Asymptomatic secondary hyperparathyroidism can mimic sacroiliitis on computed tomography

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Secondary hyperparathyroidism (sHPT) as a result of chronic kidney disease (CKD) is a common health problem and has been reported to manifest at the sacroiliac joints (SIJ). The aim of this investigation was to systematically assess sacroiliac joint changes in asymptomatic sHPT as detected by high-resolution CT. Included in this IRB-approved retrospective case–control study were 56 patients with asymptomatic sHPT as well as 259 matched controls without SIJ disease. Demographic data were retrieved from electronic patient records. High-resolution computed tomography datasets of all patients were subjected to a structured scoring, including erosions, sclerosis, osteophytes, joint space alterations and intraarticular calcifications. Chi² tests were used to compare frequencies of lesions. Erosions were significantly more prevalent in patients with sHPT, and were found mainly in the ventral (28.6% vs. 13.9%; p = 0.016) and middle (17.9% vs. 7.7%; p = 0.040) iliac portions of the SIJ. Partial ankylosis was rare in both cohorts (3.6% vs. 5.0%; p > 0.999); complete ankylosis was not observed. Neither extent not prevalence of sclerosis or calcifications differed significantly between groups. Joint lesions reminiscent of sacroiliitis can be found in a substantial portion of asymptomatic patients with secondary hyperparathyroidism. Further investigations into the clinical significance of these findings are warranted.

Chronic kidney disease (CKD) is a global health problem, estimated to affect up to 10% of the general population, with a rising prevalence over the last decades1,2. A frequent complication in patients requiring haemodialysis is the development of osteo-articular disease1, especially secondary hyperparathyroidism (sHPT)3. Parathyroid hormone (PTH) has a catabolic effect on bone metabolism and has been shown to decrease bone-mineral density of cortical bone3; longstanding elevated PTH levels may lead to osteitis fibrosis cystica, a high turnover bone disease presenting with lytic lesions on imaging as a result of replacement of mineralized bone with fibrous tissue6. These findings are most likely the reason why HPT is sometimes considered a differential diagnosis in sacroiliitis imaging7, as subchondral bone resorption may be difficult to distinguish from true erosions on imaging. Additionally, HPT is an important predisposing factor of calcium pyrophosphate dihydrate deposition (CPPD)8, which in turn manifests at the sacroiliac joints in up to 50% of CPPD patients and may cause bilateral erosions, joint space narrowing and sclerosis9,10.

A recent study by Tezcan et al. has investigated MRI features of asymptomatic primary hyperparathyroidism in 49 patients11 and found bone marrow edema in 16.3% of patients, though no significant difference to healthy controls could be detected. In terms of secondary hyperparathyroidism, published evidence of manifestations at the SIJs to date is limited to case reports12, investigations undertaken more than 30 years ago13 or radiographic studies14.

To our knowledge, no systematic investigation on the pattern of arthropathy of the SIJ in sHPT as detected by computed tomography has been undertaken thus far. The aim of this study was to systematically describe the pattern of arthropathy in asymptomatic secondary hyperparathyroidism compared the normal population.

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Materials and methods

Ethical approval and patient consent. Prior to data acquisition, approval was attained from the ethics review board of the Charité Universitätsmedizin Berlin (EA1/300/19). Due to the retrospective nature of the investigation the ethics review board waived individual written informed consent. Consent for use of de-identified imaging data in scientific publications was obtained as a routine practice in our institution. The study was conducted in compliance with the Declaration of Helsinki and local legislation and ethical standards.

