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«Cortical sparing» adrenalectomy in heritable pheochromocytoma

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Prevalence of an underlying genetic disorder in apparently sporadic cases of pheochromocytoma is much higher than suggested by the traditional 10% rule, and it may reach 40% of cases.
Bilateral pheochromocytoma, more common in patients with MEN-2, von Hippel-Lindau's disease or neurofibromatosis, may require removal of both glands, exposing the patient to life-long dependency on exogenous steroids. Replacement therapy may prevent acute hypoadrenalism (a life-threatening complication, particularly in the elderly) but at the risk of over-replacement and osteoporosis, hypertension and diabetes.
In the past, to prevent the need for steroid replacement, auto-graft of fragments of adrenocortical tissue has been attempted, but this technique is no longer in use due to success being limited to just about 30% of patients.
Over the last 20 years, **«cortical sparing» adrenalectomy** (radical removal of the pheochromocytoma while leaving behind a fragment of adrenocortical tissue) has gained momentum, as it has allowed a higher percentage of patients to maintain independent adrenocortical function.

A recent **review** from several European centres with particular experience in endocrine surgery has analysed **6 studies**, each with a sample of at least 10 patients, focusing on percentages of relapse and success (defined as preservation of normal adrenal function). In most of the cases, surgery has been through a trans-peritoneal or retro-peritoneal mini-invasive approach, as this is the current standard for the treatment of non-cancer adrenal pathology.
Patients have been selected for endoscopic «cortical sparing» adrenalectomy if pre-operative CT and/or MRI showed a lesion less than 4 cm (larger lesions being more difficult to remove endoscopically) in the absence of multiple pheochromocytoma nodules in the same gland.
Following intervention, all patients received post-operative steroids as a precaution, and adrenocortical function was verified later, before discontinuing treatment.
In the course of follow-up all patients underwent annual evaluation of plasmatic and urinary metanephrines, in order to allow early detection of relapse.
The **risk of relapse** was between 0-20%, with better results in patients receiving mini-invasive treatment. This may be explained by the magnification of anatomic structures provided by the endoscopic approach, which may facilitate the definition of the cleavage between pheochromocytoma and healthy adrenal cortex, thus facilitating complete removal without excessive bleeding.
Cases of relapse have occurred, on average, 9.5 years after surgery, prompting the authors to recommend long-term follow-up. The genotype per se does not seem to modify the risk of recurrence, but it might affect the interval between surgery and recurrence.
In 57-100% of cases in which cortical sparing surgery was possible, if only unilaterally, **adrenocortical function remained normal**, as shown by lack of need of replacement therapy and normal response to stimulus test with ACTH. No adrenal crises were reported during follow–up of patients treated with this technique.

Our series

We have treated 13 patients with pheochromocytoma with cortical sparing adrenalectomy. No relapses have been observed during an average follow-up of 3.8 years. Three of 4 patients treated with bilateral surgery have maintained normal adrenocortical function, while one patient has requested low-dose replacement therapy due to cortisol serum levels at lower limits of normal despite response to ACTH stimulation test.

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Conclusions

1. Based on these data (relapse <10% and normal cortical function in over 50% of patients undergoing treatment) cortical sparing adrenalectomy seems to be the surgical gold standard in hereditary pheochromocytoma.
2. In cases of MEN-2 or von Hippel-Lindau, cortical sparing surgery must be considered even in initially unilateral cases, due to the high risk of contralateral metachronous pheochromocytoma.
3. This technique should be expanded to unilateral sporadic pheochromocytomas, when the contralateral adrenal is not functioning as a consequence of previous trauma or because of earlier removal.
4. Treatment of this disease should be concentrated in centres experienced with the procedure.

References

1. Castinetti F, et al. Outcome of adrenal sparing surgery in heritable pheochromocytoma. Eur J Endocrinol 2016, 174: R9-18.