Naama Leibushor<sup>1</sup> Einat Slonimsky<sup>2</sup> Dvora Aharoni<sup>2</sup> Merav Lidar<sup>1</sup> Iris Eshed<sup>2</sup>

Keywords: ankylosis, CT, diffuse idiopathic skeletal hyperostosis, Resnick classification criteria, sacroiliac joints

DOI:10.2214/AJR.16.16994

Received June 19, 2016; accepted after revision October 15, 2016.

<sup>1</sup>Rheumatology Unit, Sheba Medical Center, Tel Hashomer, affiliated to the Sackler School of Medicine, Tel Aviv, Israel.

<sup>2</sup>Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer, affiliated to the Sackler School of Medicine, Tel Aviv 52621, Israel. Address correspondence to I. Eshed (iriseshed@gmail.com).

AJR 2017; 208:834-837

0361-803X/17/2084-834

© American Roentgen Ray Society

# Joints of Patients With Diffuse Idiopathic Skeletal Hyperostosis OBJECTIVE. The purpose of this study is to characterize sacroiliac joints (SIJs

**OBJECTIVE.** The purpose of this study is to characterize sacroiliac joints (SIJs) findings at CT of patients with diffuse idiopathic skeletal hyperostosis (DISH), a condition characterized (using the Resnick classification criteria) by ossification of at least four contiguous vertebrae in the thoracic spine and preserved disk space, but without radiographic evidence of intraarticular SIJ abnormalities.

CT Abnormalities in the Sacroiliac

**MATERIALS AND METHODS.** Pelvic CT examinations of 104 patients with DISH (fulfilling the Resnick criteria on spinal CT) and 106 age- and sex-matched control subjects whose entire spine lacked CT evidence of DISH (total, 149 men and 61 women; mean [ $\pm$  SD] age, 72.3  $\pm$  8.7 years) were retrospectively evaluated for the presence of intra- and extraarticular bridging osteophytes, spurs, subchondral cystlike changes, erosions, and sclerosis of SIJs. Excluded were patients with known ankylosing spondylitis or inflammatory-related diseases. Data were analyzed using multivariate ANOVA to examine the degree of difference between patients with DISH and control subjects. Logistic regression analysis was used to generate odds ratios to examine their discriminatory ability. ROC analysis was then applied to examine the sensitivity and specificity of the results.

**RESULTS.** The frequency of anterior bridging, posterior bridging, entheseal bridging, and joint ankylosis was significantly higher among patients with DISH compared with control subjects (48% vs 9%, 20% vs 1%, 34% vs 4%, and 23% vs 0%, respectively; p < 0.001 for all comparisons).

**CONCLUSION.** Intraarticular ankylosis seen at CT, an entity not included in the Resnick classification criteria, is common among patients with DISH, which implies that the radiologic classification criteria for DISH need to be revised.

iffuse idiopathic skeletal hyperostosis (DISH) was first described by Forestier and Rotes-Querol in 1950 in nine men with an average age of 65 years [1]. The authors presented radiographs and autopsy reports of the subjects and defined the condition as "senile ankylosing hyperostosis of the spine" to distinguish it from ankylosing spondylitis (AS), an inflammatory disease that primarily affects vounger patients [2]. It has since become evident that this condition of calcification and ossification of soft tissue, characteristically at the paravertebral ligaments [3, 4], is not confined to older men [5, 6], nor is it limited to the spine [7]. The commonly accepted classification criteria for DISH formulated by Resnick and Niwayama (hereafter referred to as "Resnick criteria") [3] are based on analysis of radiographs and require flowing osteophytes in at least four contigu-

ous vertebrae of the thoracic spine. Although the cause of DISH remains unclear, it is considered a noninflammatory condition, in contrast to the hallmark inflammation of the sacroiliac joints (SIJs) and the spine in AS [2]. The original Resnick DISH criteria strongly emphasize the difference in SIJ involvement between the two entities by completely excluding SIJ erosions, sclerosis, or bony fusion for a positive diagnosis of DISH [3, 8]. Though this criterion was somewhat altered later to allow for the presence of osteophytes, osteoarthritis-related changes, and paraarticular bony bridging [9], there still is a common misconception that SIJs are normal in DISH. A literature review reveals only a handful of articles describing SIJ involvement in DISH, which nonetheless manage to report conflicting findings. Indeed, although Forestier and Rotes-Querol found no SIJ abnormalities in their original report [1, 10],

