Roadmap for the treatment of heart failure patients after hospital discharge: an interdisciplinary consensus paper

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Summary

The transition period from the hospital to the outpatient setting is a critical phase when managing heart failure. A well-structured transition is paramount and helps to ensure a tight follow-up schedule for the heart failure patient, thereby improving treatment outcomes. This article aims to provide guidance for the first three follow-up visits after hospital discharge, with a focus on monitoring heart failure patients and up-titrating their medication in primary care.

Keywords: heart failure, patients, hospital discharge

Introduction

Heart failure (HF) is a serious chronic condition associated with periodic exacerbations leading to frequent hospitalisation [1]. Indeed, it is the leading cause of hospitalisation in patients over 65 years of age [1, 2, 3]. HF patients are discharged from the hospital in a vulnerable phase characterised by high mortality and morbidity. In a Swiss trial, approximately 20% of HF patients were readmitted to the hospital within the first 30 days of discharge [4]. Similarly, data gathered from two other studies conducted in Switzerland showed that at 3 months mortality was 18% and the rate of rehospitalisation was 26% [3, 5].

Several strategies have been developed to reduce mortality and morbidity during the vulnerable post-discharge period, including coordinated discharge planning and the development of a well-structured follow-up treatment plan [1]. This seems to be an area where cardiology could learn a lot from oncology with its predefined treatment schedules aiming to best balance treatment efficacy and tolerability. An integrative and collaborative patient care approach following hospital discharge has been shown to reduce the mortality risk by approximately 50% (from 15.5% to 7.2%) [6]. In particular, prescheduled follow-up visits, adherence to therapy and up-titration of HF medication are important aspects of reducing the mortality risk during the transition phase after hospital discharge [1]. Consequently, according to European Society of Cardiology (ESC) Guidelines, patients with chronic HF should be followed up in a multidisciplinary environment (evidence level IA) in which general practitioners (GPs) and cardiologists play a key role [1, 7, 8].

The aim of this consensus paper is to set clear treatment targets for the first three follow-up visits, and to provide GPs and cardiologists with recommendations for an optimal patient follow-up during the transition phase after discharge of HF patients hospitalised for acute decompensation in Switzerland. We address the aspect of feasibility, highlighting current hurdles for implementation, and also concepts on how to overcome them. In particular, these recommendations also provide guidance on the optimal monitoring of HF patients when up-titrating HF medication, which may be challenging owing to its tolerability, concomitant comorbidities and polypharmacy. The recommendations for monitoring apply universally to all HF patients, whereas the recommendations for up-titration of disease-modifying drugs are specific for HF with reduced ejection fraction (HFrEF).

The benefit of a well-structured transition phase

There is a growing body of evidence suggesting that HF patients are particularly vulnerable to disruptions in care...
Review article: Biomedical intelligence in the decision to transition to palliative care. However, it the patient, the cardiologist and the GP should be involved expressed wishes regarding life-prolonging measures and of the disease while still at hospital or if the patient has been informed about the prognosis whether the patient has been informed about the prognosis of the disease while still at hospital or if the patient has expressed wishes regarding life-prolonging measures and palliative care. In the case of patients with severe HF, the patient, the cardiologist and the GP should be involved in the decision to transition to palliative care. However, it is challenging to select the time-point for this transition as symptoms and quality of life keep changing for HF patients. Thus, it is recommended to regularly assess the patients and analyse their palliative scores, which provide an objective assessment of the patient’s condition.

To ensure a timely follow-up schedule, a collaborative care network with HF specialists, cardiologists and GPs should be established. Consistently with the 2016 ESC guidelines on HF, the present author group recommends that the first follow-up visit take place within the first 7–10 days after hospital discharge. Patients with severe HF, however, should see a GP or cardiologist within 1–3 days. Recommendations for monitoring HF patients beyond the first follow-up visit are currently limited and depend on the individual patient’s needs. This author group further suggests that the second visit take place 7–10 days after the first visit. The interval between follow-up visits can be increased for the third and later follow-up visits depending on the patient’s clinical status. A referral to a cardiologist, on the other hand, is recommended every 3 months for patients with New York Heart Association (NYHA) stage III–IV HF.

Together these measures ensure a close collaboration between GPs and cardiologists, thus enabling HF patients to receive the right support and care after hospital discharge. Furthermore, these measures are a prerequisite for optimal follow-up and up-titration strategies and, therefore, contribute to reducing the risk of death or rehospitalisation.

