Associations of serum potassium levels with mortality in chronic heart failure patients

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Aims
Medication prescribed to patients suffering from chronic heart failure carries an increased risk of impaired potassium homeostasis. We examined the relation between different levels of serum potassium and mortality among patients with chronic heart failure.

Methods and results
From Danish National registries, we identified 19,549 patients with a chronic heart failure diagnosis who had a measurement of potassium within minimum 90 days after initiated medical treatment with loop diuretics and angiotensin converting enzyme inhibitors or angiotensin-II receptor blockers. All-cause mortality was examined according to eight predefined potassium levels: 2.8–3.4 mmol/L, 3.5–3.8 mmol/L, 3.9–4.1 mmol/L, 4.2–4.4 mmol/L, 4.5–4.7 mmol/L, 4.8–5.0 mmol/L, 5.1–5.5 mmol/L, and 5.6–7.4 mmol/L. Follow-up was 90 days from potassium measurement. We estimated the risk of all-cause mortality using multivariable adjusted Cox proportional hazard model, with normal serum potassium level at 4.2–4.4 mmol/L as reference. After 90 days, the mortality in the eight strata was 14.4, 8.0, 6.3, 5.0, 5.8, 7.9, 10.3, and 21.1% respectively. In multivariable adjusted analysis, patients with potassium levels of 2.8–3.4 mmol/L [hazard ratio (HR): 3.16; confidence interval (CI): 2.43–4.11], 3.5–3.8 mmol/L (HR: 1.62; CI: 1.31–1.99), 3.9–4.1 mmol/L (HR: 1.29; CI: 1.08–1.55), 4.8–5.0 mmol/L, 5.1–5.5 mmol/L, and 5.6–7.4 mmol/L (HR: 1.34; CI: 1.10–1.63), 4.5–4.7 mmol/L (HR: 1.60; CI: 1.29–1.97), and 5.6–7.4 mmol/L (HR: 3.31; CI: 2.61–4.20) had an increased risk of all-cause mortality.

Conclusion
Levels within the lower and upper levels of the normal serum potassium range (3.5–4.1 mmol/L and 4.8–5.0 mmol/L, respectively) were associated with a significant increased short-term risk of death in chronic heart failure patients. Likewise, potassium below 3.5 mmol/L and above 5.0 mmol/L was also associated with increased mortality.

Keywords
Heart failure • Serum potassium • Mortality • Chronic heart failure

Introduction
The prevalence of heart failure is increasing and it represents a significant health care issue. Despite improved treatment regimens, mortality and morbidity remain high.¹–³

Many patients suffering from chronic heart failure receive both loop diuretics, mineralocorticoid receptor antagonists (MRA) and angiotensin converting enzyme (ACE) inhibitors, or angiotensin-II-receptor blockers (ARB). Impaired potassium homeostasis, as a consequence of the above treatment, is frequently observed and both hypo- and hyperkalaemia are associated with a poor outcome⁴–⁸ although mild to moderate hyperkalaemia can be well tolerated⁹ and hyperkalaemia induced by MRA may still improve survival if carefully monitored.¹⁰

Recently, a U-shaped relation between potassium and mortality in patients suffering from acute heart failure and cardiovascular disease

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has been reported\(^1\),\(^2\) and even high and low potassium levels within the accepted normal range of potassium were associated with increased mortality suggesting a narrower safe level for these patients.

Whether this observation for acute heart failure patient also applies for chronic heart failure patients is unknown at present.

Using Danish registries, we aimed to elucidate on the association between different potassium levels and mortality in chronic heart failure patients receiving both loop diuretics and ACE-inhibitors or ARB.

**Methods**

**Databases**

All residents in Denmark have a personal, unique, and permanent civil registration number that enables individual linkage of personal data from all nation-wide administrative registries.

We used the Danish National Population Register to obtain data regarding age, sex, and survival status. From The Danish National Patient Register, we collected information about admission dates, hospital discharge dates, discharge diagnosis, dates of operation, and operation code.