### SIJ Abnormalities Seen at CT in Patients With DISH

others have noted calcinosis, osteophytes, bridging, fusion, and ankylosis [11–13]. It may be for that reason that relatively more recent and inclusive DISH classification criteria by Utsinger [14] do not include the lack of SIJ disease.

Here, we performed a comprehensive evaluation of the radiographic appearance of SIJs of patients with DISH and control subjects, on CT examinations, in an attempt to clarify the issue of SIJ involvement and its extent in DISH.

## **Materials and Methods**

Archived records of all comers in a single tertiary medical center who were incidentally found to have DISH on lateral thoracic spine radiographs, as per the Resnick spinal criteria, were retrieved, and the institution's PACS was searched for the presence of cervical, thoracic, lumbar, and pelvic CT studies performed on these subjects. Only subjects who fulfilled the Resnick criteria on thoracic spinal CT (i.e., had at least four consecutive flowing osteophytes at the thoracic spine) and had an abdominal or pelvic CT examination that included the SIJ in their entirety were included in this investigation.

The study was approved by the local ethics committee. Informed consent was waived because only imaging findings and demographics were extracted from the electronic records.

The PACS was used to identify sex- and agematched control subjects who had undergone CT examinations of their entire spine and for whom DISH was not apparent in the cervical, thoracic, or lumbar spine. To exclude patients who may potentially have DISH in early stages, patients who had flowing osteophytes in two or more vertebrae anywhere along the spine were not included in the control group. Also excluded were patients or control subjects with known AS, as well as patients with spondyloarthritis-related inflammatory diseases, such as inflammatory bowel disease and psoriasis.

The study group consisted of 104 subjects with DISH (74 men and 30 women; mean [ $\pm$  SD] age, 72.3  $\pm$  8.6 years), and the control group consisted of 106 age- and sex-matched subjects (75 men and 31 women; mean age, 72.3  $\pm$  8.8 years). The same cohort of patients with DISH and control subjects was recently evaluated for the presence of pelvic enthesopathy not including the SIJs [15], whereas in the current study, the SIJs only were evaluated.

All CT studies were performed on the following CT scanners: Mx8000 Quad 4-MDCT, Mx8000 IDT 16-MDCT, and Brilliance 40-MDCT, 64-MDCT, and 128-MDCT (all from Philips Healthcare) and 64-MDCT VCT Light-Speed (GE Healthcare). Slice thickness was 0.6-2.5 mm. Images were reconstructed in bone and soft-tissue algorithms, reformatted in multiple planes, and evaluated in the axial orientation.

### CT Evaluation

Two readers, a musculoskeletal radiologist with 15 years' experience in musculoskeletal CT reading and a board-certified rheumatologist, retrospectively and in consensus evaluated pelvic CT examinations of patients with DISH and control subjects for the presence of anterior or posterior bridging osteophytes (paraarticular), anterior or posterior spurs, subchondral cystlike changes (denoted hereafter "subchondral cysts"), subchondral sclerosis, intraarticular joint bridging or fusion, and enthesopathy at the posterior ligaments in the right and left SIJs. Readers were aware of the subjects' age and sex but were blinded to their assigned group (DISH or control). For the evaluation of intrareader reliability, two separate additional readings were performed by one of the readers with a minimum interval of 2 months between the readings, on a subset of 62 patients.

