Reply—Gender difference in GFR dependent on age

Sir,

Rook et al. have made some comments on my work on renal function in relation to age [1]. They state that my conclusion is not warranted, since I have no longitudinal data. It is true that I have no longitudinal data, but I think these authors will agree with me that it is very hard to follow longitudinally healthy adults from age 20 to 70 years with adequate renal function tests, including continuous infusion and urine sampling. They also state that I have very few donors above 50 years of age; I believe that I pointed this out adequately in my study, in the Abstract, the Introduction, the Discussion and in the Conclusion. Moreover, I think that the period before 50 years of age is of special interest, since several authors claim that the decline in GFR does not start until 40–60 years of age [2–4]. Furthermore, that age range is the time when females still have an influence of oestrogens, which I think is the reason for the absence of decline in GFR and ERPF with age in females.

Rook et al. also claim that the number of subjects studied was relatively small. Looking at the data presented by Rook et al., the age distribution of their subjects does not seem uniform. Based on the figures in their study and calculating the number of males and females in each decade up to the age of 50 years, i.e. the same age range as in mine, the numbers in their data and in mine are as follows:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–30 years</td>
<td>8</td>
<td>5</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>30–40 years</td>
<td>10</td>
<td>20</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>40–50 years</td>
<td>23</td>
<td>47</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>72</td>
<td>56</td>
<td>60</td>
</tr>
</tbody>
</table>

I think that given the preponderance of donors and especially females between 40 and 50 years in their material, several of those females might have passed menopause and thus the positive influence of oestrogens on renal function might have disappeared. Moreover, half the donors presented by Rook et al. are over 50 years of age, i.e. outside the age range of focus in my study.

Furthermore, Rook et al. find, as I do, a rise in filtration fraction with age in males but not in females, which they claim ‘supports the relevance of gender for age-related effects on the kidney’. I may be wrong but I interpret this comment as a gender difference, as shown in my work.

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Letters

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The effects of n-acetylcysteine on methotrexate-induced oxidative renal damage in rats

Sir,

Methotrexate (MTX), a folic acid antagonist, is widely used as a cytotoxic chemotherapeutic agent for several malignancies and various inflammatory diseases. However, the efficacy of this agent often is limited by severe side effects and toxic conditions. MTX can cause increased serum creatinine levels, uraemia and haematuria, while its administration in high doses has been reported to cause acute renal failure [1]. The underlying mechanism of nephrotoxicity caused by the MTX treatment remains unknown. However, it has been reported that MTX causes oxidative stress in rat kidney tissues [2]. Moreover, antioxidant compounds such as t-carnitine and taurine has been shown to decrease the MTX-induced nephrotoxicity in the recent experimental studies [3,4]. Starting from this point, the present study was undertaken to determine whether n-acetylcysteine (NAC), as a potent antioxidant compound, could ameliorate MTX-induced oxidative renal damage in rats. Forty Wistar albino rats were used in the study. Following a single dose of MTX (20 mg/kg), either saline (MTX group) or NAC (150 mg/kg, MTX ± NAC group) was administered for 5 days. In other rats, saline (control group) or NAC (150 mg/kg, NAC group) was injected for 5 days, following a single injection of saline. On the sixth day the animals were sacrificed and the kidneys were excised and stored at −80°C for later analysis of malondialdehyde (MDA) and reduced glutathione (GSH) levels, and myeloperoxidase (MPO), superoxide dismutase (SOD) and catalase (CAT) activities.

As shown in Table 1, MTX treatment increased the kidney GSH, MDA levels and SOD, CAT and MPO activities significantly in the controls, while NAC treatment following MTX decreased this elevated parameters. Our results point out that MTX has induced oxidative stress on the kidney and hence increased oxidative stress products such as MDA and MPO and antioxidant activities (GSH, SOD and CAT) as a response to the oxidative stress. We also found that following the administration of NAC, the already increased oxidative stress parameters on the kidney were all decreased significantly. In conclusion, the results of the present study encourage new experimental and clinical studies to evaluate the efficacy of NAC as an adjunctive agent to ameliorate the toxic side effects of chemotherapeutics that cause oxidative renal injury.
**Table 1. Effects of NAC on MTX-induced changes in oxidant and antioxidant parameters**

