Chapter V

Effect of First Myocardial Ischemic Event on Renal Function

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Abstract

The effects of cardiovascular dysfunction on the course of renal function have been poorly characterized. Therefore, we investigated the relationship between a first ischemic cardiac event and long-term renal function changes in the general population from the PREVEND study. We studied 6360 subjects with a total follow-up duration of 27,017 subjects-years. The estimated mean proportional increase in serum creatinine after a first ischemic cardiac event was 3.1% compared to 0.4% per year of follow-up in subjects without such an event ($P = 0.005$). This represented a significantly larger decline in estimated glomerular filtration rate after the event in subjects with a first ischemic cardiac event compared to subjects without (2.2 versus 0.5 ml/min/1.73m2 per year of follow-up respectively, $P = 0.006$). In the multivariate analysis with adjustment for renal risk factors, this event showed an independent association with serum creatinine change. In conclusion, a first ischemic cardiac event appears to enhance the natural decline in renal function. The occurrence of this event was associated with renal function change independent from other risk factors. Since even mild renal dysfunction should be considered as a major cardiovascular risk factor after myocardial infarction, enhanced renal function loss after an ischemic cardiac event could add to the risk for subsequent cardiovascular morbidity, closing a vicious circle.

Key words

Ischemic cardiac event, myocardial infarction, general population, renal function loss.
Introduction

Renal (dys)function has been shown to be one of the most powerful prognostic risk markers for cardiovascular morbidity and mortality in various populations. However, the issue whether cardiovascular morbidity has an effect on the course of renal function (i.e., cardio-renal interaction) has not been adequately addressed to date. In theory, cardiac dysfunction could be particularly detrimental for organs that require a large hemodynamic perfusion such as the kidney. Previously, we found that experimental myocardial infarction has a distinct impact on the kidney resulting in enhanced progression of proteinuria and focal glomerulosclerosis in rats. Clinical data from the Captopril and Thrombolysis Study indicated that renal function declined in a selected population of patients with a previous anterior wall myocardial infarction. However, this study neither examined renal function before myocardial infarction, nor did it include a control group providing comparative data against subjects without such an event. Furthermore, the impact of other forms of ischemic heart disease were not investigated. We therefore investigated the long-term renal impact of a first ischemic cardiac event in a well-characterized, large cohort derived from the general population. The association between this first ischemic cardiac event and renal function change was evaluated among a comprehensive set of risk factors for renal function loss.
**Materials and Methods**

**Study design and population**

The Prevention of Renal and Vascular End-stage Disease (PREVEND) Study was initiated in 1997 with the primary aim to investigate the natural course of microalbuminuria and its relationship with renal and cardiovascular disease in the general population. Detailed information regarding the design and organisation of this observational cohort study has been presented elsewhere. In short, a cohort consisting of male and female inhabitants aged 28 to 75 years drawn from the city of Groningen, the Netherlands, was screened during a baseline visit at an outpatient clinic. Pregnant women and subjects with insulin-dependent diabetes mellitus were excluded. Overall, 8592 subjects were included. After a mean follow-up duration of 4.2 years, the participants were invited for a follow-up visit. In total, 1698 patients did not complete the follow-up visit due to withdrawal from the study (n = 1328), death (n = 240), or lost to follow-up without known vital status (n = 130). Both baseline and follow-up data were available for a total of 6894 subjects (ie., 80.2% of the included population).

In this data set, an ischemic cardiac event was defined according to the World Health Organisation International Classification of Diseases (WHO-ICD-9) as the occurrence of myocardial infarction (code 410) or other acute and subacute forms of ischemic heart disease (code 411), the latter of which includes unstable angina and acute coronary occlusion without myocardial infarction. The event data were obtained from the National Medical Register of hospital admissions. In order to study the impact of a first ischemic cardiac event on long-term renal function, subjects who experienced an ischemic cardiac event before the baseline visit and/or within one year prior to the follow-up visit were excluded (n = 204). We also excluded subjects with a missing value for serum creatinine at either visit, renal disease requiring dialysis, and/or baseline urine sediment abnormalities (leukocytes > 75/μL and/or erythrocytes > 50/μL) making albumin measurement unreliable (n = 330). In total 6360 subjects were eligible for the present analysis. All subjects gave written informed consent. The local medical ethics committee approved the PREVEND study and the conduct of the project was in accordance with the guidelines of the declaration of Helsinki.

