Introduction

• Growth hormone (GH) excess in acromegaly is associated with higher mortality and morbidity
• With improved treatment for acromegaly, many studies have demonstrated latest mortality rates to be improving and comparable to the general population (Schott 2012 Eur J Endocrinol; Varadhan 2016 Pituitary)
• Though the SMR for acromegaly per se is improving with time, The mortality rates remain high largely due to cancers and circulatory disease (Esposito 2018 Eur J Endocrinol)
• Acromegaly is associated with significant morbidity (Dakkers 2008 J Clin Endocrinol Metab)
• There are not many studies that have looked at the predictors of morbidity associated with acromegaly
  ▪ Development of comorbidities such as cardiovascular events and cancers are an important cause of mortality (Varadhan 2016 Pituitary)
  ▪ A recent study used IgF1 as a marker but this may not be available in all patients who have been follow up for more than 2 decades (Jayasena 2011 Clin Endocrinol)
  ▪ The duration of diabetes preceding the diagnosis of acromegaly is unaccounted for and could contribute to morbidity of acromegaly (Valletta 2013 Clin Endocrinol)
• The frequency of pituitary surgery to aim for cure for this condition has been progressively increasing (Esposito 2018 Eur J Endocrinol)
• Patients with acromegaly continue to have significant comorbidities, especially cancers, cardiovascular diseases, diabetes and hypopituitarism, which can account for a significant financial burden on health care system (Lesan 2017 Eur J Endocrinol)

Aim

The aim of the study was to assess the differences in mortality and morbidity associated with active acromegaly compared to patients in whom disease control was achieved

Methods

• Single centre study : Retrospective clinical observational study
• Data on all patients with acromegaly who had been treated since 1948
• 1948-2014 used for data collection
• All GH results were converted to mcg/L
• Divided into ‘control-achieved’ and ‘active disease group’ for calculations
• Data at baseline including proportion with macroadenomas, pituitary axes failures and cardiovascular events (diabetes, hypertension, strokes, MI and CCF) labelled as CVE, were collected
• Details regarding treatment modalities used: surgery, radiotherapy and medical treatment were counted and the number of times each was done was counted
  ▪ Medical treatment included Somatostatin analogues, cabergoline/ bromocriptine or Pegvisomant
  ▪ Each therapy was counted as a course if treatment sustained beyond 3 months continuously
  ▪ Patients with repeated course of same therapy were counted as independent episodes
• Control was deemed achieved if latest GH consistently <1.5mcg/L.
• Data on mortality and CVE and duration to the events were calculated
• IgF-1 was not included in this analysis due to lack of sufficient data

Results

<table>
<thead>
<tr>
<th>Control-achieved</th>
<th>Active Disease</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>116</td>
<td>51</td>
</tr>
</tbody>
</table>

At diagnosis

• Age: 47.5 ± 13.3 vs. 53.9 ± 12.9, p <0.005
• GH(mcg/L): 16.6 ± 25.5 vs. 28.8 ± 36.3, p <0.05
• Patients with pt. Axes failure: 9.5% vs. 16%, NS
• Macroadenomas: 78.5% vs. 62%, p <0.001

At follow-up

• Duration follow up (months): 163 ± 118 vs. 102 ± 110, NS
• Patients surgery done: 65.5% vs. 46.2%, p <0.0005
• Mean number of surgeries among operated: 1.1 (1-3) vs. 1.3 (1-3), NS
• Patients with medical Rx: 98.3% vs. 82.7%, NS
• Mean no. of medical courses: 1 (1-5) vs. 0.8 (1-4), NS
• Total no. of treatment modalities: 2.25 vs. 1.8, NS
• New pituitary axes failure: 38.2% vs. 32%, NS
• No. of total new failed axes: 1.8 (1-3) vs. 1.5 (1-4), NS
• New CVE: 33.6% vs. 36%, NS
• Duration to CVE (months): 144 ± 112 vs. 69 ± 110, p <0.05
• Mortality: 30.2% vs. 64%, p <0.0001

Discussion

• The initial GH at diagnosis and macroadenomas were significantly higher in the active disease group, suggesting more severe disease
• The proportion of patients operated was higher in the group were control achieved, again showing surgery as the most successful form of treatment
• The number of treatment modalities required to achieve control was higher compared to group where control not achieved, suggesting that a more aggressive approach may be helpful
• Though CVE was equal in both groups, the duration to achieve control was higher in patients where control achieved, again highlighting the benefit of curing acromegaly
• The mortality rates were higher in the active disease group
• Though the total number of treatment modalities was higher, the proportion suffering with further pituitary axes failure was comparable between the two groups

Limitations of our analysis

• Retrospective analysis not allow for calculating incidence rates
• Regression analysis could not performed as data on various other confounding factors for mortality and morbidity were not available
• Data on cancer prevalence and cause of death was not available for this study

Conclusion

• Mortality rates from acromegaly were higher in patients with active disease
• Disease burden from acromegaly is significantly high in both ‘control-achieved’ as well as ‘active disease’ group; however the duration to develop these complications can be prolonged by achieving control
• The various available treatment options would need to be explored, with surgery being the preferred choice, to aim to achieve biochemical control of acromegaly to reduce the risk of complications