Original Article

Bone mineral density in pediatric heart transplanted patients: A retrospective single-center study at Skåne University Hospital in Lund 1988–2016

Eveline Löfdahl1,2 | Karin Tran-Lundmark3,4,5 | Carl Haggård1,2 | Johan Nilsson6,7 | Michal Odermarsky3,8 | Göran Rådegran1,2

1Department of Clinical Sciences Lund, Cardiology, Lund University, Lund, Sweden
2The Section for Heart Failure and Valvular Disease, VO. Heart and Lung Medicine, Skåne University Hospital, Lund, Sweden
3The Pediatric Heart Center, Skåne University hospital, Lund, Sweden
4Wallenberg Center for Molecular Medicine, Lund University, Lund, Sweden
5Department of Experimental Medical Science, Lund University, Lund, Sweden
6Department of Clinical Sciences Lund, Cardiothoracic Surgery, Lund University, Lund, Sweden
7Department of Cardiothoracic and Vascular Surgery, Skåne University hospital, Lund, Sweden
8Pediatric Cardiology, Department of Clinical Sciences Lund, Lund University, Lund, Sweden

Correspondence
Eveline Löfdahl, The Hemodynamic Lab, The Section for Heart Failure and Valvular Disease, VO. Heart and Lung Medicine, Skåne University Hospital, Lund, Sweden. Email: eveline.lofdahl@med.lu.se

Funding information
This work was funded by unrestricted research grants from Anna-Lisa & Sven-Erik Lundgren’s, as well as from ALF’s Foundations, Lund, Sweden. The contributors had no role in the collection, analysis or interpretation of the data, and had no right to restrict the dissemination or publication of the results.

Abstract

Background: Impaired bone mineral density (BMD) and osteoporosis are commonly found in patients who have undergone heart transplantation (HT), which increases the risk for bone fractures which is associated with increased morbidity and mortality in adults. However, the long-term evolution of BMD after HT in pediatric patients has not been thoroughly investigated.

Method: Bone mineral density up to 10 years after HT was investigated in 30 patients who underwent HT at an age <20 years at Skåne University Hospital in Lund 1988–2016.

Results: The total observed time was 235 person-years. Before HT, 86% had low BMD for chronologic age in the lumbar spine. In lumbar spine, BMD was significantly lower than normal for chronological age before HT (p = .034), but recovered at the 4th year (p = .009). In whole body, BMD was normal at the 4th annual check-up (p = .030) and remained so throughout the follow-up period. The median T score in the lumbar spine and femoral neck 10 years after HT did not differ between the two groups based on age at HT (<20 years vs 20 years or older; p = .779 in the lumbar spine and p = .388 in the femoral neck).

Abbreviations: ACR, acute cellular rejection; ALP, alkaline phosphatase; ARVD, arrhythmogenic right ventricular dysplasia; AZA, azathioprine; BMD, bone mineral density; BMI, body mass index; CS, corticosteroids; CSA, cyclosporine A; DF, Degrees of freedom; DXA, Dual-energy X-ray absorptiometry; EVE, everolimus; GFR, glomerular filtration rate; HT, heart transplantation; IQR, interquartile range; LHTRR, Lund Heart Transplantation Research Register; MMF, mycophenolate mofetil; MPA, mycophenolic acid; PTH, parathyroid hormone; SD, standard deviation; TA, transplant assessment; TAC, tacrolimus.

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2021 The Authors. Pediatric Transplantation published by Wiley Periodicals LLC.
Conclusions: Patients who undergo HT at an age of <20 years have low BMD for chronological age already before HT, but BMD may recover completely within the first 4 years after HT. The results indicate no difference in BMD at 10 years after HT between pediatric and adult patients.

