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Identification of Clinical Phenotypes of Hand Osteoarthritis using Hierarchical Clustering Method: Results from the Digicod Cohort

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Purpose: Hand osteoarthritis (OA) is a very heterogenous disease in terms of risk factors, localization and severity. Such heterogeneity may also include clinical presentation and symptoms but has been poorly investigated. The main objective of this study was to delineate the clinical symptomatic phenotypes in hand OA population using computational and integrative analyses base on the cardinal symptoms in hand OA (pain, functional limitation, stiffness, esthetic discomfort).

Methods: We used the baseline data from DIGICOD which is a multi- centric hospital-based hand OA cohort. Clustering segregation was performed on AUSCAN subscores (0-100) of pain, function, stiffness separately, and the visual analog scale (0-100 mm) of esthetic discomfort. Hierarchical agglomerative clustering analyses has been performed on 389 patients based on euclidean distance and Ward D2 method. Differences between cluster composition have been assessed with Kruskal-Wallis, Mann-Whitney and Chi square test, Holm-Bonferroni correction has been applied on adjusted p-values.

Results: Among the 389 patients analyzed, 5 distinct clinical clusters have been identified (Figure 1). Cluster 1 (N/488) is mainly composed of low symptomatic patients, cluster 2 (N /4 91) of patients with mild symptoms (pain, stiffness and functional limitation), cluster 3 (N/480) of patients displaying esthetic discomfort mainly (without pain), cluster 4 (N 1/442) has high level of pain, stiffness and functional disability but without esthetic discomfort and cluster 5 (N/488) combined features of cluster 4 plus high level of esthetic discomfort (Figure 2). Age and hand OA duration were significantly different amongst clusters and higher in clusters 4 and 5 (p 1/40.06 and p 1/40.0002). Men were mostly present in low and mild-symptomatic cluster 1 and 2 (p 1/40.002). The clusters did not differ significantly for BMI, metabolic syndrome and CRP level, although metabolic syndrome represented 45.4 % of highly symptomatic cluster 5 vs 26.1 % of cluster 1 (p1/4 0.01). The presence of esthetic discomfort (corresponding to clusters 3 and 4) was associated with higher number of nodes

($p=0.0003$) and with radiographic erosive hand OA ($p=0.04$). Clusters 3, 4 and 5 were more severe radiographically since they were associated with higher sum of the Kellgren Lawrence score for all hand joints ($p<0.00001$) compared to cluster 1. Clusters 4 and 5 have also higher Hospital Anxiety and Depression score ($p=0.0004$). The main expectation in all clusters was function, except pain for the highly symptomatic cluster 5. Only cluster 4 and 5 which represented a third of our cohort (130 patients over 389) have a mean AUSCAN pain score ≥ 40 .

Conclusions: The identification of these 5 clinical symptomatic phenotypes through hierarchical clustering, illustrates the heterogeneity of clinical presentation of hand OA. This may help rationalizing patient recruitment in clinical trials evaluating symptomatic drugs. This may open toward a tailored therapeutic management according to each cluster and may better identify patients who may likely participate in clinical trials evaluating symptomatic drugs.

Ref 1: Joint Bone Spine 2021 [PMID: 33689840](#)

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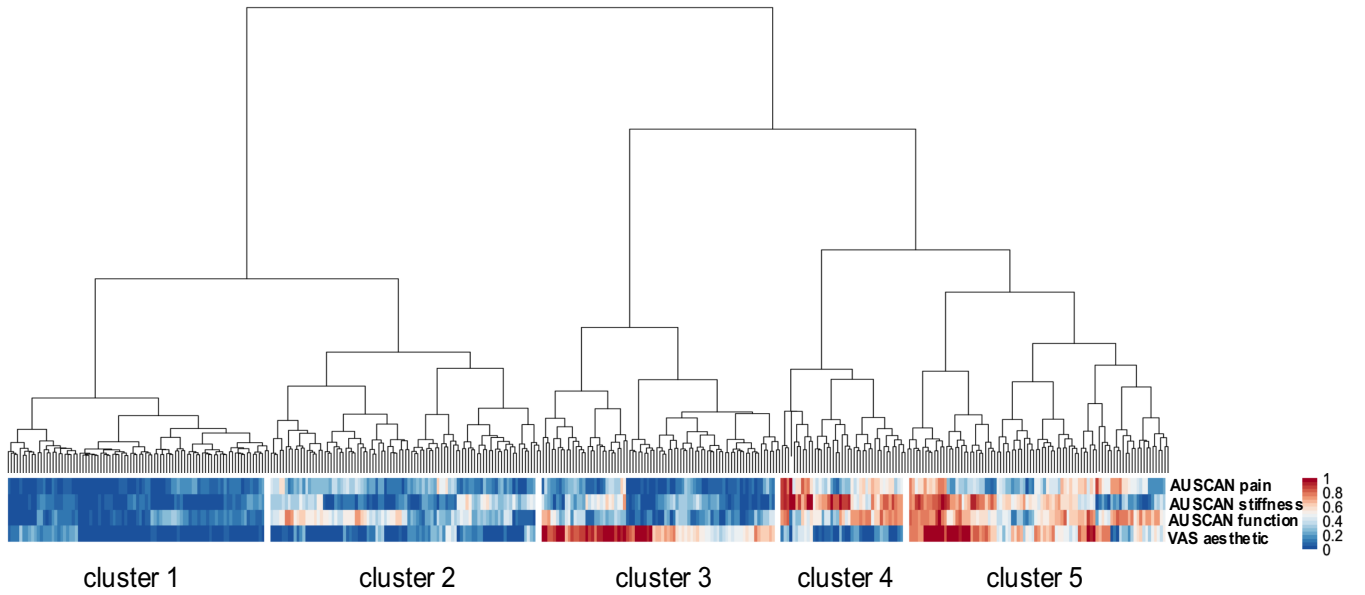


