as exercise training, might be effective for recovering serum BDNF level with resultant improvement of cognitive dysfunction, dementia and long-term prognosis in CHF patients.

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## Disclosure statement

The authors declare no conflict of interest.

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# Femoral osteoporosis is more common than lumbar osteoporosis in patients with Werner syndrome

Dear Editor,

Werner syndrome (WS) is a rare autosomal recessive genetic disorder characterized by early onset of the normal aging processes and its associated complications, including osteoporosis. Mutations in the human *WRN* gene, encoding a member of the RecQ family of DNA helicases, result in this disorder.[1] We aimed to elucidate the clinical characteristics of osteoporosis in WS. A total of 10 patients (5 men and 5 women; mean age 50 years, range 40–60 years) were included. A diagnosis of WS was made based on the presence of the cardinal signs and symptoms of the disease, which include progeroid changes in hair, bilateral cataracts, intractable skin ulcers, soft-tissue calcification, bird-like face and abnormal voice, and was subsequently confirmed by genetic testing (Table 1).[2] Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry using the same machine for all the patients, and osteoporosis was diagnosed based on the Japanese diagnostic criteria for primary osteoporosis (BMD ≤70% of young adult mean or *t*-score ≤−2.5 SD).[3] As judged by lumbar ($L_{2–4}$) BMD, only one of 10 patients (case 1) was diagnosed with osteoporosis (Table 1). In contrast, based on the femoral BMD, six of 10 patients (cases 1, 2, 3, 5, 7 and 10) were diagnosed with osteoporosis (Table 1). Examination of thoracolumbar ($T_4$–$L_4$) radiographs showed that none of the patients sustained morphological vertebral fracture, any deformity of lumbar spine and calcification of abdominal aorta. Our present observation indicates that

**Table 1** Bone mineral density of 10 patients with Werner syndrome

| Case | Sex | Age (years) | *WRN* mutation[a] | Lumbar spine BMD ($L_{2–4}$) | | | Femoral neck BMD | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | g/cm$^2$ | *T*-score (SD) | %YAM | g/cm$^2$ | *T*-score (SD) | %YAM |
| 1 | M | 57 | 6/6 | 0.730 | −2.7[c] | 70[d] | 0.601 | −2.1 | 70[d] |
| 2 | F | 60 | 6/6 | 0.804 | −2.1 | 78 | 0.452 | −3.1[c] | 57[d] |
| 3 | F | 57 | 4/6 | 0.790 | −1.9 | 78 | 0.351 | −4.0[c] | 45[d] |
| 4 | M | 40 | 4/11 | 1.116 | 0.6 | 107 | – | – | – |
| 5 | F | 60 | 4/4 | 0.803 | −1.8 | 79 | 0.533 | −2.3 | 68[d] |
| 6 | F | 40 | 11/11 | 0.983 | −0.2 | 97 | 0.582 | −1.9 | 74 |
| 7 | M | 51 | 4/7 | 0.971 | −0.6 | 93 | 0.508 | −2.8[c] | 59[d] |
| 8 | F | 42 | 4/4 | 0.892 | −1.0 | 88 | 0.598 | −1.7 | 76 |
| 9 | M | 43 | 4/4 | 0.890 | −1.3 | 85 | 0.697 | −1.3 | 81 |
| 10 | M | 53 | 4/– [b] | 0.901 | −1.1 | 85 | 0.606 | −2.0 | 70[d] |

[a]*WRN* mutation 4: IVS25–1 G > C, mutation 6: 1105 C > T (R369X), mutation 7: 3446delA (Q1148 fsX 1161), mutation 11: 2959 C > T (R987X). [b]Compound heterozygote with mutation 4 and another mutation that remains to be determined. [c]*T*-score ≤−2.5 SD. [d]Less than 70% of young adult mean (YAM; age 20–44 years). BMD, bone mineral density; F, female; M, male.

femoral osteoporosis, but not lumbar osteoporosis, is common in patients with WS.

