*. compared telephone consults and VCs to standard care in patients with chronic HF, and Offiah *et al*. compared VC to standard care for all-comers cardiac patients. Both studies reported lower amounts of ordered diagnostic tests per VC compared with standard care; in VC, 32.2% and 38.5% of the total amount of VCs resulted in the ordering of diagnostic tests compared with 55.7% and 65.5% for PCs.[41,42] Both studies also reported a lower number of prescribed medications in VCs; in the study of Offiah *et al*., 19.9% of the VCs resulted in changes in the medical treatment compared with 38.5% for PCs, while Yuan *et al*. reported a lower odds for prescribing medication in VCs compared with PCs, odds ratio: beta-blockers [0.82 (0.68–0.99)], MRAs [0.69 (0.50–0.96)], nitrates [0.18 (0.04–0.90)], hydralazine [0.29 (0.10–0.82)], and loop diuretics [0.67 (0.53–0.85)]. Yuan *et al*. also compared differences in emergency department visits, mortality, and hospitalizations of VCs to PCs, which were not significant. This might, according to the authors, be due to a low event rate. The lower orders of diagnostic tests might indicate that clinicians underestimate complaints in the patients receiving a VC. However, in both studies, there are some important limitations regarding the generalizability of the results. First, patients who are not suitable for VC (such as patients for which a physical examination is recommended) were also scheduled for a VC during the large upscaling of VCs during the COVID-19 pandemic. This is arguably not the right approach for a long-term implementation as physical examinations are beneficial for certain types of consults and patients. Second, in the study of Offiah *et al*., VCs during the COVID-19 pandemic were compared with PCs before the pandemic, while in the study of Yuan *et al*., VCs were compared with PCs during the pandemic. This means that in the study of Offiah *et al*., the observed differ-

ences might have partly occurred due to the COVID-19 pandemic. In the study of Yuan *et al*., VCs might have been more frequently employed for specific purposes such as a long-term follow-up after an intervention or as a substitute for routine checkups. This would lead to a potential bias towards more diagnostic tests and more medical changes in the PC group. Considering these limitations, VCs might still be effective for a specified group of patients. An example of this is that in patients with chronic HF who received remote support meetings instead of physical support meetings, no significant differences were found in mortality and hospital admissions.[43,44] There is thus arguably a need to further investigate which patients in cardiology can benefit from remote consults.

Remote consults for guideline-directed medical therapy optimization

Structural worldwide underuse of GDMT is likely multifactorial but includes an under-appreciation for the benefits of the medication, an overestimation of the risks, and clinician-related factors.[45] Regarding the overestimation of risks, the European Society of Cardiology guidelines accept a significant deterioration of kidney function to titrate GDMT (to a complete doubling of the creatine value). In practice, professionals are much more cautious for kidney function deterioration, and therefore, GDMT maximum dose is often not reached.

In patients with chronic HF, interventions helping patients in the form of, for example, education, reminders, or structured telephone support have been shown to be effective in increasing medication adherence in a meta-analysis by Ruppar *et al*.[46] Interventions targeting clinician have also been shown to be effective in increasing the adherence of clinicians to the guidelines in patients with chronic HF in a meta-analysis by Shanbhag *et al*.[47] Both patient- and clinician-orientated measures are thus shown to be effective for the optimization of GDMT.

In a study by Desai *et al*., GDMT is remotely optimized by paramedic navigators using a titration algorithm based on the HF guidelines of the American Heart Association.[48] The authors wanted to test if a remote algorithm-driven and navigator-administered optimization program can increase GDMT. With remote consults occurring every 2 weeks, they managed to significantly increase the dose from 70.1% to 86.3% for ACE/ARB/ARNI and from 77.2% to 91.9% for beta-blocker, while no increase was observed in the control group. However, this study has important limitations as patients who refused to participate and patients in whom the clinician declined to participate were assigned to the control group. This may have led to an important selection bias that is reflected in an older age [68 (±14.5) vs. 66 (±12.7)], less treatment by an HF specialist (33.5% vs. 44.3%), and a lower eGFR [65 (±18.7) vs. 60 (±19.1)] in the control group. A total of 1028 patients were included in this study (197 were assigned to the treatment group and 831 to the control group). In a pilot study by Artanian *et al*.,49 telemonitoring was used to titrate 42 patients [21 (treatment) and 21 (control)] using a telemonitoring app to send alerts to clinicians in case of at-home measurements and with remote consults every 2 weeks. This strategy resulted in an optimization speed of 11.8 in the treatment group vs. 18.8 in the control group. There are however limitations regarding the external applicability of the study of Artanian *et al*.49 as it is single center and requires dedicated HF staff to adopt a telemonitoring strategy with alerts sent to clinicians. Massot *et al*.22 have evaluated 96 patients in a retrospective analysis. Median duration of tele-titration consult was reported to be 42 days. And with only 2% major events in the event group, it was reported to be a fast and safe strategy. This is however a retrospective analysis, and therefore, important cofounders could influence the reported result especially because baseline characteristics were not extensively reported. The role of DC on GDMT optimization thus remains unclear. This multifaceted intervention focused on remote consults, exchange of e-learning and other digital information, and providing summaries and advice on GDMT optimization to clinicians.

Guideline-directed medical therapy optimization in practice

In GDMT optimization, a patient may have a contraindication for optimization of certain medication group. This means that guideline-indicated target dosage for a specific medication is not reached for that medication group. The contraindications of BP (≤90 mmHg) and HR (≤60 b.p.m.) occur at different dosages depending on the reaction of the patient to the treatment. This treatment reaction is different for each patient, and the maximal tolerable dosage thus varies for a large portion of patients. Because of the variability between the maximal tolerable dosages, GDMT can be considered as a sliding scale that varies between patients.

Limitations

Patients with HFrEF display a wide range of clinical profile, both in variety and in severity. Not all patients of older age use digital solutions.[50] These patients might be less inclined to participate in a study, as they feel that they have a barrier to this modern way of care delivery. Conversely, patients with good digital skills may be more likely to participate. This might create an inclusion bias. In this trial, clinicians are not informed to a control group assignment to optimally capture local practice; however, in some cases, assignment to the control group might be deduced.

Future implications

Digital technologies and communication systems have opened new avenues for efficient communication and digital control of health parameters. The familiarity of patients with these digital communication systems is likely to increase in the future, and more efficient monitoring systems are likely to become available.[25] Consequently, an increasing number of patients may become eligible to receive remote digital GDMT optimization. Adequate patient selection is and will likely in the future however still be necessary to identify patients suitable to a digital setting. For a successful adoption of a digital setting in a large patient group among multiple healthcare centers, it is likely to be essential that the systems are effective in replacing care and a solution to the issue of GDMT optimization.[51]

Conclusions

The current study is the first RCT that evaluates the effect of DC on HFrEF patients with an indication for GDMT optimization. The ADMINISTER trial is expected to offer the first robust data of GDMT prescription rates, time till full GDMT optimization, time patients spent on healthcare, patient and clinician satisfaction, and QoL for DC.

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Conflict of interest

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