Feasibility

Several hurdles for implementation exist. First, most GPs/ cardiologists have busy schedules, making it challenging to add on additional patients at rather short notice. Second, GPs/cardiologists may not have all relevant medical information to add on additional patients at rather short notice. Second, GPs/cardiologists may not have all relevant medical information.

Figure 1: Up-titration roadmap for patients with HFrEF. ACEI = angiotensin-converting-enzyme inhibitor; AE = adverse event; AHA = American Heart Association; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; BB = beta blockers; ESC = European Society of Cardiology; GP = General Practitioner; HFrEF = heart failure (HF) with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; PCP = primary care physician. Based on the scientific content of the publications from Hickey 2016 [45] with data from Ponikowski et al. 2016 [1], Yancy 2013/2017 [47, 48] and the Canadian Cardiovascular Society 2017 [30].

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mation of the recent hospitalisation available early on after discharge owing to delays in the finalisation of the discharge letter or lack of details in the discharge letter (e.g., missing details on body weight, blood pressure, potassium and renal function). Third, some patients may not have a GP/cardiologist at the time of hospitalisation. Fourth, frailty may limit the ability of the patient to visit the office of the GP/cardiologist.

For successful implementation of the transition programme, each of these hurdles must be addressed and ultimately overcome. To improve practical feasibility, the implementation of cardiology and/or HF networks that share patient information and use common electronic health records, joint online booking systems for GP/cardiology slots (similar to those used extensively to book hotel rooms worldwide), such as docbox, nurse-coordinated HF management programmes [20, 21], and tele-monitoring programmes, such as the Swiss Care4Cardio, will all have important roles [22, 23].

**General assessments during follow-up visits**

Recommended assessments to be performed during the first three follow-up visits with the GP or the cardiologist are summarised in table 1 [1]. These include the evaluation of risk factors that increase the risk of rehospitalisation due to HF. Monitoring of physical symptoms (rales, oedema, body weight changes), laboratory parameters (B-type natriuretic peptide [BNP] or N-terminal pro b-type natriuretic peptide [NT-pro-BNP], electrolytes, haemoglobin, renal function), and drug-related adverse events (hypotension, hyperkalaemia, worsening renal function) are likewise of particular relevance [1, 26].

**Patient education**

The follow-up visits should also be used to educate the HF patients on the importance of self-monitoring body weight and other signs/symptoms of deterioration. Besides the “heart failure diary”, patients may use apps such as “life with heart failure” or the “electronic heart failure diary”, for self-monitoring [27]. This authors group considers patient education and empowerment an import pillar of HF management. In addition, patients need to learn how to react to imminent decompensation (calling their GP, self-adjusting the diuretic dose).

**Medication management after hospital discharge**

The importance of up-titration after hospital discharge

Treatment of HF with angiotensin converting-enzyme inhibitors (ACEIs), or angiotensin II receptor blockers (ARBs) if the ACEI is not tolerated, angiotensin receptor-aldosterone antagonist (ARNI), beta-blockers and mineralocorticoid receptor antagonists (MRAs) form the basis of the management of patients with HFrEF (fig. 2). Adjustment and up-titration of these therapeutic agents are critical for successful HF management. Based on pivotal trials, the 2016 ESC guidelines on HF recommend tight follow-up and up-titration schedules until the highest tolerated dose is achieved [1]. However, only a minority of patients enrolled in the ESC Heart Failure Long-Term Registry received the target dose of an ACEI (29% of patients) or beta-blocker (18% of patients) despite their positive impact [28]. Conversely, a careful reduction of loop diuretics may be feasible in the majority of stable chronic HF patients without signs of volume overload [29].

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**Table 1:** Assessments in primary care for monitoring HF patient status.

| Assessments to monitor patient status [16, 24] | Patient well-being | Physical and social activities, independent care (e.g., ability to climb stairs, carry groceries, jog or run [as if to catch a bus], do housework or gardening, walk a certain distance on level ground, have sex, dress, shower/bathe) |
| | Symptoms such as shortness of breath, swelling in your feet, ankles, legs, fatigue |
| | Patient education / self-care | The patient should be aware of the importance of self-monitoring and documenting their body weight on a daily basis. |
| | Life-style: physical activity | Knowledge about "red flags" and what to do if any of the following warning signs occur: |
| | | – increase in body weight |
| | | – dyspnoea |
| | | – fainting |
| | | – worsening symptoms |
| | Palliative care: Patients with late-stage HF should be informed about palliative care options |
| Assessments to monitor HF status [16, 19, 25] | Cardiac function | Heart rate and heart rhythm |
| | Laboratory assessments | Kidney function (eGFR and SCR) |
| | Serum electrolytes (potassium) |
| | Clinical assessments | Body weight |
| | | Jugular venous pressure, crackling in the lungs (these provide valuable insights for adjusting diuretic therapy) |
| | | Peripheral oedema |
| | | Blood pressure (to assess potential orthostatic hypotension) |
| | | Palpitations |
| | | Volume status |

eGFR = estimated glomerular filtration rate; HF = heart failure; SCR = serum creatinine; NYHA: New York Heart Association

