PARATHYROID GLAND

Which surgery for MEN1 patients?

Subtotal parathyroidectomy is preferable to other surgical approaches for the treatment of primary hyperparathyroidism in patients with multiple endocrine neoplasia type 1 (MEN1) syndrome, recommend researchers from the DutchMEN1 Study Group (DMSG).

Primary hyperparathyroidism, a frequent occurrence in patients with MEN1 syndrome, is usually treated by resection of the parathyroid glands. However, partial parathyroid surgery is associated with risk of persistent or recurrent hyperparathyroidism, whereas more extensive surgery can lead to postoperative hypoparathyroidism.

“Up until now, the care of these patients has followed clinical practice guidelines that are mainly based on expert opinion,” explains senior researcher Gerlof Valk. The DMSG researchers built a database that includes the medical records of all patients with MEN1 syndrome followed up at university medical centres in the Netherlands, which constitutes 90% of all Dutch MEN1 patients. All patients aged ≥ 16 years who were treated between 1990 and 2009 were included. “Prior research was mainly done in institutional and relatively small patient groups with possible selection bias,” Valk points out, whereas the DMSG database “gives us, for the first time, the opportunity to study MEN1 in a truly unselected, national patient population with a long-term follow-up”.

In this latest study, the DMSG researchers retrospectively analyzed the outcome of a cohort of 73 patients with MEN1 syndrome and hyperparathyroidism who underwent parathyroid surgery at two of the eight Dutch university medical centres (Utrecht and Nijmegen). The median follow-up was 4.3 years and patients were observed at 3-month intervals during follow-up. The researchers compared the outcomes of resection of less than three parathyroid glands ($n=17$), subtotal resection (more than three parathyroid glands removed, but one or part of a gland left behind; $n=23$) and total resection of the parathyroid glands ($n=32$). One patient had an unknown type of parathyroid surgery.

When less than three parathyroid glands were removed, the risk of persistent or recurrent hyperparathyroidism—defined as hypercalcaemia with raised or inadequately normal parathyroid hormone levels within 6 months after surgery—was 53%, whereas this risk was only 17% when the resection was subtotal and 19% when the resection was total. Persistent hypoparathyroidism—defined as a need for vitamin D or calcium therapy ≥ 6 months after surgery—occurred in 24%, 39% and 66% of patients who underwent resection of less than three parathyroid glands, subtotal resection and total resection, respectively. Given these results, “we have abandoned the resection of less than three parathyroids as primary surgery in patients with MEN1 syndrome,” says Valk. Furthermore, he adds, “because of the rate of postoperative hypoparathyroidism after total resections, subtotal parathyroidectomy is the preferred procedure now”.

On the basis of their long-term observations, the researchers point out that postoperative hypoparathyroidism, even that lasting for 6 months or more, should not be considered permanent. “It might take months or even years to successfully taper off medication,” Valk comments, “but in almost two-thirds of the patients this will eventually be successful”.

The researchers also showed that patients with a nonsense or frameshift mutation in exons 2, 9 or 10 of the *MEN1* gene were less likely to experience disease recurrence after resection of less than three parathyroid glands than patients with mutations elsewhere in the *MEN1* gene. “In preoperative consultation, patients with other mutations can be informed of their higher recurrence risk,” says Valk.

The database will now be used to assess the effectiveness of screening and intervention protocols. “The current clinical practice guidelines will be critically evaluated with the ultimate goal of optimizing and individualizing the evidence-based care of patients with MEN1 syndrome,” concludes Valk.

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