Daily home monitoring of potassium, creatinine, and estimated plasma volume in heart failure post-discharge

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Abstract

Aims Congestive status, serum potassium, and renal function are major determinants of outcomes as well as critical elements for adjusting drug therapy in heart failure (HF) patients. This study aimed at describing the daily variations in estimated plasma volume (ePV, a surrogate of congestion computed from haemoglobin and haematocrit), blood potassium, and estimated glomerular filtration rate during 2 months post-hospitalization for decompensated HF with reduced ejection fraction.

Methods and results The study was conducted in a single tertiary referral centre. Capillary blood samples were drawn by study nurses at home (7–12 am), and haematocrit, blood haemoglobin, creatinine, and potassium were measured using an approved home-based device (ABOTT i-STAT) (ClinicalTrials.gov: NCT01655134). Among the 15 home-monitored patients, two patients died (one suddenly), and one was readmitted for ischaemic acute pulmonary oedema, with a subsequent acute coronary syndrome, and did not have a complete 2-month follow-up. The 5-day-a-week biological home monitoring revealed an ePV > 5.5 mL/g Hb, suggestive of undiagnosed residual congestion at discharge in 3 out the 15 patients. It was possible to document a number of episodes of hyperkalaemia (>5: mean ± standard deviation: 2.2 ± 2.2 or 5.5: 1.7 ± 1.6 mmol/L), hypokalaemia (<4: 1.9 ± 2.4 or 3.5: 0.5 ± 1.2 mmol/L), worsening renal function (drop in estimated glomerular filtration rate-20%: 1.3 ± 1.8 or 30%: 0.7 ± 1.2) and recongestion (ePV rise above 10%: 1.4 ± 1.5, 15%: 2.3 ± 2.4, 5.5 mL/g Hb: 1.8 ± 2.6) episodes indicative of clinically relevant and potentially actionable cardiorenal and electrolytic patterns.

Conclusions Our findings demonstrate that a 5-day-a-week home monitoring combining haemoglobin/haematocrit, potassium, and creatinine measurements was able to capture a substantial number of clinically relevant cardiorenal and electrolyte events which are frequently overlooked and potentially actionable. Whether acting on these events may help optimizing renin angiotensin aldosterone system inhibitors and diuretic therapy warrants further dedicated testing. The ongoing HERMES HF study (NCT04050904) is assessing the short-term feasibility and safety of such a monitoring strategy, complemented by a decision support system, and generating recommendations based on ESC clinical guidelines in patients discharged after an episode of worsening heart failure with reduced ejection fraction.

Keywords Hypokalaemia; Hyperkalaemia; Estimated plasma volume; Kidney function; Heart failure with reduced ejection fraction; Monitoring

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Background

After discharge from heart failure (HF) hospitalization, patients are at an unacceptably high risk of death and recurrent hospitalization for HF. Patients with chronic HF and reduced ejection fraction (HFrEF) should receive renin angiotensin aldosterone system inhibitors (RAASI) to improve survival and diuretic therapy to alleviate congestion-related symptoms. However, in daily practice, patients receive suboptimal doses of RAASI mostly due to concerns of worsening renal function (WRF) and hyperkalaemia. In addition, undiagnosed residual congestion is a major driver of post-discharge early readmission.

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Table 1 Baseline characteristics

