POS1124

IDENTIFYING POTENTIAL CLASSIFICATION CRITERIA FOR CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD): RESULTS FROM THE INITIAL PHASES

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Background: Classification criteria for calcium pyrophosphate deposition disease (CPPD) will facilitate clinical research on this common crystalline arthritis. ACR/EULAR are jointly sponsoring development of CPPD classification criteria using a multi-phase process.

Objectives: To report preliminary results from the first two phases of a four-phase process for developing CPPD classification criteria.

Methods: CPPD classification criteria development is overseen by a 12-member Steering Committee. Item generation (Phase I) included a scoping literature review of five literature databases and contributions from a 35-member Combined Expert Committee and two Patient Research Partners. Item reduction and refinement (Phase II) involved a Combined Expert Committee meeting, discussions among Clinical, Imaging, and Laboratory Advisory Groups, and an item rating exercise to assess the influence of individual items toward classification. The Steering Committee reviewed the modal rating score for each item (range -3 [strongly pushes away from CPPD] to +3 [strongly pushes toward CPPD]) to determine items to retain for future phases of criteria development.

Results: Item generation yielded 420 items (312 from the literature, 108 from experts/patients). The Advisory Groups eliminated items they agreed were unlikely to distinguish between CPPD and other forms of arthritis, yielding 127 items for the item rating exercise. Fifty-six items, most of which had a modal rating of +/- 2 or 3, were retained for future phases (see Table 1). As numerous imaging items were rated +3, the Steering Committee recommended focusing on imaging of the knee, wrist, and one additional affected joint for calcification suggestive of CPP crystal deposition.

Conclusion: The ACR/EULAR CPPD classification criteria working group has adopted both data- and expert-driven approaches, leading to 56 candidate items broadly categorized as clinical, imaging, and laboratory features. Remaining steps for criteria development include domain establishment, item weighting through a multi-criteria decision analysis exercise, threshold score determination, and criteria validation.

Table 1. Categories of items retained for future phases of classification criteria development

Age in decade at symptom onset
Acute inflammatory arthritis (e.g. knee, wrist, 1st MTP joint*)
Recurrence and pattern of joint involvement (e.g. 1 self-limited episode, >1 self-limited episode)
Physical findings (e.g. palpable subcutaneous tophus*, psoriasis*)
Co-morbidities and family history (e.g. Gitelman disease, hemochromatosis, familial CPPD)
Osteoarthritis location and features (e.g. 2nd or 3rd MCP joint, wrist)
Synovial fluid findings (e.g. CPP crystals present, CPP crystals absent on 1 occasion* or 2 occasions*, monosodium urate crystals present*)
Laboratory findings (e.g. hypomagnesemia, hyperparathyroidism, rheumatoid factor*, anti-CCP*)
Plain radiograph: calcification in regions of fibro- or hyaline cartilage+
Plain radiograph: calcification of the synovial membrane/capsule/tendon+
Conventional CT: calcification in regions of fibro- or hyaline cartilage+
Conventional CT: calcification of the synovial membrane/capsule/tendon+
Ultrasound: CPP crystal deposition in fibro- or hyaline cartilage+
Ultrasound: CPP crystal deposition in synovial membrane/capsule/tendons+
Dual-energy CT: CPP crystal deposition in fibro- or hyaline cartilage+
Dual-energy CT: CPP crystal deposition in synovial membrane/capsule/tendon+

*Potential negative predictor +Assessed in the knee, wrist, and/or 1 additional affected joint

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POS1125

DUAL ENERGY CT HAS PROGNOSTIC VALUE IN GOUT BEYOND STANDARD CLINICAL MEASURES: A BEST EVIDENCE SYNTHESIS

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Background: Dual Energy CT Scan (DECT) can detect monosodium urate crystal deposits in multiple tissues. EULAR gout guidelines (Richette, 2020) recognized the value of DECT in making a clinical diagnosis when joint aspiration is difficult. DECT shows crystal deposits in almost 50% of gout patients without tophi (Dalbeth, 2017). Tophi are known to predict all-cause and cardiovascular mortality (Vincent 2017, Perez-Ruiz 2013) and it is plausible that DECT could as well. A prognostic measure should be reliable and valid. DECT validity would be evident for death, disability and distress.

Objectives: This study used a best evidence synthesis approach to synthesize the evidence for DECT as a prognostic measure in gout.

Methods: PUBMED and EMBASE were searched from initiation to December 2019; keywords (Dual Energy Computed Tomography OR DECT, gout,

tophaceous gout, chronic gout, monosodium urate crystals OR monosodium urate burden OR tophi OR monosodium urate volume OR flares OR pain OR distress OR death OR disability OR function). Human studies in English were considered. Titles, abstracts and full articles were reviewed. A manual search of secondary sources was conducted. Key gaps identified were considered throughout 2020 when reviewing emerging articles and presentations. Data extraction was conducted by both authors; data presented represents consensus.