Diagnoses are classified as primary and/or secondary according to WHO International Classification of Disease (ICD). From 1978 until 1994, the 8th revision (ICD-8) was used, and from 1994 and onwards the 10th revision (ICD-10) was used for discharge registration. From the National Register for Medicinal Products Statistics, information on each patient’s pharmacotherapy was collected. This register includes all dispensed prescriptions from all Danish pharmacies since 1995 based on the Anatomical Therapeutic Chemical System (ATC). As the health care system is state financed and partly reimburses drug costs, all Danish pharmacies are required by law to register all dispensed drug prescriptions, providing a valid register. From three regions in Denmark, covering approximately 1.250.000 inhabitants, blood test results were obtained from electronic registries of laboratory data and were linked to data from the aforementioned Danish registers.

**Study population**

The study population consists of patients diagnosed with heart failure (see ICD-10 codes in Supplementary material online) between 1994 and 2012 during either a hospital admission or in an ambulatory outpatient setting. The heart failure diagnosis based on the I50 code has previously been validated with a high specificity.\(^3\)\(^4\)\(^5\) Besides having a diagnosis of heart failure, the patients in this study population were required to have claimed a prescription for both loop diuretics (see ATC codes in Supplementary material online) and ACE inhibitors or ARB (see ATC codes in Supplementary material online) between 1994 and onwards the 10th revision (ICD-10). The following medications were identified (see ATC codes in Supplementary material online, S2): beta-blockers, MRA, thiazides, digoxin, and potassium supplements. The concomitant pharmacotherapies were evaluated during the 365 days prior to the baseline and were not evaluated after the baseline. To evaluate the renal status, blood chemistry including serum creatinine levels at the baseline were used. The renal status was assessed by dividing the patients into six intervals stratified on sex, age and dependent on whether their serum creatinine levels were higher or lower than following serum creatinine level: 105 mmol/L for men <70 years, 125 mmol/L for men ≥70 years, 90 mmol/L for women <70 years, and 105 mmol/L for women ≥70 years.

Patients with an implantable Cardioverter/Defibrillator (ICD) were identified based on an operation code (see operation code in Supplementary material online, S3) if dated before the baseline.

**Outcomes**

The outcome of the study was all-cause mortality within 90 days after baseline serum potassium measurement.

**Statistical analysis**

The baseline potassium levels, demographics, and clinical characteristics were compared among groups of patients by dividing the normal potassium reference range (3.5–5 mmol/L) into five intervals. Furthermore, three intervals outside the normal potassium reference range were defined, one interval containing patients with a serum potassium below 3.5 mmol/L (2.8–3.4 mmol/L), one with patients with a serum potassium from 5.1 mmol/L to 5.5 mmol/L and last, one interval containing patients with a serum potassium above 5.5 mmol/L (5.6–7.4 mmol/L). Thus this study contains eight potassium intervals, where the reference interval was defined as potassium from 4.2 to 4.4 mmol/L based on analysis, which confirmed that the lowest mortality risk was found in this range. (Table 1)

The categorical variables were presented as counts and percentages and continuous values as median and interquartile range. We used Pearson’s \(\chi^2\) test to evaluate differences in categorical variables, and the Kruskal–Wallis rank sum test to evaluate differences in non-normal

**Table 1**  Pre-defined potassium intervals

<table>
<thead>
<tr>
<th>Potassium</th>
<th>Serum potassium concentration</th>
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</thead>
<tbody>
<tr>
<td>Interval 1 (Hypokalaemia)</td>
<td>2.8–3.4 mmol/L</td>
</tr>
<tr>
<td>Interval 2</td>
<td>3.5–3.8 mmol/L</td>
</tr>
<tr>
<td>Interval 3</td>
<td>3.9–4.1 mmol/L</td>
</tr>
<tr>
<td>Interval 4 (Reference interval)</td>
<td>4.2–4.4 mmol/L</td>
</tr>
<tr>
<td>Interval 5</td>
<td>4.5–4.7 mmol/L</td>
</tr>
<tr>
<td>Interval 6</td>
<td>4.8–5.0 mmol/L</td>
</tr>
<tr>
<td>Interval 7 (Mild hyperkalaemia)</td>
<td>5.1–5.5 mmol/L</td>
</tr>
<tr>
<td>Interval 8 (Severe hyperkalaemia)</td>
<td>5.6–7.4 mmol/L</td>
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</tbody>
</table>
distributed continuous variables. Kaplan–Meier survival curves were plotted for the eight potassium intervals to illustrate survival.

In order to investigate the association between the serum potassium levels and survival within 90 days, a Cox proportional hazard model was used. The proportional hazard assumption was tested for all regression models and fulfilled.

