DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS IN SUBJECTS WITH CONGESTIVE HEART FAILURE UNDERGOING CARDIAC REHABILITATION: A DECISION TREE ANALYSIS

Pasquale AMBROSINO, MD, Domenico SCRUTINIO, MD, Maurizio DE CAMPI, MD, Enzo MINIERO, MD, Roberto FORMISANO, MD, Giorgio Alfredo SPEDICATO, PhD, FCAS, FSA, CStat, Gian Luca IANNUZZI, MD and Nicola PAPPONE, MD

From the 1Istituti Clinici Scientifici Maugeri IRCCS, Pavia and 2Unipol Group, Bologna, Italy

Objective: To assess the prevalence of diffuse idiopathic skeletal hyperostosis and its relationship with vascular risk factors among patients with congestive heart failure.

Design: Population-based cross-sectional study.

Participants: A total of 584 consecutive patients admitted to a Rehabilitative Cardiology Unit.

Methods: Chi-square Automatic Interaction Detector (CHAID) decision tree analysis was used to build a predictive model.

Results: The mean age (standard deviation) of the study population was 68.1 years (standard deviation 12.3), and 77.7% of the subjects were men. The overall prevalence of diffuse idiopathic skeletal hyperostosis in the cohort was 49.8%. Logistic regression analysis showed that age was a predictor of diffuse idiopathic skeletal hyperostosis (odds ratio 1.034; 95% confidence interval: 1.021–1.047, \( p < 0.001 \)), with increasing odds ratios for increasing age tertiles. The CHAID prediction model identified 2 age “buckets”: \( \leq 69 \) and \( > 69 \) years. Patients > 69 years had a diffuse idiopathic skeletal hyperostosis prevalence of 60.1%, compared with 39.2% among those \( \leq 69 \) years. Notably, body mass index was a predictor of diffuse idiopathic skeletal hyperostosis in this younger subset of patients \( (p = 0.028) \), with 2 body mass index buckets, \( \leq 23.3 \) and \( > 23.3 \) kg/m\(^2\), the latter showing more than twice the prevalence of diffuse idiopathic skeletal hyperostosis (43.2% vs 20%).

Conclusion: Diffuse idiopathic skeletal hyperostosis is extremely frequent among patients with congestive heart failure, with age and body mass index being the strongest predictors.

Key words: diffuse idiopathic skeletal hyperostosis; spine; congestive heart failure; disability; rehabilitation; exercise; chi-square automatic interaction detector.

Accepted 10 Feb, 2020; Epub ahead of print Feb 27, 2020

J Rehabil Med 2020; 52: jrm00030

Correspondence address: Nicola Pappone, Istituti Clinici Scientifici Maugeri IRCCS, Via Maugeri 4, 27100, Pavia, Italy. E-mail: nicola.pappone@icsmaugeri.it

Diffuse idiopathic skeletal hyperostosis (DISH) is a common, but often unrecognized, systemic disorder, observed mainly in elderly people. DISH is characterized by calcification and ossification of enthesal sites, especially in the axial skeleton, but also in peripheral joints (1). A diagnosis of DISH is made when large bridging osteophytes in at least 4 adjacent thoracic vertebrae are present on conventional radiographs (2).

Despite these significant structural changes, DISH can be an asymptomatic condition. Thus DISH has been poorly investigated and its clinical relevance has been acknowledged only in recent years (3). DISH can produce incarceration syndromes, spinal immobility, radiculopathy and myelopathy, with the possibility of para- and tetraparesis, dysphagia and dysphonia, rhinolalia by irritation of the recurrent laryngeal nerve, reduced lung capacity and airway obstruction (4). Furthermore, individuals with DISH have a significantly higher risk of spinal fractures after low impact trauma compared with individuals with a non-ankylosing spine (5). Thus, although DISH is often asymptomatic, its high prevalence in the general population, and the possibility of severe and disabling complications, justify the increasing interest in this condition in recent years.
Research into the mechanisms that contribute to new bone growth in patients with DISH (6, 7) reports a strong association with individual components of the metabolic syndrome (e.g. diabetes mellitus, obesity, hypercholesterolaemia) (8) and an increased risk of cardiovascular comorbidity (9). In keeping with this, a prevalence of DISH of 30.3% has been reported recently among patients with severe atherosclerotic cardiovascular diseases (CVDs) (10), with an even higher prevalence (42.2%) in a small subgroup of patients diagnosed with congestive heart failure (CHF) (10).

