Association between chronic obstructive pulmonary disease and chronic kidney disease in vascular surgery patients

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Abstract

Background. Chronic obstructive pulmonary disease (COPD) is recognized as a source of systemic inflammation and is associated with the development of cardiovascular disease. However, little is known about the association between COPD and chronic kidney disease (CKD). Therefore, we investigated the relationship between COPD and CKD and the association between COPD and mortality in patients with CKD.

Methods. We conducted a cohort study of 3358 vascular surgery patients between 1990 and 2006. CKD was defined according to the Modification of Diet in Renal Disease equation as an estimated glomerular filtration rate (GFR) < 60 mL/min/1.73 m². In addition, the patients were divided into three categories based on the baseline estimated GFR: ≥ 90 mL/min/1.73 m²; 60–89 mL/min/1.73 m² and < 60 mL/min/1.73 m². Multivariable logistic regression analysis was used to evaluate the independent association between prevalent COPD and CKD.

Results. The prevalence of COPD was inversely related to kidney function. COPD was present in 47, 38 and 32% of patients with an estimated GFR < 60, 60–89 and ≥ 90 mL/min/1.73 m², respectively. COPD was independently associated with CKD (OR 1.22; 95% CI 1.03–1.44; P = 0.03). This association was strongest in patients with moderate COPD (OR 1.33; 95% CI 1.07–1.65; P = 0.01). Both moderate and severe COPD were associated with increased long-term mortality in patients with CKD (HR 1.27; 95% CI 1.03–1.56; P = 0.03 and HR 1.61; 95% CI 1.10–2.35; P = 0.01, respectively), compared to patients without COPD.

Conclusions. Our findings indicate that COPD is moderately associated with CKD in a large cohort of vascular surgery patients. In addition, moderate and severe COPD are related to increased long-term mortality in patients with CKD.

Keywords: chronic kidney disease; chronic obstructive pulmonary disease; vascular surgery

Introduction

Chronic kidney disease (CKD) is a growing public health problem and affects a large number of individuals, ~13% of the US adult population [1]. This is mainly due to the increased prevalence of traditional cardiovascular risk factors such as diabetes, hypertension and obesity [1, 2]. In addition, the presence of cardiovascular disease is also important in the development and deterioration of kidney disease [3]. Previous studies have found underlying atherosclerosis, an inflammatory process [4], to be associated with the pathogenesis of kidney disease [5, 6]. Hence, the relationship between cardiovascular disease and kidney function could also be due to an increased prevalence of other less well-examined cardiovascular risk factors, such as chronic obstructive pulmonary disease (COPD).

As with kidney disease, COPD is a major health care problem worldwide and is associated with cardiovascular disease as well. COPD is characterized by an abnormal inflammatory response of the lungs to noxious particles and gases [7]. However, the inflammation is not only restricted to the lungs but also extends systemically. Previous studies showed that this systemic inflammation might be the missing link between COPD and the development and progression of atherosclerosis and cardiovascular disease [8]. Consequently, given that a number of investigators [9–11] have shown that COPD is associated with cardiovascular disease in people with normal kidney function, it seems reasonable to propose that COPD in patients with vascular disease may also be associated with CKD independent of other covariates that might influence kidney function loss. Therefore, we investigated the relationship between COPD and CKD in a large cohort of vascular surgery patients with peripheral arterial disease. Moreover, we assessed the association between COPD and mortality in patients with kidney disease.
Results

Baseline characteristics

The characteristics of the 3358 patients are presented in Table 1 based on the presence or the absence of CKD. The mean serum creatinine concentration and estimated GFR in this population were 1.22 ± 1.15 mg/dL and 76 ± 30 mL/min/1.73 m², respectively. In total, 918 (27%) patients had CKD defined by an estimated GFR <60 mL/min/1.73 m² (mean estimated GFR 43 ± 15 mL/min/1.73 m²) (Table 1). Patients with CKD were older, were more likely to be female and had significantly higher proportions of hypertension, diabetes, COPD and cardiovascular disease. Importantly, CKD patients were less likely to be smokers and had a lower proportion of hypercholesterolaemia. COPD was present in 1307 (39%) patients.

