Concept for Visualisation of Guideline Adherence of Medication Prescriptions in a Heart Failure Telehealth System

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Abstract. Background: Heart failure is a chronic disease that affects around 26 million people worldwide. Projections assume a substantial increase in prevalence over the next years. To improve the survival rate and quality of life in patients suffering from heart failure, the European Society of Cardiology published guidelines for diagnosis and treatment. Adherence of healthcare professionals' medication prescriptions with regard to these guidelines is critical for optimal outcomes. Methods: Data from the conceptional phase of the existing disease management network 'HerzMobil Tirol' were analysed. Prescriptions and patient-reported intake data of the four major substances of recommended heart failure medication were used to calculate the relative prescribed doses as a percentage of the recommended target doses. A concept for visualisation of the prescription status was developed in cooperation with health professionals. Results: The documented prescriptions were analysed and used to develop a mock-up in order to visualise the prescription status for the individual patient. Conclusion: Analysis and visualisation can be managed by displaying the calculated daily relative dose per substance group in a traffic light system.

Keywords. heart failure, telemedicine, prescriptions, medication adherence, guideline

1. Introduction

1.1. Heart failure – Demographics and ESC guidelines

Heart failure (HF) is a chronic disease that affects around 26 million people worldwide. Projections assume an increase in prevalence [1]. In 2018, there were 24,315 hospital admissions for acute HF in Austria [2]. The readmission rate within the first year post discharge is 61.3% with a median survival rate of 1.75 years [3].

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In 2016, the European Society of Cardiology (ESC) published the updated version of the guidelines for the diagnosis and treatment of acute and chronic HF [4]. A substantial part of the guidelines addresses the pharmacological treatment of HF using reduced ejection fraction (HFrEF) which include:

- Angiotensin-converting-enzyme inhibitors (ACE-I)
- Beta-blockers
- Mineralocorticoid receptor antagonists (MRA)
- Angiotensin receptor blockers (ARB)
- Angiotensin receptor neprilysin inhibitors (ARNI)
- I_F-channel blockers
- Diuretics

ACE-I and beta-blockers are considered first-line therapy to improve symptoms and reduce the risk of heart-failure related hospitalisation and mortality. In case of ACE-I intolerance, it is recommended to switch to ARBs. MRAs are indicated in patients with persisting symptoms and left ventricular ejection fraction (LVEF) ≤ 35%. Ivabradine is an I_F-channel blocker used in combination with the aforementioned substances in patients with an elevated heart rate and LVEF ≤ 35% when beta-blockers are contraindicated or do not suffice to reduce the heart rate to below 70/min. Depending on symptoms, drugs should be started at a low dose and be up-titrated over the course of several weeks to a recommended target dose, whilst not contraindicated.

Diuretics are prescribed to improve signs of congestion in HFrEF patients. The dose should be adjusted to the lowest dose necessary. Thus, a tolerated maximum is recommended instead of a target dose. Therefore, diuretics were not considered in this project.

Adherence to guideline recommended target doses has proven to be crucial in the decrease of all-cause mortality [5]. There are two major aspects that have impact on whether a patient will receive the recommended dose of a drug or not: a) the patients' adherence to the prescribed medication and b) the physicians' adherence to the guidelines. Physicians' fear of overdosing has shown to be a major issue in this regard [6].

1.2. State of the Art

Telehealth services such as HF disease management networks are well established as patient support after hospital discharge [7]. Typically, services implement a closed-loop system by allowing the transmission of vital parameters, patient-reported data and medical feedback between patients and healthcare professionals. Telehealth services can provide assistance to patients as well as medical professionals. On the healthcare professionals' side, telehealth services aim to increase adherence to guidelines, e.g. by providing a mobile phone app designed for antibiotic therapy for prescribers, or an app to improve the communication with patients and to facilitate patient counselling by pharmacies [8, 9].

To the best of our knowledge, there is no system available for chronic diseases which would promote physicians' adherence to guidelines by visualising a patients' current prescription status.

1.3. Objectives

The aim of the present study was to a) retrospectively evaluate prescription data from a telehealth network for HF patients and b) to design a module for calculation and an innovative visualisation of guideline adherence of physicians in individual patients.

2. Methods

2.1. Data acquisition / HerzMobil Tirol

The data used in this study were taken from the existing disease management network 'HerzMobil Tirol'. This multidisciplinary network was implemented by the health care provider 'Tirol Kliniken' starting in 2012 and approved by the local ethics committee. It allowed for physician-controlled telemonitoring and nurse-led care, as well as the inclusion and empowerment of the patient [10].