To better address this issue, this study evaluated the prevalence of such potentially disabling condition in a larger cohort of subjects diagnosed with CHF who were undergoing exercise-based cardiac rehabilitation. Moreover, this study used decision tree analysis to build a predictive model for development of DISH in this clinical setting.

**MATERIAL AND METHODS**

**Study design**

This is a single-centre, population-based, observational study.

**Setting and participants**

From July 2016 to January 2019, 608 consecutive patients diagnosed with CHF admitted to the heart disease rehabilitation programme in our Rehabilitative Cardiology Unit were screened for enrollment in the study. The protocol was approved by the Institutional Review Board of ICS Maugeri – Institute of Cas-sano Murge, Bari, Italy on April 13, 2016.

**Inclusion and exclusion criteria**

The target study population consisted of inpatients patients of either sex and any race, with a known diagnosis of CHF (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 428.0, 428.1 and 428.9). Exclusion criteria were: any clinical condition that could alter the radiographic aspect of the spine: e.g. ankylosing spondylitis or any seronegative spondyloarthritides; rheumatic diseases; severe spine deformities; previous vertebral fractures; active metastatic cancer.

**Variables and measurements**

At admission, all patients underwent a complete cardiological examination by a trained staff member. The following information was collected from the whole population: sex, age, New York Heart Association (NYHA) class, ejection fraction, personal history of ischaemic heart disease, atrial fibrillation, chronic obstructive pulmonary disease (COPD), liver disease, thyroid disease, and cancer. Subsequently, all patients underwent measurements of systolic and diastolic blood pressure, weight, height, and body mass index (BMI) calculation. Blood samples were also collected to evaluate total cholesterol, high-density lipoprotein cholesterol (HDLc), serum fasting glucose, creatinin, and b-type natriuretic peptide (BNP) levels. According to validated criteria (11), hypercholesterolaemia with low HDLc was defined as total cholesterol ≥200 mg/dl with HDLc ≤40 mg/dl for men and ≤50 mg/dl for women, hypertension as blood pressure ≥130/85 mmHg, impaired fasting glucose as a fasting glucose level ≤100 mg/dl, and obesity as BMI values ≥30 kg/m².

The presence of end-stage renal disease (ESRD) was defined as an estimated glomerular filtration rate (eGFR) ≤15 ml/min (12). Chest radiographs were performed for formal assessment of thoracic diseases. Images were acquired with computed radiography equipment (Prestige SI, GE Healthcare, Little Chalfont, United Kingdom) using a standardized technique (125 kV with 2 lateral fields; 200-cm focus-to-film distance). Images were examined by a radiologist and a rheumatologist, both blinded to rheumatological and metabolic evaluations. DISH was established when the radiological criteria of Resnick & Niwayama were fulfilled on the posteroanterior or lateral view or both (2). These criteria require the involvement of at least 4 contiguous thoracic vertebral segments, preservation of intervertebral disc spaces, and the absence of apophyseal joint degeneration or sacroiliac inflammatory changes. Individuals with inconclusive radiographs were scored as non-DISH subjects.

**Statistical analysis**

Statistical analysis was performed with the IBM SPSS 25 system (SPSS Inc., Chicago, IL, USA). Continuous data are expressed as mean (standard deviation; SD), whilst categorical data are expressed as percentage. Preliminarily, the t-test was performed to compare continuous variables, while the χ² test was employed to analyse categorical data (using the Monte Carlo approach to compute the p-values in order to cope with small sample size).