<table>
<thead>
<tr>
<th></th>
<th>Control group (n = 10)</th>
<th>MTX group (n = 10)</th>
<th>MTX + NAC group (n = 10)</th>
<th>NAC group (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (nmol/mg protein)</td>
<td>0.028 ± 0.005</td>
<td>0.20 ± 0.05*</td>
<td>0.079 ± 0.01</td>
<td>0.04 ± 0.007</td>
</tr>
<tr>
<td>MPO (U/mg protein)</td>
<td>508.5 ± 98.5</td>
<td>917.9 ± 101.3*</td>
<td>607.2 ± 102.04</td>
<td>521.8 ± 122.3</td>
</tr>
<tr>
<td>SOD (U/mg protein)</td>
<td>2.25 ± 0.41</td>
<td>5.80 ± 1.51**</td>
<td>4.38 ± 1.05</td>
<td>3.18 ± 0.42</td>
</tr>
<tr>
<td>CAT (U/mg protein)</td>
<td>0.26 ± 0.007</td>
<td>0.64 ± 0.1***</td>
<td>0.44 ± 0.08</td>
<td>0.32 ± 0.07</td>
</tr>
<tr>
<td>GSH (μmol/mg protein)</td>
<td>0.008 ± 0.002</td>
<td>0.02 ± 0.0040***</td>
<td>0.01 ± 0.003</td>
<td>0.01 ± 0.004</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

*P < 0.001, significantly different from control, MTX + NAC and NAC groups.

**P < 0.05, significantly different from control and NAC groups.

***P < 0.05, significantly different from control, MTX + NAC and NAC groups.

Conflict of interest statement. None declared.

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An assessment of the rifle criteria for acute renal failure in severely burned patients

Sir,

RIFE is a newly developed classification for acute renal failure (ARF) that defines three grades of severity—Risk (class R), Injury (class I) and Failure (class F) [1]. Although some studies have applied this scoring system in sets of critically ill patients [2–4], its usefulness in patients with severe burns has not yet been assessed. We sought to determine retrospectively the ability of RIFE classification to predict mortality in severely burned patients admitted to the Burns Unit of our Hospital between January 2004 and December 2005. Patients were categorized on serum creatinine or urinary output, or both and the criteria that led to the worst classification were used. A total of 126 patients (83 men; mean age: 49.44 ± 19.23 years; 123 Caucasian; 10 diabetic) were evaluated. According to the RIFE criteria, 14.3% of all the patients were in the class R for ARF, 8.7% in the class I and 12.7% in the class F. In all the cases, the maximum RIFE occurred within the first 10 days of hospitalization in the Burns Unit. Patients with worst renal function were older (Normal renal function, 46 ± 19.2 years; class R, 44.3 ± 21.71 years; class I, 59 ± 17.3 years; and class F, 60.1 ± 18.5 years; P = 0.014), and had a higher burned body surface (Normal renal function, 16.3 ± 13.4%; class R, 28.4 ± 25.1%; class I, 52.3 ± 27.4%; and class F, 41.3 ± 28.9%; P < 0.0001), but did not differ in terms of comorbidity, namely cardiovascular disease and diabetes mellitus. In addition, males were more prevalent in this set of patients. Mortality rate was 17.5% and increased significantly from Normal to class F (Normal, 6%; class R, 11.1%; class I, 63.6%; and class F, 75%; P < 0.0001). Forward stepwise multivariate regression analysis showed that age, burned body surface and RIFE class were independent predictors of mortality. Class R (odds ratio 5.6, 95% CI 1.2–26.8, P < 0.0001) and class I (odds ratio 6.2, 95% CI 1.1–47.8, P = 0.008) were associated with a significantly higher risk of death than normal renal function. In sum, RIFE criteria allowed to identify close to 36% of severely burned patients as having various degrees of ARF and seems an important tool to stratify these patients according to risk of death.

Conflict of interest statement. None declared.

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