Each patient was provided with telemonitoring equipment, including a blood pressure and heart rate monitor, a body weight scale and a mobile phone. The last-mentioned was used to read out the measured data and transmit them daily. Additionally, the patients were able to document their subjective well-being and medication-intake for up to five of their currently prescribed drugs. An allocated network physician reviewed this data on a weekly basis with the possibility to adjust the treatment/medication. Alterations were performed by using the related web-based telemonitoring software of 'HerzMobil'. Healthcare professionals were also able to document notable circumstances via free text notes through the software.

Over the course of four different phases, 136 patients participated in the 'HerzMobil' program's conception phase between 2012 and 2016. Monitoring time spans varied in between one year, 6 months and 3 months. Patients that dropped out within the first two weeks or without medical recordings were excluded from the study. The final cohort comprised 104 participants, 13,064 total recorded days and 64,074 transmitted vital parameter measurements.

2.2. Data processing

The data were provided as pseudonymised PostgreSQL[2] database dumps. The following pre-processing steps were performed in KNIME[3]: the removal of outliers and never-beginners, matching drugs with their underlying agent, and adding prescription patterns and target doses. Each drug agent was then generalised in MATLAB R2019 (The MathWorks, Inc, Natick, MA). The ESC guideline 2016 recommended target doses (in mg) for each drug and day. Heart failure medication was categorised into four groups of substances. Generalisation was achieved by calculating the documented dose in percent, relative to the target dose as defined by the ESC guidelines ($dose_{rel}$). Equation 1 shows the calculation of the relative dose:

[2] https://www.postgresql.org/
[3] https://www.knime.com/

$$dose_{rel} = \frac{dose_{per-unit} * n_{units}}{dose_{target}} * 100\ [\%] \quad (1)$$

In Equation 1, $dose_{per\text{-}unit}$ denotes the dose (in mg) per unit; $dose_{target}$ is the maximum recommended dose per day according to the ESC guidelines, where potential contraindications or limitations to dose up-titration were considered; n_{units} is the sum of units taken according to the drug ingestion scheme (i.e. the sum of the number of pills taken in the morning, at noon, in the evening and at night).

The above-mentioned pre-processing was performed in order to calculate a) the medication dose as prescribed by the clinician and b) the recorded amount of taken medication for up to five drugs by the patient via smartphone each day. ACE-I, ARB and ARNI were combined into a single category called 'A-group', based on the fact that only one of them was prescribed at a time.

Within the 'HerzMobil' software system, physicians could manually enter the prescribed doses per drug for an arbitrary number of drugs. From all these prescriptions, a maximum of five could be sent to the 'HerzMobil' app on the patient's mobile phone. Each day, the patients documented whether they actually took those five drugs or not.

The relative prescription was calculated based on the physicians' and the patients` information:

- Patient-reported intake transmitted by the mobile phone (if present)
- Prescribed doses based on the medical professionals' prescription in the software (otherwise)

The prescribed dose and the patient-reported intake dose could differ in some specific situations, e.g., a dose could have been adjusted by the physician but not yet transmitted to the patient's app. Therefore, whenever both (patient-reported intake data and physician prescribed dosage data) were available, patient-reported intake data was considered. A 7-day median- filter was applied to remove outliers from the prescription data, for example when the prescription was changed. An example of a prescribed dose, a patient-reported intake and the resulting combined data is shown in Fig. 1.

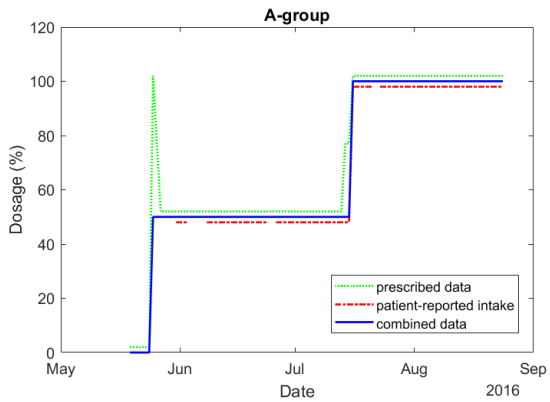

Figure 1. Example of prescribed dose in the web system (prescribed data), dose as shown on the mobile phone (patient-reported intake) and averaged resulting dose for a selected patient (combined data).