In order to evaluate the impact of different covariates on the evaluated outcome and calculate the odds ratio (OR) for the presence of DISH, a multivariate logistic regression analysis (stepwise method) was adopted, with the presence of DISH as the dependent variable and the following demographic (age, male sex) and clinical covariates related to disease severity and aetiology (NYHA class, BNP levels, ejection fraction, ischaemic CHF aetiology), presence of traditional vascular risk factors (obesity, hypertension, hypercholesterolaemia, diabe-tes), and comorbidities (cancer, ESRD, liver disease, thyroid disease, COPD, atrial fibrillation) as independent variables. A supplementary logistic regression analysis was performed, also including continuous data (age, BMI, ejection fraction, and BNP levels) categorized into tertiles as independent variables to account for possible marginal non-linearity. Finally, in order to identify possible variable interactions at different levels, a Chi-square Automatic Interaction Detector (CHAID) classification and regression tree was fitted onto the sample using a hierarchical approach (13, 14). The significance level for node splitting in the CHAID model was p<0.05.

The area under the curve of receiver operating characteristic (AUC-ROC) was estimated in order to quantify the discriminating ability of both CHAID and logistic regression methods.

All the results are shown as 2-tailed with the confidence interval for statistical significance set at 95% (95% CI).

**RESULTS**

Among the 608 patients evaluated, 24 were excluded (18 vertebral fractures, 6 diagnosed with rheumatic or spine diseases other than DISH). Therefore, 584
subjects entered the study. Clinical and demographic features of the study population are shown in Table I.

The mean (SD) age of the study population was 68.1 years (SD 12.3), and 77.7% of the subjects were men. The overall prevalence of DISH in the cohort was 49.8%. Patients with DISH showed an older age, an increased prevalence of hypertension, COPD, and atrial fibrillation, and a significantly higher ejection fraction. However, after adjusting for all the other clinical and demographic variables by means of multivariate analyses, only age was an independent predictor of the presence of DISH (OR 1.034; 95% CI 1.021–1.047, \( p < 0.001 \)). It is notable that a second logistic regression analysis, also including continuous data categorized into tertiles, showed that both age and BMI impacted significantly on the presence of DISH. The risk of development of DISH according to increasing tertiles of age and BMI is shown in Fig. 1.

Accordingly, CHAID analysis identified 2 variables significantly affecting the presence of DISH: age and BMI. The other variables did not reach significance, thus only age and BMI were used to build the CHAID decision tree. The model included a total of 5 nodes, with 3 terminal nodes (numbers 2, 3 and 4). In detail, 2 age “buckets” were identified: \( \leq 69 \) years (node 1), with a DISH prevalence of 39.2%, and \( > 69 \) years (node 2), in which DISH diagnostic criteria were achieved by 60.1% of subjects. Of interest, BMI was significantly correlated with the presence of DISH in the younger subset of patients (\( p = 0.028 \)), since 2 BMI buckets were identified, \( \leq 23.3 \) kg/m\(^2\) (node 3) and \( > 23.3 \) kg/m\(^2\) (node 4), the latter showing more than twice the rate of DISH prevalence (43.2% vs 20%) (Fig. 2).

Using a default 50% classification threshold, the overall estimated accuracy was 60.4% for the CHAID model and 62.8% for the logistic regression model.

### Table I. Demographic and clinical features of the study population and stratification according to diffuse idiopathic skeletal hyperostosis (DISH) and non-DISH criteria achievement