Patients. Included into the case-group of this retrospective case–control study were patients with known secondary hyperparathyroidism who had received a computed tomography of abdomen and pelvis between March 2016 and March 2019. Clinical data was retrieved from electronic patient records. Patients with known disease of the sacroiliac joints, known rheumatic disease, cutaneous psoriasis, inflammatory bowel disease, uveitis, malignancy of the skeletal system (both primary and metastatic) and fractures of the pelvis were excluded. The patients were matched with subjects from an existing, retrospectively acquired cohort from our institution, who had undergone imaging during the same period and for whom the same clinical information (except parameters of SHPT) were available. Indications for CT examinations in the case group were oncological staging (15/56), infection (10/56), trauma/bleeding (5/56) and other, including evaluation before kidney donation as recipient (27/56). Indications for CT examination in the control group were oncological staging (130/259), infection (83/259), trauma/bleeding (6/259) and other, including evaluation before kidney donation (27/56). Matching was performed in a ratio of 4 controls for every case.

Imaging technique. For all CT scans a special reconstruction of the pelvic skeleton was available, yielding images in a similar quality as in dedicated SIJ imaging. All image datasets were scored by one radiological resident with 7 years of experience in MSK imaging (KZ), blinded for all clinical data. Images were read using dedicated software (Horos v3.3.6, The Horos Project, public license) in random order and predominantly in oblique-coronal and axial orientation, using bone-window settings.

Scoring system. Expanding on previous work of our research group, a scoring system was used that divides the sacroiliac joints into 12 joint regions on each side. In each region, erosions and sclerosis were assessed in a categorical fashion, laid out in Table 1.

Additionally, joint space alterations (including pseudo-widening and ankylosis) and intraarticular calcifications (both per side) as well as osteophytes (ventral and dorsal, separately for each side) were scored. Prior to scoring, an atlas was assembled from example patients not included in this analysis, which was used as a reference during scoring. A teaching session on 15 test cases (not included in the study) was carried out with a consultant radiologist with expertise in MSK radiology (TD) before commencement of the scoring process. In order to calculate inter- and intra-reader reliability, a random sample of 50 study patients was scored by both junior (KZ) and senior reader (TD)—in case of the junior reader a second time.

Statistical analysis. Statistical analyses were carried out using SPSS Version 25 (IBM Corporation, New York, USA). Patients were matched with controls using the dedicated propensity score matching tool; age, gender and weight were chosen as covariables, with a defined tolerance of 0.01. Scoring results were summarised as sum scores for each structural lesion separately; on the patient level, positivity for erosions was defined as a sum score ≥ 2. Frequencies of structural lesions were compared using Chi² tests. Sum scores of structural lesions were compared using Mann–Whitney-U tests. Intraclass-correlation coefficients were calculated for inter- and intra-reader reliability, using a two-way mixed model ICC(3,2) on sum scores for each lesion type. A significance level of p < 0.05 was assumed for all tests.

Results

Patients’ characteristics. A total of 315 patients (56 SHPT, 259 controls) were included in this investigation; a summary of patient flow and clinical characteristics is provided as Fig. 1. As per study design, mean age and gender distribution did not differ between groups.

Frequency and distribution of structural lesions. A complete table of frequencies of structural lesions as well as mean sum scores is provided as Table 2.

| Erosions | Sclerosis | Joint space | Osteophytes | Calcifications |
|----------|-----------|-------------|-------------|---------------|
| 0        | None      | Normal      | None        | None          |
| 1        | 1–2 erosion | Possible/very little sclerosis | Possible widening/narrowing | Small osteophyte (≤ 5 mm) | Few or punctuate calcifications |
| 2        | 3–5 erosions | Marked sclerosis | Pseudo-widening/narrowing | Larger osteophyte (> 5 mm) | Extensive or linear calcifications |
| 3        | > 5 erosions | Partial ankylosis | Bridging osteophyte |
| 4        | Complete ankylosis |

Table 1. Scoring system. Overview of scoring system.
Erosions were observed in significantly more sHPT patients than their matched controls (11/56 vs. 10/259; \( p < 0.001 \)). The difference was most pronounced in the iliac joint portions with 28.6% vs. 13.9% ventrally \( (p = 0.001) \), 17.9% vs. 7.7% in the middle \( (p = 0.040) \) and 10.7% vs. 3.5% dorsally \( (p = 0.033) \). Neither sclerosis nor joint space alterations including partial ankylosis differed in frequency and extent between sHPT patients and controls; there was no instance of complete ankylosis in either cohort of this investigation. Intraarticular calcifications were seen in 26.8% of sHPT patients and 17.4% of controls—the difference was not statistically significant \( (p = 0.132) \). Osteophytes were more prevalent in controls than sHPT patients with 51.7% vs. 32.1% \( (p = 0.008) \) in the dorsal aspect of the joint. Imaging examples from the patient cohort are supplied as Fig. 2.