Findings were defined as follows: an anterior bridging osteophyte is a bony projection arching over the anterior margin of the SIJ bridging the ilium and sacrum bones, but not involving the intraarticular part of the joint. A posterior bridging osteophyte is a bony projection arching over the posterior margin of the SIJ bridging the ilium and sacrum bones, but not involving the intraarticular part of the joint. An anterior spur is a bony projection at the anterior aspect of the SIJ that does not bridge over the joint line. A posterior spur is a bony projection at the posterior aspect of the sacroiliac joint that does not bridge over the joint line. Subchondral cysts are small hypodense round lucencies in the bone proximal to the cartilage on either side of the joint line (sacrum or ilium). Subchondral sclerosis is increased bone density along either side of the joint line (sacrum or ilium). Erosions involve local cortical breakthrough and resorption at the SIJ articular surface. Joint bridging or joint fusion is a transverse bony projection within the SIJ connecting the sacrum and ilium bones. An entheseal spur is a bony projection at the posterior sacroiliac ligaments. Finally, entheseal bridging is a transverse bony projection within the posterior sacroiliac ligaments connecting the sacrum and ilium bones.

The absence of any evaluable findings on either side of the SIJs (right or left) was scored as 0. A unilateral finding of anterior or posterior bridging osteophytes, subchondral cysts, subchondral sclerosis, joint fusion, or entheseal bridging was scored as 1. The bilateral presence of such findings was scored as 2. Entheseal, anterior, and posterior spurs were further scored according to size: The presence of a unilateral small spur (defined as a spur smaller than the SIJ space width) was scored as 1, whereas the presence of a unilateral large spur (defined as a spur equal to or larger than SIJ space width) was scored as 2. The maximum score per spur finding per patient was 4, bilaterally.



Fig. 1—75-year-old man with diffuse idiopathic skeletal hyperostosis. Axial CT image of sacroiliac joints (SIJs) shows bilateral anterior bridging (*arrows*). There is some iliac cortical irregularity with subchondral cysts in right SIJ and no evidence of intraarticular abnormality in left SIJ.



Fig. 2—74-year-old man with diffuse idiopathic skeletal hyperostosis. Axial CT image of sacroiliac joints (SIJs) shows bilateral entheseal bridging and ankylosis (*arrowheads*). Anterior bridging of right SIJ can also be detected. There is no evidence for intraarticular SIJ abnormality.



Fig. 3—84-year-old man with diffuse idiopathic skeletal hyperostosis. Axial CT image of sacroiliac joints (SIJs) shows right-sided intraarticular SIJ ankylosis (*arrowheads*) as well as anterior bridging. Left SIJ is intact.

|                       | Mean Score (Percentage Prevalence) |                  |                 | Odda Patia     | Consitivity | Creativity | Positive  | Negative  |
|-----------------------|------------------------------------|------------------|-----------------|----------------|-------------|------------|-----------|-----------|
| Finding               | Patients With DISH                 | Control Subjects | F Value (p)     | ( <i>p</i> )   | (%)         | (%)        | Value (%) | Value (%) |
| Anterior bridging     | 0.57 (48)                          | 0.12 (9)         | 26.20 (< 0.001) | 9.1 (< 0.0001) | 48.5        | 90.6       | 83.3      | 64.4      |
| Posterior bridging    | 0.32 (20)                          | 0.02 (1)         | 16.47 (< 0.001) | 26.9 (0.002)   | 20.4        | 99.1       | 95.5      | 56.2      |
| Anterior spur         | 1.58 (76)                          | 1.12 (72)        | 6.52 (0.011)    | 1.3 (0.410)    | 76.7        | 28.3       | 51.0      | 55.6      |
| Posterior spur        | 1.00 (43)                          | 0.92 (52)        | 0.29 (0.589)    | 0.7 (0.185)    | 42.7        | 48.1       | 44.4      | 46.4      |
| Joint fusion          | 0.28 (23)                          | 0.00 (0)         | 15.74 (< 0.001) | 31.9 (0.001)   | 23.3        | 99.1       | 96.0      | 57.1      |
| Subchondral cyst      | 0.25 (19)                          | 0.27 (22)        | 0.07 (0.800)    | 0.9 (0.684)    | 19.4        | 78.3       | 46.5      | 50.0      |
| Entheseal bridging    | 0.43 (34)                          | 0.02 (4)         | 25.97 (< 0.001) | 13.1 (< 0.001) | 34.0        | 96.2       | 89.7      | 60.0      |
| Entheseal spur        | 0.15 (12)                          | 0.00 (0)         | 8.67 (0.004)    | 29.1 (0.020)   | 11.7        | 100.0      | 100.0     | 53.8      |
| Erosion               | 0.05 (4)                           | 0.02 (2)         | 1.23 (0.269)    | 2.1 (0.397)    | 3.9         | 98.1       | 66.7      | 51.2      |
| Subchondral sclerosis | 0.70 (40)                          | 0.75 (45)        | 0.10 (0.747)    | 0.8 (0.511)    | 40.8        | 54.7       | 46.7      | 48.7      |

