Less use of standard guideline-based treatment of myocardial infarction in patients with chronic kidney disease: a Danish nation-wide cohort study

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Aims
The aim of this Danish nationwide study was to evaluate the treatment of myocardial infarction (MI) in patients with non-end-stage chronic kidney disease (CKD) and in patients requiring renal replacement therapy (RRT). Upgraded guidelines for the management of MI were implemented around 2004; hence, the treatment of MI in the time periods before and after 2004 was compared in order to evaluate the impact for patients with CKD.

Methods and results
By linking nationwide registries by the personal registration number, we identified patients admitted to Danish hospitals with first time MI in the period 2000–09 (79 585 with no renal disease, 3144 with non-end-stage CKD, and 725 requiring RRT). Cox proportional hazards model was used to estimate the chance of invasive treatment within 60 days after MI and the chance of filling prescriptions on recommended post-MI drugs within 90 days before and after 2004. Significantly less use of relevant MI treatment in patients with non-end-stage CKD and patients requiring RRT compared with patients with no renal disease were seen; however, the absolute frequencies of invasive procedures and filled prescriptions on post-MI drugs increased after 2004 in all patients.

Conclusions
After 2004, invasive and pharmacological treatment of first-time MI improved in patients with non-end-stage CKD and patients requiring RRT; however, all CKD patients were less treated with standard MI care compared with patients with no renal disease.

Keywords
Chronic kidney disease • Renal replacement therapy • Myocardial infarction • Angiography • Coronary revascularization • Pharmacological treatment

Introduction
Cardiovascular disease is a common cause of death in patients with chronic kidney disease (CKD). Fifty per cent of dialysis patients die within 2 years after a myocardial infarction (MI).1 Even mild CKD is a major risk factor for cardiovascular complications after MI.2,3 Chronic kidney disease patients, including those requiring renal replacement therapy (RRT) with dialysis or renal transplantation, are often excluded from clinical trials.4 Despite the lack of evidence from randomized trials concerning the treatment of MI in CKD, the National Kidney Foundation KDOQI Guidelines recommend that all CKD patients presenting with acute MI should be treated as patients with no renal disease, with the exception of specific attention to drugs that have altered clearances in kidney failure.5 These recommendations are also applicable in Denmark, where the national guidelines suggest coronary angiography and percutaneous coronary intervention (PCI) performed along with pharmacological treatment with antiplatelet agents, beta-blockers, thrombolytic therapy, and lipid-lowering agents. Previously, studies have shown that patients with CKD were subject to underuse of treatment options after MI—9 and factors such as the risk of contrast-induced kidney injury (CI-AKI) and severe comorbidity in CKD patients might influence...
treatment decisions in these patients. Early invasive strategies for the treatment of MI were implemented in Denmark around 2004 in line with the upgraded European Society of Cardiology (ESC) guidelines and it is presently unknown whether the handling of MI in CKD patients has changed accordingly. Therefore, the objective of the present study was to describe the treatment of MI in patients with and without CKD before and after 2004 in this Danish nationwide cohort study.

Methods

Data sources

Linkage of nationwide administrative registries by the personal unique civil registration number provided information on patients admitted to Danish hospitals. The National Patient Registry holds information on all admissions to Danish Hospitals since 1978, including information on primary discharge diagnosis, secondary discharge diagnoses, procedures, and operations. Diagnoses are classified according to the international classification of diseases (ICD); version 8 (ICD-8) were used before 1994 and version 10 (ICD-10) since 1994. The Danish Register of Medicinal Product Statistics holds information on dispensed prescription medicines (ATC code, date of dispensing, strength, and number of tablets) from Danish pharmacies since 1995. Patients requiring chronic (>3 months) RRT are registered in The Danish National Registry on Regular Dialysis and Transplantation. The registry is complete and valid. Administrative codes are listed in Supplementary material online, appendix.