**Serum creatinine**

At baseline, serum creatinine was determined by Kodak Ektachem dry chemistry (Eastman Kodak, Rochester, NY), an automatic enzymatic method. During the follow-up visit, serum creatinine was determined by photometric determination with the Jaffé method without deproteinization (Merck KGaA, Darmstadt, Germany). To prevent this
change in analytical method for serum creatinine to cause a systematic bias, a correction formula was introduced as described previously. The crude proportional change in serum creatinine was calculated as 100 percent x [(serum creatinine at follow-up minus serum creatinine at baseline) divided by (serum creatinine at baseline multiplied by follow-up duration)]. A more detailed analysis of the change in serum creatinine related to the occurrence of a first ischemic cardiac event was provided by means of calculating the change in serum creatinine after the event. Given the unexpected nature of the occurrence and timing of a first ischemic cardiac event in subjects from the general population, serum creatinine measurements could not be obtained immediately before the occurrence of this event. Therefore, the change in serum creatinine after the event was estimated using the individual change in serum creatinine between the baseline and follow-up visit subtracted by the expected serum creatinine increase prior to this cardiac event, based on the timing of the event after baseline for each individual and the natural course of serum creatinine in the large control group. For subjects with a first ischemic cardiac event, the zero index time point was defined as the moment this event occurred between baseline and follow-up. This time point was equal to the baseline visit for subjects without such an event during the follow-up period.

To investigate the robustness of the outcome, the change in serum creatinine after the first ischemic cardiac event was also calculated assuming a doubled rate of the expected (natural) serum creatinine increase prior to the occurrence of this cardiac event, yielding a conservative estimation of serum creatinine change after its occurrence. A second robustness analysis was conducted to provide a more direct comparison of subjects with and without an ischemic cardiac event, by means of defining a matched control cohort without a cardiac event. This matched cohort of subjects without a cardiac event was established on the basis of main predictors of renal function loss (i.e., age, gender, serum creatinine, body mass index, mean arterial pressure, serum cholesterol, triglycerides, plasma glucose, urinary albumin excretion, and smoking). A third robustness analysis was performed using a cut-off value of 6 months for the occurrence of the first ischemic cardiac event prior to the follow-up visit, thereby including subjects with medium-term renal function follow-up data after the event as well.

Other variables

Body mass index was calculated as weight (kg) divided by the square of height (m²). Blood pressure was automatically measured (Dinamap Model 9300 series, Johnson-Johnson Medical Inc., Tampa, FL) during 10 minutes at both visits. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or
the use of anti-hypertensive medication. Smoking was defined as current smoking or cessation < 1 year before the study. Triglycerides were measured enzymatically, and a commercially available assay system was used to assess high-density lipoprotein (HDL) (Abbott Inc., Abbott Park, IL). Serum cholesterol and plasma glucose were determined by Kodak Ektachem dry chemistry (Eastman Kodak, Rochester, NY, USA). Hypercholesterolemia was defined as serum cholesterol of ≥ 6.5 mmol/L or the use of lipid lowering medication. Diabetes mellitus was defined as a fasting glucose level of ≥ 7.0 mmol/L, a non-fasting glucose level of ≥ 11.1 mmol/L or the use of oral antidiabetic drugs. Urinary leukocyte and erythrocyte measurements were done by Nephurtest leucosticks (Boehringer Mannheim, Mannheim, Germany). Urinary albumin concentration was determined by nephelometry with a threshold of 2.3 mg/l (Dade Behring, Marburg, Germany). Urinary albumin excretion is given as the mean of the two 24-hour urine excretions. Serum C-reactive protein was also determined by nephelometry with a threshold of 0.175 mg/l (BNIIN, Dade Behring, Marburg, Germany). The estimated glomerular filtration rate was calculated using the 4-variable Modification of Diet in Renal Disease (MDRD) equation. 10

