Incidence Rates of Retinal Detachment in 2 Cohorts of Patients Treated With Oral Fluoroquinolones or Amoxicillin

To the Editor—We read with interest the article by Kuo and colleagues, which reported a large increase in the risk of rhegmatogenous retinal detachment (RRD) within 90 days from the prescription of oral fluoroquinolones, as compared to amoxicillin [1]. The association between oral fluoroquinolones and RRD is of great relevance, as little is known on the etiology of this disease. Furthermore, these results from a population-based study provide an important contribution to better understand an association that is still controversial [2–4].

The key findings were elevated hazard ratios for RRD from 2 cohorts of patients followed up for 90 day after the prescription of fluoroquinolones or amoxicillin (reference group). In reviewing these intriguing findings, we looked to see if the article provided the incidence rates (IRs) from which the hazard ratios were calculated. These figures were not included, but we could estimate them based on the number of patients and on reasonable assumptions about the expected average follow-up. From these 2 figures, we could estimate an upper bound for the person-years in the study. Using these figures for the 2 cohorts, we conservatively estimated the IRs of RRD in the 2 cohorts and in the entire study population (Table 1). The resulting (conservative) estimates of the IRs are quite high—104.7 per 100 000 person-years in the amoxicillin group, and 218.5 in the fluoroquinolone group.

These figures are much higher than the IRs usually reported in the literature. The yearly incidence of RRD in Taiwan in 1999–2009 was estimated to be between 7.8 (2000) and 10.8 (2008) cases per 100 000 residents [5]. These rates are in line with those reported worldwide [6]. The incidence of RRD is strongly age-dependent, but this is not likely to be an explanation; the incidence of RRD is generally not higher than 19–27 cases per 100 000 person-years in the sixth decade whereas the mean age in the Kuo et al cohort was 47 years [1, 6]. Also, our estimates are probably lower than the actual rates, as we assumed no death or loss to follow-up in calculating the person-years.

The surprisingly high rates of RRD calculated from Kuo et al might raise questions on the validity of their findings. It is possible that the underlying medical conditions for which the medications were prescribed might have elevated the IRs (a sort of confounding by indication). However, based on the data presented in Table 3 of Kuo et al, the number of cases experienced among patients affected by respiratory infection—which has been suggested as a trigger for RRD [7]—was relatively low (29 in 145 546 patients). Another possible explanation for the observed figures is an overascertainment of RRD cases; this bias could threaten the validity of the findings.

We suggest that Kuo and colleagues might want to calculate the rates of RRD observed in their study, and compare them to published estimates more rigorously than we are able to do from the data provided in their article. This would greatly strengthen the impact of these potentially influential findings.

Note

Potential conflicts of interest. Both authors: No reported conflicts.

Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

Table 1. Incidence Rates of Rhegmatogenous Retinal Detachment in a Taiwanese Cohort

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Patients, No.</th>
<th>PY(^a)</th>
<th>Cases, No.</th>
<th>Rate</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>178 179</td>
<td>43 935</td>
<td>96</td>
<td>104.7</td>
<td>(78.4–139.8)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>178 179</td>
<td>43 935</td>
<td>46</td>
<td>218.5</td>
<td>(178.9–266.9)</td>
</tr>
<tr>
<td>All patients</td>
<td>356 358</td>
<td>87 869</td>
<td>142</td>
<td>161.6</td>
<td>(137.1–190.5)</td>
</tr>
</tbody>
</table>

Estimates based on Kuo et al [1].
Abbreviations: CI, confidence interval; PY, person-years.
\(^a\) Upper bound estimates calculated assuming no death or loss to follow-up.
Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Reply to Farioli and Kriebel
To the Editor—Drs Farioli and Kriebel requested the incidence of rhegmatogenous retinal detachment (RRD) in the database we used, which was 11.7 per 100,000 person-years, similar to the previous study [1]. The incidence of RRD in selected patients receiving fluoroquinolones is higher than that in the general population because many of our patients had underlying diseases. For example, the prevalence of diabetes in the fluoroquinolone cohort is 17.9%, which is much higher than that in the general population (3.15%–4.22%) [2]. In addition, these patients visited physicians more frequently, which could also increase the incidence of RRD (surveillance bias). That is why patients prescribed amoxicillin were selected as a control cohort, which was matched on possible confounding factors described in the literature [3] and propensity score. After matching, the control cohort therefore had a higher incidence of RRD than the general population.

Note
Potential conflicts of interest. T.-L. C. is a medical advisor for TTY Biopharm. All other authors report no potential conflicts.
All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References

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