Study population

In the National Patient Registry, we identified patients aged 25 years or older admitted to Danish hospitals with first-time MI (ICD10 codes I21-I22) in the period 2000–09. The National Patient Registry does not hold valid information of STEMI and NSTEMI and MI was evaluated as one entity. To study first-time MI, we excluded patients with a MI diagnosis before 2000. Both patients that did not survive or were discharged on the first hospital day were excluded from the study population. Patients that did not survive the first hospital day were excluded due to insufficient observation time and patients who were discharged on the first hospital day were defined as not having MI. As we compared the treatment of MI among patients with and without CKD at the time of admission, we excluded patients who started RRT or were diagnosed with CKD within 3 months after MI as an undiagnosed kidney disease at admission would blur the treatment in the group of patients with no renal disease. Patients requiring RRT were identified in The Danish National Registry on Regular Dialysis and Transplantation and patients with non-end-stage CKD were identified in the National Patient Registry with one of the following diagnoses prior to MI: diabetic nephropathy, chronic glomerulonephritis, chronic tubulo-interstitial nephropathy, hypertensive nephropathy, adult polycystic kidney disease, chronic nephropathy of other origin, or chronic nephropathy of unknown aetiology.

Invasive coronary procedures

Performed coronary angiography, PCI, and coronary artery by-pass grafting (CABG) were coded according to the Nordic Medical Statistics Committee’s Classification of Surgical Procedures (NCSP) which is registered in the National Patient Registry. The codes are used as measures of activity and form the basis for the reimbursement system in the Danish National Health Service.

Pharmacological treatment

Information on filled prescriptions 180 days before MI and 90 days after MI on clopidogrel, aspirin, statins, and cardio-protective drugs was retrieved from the Danish Register of Medicinal Product Statistics. Cardio-protective drugs were a composite of beta-blockers, alpha-beta blockers, and renin–angiotensin blockers.

Comorbidity

Comorbidity was defined as primary and secondary discharge diagnoses up to 1 year before the index admission, including diabetes with complications, congestive heart failure, cancer, cerebrovascular disease, pulmonary oedema, cardiac dysrhythmias, and shock.

Main outcome parameters

The main outcome parameters were invasive treatment with coronary angiography and PCI/CABG (coronary revascularization) and pharmacologic treatment with clopidogrel, aspirin, statins, and cardio-protective drugs. For invasive treatment, outcomes within 60 days after first-time MI were recorded. A 60-day period was chosen in order to include as many examinations as possible and at the same time avoid examinations due to reinfarction. Filled prescriptions within 90 days were recorded for the pharmacologic treatment outcome parameters. The absolute frequencies of coronary angiography and PCI performed within 1, 3, and 60 days and filled prescriptions 180 days before MI and 90 days after MI are presented as well.

Statistics

Baseline variables are presented as percentages and medians with inter-quartile ranges. Chi-squared and Fisher’s exact tests are used where appropriate. We analysed the probability of coronary angiography, coronary revascularization, and filled prescriptions with Cox proportional hazards model adjusting for age, gender, and comorbidity before and after 2004. The time periods before and after 2004 were defined a priori as we wanted to evaluate if the upgraded guidelines for the management of MI that were implemented around 2004 had any impact on the treatment of MI after 2004. The hazards for the time periods before and after 2004 were compared using the Wald test. Model assumptions of linearity of continuous covariates, proportional hazards, and lack of interactions were tested and found valid unless otherwise indicated. Adjustments for multiple comparisons have not been made. A two-sided P-value of <0.05 was considered to be statistically significant. SAS version 9.2 was used for the statistical analysis.

Ethical considerations

The study was approved by the Danish Data Protection Agency (Reference: 2007-58-0015, int. ref. GEH-2010-001). Registry studies do not require ethical approval in Denmark.

Results

A total of 90676 patients were admitted with first-time MI from 1 January 2000 to 31 December 2009. Totally, 7222 patients were excluded because of death or discharge on the first hospital day. The study population therefore consisted of 83454 patients where 3144 (3.8%) were non-end-stage CKD patients and 725 (0.9%) were patients requiring RRT. Among those patients requiring RRT, approximately 20% were kidney transplanted. There was an even distribution of patients before and after 2004 (Figure 1).