KEYWORDS
bone mineral density, heart transplantation, immunosuppression, pediatric

1 | INTRODUCTION

Patients who undergo heart transplantation (HT) have increased risk for impaired bone mineral density (BMD) and osteoporosis.1 The pathophysiology behind impaired BMD in HT patients is multifactorial and includes side effects of the immunosuppressive regimen, given to prevent allograft rejection.2 Out of the immunosuppressive agents, corticosteroids (CS) have the greatest negative impact on BMD, but calcineurin inhibitors, such as tacrolimus, also impair BMD.3-6 Osteoporosis furthermore increases the risk of fracture-related morbidity and mortality in adults.7,8 However, in children and adolescents, the association between BMD and fractures is not clear. Thus, it is not possible to diagnose osteoporosis based on BMD alone.9 In pediatric patients, the BMD is related to an age-, race-, and gender-matched control, resulting in a Z score, which may indicate low BMD for chronological age.10 Previous studies have shown that pediatric solid organ recipients have impaired bone health post-operatively, and that patients who underwent HT in adolescence have increased prevalence of osteoporosis in adulthood, mainly due to mild renal impairment, secondary hyperparathyroidism, and altered bone turnover.11-13 Pediatric HT has also been found to be a significant risk factor for scoliosis.14 However, the long-term evolution of BMD after HT in pediatric patients has not been thoroughly investigated. Our objective was therefore to investigate the BMD as evaluated by the Z score before and up to 10 years after HT in pediatric patients, as well as to investigate the BMD in adults who underwent HT during childhood.

2 | PATIENTS AND METHOD

2.1 | Study design and patient selection

This retrospective cohort study was conducted at Skåne University Hospital in Lund, Sweden, as part of establishing Lund Heart Transplantation Research Register (LHTRR). Included subjects underwent HT between January 1988 and June 2016, at an age younger than 20 years, and were followed at Skåne University Hospital in Lund until 31st of December 2019. Patients who underwent re-HT were excluded. Part of the patient cohort has previously been described in a separate report on acute cellular rejection (ACR).15 The present study was approved by the local ethics board in Lund (approval No. 2010/114, 2011/777, 2014/92).

2.2 | Data collection

Data were collected from clinical records from the transplant assessment (TA) before HT and annually up to 10 years after HT. BMD was obtained using Dual-energy X-ray absorptiometry (DXA) at the lumbar spine and whole body before HT and up to 10 years after HT. The term "low BMD for chronological age" was defined as a Z score of at least 2 standard deviations (SD) below the age-, race-, and gender-matched control, according to the official positions of the International Society for Clinical Densitometry.16 In addition to BMD, data on age, gender, body mass index (BMI), maintenance immunosuppressive treatment, time on waiting list, urine albumin/creatinine ratio, frequency and grade of ACR, osteoporosis preventive treatment, as well as serum levels of creatinine, urea, calcium, alkaline phosphatase (ALP), and parathyroid hormone (PTH) were collected. Glomerular filtration rate (GFR) was measured through plasma clearance of iohexol.

To investigate the BMD in adults who underwent HT at an age younger than 20 years, a comparison was performed between patients who had undergone HT at an age younger than 20 years and patients who underwent HT at an age of at least 20 years. In this analysis, BMD was obtained through DXA at the lumbar spine and femoral neck at the 10th annual check-up, using T score. The adult patient cohort has previously been described in a separate report on HT and chronic kidney disease.17 Osteoporosis was defined as a T score of ≥−2.5 SD from normal BMD of young and healthy adults, in accordance with the recommendation from the World Health Organization.18

2.3 | Statistical analysis

Statistical analyses were performed using IBM SPSS for Windows (version 26.0, IBM Corp). All statistical analyses were two-tailed with a 5% level of significance. The median and interquartile range (IQR) were calculated for continuous variables.

One-sample Wilcoxon signed rank tests were performed in order to investigate whether the observed medians of Z scores
differed significantly from the limit which define low BMD for chronologic age.

In order to compare the median T score at 10 years post-HT in patients who had undergone HT at an age younger than 20 years versus patients who were transplanted at an age of at least 20 years, independent samples Mann-Whitney U-tests were performed.

In an attempt to control for missing data at TA, a binary logistic regression was implemented to investigate whether primary indication for HT, urgency of HT, and need of mechanical support were predictors for missing BMD data before HT.