| Overall | DISH (49.8%) | No-DISH (50.2%) | \( p \)-value |
|---------|--------------|-----------------|--------------|
| Age, years, mean (SD) | 68.1 (12.3) | 70.5 (11.0) | 65.6 (13.0) | \( < 0.001 \) |
| Male, sex, n (%) | 454 (77.7) | 225 (49.6) | 229 (50.4) | 0.443 |
| Ischaemic CHF aetiology, n (%) | 283 (48.5) | 145 (51.2) | 138 (48.8) | 0.282 |
| NYHA class, mean (SD) | 3.4 (0.6) | 3.4 (0.6) | 3.4 (0.6) | 0.349 |
| BNP (pg/ml), mean (SD) | 6,111.7 (8,957.5) | 5,666.1 (7,796.8) | 6,560.4 (9,984.5) | 0.228 |
| Ejection fraction, %, mean (SD) | 30.1 (11.4) | 31.4 (11.5) | 28.8 (11.2) | \( 0.006 \) |
| Obesity, mean (SD) | 153 (26.7) | 73 (26) | 80 (27.5) | 0.377 |
| Height, cm | 162.8 (9.0) | 162.5 (8.6) | 163.0 (9.4) | 0.508 |
| Weight, kg | 75.0 (16.6) | 76.0 (16.0) | 74.0 (17.2) | 0.172 |
| BMI, kg/m\(^2\) | 27.9 (5.7) | 28.2 (5.5) | 27.5 (5.8) | 0.112 |
| Hypertension, n (%) | 335 (57.4) | 178 (61.2) | 157 (53.6) | \( 0.038 \) |
| Hypercholesterolaemia, n (%) | 72 (12.4) | 36 (12.4) | 36 (12.4) | 0.544 |
| Diabetes mellitus/IFG, n (%) | 203 (34.8) | 101 (37.8) | 93 (31.7) | 0.073 |
| COPD, n (%) | 166 (28.4) | 95 (32.6) | 71 (24.2) | \( 0.015 \) |
| Atrial fibrillation, n (%) | 214 (37.7) | 118 (41.7) | 96 (33.7) | \( 0.030 \) |

DISH: diffuse idiopathic skeletal hyperostosis; CHF: congestive heart failure; NYHA: New York Heart Association; BNP: b-type natriuretic peptide; BMI: body mass index; IFG: impaired fasting glucose; COPD: chronic obstructive pulmonary disease. Continuous variables with normal distribution are presented as mean (standard deviation; SD). Significant values are shown in bold.

Fig. 1. Risk of development of diffuse idiopathic skeletal hyperostosis (DISH) according to increasing tertiles of (A) age and (B) body mass index (BMI). OR: odds ratio; 95% CI: 95% confidence interval; BMI: body mass index.
When the 2 models were compared they were found to be statistically equivalent in terms of predictive power, since similar AUC-ROC with similar confidence intervals were found (Fig. 3).

**DISCUSSION**

To our knowledge, this is the first population-based study specifically designed to report on the prevalence of DISH in patients with CHF who are undergoing cardiac rehabilitation. In addition, it is the first time that the CHAID decision tree analysis has been used to identify potential risk factors for the presence of DISH. The study documented a 49.8% overall prevalence of DISH in patients with CHF. This prevalence is higher than that reported in other clinical settings (15–17), but it is in line with the results of a previous study, showing a prevalence of DISH of 30.3% in subjects with severe atherosclerotic CVDs and a prevalence of 42.2% in the small subgroup of patients with CHF \((n=45)\) (10). One of the largest population-based studies on DISH documented a prevalence of only 25% in men and 15% in women (15). Thus, our group previously reported a similar prevalence (15.1%) in 93 Italian women (17). In contrast, only 3.8% of men and 2.6% of women achieved DISH diagnostic criteria in the Finnish general population (18). These apparently contrasting results are probably due to the different populations evaluated in each study, and it can be hypothesized that the cardiometabolic status of the patients enrolled in our study may account for the ≈50% reported prevalence of DISH. The association of DISH with metabolic syndrome and its individual components (e.g. diabetes mellitus, obesity, hypertension) has been documented previously (7–9). Increasing evidence is emerging about the presence of a common pathogenic substrate for metabolic syndrome-associated disorders (including atherosclerosis) and the process of new bone formation in patients with DISH (6, 10, 19). In fact, approximately half of the patients in the current study had a history of ischaemic cardiovascular events, with a high prevalence of hypertension (57.4%) and diabetes mellitus (34.8%) and a mean BMI of 27.9 kg/m\(^2\).