Patients requiring RRT were younger than both non-end-stage CKD patients and patients with no renal disease (Table 1). Approximately
one-third of all patients were women. Diabetes, cancer, cerebrovascular disease, pulmonary oedema, and cardiac dysrhythmias were more frequently seen in non-end-stage CKD patients and in patients requiring RRT compared with patients with no renal disease (Table 1).

**Mortality**

Non-end-stage CKD patients and patients with no renal disease had significant lower all-cause mortality rates after 30 and 365 days after 2004 compared with the time before 2004. The improved survival rates were not observed for patients requiring RRT (Table 1).

**Coronary angiography and coronary revascularization (PCI and CABG)**

Overall, significantly more patients in all three patient groups were examined with coronary angiography and PCI within 60 days after 2004 (Table 2).

The increase was more pronounced in patients with no renal disease: 24% (no renal disease), 12% (non-end-stage CKD), and 14% (requiring RRT) for coronary angiography and 20% (no renal disease), 9% (non-end-stage CKD) and 6% (requiring RRT) for PCI, respectively (Table 2). A substantial reduction after 2004 in median time from hospital admission to coronary angiography and coronary revascularization was seen (Table 2).

Compared with patients with no renal disease, the chance of coronary angiography within 60 days for non-end-stage CKD patients was significantly reduced over time with a hazard ratio (HR) of 0.69 [95% confidence intervals (CI), 0.62–0.77] before 2004 to a HR after 2004 of 0.60 (95% CI, 0.55–0.65; P = 0.026 for difference between hazard ratios). For patients requiring RRT, no change was seen [HR 0.56 (95% CI, 0.47–0.68) before 2004 and HR 0.47 (95%, CI 0.40–0.55) after 2004] P = 0.14 for difference between hazard ratios (Figure 2). The chance of coronary revascularization within 60 days in non-end-stage CKD patients and in patients requiring RRT compared with patients with no renal disease was unchanged across the study period (Figure 2). Both before and after 2004, non-end-stage CKD patients and patients requiring RRT were significantly less treated with coronary angiography and coronary revascularization compared with patients with no renal disease (Figure 2). We performed an additional analysis to evaluate the possible treatment differences between dialysis patients and patients with a kidney transplant (Table 3). Data showed that the percentages of patients with a kidney transplant having a coronary angiography performed within 60 days were almost similar to that of patients with no renal disease, whereas PCI was performed to a lesser extent. For both dialysis patients and patients with a kidney transplant treatment with both coronary angiography and PCI increased significantly after 2004 (Table 3). In our study population, the MI diagnosis was coded as

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**Figure 1** Study population, according to status on renal disease. Of the 90,676 patients discharged with a myocardial infarction diagnosis between 2000 and 2009, 86,557 patients had no renal disease, 3,345 had non-end-stage chronic kidney disease, and 774 had disease requiring renal replacement therapy.
STEMI in 8081 (10%) patients, NSTEMI in 26 435 (31%) patients, and the remaining 48 938 (59%) patients were coded as unspecified MI. Among patients coded with either STEMI or NSTEMI, STEMI was more often coded in patients with no renal disease (24%) compared with non-end-stage CKD patients (15%) and patients requiring RRT (14%). The frequency of acute PCI (PCI within 1 day of MI) was evaluated among coded STEMI patients: before 2004, 48% (n = 1439) of coded STEMI patients with no renal disease were treated with acute PCI compared with 75% (n = 3628) after 2004. In coded STEMI patients with non-end-stage CKD 28% (n = 23) had an acute PCI before 2004 compared with 41% (n = 48) after 2004 and 35% (n = 6) of coded STEMI patients requiring RRT had an acute PCI before 2004 compared with 38% (n = 8) after 2004. In the subgroup of coded STEMI patients, treatment with acute PCI increased after 2004 and was performed more frequently in patients with no renal disease compared with patients with CKD.