Figure 1. identification by clusters of hand OA phenotypes. The heatmap represents the results of hierarchical agglomerative clustering performed on AUSCAN pain, function and stiffness, and VAS esthetic data collected on 389 patients from the DIGICOD cohort.

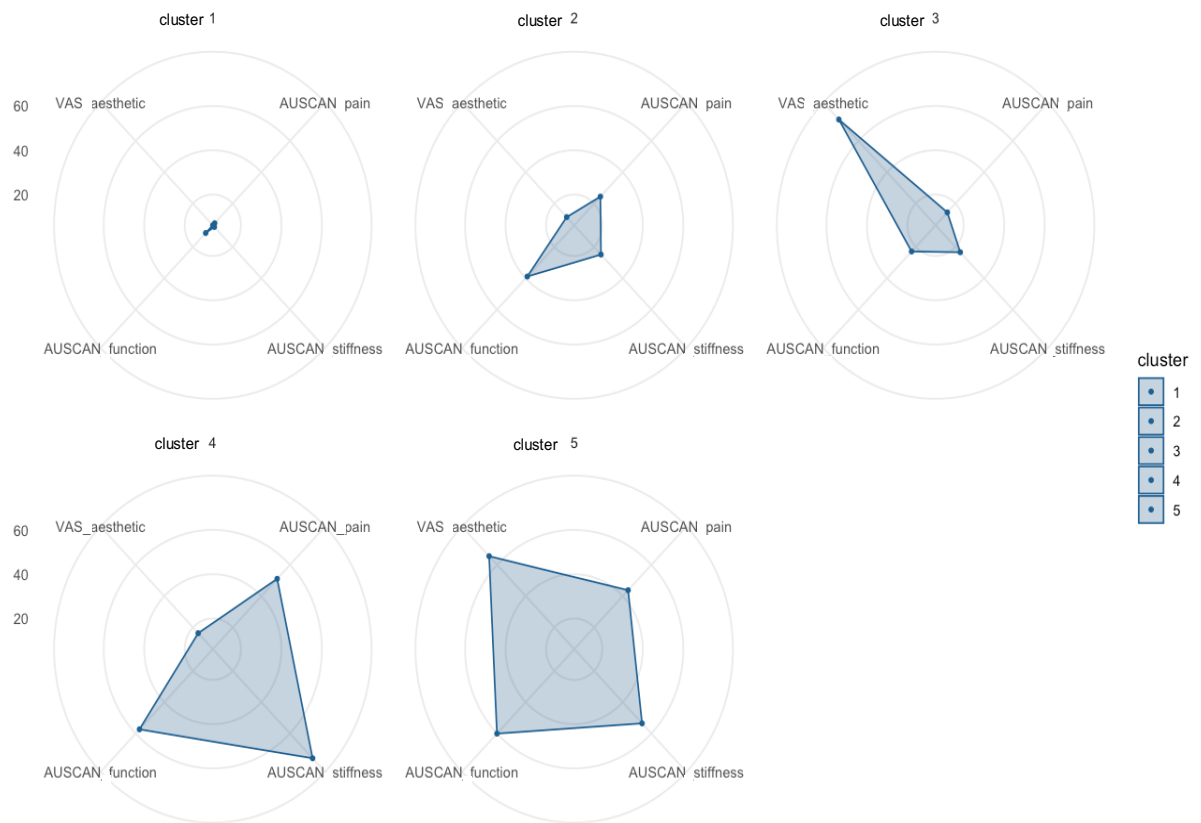


Figure 2. Contribution of the different symptoms to hand OA clusters. Radar plots represent for each cluster the contribution of each symptom based on the AUSCAN pain, function and stiffness, and the VAS esthetic. The values correspond to the mean of the 4 values expressed in each cluster.