Statistical analyses

Comparisons of the population characteristics for subjects with and without an ischemic cardiac event during follow-up were tested using Student’s t-test for continuous variables and the Chi-Square test for categorical variables. Because of its skewed distribution, urinary albumin excretion was tested using the Kruskal-Wallis test. The difference in the change in serum creatinine between the groups with and without a first ischemic cardiac event was tested using Student’s t-test. The main response variable in the multivariate regression analysis was the estimated proportional change in serum creatinine from the zero index time point per year of follow-up. The analysis was conducted with adjustment for the baseline covariates gender, age, urinary albumin excretion, mean arterial pressure, body mass index, serum creatinine, cholesterol/HDL ratio, triglycerides, plasma glucose, C-reactive protein, smoking, and the presence of hypertension (definition included use of anti-hypertensive medication), diabetes mellitus or hypercholesterolemia (backward selection method). The analysis was also adjusted for the execution of percutaneous transluminal coronary angioplasty and coronary artery bypass grafting during follow-up, since these surgical procedures could have the potential to affect renal function in individual cases. For optimal goodness of fit, the variables serum creatinine, urinary albumin excretion and body mass index at baseline were transformed by a natural logarithm. Interaction (effect modification) was tested by entering product-terms into the model. A two-tailed P value of < 0.05 was considered statistically significant.
Results

The incidence of a first ischemic cardiac event was \( \frac{66}{6360} = 1.0\% \) in our sample of the general population, of which 61% was classified as myocardial infarction and 39% as ischemic heart disease. The total follow-up duration was 27.017 subject-years, yielding an event rate of 2.4 per 1000 subject-years. Baseline characteristics for subjects with and without a first ischemic cardiac event are presented in Table 1. Subjects who experienced a first ischemic cardiac event were older and had a higher body mass index, mean arterial pressure, cholesterol/HDL ratio, and urinary albumin excretion compared to subjects without a cardiac event. Also, a larger proportion of subjects with a cardiac event was male and more likely to have cardiovascular comorbid conditions such as hypertension or hypercholesterolemia. At baseline, renal function appeared to be slightly lower in the group with a cardiac event, as evidenced by a small and statistically insignificant difference in estimated glomerular filtration rate compared to the control group (Table 1). Subject characteristics at baseline were comparable between subgroups with myocardial infarction and ischemic heart disease. The crude mean proportional serum creatinine change between the baseline and follow-up visit was significantly larger in subjects with versus without a first ischemic cardiac event at rates of 1.8% and 0.4% per year of follow-up, respectively \((P=0.005)\). Accordingly, a consistently larger proportion of subjects from the group with a first ischemic cardiac event showed an increase in serum creatinine of at least a given magnitude between the baseline visit and the follow-up visit after 4.2 years on average (Table 2).

Main analysis

The main analysis concerned the estimated proportional serum creatinine change after the first ischemic cardiac event, thereby taking into account the timing of the event during the follow-up period. The mean duration between the occurrence of a first ischemic cardiac event and the follow-up visit was 943 days (range: 404-1653 days). In subjects with a first ischemic cardiac event, the estimated mean proportional increase in serum creatinine after the event was 3.1% per year of follow-up (Figure 1). This rate was significantly larger compared to the rate observed in subjects without a first ischemic cardiac event (0.4% per year of follow-up, \(P=0.005\)). These results represented a significantly larger decline in estimated glomerular filtration rate after the event in subjects with a first ischemic cardiac event compared to the decline observed in subjects without an event (2.2 versus 0.5 ml/min/1.73m\(^2\) per year of follow-up respectively, \(P=0.006\)). The mean proportional changes in serum creatinine after the event in the two subgroups with a first myocardial infarction or first event of ischemic heart disease were 2.9% and 3.6% per year of follow-up, respectively (Figure 1). The
expected course of the mean level of serum creatinine between the baseline and follow-up visit for subjects with a cardiac event and subjects without a cardiac event is depicted in Figure 2. At baseline, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers were used in 9% and 5% of subjects with and without a first ischemic cardiac event during follow-up, while 29% and 8% of subjects took these medications at the follow-up visit, respectively. In the multivariate regression analysis, a first ischemic cardiac event was significantly associated with the proportional change in serum creatinine independent from other risk factors for renal function loss (Table 3). Interactions with a first ischemic cardiac event were found for age and gender. Female and older subjects with a first ischemic cardiac event had a larger proportional serum creatinine increase compared to male and younger subjects, respectively.