| Characteristics          | N   | Mean ± SD or n (%) | Median (Q1–Q3) | Range |
|--------------------------|-----|--------------------|-----------------|-------|
| Demography               |     |                    |                 |       |
| Age (years)              | 15  | 71 ± 10            | 71 (68–76)      | 38–84 |
| Male gender              | 15  | 11 (73%)           |                 |       |
| Physical examination     |     |                    |                 |       |
| BMI (kg/m²)              | 15  | 28.3 ± 5.7         | 28.1 (24.4–33.0)| 17.6–36.7|
| Blood pressure systolic (mmHg) | 15  | 117 ± 14           | 117 (107–126)   | 95–145|
| diastolic (mmHg)         | 15  | 70 ± 11            | 67 (63–81)      | 51–89 |
| MAP (mmHg)               | 15  | 86 ± 11            | 85 (78–95)      | 66–108|
| Cardiac examination      |     |                    |                 |       |
| LVEF (%)                 | 15  | 31 ± 9             | 30 (25–35)      | 10–45 |
| Sinus rhythm             | 15  | 7 (47%)            |                 |       |
| Pacing                   | 15  | 2 (13%)            |                 |       |
| ICD                      | 15  | 5 (33%)            |                 |       |
| NYHA class               | 15  |                    |                 |       |
| I                        |     | 1 (7%)             |                 |       |
| II                       |     | 6 (40%)            |                 |       |
| III                      |     | 7 (47%)            |                 |       |
| IV                       |     | 1 (7%)             |                 |       |
| Acute coronary syndrome  |     |                    |                 |       |
| Previous history         |     |                    |                 |       |
| Ischaemic cardiopathy    | 15  | 7 (47%)            |                 |       |
| Hypertension             | 15  | 7 (47%)            |                 |       |
| COPD                     | 15  | 2 (13%)            |                 |       |
| Neoplasia                | 15  | 5 (33%)            |                 |       |
| Risk factors             |     |                    |                 |       |
| Smoker (past or current) | 15  | 6 (40%)            |                 |       |
| Dyslipidaemia            | 15  | 6 (40%)            |                 |       |
| Diabetes                 | 15  | 8 (53%)            |                 |       |
| Biochemistry             |     |                    |                 |       |
| Kalaemia (mmol/L)        | 15  | 4.5 ± 0.6          | 4.4 (3.9–4.9)   | 3.8–5.8|
| eGFR (mL/min/1.73 m²)    | 15  | 60 ± 17            | 61 (47–78)      | 27–87 |
| ePV (mL/g Hb)            | 15  | 4.6 ± 1.3          | 4.4 (3.5–5.0)   | 2.8–7.9|
| Myocardial stretch biomarker |     | 588 ± 405         | 432 (258–994)   | 94–1286|

BMI, body mass index; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate (CKD-EPI formula); ePV, estimated plasma volume; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; NYHA, New York Heart Association.

N: count; SD: standard deviation; Q1–Q3: 1st and 3rd quartiles.

Table 2 Individual clinical characteristics

| Patient | Gender | Age (years) | Sinus rhythm | PM Y/N | ICD Y/N | Baseline values | Blood level ranges during follow-up |
|---------|--------|-------------|--------------|--------|---------|-----------------|-----------------------------------|
|         |        |             |              |        |         | SBP/DBP (mmHg)  | EF (%) | eGFR (mL/min/1.73 m²) | K+ (mmol/L) | ePV (mL/g Hb) |
| 01      | M      | 68          | Y            | N      | N       | 133/86         | 10     | 4.4 (3.9–4.9)       | 3.8–5.8     | 2.9–4.4      |
| 02      | M      | 68          | N            | Y      | N       | 117/70         | 30     | 4.8–6.2             | 3.5–7.2     | 2.8–7         |
| 03      | M      | 60          | N            | Y      | Y       | 112/64         | 35     | 4.1–6.8             | 3.5–9.9     | 2.6–4.6      |
| 04      | M      | 88          | N            | N      | N       | 114/67         | 25     | 4.4–6.7             | 3.7–5.0     | 3.5–7.2      |
| 05      | M      | 78          | Y            | N      | N       | 126/63         | 30     | 4.1–6.8             | 5.3–9.9     | 2.6–4.6      |
| 06      | M      | 66          | Y            | N      | Y       | 95/63          | 25     | 3.9–7.4             | 2.6–4.6     | 3.5–7.2      |
| 07      | W      | 38          | Y            | N      | Y       | 125/86         | 45     | 3.9–5.4             | 2.9–4.7     | 3.5–7.2      |
| 08      | W      | 79          | Y            | N      | N       | 114/61         | 33     | 3.7–5.7             | 3.6–5.3     | 3.5–7.2      |
| 09      | M      | 72          | Y            | N      | N       | 107/74         | 35     | 4.0–5.4             | 2.5–3.7     | 3.5–7.2      |
| 10      | M      | 71          | N            | N      | Y       | 125/69         | 30     | 4.0–5.6             | 3.8–5.3     | 3.5–7.2      |
| 12      | M      | 76          | N            | Y      | N       | 125/67         | 35     | 4.4–5.7             | 3.7–4.6     | 3.5–7.2      |
| 13      | W      | 75          | Y            | N      | N       | 145/89         | 20     | 3.9–6.0             | 3.0–4.6     | 3.5–7.2      |
| 15      | M      | 79          | N            | N      | Y       | 96/51          | 40     | 3.6–6.0             | 5.0–7.6     | 3.5–7.2      |
| 16      | M      | 68          | Y            | N      | N       | 124/81         | 30     | 3.8–4.9             | 4.6–6.0     | 3.5–7.2      |
| 18      | W      | 84          | MD           | N      | N       | 124/81         | 30     | 3.0–5.6             | 3.9–6.1     | 3.5–7.2      |