### Pharmacologic treatment

Filled prescriptions on clopidogrel, aspirin, statins, and cardio-protective drugs after MI are shown in Table 4. Except for cardio-protective drugs in patients requiring RRT, the frequency of filled prescriptions increased over time for all patients irrespective of renal disease (Table 4). Cox proportional hazards analysis of filled prescriptions within 90 days after MI before and after 2004 is shown in Figure 2. For non-end-stage CKD patients, there was a significant increase in filled prescriptions for clopidogrel [HR 0.68 (95% CI 0.61–0.76) before 2004 and HR 0.78 (95% CI 0.72–0.84) after 2004; P = 0.04 for difference between hazard ratios] (Figure 2). No improvement after 2004 in the relative chance of filling prescriptions in patients requiring RRT was seen (Figure 2). Following coronary angiography, fewer patients with CKD filled a prescription on clopidogrel compared with patients with no renal disease, and no change after 2004 was seen. Hazard ratios of clopidogrel 90 days after coronary angiography for non-end-stage CKD patients were 0.64 (95% CI 0.56–0.72) before 2004 and 0.63 (95% CI 0.58–0.69) after 2004; P = 0.91 for difference between hazard ratios. For patients requiring RRT, the corresponding numbers were 0.50 (95% CI 0.39–0.63) before 2004 and 0.50 (95% CI, 0.42–0.60) after 2004; P = 0.93 for difference between hazard ratios. Following coronary revascularization with PCI or CABG, the chance of filling a prescription on clopidogrel within 90 days was also significantly lower in all CKD patients compared with patients requiring RRT, the frequency of filled

### Table 1 Baseline characteristics of patients with first time myocardial infarction in the periods 2000–04 and 2005–09

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<tbody>
<tr>
<td>Study population</td>
<td>372</td>
<td>353</td>
<td>1514</td>
<td>1630</td>
<td>42 811</td>
<td>36 774</td>
</tr>
<tr>
<td>Disease requiring RRT</td>
<td>66 (55–74)</td>
<td>68 (59–76)</td>
<td>76 (67–82)</td>
<td>77 (68–84)</td>
<td>72 (60–81)</td>
<td>70 (60–81)</td>
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<tr>
<td>Female gender (%)</td>
<td>34</td>
<td>37</td>
<td>38</td>
<td>36</td>
<td>40</td>
<td>38</td>
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<tr>
<td>Admission length, days (IQR)</td>
<td>6 (4–9)</td>
<td>6 (3–11)</td>
<td>7 (4–12)</td>
<td>6 (4–12)</td>
<td>6 (4–10)</td>
<td>5 (3–9)</td>
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<tr>
<td>RRT modality at MI, n (%)</td>
<td></td>
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<tr>
<td>Dialysis</td>
<td>296 (80)</td>
<td>290 (82)</td>
<td></td>
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<td>RTX</td>
<td>76 (20)</td>
<td>63 (18)</td>
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<td>Comorbidity, n (%)</td>
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<tr>
<td>Diabetes with complications</td>
<td>108 (29)*</td>
<td>117 (33)*</td>
<td>618 (41)*</td>
<td>633 (39)*</td>
<td>4515 (11)</td>
<td>3459 (9)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>62 (17)**</td>
<td>49 (14)**</td>
<td>458 (30)*</td>
<td>421 (26)*</td>
<td>5796 (14)</td>
<td>4179 (11)</td>
</tr>
<tr>
<td>Cancer</td>
<td>25 (7)*</td>
<td>30 (9)*</td>
<td>107 (7)*</td>
<td>125 (8)*</td>
<td>1735 (4)</td>
<td>1568 (4)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>30 (8)**</td>
<td>35 (10)*</td>
<td>184 (12)*</td>
<td>213 (13)*</td>
<td>2713 (6)</td>
<td>2117 (6)</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>36 (10)*</td>
<td>17 (5)*</td>
<td>67 (4)*</td>
<td>51 (3)*</td>
<td>787 (2)</td>
<td>461 (1)</td>
</tr>
<tr>
<td>Cardiac dysrhythmias</td>
<td>62 (17)*</td>
<td>75 (21)*</td>
<td>304 (20)*</td>
<td>335 (21)*</td>
<td>5375 (13)</td>
<td>4862 (13)</td>
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<tr>
<td>Shock</td>
<td>4 (1)**</td>
<td>5 (1)**</td>
<td>23 (2)*</td>
<td>30 (2)*</td>
<td>335 (1)</td>
<td>308 (1)</td>
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<tr>
<td>Mortality, n (%)</td>
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<tr>
<td>30 days</td>
<td>69 (19)</td>
<td>72 (20)**</td>
<td>419 (28)</td>
<td>371 (23)*</td>
<td>5933 (14)</td>
<td>4282 (12)*</td>
</tr>
<tr>
<td>365 days</td>
<td>162 (44)</td>
<td>151 (43)**</td>
<td>722 (48)</td>
<td>714 (44)*</td>
<td>10 035 (23)</td>
<td>7470 (20)**</td>
</tr>
</tbody>
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| RRT, renal replacement therapy; CKD, chronic kidney disease.  
| aHaemo- or peritoneal dialysis.  
| bRenal transplantation; frequency of comorbidity was compared with patients with no renal disease. IQR: 25–75% range.  
| nP < 0.05. All-cause mortality was compared before and after 2004. |
with no renal disease and did not change during the study period. The hazard ratios were almost the same as for coronary angiography. Overall CKD patients, including patients requiring RRT filled significantly fewer prescriptions on recommended post-MI drugs compared with patients with no renal disease. Treatment with aspirin, statins, and cardio-protective drugs were more frequent in non-end-stage CKD patients and in patients requiring RRT before MI compared with patients with no renal disease, probably reflecting more comorbidity.