We considered a two-sided P-value below 0.05 statistically significant.

The association of potassium with mortality was also assessed using restricted cubic splines with knots at the 10th, 25th, 50th, 75th, and 90th percentiles of potassium.

The selected interactions in the multivariable analysis were sex, age, AMI, COPD, diabetes, a high serum creatinine level, an ICD, atrial fibrillation, ventricular fibrillation, atrioventricular block (2nd and 3rd degree), and prescriptions for beta-blockers, MRA, thiazides, digoxin, and potassium supplements.

Age was included in the regression model as five groups defined using cut values from 20th percentiles.

All data management and analyses were performed using SAS 9.4 (SAS Institute Inc.) and R version 3.2.4 (R Development Core Team).

Results

Baseline characteristics

A total of 19 549 patients were included in the study. The baseline characteristics of the study population according to each potassium level are presented in Table 2. This study population was characterized by advanced age and there were more men than women. Around 35% had a prior myocardial infarction. More patients with a high potassium level had an elevated creatinine level than patients with a lower potassium level (see Table 2).

Survival analysis

Within 90 days from qualifying serum potassium measurement, 1384 (7.1%) patients died. The 90-day mortality in the eight potassium intervals from the lowest (K=2.8–3.4 mmol/L) to the highest (K=5.6–7.4 mmol/L) were 14.4, 8.0, 6.3, 5.0, 5.8, 7.9, 10.3, and 21.1% respectively as illustrated in Kaplan–Meier survival curves in Figure 1. There was a significant increased risk of death in hypokalaemia patients (K=2.8–3.4 mmol/L, P < 0.001) and hyperkalaemia patients (K=5.1–5.5 mmol/L, P = <0.001 and K=5.6–7.4 mmol/L, P = <0.001) compared with the reference interval with potassium level ranging from 4.2 to 4.4 mmol/L. Moreover, potassium intervals within the normal range showed significant increased risk for patients between 3.5–3.8 mmol/L (P = <0.001), 3.9–4.1 mmol/L (P = 0.0076), and 4.8–5.5 mmol/L (P = <0.001).

The results of the multivariable adjusted analysis with potassium 4.2–4.4 mmol/L as reference are shown in Figure 2. In the adjusted analysis, the mortality remained significantly increased in patients with hypo- [hazard ratio (HR) 3.16, P = <0.01] and hyperkalaemia (HR 1.60, P = <0.01 and HR 3.31 P = <0.001). Risk of all-cause mortality was also increased in the following potassium intervals within the normal range: 3.5–3.8 mmol/L (HR 1.62, P = <0.01), 3.9–4.1 mmol/L (HR 1.29, P = <0.01) and 4.8–5.5 mmol/L (HR 1.34, P = <0.01).

The covariates with a significant impact on mortality are age, gender, AMI, COPD, diabetes, a high serum creatinine level, and prescriptions for digoxin and potassium supplements.

The U-shaped restricted cubic spline curve is shown in Figure 3. The spline curve shows an increase in mortality for both high and low potassium levels. In addition, the spline curve shows a difference within the normal potassium range, where the interval from 4.0 to 4.8 mmol/L is associated with the lowest risk of death.

Additional analyses

We performed nine sensitivity analyses to test the robustness of our results.

First, we changed the maximum number of days, between treatment initiation and serum potassium measurement. These analyses showed that different inclusion criteria did not change the overall results. See Supplementary material online, S4 for these analyses.

Secondly, we divided the population into two periods (1994–99 and 2000–12) to analyse whether the effect of potassium on mortality is different in the two periods where treatment of heart failure patients was slightly different. We observed that the results were generally similar to our main analysis. However, in the period 1994–99, the confidence intervals were large and P-values not significant in the intervals 3.5–3.8 mmol/L, 3.9–4.1 mmol/L, 4.8–5.0 mmol/L, and 5.1–5.5 mmol/L (P = 0.09, P = 0.12, P = 0.06, and P = 0.06, respectively). In the period 1994–1999, there were fewer patients included in the study compared to 2000–12 (3980 and 15 569, respectively). See Supplementary material online, S5 for the analyses.