In addition to the 918 patients with an estimated GFR <60 mL/min/1.73 m², 1500 and 940 patients had an estimated GFR level of 60–89 and ≥90 mL/min/1.73 m², respectively. The distribution of the prevalence of COPD according to kidney function is presented in Figure 1. Across decreasing estimated GFR groups 32%, 38% and 47% had COPD ($P < 0.001$).

Cross-sectional relationship between COPD and CKD

Table 2 shows that COPD was associated with a higher risk of prevalent CKD. After adjustment for age, gender, type of surgery, current smoking, previous heart failure, hypertension, diabetes and hypercholesterolaemia, patients with COPD had increased odds of CKD (adjusted OR 1.22 95% CI: 1.03–1.44; $P = 0.03$). This relationship was further explored by examining the association between COPD severity and CKD. A borderline significant relationship was observed for mild COPD while moderate COPD was independently associated with kidney disease (OR 1.23; 95% CI 0.99–1.53; $P = 0.06$ and OR 1.33; 95% CI 1.07–1.65; $P = 0.01$, respectively). No significant association was found between severe COPD and kidney disease (OR 0.80; 95% CI 0.54–1.20; $P = 0.29$) (Table 2).

Short- and long-term outcome in patients with CKD

In total, 178 (5%) patients died within 30 days after surgery and 80 (9%) of those with CKD. No relationship between COPD and short-term mortality was observed in patients with CKD (adjusted OR 0.94 95% CI: 0.58–1.54; $P = 0.82$). During 10 years of follow-up, 1555 (46%) patients died. COPD was associated with a higher risk of long-term mortality (Table 3). After adjustments for demographics, type of surgery, current smoking, previous heart failure, hypertension, diabetes and hypercholesterolaemia, moderate and severe COPD remained significantly associated with all-cause mortality in patients with CKD (HR 1.27; 95% CI 1.03–1.56; $P = 0.03$ and HR 1.61; 95% CI 1.10–2.35; $P = 0.01$, respectively).

Discussion

To date, several risk factors have been identified for the development and progression of CKD, e.g. older age,
Table 1. Baseline characteristics according to CKD

<table>
<thead>
<tr>
<th>Total (n = 3358)</th>
<th>No CKD (GFR ≥ 60) (n = 2440)</th>
<th>CKD (GFR &lt;60) (n = 918)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean estimated GRF (SD)</td>
<td>76 (30)</td>
<td>89 (23)</td>
<td>43 (15)</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>66 (12)</td>
<td>64 (12)</td>
<td>70 (11)</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>73</td>
<td>75</td>
<td>68</td>
</tr>
<tr>
<td>Type of surgery (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAA</td>
<td>36</td>
<td>33</td>
<td>40</td>
</tr>
<tr>
<td>CEA</td>
<td>24</td>
<td>28</td>
<td>15</td>
</tr>
<tr>
<td>LLR</td>
<td>40</td>
<td>39</td>
<td>45</td>
</tr>
<tr>
<td>Cardiovascular history (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>22</td>
<td>19</td>
<td>29</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>16</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>Heart failure</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>14</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>30</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No COPD</td>
<td>61</td>
<td>64</td>
<td>54</td>
</tr>
<tr>
<td>Mild COPD</td>
<td>17</td>
<td>16</td>
<td>21</td>
</tr>
<tr>
<td>Moderate COPD</td>
<td>17</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>5</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Clinical characteristics (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>38</td>
<td>34</td>
<td>50</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>18</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Current smoking status</td>
<td>28</td>
<td>30</td>
<td>24</td>
</tr>
</tbody>
</table>

Fig. 1. Percentages of COPD severity according to kidney function.

Table 2. Association between COPD severity and CKD (estimated GFR <60 mL/min/1.73 m²)

<table>
<thead>
<tr>
<th>Univariable</th>
<th>Multivariable a</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>COPD</td>
<td>1.54</td>
</tr>
<tr>
<td>No COPD</td>
<td>1.00</td>
</tr>
<tr>
<td>Mild COPD</td>
<td>1.57</td>
</tr>
<tr>
<td>Moderate COPD</td>
<td>1.67</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>1.01</td>
</tr>
</tbody>
</table>

aAdjusted for age, gender, type surgery, current smoking, previous heart failure, hypertension, diabetes and hypercholesterolaemia.
in patients with kidney dysfunction. The Cardiovascular Health Study found kidney dysfunction to be independently associated with elevated levels of high-sensitivity C-reactive protein (hsCRP), fibrinogen and interleukin-6 in participants of 65 years and older [22]. This might suggest that the inflammatory response observed in patients with kidney disease might be exacerbated by concomitant COPD.