3 | RESULTS

3.1 | Study population

A total of 50 patients had undergone HT at an age younger than 20 years at our center between January 1988 and June 2016. Of those, 18 patients were pre-evaluated and followed at other referral university hospitals, one who had undergone re-HT, and one patient with severe connective tissue disorder, Loeys-Dietz syndrome, were excluded. Ultimately, a total of 30 patients were included in the study. Of the included patients, one had total cavopulmonary connection and one had previously undergone the Glenn procedure. None had 22q11.2 deletion syndrome. Median follow-up was 10 years (5;10), the total observed time was 235 person-years, and 23 patients (77%) reached the end of follow-up alive. Baseline characteristics, with stratification based on age group, are displayed in Table 1.

Dual-energy X-ray absorptiometry was performed once pre-HT and annually after HT according to the local routine. However, BMD was missing for the younger patients since DXA was only performed in patients with an age of at least 10 years. However, as the cohort aged during the follow-up, BMD measurements were subsequently more frequent. Treatment with vitamin D or calcium supplementation, or antiresorptive therapies, was given to patients with abnormal DXA results after discussion with an endocrinologist, according to the local routine.

3.2 | Maintenance immunosuppressive therapy

All pediatric HT patients had received daily CS from the time of HT, and the aim was complete CS cessation at approximately 6 months after HT if no rejection of higher grade than 1R had occurred. At the first annual check-up, nine patients (30%) received a combination of tacrolimus and mycophenolate mofetil (MMF), seven patients (23%) received cyclosporine A (CSA) and MMF, and the remaining patients received other combinations of immunosuppressive agents. At the 5th annual check-up, 7 (39%) received tacrolimus and MMF, and 7 (39%) received CSA and MMF. At the 10th annual check-up, 3 (30%) received tacrolimus and MMF, and 3 (30%) received CSA and MMF.

3.3 | Bone mineral density evolution

At baseline (TA), a striking 86% had low BMD for chronologic age in the lumbar spine, whereas only 13% were affected in the whole-body measurements. At TA, 100% of patients aged 15–20 years at the HT had low BMD for chronologic age in the lumbar spine, but 100% of the same age group had normal BMD in the whole-body measurements.

The median Z score in the lumbar spine at the TA, and at 1, 5, and 10 years after HT was −2.9 SD (−3.2;−2.6), −2.5 SD (−3.2;−2.1), −0.8 SD (−1.4;0.4), and −1.0 SD (−1.6;0.1), Figure 1A. The median Z score in whole-body measurements at the TA, and at 1, 5, and 10 years after HT was −1.4 SD (−1.9;−1.3), −1.4 SD (−2.4;−0.9), −0.6 SD (−1.3;0.3), and −0.7 SD (−1.0;0.2), Figure 1B.

In the lumbar spine, BMD was significantly lower than −2.0 SD at TA (p = .034), but normalized at the 4th annual check-up (p = .009), Figure 1A. In whole-body measurements, BMD normalized at the 4th annual check-up (p = .030) and remained so throughout the follow-up period, Figure 1B.

3.4 | Comparison of BMD 10 years after HT based on age at HT

Of the included 30 patients who had undergone HT at an age younger than 20 years, a total of fourteen had reached an age of at least 20 years at their 10th annual check-up. Of these, six had available DXA measurements from both the lumbar spine and femoral neck. Their median T score was −1.2 SD (−1.6;0.2) in the lumbar spine and −0.9 SD (−1.9;−0.7) in the femoral neck, Figure 2.

Dual-energy X-ray absorptiometry measurements from the lumbar spine and the femoral neck at the 10th annual check-up post-HT were available in a total of 63 and 60 patients, respectively, who had undergone HT at an age of at least 20 years. Their median T score was −0.7 SD (−1.6;0.2) in the lumbar spine and −1.3 SD (−1.9;−0.8) in the femoral neck, Figure 2.

The median T score in the lumbar spine and femoral neck 10 years after HT did not differ between the two groups based on age at the time of HT (p = .779 in the lumbar spine and p = .388 in the femoral neck, respectively).