Use of clopidogrel after MI for both dialysis patients and patients with a kidney transplant increased significantly after 2004 (Table 3). Aspirin, statin, and cardio-protective drug use in patients with a kidney transplant were unchanged over time, whereas in dialysis patients a significantly increase in use of statins after 2004 was seen (Table 3).

### Discussion

The present study shows, at a national level, that the significant implementation of invasive procedures after MI has to a lesser degree included the CKD population. In non-end-stage CKD patients, the frequency of coronary angiography within 60 days after MI increased significantly from 25% before 2004 to 37% after 2004, and in patients requiring RRT from 31% before 2004 to 45% after 2004. Myocardial infarction patients with no renal disease had a significantly increase in coronary angiography procedures from 44% before 2004 to 68% after 2004. The relative chance for coronary angiography fell significantly from 69 to 60% in non-end-stage CKD patients and from 56 to 47% (non-significant) in patients requiring RRT compared with MI patients with no renal disease. The frequency of PCI within 60 days showed the same pattern with a significantly increase in patients with no renal disease from 30% before 2004 to 50% after 2004, in non-end-stage CKD patients from 15 to 24% and 19 to 25% in patients requiring RRT. As for coronary angiography, the relative chance for coronary revascularization with PCI/CABG fell (non-significant) in patients with CKD. Furthermore, both coronary angiography and coronary revascularization were performed some days later in MI patients with CKD. For patients requiring RRT, there was a marked difference between the frequency of invasive coronary procedures in dialysis patients and renal transplanted patients.