EF, ejection fraction; eGFR, estimated glomerular filtration rate; ePV, estimated plasma volume; ICD, implantable cardioverter defibrillator; MD, missing data; N, no; PM, pacemaker; SBP/DBP, systolic/diastolic blood pressure; Y, yes.
Instantaneous plasma volume estimated from haemoglobin/haematocrit and its changes are indicative of congestion status and are associated with prognosis in acute or chronic HF. We hypothesized that daily post-discharge home monitoring of plasma volume, blood potassium, and estimated glomerular filtration rate (eGFR) could identify electrolyte and cardiorenal changes that could benefit outpatient optimization of diuretic and RAASi therapy.

Aims

The aim of this study is to assess the daily variations in estimated plasma volume (ePV), blood potassium, and eGFR after discharge from hospitalization for decompensated heart failure, using a home-based finger capillary blood measurement 5 days a week during 2 months post-discharge and an approved bioassay device (ABOTT i-STAT) (ClinicalTrials.gov: NCT01655134).

Methods

The study was performed in a single tertiary referral centre, sponsored and funded by the University Hospital (CHRU) of Nancy, France. The protocol was approved by the Comité de Protection de Personnes Est-III prior to study initiation. All patients provided written informed consent before

Table 3 Individual treatments and events

| Patient | Baseline medications and daily doses (mg) | Drug changes | Clinical event |
|---------|------------------------------------------|--------------|----------------|
| 01      | Ramipril 5, Bisoprolol 2.5, Furosemide 120, Eplerenone 12.5 | D13: Biso 3.75, D29: Biso 5, D30: Eple 25, D45: Eple 50 | None |
| 02      | Ramipril 10, Celiprolol 200, Furosemide 125, Eplerenone 25, Diffu-K 600 | D07: Furo 500, D16: K+ 5400, D17: K+ 4200, D21: K+ decrease, D28: K+ 3600, D30: K+ 3000, D42: Furo 625 | None |
| 03      | Ramipril 10, Bisoprolol 10, Furosemide 375, Spiro. 25, Diffu-K 4200 | None | D40: sudden death |
| 04      | Candesartan 8, Bisoprolol 1.25, Furosemide 40, None | None | D13: septic shock |
| 05      | Perindopril 5, Bisoprolol 5, Furosemide 40, None, Diffu-K 1200 | None | D27: bladder infection |
| 06      | Candesartan 8, —, Furosemide 250, Eplerenone 50, Diffu-K 7200 | None | D28: raised creatinine |
| 07      | Perindopril 10, Bisoprolol 2.5, Furosemide 40, Spiro. 25 | None | D21: chest pain |
| 08      | Perindopril 7.5, Bisoprolol 2.5, Furosemide 40, Spiro. 25 | None | D48: viral infection of upper respiratory tract |
| 09      | Ramipril 5, Bisoprolol 7.5, Furosemide 375, None, Diffu-K 5400 | D03: Diffu-K 3600, D03: Biso 10, D03: Furo 125 | None |
| 10      | Fosinopril 20, Bisoprolol 10, Furosemide 125, None, Diffu-K 1800 | D21: Furo 120, D34: Furo 140 | None |
| 12      | Ramipril 10, Bisoprolol 10, Furosemide 40, Eplerenone 50 | None | D45: stent (planned) |
| 13      | Fosinopril 20, —, Furosemide 120, Spiro. 25 | None | D52: dry cough |
| 15      | Ramipril 2.5, Bisoprolol 3.75, Furosemide 60, None, Diffu-K 1800 | None | D22: ischemic acute pulmonary edema |
| 16      | Perindopril 5, Bisoprolol 10, Furosemide 375, Eplerenone 12.5, Diffu-K 1800 | D32: Diffu-K 3000, D32: Rami 10 | D42: severe chest pain |
| 18      | Yes | Yes | None | D05: Diffu-K 600, D39: Bumetan. 2, D54: Fosi. 10 | D36: dehydration |

Yes: drug intake, no other specification.
participating in the study. Assuming 8% of nonanalysable observations, a sample size of 20 patients was required to ensure a 0.5 SD accuracy for daily measurements and a corresponding 0.2 mmol/L accuracy for serum potassium.