**Figure 1.** Patient flow. sHPT secondary hyperparathyroidism, GFR glomerular filtration rate, SD standard deviation, iPTH intact parathyroid hormone, ADPKD autosomal dominant polycystic kidney disease, GN glomerulonephritis. Distribution of clinical characteristics was compared between sHPT and controls with appropriate statistical tests (t-test, Chi\(^2\) test)—no significant differences were detected.

Inter-and intra-reader agreement. Interreader reliability, interpreted according to Koo et al.\(^{16}\), was moderate for erosions \((0.57; 95\% \text{CI} 0.25–0.76; \ p = 0.002)\), good for sclerosis \((0.78; 95\% \text{CI} 0.64–0.87; \ p < 0.001)\), moderate for joint space alterations \((0.74; 95\% \text{CI} 0.53–0.85; \ p < 0.001)\), good for osteophytes \((0.83; 95\% \text{CI} 0.70–0.90; \ p < 0.001)\).
0.71–0.91; \( p < 0.001 \)) and good for calcifications (0.85; 95% CI 0.74–0.91; \( p < 0.001 \)). Intrareader reliability was good for erosions (0.77; 95% CI 0.59–0.87; \( p < 0.001 \)), good for sclerosis (0.88; 95% CI 0.78–0.93; \( p < 0.001 \)), good for joint space alterations (0.82; 95% CI 0.68–0.90; \( p < 0.001 \)), good for osteophytes (0.87; 95% CI 0.77–0.93; \( p < 0.001 \)) and good for calcifications (0.86; 95% CI 0.76–0.92; \( p < 0.001 \)).

### Discussion

To our knowledge the data presented here is the first systematic exploration of structural lesions of the sacroiliac joints of patients with asymptomatic sHPT. We found a significantly higher prevalence of erosions in sHPT patients, while ankylosis and sclerosis were equally rare in both groups. These findings carry significance in the context of sacroiliitis imaging, where erosions are considered a specific finding of inflammatory joint disease.

Our findings somewhat contradict those of Tezcan et al., who examined inflammatory MRI lesions in primary hyperparathyroidism and did not find significant differences between HPT patients and controls. The most likely explanation for this incongruence is that standard SIJ-MRI imaging has known deficits in the depiction of small structural lesions, such as erosions. Osteophytes, which are considered degenerative rather than inflammatory joint lesions were significantly less prevalent in the sHPT group. This is surprising, as osteoarthritis is considered a common finding in patients with advanced CKD, and patients were matched with regards to predisposing factors for mechanical SIJ disease such as obesity and parity in women. A possible explanation may be a comparably larger proportion of immobile patients in the sHPT group. This is surprising, as osteoarthritis is considered a common finding in patients with advanced CKD, and patients were matched with regards to predisposing factors for mechanical SIJ disease such as obesity and parity in women. A possible explanation may be a comparably larger proportion of immobile patients in the sHPT group. This is surprising, as osteoarthritis is considered a common finding in patients with advanced CKD, and patients were matched with regards to predisposing factors for mechanical SIJ disease such as obesity and parity in women. A possible explanation may be a comparably larger proportion of immobile patients in the sHPT group.

Due to the retrospective nature of the investigation, data on back pain in sHPT patients could only be captured from electronic patients records, so that we cannot exclude the possibility that some of the patients may in fact have symptomatic joint disease, somewhat limiting the validity of our results. The results are limited further by the small size of the patient group—larger, prospective cohorts with more detailed information on severity and duration of the secondary hyperparathyroidism, including information on vitamin D, calcium and alkaline phosphatase are needed to illicit the factors that contribute to the development of the lesions described in this analysis.