Results: Of 344 articles, 81 titles/abstracts met screening inclusion criteria (24%) in the 2019 search; review of the full manuscript led to 41 articles selected (51%). Additionally, 3 key papers and 2 ACR 2020 presentations were identified through 2020. DECT is highly reliable with inter-class correlation coefficients >0.9. DECT has content validity. Dalbeth (2015) showed DECT and X-Rays findings correlated in tophaceous patients, r=0.70, p<0.001. Hand function correlates with DECT burden, with r^2=0.59, p=0.024 (Dalbeth 2007). Dalbeth (2017) showed DECT associated with greater flares at 3 and 12 months (p<0.01) in 152 patients. Pascart (2018) confirmed that subjects with flares had nearly doubled DECT feet volumes (0.9 vs 2.1 cm^3, p=0.05) versus those not flaring. Dalbeth (2017) showed abnormal DECT scans occurred in 47% of patients with normal uric acid (<6.0 mg/dL) without palpable tophi and in 90% with elevated uric acid and palpable tophi. DECT is very sensitive to change (Araujo 2015) with 95% volume reduction in 152 patients on pegloticase treated up to 12 months. Three studies show DECT is correlated to cardiovascular risk factor prevalence (Pascart 2020, Gamala 2018, Lee 2017). Marty-Ané reported that DECT volume predicts mortality (Marty-Ané ACR 2020). Limited evidence from 3 studies suggests that the minimum important volume for DECT is 1.0 cm^3 at feet and ankles, including Pascart 2020.

Conclusion: DECT imaging is highly reliable, has evidence for content validity and is highly sensitive to change. DECT appears to predict future gout flares, cardiovascular risk factor prevalence and mortality. Minimum important DECT volume approximates 1.0 cm^3. DECT requires further study but appears to be a relevant outcome for clinical trials and staging gout patients.

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POS1126 PREVALENCE OF HYPOPHOSPHATASIA IN ADULT RHEUMATOLOGY PATIENTS SCREENED BY LOW LEVELS OF ALKALINE PHOSPHATASE

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Background: Hypophosphatasia (HPP) is a genetic disease caused by one or more mutations in the alkaline phosphatase (ALP) gene, which encodes tissue-specific ALP and affects the mineralization process. Accordingly, arthralgia, fractures, and dental abnormalities have been reported in adults, and fatal courses in children. This metabolic disorder is commonly misdiagnosed with other more prevalent bone diseases due to its low prevalence and lack of recognition (i.e. chrondrocalcinosis). However, no epidemiological studies on the prevalence of HPP in the rheumatological patient population have been available to date.

Objectives: To identify the prevalence of HPP in rheumatological patients screened for persistent low levels of ALP and association with mutations in the ALP gene.

Methods: All adult rheumatology patients were screened for pathological low levels of ALP (< 35 IU/L) between January 1, 2017 and June 30, 2019 at the Department of Rheumatology, Clinic of Internal Medicine III, University Hospital Bonn, Germany. Medical files of patients with pathological low ALP levels were then reviewed for clinical signs and symptoms as well as results of genetic testing for HPP (full sequencing using Next Generation Sequencing).

Results: In total, 2,289 rheumatology patients were screened for low ALP levels. In 60 patients (2.62 %), pathological low ALP levels were identified, while in 30 of these (1.31 %), persistent low ALP levels were detected. In 19 of the 30 patients, genetic tests for ALPL gene mutations were done. Seven out of 19 patients (36.84 %) had HPP-related symptoms (fracture, dental abnormalities) with normal bone densitometry, while four of these patients (21.05 %) had a history of fracture and three patients (15.78 %) showed dental abnormalities. In addition to the typical HPP signs and symptoms, 13 patients (68.42%) showed mutations in the ALPL gene. One of the ALP mutations was found to be a novel genetic variant, classified as pathological. Interestingly, no association with chondrocalcinosis was detected.

Conclusion: In summary, it can be concluded that HPP is an under-diagnosed condition with a higher proportion of affected rheumatologic patients than previously thought (at least 0.56 percent of rheumatologic patients vs. 0,01 percent in a spanish healthy population). If we replicate these numbers for the german population (83 million, 5 percent of whom suffer from rheumatic conditions) the yield is approximately 4.15 million. This possibly indicates that 23,240 potential cases of HPP are currently not diagnosed. Therefore, implementation of a protocol in clinical practice to prevent underdiagnosis of HPP and to treat this disease appropriately is essential.

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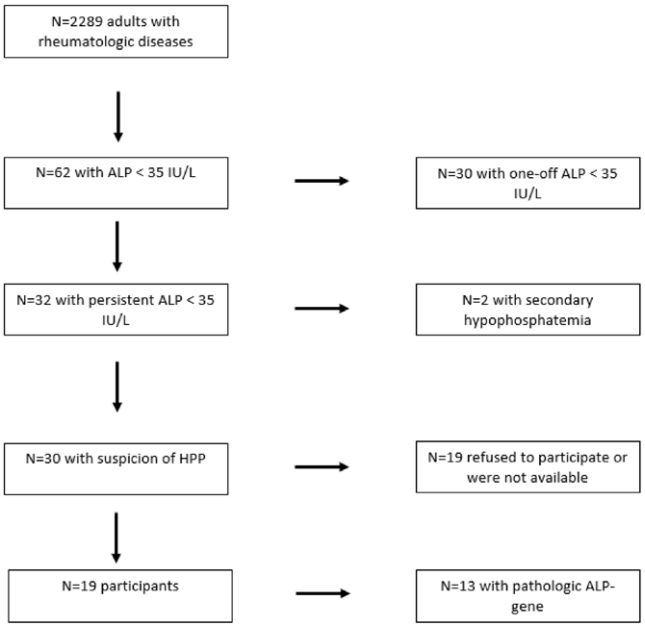

Figure 1.

Flow chart of identification of potential hypophosphatasia (HPP) patients from an adult rheumatology population. Threshold alkaline phosphatase < 35 IU/L at 37`C. ALP: alkaline phosphatase

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