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Abstract of PhD Thesis:

**CLINICAL AND PATHOLOGICAL PROGNOSTIC FACTORS IN PITUITARY
NEUROENDOCRINE TUMORS OF THE ELDERLY**

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Pituitary tumors are the third most common intracranial pathology following gliomas and meningiomas. Increased occurrence of pituitary tumors in the elderly has been known from autopsy studies for over 35 years, but recently also an increased clinical incidence has been seen. As the general population undergoes an overall aging, occurrence of pituitary tumors in elderly and very elderly is expected to continue to rise.

In the **first study**, a research was conducted of the prevalence of pituitary tumors in the elderly and of surgical results of patients aged over 80 treated by endoscopic transsphenoidal approach for non-secreting pituitary tumors.

Out of the 623 patients neurosurgically operated for pituitary tumors between 2007 -2015 at the Groupement Hospitalier Est, Lyon, France, the prevalence of pituitary tumors of the elderly, aged over 65 years, was 23% (n=143) of all surgeries. The prevalence of non-functional pituitary (gonadotroph and non-immunoreactive) tumors in the elderly was also representing 81% (n=116).

Regarding the surgical results of transsphenoidal surgery in the very elderly, aged over 80, a group of 15 elderly patients were compared to a control group of elderly patients of 49 cases, aged 65-75 years at the time of surgery.

All preoperative clinical data including: tumor size and invasion as seen on MRI, visual status, anterior pituitary status and previously known comorbidities, were studied between the study groups. Postoperative the tumor resection, visual outcome, pituitary improvements and complication were also studied.

Very elderly patients presented good outcomes of surgery, with significant visual recovery (80%) ($p=0.0012$), no deaths were recorded in the immediate postoperative period and during the first 3 months following surgery. Very elderly patients had reduced rates of postoperative complications and short hospital stay (mean of 6 days).

These results showed that age by itself is not a prognostic factor of poorer outcome and contradicted a previous meta-analysis that showed a 1.85 odds ratio of death from surgery in this extreme age group.

In the **second study**, we studied the effects of age over the morphology of the pituitary gland, especially on the size and number of gonadotroph cells in elderly and young, as senescence changes in the structure of the pituitary and their possible linkages to the increased incidence of non-functioning pituitary tumors are still poorly understood.

We have found that a significant increase of interstitial fibrosis appears in elderly without differences between men and women. In addition, a gonadotroph cellular hypertrophy was seen in pituitary glands of elderly, predominantly in females, but without pituitary hyperplasia. The gonadotroph hypertrophy, predominant in women may explain the difference in plasma levels of FSH and LH between men and menopausal women. Our observations support the hypothesis of Kastelan and collaborators that age-related hormone decrease and “lack of feedback suppression” could be the causes of higher numbers of tumors in elderly due to the continuous overstimulation of the gonadotroph cells, but this hypothesis needs to be confirmed.

This study represents the first mapping of gonadotroph cells using immunohistochemical and statistical methods and clearly shows that cell counting is feasible and necessary to confirm a histological observation.

Key words: non-functioning pituitary tumors, elderly, endoscopic transsphenoidal surgery, immunohistochemistry, gonadotroph cells, fibrosis, hyperplasia, hypertrophy.