However, most individual components of metabolic syndrome did not impact on the prevalence of DISH in our study, nor did the aetiology or disease severity of CHF (NYHA class, BNP levels, ejection fraction). In addition, the high prevalence of traditional cardiovascular risk factors, one of the main differences between our study population and those of previous studies reporting lower percentages of DISH is older age. Our patients had a mean age of 68.1 years, and the results of our multivariate analyses consistently confirmed the impact of age on the presence of DISH, with an
increasing OR for increasing age tertiles. The other variable significantly impacting on the prevalence of DISH was BMI. The role of age and BMI as predictors of DISH was better described by CHAID decision tree analysis. CHAID is a frequently used data-mining approach, which has been developed as a useful tool for epidemiological investigations. Compared with conventional logistic regression analysis, CHAID reveals possible partitions of the data-set, by using the predictor that, at that precise stage, most significantly explains the outcome. In the current study, the CHAID prediction model identified 2 age buckets: ≤ 69 and > 69 years. Patients > 69 years had a prevalence of DISH of 60.1%, compared with a prevalence of 39.2% among those ≤ 69 years. It is notable that, in this younger subset of patients, BMI was the only predictor of the presence of DISH, since 2 BMI buckets were identified, ≤ 23.3 and > 23.3 kg/m², the latter showing more than twice the rate of prevalence of DISH (43.2% vs 20%).

Although this predictive model showed only moderate accuracy, it substantially confirmed the results of logistic regression analysis. Overall, these findings suggest that age and BMI are the strongest predictors of the presence of DISH among patients with established cardiovascular disorders, in line with our previous report on a different subset of patients (10). While ageing is inevitable, body weight is a modifiable risk factor, in which both patients and clinicians may intervene. In our study population, a BMI ≤ 23.3 kg/m² was associated with significantly lower percentages of DISH among younger patients with CHF. Whether a BMI lower than this cut-off value could also be a reasonable “target” in other clinical settings is unknown. Moreover, it is not known whether a reduction in body weight could be able to slow down, stop or even reverse the progression of DISH. Overall, our results suggest the need for larger population-based studies with appropriate prediction models to better address these issues, also taking into account that no comparable study has been found in current literature that could be used as a “benchmark” for predictive accuracy.

Despite these unresolved queries, the results of this study may have some relevant clinical implications. DISH is a systemic condition with a wide spectrum of clinical manifestations, ranging from complete absence of symptoms to severe disability (6). Patients with DISH often report pain, stiffness, loss of range of motion, and even difficulty breathing or swallowing (9). Involvement of the axial skeleton, with postural abnormalities and severe limitations of spinal mobility, may be such as to be differentiated from the manifestations of ankylosing spondylitis (20, 21). As a consequence, the presence of such disabling symptoms may interfere with activities of daily living and significantly reduce the patient’s perceived quality of life (22). Moreover, it is well known that the ankylosed spine in patients with DISH is prone to unstable fractures due to long lever arms and consecutive stress concentration (23), thus exposing patients to a considerable risk of secondary spinal cord injury (24, 25) and increased mortality (26). A recent multicentre study on 285 patients with DISH showed that trivial trauma accounts for 77.2% of spinal fractures in this clinical setting, with delayed diagnosis being significantly associated with neurological deterioration and subsequent disability (27). Our population-based study was conducted in a rehabilitation centre, where subjects with CHF underwent a comprehensive intervention, based on a thorough patient assessment followed by patient-tailored therapies, which include, but are not limited to, exercise training, education, and behaviour changes. However, exercise remains the cornerstone of a rehabilitation programme for patients with heart disease (28–32). The results of the current study showed an exceptionally high prevalence of DISH among patients with CHF undergoing a programme of in-hospital rehabilitation, particularly in obese and older individuals. Given the risk of spinal fractures even after low impact trauma and of severe disability, we believe that the presence of DISH should always be investigated in patients with CHF who report spine stiffness or chronic back pain, especially in those undergoing exercise-based activities. Thus, more tailored rehabilitation programmes should be administered to patients with CHF with concomitant symptoms or a diagnosis of DISH. In this regard, physiatrists might be particularly suited to take a leadership role in the design phase of a cardiac rehabilitation programme for patients with such comorbidity, since cardiologists may have limited experience of the needs of physically disabled patients. Thus, a strict collaboration between cardiologists and physiatrists could be exorted in order to identify the best rehabilitative approach for patients with CHF and concomitant DISH.