3.5 | Primary indications for HT and pre-transplant status

A total of 17 (57%) patients had dilated cardiomyopathy as primary indication for HT, Table 2. The primary indication for HT did not correlate to if BMD had been measured before HT (χ² = 1.266, DF = 3, p = .737 in the lumbar spine, and χ² = 1.255, DF = 3, p = .740 in whole-body measurement). Urgency for HT did not correlate to if BMD had been measured before HT (χ² = 2.949, DF = 1, p = .999 in the lumbar spine, and χ² = 3.451, DF = 1, p = .999 in whole-body measurement). Likewise, mechanical support did not correlate to if BMD had been measured before HT (χ² = 0.031, DF = 1, p = .860
in the lumbar spine, and $\chi^2 = 0.029$, DF = 1, $p = .866$ in whole-body measurement).

### 3.6 Kidney function and serum calcium, ALP, and PTH

Kidney function, measured as GFR, as well as serum concentrations of calcium, ALP, and PTH from TA up to 10 years after HT are displayed in Figure 3. GFR, as well as serum concentrations of calcium, ALP, and PTH remained relatively stable throughout the follow-up. None of the patients suffered from end-stage renal disease at any time during follow-up.

### 3.7 Supplementation and antiresorptive therapy

The number of patients who received vitamin D or calcium supplementation, or bisphosphonates, is displayed in Table 3.

### DISCUSSION

It is well known that osteoporosis frequently affects adult HT patients which increases morbidity and mortality, but BMD and bone fracture risk in pediatric HT patients remain to be thoroughly investigated. This single-center retrospective cohort study aimed to describe the BMD evolution in pediatric patients up to 10 years after HT, as well as to analyze the BMD in adults who underwent HT during childhood.

The results of the present study suggest that patients who underwent HT at an age of <20 years had significantly reduced BMD in the lumbar spine compared with the limit for low BMD for chronological age of $-2.0$ SD at the TA before HT, Figure 1A. However, by the fourth-year post-HT, BMD had normalized in both lumbar spine and whole-body measurements, Figure 1. This evolution is likely due to factors related to the end-stage heart failure preceding the HT, such as renal impairment, nutritional deficiency, immobilization, and administration of heart failure medications. An early decrease in BMD after HT in pediatric

### TABLE 1 Baseline recipient characteristics

| Recipient characteristics | Total ($N = 30$) | Age (years) at HT |
|---------------------------|------------------|------------------|
|                           |                  | <10 ($N = 10$)   | 10-15 ($N = 14$) | >15 ($N = 6$) |
| Age at HT, years          | 12 (5:15)        | 3 (1:5)          | 13 (12:14)       | 16 (16:18)    |
| Female, N (%)             | 18 (60)          | 7 (70)           | 7 (50)           | 4 (67)        |
| BMI, kg/m$^2$             | 16 (15:19)       | 14 (13:17)       | 18 (16:21)       | 17 (15:21)    |
| Follow-up, years          | 10 (5:10)        | 10 (6:10)        | 10 (4:10)        | 10 (8:10)     |
| Person-years              | 235              | 83               | 102              | 50            |
| Biopsies per patients within the first year after HT, N | 11 (9:13) | 10 (9:12) | 13 (11:14) | 13 (10:13) |
| ACR grade 2R, % of biopsies for each patient | 0 (0:1) | 0 (0:16) | 0 (0:11) | 0 (0:2) |
| Waiting time, days        | 105 (15:229)     | 105 (20:193)     | 49 (7:359)       | 190 (126:267) |
| Ischemic time, min        | 198 (157:223)    | 209 (188:242)    | 197 (154:229)    | 194 (98:219)  |
| Serum creatinine, µmol/L  | 42 (32:73)       | 30 (23:35)       | 58 (41:80)       | 73 (41:99)    |
| Serum urea, mmol/L        | 6.4 (4.6:7.9)    | 5.3 (4.5:6.4)    | 7.1 (4.3:9.1)    | 6.8 (4.3:10.6) |
| Iohexol-GFR, ml/min/1.73 m$^2$ | 71 (67:96) | 69 (67:86) | 75 (67:105) | 71 (53:102) |
| Urine albumin/creatinine ratio, g/mol | 17 (2:57) | – (–) | 17 (10:24) | 10 (2:17) |
| Daily CS at 1 year after HT, N (%) | 7 (23) | 3 (33) | 2 (22) | 2 (40) |
| Daily CS dose at 1 year after HT, mg | 0 (0:5) | 0 (0:4) | 0 (0:1) | 4 (0:8) |
| BMD, g/m$^2$              |                  |                  |                  |                |
| Lumbar spine              | 0.769 (0.608:0.883) | – (–) | 0.608 (0.524:0.719) | 0.884 (0.883:0.905) |
| Whole body                | 0.977 (0.876:1.031) | – (–) | 0.876 (0.799:0.910) | 1.031 (1.020:1.054) |
| Z score, SD               |                  |                  |                  |                |
| Lumbar spine              | –2.9 (–3.2:–2.6) | – (–) | –2.9 (–4.0:–2.0) | –2.9 (–3.0:–2.9) |
| Whole body                | –1.4 (–1.9:–1.3) | – (–) | –1.6 (–3.1:–0.9) | –1.4 (–1.6:–1.3) |

