Mortality of patients with non-functioning pituitary macroadenoma is significantly elevated: systematic analysis of 546 cases in a tertiary referral centre in the UK

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Introduction
Data on the mortality of patients with non-functioning pituitary macroadenoma (NFA) are limited.

Aim
To assess the mortality of patients with NFA and predictive factors.

Patients and Methods
All patients presenting to our Department with NFA between 1963-2011 were studied. Status was recorded as either dead or alive, as of 31 December 2011.

<table>
<thead>
<tr>
<th>Data on mortality</th>
<th>Patients (n)</th>
<th>Males (n)</th>
<th>Median age at surgery (years) (range)</th>
<th>Median time between surgery and known survival status (years) (range)</th>
<th>Number of deaths</th>
<th>Median age of death (years) (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>546</td>
<td>333</td>
<td>58.7 (16.1-94.2)</td>
<td>8 (1 month-48.5 years)</td>
<td>83</td>
<td>77.8 (36.4-98.3)</td>
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</tbody>
</table>

Results

SMR for the total group 3.62 (95%CI:2.90-4.47; p<0.001)

SMR for those diagnosed before 1990 4.66 (95%CI:2.65-7.63; p<0.001)

SMR for those diagnosed after 1990 3.53 (95%CI:2.77-4.44; p<0.001)

Clinical follow-up data (until date of death or date the database was frozen)

- Number of patients 436 (269 males)
- Median age at surgery (years) 58.5 (16.11-94.19)
- Number of patients with no or intrasellar remnant after surgery 203/431
- Number of patients with extrasellar remnant after surgery 228/431
- Median follow-up 6.9 years (1 month-48.5 years)
- Number of patients with NFA regrowth 111/436
- Number of patients who received radiotherapy (adjuvant or for regrowth) 188/436

Causes of death in NFA patients

- Infections 30%
- Malignancies 29%
- Cardio/cerebrovascular 34%
- Old age 1%
- Unknown 3%
- Suicide 1%
- Gastrointestinal hemorrhage 1%
- Perioperatively 1%

Cox regression analysis (univariate followed by multivariate approach) demonstrated that amongst: age at surgery, NFA regrowth, radiotherapy, sex, extent of removal, untreated GH deficiency, untreated FSH/LH deficiency, ACTH deficiency, TSH deficiency and treatment with DDAVP, ONLY AGE remained an independent significant factor (HR 1.099, 95%CI:1.073-1.126; p<0.001)

Conclusions
This is the first study assessing systematically mortality in a large series of non-selected patients with NFA in the UK. Despite the improvement in the last three decades, mortality remains high. Apart from age, factors related with the management/outcome of the tumour are not independent predictors and pituitary hormone deficits managed with the currently-used substitution protocols do not adversely affect mortality in this group of patients.