Robustness analyses

Several robustness analyses were conducted, since the statistically insignificant difference in baseline renal function in subjects with and without a first ischemic cardiac event might have influenced the course of renal function during the follow-up period. The first robustness analysis assuming a doubled rate of the expected (natural) serum creatinine increase prior to the occurrence of the first ischemic cardiac event, yielded an estimated mean proportional change in serum creatinine after the event of 2.9% per year of follow-up ($P = 0.010$, $n = 66$). In the multivariate analysis, a first ischemic cardiac event remained significantly associated with the change in serum creatinine independent from other risk factors for renal function loss. In the second robustness analysis, a more direct comparison of the increase in serum creatinine in subjects with and without a first ischemic cardiac event was provided by defining a matched cohort without a cardiac event on the basis of main risk factors for renal function loss. A significantly larger increase in serum creatinine was found in the group with a first cardiac event compared to the matched group without a cardiac event (3.1% versus 0.4% per year of follow-up respectively, $P = 0.007$), which represented a significantly larger decline in estimated glomerular filtration rate after the event in subjects with a first ischemic cardiac event compared to the decline observed in the matched group without an event (2.2 versus 0.5 ml/min/1.73m$^2$ per year of follow-up respectively, $P = 0.011$). Overall, both robustness analyses further support that the enhanced decline in renal function is related to the occurrence of a first ischemic cardiac event. The third robustness analysis using a more permissive cut-off value for the timing of the first ischemic cardiac event before the follow-up visit (i.e., 6 months), yielded a mean proportional change in serum creatinine after the event of 3.6% per year of follow-up ($P = 0.008$, $n = 77$). Again, a first ischemic cardiac event remained significantly associated with the change in serum creatinine independent from other renal risk factors.
Table 1. Population characteristics at baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subjects without ischemic cardiac event</th>
<th>Subjects with ischemic cardiac event</th>
<th>Subjects with myocardial infarction</th>
<th>Subjects with ischemic heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49 (12)</td>
<td>58 (9)</td>
<td>57 (9)</td>
<td>60 (9)</td>
</tr>
<tr>
<td>Men</td>
<td>50.0%</td>
<td>66.7%</td>
<td>72.5%</td>
<td>57.7%</td>
</tr>
<tr>
<td>White</td>
<td>96.0%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0 (4.1)</td>
<td>28.6 (5.5)</td>
<td>28.6 (6.6)</td>
<td>28.6 (3.4)</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>92 (12)</td>
<td>101 (12)</td>
<td>102 (13)</td>
<td>100 (11)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.6 (1.1)</td>
<td>6.3 (1.0)</td>
<td>6.3 (0.8)</td>
<td>6.4 (1.2)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.3 (0.4)</td>
<td>1.1 (0.3)</td>
<td>1.1 (0.4)</td>
<td>1.0 (0.2)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>1.2 (0.8-1.7)</td>
<td>2.1 (1.2-2.2)</td>
<td>1.9 (1.2-2.2)</td>
<td>1.9 (1.3-2.2)</td>
</tr>
<tr>
<td>UAE (mg/day)</td>
<td>8.9 (6.2-15.2)</td>
<td>16.3 (9.4-33.6)</td>
<td>17.8 (9.7-43.8)</td>
<td>14.8 (8.8-24.4)</td>
</tr>
<tr>
<td>sCreat (µmol/L)</td>
<td>83.3 (14.1)</td>
<td>86.6 (14.1)</td>
<td>87.3 (15.2)</td>
<td>85.5 (12.3)</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m²)</td>
<td>81.2 (14.0)</td>
<td>78.4 (13.0)</td>
<td>79.9 (14.2)</td>
<td>76.0 (10.9)</td>
</tr>
<tr>
<td>Smokers</td>
<td>36.0%</td>
<td>48.5%</td>
<td>45.0%</td>
<td>53.8%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28.9%</td>
<td>58.5%</td>
<td>53.8%</td>
<td>65.4%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>3.1%</td>
<td>6.2%</td>
<td>7.5%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>24.4%</td>
<td>53.8%</td>
<td>53.8%</td>
<td>53.8%</td>
</tr>
</tbody>
</table>