In conclusion, secondary hyperparathyroidism can mimic sacroiliitis on SIJ CT in a substantial portion of patients and should be considered when assessing joints for inflammatory changes. Further investigations into the clinical significance of these lesions for affected patients are warranted.

### Table 2. Structural CT lesions in secondary hyperparathyroidism compared with controls. sHPT secondary hyperparathyroidism, SD standard deviation. Significantly (\( p < 0.05 \)) values are printed in bold. P-values were derived from Chi² tests for nominal and Mann–Whitney–U tests for continuous data.

| Lesion type          | sHPT (n=56) | Controls (n=259) | p-values |
|----------------------|------------|-----------------|----------|
| Erosion              |            |                 |          |
| Erosion score (0–72), mean (SD) | 2.6 (7.4) | 0.6 (2.7) | 0.001    |
| Erosion ventral ilium present, n (%) | 16 (28.6)* | 36 (13.9) | 0.016    |
| Erosion ventral sacrum present, n (%) | 6 (10.7)  | 12 (4.6) | 0.165    |
| Erosion middle ilium present, n (%) | 10 (17.9)* | 20 (7.7) | 0.040    |
| Erosion middle sacrum present, n (%) | 2 (3.6)  | 2 (0.8) | 0.147    |
| Erosion dorsal ilium present, n (%) | 6 (10.7)* | 9 (3.5) | 0.033    |
| Erosion dorsal sacrum present, n (%) | 3 (5.4)*  | 1 (0.4) | 0.019    |
| Sclerosis            |            |                 |          |
| Sclerosis score (0–48), mean (SD) | 3.0 (3.0) | 3.5 (3.2) | 0.300    |
| Sclerosis ventral ilium present, n (%) | 34 (60.7) | 151 (58.3) | 0.767    |
| Sclerosis ventral sacrum present, n (%) | 9 (16.1)  | 68 (26.3) | 0.124    |
| Sclerosis middle ilium present, n (%) | 15 (26.8) | 74 (28.6) | 0.871    |
| Sclerosis middle sacrum present, n (%) | 2 (3.6)  | 14 (5.4) | 0.746    |
| Sclerosis dorsal ilium present, n (%) | 14 (25.0) | 91 (35.1) | 0.162    |
| Sclerosis dorsal sacrum present, n (%) | 8 (14.3)  | 45 (17.4) | 0.695    |
| Joint space alterations |            |                 |          |
| Joint space alterations score, mean (SD) | 0.6 (1.3) | 0.4 (1.3) | 0.586    |
| Pseudo-widening present, n (%) | 3 (5.4)  | 4 (1.5) | 0.110    |
| Partial ankylosis present, n (%) | 2 (3.6)  | 13 (5.0) | > 0.999  |
| Osteophytes           |            |                 |          |
| Osteophyte score (0–12), mean (SD) | 1.5 (2.0) | 2.3 (2.3)* | 0.020    |
| Osteophyte ventral present, n (%) | 18 (32.1) | 102 (39.4) | 0.364    |
| Osteophyte dorsal present, n (%) | 18 (32.1) | 134 (51.7)* | 0.008    |
| Calcification         |            |                 |          |
| Calcification score, mean (SD) | 0.6 (1.1) | 0.4 (0.9) | 0.091    |
| Calcification present, n (%) | 15 (26.8) | 45 (17.4) | 0.132    |
Figure 2. Example of joint alterations in sHPT. Axially reconstructed high-resolution CT images. (A) Healthy control patient with normal SIJ. (B) Patient with secondary hyperparathyroidism: note the subchondral bone resorption mimicking erosions (black arrowheads) as well as the sclerotic rim around the resorption zone (white arrowheads). (B) Patient with secondary hyperparathyroidism: note the irregular, pseudo-widened left joint space (black arrowheads) compared to the regular joint space on the right.

Data availability
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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