Third, we looked at cardiovascular death as outcome and the results were similar to the main analysis. We observed increased risk of cardiovascular death in the following potassium intervals within the normal range: 3.5–3.8 mmol/L (HR 1.51, P = <0.01), 3.9–4.1 mmol/L (HR 1.27, P = 0.02), and 4.8–5.0 mmol/L (HR 1.32, P = 0.01). See Supplementary material online, S6 for the analysis.

Fourth, we performed an analysis where patients were identified from the registry with only a heart failure diagnosis, and thus they did not fulfil the medical treatment required for inclusion in the main analysis. The result of this analysis was comparable to the main analysis. See Supplementary material online, S7 for the analyses.

Fifth, we performed an additional analysis including patients from the main study population who did not receive a prescription on MRAs prior to the baseline. See Supplementary material online, S8 for this analysis.

Sixth, a subgroup analysis was conducted in which patients with a high serum creatinine level were separated from those at a normal serum creatinine level. The result is generally similar to our main results (see Supplementary material online, S9). In addition an interaction analysis was performed and no interaction was identified between hyperkalaemia and renal function on outcome, P = 0.3047 for the interval 5.1–5.5 mmol/L and P = 0.3410 for the interval 5.6–7.4 mmol/L.

Seventh, we performed subgroup analyses for patients with and without potassium supplement treatment. These analyses both show the same trend as the main analysis. See Supplementary material online, S10.

Eight, an additional survival analysis with a follow-up time at 20 days was performed. The result was very comparable with the results of the main analysis (see Supplementary material online, S11).

Finally, we performed a time-varying analysis considering if patients had additional potassium measurements other than the baseline.
Table 2  Baseline demographics

