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Should the duration of primary hyperparathyroidism impact guidelines for evaluation and treatment?

Primary hyperparathyroidism (PHPT) manifests itself in a wide and variable constellation of symptoms. Parathyroidectomy in skilled hands offers a low-risk procedure resulting in a durable cure with symptomatic relief, although for those without symptoms or for those with symptoms that are misattributed to other causes, the benefits of treatment are less obvious. Current clinical guidelines recommend parathyroidectomy based on objective and measurable factors, including skeletal and renal manifestations of the disease, serum calcium levels, and age.[1,2] In the current issue of *Surgery,* Assadipour and colleagues detail the timing of disease progression to end-organ effects, and in doing so, raise the question of whether or not the duration of PHPT should impact the decision to treat the disease.[3]

Currently, the duration of disease is not factored into recommendations to treat PHPT, according to the international guidelines[1] or those from the American Association of Endocrine Surgeons.[2] Both sets of guidelines, however, list age less than 50 as an indication for parathyroidectomy even when patients are asymptomatic.[1,2] The inclusion of age stems from research suggesting that a greater proportion of younger patients develop another indication for parathyroidectomy than do older patients.[4] In a much larger cohort with an older mean age of 64 years, Assadipour et al[3] identified evidence of end-organ effects on the skeleton (osteoporosis) and kidneys (decreasing renal function, nephrolithiasis, and hypercalciuria) in 51% of patients at the time of diagnosis; 23% of the other patients went on to develop end-organ effects within 5 years.[3] In a smaller yet prospective study, Silverberg et al[5] found that 27% of asymptomatic patients developed an indication for operative treatment during their follow-up.[5] Even if younger patients are more likely to experience end-organ effects of PHPT, the risk for those older than 50 remains substantial, especially considering the current US life expectancy of about 79 years.

Although medical options might address symptoms of PHPT, only parathyroidectomy can address the underlying pathology. Even though some define symptomatic patients with PHPT as those with objective signs of disease, such as low bone density, nephrolithiasis, or proximal muscle atrophy,[5] subjective symptoms can be equally debilitating. We consider any patient with PHPT and manifestations consistent with the disease to be symptomatic even in the absence of objective signs, and we believe symptomatic patients at least deserve to hear about and be given the option of operative treatment. For truly asymptomatic patients, the main alternative to parathyroidectomy is observation. Before planning to observe these patients, however, clinicians should decide what endpoint merits treatment. The guidelines help in this situation, but ultimately these guidelines suggest that for patients over 50 with only moderately increased serum calcium, clinicians might wait until osteoporosis, fragility fractures, nephrolithiasis, or stage 3 chronic kidney disease develop before suggesting treatment. Perhaps setting a 5-year disease duration as a cut-off for parathyroidectomy will prevent end-organ damage in over 75% of patients where such disease manifestations are not present at diagnosis; but why wait at all if afforded the opportunity to prevent bone and kidney disease in clearly high-risk patients? Of course, any effort to prevent the outcomes associated with observation requires appraisal in the context of its risks. With an experienced parathyroid surgeon, parathyroidectomy offers a very high chance of success and an exceedingly low risk of complications, often on an outpatient basis.

So, should the duration of disease impact guidelines for the treatment of PHPT? Yes, but not with an arbitrary cutoff for intervention based on the time elapsed since diagnosis. Rather, the end-organ damage associated with the duration of PHPT should serve as a reminder that observation or delaying treatment yields consequences that may very well outweigh the risk of parathyroidectomy even in older patients. In addition, measuring the impact of lesser-recognized and underappreciated symptoms of PHPT and their associated effect on personal health and quality of life is much more difficult than calculating bone density or creatinine clearance. A better way to prevent the negative sequelae associated with a greater duration of disease in truly asymptomatic patients may be to consider estimated life expectancy as part of the guidelines rather than chronologic age or disease duration. As it is, PHPT remains underdiagnosed and undertreated. Even in a population with reliable access to quality health care, evidence of end-organ effects are already present in over 50% of patients at the time PHPT is diagnosed.[3] For these patients, the opportunity for prevention is already lost, but for many others, we should not let the chance to prevent the complications of this diesease slip away.

Conflicts of interest

The authors have indicated that they have no conflicts of interested regarding the content of this article.

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