# TABLE I: Distribution and Statistical Analysis of Sacroiliac Joint Findings on CT in Patients With Diffuse Idiopathic Skeletal Hyperostosis (DISH) and Control Subjects

### Statistical Analysis

Data were analyzed with Statistica (version 10, StatSoft). A multivariate ANOVA was applied to examine the degree of difference (i.e., F value) between patients with DISH and control subjects [16]. The higher the F value, the greater the difference between the DISH and control groups with respect to each type of finding examined. The smaller the *p* value, the more significant the observed difference between the two groups. A p < 0.001 was chosen, meaning that the probability that the results are inaccurate is less than 0.1%; hence, their accuracy is greater than 99.9%.

Logistic regression analysis was used to generate odds ratios [17]. In addition, a ROC analysis was conducted to examine the sensitivity, specificity, positive predictive value, and negative predictive value of the results for each observed finding [18]. This analysis assesses the likelihood that the observed differences between patients with DISH and the control subjects are indeed significantly associated with DISH.

Intraclass correlation coefficients (ICCs) were calculated for intraobserver reliability by the twoway random ANOVA for absolute agreement. The *p* value for ICC is presented. A *p* < 0.05 was considered to be statistically significant. ICC values were interpreted as follows: 0-0.2 denotes poor agreement, 0.3-0.4 denotes fair agreement, 0.5-0.6 denotes moderate agreement, 0.7-0.8 denotes strong agreement, and greater than 0.8 denotes almost perfect agreement.

## Results

Pelvic CT examinations of a total of 210 individuals (149 men and 61 women; mean age,  $72.3 \pm 8.7$  years; age range, 50-94 years) were evaluated. No significant demographic differences were found between the study and control groups.

Intrareader reliability for the evaluated SIJ findings was fair to excellent (ICC = 0.5-0.9; p < 0.01). With respect to each of the evaluated SIJ findings, there was no significant difference between men and women (data not shown). Distribution of the different SIJ-detected features in the DISH and control groups is shown in Table 1.

Anterior and posterior bridging (Fig. 1), entheseal bridging (Fig. 2), and joint fusion (Fig. 3) of the SIJ were detected significantly more frequently in patients with DISH compared with control subjects. These findings were of highest discriminatory factor with p < 0.001, specificity greater than 90%, and positive predictive value greater than 83%. Anterior bridging was the most robust discriminatory finding between the groups.

Anterior spurs were a common occurrence among both groups, with large anterior spurs more frequent in patients with DISH than in control subjects (44 vs 32 spurs; p >0.05). Additional SIJ findings that were not significantly different between groups were posterior spurs, subchondral cysts, and subchondral sclerosis.

Although entheseal spurs and erosions were more frequent among patients with DISH than control subjects and their positive predictive value (100% for entheseal spurs and 66.7% for erosions) and specificity (100% for entheseal spurs and 98.1% for erosions) were remarkably high, their sensitivity for the detection of DISH was quite low.

### Discussion

In this study, we evaluated the SIJs on pelvic CT examinations for the presence of multiple pathologic features in patients with DISH and in age- and sex-matched control subjects without DISH. We have shown that SIJ fusion, anterior and posterior bridging, and entheseal bridging occur significantly more frequently in subjects with DISH compared to those without DISH. Moreover, these features can be used to characterize patients with DISH and to distinguish them from subjects who do not have DISH. The presence of joint bridging and fusion in DISH, similar to that seen in patients with AS, stands in bold contrast to this exclusion criterion of the Resnick DISH classification criteria and challenges the notion that such SIJ intraarticular involvement rules out the diagnosis of DISH [3, 9].

