Bone loss in patients with SAPHO syndrome: a preliminary study

Synovitis, acne, palmoplantar pustulosis, hyperostosis and osteitis (SAPHO) syndrome is a rare entity that involves the skin, bones and joints. The estimated prevalence of SAPHO syndrome is lower than 1/10 000.[1] The real prevalence may be underestimated because of lack of typical symptoms.[2] Bone is one of the critical affected organs for SAPHO. The most common site is the anterior chest wall (65%–90%), followed by the thoracic spine.[1] However, the effects of SAPHO syndrome on bone loss or osteoporosis have not been clarified. We performed a case–control study to show bone loss in patients with SAPHO syndrome in a Chinese population.

From June 2014 to August 2019, a total of 27 new-onset SAPHO patients were included in the study after excluding patients who had been diagnosed for more than 6 months and who were younger than 25 years old. The diagnosis of SAPHO syndrome was based on clinical symptoms and radiological examinations.[2] The diagnosis is based on the presence of at least one of four features: (1) osteoarticular manifestations with severe acne; (2) osteoarticular manifestations with palmoplantar pustulosis; (3) hyperostosis with or without skin lesions; (4) recurrent multifocal chronic osteomyelitis involving the axial or peripheral skeleton, with or without skin lesions. Two or three age-matched and gender-matched control subjects who underwent chest CT scan for physical examinations were matched for each patient. The demographic data, medical history, clinical symptoms, erythrocyte sedimentation rate and C reactive protein were collected.

All CT scan was obtained from multi-detector CT system (GE Healthcare, Tokyo, Japan). The images were reconstructed in the work station using a 0.625 mm section thickness and 0.5 mm increments. CT attenuation (Hounsfield units, HU) of thoracic spine 10–12 (T10–T12) and lumbar spine (L1) was measured on the region of interests (ROIs) avoiding erosion and sclerosis. Five ROIs were measured for each vertebral body (central section and extended two upper and lower sections) and the average of CT attenuation was obtained. Bone loss and osteoporosis were defined based on CT attenuation.[3] Briefly, normal bone mineral density was considered when HU was larger than 160; osteopenia and osteoporosis were defined when HU was ranged from 135 to 160 and less than 135.

70.4% and 77.8% patients had skin lesions and osteoarticular manifestations, respectively (table 1). The CT values of vertebral bodies in SAPHO patients were all significantly lower than those in control ($p<0.01$ or $p<0.05$) (figure 1A,B). Similar results were observed when considering the effect of gender and age (figure 1C,D). The prevalence of bone loss was 55.6% and osteoporosis was 40.7% in total SAPHO population. The prevalence of osteoporosis or bone loss in SAPHO group was significantly higher than those in control for total population and women (table 1, all $p<0.001$). Univariate and multivariate logistic regression analysis both showed that the risk of bone loss and osteoporosis in SAPHO patients (online supplemental table 1) were both higher than the control (OR=11.52, 95% CI 3.10 to 42.81; OR=20.59, 95% CI 4.18 to 101.17). Subgroup analysis showed similar trends in men and women (online supplemental table 2).

The bone loss in SAPHO patients may be caused by the overexpressed proinflammatory cytokines.[4] In addition, glucocorticoid using which may induce bone loss are also widely used in SAPHO patients. Our patients were new-diagnosed SAPHO. Only three patients received long term (>2 weeks) systematic therapy of steroids. The influence of pharmacological treatment on bone may be little in our study. SAPHO syndrome may directly induce bone loss. The prevalence of osteoporosis in SAPHO patients is higher than a recent national quantitative CT (qCT) survey in China.[5] The bone loss in SAPHO patients needs to be paid attention to because SAPHO usually occurs