The translational relevance of our results can be better understood if we consider that different subsets of patients undergoing other forms of exercise-based rehabilitation (e.g. rheumatological, orthopaedic, pulmonary, neurological) often have several comorbidities (33–35), including an increased cardiovascular risk (36–38). Thus, the presence of DISH may represent a concern, not only for cardiologists, but also for other health professionals working in the field of rehabilitation. Further, population-based, studies with appropriate prediction models are needed in order to assess the prevalence of DISH in different settings and the impact that this condition may have on the effectiveness of rehabilitation programmes.
Study limitations

This study has a number of limitations. First, no healthy control group was enrolled, and an observational analysis of the setting was performed. Overall, characteristics of our study population reflect the heterogeneity of the population that is referred to a cardiac rehabilitative programme.

Secondly, although no significant association was found between the ischaemic CHF aetiology and the presence of DISH, we are aware that other aetiologies (valvular, arhythmic, etc.) accounted for the remaining 51.5% of patients with CHF in our study population. Unfortunately, no information about the isolated prevalence of each non-ischaemic condition related to insurgence of CHF was recorded in our database. Thus, we could not assess the impact of the different non-ischaemic aetiologies on the evaluated outcome.

A further consideration is the ~60% estimated accuracy of our predictive models. Although the accuracy of both CHAID and logistic regression may appear to be low, 2 main aspects should be taken into account. First, more sophisticated models (e.g. machine-learning models) could be tested, but a much larger sample size would be necessary. This would eventually allow us to assess the predictive performance of the presented models on a separate validation set. Secondly, the residual variability of our models could be due to predictors that have not been considered in this study (e.g. hypertriglyceridaemia, presence/absence of metabolic syndrome). However, to the best of our knowledge, no study is currently available in the existing literature reporting on the predictive ability of estimating the risk of DISH in this specific clinical setting. Therefore, our study would serve as an initial “benchmark” for future research.

Conclusion

The results of this study consistently show that DISH is extremely frequent among patients with CHF, and that age and BMI are the strongest predictors of the presence of DISH in this clinical setting. Given the risk of spinal fractures and the presence of DISH-related disabling symptoms, a strict collaboration between cardiologists and physiatrists should be exhorated in order to identify the best rehabilitative approach for patients with such comorbidity. Larger controlled studies are needed to delineate the entire spectrum of this condition in patients with cardiovascular diseases.

Authors’ contribution. Ambrosino P and Pappone N conceived and designed the study, performed statistical analysis, interpreted results and drafted the manuscript. Minieno D, De Campi M, Miniero E, Formisano R and Iannuzzi GL acquired clinical data and drafted the manuscript. Specidato GA performed statistical analyses and critical revisions. All Authors read and approved the final version of the manuscript. Pappone N had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of data analysis.

The authors have no conflicts of interest to declare.