### Table 2 Invasive procedures with coronary angiography and coronary revascularization in patients with first time myocardial infarction before and after 2004

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<tbody>
<tr>
<td></td>
<td>Disease requiring RRT (N = 372)</td>
<td>166 (45)</td>
<td>184 (53)</td>
<td>464 (31)</td>
<td>680 (42)</td>
<td>22 494 (53)</td>
<td>25 977 (71)</td>
</tr>
<tr>
<td></td>
<td>Disease requiring RRT (N = 353)</td>
<td>121 (8)</td>
<td>163 (11)</td>
<td>371 (25)</td>
<td>610 (37)</td>
<td>18 819 (44)</td>
<td>25 117 (68)</td>
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<td>Examination with CAG, n (%)</td>
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<tr>
<td>Within</td>
<td>1 day</td>
<td>35 (9)</td>
<td>48 (14)</td>
<td>266 (16)</td>
<td>6990 (16)</td>
<td>13 351 (36)</td>
<td>16 404 (45)</td>
</tr>
<tr>
<td></td>
<td>3 days</td>
<td>56 (15)</td>
<td>79 (22)</td>
<td>347 (21)</td>
<td>8698 (20)</td>
<td>16 404 (45)</td>
<td>16 404 (45)</td>
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<td></td>
<td>60 days</td>
<td>115 (31)</td>
<td>158 (45)</td>
<td>610 (37)</td>
<td>18 819 (44)</td>
<td>25 117 (68)</td>
<td>25 117 (68)</td>
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<tr>
<td>Days from admission to CAG (median, IQ range)</td>
<td></td>
<td>11 (2–122)</td>
<td>4 (1–15)</td>
<td>8 (1–33)</td>
<td>3 (0–9)</td>
<td>6 (0–22)</td>
<td>1 (0–6)</td>
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<tr>
<td>Coronary revascularization, n (%)</td>
<td></td>
<td>93 (25)</td>
<td>109 (31)</td>
<td>276 (18)</td>
<td>426 (26)</td>
<td>14 890 (35)</td>
<td>18 928 (52)</td>
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<tr>
<td>PCI</td>
<td></td>
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<tr>
<td>Within</td>
<td>1 day</td>
<td>31 (8)</td>
<td>36 (10)</td>
<td>124 (8)</td>
<td>258 (16)</td>
<td>7273 (17)</td>
<td>13 265 (36)</td>
</tr>
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<td></td>
<td>3 days</td>
<td>43 (12)</td>
<td>46 (13)</td>
<td>227 (15)</td>
<td>385 (24)</td>
<td>12 713 (30)</td>
<td>18 361 (50)</td>
</tr>
<tr>
<td></td>
<td>60 days</td>
<td>70 (19)</td>
<td>90 (25)</td>
<td>227 (15)</td>
<td>385 (24)</td>
<td>12 713 (30)</td>
<td>18 361 (50)</td>
</tr>
<tr>
<td>CABG</td>
<td></td>
<td>33 (9)</td>
<td>22 (6)</td>
<td>90 (6)</td>
<td>3898 (9)</td>
<td>2439 (7)</td>
<td>2439 (7)</td>
</tr>
<tr>
<td>Days from admission to PCI/CABG (median, IQ range)</td>
<td></td>
<td>11 (1–122)</td>
<td>7 (1–42)</td>
<td>11 (1–45)</td>
<td>3 (0–17)</td>
<td>8 (0–32)</td>
<td>1 (0–9)</td>
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</table>

RRT, renal replacement therapy; CKD, chronic kidney disease; CAG, coronary angiography; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; NS, not significant; IQ range, 25 and 75% quartile range. *P < 0.05 if difference exists before and after 2004.
The percentage of patients with a kidney transplant treated with coronary angiography within 60 days was almost the same as for patients with no renal disease, whereas the percentage for PCI was slightly lower. Only limited literature concerning coronary invasive treatment after MI in patients with a kidney transplant was found; however, kidney transplant status did not seem to influence the medication use after MI.20 In the subgroup coded STEMI patients, patients with no renal disease were treated with acute PCI more frequently after 2004 and to a greater extent than patients with CKD, confirming the overall conclusion that patients with CKD are less treated with standard guideline-based therapies than patients with no renal disease. The lower use of coronary angiography and coronary revascularization in MI patients with CKD may have several reasons. One explanation might be the sparse evidence pertaining to an improved outcome after invasive procedures in these patients and another probably more important explanation is the risk of CI-AKI which in patients with non-end-stage CKD might lead to worsening of an already reduced renal function and, in patients requiring dialysis, it might cause the loss of residual renal function. Furthermore, the use of invasive procedures might also be influenced by comorbidity, which is often severe in patients with CKD. Compared with the results from this study, other studies have shown even worse rates of reperfusion therapies in patients with moderate CKD after MI.8,9,21