Table 1 Prevalence of bone loss

	Total population			Women			Men		
	SAPHO (n=27)	Control (n=70)	P value	SAPHO (n=15)	Control (n=42)	P value	SAPHO (n=12)	Control (n=28)	P value
Age	44.6±10.4	46.4±9.8	>0.05	46.3±10.6	47.9±9.3	>0.05	42.3±10.1	44.1±10.1	>0.05
BMI	22.6±3.9	23.7±3.4	>0.05	21.4±3.5	22.4±4.3	>0.05	22.5±4.1	23.2±3.6	>0.05
Disease duration, months	5.4 (2.0–12.0)	–		5.8 (1.0–12.0)	–		5.2 (2.0–9.0)	–	
Skin manifestations (n)	19 (70.4%)	–		10 (66.7%)	–		9 (75.0%)	–	
Osteoarticular manifestations (n)	21 (77.8%)	–		12 (80.0%)	–		9 (75.0%)	–	
Anterior chest wall	17 (63.0%)	–		9 (60.0%)	–		8 (66.7%)	–	
Peripheral joints	3	–		1	–		2	–	
Spine	10(37.0%)	–		6 (40.0%)	–		4 (33.3%)	–	
Steroids using (n)	3 (11.1%)	–		2 (10.3%)	–		1 (8.3%)	–	
CRP elevated (n)	12 (44.4%)	–		7 (46.7%)	–		5 (41.7%)	–	
ESR elevated (n)	10 (37.0%)			6 (40.0%)			4 (33.3%)		
Prevalence of osteoporosis (n)			<0.001			<0.001			>0.05
Normal BMD	12 (44.4%)	60 (85.7%)		6 (40.0%)	38 (90.5%)		6 (50.0%)	22 (78.6%)	
Osteopenia	4 (14.8%)	4 (5.7%)		3 (20.0%)	3 (7.1%)		1 (8.3%)	1 (3.6%)	
Osteoporosis	11 (40.7%)	6 (8.6%)		6 (40.0%)	1 (2.4%)		5 (41.7%)	5 (17.6%)	
Prevalence of bone loss (n)			<0.001			<0.001			0.07
Normal BMD	12 (44.4%)	60 (85.7%)		6 (40.0%)	38 (90.5%)		6 (50.0%)	22 (78.6%)	
Bone loss	15 (55.6%)	10 (14.3%)		9 (60.0%)	4 (9.5%)		6 (50.0%)	6 (21.4%)	
Diabetes (n)	1	2	>0.05	0	1		1	1	>0.05

The osteoporosis or bone loss was evaluated based on the CT attenuation (Hounsfield units, HU) of thoracic spine 10–12 (T10–T12) and lumbar spine (L1). Normal bone mineral density (BMD) was considered when HU was more than 160; osteopenia and osteoporosis were defined when HU was ranged from 135 to 160 and less than 135. Bone loss was defined as osteoporosis or osteopenia. Steroids using means receiving long term (>2 weeks) systematic therapy. Elevated C reactive protein (CRP) was defined when CRP was larger than 8.0 mg/L. Elevated erythrocyte sedimentation rate (ESR) was defined when ESR was >20 mm/hour. The continuous data were shown as mean±SD or range, and was analysed by independent-sample t-test. Qualitative data were shown as number (percentage), and was compared by χ^2 test or Fisher's exact test.
BMI, body index mass; SAPHO, synovitis, acne, palmoplantar pustulosis, hyperostosis and osteitis.