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Guidance on up-titrating heart failure medication

Table 2 provides both GPs and cardiologists with a checklist for initiating and up-titrating HF medication. An overview is depicted in figure 1. This up-titration strategy should be followed in all HFpEF patients as long as the therapy is tolerated. The up-titration strategy should be adjusted in the case of adverse events such as hypotension, hyperkalaemia or worsening renal function [1, 30]. Recommendations for adjusting HF medication in HFpEF patients experiencing such adverse events are summarised in table 3.

Management of adverse events is part of the up-titration strategy. Patients with asymptomatic hypotension (systolic blood pressure [SBP] 90–100 mm Hg) usually do not require any changes to therapy [45]. In patients with symptomatic hypotension (characterised by dizziness, light-head-
edness and confusion; SBP <90 mm Hg), however, treatment with nitrates, calcium-channel blockers and other vasodilators should be either stopped entirely or administered at reduced doses [45].

The probability for symptomatic hypotension is increased in patients with volume and sodium depletion [31–33, 35–37, 44]. Therefore, a reduction of the diuretic dose should be considered in compensated patients not showing signs or symptoms of congestion [45]. If these measures do not improve the patient’s clinical status, the dose of ACEI, ARB, ARNI or beta-blocker may be temporarily reduced in a step-by-step manner [38–41] and the patient has to be reassessed within one week [45]. Renal insufficiency may also increase the risk of hypotension [32, 35]. Furthermore, postural hypotension in HF patients with autonomic dysfunction or stroke can limit the optimal dosing of HF medication [1]. In these patients, a reduction of the diuretic dose may reduce the severity of the interaction [1].

Treatment of other pharmacological conditions such as depression (tricyclic antidepressants) or prostatic obstruction (alpha-adrenoceptor blockers) may cause hypotensive interactions with HF medication [1].

As hyperkalaemia may occur in HF patients, regular monitoring of serum potassium levels is necessary [1]. Particularly in dehydrated or septic patients, serum potassium, creatinine and urea levels should be closely followed [45]. Additional risk factors for hyperkalaemia include age, renal failure and diabetes mellitus [43]. If serum potassium levels increase to ≥5.5 mmol/l, the doses of potassium-retaining agents and renin-angiotensin-aldosterone system (RAAS) inhibitors should be halved and levels rechecked after few days. Short term cessation is required if potassium rises to >6.0 mmol/l [1]. However, RAAS inhibitors should be reintroduced as soon as possible with continued close monitoring of potassium levels [1].

Furthermore, worsening renal function or chronic kidney disease (CKD) are also commonly seen among HF patients [1]. Both CKD and HF share many risk factors, including diabetes, hypertension and hyperlipidaemia [1]. Heart failure patients are more vulnerable to acute renal failure following a destabilising event, such as a dehydrating illness, over-diuresis or the addition of nephrotoxic medication (e.g., antibiotics such as trimethoprim or gentamicin, or non-steroidal anti-inflammatory drugs, which are even contraindicated in HFrEF) [1]. Worsening renal function is common during initiation and up-titration of RAAS inhibitors [1]. Usually, the reduction in renal function is minor and should not lead to treatment discontinuation [1]. However, patients showing a substantial increase in serum creatinine levels (50% above baseline, 266 μmol/l / 3 mg/dl or estimated glomerular filtration rate <25 ml/min/1.73 m²) should be evaluated thoroughly and assessed for possible renal artery stenosis, excessive hyper- or hypovolaemia and concomitant medication [1].