The capillary blood samples were drawn by study nurses at home (7–12 am). No data were communicated to the treating physician except in instances where blood potassium was ≥5.8 mmol/L. Haematocrit was determined using conductometry by i-STAT, which provides a calculated haemoglobin result as follows:

\[ \text{haemoglobin (g/dL)} = \text{haematocrit (\%)} \times 0.34, \]

which was shown to be well correlated with the reference methods over a broad range of values between 6 and 16 g/dL.

Estimated plasma volume and its changes were computed as previously described. A threshold of 5.5 mL/g Hb at discharge was deemed clinically relevant since associated with both congestion features and poor clinical outcomes.

Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration formula. Biological events are described as episodes (mean number of separate sequences with values persistently above or below a given threshold, i.e., hyperkalaemia >5.5 mmol/L or >5 mmol/L, hypokalaemia <4 or 3.5 mmol/L, WRF (drop in eGFR) >20% or 30%, ePV increase >10% or 15% or above 5.5 mL/g Hb) and mean number of measurements per episode.

Results

Among the 15 home-monitored patients, two patients died (one suddenly), and one was readmitted for ischaemic acute pulmonary oedema, with a subsequent acute coronary
syndrome, and thus did not have a complete 2-month follow-up (see study flowchart in online supplement).

Baseline patient characteristics are presented in Table 1. Individual follow-up data and post-discharge treatment changes are presented in Tables 2 and 3. The 5-day-a-week biological home monitoring (Figure 1) enabled documenting a number of hyperkalaemia, hypokalaemia, WRF and recongestion episodes (Table 4).

At the individual level (Data S1), relevant and consistent profiles (e.g. persistent and/or recurrent dyskalaemia, WRF, recongestion, or decongestion patterns) were easily identified. For instance, Patient #2 (who suddenly died at Day 40), Patients #6 and #13 were chronically hyperkalaemic and displayed sustained trends towards worsening renal function and recongestion, without any recorded change in cardiovascular medications. Before being rehospitalized for an acute pulmonary oedema of ischaemic origin, Patient #16 had a decrease in ePV and became hypokalaemic, with a transient WRF. When considering congestion separately, six patients presented ePV >5.5 mL/g Hb at inclusion (Patients #05 and #15: permanently raised ePV; Patient #16: ePV oscillating at around the 5.5-threshold value), indicative of post-discharge residual congestion, and/or ePV >5.5 mL/g Hb during follow-up. Patient #02 had an ePV <5.5 at inclusion, which continued to increase steadily until sudden death, which occurred in conjunction with massive leg oedema. Patient #03 had an ePV close to the threshold, with short occasional excursions above 5.5, while Patient #18 had a slow increase in ePV during follow-up, with values oscillating around 5.5 after Day 28. Of note, this latter Patient #18 was nevertheless documented as “clinically dehydrated” by the treating physician at Day 36, concomitant with an obvious decrease in ePV, a WRF, and hypokalaemia.

### Conclusions

To the best of our knowledge, this is the first attempt of a daily home monitoring of blood potassium, eGFR, and ePV in HFrEF patients within the vulnerable post-discharge phase. Despite its small sample size and related limitation, such home monitoring study was already able to capture a substantial number of clinically relevant cardiorenal and electrolytic changes which are otherwise undiagnosed in routine daily practice with no monitoring. Additionally, given that (i) undiagnosed residual congestion is a major driver of post-discharge early readmission; (ii) excessive decongestion and use of diuretic therapy is associated with dehydration, hypotension, WRF, and poor prognosis; (iii) dyskalaemia is associated with poor outcome; and hyperkalaemia and WRF are the main reasons for the underuse, underdosing and frequent discontinuation of RAASi, and mineralocorticoid antagonists; and (iv) use of the newly available potassium binders warrants proper biological monitoring, we believe that concomitant monitoring of plasma volume, blood potassium, and renal function is a relevant strategy for assessing congestion and the delicate cardiorenal balance. Plasma volume, blood potassium, and renal function are potentially the most clinically actionable variables for the dynamic optimization of diuretic therapy and of life-saving RAASI therapy.