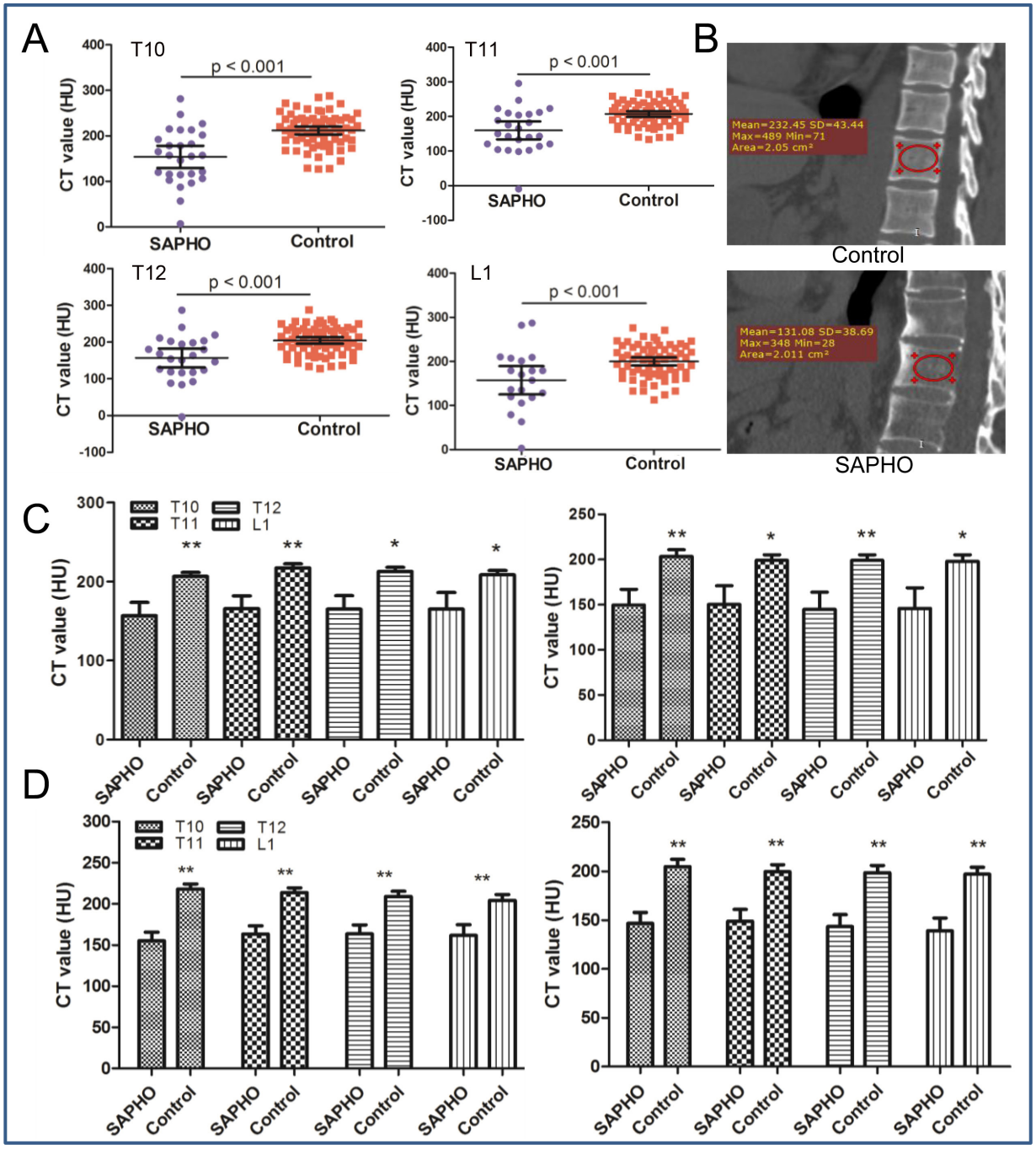

Figure 1 CT attenuation (Hounsfield units, HU) in thoracic spine 10–12 (T10–T12) and lumbar spine (L1) (A), and sagittal CT images of T12 in patients with synovitis, acne, palmoplantar pustulosis, hyperostosis and osteitis (SAPHO) syndrome and age/gender-matched control (two 64 years old men) (B). Cortical sclerosis and osteoporosis both occurred in T12 in a SAPHO patient. CT values of T10–T12 and L1 in women (left) and men (right) (C). Age-adjusted CT values of T10–T12 and L1 in women (left) and men (right) (D). SAPHO versus control: **p<0.01; *p<0.05. Data are shown as mean with 95% CI (A) and mean with SE (C, D). The data were analysed using Mann-Whitney U test (A, C).

in young adult (mean age 37–48).[1] Bisphosphonates that have been widely used to treat osteoporosis may be potential drugs for SAPHO.[6] The sample size is small because the rarity of the SAPHO syndrome. Our study is just a preliminary exploration. Further studies are needed.

In conclusion, our study reports that CT attenuations of vertebral bodies in SAPHO patients are lower than those in control. The prevalence of bone loss or osteoporosis in SAPHO patients is higher than that in general population. Osteoporosis should be paid attention to in the management of SAPHO syndrome.

Xiao Chen ,[1] **Miaomiao Wang**,[1,2] **Wenjing Cui**,[1] **Zhongqiu Wang**[1]

[1]Department of Radiology, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, China
[2]The First College of Clinical Medicine, Nanjing University of Chinese Medicine, Nanjing, China

Correspondence to Dr Xiao Chen, Department of Radiology, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China; chxwin@163.com

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ORCID iD
Xiao Chen http://orcid.org/0000-0002-8354-9087

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