Note: Data are displayed as medians (IQR) if not stated otherwise. Abbreviations: ACR, acute cellular rejection; BMD, bone mineral density; BMI, body mass index; GFR, glomerular filtration rate; HT, heart transplantation; IQR, interquartile range; SD, standard deviations.

*At TA.
patients has previously been described in the literature. The immunosuppressive regimen in the present cohort strived for complete CS cessation within the first postoperative year, which may partly explain the increased BMD over time. Thus, with the present regimen, the results suggest BMD recovery within the first four postoperative years after HT.

Patients aged 15–20 years at the time of the HT were more likely to suffer from low BMD for chronological age in the lumbar spine than in the whole-body measurements at baseline. This may be a reflection of the heart failure preceding HT and its different impact on trabecular and cortical bone. In a cross-sectional study, using quantitative CT to assess bone density in young healthy girls, it was reported that trabecular bone may be influenced by sexual development to a greater extent than cortical bone, which may be more correlated to weight-bearing or mechanical stress. In another cross-sectional multicenter study which included subjects with Fontan patients, both boys (58%) and girls (58%) had a delay of 1.5–2 years in ≥1 Tanner stage parameter compared with a control population. Although the mechanisms behind BMD regulation in growing subjects in relation to puberty are complex, the findings may suggest that trabecular bone, which is more abundantly found in the lumbar spine, may be more vulnerable to hormonal changes in relation to heart failure per se.

The main limitation of the present study was the limited amount of included patients which was further limited by the fact that a substantial amount of DXA measurements were missing at baseline. Since bone densitometry could have been down-prioritized in more urgent cases of HT and therefore missing in these cases, it was hypothesized that this may bias the results. However, in a regression analysis, no evidence was found on correlations between

---

**FIGURE 1** Boxplot of Z score in (A) Lumbar spine and (B) whole body. One-sample Wilcoxon signed-rank test was used to compare the observed median and a Z score of −2 SD. * Outlier. SD, standard deviation; TA, transplant assessment.
missing bone densitometry before HT and primary indication for HT, urgency of HT, or need of mechanical support. Thus, there is no evidence against the representativeness of the present cohort despite the small sample size. However, the small sample size limits the possibility to draw final conclusions about BMD evolution after pediatric HT. Additionally, the lack of fracture data further limits the significance of the results. Data on fractures had not been registered systematically, and since vertebral fractures often are asymptomatic, this would have led to a significant data collecting error in this retrospective study.

No difference was found between BMD in patients who had undergone HT at an age of <20 years and patients who had undergone HT at an age of ≥20 years, Figure 3. Also, as previously described, BMD normalized at the fourth annual check-up in the latter group, Figure 1. The findings suggest the skeletal health had recovered in both age groups within 10 years after HT, supporting the idea that the timing of the heart transplantation in relation to patient age does not affect bone strength long term.

Bone health and renal disease are known to be closely related. In a previously published study on an adult cohort from the same center, the issue of chronic kidney disease in relation to DXA, particularly in the lumbar spine, was discussed. The DXA results were found to be a potential result of vascular disease and aortic calcification which is associated with renal disease. In the
present study, GFR remained stable throughout the follow-up and none of the included subjects suffered from end-stage renal disease at any time, suggesting that kidney function did not significantly influence the results.