**Table 4 Biological events during follow-up**

| Parameter | Number of\(^a\) | Mean ± SD | Median (Q1–Q3) | Range |
|-----------|-----------------|-----------|----------------|-------|
| Potassium >5.5 mmol/L | Episodes | 1.7 ± 1.6 | 1.5 (0.5–0.5) | 0–5 |
| Potassium >5.0 mmol/L | Episodes | 4.4 ± 6.9 | 1.5 (0.5–0.5) | 0–22 |
| Potassium <4.0 mmol/L | Episodes | 9.1 ± 10.1 | 5.5 (2.5–2.5) | 1^b–33 |
| Potassium <3.5 mmol/L | Episodes | 9.1 ± 10.1 | 5.5 (2.5–2.5) | 1^b–33 |
| WRF > 20% | Episodes | 3.7 ± 5.7 | 1.0 (0.0–0.0) | 0–6 |
| WRF > 30% | Episodes | 0.5 ± 1.2 | 0.0 (0.0–0.0) | 0–3 |
| ePV >5.5 mL/g Hb | Episodes | 1.3 ± 1.8 | 0.5 (0.0–0.0) | 0–6 |
| ePV increase >10% | Episodes | 5.3 ± 7.2 | 2.5 (0.0–0.0) | 0–22 |
| ePV increase >15% | Episodes | 0.7 ± 1.2 | 0.0 (0.0–0.0) | 0–3 |
| ePV increase | Episodes | 2.4 ± 5.0 | 0.0 (0.0–0.0) | 0–16 |
| ePV increase | Episodes | 6.8 ± 11.6 | 0.0 (0.0–12.0) | 0–37 |
| ePV increase | Episodes | 1.4 ± 1.5 | 1.0 (0.0–0.0) | 0–5 |
| ePV increase | Episodes | 10.4 ± 9.1 | 12.0 (1.0–1.0) | 0–30 |
| ePV increase | Episodes | 7.7 ± 8.0 | 8.0 (0.0–0.0) | 0–25 |

Note that an episode with values >x may include several shorter episodes with values y > x, and conversely for values <x and y with y < x. For instance, the mean number of episodes with ePV increases >10% (1.4 ± 1.5) was lower than for increases >15% (2.3 ± 2.4), although the mean number of measurements per episode was higher (10.4 ± 9.1 vs. 7.7 ± 8.0).

- ePV, estimated plasma volume; WRF, worsening renal function from baseline.
- ^a^12 complete observations, excluding three premature (two deaths and one hospitalization for ischaemic acute pulmonary oedema) and five consent withdrawals.
- ^b^One patient had only one 1-day hyperkalaemia >5.5 mmol/L.
The ongoing HERMES HF study (NCT04050904) is currently assessing the short-term feasibility and safety of such a monitoring strategy, complemented by a decision support system (“ExpHeart”), and generating recommendations based on ESC clinical guidelines (CardioRenal ExpHeart) in patients discharged after an episode of worsening HFrEF.

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Conflict of Interest

Dr. Rossignol reports grants and personal fees from AstraZeneca, Bayer, CVRx, personal fees from Fresenius, grants and personal fees from Novartis, personal fees from Grunenthal, Servier, Stealth Peptides, Vifor Fresenius Medical Care Renal Pharma, Idorsia, NovoNordisk, Ablative Solutions, G3P, Corvidia, Relypsyra, outside the submitted work; and Cofounder: CardioRenal. Cofounder: CardioRenal, a company developing a telemonitoring loop in heart failure (including creatinine, potassium and Hb measurements) Nicolas Girerd: personal fees from Novartis, personal fees from Boehringer, outside the submitted work; Renaud Fay: none Faiez Zannad: personal fees from Novartis, personal fees from Cardior, personal fees from Cereno pharmaceutical, personal fees from Applied Therapeutics, personal fees from Merck, other from CVCT, personal fees from Novartis, outside the submitted work; Cofounder: CardioRenal, a company developing a telemonitoring loop in heart failure (including creatinine, potassium and Hb measurements)

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Supporting information

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

Data S1: Study flowchart.

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