Cohort studies and subgroup analyses have provided somewhat diverging results on which treatment strategy should be applied and favourable outcomes after recommended therapies have been shown as well as less significant effects of recommended treatment.22–33 Data from the SWEDHEART registry showed that a 1-year mortality benefit of early revascularization over medical therapy was seen in patients with estimated GFR (eGFR) above 30,22 whereas no benefit was seen in patients with eGFR below 30; however, only 44 patients with eGFR below 30 were included in the study. Incidence of reinfarction was not evaluated. A subgroup analysis from the TACTICS-TIMI trial34 showed a benefit of early revascularization on the composite endpoint death, MI, and revascularization in patients with creatinine clearance of 30–60 mL/min and similar results were found in the GRACE registry.35 Although these studies suggest a therapeutic benefit in patients with mild to moderate renal insufficiency, evidence from clinical trials regarding a therapeutic threshold of a certain level of renal function is lacking probably contributing to the less use of standard MI therapy in CKD patients. Contrast-induced kidney injury is important but the risk has to be evaluated in light of the marked cardiovascular morbidity and mortality in CKD patients. A recently published retrospective study of more than 33 000 patients with MI between 2000 and 2008 showed that the overall incidence of acute kidney injury (defined as an absolute increase in creatinine level of at least 0.3 mg/dL or a relative increase of at least 50% during hospitalization) declined from 26.6% in 2000 to 19.7% in 2008 despite the ageing population and rising prevalence of risk factors for acute renal failure, including CKD. It was suggested that the decline in acute kidney injury may be due to improved efforts at preventing CI-AKI in MI patients.36

The percentage of patients with a kidney transplant treated with coronary angiography within 60 days was almost the same as for patients with no renal disease, whereas the percentage for PCI was slightly lower. Only limited literature concerning coronary invasive treatment after MI in patients with a kidney transplant was found; however, kidney transplant status did not seem to influence the medication use after MI.20 In the subgroup coded STEMI patients, patients with no renal disease were treated with acute PCI more frequently after 2004 and to a greater extent than patients with CKD, confirming the overall conclusion that patients with CKD are less treated with standard guideline-based therapies than patients with no renal disease. The lower use of coronary angiography and coronary revascularization in MI patients with CKD may have several reasons. One explanation might be the sparse evidence pertaining to an improved outcome after invasive procedures in these patients and another probably more important explanation is the risk of CI-AKI which in patients with non-end-stage CKD might lead to worsening of an already reduced renal function and, in patients requiring dialysis, it might cause the loss of residual renal function. Furthermore, the use of invasive procedures might also be influenced by comorbidity, which is often severe in patients with CKD. Compared with the results from this study, other studies have shown even worse rates of reperfusion therapies in patients with moderate CKD after MI.8,9,21

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Figure 2 Probability of coronary angiography and coronary revascularization within 60 days and filled prescriptions on clopidogrel, aspirin, statins, and cardio-protective drugs within 90 days after myocardial infarction in patients with non-end-stage chronic kidney disease and patients requiring renal replacement therapy compared with patients with no renal disease. Values are shown as hazard ratios (HR) with error bars illustrating the 95% confidence intervals. *P*-values demonstrate difference between time periods. Statistically significance at *P* < 0.05.
The recommended post-MI drugs, as judged by filled prescriptions within 90 days, generally increased after 2004, although the chance of filling prescriptions was lower compared with patients with no renal disease. When non-end-stage CKD patients and patients requiring RRT were treated with invasive procedures, the chance of filling a prescription on clopidogrel afterwards was significantly reduced compared with patients with no kidney disease. Same result was found in a study by Gibney et al. Benefits and less apparent benefits of long-term clopidogrel have been demonstrated. However, the treatment with clopidogrel was not associated with a greater relative risk of bleeding based on renal function. No relevant differences in the use of post-MI drugs after 2004 between dialysis patients and patients with a kidney transplant were observed, and for both groups a significant increase in use of clopidogrel after MI was seen.