In conclusion, the present study showed that patients who underwent HT at an age of <20 years had low BMD for chronological age in the lumbar spine already before HT. BMD then recovered at the fourth-year after HT in both lumbar spine and whole-body measurements. No difference in BMD at 10 years after HT was found between patients who underwent HT at an age of <20 years versus patients who underwent HT at an age of ≥20 years. The results suggest that pediatric HT patients may recover completely in measures of skeletal health within the first years after HT. For the future, it would be desirable to investigate the skeletal health using advanced imaging techniques, such as quantitative magnetic resonance, and measurement of sex hormones, using a prospective study design.

ACKNOWLEDGEMENTS
We acknowledge the support of the staff at the Section for Heart Failure and Valvular Disease at Skåne University Hospital, and the staff at the Department of Clinical Sciences Lund, Cardiology, at Lund University, Lund, Sweden, as well as the staff at The Pediatric Heart Center, Skåne University Hospital, Lund, Sweden.

CONFLICT OF INTEREST
None.

AUTHOR CONTRIBUTIONS
EL involved in study design, data collection, data analysis, and writing of the article. KTL involved in study design, data acquisition,
and writing and reviewing of the article. JN involved in writing and reviewing of the article. MO involved in data acquisition, and writing and reviewing of the article. CH involved in data collection and reviewing the article. GR involved in study design, data acquisition, and writing and reviewing of the article.

DATA AVAILABILITY STATEMENT
Data available on request due to privacy/ethical restrictions.

ORCID
Eveline Löfdahl https://orcid.org/0000-0002-8976-0801
Carl Haggård https://orcid.org/0000-0003-0415-6555
Johan Nilsson https://orcid.org/0000-0001-6860-6090
Michal Odermarsky https://orcid.org/0000-0002-0852-5691