| Parameters          | K: 2.8–3.4 mmol/L n = 514 | K: 3.5–3.8 mmol/L n = 1783 | K: 3.9–4.1 mmol/L n = 3645 | K: 4.2–4.4 mmol/L n = 5055 | K: 4.5–4.7 mmol/L n = 4285 | K: 4.8–5.0 mmol/L n = 2336 | K: 5.1–5.5 mmol/L n = 1442 | K: 5.6–7.4 mmol/L n = 489 | Total n = 19549 | P-value
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<tbody>
<tr>
<td>Sex, female</td>
<td>264 (51.4%)</td>
<td>858 (48.1%)</td>
<td>1614 (44.3%)</td>
<td>2047 (40.5%)</td>
<td>1693 (39.5%)</td>
<td>967 (41.4%)</td>
<td>650 (45.1%)</td>
<td>231 (47.2%)</td>
<td>8326 (42.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex, male</td>
<td>250 (48.6%)</td>
<td>925 (51.9%)</td>
<td>2029 (55.7%)</td>
<td>3008 (59.5%)</td>
<td>2592 (60.5%)</td>
<td>1369 (58.6%)</td>
<td>792 (54.9%)</td>
<td>258 (52.8%)</td>
<td>11233 (57.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>76.2 (67.1–82.5)</td>
<td>75.5 (66.4–82.3)</td>
<td>75.3 (66.6–82.3)</td>
<td>74.8 (66.0–81.9)</td>
<td>75.5 (67.0–82.5)</td>
<td>76.7 (68.7–83.3)</td>
<td>78.1 (70.0–84.5)</td>
<td>78.1 (70.5–85.2)</td>
<td>75.8 (67.0–82.6)</td>
<td>&lt;0.001</td>
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<td>Comorbidities</td>
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<tr>
<td>AMI</td>
<td>164 (31.9%)</td>
<td>566 (31.7%)</td>
<td>1189 (32.6%)</td>
<td>1796 (35.5%)</td>
<td>1486 (34.7%)</td>
<td>843 (36.1%)</td>
<td>497 (34.5%)</td>
<td>154 (31.5%)</td>
<td>6695 (34.2%)</td>
<td>0.006</td>
</tr>
<tr>
<td>ICD</td>
<td>17 (3.3%)</td>
<td>33 (1.9%)</td>
<td>79 (2.2%)</td>
<td>153 (3.0%)</td>
<td>113 (2.6%)</td>
<td>71 (3.0%)</td>
<td>33 (2.3%)</td>
<td>5 (1.0%)</td>
<td>504 (2.6%)</td>
<td>0.010</td>
</tr>
<tr>
<td>COPD</td>
<td>115 (22.4%)</td>
<td>408 (22.9%)</td>
<td>771 (21.2%)</td>
<td>1058 (20.9%)</td>
<td>908 (21.2%)</td>
<td>520 (22.3%)</td>
<td>342 (23.7%)</td>
<td>127 (26.0%)</td>
<td>4249 (2.1%)</td>
<td>0.055</td>
</tr>
<tr>
<td>Diabetes</td>
<td>93 (18.1%)</td>
<td>305 (17.1%)</td>
<td>642 (17.6%)</td>
<td>935 (18.5%)</td>
<td>880 (20.5%)</td>
<td>523 (22.4%)</td>
<td>370 (25.7%)</td>
<td>130 (26.6%)</td>
<td>3878 (19.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High serum creatinine</td>
<td>172 (34.4%)</td>
<td>596 (34.4%)</td>
<td>1227 (34.7%)</td>
<td>1917 (39.3%)</td>
<td>1878 (45.3%)</td>
<td>1281 (56.8%)</td>
<td>943 (68.3%)</td>
<td>405 (84.9%)</td>
<td>8419 (44.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td></td>
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<tr>
<td>Beta-blockers</td>
<td>283 (55.1%)</td>
<td>1041 (58.4%)</td>
<td>2175 (59.7%)</td>
<td>3181 (62.9%)</td>
<td>2776 (64.8%)</td>
<td>1475 (63.1%)</td>
<td>893 (61.9%)</td>
<td>265 (54.2%)</td>
<td>12089 (61.8%)</td>
<td>&lt;0.001</td>
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<tr>
<td>Mineralocorticoid</td>
<td></td>
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<tr>
<td>receptor antagonists</td>
<td>116 (22.6%)</td>
<td>382 (21.4%)</td>
<td>927 (25.4%)</td>
<td>1423 (28.2%)</td>
<td>1450 (33.8%)</td>
<td>911 (39.0%)</td>
<td>609 (42.2%)</td>
<td>263 (53.8%)</td>
<td>6083 (31.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thiazides</td>
<td>11 (2.1%)</td>
<td>33 (1.9%)</td>
<td>40 (1.1%)</td>
<td>66 (1.3%)</td>
<td>61 (1.4%)</td>
<td>43 (1.8%)</td>
<td>40 (2.8%)</td>
<td>9 (1.8%)</td>
<td>303 (1.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Digoxin</td>
<td>166 (32.3%)</td>
<td>623 (34.9%)</td>
<td>1276 (35.0%)</td>
<td>1705 (33.7%)</td>
<td>1501 (35.0%)</td>
<td>777 (33.3%)</td>
<td>510 (35.4%)</td>
<td>180 (36.8%)</td>
<td>6738 (34.5%)</td>
<td>0.456</td>
</tr>
<tr>
<td>Potassium supplements</td>
<td>447 (87.0%)</td>
<td>1500 (84.1%)</td>
<td>3040 (83.4%)</td>
<td>4105 (81.2%)</td>
<td>3426 (80.0%)</td>
<td>1785 (76.4%)</td>
<td>1094 (75.9%)</td>
<td>375 (76.7%)</td>
<td>15772 (80.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death (90 days)</td>
<td>74 (14.4%)</td>
<td>142 (8.0%)</td>
<td>231 (6.3%)</td>
<td>253 (5.0%)</td>
<td>249 (5.8%)</td>
<td>184 (7.9%)</td>
<td>148 (10.3%)</td>
<td>103 (21.1%)</td>
<td>1384 (7.1%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are presented as number of patients (column percentage) in all parameters except for age. Data are in the age parameter presented as median and IQR using the 25th and 75th percentiles.

AMI, acute myocardial infarction; COPD, chronic obstructive pulmonary disease; ICD, implantable cardioverter defibrillator; IQR, interquartile range.
measurement during the 90-days follow-up. This analysis did not change our conclusions (see Supplementary material online, S12).