2.3. Time interval selection

Two equally sized time intervals at different points in time were chosen for further evaluation: a) 10 days in the beginning of the program and b) 10 days before the patient finished the 'HerzMobil' program. For each patient, the relative dose of each agent was averaged within these intervals. This resulted in a dataset with two values (one at the beginning and one at the end of the program) per patient and per drug agent.

2.4. Developing a concept for visualisation

The pre-existing 'HerzMobil' software system constituted an important tool for health professionals to observe changes in a patient's vital signs. Furthermore, it gave information about drug intake and allowed an immediate reaction to changes in health parameters by adjustment of the prescription. To provide a useful addition to this existing system, a concept for visualising the recommended prescription according to the ESC guidelines was designed in a focus group. This focus group consisted of a heart failure specialist, two HF nurses, a medical PhD in the field of data science, an IT specialist and a data scientist. The primary goal was to display the current prescription status of the patient for each group and day. Several approaches were considered before the group decided on the visualisation of the generalised doses of the four major HF groups relative to their recommended target dose.

3. Results

Figure 2 presents histograms comparing three groups of drug agents: A-group, beta-blockers and MRAs. The y-axis represents the number of patients taking the respective documented relative dose as compared to the ESC guideline target dose (as far as documented in the 'HerzMobil' system). As described above, data from the first (left) and final (right) 10 days of recording were averaged for each patient.

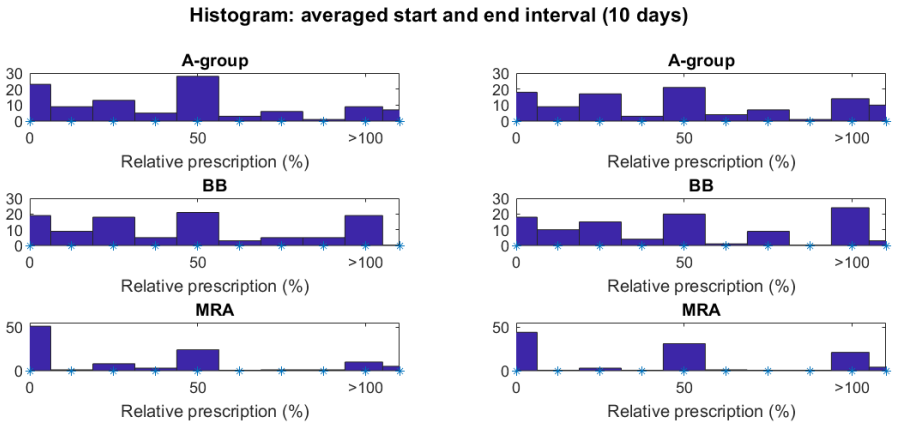

Figure 2. Histogram of the documented relative dose per drug agent,group and patient. The left side shows three agents averaged over the first 10 days of treatment, the right side shows the same agents averaged over the final 10 days. The A-group combines Angiotensin-converting-enzyme inhibitors (ACE-I), Angiotensin receptor blockers (ARB) and Angiotensin receptor neprilysin inhibitors (ARNI).

A proposal for visualising the currently prescribed doses in relation to the ESC guidelines target doses in the web system is shown in the form of a mock-up in Figure 3. On its left side, the recorded vital signs of the patient (a), as well as the taken medication (b), are visualised. The right-hand side shows a colour-coded overall prescription status (c) which depends on the lowest prescribed drug agent, excluding diuretics (in this case the lowest prescription is MRA). On the top, the status of the 'total relative prescription' is indicated. The gauge underneath shows more details, such as thresholds and the measured value of the current total relative prescription. Thus, more detailed information for each drug agent can be displayed (d): pointers show the current relative prescription per group and the different coloured areas visualise the individual statuses.