Dar et al. [12] studied 2845 skeletons and discovered that 12.27% of all male skeletons and 1.83% of all female skeletons had some degree of SIJ bridging, emphasizing that this is not an uncommon occurrence. In their study, the diagnosis of those individuals with SIJ bridging was not indicated, though it was significantly age and sex dependent, and occurred predominantly at the superior aspect of the joint. In a different study of 289 male skeletons [9], the same group observed a strong association between SIJ bridging and general entheseal reaction. In that study, individuals with SIJ bridging were three times more likely to have DISH rather than spondyloarthropathy, strongly supporting the finding of our current study.

The presence of SIJ fusion or ankylosis may, in some individuals, pose a diagnostic dilemma in distinguishing between DISH and AS, an inflammatory disease of which enthesitis of the spine and SIJs is a hallmark. Such a dilemma also arises in cases in which a combination of syndesmophytes and bridging osteophytes occurs concomitantly in the same patient [19]. The presence of SIJ fusion in patients with DISH and in those with AS may also suggest that the diseases have a similar pathogenetic route that leads to an inflammatory-related enthesitis in younger individuals, perhaps in association with a genetic background of human leukocyte antigen B27 positivity, and to a more mechanically related enthesopathy in older patients.

Although the pathogenesis of DISH is poorly understood, it is clear that entheseal and ligamentous ossification, osteophyte formation, and, finally, bone bridging and ankylosis are a continuum [20]. We also know that this excessive and robust enthesopathy in DISH is not limited to the spinal column but is evident in the peripheral joints as well [7, 15, 21, 22]. Given that SIJ anterior and posterior bridging occur at the entheseal sites and that the SIJ itself is considered by some to be a unique type of entheses [23, 24], our robust findings in and around the SIJs in patients with DISH are in concert with the excessive enthesopathy detected elsewhere in this group.

Spinal flowing osteophytes are considered the hallmark of DISH and are included in the diagnostic criteria [3], as well as extraspinal manifestations [14]. We have currently shown that typical SIJ changes are also present. However, the sequence in which bone is formed into spinal osteophytes and extraspinal enthesophytes is not clear. Thus, potentially, SIJ or entheseal DISH-related findings may develop before the typical spinal findings in patients with DISH. If this theory would be prospectively substantiated, a change in the current diagnostic criteria may be warranted.

Our study limitations include the relatively small sample size and the retrospective and observational cross-sectional nature of the study, as opposed to a longitudinal study. Larger prospective studies are needed to substantiate our results and to determine whether such SIJ findings may be used to predict the development of DISH in a particular individual.

In conclusion, the results of the current study suggest that CT findings of SIJ fusion, anterior and posterior bridging, and entheseal fusion are discriminative and specific for the diagnosis of DISH. The convergence of these highly significant findings would appear to justify the consideration to include them as criteria for the differential diagnosis of DISH.