Limitations

Many recommendations provided in this review are supported by the latest European Society of Cardiology and American Heart Association / American College of Cardiology guidelines for the management of patients with HF (see also fig. 1). However, as we tried to provide as concrete and specific suggestions as possible to facilitate m-

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Table 2: Target doses and contraindications of common therapies for HFrEF patients, according to the Swiss Summary of Product Characteristics.

| Class | Class contraindications | Drug | Target Dose | Up-titration interval [80] | Specific contraindications |
|-------|--------------------------|------|-------------|---------------------------|--------------------------|
| ACEI  | Hypersensitivity (hereditary angio-oedema, or angio-oedema in the past during therapy with ACEI/ARB), combination with aliskiren in DM II/renal insufficiency, pregnancy/breastfeeding | Enalapril [31] | 10–20 mg b.i.d. | 2–4 weeks | – |
|       |                          | Lisinopril [32] | 5–20 mg o.d. |  | Dialysis and haemofiltration |
|       |                          | Perindopril[29] | 2.5–5.0 mg o.d. |  | Dialysis and hemofiltration, uni- or bilateral renal stenosis, creatinine clearance <20 ml/min |
|       |                          | Ramipril [33] | 10 mg o.d. |  | Severe hepatic impairment and/or cholestasis |
| ARB   |                          | Candesartan [34] | 32 mg o.d. |  | Creatinine clearance <10 ml/min |
|       |                          | Losartan [35] | 150 mg o.d. |  | eGFR <10 ml/min |
|       |                          | Valsartan [36] | 160 mg b.i.d. |  | Hepatic insufficiency/impairment, acute decompensated heart failure, cardiogenic shock, pregnancy/breastfeeding, bradycardia (<50 beats/minutes) |
|       |                          | Sacubitril/Valsartan [37] | 200 mg b.i.d. |  | Stable dose of diuretics, digoxin, ACEI, ARB for at least 2 weeks before initiating of nebivolol |
| BB    | Hypersensitivity, AV-block 2nd/3rd degree; sick sinus syndrome, sinusoidal block, symptomatic bradycardia (<60 beats/min) before initiation; symptomatic hypotension (<100 mm Hg) before initiation, severe pAVK / Raynaud’s syndrome, severe bronchial asthma, untreated phaeochromocytoma, metabolic acidosis | Bisoprolol [38] | 10 mg o.d. |  | Acute renal failure (creatinine clearance <30ml/ml), anuria, Addison’s disease, hypoponatraemia, combination with eplerenone |
|       |                          | Carvedilol [39] | 25–100 mg b.i.d. |  | Hepatic insufficiency/impairment, acute decompensated heart failure, cardiogenic shock, pregnancy/breastfeeding, bradycardia (<50 beats/minutes) |
|       |                          | Metoprolol succinate [40] | 200 mg o.d. |  | Stable dose of diuretics, digoxin, ACEI, ARB for at least 2 weeks before initiating of nebivolol |
|       |                          | Nebivolol [41] | 10 mg o.d. |  | Potassium >5.0 mmol/l before initiation, eGFR <30 ml/min/1.73 m², hepatic insufficiency (Child-Pugh C), combination with potassium-sparing diuretics, Cyp3A4-inhibitors, potassium supplements, dual RAAS blockade |
| MRA  | Hypersensitivity, hyperkalaemia | Spironolactone [42] | 25–50 mg o.d. | 4 weeks | – |
|       |                          | Eplerenone [43] | 50 mg o.d. |  | – |

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; AV = atrioventricular; BB = beta blocker; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; pAVK = peripheral arterial occlusive diseases *MRA in combination with ARB/ACEI usual daily dose: 50 mg; MRA without combination of ACEI/ARB: 100–200 mg. † Common contraindications cited, individual contraindications should be checked with the Swiss Prescribing Information. ‡ Target dose 2 × 50 mg, if >85kg
Table 3: Adjustment of HF medication in the case of adverse events. Adapted from Ponikowski et al. 2016 [1, 44].