Another possible explanation of our findings might be pulmonary hypertension secondary to COPD, which has been associated with the progression of kidney disease. Patients with COPD have severe retention of salt and water, reduction in renal blood flow and glomerular filtration and neurohormonal activation [23]. However, as our study was not designed to examine the mechanisms responsible for the association between COPD and kidney disease, further studies are needed to elucidate the rationale behind these relationships.

The fact that we did not find severe COPD associated with kidney disease might be explained by the following: first, only those patients who underwent vascular surgery were included in our study, so it might be possible that surgery was cancelled in those patients with a poor pulmonary function. Moreover, cardiovascular disease and cancer are major comorbidities in patients with COPD, with the inflammatory state as a possible link. These comorbidities are the leading causes of death in patients with mild and moderate COPD, while in those with severe COPD respiratory failure is the predominant cause [24]. So it might be suggested that patients with severe COPD died because of their respiratory failure before they could develop kidney disease.

Given that early stages of impaired kidney function are associated with increased risk of death, cardiovascular events and hospitalization [25], it is important to identify and consequently treat these patients to improve prognosis. Adequate treatment with angiotensin-converting enzyme (ACE) inhibitors or angiotensin-II receptor blockers (ARB) is required in those patients to slow the progression of kidney disease. In addition, a recent meta-analysis of randomized controlled trials demonstrated that statin therapy significantly reduces lipid concentrations and cardiovascular end points in patients with prevalent cardiac disease and CKD [26]. Therefore, an important aspect of the treatment of patients with kidney disease is to control the underlying cause and management of cardiovascular risk factors.

Hence, the observed association between moderate and severe COPD and increased long-term mortality in patients with CKD advocates the importance of the optimal management of COPD in patients with kidney disease as well.

Our study has some limitations as seen with retrospective studies. Unfortunately, we do not have any information on patients who were declined for surgery because of their pulmonary or kidney function that might explain the absence of a relationship between patients with severe COPD and kidney disease. Data on markers of inflammation were not available. Hence, the proposed mechanism that inflammation might be the underlying link between COPD and CKD could not be examined. In addition, due to the cross-sectional design of the study, the results need to be interpreted cautiously. As both pulmonary and kidney functions are assessed at one time point, it is difficult to infer causality as the sequence of COPD and kidney disease could not be ascertained. Consequently, the results of our study need to be interpreted cautiously. Finally, only 5% of the cohort had advanced kidney disease (i.e. estimated GFR ≤30 mL/min/1.73 m²). Hence, the prevalence of COPD in this group of patients could not be examined.

In summary, mainly moderate COPD was found to be associated with kidney disease in vascular surgery patients with peripheral arterial disease. Furthermore, advanced stages of COPD are associated with increased long-term mortality in patients with kidney disease. The presence of COPD might be responsible for the progression of atherosclerosis inducing further kidney disease. Further experimental and longitudinal studies are necessary to elucidate the role of COPD in the pathway by which kidney disease contributes to an increased risk of death.

Conflict of interest statement. None declared.

**References**

Glomerular filtration rate is related to carotid intima–media thickness in middle-aged adults

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Abstract

Background. Severe renal dysfunction is associated with increased cardiovascular risk. The aim of this study was to investigate the association between renal function and carotid intima–media thickness (cIMT) in a middle-aged population-based cohort.

Methods. A total of 247 males and 258 females aged 40–62 years participated in this cross-sectional study. Renal function was assessed with estimated glomerular filtration rate (eGFR) and carotid atherosclerosis with ultrasonography as the mean IMT of the far carotid wall.

Results. The mean eGFR values were 90.2 (SD 16.8) ml/min/1.73 m² for men and 78.0 (SD 14.0) ml/min/1.73 m² for women.

Received for publication: 16.1.09; Accepted in revised form: 23.3.09

doi: 10.1093/ndt/gfp172
Advance Access publication 15 April 2009