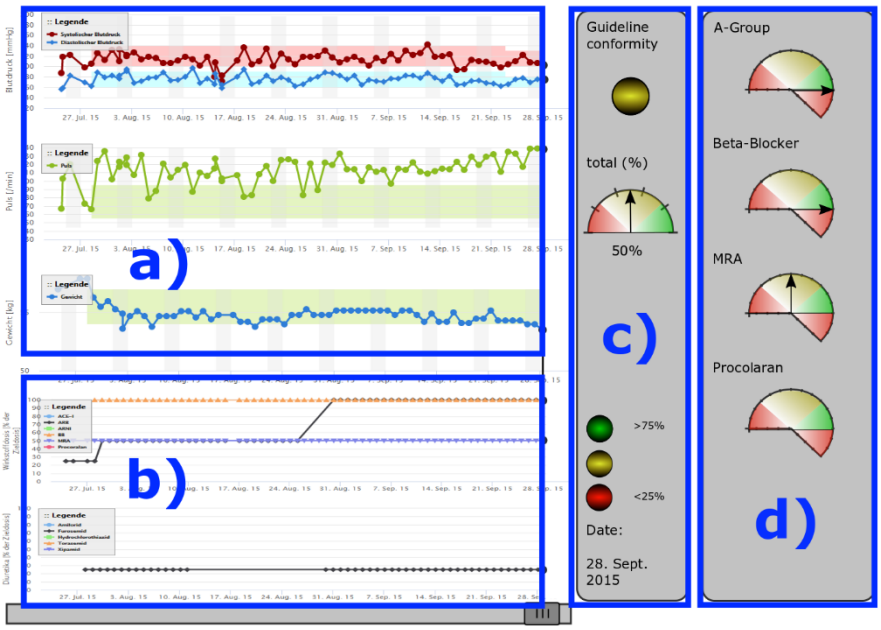

Figure 3. Mock-up of a traffic light system for visualising accordance with the target doses.

4. Discussion

4.1. Interpretation of the results

Our results indicate that the calculation of the documented relative dose of major HF medication as compared to the ESC guideline target dose as a measure of guideline adherence is feasible. A mock-up on how such data could be visualised in the web system has been designed and discussed in a focus group with telehealth experts from the 'HerzMobil' programme.

Computing the relative doses in relation to the by the guideline recommended target dose may help a) to generalise the information between groups of drugs and b) to counteract the 'cognitive illusion based on the maximum target dosage' [6]. The distribution of the relative daily dose over the first and final 10 days of each patient can

be seen in Figure 2. Obviously, relative prescribed doses accumulate around 25%, 50% and 100%, representing the titration status of the respective drug. Colour coding each status to create a traffic light system will also help to identify the prescription of each substance class more quickly (compared to daily prescriptions and schemes as plain text). Fig. 3. shows the concept of the traffic light system with additional gauges for a detailed illustration. In the patient overview, the overall relative prescription will be shown which is governed by the lowest prescribed group. More in-depth information will only be revealed by clicking on the overall relative prescription. Non-prescribed drugs will not affect the traffic light.

Since there are various reasons why the guideline's target dose cannot be reached in individual patients, we plan to support the temporal and continuous adaption of an individual patient's target dose by the physician. However, in such cases, the reason for the target dose adaption has to be documented. Additionally, the adaption of the target dose will be visualised in the web-system.

Some previously unexpected occurrences were identified (e.g. outliers with more than twice the target dose for a specific group). Therefore, the filtering of the prescribed data and merging of prescribed and documented intake data was considered in the retrospective data. These precautions are not necessary in the real-time system, since, in a prospective setting, only the prescribed dose at the current point in time will be considered for visualisation.

4.2. Limitations

The data used for this paper were taken from the conception phase of the HerzMobil program. A lot of insights from this phase were used to optimise the subsequent phases. The main purpose of the initial phases was to stabilise patients by preventing hospitalisations and cardiovascular events. We suppose that the prescription adherence would increase towards the end of the recordings.

Our approach was developed based on retrospective data, although it will be applied to prospective data in a real-world application. Therefore, especially the histograms provided in Figure 2 must be interpreted with care.

Our tool is not intended to replace the work of doctors and nurses. A static threshold is used for the calculation of the relative prescription. Potential limitations to dose escalation like hypotension or bradycardia and/or according symptoms such as dizziness are not considered. The medical staff's perception of potential limitations is still needed. The system only shows the medical professionals' adherence (in form of the prescription status) and assumes the patients' perfect adherence. Therefore, a suboptimal adherence of the patient is currently not considered.

4.3. Outlook

As a next step, we will take a closer look at the current system, regarding which further steps have to be considered before deploying our concept in routine care. Analytical tests should be performed prior and post implementation to evaluate if changes in the prescription patterns can be identified due to our approach.

Furthermore, we will analyse, whether guideline adherence can be utilised as a valuable additional feature in our artificial intelligence approach for predicting outcomes, such as hospitalisation or death in telehealth scenarios [11].

5. Conclusion

Guideline adherence of medication prescriptions for HF telehealth patients can be visualised by calculating the daily relative dose per drug group and by using a traffic light system. Such a system provides an overview of the prescription status of each group via a coloured classification, as well as an overall status of the relative prescription. Future steps in the development of the 'HerzMobil' telehealth system include a) a guideline adherence visualisation and b) a comprehensive drug documentation concept.

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