| Adverse event                                                                 | ACEI/ARB/ARNI | BB | MRA | Diuretic |
|-------------------------------------------------------------------------------|---------------|----|-----|----------|
| Worsening signs or symptoms (increasing dyspnoea, fatigue, oedema, weight gain) | In patients with signs of increasing congestion, the diuretic dose should be increased. In the event of severe deterioration, the BB dose should be reduced to 50%. In the case of marked fatigue, the BB dose should be reduced to 50% and it should be taken in the night. The patient should be reassessed within 1–2 weeks. | No change in therapy required. | Dose may be reduced if the patient shows no signs or symptoms of congestion. | |
| Asymptomatic hypotension                                                      | No change in therapy required. | Dose may be reduced if the patient shows no signs or symptoms of congestion. | | |
| Symptomatic hypotension                                                       | Dizziness and light-headedness are common adverse events and improve over time. Reduce the dose if the patient experiences dizziness or light-headedness without showing signs or symptoms of congestion. Dose adaption of diuretics, antihypertensive medication [44]; treatment with nitrates, calcium-channel blockers and other vasodilators should be stopped or the dose reduced. If the patient shows no signs or symptoms of congestion, a reduction of the diuretic dose can be considered. Alternative causes for hypotension, e.g. hypovolaemia, should be treated [44]. | | |
| Cough                                                                         | ACEI-induced cough does not usually require a change in therapy. However, substitution of an ARB is recommend- ed in case of troublesome, ACEI-in- duced cough. | No change in therapy required. | Due to an increased risk of renal dysfunction, the triple combination of an ACEI, ARB and MRA is not recommended. Thiazide diuretic therapy should be stopped if used with concomitant loop diuretics. A reduction of the diuretic dose should be considered if urea or creatinine levels rise excessively. Male HF patients treated with spironolactone should be switched to eplerenone if they develop breast discomfort or gynaecomastia. | |
| Worsening renal function                                                      | Concomitant nephrotoxic drugs, includ- ing NSAIDs should be stopped if urea or creatinine levels rise excessively. ACEI (or ARB) dose should be reduced to half and blood chemistry re-checked within 1–2 weeks if the rise in creatinine levels persists at 50% above baseline, 286 μmol/l (3 mg/dl) or eGFR <25 ml/min/1.73 m². ACEI (or ARB) therapy should be stopped if creatinine levels increase by >100%, to >310 μmol/l (3.5 mg/dl) or eGFR <20 ml/min/1.73 m². ARNI therapy (Swiss Summary of Product Characteristics): In the case of renal dysfunction, concomitant medication should be evaluat- ed and a temporary dose reduction or withdrawal of ARNI is recommended [44]. ARNI therapy is contra-indicated in pa- tients with eGFR <10 ml/min/1.73 m² [1, 44]. | No change in therapy re- quired. | Thiazide diuretic therapy should be stopped if used with concomitant loop diuretics. A reduction of the diuretic dose should be considered if urea or creatinine levels rise excessively. Thiazide diuretic therapy should be stopped if used with concomitant loop diuretics. | |
| Hyperkalaemia                                                                | Potassium supplements or retaining agents should be stopped. A reduction of the diuretic dose should be consid- ered if potassium levels rise excessive- ly, if there are no signs of congestion. Close monitoring of potassium levels is recommended especially for patients with risk factors: severe renal insufficiency, diabetes mellitus, hyperaldos- teronism [44]. If the increase in potassium levels per- sists above ≥5.5 mmol/l, the ACEI (or ARB) dose should be reduced to half and blood chemistry re-checked within 1–2 weeks. ACEI (or ARB) therapy should be stopped temporarily if potassium levels rise to >6.0 mmol/l. In the event of hyperkalaemia, concomitant medication should be evaluat- ed and a temporary dose reduction or withdrawal of ARNI is recommended [44]. | No change in therapy re- quired. | The triple combination of an ACEI, ARB and MRA is not recommended. Other potassium-sparing or -re- taining agents should be avoid- ed. Some low-salt supplements can lead to increased serum potassium levels. Normal-to-high potassium lev- els are described in HF pa- tients if they are receiving digoxin. | |
| Hypokalaemia or hypomagnesaemia                                               | The ACEI or ARB dose should be increased. MRA should be added.Potassium/magnesium supplements | | | |
| Hyponatraemia                                                                | If the patient is volume deplet- ed, either: | | | |
Insufficient diuretic response or diuretic resistance

- Consider adding an MRA or increasing the MRA dose. The diuretic (loop, thiazides, non-thiazide-sulphonamide) dose should be increased.
- The loop diuretic should be administered more frequently or on empty stomach.
- Loop diuretics may be combined with thiazide or metolazone.
- Patients on furosemide may be switched to bumetanide or torasemide.
- Ultrafiltration or short term i.v. infusion of loop diuretic can be considered.

Hyponatraemia or dehydration

- The diuretic dose may be reduced depending on the volume status.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; AVP = arginine vasopressin; BB = beta-blocker; eGFR = estimated glomerular filtration rate; HF = heart failure; i.v. = intravenous; MRA = mineralocorticoid receptor antagonist; NSAID = nonsteroidal anti-inflammatory drug

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Potential competing interests

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