was exclusively in patients with diabetes and was asking a subtly different question with a different methodology. It included patients who were not on a stable dose of thyroxine, unlike our study. Diez and Iglesias are correct that only a detailed analysis at the patient level will help elucidate the mechanism of any putative mechanism of interaction.

From a practical stand point, a reduction in TSH of 0.21 mU/l is unlikely to be of clinical significance to a patient. However, a difference of 0.21 mU/l within a population is likely to reflect a much greater change for a small number of patients, and thus may be significant for a small minority. However, we were unable to determine the impact of these changes on free T4 or clinical end-points for individual patients.

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'Hyperaldosteronaemic or normocalcaemic' hyperparathyroidism?

Normocalcaemic hyperparathyroidism (NCHP) is increasingly diagnosed among patients presenting with fractures. However, the aetiology of this condition and its optimal treatment remain unclear.[1] NCHP is characterized biochemically by normal calcium and elevated parathyroid hormone (PTH) levels in the absence of demonstrable secondary causes of hyperparathyroidism.[1] While some view NCHP as an early manifestation of primary hyperparathyroidism, parathyroid adenoma is present in some, but not all, cases,[1] and parathyroidectomy does not always normalize NCHP,[1] suggesting the presence of yet unidentified aetiological factors.

Recent evidence has emerged suggesting primary aldosteronism (PA) could be a hyperparathyroid state, stemming from bidirectional interaction between calcium-PTH and the renin–angiotensin–aldosterone system (RAAS).[2] Circulating PTH levels are elevated in PA, leading to suggestion of PTH measurement incorporation into the PA diagnostic workup.[3] An unexplored question is whether the high PTH levels observed in patients with NCHP heralds early PA.

To date, no studies have examined the RAAS in patients with NCHP. Since the earliest manifestation of PA is hypertension, this question could be probed by examining blood pressure (BP) in patients with/without NCHP.

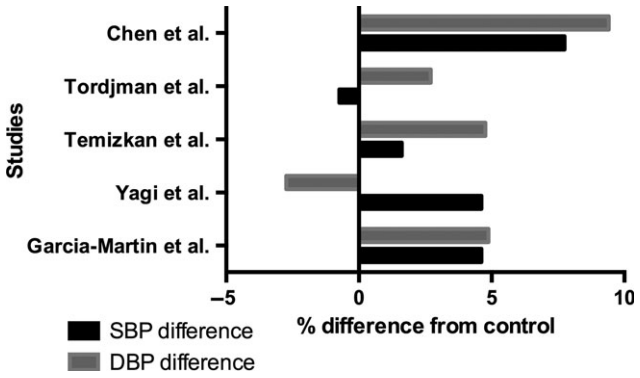

Fig. 1 Comparison of systolic (SBP) and diastolic blood pressure (DBP) in published studies[1,4–8] between patients with normocalcaemic hyperparathyroidism and age- and gender-matched controls.

A PubMed search using the key words 'normocalcaemic hyperparathyroidism' returned 453 articles, of which 54 were original clinical NCHP studies. BP was reported in five studies[1,4–8] including 553 individuals (70 patients with NCHP and 662 controls). Systolic BP was 3·6% (95% CI: −0·4 to 7·6%), and diastolic BP was 2·9% (95% CI: −1·7 to 9·3%) higher in patients with NCHP compared to controls (Fig. 1). Calculated mean arterial BP was higher among patients with NCHP (97 ± 4 *vs* 93 ± 1 mmHg, $P = 0{\cdot}06$).

When studies reporting PTH levels in patients with PA were reviewed, the results were striking: all hyperparathyroid patients with PA were normocalcaemic.[3] Interestingly, PA also independently increases the risk of fractures, a consequence shared with NCHP.[9] In other words, high PTH eucalcaemic state in PA appears to be a 'yin and yang' reminiscence of NCHP. Finally, adenoma resection or aldosterone antagonist therapy normalizes hyperparathyroidism in patients[3] with PA, demonstrating reversibility of PA-induced high PTH state.

While these interpretations should be viewed as hypothesis generating, their implications are clinically relevant. First, BP was reported in less than 10% of NCHP studies, highlighting the underappreciation of possible RAAS involvement in the pathogenesis of NCHP, despite clues from parallel PA literature. Second, parathyroid localization studies are costly, averaging between US$6000 and 8000,[10] and could lead to unnecessary surgery with no guarantee of cure. In contrast, pharmacological aldosterone antagonism may not only be a simple 'diagnostic test', but also an inexpensive therapeutic option. Finally, the proposed hypothesis may stimulate research into the relation between NCHP and RAAS, thereby shedding new insight on appropriate investigations and treatment.

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