REFERENCES
1. Lofdahl E, Soderlund C, Radegran G. Bone mineral density and osteoporosis in heart transplanted patients: a single-center retrospective study at Skane University Hospital in Lund 1988–2016. Clin Transplant. 2019;33(3):e13477.
2. Soderlund C, Radegran G. Immunosuppressive therapies after heart transplantation—the balance between under- and over-immunosuppression. Transplant Rev. 2015;29(3):181-189.
3. Canalis E, Mazzotti G, Giustina A, Bilezikian JP. Glucocorticoid-induced osteoporosis: pathophysiology and therapy. Osteoporos Int. 2007;18(10):1319-1328.
4. Sun L, Blair HC, Peng Y, et al. Calcineurin regulates bone formation by the osteoblast. Proc Natl Acad Sci USA. 2005;102(47):17130-17135.
5. Sun L, Peng Y, Zaidi N, et al. Evidence that calcineurin is required for the genesis of bone-resorbing osteoclasts. Am J Physiol Renal Physiol. 2007;292(1):F285-F291.
6. Tamlor R, Epstein S. Nonsteroid immune modulators and bone disease. Ann N Y Acad Sci. 2006;1068:284-296.
7. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. Lancet. 2002;359(9319):1761-1767.
8. Abrahamsen B, van Staa T, Ariely R, Olson M, Cooper C. Excess mortality following hip fracture: a systematic epidemiological review. Osteoporos Int. 2009;20(10):1633-1650.
9. Laine CM, Laine T. Diagnosis of osteoporosis in children and adolescents. Eur Endocrinol. 2013;9(2):141-144.
10. Bogunovic L, Doyle SM, Vogiatzi MG. Measurement of bone density in the pediatric population. Curr Opin Pediatr. 2009;21(1):77-82.
11. Bechtold S, Putzker S, Birnbam J, Schwarz HP, Netz H, Dalla PR. Impaired bone geometry after heart and heart-lung transplantation in childhood. Transplantation. 2010;90(9):1006-1010.
12. Acott PD, Crocker JF, Wong JA. Decreased bone mineral density in the pediatric renal transplant population. Pediatr Transplant. 2003;7(5):358-363.
13. Cohen A, Addonizio L, Lamour JM, et al. Osteoporosis in adult survivors of adolescent cardiac transplantation may be related to hyperparathyroidism, mild renal insufficiency, and increased bone turnover. J Heart Lung Transplant. 2005;24(6):696-702.
14. Helenius I, Jalanko H, Remes V, et al. Scilosis after solid organ transplantation in children and adolescents. Am J Transplant. 2006;6(2):324-330.
15. Soderlund C, Ohman J, Nilsson J, et al. Acute cellular rejection the first year after heart transplantation and its impact on survival: a single-centre retrospective study at Skane University Hospital in Lund 1988–2010. Transpl Int. 2014;27(5):482-492.
16. Rauch F, Plotkin H, DiMeglio L, et al. Fracture prediction and the definition of osteoporosis in children and adolescents: the ISCD 2007 pediatric official positions. J Clin Densitom. 2008;11(1):22-28.
17. Löfdahl E, Haggård C, Rådegran G. Bone mineral density in relation to chronic kidney disease after heart transplantation: a retrospective single-center study. Transplant Rev. 2014;28(3):132-138.
18. Prevention WHOSGöt, management of O. Prevention and management of osteoporosis: report of a WHO scientific group. In: Geneva: World Health Organization. 2003.
19. Löfdahl E, Rådegran G. Osteoporosis following heart transplantation and immunosuppressive therapy. Transplant Rev. 2017;31(4):232-239.
20. Aluoch AO, Jesse R, Habal H, et al. Heart failure as a risk factor for osteoporosis and fractures. Curr Osteoporos Rep. 2012;10(4):258-269.
21. Lim LS, Fink HA, Blackwell T, Taylor BC, Ensrud KE. Loop diuretic use and rates of hip bone loss, and risk of falls and fractures in older women. J Am Geriatr Soc. 2009;57(5):855-862.
22. Gajic-Veljanoski O, Phua CW, Shah PS, Cheung AM. Effects of long-term low-molecular-weight heparin on fractures and bone density in non-pregnant adults: a systematic review with meta-analysis. J Gen Intern Med. 2016;31(8):947-957.
23. Daniels MW, Wilson DM, Paguntalan HG, Hoffman AR, Bachrach LK. Bone mineral density in pediatric transplant recipients. Transplantation. 2003;76(4):673-678.
24. Mora S, Goodman WG, Loro ML, Roe TF, Sayre J, Gilson V. Age-related changes in cortical and cancellous vertebral bone density in girls: assessment with quantitative CT. AJR Am J Roentgenol. 1996;162(2):405-409.
25. Menon SC, Al-Dulaimi R, McCrindle BW, et al. Delayed puberty and abnormal anthropometry and its associations with quality of life in young fontan survivors: a multicenter cross-sectional study. Congenit Heart Dis. 2018;13(3):463-469.
26. Ensrud KE, Lui LY, Taylor BC, et al. Renal function and risk of hip and vertebral fractures in older women. Arch Intern Med. 2007;167(2):133-139.
27. Klawansky S, Komaroff C, Cavanaugh PF, et al. Relationship between age, renal function and bone mineral density in the US population. Osteoporos Int. 2003;14(7):570-576.
28. Löfdahl E, Haggård C, Rådegran G. Bone mineral density in relation to chronic kidney disease after heart transplantation: a retrospective single-center study at Skåne University Hospital in Lund 1988–2016. Transplantation Direct. 2020;6(3):e537-e537.
29. Palit S, Kendrick J. Vascular calcification in chronic kidney disease: role of disordered mineral metabolism. Curr Pharm Des. 2014;20(37):5829-5833.
30. Toussaint ND, Lau KK, Strauss BJ, Polkinghorne KR, Kerr PG. Associations between vascular calcification, arterial stiffness and bone mineral density in chronic kidney disease. Nephrol Dial Transplant. 2007;22(3):586-593.

How to cite this article: Löfdahl E, Tran-Lundmark K, Haggård C, Nilsson J, Odermarsky M, Rådegran G. Bone mineral density in pediatric heart transplanted patients: A retrospective single-center study at Skåne University Hospital in Lund 1988–2016. Pediatr Transplant. 2022;26:e14127. https://doi.org/10.1111/petr.14127