To our knowledge, this is the first study in which BMD was measured by dual-energy X-ray absorptiometry in patients with WS. It has been reported that patients with WS exhibit osteoporosis[4,5] with possible impaired osteoblastic bone formation,[6] but normal osteoclastic bone resorption.[7] A target of the WRN protein is telomeric DNA, but long telomeres and abundant telomerase in mice minimize the need for WRN, and thus *WRN* knockout mice are relatively healthy.[8] However, in a model of accelerated aging that combined a *WRN* mutation with the shortened telomeres of telomerase (*TERC*) knockout mice, the simultaneous loss of *WRN* and *TERC* genes produced a low bone mass phenotype, and age-related osteoporosis resulted from impaired osteoblast differentiation.[9] Although there is no evidence to date for the expression and function of the WRN protein in human bone cells including osteoblasts, this, along with a subsequent report,[10] suggests that defective osteoblast differentiation as a result of telomere dysfunction is an important cellular mechanism that could partly explain the early onset of osteoporosis in patients with WS. It is unclear why femoral bone is more susceptible to osteoporosis than lumbar vertebral bone is, in this patient population, but it might be the case that mechanical offloading of the femur as a result of muscle atrophy and intractable leg ulcers could contribute to skeletal atrophy of the lower extremities in patients with WS.

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## Disclosure statement

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# Effect of sex on the association of isokinetic quadriceps strength with hypertension among older Americans

Dear Editor,

Few studies have examined whether muscle strength is associated with hypertension (HTN).[1–5] We tested this hypothesis in a cross-sectional analysis of data from a USA national sample National Health and Nutrition Examination Survey (NHANES) 1999–2002.[6–9] Participants were adults aged ≥50 years with no history of cardiovascular disease ($n$ = 2335**)**. HTN was either a reported HTN diagnosis or blood pressure measurement of ≥140/90 or the use of HTN medication. Isokinetic muscle strength was measured by dynamometer.

Our sample size of 2266 (37 % aged ≥65 years, 52% women, 82% white) represented 42 225 702 persons in the USA after the sampling rate; oversampling of certain groups and non-response were taken into account by weighting. Mean quadriceps strength (Newtons) was significantly higher in normal individuals: undiagnosed HTN ($n$ = 355, mean 355, 95% CI 337–374), diagnosed HTN ($n$ = 1007, mean 357, 95% CI 346–367) and no HTN ($n$ = 904, mean 393, 95% CI 379–406).

There was a significant effect modification by sex; therefore, sex-specific analyses are presented. Table 1 shows multivariate analyses. Model 1 controlled for the variables of age, race, body mass index and HTN status. Model 2 included model 1 plus blood relatives with a history of heart attack (yes/no) and smoking status (never/former/current). In model 1, the results showed that men aged ≥65 years had significantly lower quadriceps strength ($P$ = 0.00) than men aged 50–64 years. In addition, men with a high body mass index also had lower quadriceps strength in comparison with persons with a healthy body mass index ($P$ = 0.01). As with model 1, the results of model 2 also showed that quadriceps strength was significantly lower in diagnosed HTN ($P$ = 0.02) than in those with no HTN. Quadriceps strength was lower in undiagnosed HTN than in normal individuals, but this difference was not significant. Women did not show such an association (Table 1).

In adults, limb muscle strength declines while HTN increases with aging.[10] In the present study we found that among adults aged ≥50 years without a history of cardiovascular disease, isokinetic quadriceps strength was significantly lower in men with diagnosed and undiagnosed HTN than in men with no HTN. No such association was seen in women. Previous studies have not reported an effect modification by sex. This and other findings should be confirmed in follow-up studies. A greater understanding of the role of muscle strength and mass in hypertension pathogenesis might clarify the role of resistance versus dynamic physical activity in hypertension prevention.

## Disclosure statement

The authors declare no conflict of interest.

**Table 1** Linear regression of hypertension status and quadriceps strength in persons aged 50 years and older: National Health and Nutrition Examination Survey 1999–2002

| Hypertension status | β coefficient model 1 | *P*-value | β coefficient model 2 | *P*-value | β coefficient model 1 | *P*-value | β coefficient model 2 | *P*-value |
|---|---|---|---|---|---|---|---|---|
| | Men | | | | Women | | | |
| Diagnosed hypertension | –21.79 | 0.02 | –23.77 | 0.01 | 5.15 | 0.52 | 4.83 | 0.54 |
| Undiagnosed hypertension | –0.34 | 0.98 | 0.25 | 0.98 | 6.25 | 0.45 | 5.67 | 0.48 |
| No hypertension | 1.00 | | 1.00 | | 1.00 | | 1.00 | |