The mean ± SD is given, except for urinary albumin excretion, C-reactive protein and triglycerides, which are expressed as median with the 25th and 75th percentiles. †With versus without ischemic cardiac event. BMI; body mass index, MAP; mean arterial pressure, HDL; high-density lipoprotein, CRP; C-reactive protein, eGFR; estimated glomerular filtration rate, sCreat; serum creatinine, UAE; urinary albumin excretion.  
†Defined as a systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or anti-hypertensive medication usage.  
&Defined as a fasting glucose level of ≥ 7.0 mmol/L, a non-fasting glucose level of ≥ 11.1 mmol/L or oral antidiabetic drugs usage.  
*Defined as serum cholesterol of ≥ 6.5 mmol/L or lipid lowering medication usage.
Table 2. Proportion of subjects in groups with and without a first ischemic cardiac event by serum creatinine change between baseline and follow-up visit

<table>
<thead>
<tr>
<th>Change during follow-up</th>
<th>Proportion of subjects in group without first ischemic cardiac event</th>
<th>Proportion of subjects in group with first ischemic cardiac event</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 5%</td>
<td>33.4%</td>
<td>42.4%</td>
</tr>
<tr>
<td>≥ 10%</td>
<td>16.9%</td>
<td>31.8%</td>
</tr>
<tr>
<td>≥ 20%</td>
<td>3.8%</td>
<td>13.6%</td>
</tr>
<tr>
<td>≥ 40%</td>
<td>0.3%</td>
<td>3.0%</td>
</tr>
</tbody>
</table>

Table 3. Univariate and multivariate regression models with the proportional change in serum creatinine (% per year) as outcome variable

<table>
<thead>
<tr>
<th>Univariate</th>
<th>Multivariate</th>
<th>n = 6244</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Unstandardized</td>
</tr>
<tr>
<td>Ischemic cardiac event^a</td>
<td>2.793</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Age</td>
<td>0.014</td>
<td>$&lt; 0.001$</td>
</tr>
<tr>
<td>Gender^b</td>
<td>-0.081</td>
<td>0.207</td>
</tr>
<tr>
<td>Ischemic cardiac event x Age</td>
<td>0.212</td>
<td>0.033</td>
</tr>
<tr>
<td>Ischemic cardiac event x Gender</td>
<td>2.498</td>
<td>0.645</td>
</tr>
</tbody>
</table>

^aReference group is subjects without a first ischemic cardiac event. ^bReference group is male subjects. Analysis adjusted for the baseline covariates mean arterial pressure, body mass index, serum creatinine, urinary albumin excretion, cholesterol/HDL ratio, triglycerides, plasma glucose, C-reactive protein, smoking, and the presence of hypertension, diabetes or hypercholesterolemia. The analysis was also adjusted for the execution of percutaneous transluminal coronary angioplasty and the execution of coronary artery bypass grafting during follow-up.
Figure 1. Impact of first ischemic cardiac event on long-term renal function. Barcharts show mean and 95% confidence interval of the mean. ICE; ischemic cardiac event, MI; myocardial infarction, IHD; ischemic heart disease.

Figure 2. Expected course of serum creatinine between baseline and follow-up visit per group. *Robustness analysis, assuming doubled rate of serum creatinine increase prior to cardiac event. **Matched control cohort of subjects without ischemic cardiac event, based on age, gender, serum creatinine, urinary albumin excretion, body mass index, mean arterial pressure, serum cholesterol, triglycerides, plasma glucose, and smoking.
Renal function gradually decreases over the years, but a first ischemic cardiac event appears to enhance this deterioration. The estimated mean proportional increase in serum creatinine after a first ischemic cardiac event was significantly larger compared to the rate observed in the control group of subjects without a cardiac event (3.1% versus 0.4% per year of follow-up, respectively). A comparable pattern was observed regarding the change in estimated glomerular filtration rate, showing a significantly larger decline in glomerular filtration rate after the event in subjects with a first ischemic cardiac event compared to the decline observed in subjects without an event (2.2 versus 0.5 ml/min/1.73m² per year of follow-up, respectively). The occurrence of a first ischemic cardiac event was associated with renal function change independent from other risk factors for renal function loss.