**Discussion**

Our study showed that hypo- and hyperkalaemia were highly associated with increased mortality. Further, our data suggested that low and high normal levels of potassium were also associated with an increased all-cause 90-days mortality in patients with chronic heart failure and that excess mortality was evident as early as 20 days after enrolment. Moreover, the ‘safest’ potassium interval is narrow between 4.1 and 4.8 mmol/L. Hypokalaemia is frequently seen in patients with heart failure despite the use of ACE/ARB and MRA although the use of MRA significantly reduce mortality, with the presumption that a significant
contribution to a lower mortality was conditional on reduced potassium loss. Several retrospective analyses from the digitals investigation group trial all suggest that a potassium level below 4 mmol/L was associated with excess mortality and diuretic induced potassium depletion has been suggested as a potential cause of arrhythmic death in chronic heart failure patients despite the fact that no direct analysis on the effect of serum potassium levels on mortality was made. Finally, Nolan et al. showed that chronic heart failure patients who survived during a follow-up period had an average serum potassium level of 4.4 mmol/L ± 0.5, whereas non-survivors had an average serum potassium level of 4.1 mmol/L ± 0.6. Although many of the above studies are retrospective in nature they all point towards the fact that a potassium level below 4.0 mmol/L is associated with increased mortality in heart failure patients. The current study agrees with this assumption. Moreover, we observed that patients with hypokalaemia as well as low normal potassium have less frequent prescriptions of MRA, which is in line with a recent report. The reasons for this apparent underutilization and lack of compliance with current guidelines are not clear but could include a physician fear of MRA-related side effects.

Recent retrospective studies also not designed to investigate the association between potassium levels and mortality in chronic heart failure patients suggest that levels of potassium between 5.0 and 5.5 mmol/L appear relatively safe. This statement regarding potassium levels of as high as 5.5 mmol/L possibly being an advantage for patients suffering from chronic heart failure stands in contrast to the findings of the current study. Our data are in fact in line with another recent publication concerning acute heart failure patients suggesting a rather narrow optimum potassium interval covering only the mid-range of the reference interval with a U-shaped relation between potassium and outcome. However, recent data suggest that the use of MRA even in the case of moderate hyperkalaemia still improve patient outcome if careful surveillance is performed. In the present study, patients with hyperkalaemia received MRA treatment in about one-third of cases. We performed an additional sensitivity analysis (see Supplementary material online, S8) and our findings suggest that the observed excess mortality in high normal potassium and hyperkalaemia is related to potassium but unaffected by concomitant treatment with MRA supporting the above assumption. Thus, optimum handling of high potassium should therefore include careful dietary counselling and potentially newer generation potassium lowering drugs before adjusting MRA dosage.

The current study had a relatively short follow-time compared with previous studies. This choice was deliberate to ensure that the potassium measurement was more related with the outcome considering the risk of confounding factors in the study design. Further, we performed an additional analysis, where we changed the maximum number of days, between treatment initiation and serum potassium measurement to test if a longer treatment-time would have an effect on potassium and on the outcome subsequently. These analyses did not change our results (see Supplementary material online, S4).

The current study is based on a large number of data, and contrary to previous studies, it has only few exclusion criteria. Notably, this study included both patients with abnormal and normal potassium levels, of high age, with comorbid conditions and patients who might receive different types of medication.

Study limitations
Due to the observational design, we cannot exclude that residual confounding contributes to the findings, thus if potassium levels reflect severity of heart failure this could contribute. Information on ejection fraction for each heart failure patient was not available. Consequently, we were not able to subdivide our heart failure population according to e.g. reduced or preserved ejection fraction. Further, we did not have electrocardiogram data available. Consequently, we were not able to examine whether the heart failure patient had e.g. a left bundle branch block. The mechanism of death was also not evaluated. In this nation-wide registry study, we cannot identify arrhythmic death with reasonable certainty, as in some situations previous cardiac diagnoses are registered as cause of death. This could lead to an overestimation of the risk when looking at the cardiovascular death. Since we are examining mortality over a short period after a diagnosis of heart failure we did not find it beneficial to distinguish between cardiovascular and non-cardiovascular death. Danish patients are a quite homogeneous population, so it is not known whether it is possible to apply the findings of the study on other ethnicities.

Conclusion
This study identifies potassium levels in the intervals 2.8–3.4 mmol/L and 5.0–7.4 mmol/L to be associated with an increased short-term mortality in chronic heart failure patients. Likewise, a potassium level within the lower and upper levels of the normal serum potassium range (3.5–<4.1 mmol/L and from 4.8–5.0 mmol/L, respectively) was also associated with increased mortality compared with the reference interval of 4.2–4.4 mmol/L.

Supplementary material
Supplementary material is available at European Heart Journal online.

Conflict of interest: S.H. has received support from the Danish Heart Foundation and the Laerdal Foundation. The remaining co-authors had nothing to declare.

References