Aspirin and statin use after MI was shown to improve outcome in patients with underlying kidney disease and more than two-thirds of the non-end-stage CKD patients and half the patients requiring RRT filled a prescription on aspirin and statins, respectively, after 2004. Compared with patients with no renal disease, no increase during the study period was seen.

Use of cardio-protective drugs was shown to be beneficial after MI with an overall mortality risk reduction, and more than 80% of both non-end-stage CKD patients and patients requiring RRT filled a prescription on cardio-protective drugs after 2004.

The overall lower use of post-MI drugs could be related to the prevailing poly-pharmacy in patients with CKD increasing the risk of drug-related adverse reactions and drug interactions. Cohort studies from the USA have shown a substantial underuse of invasive and medical treatments after MI. However, opposite USA, Denmark offers free medical care to all citizens regardless of income as well as a reimbursement of parts of the medicine expenses, so at least this should not be an obstacle for the treatment of patients with CKD.

Overall, the increases after 2004 in invasive procedures performed within 60 days after MI and in filled prescriptions on clopidogrel, aspirin, and statins within 90 days suggest increased awareness on providing CKD patients recommended MI treatment and less therapeutic nihilism. However, compared with patients with no renal disease, patients with CKD are less treated with invasive procedures and post-MI drugs with the exception that patients with a kidney transplant were treated with coronary angiography to the same extent as patients with no renal disease.

**Strengths and limitations**

The major strength of the present study is that it is based on nationwide registries, i.e. the description of the MI treatment pertains to all citizens in Denmark. The diagnosis of MI in the National Patient Registry has been validated with a positive predictive value of 92.4%. The Danish Registry on Regular Dialysis and Transplantation is valid and complete. One major limitation in our study was that we did not have valid information regarding whether the MI was STEMI or NSTEMI as the guidelines differ for these two presentations of MI. However, our main outcome was coronary angiography and revascularization within 60 days and hence would include both STEMI and NSTEMI patients. Another major limitation was that patients diagnosed with a CKD at any time before MI were analysed as one group as we did not have access to measures of kidney function and therefore not able to describe the treatment of MI according to CKD stages. On the other hand, previous studies have evaluated MI treatment according to plasma creatinine levels measured at admission, which might not reflect any CKD but rather be a snapshot of the acute illness. Therefore, eGFR at admission might cause a higher rates of CKD in the MI population seen in these
Yet another limitation was that we did not have access to information about risk factors such as smoking habits and body weight and we did not have access to information about the activity of daily living. Compliance is also an important limitation. Even if patients filled their prescriptions, we could not be sure that they were actually taking the medicine and for those not filling prescriptions we could not differentiate whether the patients did not receive a prescription at discharge or chose not to fill it.

### Conclusions and implications

We demonstrated that the absolute frequencies of invasive procedures and filled prescriptions on post-MI drugs increased after 2004 in all patients irrespective of renal disease and that patients with a kidney transplant were offered same level of care as patients with no renal disease regarding treatment with coronary angiography within 60 days. Compared with patients with no renal disease, significantly less use of standard MI treatment in patients with CKD was demonstrated in this nationwide study. Explanations for this less use of standard MI treatment in CKD patients could be the sometimes severe comorbidity among CKD patients and the risk of CI-AKI, but this study was not able to confirm this.

### Supplementary material

Supplementary material is available at European Heart Journal online.

### Conflict of interest

None declared.

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