REFERENCES

1. Utsinger PD. Diffuse idiopathic skeletal hyperostosis. Clin Rheum Dis 1985; 11: 325–351.
2. Resnick D, Niwayama G. Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). Radiology 1976; 119: 559–568.
3. Mader R, Verlaan JJ, Buskila D. Diffuse idiopathic skeletal hyperostosis: clinical features and pathogenic mechanisms. Nat Rev Rheumatol 2013; 9: 741–750.
4. Littlejohn GO. Diffuse idiopathic skeletal hyperostosis. In: Hochberg M, Silman A, Weinblatt M, Weismann M, editors. Rheumatology. Philadelphia: Mosby Elsevier; 2011, p. 1801–1806.
5. Taljanovic MS, Hunter TB, Wisneski RJ, Seeger JF, Friend CJ, Schwartz SA, et al. Imaging characteristics of diffuse idiopathic skeletal hyperostosis with an emphasis on acute spinal fractures: self-assessment module. Am J Roentgenol 2009; 193: S20–S24.
6. Pappone N, Ambrosino P, Di Minno MND, Iervolino S. Is diffuse idiopathic skeletal hyperostosis a disease or a syndrome? Rheumatology (Oxford) 2017; 56: 1635–1636.
7. Kiss C, Szilágyi M, Paksy A, Poór G. Risk factors for diffuse idiopathic skeletal hyperostosis: a case control study. Rheumatology (Oxford) 2002; 41: 27–30.
8. Pillai S, Littlejohn G. Metabolic factors in diffuse idiopathic skeletal hyperostosis – a review of clinical data. Open Rheumatol J 2014; 8: 116–128.
9. Mader R, Novofestovski I, Adawi M, Lavi I. Metabolic syndrome and cardiovascular risk in patients with diffuse idiopathic skeletal hyperostosis. Semin Arthritis Rheum 2009; 38: 361–365.
10. Zincarelli C, Iervolino S, Di Minno MN, Miñiero E, Rengo C, Di Gioia L, et al. The prevalence in subjects with severe atherosclerotic cardiovascular diseases. Arthritis Care Res (Hoboken) 2012; 64: 1765–1769.
11. Di Minno MN, Peluso R, Iervolino S, Russolillo A, Lupoli R, Scarpa R, et al. Weight loss and achievement of minimal disease activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor α blockers. Ann Rheum Dis 2014; 73: 1157–1162.
12. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009; 150: 604–612.
13. Haughton D, Oulabi S. Direct marketing modeling with CART and CHAID. J Direct Market 1993; 7: 16–26.
14. Podgorelec V, Kokol P, Stiglic B, Rozman I. Decision trees: an overview and their use in medicine. J Med Systems 2002; 26: 445–463.
15. Weinfeld RM, Olson PN, Maki DD, Griffiths HJ. The prevalence of diffuse idiopathic skeletal hyperostosis (DISH) in two large American Midwest metropolitan hospital populations. Skeletal Radiol 1997; 26: 222–225.
16. Kiss C, O’Neill TW, Mitzusova M, Szilágyi M, Poór G. The prevalence of diffuse idiopathic skeletal hyperostosis in a population-based study in Hungary. Scand J Rheumatol 2002; 31: 226–229.
17. Pappone N, Lubrano E, Esposito-del Puente A, D’Angelo S, Di Girolamo C, Del Puente A. Prevalence of diffuse idiopathic skeletal hyperostosis in a female Italian population.
Clin Exp Rheumatol 2005; 23: 123–124.

18. Julkunen H, Knekt P, Aromaa A. Spondylosis deformans and diffuse idiopathic skeletal hyperostosis (DISH) in Finland. Scand J Rheumatol 1981; 10: 193–203.

19. Oudkerk SF, Mohamed Hoessein F, Pthm MA, Öner FC, Verlaan JJ, de Jong PA. Subjects with diffuse idiopathic skeletal hyperostosis have an increased burden of coronary artery disease: an evaluation in the COPDGene cohort. Atherosclerosis 2019; 287: 24–29.

20. Dan Lantsman C, Herman A, Verlaan JJ, Stern M, Mader R, Eshed I. Abdominal fat distribution in diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis patients compared to controls. Clin Radiol 2018; 73: 910e15–910e20.

21. Olivieri I, D’Angelo S, Palazzi C, Padula A, Mader R, Khan MA. Diffuse idiopathic skeletal hyperostosis: differentiation from ankylosing spondylitis. Curr Rheumatol Rep 2009; 11: 321–328.

22. Mader R, Novofastovski I, Rosner E, Adawi M, Herer P, Buskila D. Nonarticular tenderness and functional status in patients with diffuse idiopathic skeletal hyperostosis. J Rheumatol 2010; 37: 1911–1916.