#### References

- Forestier J, Rotes-Querol J. Senile ankylosing hyperostosis of the spine. Ann Rheum Dis 1950; 9:321–330
- Moll JM, Wright V. New York clinical criteria for ankylosing spondylitis: a statistical evaluation. *Ann Rheum Dis* 1973; 32:354–363
- Resnick D, Niwayama G. Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). *Radiology* 1976; 119:559–568
- Taljanovic MS, Hunter TB, Wisneski RJ, et al. Imaging characteristics of diffuse idiopathic skeletal hyperostosis with an emphasis on acute spinal fractures: review. *AJR* 2009; 193(3 suppl):S10–S19; quiz, S20–S24
- Westerveld LA, van Ufford HM, Verlaan JJ, Oner FC. The prevalence of diffuse idiopathic skeletal hyperostosis in an outpatient population in The Netherlands. J Rheumatol 2008; 35:1635–1638
- Kiss C, O'Neill TW, Mituszova M, Szilagyi M, Donath J, Poor G. Prevalence of diffuse idiopathic skeletal hyperostosis in Budapest, Hungary. *Rheumatology (Oxford)* 2002; 41:1335–1336
- Mader R, Sarzi-Puttini P, Atzeni F, et al. Extraspinal manifestations of diffuse idiopathic skeletal hyperostosis. *Rheumatology (Oxford)* 2009; 48:1478–1481
- Resnick D, Shaul SR, Robins JM. Diffuse idiopathic skeletal hyperostosis (DISH): Forestier's disease with extraspinal manifestations. *Radiology* 1975; 115:513–524
- Resnick D, Kransdorf M. Bone and joint imaging, 3rd ed. Philadelphia, PA: Elsevier Saunders, 2005
- Branten AJ, de Jong AJ, Janssen M. Familial presentation of bamboo spine, peripheral calcifications, and normal sacroiliac joints. *Scand J Rheumatol* 2009; 38:156–157
- Durback MA, Edelstein G, Schumacher HR Jr. Abnormalities of the sacroiliac joints in diffuse idiopathic skeletal hyperostosis: demonstration by computed tomography. *J Rheumatol* 1988; 15:1506–1511
- Dar G, Peleg S, Masharawi Y, et al. Sacroiliac joint bridging: demographical and anatomical as-

pects. Spine 2005; 30:E429-E432

- Bruges-Armas J, Couto AR, Timms A, et al. Ectopic calcification among families in the Azores: clinical and radiologic manifestations in families with diffuse idiopathic skeletal hyperostosis and chondrocalcinosis. *Arthritis Rheum* 2006; 54:1340–1349
- Utsinger PD. Diffuse idiopathic skeletal hyperostosis. *Clin Rheum Dis* 1985; 11:325–351
- 15. Slonimsky E, Leibushor N, Aharoni D, Lidar M, Eshed I. Pelvic enthesopathy on CT is significantly more prevalent in patients with diffuse idiopathic skeletal hyperostosis (DISH) compared with matched control patients. *Clin Rheumatol* 2016; 35:1823–1827
- 16. Tabachnick BG, Fidell LS. Using multivariate statistics. Boston, MA: Allyn and Bacon, 2001
- Hill T, Lewicki P. Statistics: methods and applications—a comprehensive reference for science, industry, and data mining. Tulsa, OK: StatSoft, 2006
- Boyko EJ. Ruling out or ruling in disease with the most sensitive or specific diagnostic tools: short cut or wrong turn. *Med Decis Making* 1994; 14:175–179
- Moreno AC, Gonzalez ML, Duffin M, López-Longo FJ, Carreño L, Forrester DM. Simultaneous occurrence of diffuse idiopathic skeletal hyperostosis and ankylosing spondylitis. *Rev Rhum Engl Ed* 1996; 63:292–295
- 20. Yaniv G, Bader S, Lidar M, et al. The natural course of bridging osteophyte formation in diffuse idiopathic skeletal hyperostosis: retrospective analysis of consecutive CT examinations over 10 years. *Rheumatology (Oxford)* 2014; 53:1951–1957
- Mader R, Novofastovski I, Iervolino S, et al. Ultrasonography of peripheral entheses in the diagnosis and understanding of diffuse idiopathic skeletal hyperostosis (DISH). *Rheumatol Int* 2015; 35:493–497
- 22. Weiss BG, Bachmann LM, Pfirrmann CW, Kissling RO, Zubler V. Whole body magnetic resonance imaging features in diffuse idiopathic skeletal hyperostosis in conjunction with clinical variables to whole body MRI and clinical variables in ankylosing spondylitis. J Rheumatol 2016; 43:335–342
- Egund N, Jurik AG. Anatomy and histology of the sacroiliac joints. Semin Musculoskelet Radiol 2014; 18:332–339
- 24. Hermann KG, Bollow M. Magnetic resonance imaging of sacroiliitis in patients with spondyloarthritis: correlation with anatomy and histology. *RoFo Fortschr Geb Rontgenstr Nuklearmed* 2014; 186:230–237