Cardio-renal interaction

The existence of cardio-renal interaction was previously suggested in an experimental setting showing that myocardial infarction enhances kidney damage, as evidenced by the enhanced development of progressive albuminuria and focal glomerulosclerosis in rats with pre-existent mild renal dysfunction induced by unilateral nephrectomy. Mild pre-existent renal dysfunction was also present in our subjects experiencing a first cardiac event, as evidenced by a decreased estimated glomerular filtration rate and increased urinary albumin excretion at baseline (Table 1). This may have added to their risk of experiencing a first cardiac event during the course of the study, in view of the well-known association between renal dysfunction and cardiovascular morbidity.

Based on the preclinical finding of an increased level of focal glomerulosclerosis after myocardial infarction, our finding of a larger decline in renal function may reflect this enhanced progression of glomerulosclerosis. This, however, needs further confirmation in the absence of renal biopsies in this population-based study. The underlying mechanism of this cardio-renal interaction is not well understood, but finding the exact underlying mechanism would constitute a major advance in the search for a more effective, targeted treatment of subjects at risk. Recent experimental data suggest that renin-angiotensin-aldosteron-system activity is involved in renal damage secondary to myocardial infarction. Collectively, the current data on cardio-renal interaction related to a first ischemic cardiac event and the previously described reno-cardiac interaction define a vicious circle. This is of clinical importance, especially since even mild renal dysfunction is considered as a major cardiovascular risk factor after myocardial infarction.

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**Limitations and outcome variable**

It should be noted that the PREVEND study was not primarily designed to investigate the effect of a first ischemic cardiac event on renal function, resulting in bias by indication. As expected, a limited number of subjects experienced a first ischemic cardiac event in this cohort obtained from the general population. Since renal angiography was not performed during this study, we cannot exclude that ‘silent’ renal artery disease may have affected the course of renal function in individual subjects. Subjects who experienced an ischemic cardiac event during the follow-up period generally had a worse cardiovascular and renal status at baseline, as reflected by a higher mean arterial pressure, serum creatinine, urinary albumin excretion, cholesterol/HDL ratio, body mass index, and an associated increased prevalence of hypertension and hypercholesterolemia. However, ethical considerations would obviously preclude to investigate the renal impact of a first ischemic cardiac event such as myocardial infarction in a prospective randomised intervention study in an effort to conclusively demonstrate cause and effect in humans. It is therefore important to note that the estimated proportional serum creatinine increase after a first ischemic cardiac event also was significantly larger compared to the rate observed in the matched cohort of subjects without this event. Further confirmatory evidence was obtained in the analysis assuming a doubled rate of the expected (natural) serum creatinine increase prior to the occurrence of the first ischemic cardiac event, yielding a conservative estimation of the serum creatinine change after its occurrence. This analysis also demonstrated a significantly larger estimated serum creatinine increase after the event compared to the rate observed in the control group. Again, an independent association of a first ischemic cardiac event with the change in serum creatinine was found in the multivariate model. Altogether, these findings show that enhanced renal function loss is related to the occurrence of a first ischemic cardiac event.

It is recognized that serum creatinine may be a less accurate measurement of renal function in an individual subject at a certain point in time, as the serum creatinine level is determined by multiple factors including muscle mass and glomerular filtration of creatinine. Therefore, renal function can also be assessed by calculating a Modification of Diet in Renal Disease or Cockcroft-Gault equation based estimated glomerular filtration rate. The use of estimated glomerular filtration rate as primary outcome variable would however introduce co-linearity since age and gender are generally considered as relevant predictor variables and contained as factors in the glomerular filtration rate equations describing the outcome variable as well. The current analysis relates to a between group comparison of an intra-individual serum creatinine change, thereby reducing variability caused by between-subject differences.
in factors such as muscle mass. Thus, the change in serum creatinine can be considered as an accurate reflection of altered renal function within a given subject, not introducing an artificial association between predictor variables and the primary outcome variable. The use of the estimated glomerular filtration rate has therefore been restricted to provide a descriptive clinical measure of the change in renal function in the groups with and without a first ischemic cardiac event.
Conclusion

Renal function gradually decreases over the years. However, a first ischemic cardiac event appears to enhance this deterioration, implicating that apparently healthy subjects experiencing a first cardiac event are at risk for renal function loss. Enhanced renal function loss in subjects who previously experienced a first ischemic cardiovascular event such as myocardial infarction could add to their risk for subsequent cardiovascular events, in particular since even mild renal dysfunction should be considered as a major cardiovascular risk factor after myocardial infarction.
Acknowledgements

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Reference List