23. Hirasa A, Robinson Y, Olerud C, Wakao N, Kaniya M, Muratani K, et al. Regional differences in diffuse idiopathic skeletal hyperostosis: a retrospective cohort study from Sweden and Japan. Spine (Phila Pa 1976) 2018; 43: E1474–E1478.

24. Robinson Y, Willander J, Olerud C. Surgical stabilization improves survival of spinal fractures related to ankylosing spondylitis. Spine (Phila Pa 1976) 2015; 40: 1697–1702.

25. Redjati R, Damade R, Royant V. Spinal fracture in diffuse idiopathic skeletal hyperostosis. Joint Bone Spine 2018; 85: 489.

26. Hirsch JA, Beall DP, Chambers MR, Andreshak TG, Brook AL, Bruel BM, et al. Management of vertebral fragility fractures: a clinical care pathway developed by a multispecialty panel using the RAND/UCLA Appropriateness Method. Spine J 2018; 18: 2152–2161.

27. Okada E, Yoshii T, Yamada T, Watanabe K, Katsumi K, Hiyama A, et al. Spinal fractures in patients with Diffuse idiopathic skeletal hyperostosis: a nationwide multi-institution survey. J Orthop Sci 2019; 24: 601–606.

28. Long L, Mordi IR, Bridges C, Sagar VA, Davies EJ, Coats AJ, et al. Exercise-based cardiac rehabilitation for adults with heart failure. Cochrane Database Syst Rev 2019; 1: CD003331.

29. van Geffen ME, Ter Hoeve N, Sunamura M, Stam HJ, van Domburg RT, van den Berg-Emons RJ. Fatigue during and after cardiac rehabilitation. J Rehabil Med 2015; 47: 569–574.

30. Pasquini G, Vannetti P, Molino-Lova R. Ability to work in anaerobic condition is associated with physical performance on the six-minute walk test in older patients receiving cardiac rehabilitation. J Rehabil Med 2015; 47: 472–477.

31. Bonsignore A, Marzolini S, Oh P. Cardiac rehabilitation for women with breast cancer and treatment-related heart failure compared with coronary artery disease: a retrospective study. J Rehabil Med 2017; 49: 277–281.

32. Mungovan SF, Singh P, Gass GC, Smart NA, Hirschhorn AD. Effect of physical activity in the first five days after cardiac surgery. J Rehabil Med 2017; 49: 71–77.

33. de Laat FA, Dijkstra PU, Rommers GM, Geerzen JHB, Roorda LD. Prevalence of comorbidity and its association with demographic and clinical characteristics in persons wearing a prosthesis after a lower-limb amputation. J Rehabil Med 2018; 50: 629–635.

34. Lupoli R, Di Minno A, Spadarella G, Ambrosino P, Panico A, Tarantino L, et al. The risk of osteoporosis in patients with liver cirrhosis: a meta-analysis of literature studies. Clin Endocrinol (Oxf) 2016; 84: 30–38.

35. Karatepe AG, Gunaydin R, Kaya T, Turkmen G. Comorbidity in patients after stroke: impact on functional outcome. J Rehabil Med 2008; 40: 831–835.

36. Tsujikawa M, Otaka Y, Hasegawa R, Kondo K, Liu M. Echocardiographic abnormalities in patients with stroke during the subacute rehabilitation phase. J Rehabil Med 2015; 47: 38–44.

37. Milone M, Lupoli R, Maietta P, Di Minno A, Bianco P, Ambrosino P, et al. Lipid profile changes in patients undergoing bariatric surgery: a comparative study between sleeve gastrectomy and mini-gastric bypass. Int J Surg 2015; 14: 28–32.

38. Ambrosino P, Lupoli R, Iervolino S, De Felice A, Pappone N, Storino A, et al. Clinical assessment of endothelial function in patients with chronic obstructive pulmonary disease: a systematic review with meta-analysis. Intern Emerg Med 2017; 12: 877–885.